Childhood epilepsy in Bangladesh:
Clinical profile, predictors of outcome and randomized controlled trial of efficacy and side effects of drug treatment.

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ABSTRACT

Around 80% of the world’s patients with epilepsy live in countries with limited resources, and are predominantly young, 90% of whom are not appropriately treated. Bangladesh is probably typical in this respect, with an estimated 6.5/1000 affected in the 2-9 years age group, but detailed information about childhood epilepsy is limited, and services are almost non-existent outside the 2 major cities.

A study of childhood epilepsy was carried out in 3 stages. In the 1st, retrospective stage, an epilepsy profile was compiled in children aged 2 months to 15 years and predictors of poor seizure remission identified. Primary care physicians and multidisciplinary health workers were trained on short courses to diagnose and manage epilepsy and additional impairments. An extensive system of patient care, regular follow up and patient recall was set up in collaboration with a community service. The 2nd, prospective, stage was designed to validate the predictors of poor seizure remission using two groups of patients: those with newly diagnosed epilepsy from the community and the second from the child development centre (CDC) who were anticipated to have more neurodevelopmental impairments. In the 3rd stage, 108 patients from the 2nd stage study were enrolled in a randomized controlled trial (RCT) to compare the behavioural side effects of phenobarbitone (PB) and carbamazepine (CBZ).

The pilot study of 151 children showed a high rate of neurodevelopmental disabilities (73% had cognitive and 57% had motor problems). Seizure remission was obtained in 45.7%, and predictors of poor seizure remission were multiple seizure types, cognitive impairment, and an abnormal EEG. The poor were under-represented in this study. The socio-economic profile of the newly recruited children in the 2nd stage was more representative of the general population, with around 60% from the poor, both urban and rural. As anticipated, the community group had less associated non-convulsive neurological-disorder(s) than that from CDC (38.8% vs 70.5% for motor and 47% vs...
76.3% for cognitive impairment). After 12 months regular treatment, seizure remission was obtained in 77% who did not have additional non-convulsive disorder. In this population, multiple logistic regression analysis showed multiple seizure types ($p<0.01$), cognitive impairment ($p<0.02$) and associated motor disorder ($p<0.04$) predicted poor seizure remission. In the RCT there was no difference in efficacy between PB and CBZ, and no significant difference in behavioural problems between the two treatments.

The study suggests that epilepsy outcome can be broadly predicted at first presentation using the 3 factors (associated motor disability, cognitive impairment and multiple seizure types), which could be applied by a community health care physician. A multidisciplinary service in a community health care setting is an appropriate model for managing childhood epilepsy in a developing country such as Bangladesh. The result from the RCT study suggests that and PB does not produce increased behavioural problems compared with CBZ.
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INDEX OF ABBREVIATIONS

AED  Antiepileptic drugs
BD   Bangladesh
BICH Bangladesh Institute of Child Health
CBZ  Carbamazepine
CDC  Child Development Centre
CLZ  Clonazepame
CPRS Conners’ Parental rating Scale
DSH  Dhaka Shishu (Children’s) Hospital
EEG  Electroencephalogram
ERC  Ethical review committee
GIT  Gastrointestinal
IBAS Infantile behavioural assessment scale
LTZ  Lamotrigine
MH   Mahmuda Hossain
NTZ  Nitrazepame
PB   Phenobarbitone
PCP  Primary care physician
PD   Prednisolone
PHT  Phenytoin
RTI  Respiratory tract infection
SBK  Shishu Bikash Kendro (Bangla for child developmental centre)
SBN  Shishu Bikash Network (Child development network)
SHB  Selina Husna Banu
TORCH Toxoplasma, Rubella, Cytomegalovirus, Herpes simplex virus
VPA  Valproic Acid, Sodium Valproate
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CHAPTER ONE

1: Elements of the study

1.1.1: Overview of the thesis

Epilepsy is the most common yet frightening neurological condition that can occur in children. This study on childhood epilepsy in Bangladesh (BD) attempts to examine seizure outcome in children who come voluntarily for treatment, and to test the hypothesis that at initial diagnosis it is possible to identify the severity of the epilepsy, and predict the medium-term outcome using the information available on the first day of diagnosis. It also investigates the hypothesis that the children treated with phenobarbitone will have 25% higher incidence of behavioural side effects compared to those treated with carbamazepine.

1.1.2: The ultimate aim or the broader outcome of the study

The broad aim of the study is to develop a simple guideline ('slimmed down treatment protocol') for caregivers, which would be appropriate for Bangladesh and other countries with limited resources and which could be applicable at primary to tertiary levels of care. It would provide appropriate models of management for children with epilepsy and the common associated neurodevelopmental disorders of childhood epilepsy.

1.1.3: Chapter contents

The first part of the thesis describes the background of the study. Chapter Two presents a systematic overview of childhood epilepsy, highlighting the identification of different types of seizures in children, its classification, and limitations, and associated
non-convulsive disorders and their inter-relationships with epilepsy. It also looks into the relationship between insults to the developing brain and early childhood epilepsy and discusses the literature on treatment of different types of epilepsy, the first line antiepileptic drugs (AEDs).

Chapter Three describes the geographical and social aspects of Bangladesh (BD) and the epidemiology of epilepsy and other disabilities in BD, and other countries. The chapter also describes the multidisciplinary services developed at the national children’s hospital; and discusses the experience of developing a paediatric electroencephalography (EEG) service in Bangladesh.

Chapter Four presents an overview of the methods and materials used at different stages of the study, and describes the theoretical and practical training of the team workers. The application of the Conners’ behavioural assessment tool (Conner’s Rating Scale-Revised) is discussed, and the definitions of terms used in the study are presented.

Chapter Five presents the retrospective study methods, and the results, and comments on their implication for the prospective study.

Chapter Six presents the design, methods and materials of the prospective study, the results, and a discussion comparing the findings with those of the retrospective study.

Chapter Seven presents the randomized controlled trial study, the results of this stage and a discussion.
Chapter Eight discusses the implications of the findings for children with epilepsy and other neurodisabilities in Bangladesh, which may be useful in other countries with limited resources. The results indicate that

1. the children with epilepsy attending a special epilepsy service centre commonly have other disabilities; there is strong association with perinatal problems which requires the possibility of prevention at the pregnancy, birth, and neonatal levels; and that

2. the response to appropriate drug treatment in childhood epilepsy is comparable to that of developed countries despite the start of appropriate treatment being delayed.

3. Correlation analysis of seizure outcomes suggests that it is possible to predict seizure outcome with the information available on the first day of diagnosis in the community setting, using a team trained for a short period on childhood epilepsy and associated disorders.

4. The chapter also discusses the fact that EEG has an important role in the diagnosis of epilepsy syndromes and assessing the prognosis independently and that it does not affect the model of predictors.

5. This study suggests that a team recently trained for a short period of time (primary care physician (PCP), developmental therapist (DT) and a child psychologist) can provide an appropriate, multidisciplinary service for the children with epilepsy and associated disabilities in a clinic setting in Bangladesh (BD).

6. Through the drug trial study in children with generalised tonic-clonic (GTCS), secondary generalised and partial seizures, this study suggests that phenobarbitone (PB) does not produce unacceptable behavioural side-effects, and that there is no difference in efficacy when compared with carbamazepine (CBZ).
The chapter concludes with a discussion of possibilities for further studies and the proposition that the same cohort may be followed up for a long period for further evaluation of the results.

1.2: The candidate’s role in this study

1.2.1: Background preparation

- Involved in original conception of the study.
- Established the first electroencephalogram (EEG) service for children, in the country.
- Performed literature review and generated the hypotheses.
- Planned the retrospective study and prepared the prospective study design.
- Prepared the proposal for retrospective study and arranged funding for the prospective study.
- Prepared the proposal for research ethical approval in London and in the Dhaka Shishu Hospital.

1.2.2: Preparation of the entry forms and training for the personnel

- Questionnaire for the prospective epilepsy study (based on the Ten Question with probe, used in the disability survey among the children from 2 to 9 years in BD (Khan & Durkin 1995b; Zaman et al. 1990).
- Questionnaire to assess the socio-economic status (SES) following the one that has been used in the epidemiological survey of developmental disabilities in children in BD (Khan and Durkin 1-9)
Conducted translation, back-translation and pilot study of the Conners' parental questionnaire (Conners 1997b) to assess behavioural disorders in children.

Ran training sessions for primary care physicians in the diagnosis of epilepsy, neurodevelopmental assessment, grading of motor disorders, cognitive impairment, behavioural problems of children with epilepsy and acute and long-term treatment of epilepsy in children.

Conducted training for college graduates in developmental therapy, play therapy, and stimulation for children with special needs, or impending cerebral palsy. Organized training for a feeding programme for children with multiple disabilities, and family counselling regarding the disabilities and coping strategies.

Helped in training child psychologists.

Trained child neurologists in clinical Electroencephalography (EEG).

Trained technicians and established EEG services at the national paediatric hospital (Dhaka Shishu Hospital).

1.2.3: Procedure

- Designed the protocol for the prospective study of 400 children.
- Designed the RCT study to identify the efficacy of the two commonly used AEDs and to compare their side-effects.
- Trained one person to randomize by minimization, and prepared the envelopes and cards for randomization. The person had no knowledge about the drugs.
- Managed the whole project at two sites, at the special centre-CDC and at the community based OPD involving the team of primary physicians, neurologists, therapists, clinical neurophysicians, engineers at the EEG centre and technicians and the research assistants.
• Managed the quality control, involving cross-checking of the medical assessment forms, investigating the assessment procedures, organizing regular team meetings; daily at the start of the study, and once in a week later.

1.2.4: Data storage and analysis

• Created the Microsoft Access database for the data storage in separate tables for patient information, complaints on the first visit, seizure details, past medical histories, birth and pregnancy related information, general examinations, neurodevelopmental examination findings and for a summary. In addition a management plan, final follow up information, EEG and other investigation information, socio-economic status information and maternal stress assessments were also included.

• Data handling and transformation from access to SPSS for analysis.

• Designed the protocol for statistical analysis.

• Prepared for a publication (Banu et al. 2003) and presentation of the results. The results were presented at the paediatric neuroscience conference, All India Institute of Medical Sciences, October 2000, and at neurosciences meeting in London, September 2003.
PART ONE

Background to the study

Introduction
Most children with epilepsy outgrow the condition; this has been shown in studies in both developed (Berg, Hauser, & Shinnar 1995; Camfield et al. 1993; Carpay et al. 1998), and countries with limited resources, for example in Bangladesh, Kenya, India, Ecuador, and Papua New Guinea (Banu et al. 2003; Danaya, Johnson, & Ambihaipahar 1994; Feksi et al. 1991; Pal et al. 1998a; Placencia et al. 1993). However, such children need appropriate, and timely diagnosis and management in order to prevent complications and reduce neurodisability. Repeated generalised seizures and prolonged seizures are reported to cause permanent cognitive and motor disability (Christiaens et al. 2003; Meierkord et al. 1997). Such disabilities are potentially preventable by early and effective treatment of the epilepsy (Besag 2002).

It is estimated that 50 million people around the world are affected by the condition, and 40 million of them live in countries with limited resources. Annual incidence rate of epilepsy in these countries may be as high as 190 per 100,000 of the population (Sander & Shorvon 1996). In BD the estimated prevalence of ‘any seizure history’ is reported to be 68.3 per 1000 children aged 2 to 9 years (Durkin et al. 1992).

The WHO suggests that in the context of the large and rapidly increasing populations in these countries, epilepsy is a significant health and socio-economic burden requiring urgent attention (WHO, 1999). With the high prevalence rate of seizure disorders in children (who make up 45% of the population) a cost-effective, sustainable epilepsy programme is urgently required in Bangladesh. However, doctor to patient ratio is seriously deficient (1 doctor for 6000 persons); as in other developing countries, there are in particular few trained neurologists. Health services are mostly city-based. It is therefore, essential to develop alternative strategies to provide appropriate, population oriented services for the majority of the population, which live in rural areas.
Attitude, knowledge, and education of the population

A long-term treatment requires motivation and cooperation from the patient, and family members, who will require specific education about the condition. Socio-cultural context and public awareness is an important issue to be addressed in this regard. Although, cost and unavailability of appropriate treatment for epilepsy is considered to be the major cause of the epilepsy treatment gap in the developing countries, the existing negative social and cultural factors also have a significant influence. Among other chronic conditions, epilepsy is still regarded as a major stigma in many countries (Shorvon & Farmer 1989) including, for example, northern Ecuador (Placencia et al. 1995).

An educational programme for the general population might be introduced to bring change in the negative attitude. The approach used in Malawi (Watts 1989) is an example of a successful programme with widely publicized, free, easily available treatment, maintenance of regular medicine supplies and frequent and regular follow-ups. In that study only 7 patients started AED treatment at the beginning, there were 461 after two years, 68% of whom were still attending regularly. Many of them had to walk as far as 20 miles to attend the clinic. Two additional mobile clinics were set up to bring the service nearer to the peoples residence.

Why a systematic epilepsy programme is needed for this country

There is little information available about range of seizure types, risk factors, predictive factors, treatment and overall management in developing countries (Shorvon & Farmer 1988). Despite the major burden for populations by epilepsy, there are hardly any systematic services established in developing countries except in the major cities [Nepal, India, BD]. The WHO and the International League Against Epilepsy (ILAE) have, since 1975, made a series of recommendations for the control of epilepsy in developing countries, and these have embraced three main service principles (i) decentralization; (ii) integration into general health services and multi-agency (e.g. Welfare and development) collaborations and (iii) partnership with non-governmental
organization to promote public understanding and extend coverage (Gastaut & Osontokun 1976; WHO 1975).

A well-established treatment protocol is available worldwide, which is feasible for the developed countries with their well-structured health care facilities, greater awareness, and generally positive perception among the population (Caveness & Gallup 1980b). Ganger and Carnaggia have compared the knowledge and attitude of the Italian population with those of USA and West Germany (Canger & Carnaggia 1985; Caveness & Gallup 1980). Hills MD et al., studied this in the New Zealand population, and compared it with other western countries (Hills & MacKenzie 2002). These studies suggest that the knowledge is comparable and attitudes are generally positive, however, they recommend continuing public education on epilepsy.

By contrast, surveys from developing countries revealed that awareness and understanding of epilepsy among the population are the same, or even greater in some cases (China), but that attitudes towards epilepsy are much more negative (Dantas et al. 2001; Fong & Hung 2002; Gambhir et al. 1995; Lai et al. 1990; Radhakrishnan et al. 2000). Social morbidity is reported in 53% of the people with epilepsy in Sri Lanka, and 45.9% are using alternative modes of treatment (Seneviratne et al. 2002).

All of these findings strongly suggest the need to improve public awareness of, attitude towards and an understanding of epilepsies through school education, and epilepsy services should include such a programme. This will help an appropriate management protocol to be developed based not only on the disease profile and socio-economic condition of the country, but also taking account of the existing strength and weakness of the cultural belief and practices.

Why there is a need to predict the outcome on first diagnosis

When parents accept that their child has a chronic illness, treatable by appropriate medication, the next question most commonly asked is what is the outcome of the condition, followed by how, and from where, are they going to get help. Accordingly, they will utilize their limited resources.
From the professional’s point of view, they would make plans for immediate and long-term treatment, investigation, and rehabilitation in collaboration with the secondary and tertiary centres depending on the predicted outcome. Identifying the children destined to have poor seizure remission with the help of clinical evidence on first presentation may be useful at the primary level in a country with limited resources, to help plan for the long-term management. The predictors of seizure outcome have been studied in developed countries but there is no such study carried out in the countries with limited resources to compare with them.

For the first time in Bangladesh this study provides information on clinical and neurodevelopmental profiles, diagnosis, outcomes and predictors of seizure remission in children presenting to a national children's hospital. This study is expected to generate important guidelines for planning appropriate service for childhood epilepsy in countries where experts are scarce.

Which AED to use
The aim of epilepsy drug treatment is to reduce the burden of seizure attacks, and to prevent the neurodevelopmental disorders. The drug selection ideally depends on the type of seizures and epilepsy. However, for the countries with limited resources, cost of the prescribed drug is very important to consider. Phenobarbitone is suggested by the WHO as the first line AED for the developing countries mainly because of its low production cost however, it has been shown to cause behavioural problems in developed country studies (de Silva et al. 1996; Vining et al. 1987; Wolf & Forsyth 1978). If this is the case, then it should not be expected that the parents in a country who primarily would prefer to get an alternative treatment (as shown in Sri Lanka, (Seneviratne et al. 2002)), would accept AED treatment at the cost of unacceptable side-effects. Therefore, it is important to identify and qualify the level of behavioural disorder caused by the low cost AEDs compared to higher cost AED, and then decide which one we aught to accept.
CHAPTER TWO

2.1: Introduction

The word epilepsy derives from the Greek word επιλαμβανειν (Aicardi 1994a), which means to 'seize'. The classical and widely accepted definition of Hughlings Jackson was that ‘epilepsy is a condition occurring repeatedly due to occasional, sudden, excessive, rapid, general and local discharges of gray matter’. For practical purposes, the simpler definition of epilepsy widely used among the clinicians is that ‘epilepsy is diagnosed when there is a history of two or more unprovoked seizure attacks’; this excludes a single episode which may occur due to a transient biochemical change in the body, or provoked by sudden injury, high temperature or CNS infection. This simple definition is useful to prevent over-diagnosis and unnecessary treatment. The combination of conditions such as age of onset, seizure type(s), interictal condition, EEG characteristics and outcome when considered in a given patient it is termed as epilepsy syndrome and is usually more helpful in prognosis.

2.2: Epidemiology

The overall incidence of epilepsies, is about 50 cases per 100,000 persons per year (range 40 to 70 per 100,000) in the industrialized countries. In contrast this ranges from 100 to 190 per 100,000 per year in developing countries (APA 1980; Hauser 1994; Sander & Shorvon 1987; Sander & Shorvon 1996). The prevalence rates of epilepsy is estimated to be 4-10/1000 for all ages (Sander & Shorvon 1987) excluding febrile seizures, single seizures and inactive cases. The lifetime prevalence of seizures is between 2% and 5%.
Although the reported incidence and prevalence rates of epilepsy vary widely, the highest rates are reported from studies in developing countries compared with those in industrialized countries. There are multiple reasons identified for this: firstly the rate of perinatal brain damage, and intracranial infections with their consequent secondary epilepsy (Leary et al. 1999; Senanayake & Roman 1993) are high in developing countries due to poor living standards, malnutrition and poor antenatal care (Indian study and WHO bulletin); and secondly the child population is high in developing countries, and it is suggested by Sander and Shorvon that the incidence of epilepsy is higher in childhood (Sander et al. 1990; Sander & Shorvon 1996).

2.3: Epilepsy classification

The ILAE classification (ILAE 1981; ILAE 1989) of epilepsy is syndromic, based on a cluster of signs and symptoms, which includes age at onset, seizure types, EEG features and findings of neuroimaging. According to the international classifications (op.cit.) the epilepsies and epilepsy syndromes are classified initially according to their corresponding types of seizures into localization-related and generalised disorder. Each disorder is further classified according to the relationship to etiologic or predisposing factors into symptomatic, cryptogenic and idiopathic types. For epidemiological studies another category of ‘remote symptomatic’ with no immediate cause but occurring in persons with a prior brain injury or a static encephalopathy has been suggested (ILAE 1993).

The concept of epilepsy syndromes is useful for diagnosis, prognosis and management. However, it has some intrinsic limitations, for example in seizure classification, classifying simple and complex partial seizures (SPS and CPS) in children, and the syndromic classification is also limited to the well-defined generally accepted syndromes. There are cases with seizures, which do not fit within the clearly described syndrome types and categorized as unclassified. The practical usefulness of the ILAE classification in the diagnosis and management of childhood epilepsy remains
Aicardi and Manford et al. have focused on the limitation in diagnosis of a wide range of epilepsies which have non-specific categories (66.4% in Manford’s study), and found that usefulness of the concept is limited to well defined and generally accepted syndromes.

Murthy et al. have shown that partial epilepsies with unremarkable clinical features would have been diagnosed as cryptogenic epilepsies without modern neuroimaging. This means that the ILAE classification can only be fully applied within specialized centres. However, less experienced professionals still need a simpler classification at initial diagnosis, which takes the complete classification into account: very recently Rinaldi et al. (Rinaldi et al. 2000) have developed and validated an algorithm based on the ILAE classification to be used in clinical practice by less experienced physicians in newly diagnosed patients.

Despite these difficulties, the syndromic classification of the ILAE has been widely used in developed and developing countries and some authors have found that they were able to classify 78.7% to 98.2% of their cases (Beilmann & Talvik 1999; Berg et al. 2000; Shah et al. 1992).

We have used a slightly modified broader classification based on the ILAE epilepsy and epilepsy syndrome classification. (Table 4.1, Chapter 4). Following the method suggested by Rinaldi (op.cit.), we classified epilepsy in two steps, the first based on the clinical information only, on the first day of diagnosis and the second based on combined clinical and investigation data (Section 4.4).

2.4: Childhood epilepsy and associated non-convulsive neurological disorders

Motor, cognitive and behavioural non-convulsive disorders are commonly associated with childhood epilepsy. Benign generalised epilepsies are usually expected to be without any associated neuro-developmental disorders, for example there seems to be little residual effect of childhood absence seizures on cognitive or neurological
function (Panayiotopoulos, 1997). However, certain benign partial epilepsy syndromes are reported to be associated with cognitive, and functional deterioration or transient speech and memory loss or cognitive impairment (Binnie et al. 1987; Gunduz, Demirbilek, & Korkmaz 1999; Hian-Tat, Elaine, & Wyllie 2000). Early onset epileptic encephalopathy, and the presence of interictal, sub-clinical EEG discharges, or continuous spikes and waves during sleep (CSWS) are well known to be associated with psychomotor disorders (Tassinari et al. 2000). Hian et al’s study (Hian-Tat, Elaine, & Wyllie 2000) showed the effects of frequent seizures on cognitive, functional and behavioural state of children with epilepsy, while in Dunn et al’s study, children with epilepsy were found to be at risk for symptoms of attention-deficit-hyperactivity disorder (ADHD) compared to a control group (Dunn et al. 2003). In addition, Nolan et al. have found a significant association between ‘generalised symptomatic epilepsy’, and low IQ (Nolan et al. 2003).

Although the association of epilepsy and developmental deterioration or developmental delay is multifactorial, certain factors are suggested to be predictors of the associated consequences, which are: (i) seizure or epilepsy type; (ii) early onset; (iii) seizure frequency; (iv) repeated prolonged seizures; and (v) longstanding, drug-resistant, symptomatic epilepsy (Andrew 2000; Jekeit & Ebner 2002; Meastu et al. 2000).

2.5: Pregnancy and birth-related problems, and epilepsy

Maternal medical problems, such as diabetes melitus is a significant cause of fetal and neonatal morbidity and mortality (Fraster 1994). Insulin dependent diabetes particularly affects the fetal brain (Barr, Hanson, & Currey 1983). Prenatal infection with Cytomegalovirus (CMV), Rubella, and Toxoplasmosis are cytopathic for fetal cells or cause reduction or arrest of cell growth and multiplication which may result in mild to severe cerebral lesions mainly by causing damage to the endothelium of fetal blood vessels with frequent development of subependymal cysts (Rademaker, de Vries, & Barth 1993).
A proportion of cases with strictly defined birth asphyxia (which essentially includes decompensatory fetal response and neonatal encephalopathy), has been shown to be associated with subsequent neurological deficits and epilepsy. About 30% of the children who suffered from perinatal asphyxia were found to develop subsequent epilepsy, mental retardation and/or cerebral palsy (Rantakallio, Wendt, & Koivu 1987; Watanabe et al. 1982).

There may be a direct or indirect relationship between early childhood epilepsy and under-resourced health care at the pre-, peri- and post-natal levels in countries with limited resources, as shown by the studies from India, South Africa and Nigeria. Veena et al, have shown an association between poor perinatal and neonatal histories, and early onset epileptic encephalopathy with a high rate of multiple seizure types (Veena et al. 2002), Hackett et al. in their prevalence study in India, identified a significant association between active epilepsy and perinatal complications in their population (Hackett, Hackett, & Bhakta 1997). Leary and Morries, in a clinic based prevalence study of symptomatic epilepsy among the poor community people of South Africa (Leary & Morris 1998) and Asindi in a study of infants with epilepsy in Nigeria (Asindi 1995) have identified perinatal complications and meningitis as risk factors of epilepsy in 32% and 48% of their patients respectively.

The above findings are showing an association between potentially preventable problems and childhood epilepsy particularly in the rural, poor population of the developing countries. The identification of pre-, peri-, and post-natal problems and their association with childhood epilepsy is necessary to plan preventative strategies in this population.

2.6: Interrelationship between epilepsy, motor disorder and cognitive impairment

Epilepsy may affect motor development, cognition and behaviour in a number of different ways:
**Age at onset and seizure type:** early onset of generalised seizures are seen to be associated with lower IQ scores rather than early onset of partial seizures (O'Leary, Lovell, & Sackellaes 1983)

**Cortical dysplasia:** age at onset is not the only factor. It has been found in several studies that epilepsy with psychomotor developmental delay is the common phenotype in cortical dysplasia (Barkovich & Kjos 1992; Guerrini et al. 1999).

**A long history or high frequency of seizures or both:** increases the risk of cognitive impairment (Dikmen & Mathews 1977; Sillanpaa 1973).

**Status epilepticus or repeated generalised convulsions:** are reported to carry a risk of inducing brain damage, resulting in permanent cognitive and motor deterioration (Christiaens et al. 2003; Meierkord et al. 1997). Animal studies have demonstrated structural damage on experimentally-induced status epilepticus (Meldrum, Horton, & Brierley 1974).

**The effects of AEDs:** on cognitive function are discussed in section 2.7.

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**2.7: AEDs as a cause of behavioural side-effects**

Effects of AEDs on cognition and behaviour have been studied in many ways. With the background of seizures, which has direct effect on both cognition and behaviour (see above), it is not easy to comment whether such defect is caused by seizure or by drug itself. Blennow et al. (1990) and Gallasi, Morreale and Lorusso (1988) have examined this issue in children and in adolescent and adults, after they had been seizure free for one year and two years respectively (Blennow et al. 1990); (Gallasi, Morreale, & Lorusso 1988). Both of the studies suggested that only short-term memory was affected by AED treatment compared with a control group. The above findings may suggest that maintenance of AED treatment after seizure remission for a sufficient period needs to be justified.

Farwell et al. (1990) have studied the effect of PB on intelligence and found that it depress the cognitive performance in children treated for febrile seizures (Farwell et al. 1990).
It is suggested after reviewing these studies that intrinsic and environmental variables play a more significant role in predisposing children to cognitive and behavioural problems than does antiepileptic medication itself (Mandelbaum & Burack 1997).

Mandelbaum and Burak examined the effect of seizures and medication on cognitive and behavioural functioning in children with idiopathic epilepsy. They have found, as Mitchell et al. (1991) emphasized, the importance of the confounding factors while examining the effect of AED (Mitchell & Chavez 1987). The confounding factors suggested by the authors are socio-economic and cultural variables, and the baseline cognitive impairment, including the seizure type. The dose-related side-effects might be the same for all AEDs and probably for all ages. Polytherapy and/or excessive dosing may cause drowsiness in children, who may, as a result remain irritable during daytime. However, seizure frequency, seizure type, underlying cause of epilepsy, age and pre-existing cognitive state, family environment, parental tolerance and anxiety level seem to have greater influence on the behaviour of the child. In the situation of low seizure frequency or where the child has seizure remission for a long time (more than 2 years) and the child is still on AED treatment at the same maintenance dose, the effect on cognitive function and behaviour may be explained as caused by the AED as shown by Blennow et al. and Gallasi et al (op.cit.).

2.8: Availability of first line AEDs, and new antiepileptic medications in Bangladesh

Commonly used drugs in the treatment of epilepsy are barbiturates, benzodiazepins, carbamazepine, sodium valproate, prednisolone, phenytoin, clobazam, acetazolamide, lamotrigine, vigabatrin, topiramate, tiagabine and gabapentine.

The first six or seven of these drugs are commonly available in Bangladesh but only in main cities. Phenobarbitone, carbamazepine and phenytoin are usually available in
wider areas of the country, but a recent government policy of putting PB among the
narcotic group of drugs has created a crisis.

2.9: Epilepsy treatment gap in developing countries, and
seizure outcome

2.9.1: Treatment gap

A simple definition of treatment gap is 'the proportion of people with a condition or
disease who need treatment for it but who do not get it'.
The WHO accepted definition of epilepsy treatment gap is the difference between the
number of people with active epilepsy and the number whose seizures are being
appropriately treated in a given population at a given point of time, expressed as a
percentage. The appropriate treatment includes the diagnosis and treatment of any
underlying cause and the treatment of recurrent seizures (Meinardi et al. 2001). In
epilepsy the treatment gap may be estimated directly during prevalence studies (only if
studied) and indirectly from the amount of AEDs sold in the country and the number
of people with active epilepsy (defined as one episode of seizure in the past year). The
world wide treatment gap is an estimated 85%, but exceeds 92% in some developing
countries (Meinardi, Scott, Reis, & Sander 2001).

2.9.2: AED selection, developed and developing countries

AED selection is very important once the diagnosis is confirmed. The principle of
drug selection is based on seizure type, syndrome type, aetiological issues and the risk
of adverse effects of the drug. In developing countries, where resources are very
limited, drug availability and cost of drugs are major factors to consider. The
treatment of epilepsy with AEDs has been well studied in developed countries which
have established that first line AEDs are highly effective and that there is no large
difference in efficacy between the four major drugs (CBZ, PB, PHT & VPA) (Kwan &
many others, Kwan and Brodie (op.cit.) have shown that dose related tolerability is as important a confounding factor as efficacy in determining overall drug effectiveness. However, in many individual cases a particular drug may be poorly tolerated even in low dosage for reasons, which are poorly understood.

2.9.3: Seizure remission and treatment gap

In developed countries the majority of people with epilepsy are started on appropriate treatment at the beginning of the condition. The picture is different in countries with limited resources, where 85% of people with epilepsy are either inappropriately treated or not treated at all. However, despite a large treatment gap and a high rate of seizures before starting appropriate treatment, seizure control when AEDs are used is comparable to that found in developed countries (Feksi et al. 1991; Placencia, Sander, Shorvon, Roman, Alarcon, Bimos, & Cascante 1993). In their 12 months follow-up study, Feksi et al. (1991) and Placencia et al. (1993) reported 53% of the all age population were seizure free and another 26% and 14% had more than 50% seizure remission. One study from Papua New Guinea, reported 45% of the studied children became seizure free at one-year follow-up (Danaya, Johnson, & Ambihaipahar 1994). Most of the studies in developed countries are of long-term follow-ups with a minimum period of follow-up of 3 years. However, it is a frequent finding in many long-term studies that the initial response to AED treatment is an important prognostic factor (Arts et al. 1999; Kwan & Brodie 2000; Kwan & Brodie 2001). In newly diagnosed patients, seizure control was achieved among 63-82% (Elwes et al. 1984; Matson, Cramar, Collins, & Smith 1985). Childhood onset epilepsies studied by Camfield et al. (1993) and Sillanpaa et al. (1995) found that 70% (at 3 years follow-up), and 60% (at 30 years follow-up) of the population achieved seizure freedom for a period sufficient to withdraw antiepileptic medication (Camfield, Camfield, Gordon, Smith, & Dooley 1993; Sillanpaa, Camfield, & Camfield 1995). Seizure remission for 1-2 years was recorded in 63% in Brorson and Wranne’s (1987) study, 73% in de Silva’s (1996); 74% in Berg’s (1995); 77.9% in Hauser’s (1996) and 69% in Arts’s
2.9.4: Prognosis and response to treatment (based upon the syndromic classification)

1. Benign idiopathic or familial neonatal seizures (Miles & Holmes 1990), benign partial seizures (BRE), benign myoclonic epilepsy of infancy and acute symptomatic seizures (Aicardi 1994a; Aicardi 1994b; Wallace 1993) are the conditions in which spontaneous remission is the rule.

2. In childhood absence epilepsy, epilepsy with generalised tonic-clonic seizures on awakening, non-specific generalised atonic clonic seizures in patients with no abnormal neurological signs and some of the localization related epilepsies, seizures are usually easily controlled with AEDs. Once remission is achieved, it is usually permanent (op.cit.).

3. In conditions such as Juvenile myoclonic epilepsy and some of the localization related epilepsies, patients may achieve remission through AEDs but may relapse if AEDs are withdrawn (op.cit.).

4. Where seizures are associated with neurological deficits (e.g., TS, Sturge-Weber syndrome, cerebral malformations, cerebral palsy, (Aicardi 1994a;Wallace 1993), myoclonic epilepsies, and West syndrome, Lennox-Gastaut syndrome (Aicardi 1994a; Wallace 1993; Wong & Trevathan 2001), are examples of epilepsies with a very poor prognosis, despite intensive treatment with AEDs and seizures tend to continue in them. The aim of AED treatment in this group often is seizure reduction rather than remission.

2.10: Best practices and predictors of seizure remission: lessons learnt from developed countries
2.10.1: Clinical factors as predictors of seizure remission

Seizure remission is the immediate, primary outcome aim in the management of epilepsies, and this can be influenced by multiple factors. Different studies, mostly from developed countries, have found degrees of intellectual loss, age at onset of first seizure, severity of grand-mal experience, seizure frequency, epilepsy type and other associated disabilities, as important predictors for seizure remission.

A review of the various strategies used to predict outcomes in different populations, both adult and children, is given below.

Using a scoring system in children

Carol Camfield and colleagues undertook a retrospective study in Nova Scotia, to ascertain predictive factors in children with epilepsy having specific types of seizures (GTCS, and secondary generalised seizures) (Camfield, Camfield, Gordon, Smith, & Dooley 1993). The patients had been selected from an EEG centre and a simple scoring system for seizure remission was developed. Seizure ‘onset before 12 years’ of age, ‘normal intelligence’, ‘no history of neonatal seizures’ and ‘fewer than 21 seizures before treatment’ were found to be the best predictors of seizure remission. The same scoring system for prediction of remission at the time of diagnosis was applied in Nova Scotia, Canada, and Finland (Sillanpaa, Camfield, & Camfield 1995). Poor outcome (i.e. no seizure remission) was more accurately predicted in the short follow-up in Nova Scotia than seizure remission. A limitation of both of these studies was that the scoring system was developed on the children with GTCS and secondary generalised seizures. Testing in a broad range of seizure types and epilepsy in children is a prerequisite of the wider application of this scoring system.

Brorson and Waranne in their prospective study, have found that 89% of children who had none of the following risk factors, became seizure free: (a) abnormal neurology, (b) poor cognitive development, (c) seizure frequency ≥2 in 6 months and (d) multiple seizures (Brorson & Wranne 1987). The presence of a motor disorder, cognitive
impairment, frequent seizures and multiple seizure types were found to be poor prognostic factors in their study.

Studies in the general population
In Sillanpaa's long-term prospective study in a general population (Sillanpaa 1993) the authors found that 'one type of seizure', 'good short-term treatment results', 'no status epilepticus' and 'normal mental development' are strong predictors of a favourable outcome. In another long term study, similar findings, i.e., early response to therapy, low frequency of seizures or absence of status epilepticus prior to treatment and normal mental development are found to be the best predictors of seizure remission amongst adults with epilepsy who had a history of 'childhood onset' of epilepsy (Wakamoto et al. 2000).
Annegers et al. included both children and adults, and made a distinction between individuals with and without neurodeficits (Annegers, Hauser, & Elveback 1979). Among those individuals who had no signs of neurological deficit, 77% went into remission after 15 years of observation but only 46% of those who had motor and/or cognitive impairments did so. However, the prognosis for children was not reported separately from that of adults.

Control case studies
Berg et.al.(1996) and Casetta et. al.(1999) studied the predictors of intractable epilepsy in childhood. In their case control studies (Berg et al. 1996;Casetta et al. 1999) the authors found that 'early age at onset', 'high seizure frequency before starting treatment' and 'remote symptomatic etiology' are the predominant predictors of intractability. They also noted, as did Sillanpaa (Sillanpaa 1993), that 'status epilepticus' and 'intractability' were strongly associated with each other, partly because children who had remote symptomatic epilepsy were more likely to have had an episode of status epilepticus.
Arts et al.(1999) in their prospective study examined the association of variables available in the early course of childhood epilepsy with poor short-term outcome. The authors identified that the 'number of seizures before treatment', 'seizure types' and
'remote symptomatic epilepsy' were associated with poor seizure outcome (Arts et al. 1999).

Chawla (2002) performed a case control study in 100 children (50 cases) (Chawla et al. 2002) to determine the etiology and clinical predictors of intractable epilepsy. The authors identified that the presence of neurological impairment OR 12.25, 95% CI 3.58-41.89, age at onset of seizure less than 1 year (OR 11.70; 95% CI 2.95-46.43), myoclonic seizures /infantile spasm (OR 2.9; 95% CI 1.13-7.43) had correlation with poor seizure remission on multiple logistic regression.

2.10.2: EEG as a predictor of seizure remission

A few research studies have examined clinical factors and EEG findings as potential predictors of epilepsy outcome.

Camfield et al.'s (1993) data shows that a normal EEG record has significant univariate association with seizure remission (op.cit). Berg et al. (2001) in their study of two years remission and subsequent relapse in children have examined the initial EEG feature as an indicator of seizure relapse and have found that slowing on the initial EEG in combination with clinical factors (i.e., seizure frequency, remote symptomatic aetiology and family history of epilepsy) were associated with a decreased likelihood of attaining remission (Berg et al. 2001). Another study examined combined EEG and clinical predictors associated with both seizure control and medical intractability in children with epilepsy (Ko & Holmes 1999). They have found a number of EEG and clinical factors associated with intractable epilepsy. There was strong univariate association between intractability and 'abnormal EEG background' (including diffuse slowing, asymmetry, and abnormal amplitude), a 'high number of spikes or sharp waves' and 'focal spike and wave activity'. Conversely, 'reactivity to photic stimulation' and '3 Hz spike and wave discharges' were predictive of good outcomes for seizure control. 'Diffuse slowing', and 'focal spike and wave activity' were found to be independent predictors of poor outcome.
Shafer et al. (1988) have examined the predictors of 5 years seizure remission in Minnesota, in all age group. The authors have identified two clinical, and one EEG factors significantly associated with five years seizure remission. These were: no early-life brain damage, never having GTCS, and no generalised epileptiform activity (Shafer et al. 1988).

We may say in conclusion that:

1) the total phenotype of any child with epilepsy includes behavioural, cognitive, motor and sensory impairments, which need assessment and management in their own right and have prognostic significance for the epilepsy;

2) It is logical therefore to include at some level such a multidisciplinary service as part of the epilepsy program; and

3) the level and use of this expert team is yet to be evaluated.
<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Country</th>
<th>Study design</th>
<th>Poor sz. remission significantly influenced by the presence or absence of the following:</th>
<th>Age at onset; low IQ; neonatal seizures, number of sz. before treatment in MVA, EEG in UVA.</th>
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<td>Sillanpaa et al.</td>
<td>1995</td>
<td>Turku, Finland</td>
<td>Long term (30 years) follow-up of incidence cohort</td>
<td>Retrospective</td>
<td>N.D, high initial seizure rate, SE, poor short-term effects of AED therapy.</td>
</tr>
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<td>Wakamoto et al.</td>
<td>2000</td>
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<td>Childhood onset epilepsy, in 20 years or older. Retrospective</td>
<td>Remote symptomatic epilepsy (mostly represented by perinatal injury); sz. frequency, age at onset (not confirmed in all age group)</td>
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<td>Casetta et al.</td>
<td>1999</td>
<td>Copparo, Italy</td>
<td>Case-control Community based</td>
<td>Symptomatic epilepsy, number of sz. before treatment, sz. Types.</td>
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<tr>
<td>Arts et al.</td>
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<td>Tae-Sung Ko et al.</td>
<td>1999</td>
<td>Boston, U.S.A.</td>
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<td>Early brain damage, GTCS, abnormal first EEG</td>
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<tr>
<td>Shafer et al.</td>
<td>1988</td>
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<td>ND; low IQ; sz. frequency.</td>
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</tr>
<tr>
<td>Brorson And Wranne Chawla et al.</td>
<td>2002</td>
<td>India</td>
<td>Retrospectively traced 12 years followed up</td>
<td>N.D., age of onset before 1 year, MCS/IS, remote symptomatic epilepsy.</td>
<td></td>
</tr>
</tbody>
</table>

N.D., neurological deficits; MVA, multivariate analysis; UVA, univariate analysis; sz, seizure; SE, status epilepticus; IS, infantile spasm; FHO, family history of; MCS, myoclonic seizures.
CHAPTER THREE

3.1: Introduction

This chapter will discuss the prevalence of epilepsy in Bangladesh in the context of its socio-economic and geographical background and relate these to other countries with limited resources. The development of multidisciplinary services including EEG services for children in a country with limited resources will also be discussed.

3.2: Geographical and social aspects of Bangladesh

Bangladesh is a densely populated country with 130 million people, 45% of which are under 18 years of age (UNICEF 2001). The economy is predominantly agriculture-based and 85% of the population lives in rural areas. Lying in the foothills of the Himalayas and receiving two of the major rivers flowing from it, the Ganges and the Brahmaputra, over half of the country is flooded each year during the monsoons, sometimes with only two-fifths of the area remaining above water. This extensive flooding causes problems in transportation. The poverty level is high as more than 60% of the population live below the 'poverty line' (Sen 1997). Despite many geographical and social problems, since its independence from Pakistan three decades ago in 1971, Bangladesh has made considerable strides in improving its quality of primary health care. For example, the mortality of children under 5 years has decreased from 248 per 1000 in 1960 to 89 per 1000 in 1999, of which 58 per 1000 occur in the first year of life, mostly in the neonatal period (UNICEF, 2001). Recent trends show, however, that the frequent causes of mortality in children remain acute respiratory infections and diarrhoeal diseases. Malnutrition is still prevalent and present in over 60% of the population of children under 5, and only about 25% of pregnant mothers ever receive an antenatal check-up (UNICEF, 2001). On a more
positive note, the number of children per family has also decreased to 2.6, a fact that is causing families to focus more attention on the 'quality of survival' of their children. Primary education has also made considerable progress with school enrolment increased from 45% to 97% within a decade. Feudal value systems have given way to progressive policies such as the increasing number of girls being enrolled into schools every year. This is due to the government policy of providing free education for all children up to primary school level (10 years of age) and for female children until high school level (18 years of age). Traditional cultural practices from the feudal era continue such as delivery by family members or by untrained traditional birth attendants (TBA) at home in more than 80% of women, treatment by shamams and other traditional healers (Kabiraj, religious persons) for seizures and epilepsy, gender bias towards male children, covert and overt violence against women such as domestic violence. However, many practices need to be addressed in a positive manner. The close community ties, joint family system (i.e. extended family living in the same house, sharing undivided land property, having daily meal served from a common store etc.), ecological farming, use of medicinal herbs and indigenous medicine, universal breast feeding practices etc., may have positive effects on the rearing of infants and young children living in high risk environments.

3.3: Epidemiology of childhood disabilities and seizure disorders in Bangladesh and other developing countries

In Bangladesh no comprehensive national survey has been undertaken for estimating the prevalence of disabilities in children. According to the WHO, about 12 million people in all age groups with disabilities live in Bangladesh. Based on two surveys in BD in 1982 and 1986, the government estimated the national prevalence rate of disability to be 0.64%, and 0.52% respectively. The Bangladesh Bureau of Statistics (BBS) yearbook for 1995 showed the national rate to be 1.06%. According to the BBS, 1.26% of children up to 14 years of age (with a higher incidence among 5-14 years) were disabled. However the ACTIONAID Bangladesh survey in 1996 among
470,000 people revealed a higher rate of disability (14%). Most of these studies had limitations in identifying childhood disabilities accurately.

An epidemiological survey of childhood disability using a brief ten-questions with probes (Khan & Durkin 1995), was designed to screen five major disabilities, i.e., motor, cognition, seizures, vision and hearing disabilities, in a door-to-door study in both rural and urban populations. The pilot study was first conducted to validate the questionnaire in twelve developing countries, including Bangladesh (Belmont 1986; Zaman, Khan, Islam, Banu, Dixit, Shrout, & Durkin 1990). This was further refined on a population of over 10,000 children aged from 2 to 9 years in rural and urban areas of Bangladesh and also conducted in Jamaica and Pakistan (Durkin et al. 1992). This study reveals a high prevalence of disability in Bangladesh: nearly 7% of 2 to 9 year old children (Khan & Durkin 1995).

Table 3.1: Estimated prevalence of disabilities per 1000 in 2 to 9 year-old children in Bangladesh.

<table>
<thead>
<tr>
<th>Type of disability</th>
<th>Total ( (n=10,299) )</th>
<th>Urban ( (n=5103) )</th>
<th>Rural ( (n=5196) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any disability</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serious</td>
<td>15.68</td>
<td>19.90</td>
<td>11.75</td>
</tr>
<tr>
<td>Mild</td>
<td>52.84</td>
<td>45.26</td>
<td>59.98</td>
</tr>
<tr>
<td>Cognitive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serious</td>
<td>5.93</td>
<td>6.05</td>
<td>5.84</td>
</tr>
<tr>
<td>Mild</td>
<td>14.84</td>
<td>15.80</td>
<td>13.18</td>
</tr>
<tr>
<td>Motor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serious</td>
<td>3.79</td>
<td>3.58</td>
<td>4.01</td>
</tr>
<tr>
<td>Mild</td>
<td>2.17</td>
<td>2.02</td>
<td>2.32</td>
</tr>
<tr>
<td>Vision</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serious</td>
<td>2.46</td>
<td>3.74</td>
<td>1.27</td>
</tr>
<tr>
<td>Mild</td>
<td>13.33</td>
<td>22.04</td>
<td>5.14</td>
</tr>
<tr>
<td>Hearing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serious</td>
<td>5.87</td>
<td>9.66</td>
<td>2.32</td>
</tr>
<tr>
<td>Mild</td>
<td>23.06</td>
<td>6.37</td>
<td>38.77</td>
</tr>
<tr>
<td>Seizures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serious</td>
<td>0.33</td>
<td>0.45</td>
<td>0.21</td>
</tr>
<tr>
<td>Mild</td>
<td>4.57</td>
<td>3.52</td>
<td>5.57</td>
</tr>
</tbody>
</table>

Taken with permission from: Khan and Durkin, 1995.
Of the children screened by door-to-door household surveys (i.e., over 10,000 children from both urban and rural sites equally distributed), the prevalence of serious disability was found to be 1.6 per cent. In the same study, the prevalence of seizure disorders was also estimated. Lifetime prevalence of epilepsy was estimated to be 6.5 per 1000 in BD (Durkin et al. 1992).

Table 3.2: *Prevalence estimates/1000 of seizure disorders in 2-9 years old children in three populations and percentage with positive screening results specifically on seizure questions (95% CI)

<table>
<thead>
<tr>
<th>Prevalence</th>
<th>Bangladesh</th>
<th>Jamaica</th>
<th>Pakistan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonatal seizures</td>
<td>8.4 (5.6-11.2)</td>
<td>0.9 (0.4-1.3)</td>
<td>13.0 (9.4-16.7)</td>
</tr>
<tr>
<td>Febrile seizures</td>
<td>50.6 (43.7-57.5)</td>
<td>10.9 (2.6-19.3)</td>
<td>62.8 (54.8-70.9)</td>
</tr>
<tr>
<td>Provoked seizures</td>
<td>57.7 (50.5-65.0)</td>
<td>11.8 (3.5-20.2)</td>
<td>70.4 (61.9-78.9)</td>
</tr>
<tr>
<td>Unprovoked sz.*</td>
<td>8.7 (6.7-11.3)</td>
<td>6.3 (3.5-12.2)</td>
<td>17.8 (10.9-24.7)</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>6.5 (2.2-10.6)</td>
<td>5.8 (0.0-11.7)</td>
<td>15.5 (9.6-21.4)</td>
</tr>
<tr>
<td>Active epilepsy b</td>
<td>5.8 (1.6-10.1)</td>
<td>5.2 (0.0-11.1)</td>
<td>12.4 (6.6-18.2)</td>
</tr>
<tr>
<td>Any seizure history</td>
<td>68.3 (60.5-76.1)</td>
<td>17.7 (12.4-22.9)</td>
<td>91.2 (82.2-101.2)</td>
</tr>
</tbody>
</table>


*Prevalence estimates refer to lifetime prevalence; a, Includes children with epilepsy or history of one unprovoked seizure; b, Recurrent unprovoked seizures with at least in the past year.

Despite such high rates of disability identified in the population study (Tables 3.1 & 3.2), services for the children with such neurological impairments and neuro-disabilities are practically non-existent in Bangladesh except in two major cities.
3.4: Multidisciplinary child development and neurodisability services in Bangladesh: a new dimension to child health

In 1992 a Child Development and Neurology centre (CDC) was established for the first time in the country within a 350 bed national hospital for children, the Dhaka Shishu (Children’s) Hospital (DSH). The aim was to provide a comprehensive, multidisciplinary service for children presenting with both acute and longstanding neurodevelopmental impairments and disabilities. Since it was founded, the CDC has trained a multidisciplinary team of professionals including developmental paediatricians, paediatric neurologists, paediatric clinical neurophysiologists, clinical and developmental psychologists, developmental therapists and social workers, as part of a core team. There are very close links with professionals from other disciplines including ophthalmologists, neurosurgeons, orthopaedic surgeons, audiologists, special education teachers and rehabilitation specialists. For the past five years the CDC has been able to disseminate the services by training teams of professionals in several major hospitals in the country (shown on the map of Bangladesh, (Figure 3.1).
Figure 3.1: map showing the areas where comprehensive services for disabled children are disseminated.
Over one-third of children presenting to the CDC have seizure disorders.

Figure 3.2: Incidence of developmental disabilities at the *Shishu Bikash Kendro*, Dhaka *Shishu* Hospital in 4100 children from 1992-1998 (unpublished data)

3.5: Developing EEG services in Bangladesh

Until 1996, the diagnosis of epilepsy and associated disorders was based entirely upon clinical history and examination. In 1996 a paediatric EEG service was started with initiative of the CDC by SHB, who was trained in the Department of Clinical Neurophysiology, Great Ormond Street Hospital for Children, Institute of Child Health, London, UK, under the supervision of Dr. Stewart G.Boyd, for over a year. Since then two more child health physicians have been trained to perform and interpret EEGs in Dhaka. We believe that that this service has improved the quality of diagnosis and management of children with neurodisabilities and epilepsy.
The referral of children has greatly increased. Twenty percent of 1581 children attending the CDC in 1996 presented with seizure disorders (Jahan 1996). This proportion increased to 38% out of 4500 children at the same centre in 1999 (CDC, unpublished data), indicating that a higher proportion of families with children affected by seizures are seeking services. This rising demand for service is similar to that seen in other countries with limited resources, where seizure disorders form a greater proportion of the case-load than in developed countries. In Saudi Arabia, 48% of all cases referred to a children’s neurological clinic were convulsive disorders (Alfrayh & Al Naquib 1987). A similar proportion of epilepsy cases are reported in neurology clinics in India (Mani 1987). Epilepsy was identified as most common neurological condition in a study conducted to identify several neurological disorders in Nigeria (Osontokun 1982). Epilepsy therefore, is a major health care problem in developing countries, both for specialist and primary care services.

3.6: Social and public health concerns relating to childhood epilepsy in developing countries

Epilepsy is a common clinical presentation of many preventable diseases and conditions. A number of chronic infectious diseases (schistosomiasis, cerebral cystercerosis, hydatid diseases and tuberculoma), sequelae of acute CNS infections, perinatal insult, head injuries and recurrent febrile seizures are associated with epilepsy particularly in developing countries (Durkin, Leislie, Devidson, Hasan, Hasan, Khan, & Shrout 1992; Miller et al. 1983; Pal, Arturo, & Sander 2000). The majority of such problems require primary and secondary levels of health care. In another study, a history of perinatal complications, low Body Mass Index (BMI) and recent physical symptoms were found to be independently associated with active epilepsy in a study of persons of all ages in Calicut, India (Hackett, Hackett, & Bhakta 1997). When the findings of the prevalence study of childhood disabilities in three countries (Jamaica, Pakistan and Bangladesh) were compared, trauma and brain infections were found to be strongly associated with epilepsy (Durkin, Leislie, Devidson, Hasan, Hasan, Khan, & Shrout 1992; Zaman, Khan, Islam, Banu, Dixit, Shrout, & Durkin 1990). In the
latter study a history of febrile seizures was strongly associated with epilepsy in 
Pakistan and Jamaica, but not in Bangladesh. Any association with perinatal problems 
could not be analysed due to a lack of information. However, neonatal seizures were 
found to be a high risk factor for mental retardation in this study (Durkin et al. 2000; 
Durkin, Hasan, & Hasan 1998). The issue is still to be addressed in most developing 
countries.

The vast majority of seizures, especially those occurring during early infancy, remain 
unrecognised and even after identification they may not be treated appropriately. The 
reasons behind this are several, some related to social and cultural views towards 
epilepsy and unawareness among the population, and some related to the scarcity of 
specialists and lack of proper training among the care-providers at the primary, 
secondary and tertiary levels of health care. A lack of a consistent supply of AEDs is 
also a factor (Shorvon & Farmer 1988).

Studies in other countries have also revealed that different beliefs, fear of 
stigmatisation and negative attitudes towards epilepsy prevent family members from 
seeking advice for, or talking about the condition. In West Bengal, India, a probable 
cause of poor ascertainment of epilepsy in children was noted to be the deliberate 
tendency to conceal information about seizures in the family (Pal, Arturo, & Sander 
2000). In an African study, it was seen that children with seizure disorders are only 
brought to health services when they are injured as a result of a seizure episode, and 
not before (Watts 1989).

In Bangladesh, clinical experience suggests that most of children are first taken either 
to the traditional or religious healer and given herbal or other treatment with a belief 
that this is a curse from God or that an evil spirit has entered into the body. Such 
beliefs need to be studied to verify and to take steps to develop epilepsy management.
3.7: Developing epilepsy services for children in a country with limited resources

Any planning for service development within the health care infrastructure of a developing country should look first towards its existing strengths and weaknesses. The modern system of early identification and treatment being practiced in more developed countries utilizes a vast amount of its resources including those spent on investigative procedures. Yet, even in these countries the focus is also shifting towards a more holistic management to include co-existing disabilities, associated cognitive and behavioural problems and family needs as being equally important to seizure control, and that they should be provided by multidisciplinary and multi-agency co-ordination (Neville 1997). Probably the best use of resources can be made by developing a simple means of identification of epilepsies at the early stage of the condition by lesser-trained professionals. This has been shown to be possible in Bangladesh by utilising community trained health workers for the identification of a range of disabilities including seizure disorders (Khan 1998). However, these developments need to be backed up by rational management and appropriate investigations when required at the secondary (at the district) and tertiary (at the division) levels. At the moment such services are only available in the capital of the country, Dhaka (CDC) and in very few other places. Before large-scale policies are adopted an evaluation of the benefits of the existing services needs to be conducted.

Human resource development, which will provide optimum services within minimum a period of time needs to be considered. The CDC team has in the meantime developed a network of professionals and para-professionals working in the field of neurodisability and child development called the Shishu Bikash Network (SBN, 'Bangla' for Child Development Network). This not only includes child care physicians but also psychologists, social workers, counsellors and many others who are working towards optimising the development of delayed children. Innovative methods of training have been adopted, such as training college graduates in 'developmental therapy', which combines the basic disciplines of physiotherapy, occupational therapy, and speech therapy within a framework of normal child
development. Parallels can be made with the Peto School for Conductive Education in Hungary and the single nurse-teacher-therapist advocated many years ago by professionals in the UK. In a similar vein, the adoption of appropriate technology is required for the benefit of the children. Both the theoretical basis of such technologies and their practical applications are necessary to develop curricula for training. The value of such services needs to be evaluated also so that long-term planning can benefit from the messages emerging from such studies. For example, which children with seizures need to be referred from primary care (where diagnosis is based upon clinical history only), to tertiary care services for further investigation, is a question that needs to be answered. The present health care system in Bangladesh is divided as a primary care service at the thana level (Thana Health complex) where medical officers (MBBS doctors) are posted under a thana health officer (THO), secondary care service at the district level (district hospital) where a paediatric specialist including other specialists are posted, and the tertiary health care at the division level. The tertiary care with the extensive investigation facilities is only present in the capital, Dhaka and in Chittagong port city (Fig 3.1).

3.8: Experience with first 1000 EEGs, conducted between May 1996 and October 1997

The EEG is a relatively inexpensive investigation, and is often invaluable in making an appropriate diagnosis. We therefore needed to develop an EEG service for the children at the tertiary level. The experience from the first 1000 EEGs has shown the variability of referred cases. This is not unexpected given the novelty of the service for practitioners and the considerable load of chronic cases with multiple disabilities. However, this scenario was changed with time and further experience among the professionals.
Figure 3.3: Flow chart of the 1000 population from the first reviewed from the EEG centre to last follow-up

First 1000 EEGs reviewed, patients categorized as follows:
60.6% with recurrent unprovoked seizures
21.5% non-convulsive disorders
17.9% recurrent febrile seizures

539 from CDC

Medical record reviewed
151 fell into study criteria

Medical records were not available, and excluded from study

461 from other hospitals & private clinics

Epilepsy classification 1st step
63.6% generalised
25.2% Partial
11.2% unclassified

Epilepsy classification 2nd step
61.0% Symptomatic & cryptogenic
39.0% Idiopathic

EEG features in 151 children
40.3% Only epileptiform discharges
21.2% both epileptiform discharges and background abnormality
19.2% only background abnormality
19.2% normal record for the age and state of the child.

122 (80%) EEGs were abnormal
36.4% had focal discharges
25.2% generalised discharges
19.2% non-epileptiform abnormalities
19.2% normal record for the child

Seizure outcome after > 1 year of AED treatment
Seizure remission in 49.7%
50% seizure reduction in 32.2%
< 50% seizure reduction in 19.2%
Table-3.3: Clinical profile of 1000 children referred for EEG:

<table>
<thead>
<tr>
<th>Possible epilepsy</th>
<th>606</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-convulsive disorders</td>
<td>215</td>
</tr>
<tr>
<td>Developmental delay with movement disorder</td>
<td>72</td>
</tr>
<tr>
<td>Behavioural disorder</td>
<td>65</td>
</tr>
<tr>
<td>Speech and communication disorder</td>
<td>46</td>
</tr>
<tr>
<td>Headache</td>
<td>11</td>
</tr>
<tr>
<td>Autistic trait</td>
<td>9</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>8</td>
</tr>
<tr>
<td>School failure</td>
<td>4</td>
</tr>
<tr>
<td>Recurrent febrile convulsion</td>
<td>179</td>
</tr>
<tr>
<td>Total</td>
<td>1000</td>
</tr>
</tbody>
</table>

Table 3.4: Salient features of the 179 children who presented with febrile-convulsion.

<table>
<thead>
<tr>
<th>Age in years</th>
<th>n =179</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2-4 years</td>
<td>114</td>
<td>63.7</td>
</tr>
<tr>
<td>&gt;4-7 years</td>
<td>65</td>
<td>36.3</td>
</tr>
<tr>
<td>Total</td>
<td>179</td>
<td>100.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sex</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>132</td>
</tr>
<tr>
<td>Female</td>
<td>47</td>
</tr>
<tr>
<td>Total</td>
<td>179</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Number of febrile convulsions</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2</td>
<td>69</td>
</tr>
<tr>
<td>3-5</td>
<td>69</td>
</tr>
<tr>
<td>&gt;5</td>
<td>41</td>
</tr>
<tr>
<td>Total</td>
<td>179</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Non-convulsive disorders *</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Absent</td>
<td>145</td>
</tr>
<tr>
<td>Present</td>
<td>34</td>
</tr>
<tr>
<td>History of non-febrile seizure present</td>
<td>15</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>AED history</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>98</td>
</tr>
<tr>
<td>On long-term AEDs</td>
<td>81</td>
</tr>
<tr>
<td>Total</td>
<td>179</td>
</tr>
</tbody>
</table>

* Defined in section 4.6
Table 3.5 Abnormal EEG findings in children who presented with febrile seizures
(total 43)

<table>
<thead>
<tr>
<th>EEG findings</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonspecific dysrhythmia</td>
<td>23</td>
<td>53.5</td>
</tr>
<tr>
<td>Diffuse slow wave activities</td>
<td>8</td>
<td>18.6</td>
</tr>
<tr>
<td>Localized epileptiform discharges</td>
<td>6</td>
<td>14.0</td>
</tr>
<tr>
<td>3c/s spike wave discharges on HV</td>
<td>3</td>
<td>7.0</td>
</tr>
<tr>
<td>Long standing slow waves after HV</td>
<td>1</td>
<td>2.3</td>
</tr>
<tr>
<td>Centro temporal spikes</td>
<td>1</td>
<td>2.3</td>
</tr>
<tr>
<td>Transient Bursts of Generalised epileptiform</td>
<td>1</td>
<td>2.3</td>
</tr>
<tr>
<td>discharges</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>43</td>
<td>100.0</td>
</tr>
</tbody>
</table>

With this background of a high proportion of epilepsy and other disabilities in the early age group (Section 3.3, Chart 3.2), it would be appropriate to include an epilepsy service as part of a comprehensive programme for disability in childhood. This will be cost-effective, for both patients and service providers.

Epilepsy can be diagnosed from the history and clinical evidence; however, an appropriate treatment, (WHO definition for treatment gap; (Meinardi, Scott, Reis, & Sander 2001), should include the identification and treatment of the underlying cause. This would require a cost-effective and time-appropriate investigation facility. We included EEG within a short time after presentation at the clinic. The effectiveness of this not examined in this study.

We believe, that a substantial proportion of children with newly diagnosed, unprovoked seizures have a decelerating disease process, as shown by van Donselaar et al. in the course of untreated tonic-clonic seizures in childhood,(van Donselaar et al. 1997). The authors suggest that not all children with an early diagnosis of epilepsy would need regular AED treatment. However, timely identification of children needing AED treatment would prevent further complications and neurodisabilities. We therefore need to develop a simple and effective method of identifying those who really need treatment for epilepsy and who need further investigation. We also need to develop a definite guideline to regulate the AED treatment within a limited resource. However, such a guideline must also take account of the acceptability and efficacy of commonly used AEDs in an appropriate setting.
PART TWO

BACKGROUND OF PART TWO

Part One has shown that childhood epilepsy is common in Bangladesh (Section 3.3). Epilepsy management services are only available within two large cities (Fig-3.1) where, the specialist team includes a physician, developmental therapist and child psychologist, and aim to provide comprehensive management for children with epilepsy and other disabilities.

This part of the thesis will present the methods and material, and results of the childhood epilepsy research performed at the national children’s hospital in Bangladesh. It will discuss the seizure criteria, co-existing non-convulsive disabilities at first presentation at the clinic, and their correlation with seizure outcome after more than one year of comprehensive treatment. This will raise the possibility of predicting epilepsy outcome from the information available on first diagnosis, which may help caregivers to plan long-term and short-term management for children with multiple impairments, which include epilepsy.

The present part will also illustrate that even in a country with limited resources, a multidisciplinary team approach is practicable. It can be achieved by providing short-term training to (i) primary health care physicians about the diagnosis and management of epilepsy and co-existing non-convulsive disabilities, (ii) the local medical assistants on developmental therapy, and (iii) clinical child psychologists.
CHAPTER FOUR

4.1: Introduction

This chapter will present the overview of the methods and preparation for the prospective study

4.2: Methods and material

The whole study was arranged in three stages:

Stage 1
A retrospective study: this was done to compile the epilepsy profile and associated non-convulsive disorders of the children attending a specialized centre, and to identify the predictors of poor seizure remission. Methods, results and implications of this stage will be presented in chapter 5

Stage 2
A prospective study: this was designed to validate the predictors of seizure outcome using two strata of the sample. Introduction, methods, result, and discussion will be presented in Chapter 6

Stage 3
Randomized Controlled Trial study: this was done with part of the population recruited for the prospective study. Introduction, methods, results and discussion will be described in Chapter 7
4.3: Definitions

To help the identification and management of epilepsy in children, the condition needs to be clearly defined to the service providers as well as to the population. From past experience it was noted that clear identification of generalised clonic seizures, myoclonic (MC), generalised tonic (GT) and infantile spasms (IS) are difficult for the primary care physicians if not demonstrated. Similarly, a publicity campaign of seizures and epilepsy in general and the availability of treatment, may be helpful so that the demand for services can be identified. We therefore felt the need for a series of simple definitions and a modified classification. A classification system is required in order to facilitate understanding and to organize the observations. Such information needs to be well distributed, accepted and problem oriented at different levels. We also felt it would be useful to educate the population, through radio and television programmes and leaflets.

4.3.1: Definitions related to seizures and epilepsy

1. Epileptic seizures: These are defined as seizures which are manifestations of excessive, and/or hypersynchronous and usually self-limited abnormal discharges of neurons in the brain. Clinically epilepsies are diagnosed when a child has two or more unprovoked seizures (Brett & Neville 1997).

2. Convulsion: This definition, not necessarily different from that of epileptic seizures, was applicable in the context of less experienced physicians, to help them differentiate seizures with non-motor involvement. It describes involuntary, simultaneous, sustained contraction and relaxation of muscles, which may be non-CNS origin or may be the result of excessive and/or hypersynchronous neuronal activities in the brain (Aicardi 1994a; Brett & Neville 1997).

3. Active Epilepsy: Active epilepsy is diagnosed when there is a history of two or more epileptic seizures in the past one year (ILAE 1989; ILAE 1993a).
4. Febrile seizures: Generalised tonic-clonic seizures with associated fever, in which the infection is of non-CNS origin, occurring from the ages of 6 months to 7 years (ILAE 1993).

5. Atypical (complicated) febrile seizures: This was recorded when there is a history of febrile seizures with residual neurological signs after the seizure episode or partial seizures with associated fever.

6. Evolved epilepsy: We defined this in children who initially had recurrent febrile seizures followed by two or more episodes of non-febrile seizures.

7. Epilepsy as post CNS infection sequelae: A past history of CNS infection was recorded when there was hospital evidence of meningitis or meningoencephalitis, or a history of high fever followed by a prolonged seizure and unconsciousness lasting hours or days or repeated seizures without complete recovery of the previous functional state. Recurrent unprovoked seizures following CNS infection were recorded as post CNS infection sequelae.

8. Early seizure types: This was categorized in this study as ‘febrile’, ‘evolved epilepsy’, ‘post-CNS infection’, ‘and primary epilepsy’, taking the past history into consideration and the nature of early seizures.

9. Malignant epilepsy syndromes: Infantile spasms and West syndrome, Lennox Gastaut syndrome, very early onset myoclonic encephalopathy, and Landau Kleffner Syndrome were defined in this study as malignant epilepsy syndromes. Most of these syndromes have poor seizure remission and include neurodevelopmental consequences; they also have characteristic EEG patterns.

10. Age at onset of first seizure: To determine the age at the first unprovoked seizure we asked the family: “how long or up-to what age was the child well/without any complaint?” The next question focused on the seizure onset (Appendix II). Most of
the parents could recall the age of the first attack when the question was put in this way, rather than a direct question about seizure onset. We categorized age at onset as 'early' when there was a history of the first unprovoked repeated seizures at or before 12 months of age. Age at onset does not include the neonatal seizure history.

11. Type of seizures during each attack: Parents were asked to show from beginning of the arracks, and how the attacks ended. Thereby categorizing the seizures as generalised, partial, secondarily generalised, uncertain or unclassifiable.

12. Multiple seizure types: Epilepsy was categorized as with either 'single' or 'multiple seizure types'. A multiple seizure type was categorized when there was a history of more than one type of seizure (e.g., major attacks such as generalised tonic-clonic seizures, and other attacks, e.g., absences, myoclonic jerks, head drops or reflex attacks).

A single seizure type was identified by one type of seizure in the history.

13. Seizure frequency: This was defined as a frequency of episodic attacks up to the first presentation at the epilepsy clinic, and recorded as per day, per week, per month, or per year. One or more attacks per week were categorized as 'high-rate seizures'.

14. Seizure description: A complete seizure description was obtained by asking eight structured questions to the parents or family (Appendix II). The description includes “how the seizures start”, “any associated phenomena”, e.g., if there is an aura, vocalization, screaming, fear, sensory symptom or automatism or hallucination at the beginning of attack, “usual time of attacks”, “state of the child during attacks”, e.g., start in sleep, awake or both in sleep and awake, while playing or reading, “if any provoking factors”, e.g., noise, light, touch, sleep, physical exercise, reading etc., “duration of attacks” and the “recovery phase”.
15. **Family history of epilepsy:** This was recorded when there was history of epilepsy either diagnosed, or a history suggestive among first-degree relatives (siblings, parents, and first cousins).

16. **History of consanguinity:** A consanguineous marriage was recorded when there was history of marriage between first cousins.

17. **Parental perception:** To identify existing perceptions the parents were asked two direct and one indirect question: (1) where did they go for help when the child had first seizure attack; (2) their knowledge or idea about the problem (seizures, epilepsy or *mrigi rog*) and (3) what did they do during the child’s recent past illness (other than seizure) (Appendix II, Appendix IX).

18. **Seizure remission:** Although other authors have used varied criteria, to define this in their studies, I have defined this as follows: 100% seizure free for the last three months of 12 month’s follow-up period. Seizure frequencies over the previous 3 month period prior to the last follow-up appointment was used to assess the percentage of seizure remission. The highest rate of seizure occurrence during this last three months of the 12 months follow up period was taken as the present seizure status.

For analysis the frequency of seizures was calculated for the entire year and this was subtracted from the frequency (calculated again in years) at the time of entry of the child into the study and expressed as the **percentage seizure reduction.** This was taken as the seizure outcome of the child. Those children who had 100% reduction were categorized as having undergone 'seizure remission'. Those who had <100% reduction were categorized as having 'poor seizure remission'.

### 4.4: Classification of epilepsies and epilepsy syndromes

We followed the ILAE classification of seizures and epilepsy (ILAE 1989) using broader headings (Table 4.1). Epilepsy was classified in two steps with as much
precision as possible using information available at the time of assessment. In the first step, the patient’s epilepsy was classified according to a major syndromic group, e.g., localization related or primary generalised epilepsy, based on the history and clinical features. In the second step classification was done in a syndromic subgroup (aetiological classification) e.g., idiopathic/symptomatic/cryptogenic, based on combined seizure history, clinical presentation, EEG features and neuroimaging when possible.

**Generalised epilepsy:** This was recorded when the descriptions of seizure attacks were suggestive of involving both of the hemispheres from the beginning of an attack.

**Partial epilepsy:** This was diagnosed if the semiology was suggestive as partial in origin.

**Unclassifiable:** This was recorded when the description of seizure attacks were discrete focal, not definitely generalised or partial, when seizures were not easily describable or not convincingly identified as partial or generalised seizures, such as frequent startling provoked by sudden noise, and flickering of fingers or limbs provoked by sleep, discrete multifocal jerks.

**Etiological classification**

Using standard clinical and investigation criteria (ILAE 1989; ILAE 1993b) an epilepsy was classified as ‘symptomatic or cryptogenic’ if the child had a history of static encephalopathy from birth and/or stroke or significant head trauma with clear signs of a cerebral lesion or a sign of a neurological deficit on examination or if there was definite structural abnormality found in neuroimaging. An epilepsy was classified as ‘idiopathic’ if there was no such clinical or investigative evidence of a cerebral lesion. A ‘remote symptomatic’ type was identified, in those who had a definite history of perinatal asphyxia and/or neonatal seizures, CNS infection or head injury without any obvious clinical sign of cerebral lesions. A review of the classification
after 6 months' follow up enabled us to classify this group into either symptomatic or idiopathic group with the help of investigations.

Table- 4.1: Classification of seizures and epilepsies adapted from the ILAE classification

A1. Partial epilepsy with focal or localized epileptiform discharge in interictal EEG
   Simple partial seizures;
   Complex partial seizures;
   Benign rolandic seizures; or
   Benign childhood epilepsy with centro-temporal spikes;
   Benign childhood epilepsy with occipital paroxysm;
   Primary reading epilepsy;

A 2. Secondary generalised epilepsy,
   Simple or complex partial seizure with secondarily generalization
   EEG evidence of secondary generalization of a focal epileptiform discharge

B1.1. Idiopathic localization related epilepsy

B1.2. Symptomatic and cryptogenic localization related epilepsy

A.2. Generalised epilepsy: generalised or widespread epileptiform discharges in EEGs involving both the hemispheres.
   Myoclonic seizures;
   Akinetic seizures;
   Atonic seizures;
   Absence seizures;
   Generalised tonic-clonic seizures;
   Generalised tonic seizures;
   Generalised clonic seizures;
   Status epilepticus with overt generalised seizures;
   Nonconvulsive status epilepticus with supportive EEG findings;
B 2.1 Idiopathic generalised epilepsies;
B 2.2 Symptomatic and cryptogenic generalised epilepsy.

A.3 Unclassified epilepsy with mixed seizures, without unequivocal focal or generalised features
   Multifocal asymmetric spikes/sharp waves in EEG record.
   Multifocal and mixed types of seizures
   Neonatal seizures;
   Reflex seizures provoked by sound or touch.

B 3.1 Idiopathic
B 3.2 Symptomatic and cryptogenic

A.4 Severe epilepsy syndrome with characteristic EEG pattern abnormality
   Epileptic Infantile spasm/ West syndrome
   Lannox Gastaut syndrome
   Landau Kleffner syndrome
   Myoclonic epileptic encephalopathy
   Epilepsy with CSWSS in EEG sleep recording
4.5: Risk factors: pregnancy and birth related factors and past medical histories defined

We collected the following information to assess the pregnancy and birth related problems, in other words to identify the probably preventable causes of early onset epilepsies, and to get evidence about an aetiological classification of epilepsy.

The following information were recorded in this regard i.e., mother’s age during the related pregnancy, history of antenatal check up, history of any maternal medical problem, any medicine intake including indigenous abortificients during the pregnancy and previous obstetric history. Information about place and mode of delivery and who attended, delivery events recalled during birth to neonatal period (within one month of delivery), birth weight (where available) or whether the new-born size was usual, smaller or bigger compared with other new-born babies were recorded in the medical assessment forms (MAF).

4.5.1: History of perinatal asphyxia

A history of perinatal asphyxia was taken to be positive if there was hospital documentation of active resuscitation, and/or if there was a history of prolonged second stage of labour, and/or difficult labour, and/or a clear history of delayed establishment of spontaneous respiration in the newborn, and/or delayed cry (e.g. not within first 15 minutes), and/or change of skin colour to either bluish or white. This arbitrary definition was used following the study done in Nepal (Ellis et al. 1999). The concept of birth asphyxia is that the foetus is deprived of oxygen during the process of labour and that this hypoxia may have an irreversible and detrimental effect on function.

The definition used in the Swedish cerebral palsy study was that ‘perinatal asphyxia’ meant that respiration was not established after one minute and/or active resuscitation was needed (Hagberg & Hagberg 1984). Our definition was based upon the parents’ and the family members recall of events.
4.5.2: Any problems during the neonatal period and history of neonatal seizures

A history of neonatal seizures was obtained from the clear description of seizure attacks within 4 weeks of birth and/or from hospital discharge certificates produced by the family. The question put to the parents was ‘whether there had been any problem noted during first four weeks of the child’s life’. The next question was to clarify ‘what the problem was’. This included, poor feeding, excessive or very poor cry, frequent change in skin colour, stiffening and sudden repeated focal or generalised jerks with clear impression of un-wellness in the baby for which they needed to consult a physician, village doctor or a natural healer (religious person or kabiraj).

4.5.3: Previous obstetric history

History of abortion and/or threatened abortion, still-birth, intra-uterine death were recorded and categorized as ‘poor obstetric history’ if there was a history of any of these mentioned.

4.5.4: Preceding history of febrile seizures

If there was a history of recurrent seizures associated with high fever (Section 4.3.1, point 4) prior to the development of unprovoked seizures, it was taken as a 'positive history' of febrile seizures.

4.5.5: Family history of epilepsy

If there was a history of diagnosed epilepsy or unprovoked seizures in first-degree and second-degree relatives (parents, siblings, first cousins) it was considered as a 'positive family history'.
4.5.6: Previous history of CNS infection

A previous history of CNS infection was recorded as positive when there was a history suggestive of or there was a hospital evidence of such infection (Defined in section 4.3).

4.5.7: History of significant head injury

This was recorded positive, when there was a clear history of head injury or fall followed by bleeding through the nose or ear, unconsciousness or convulsion within 24 hours or a confused state after injury.

4.5.8: History of status epilepticus before entry

This was recorded when there was a history of prolonged seizures lasting for 30 minutes or more. An approximate time was calculated by the descriptions of activities of the parents when they were unable to state the duration of attacks.

4.5.9: Previous history of AED treatment

This was recorded when the child was on regular daily AED treatment for a minimum of 2 months outside the hospital. AED treatment for a short period, during any acute illness or during hospital admission was not included.

4.5.10: Time gap

This was recorded as the period in months between the onset of recognizable second attack of unprovoked seizures and starting the appropriate AED treatment.
4.5.11: Treatment gap

This was defined as the percentage of the population who were not getting appropriate treatment when it was clearly indicated (Section 2.9.1).

4.6: Non-convulsive disorders

Associated neurological disorders were defined as ‘non-convulsive disorders’, which include motor and sensory deficits leading to functional developmental delay, and cognitive impairment.

4.6.1: Motor disorder

Motor disorder was rated based on the child’s mobility (WHO severity grading- see Appendix XV) and coded as: ‘normal’ with no disability, ‘mild’ with some limitation of hand function and mobility but the child was independent in daily living activities, ‘moderate’ when the child had functional limitations, difficulty in holding implements and dressing, needed support to sit upright, but were able to move around with substantial help and ‘severe’ when the child was unable to walk and had no hand function.

Sensory deficit: This was rated as ‘present’ when the child had vision and/or hearing impairment associated with developmental motor delay.

Speech and communication regression: This was considered to be ‘present’ if the child had had a period of normal speech development followed by regression.

History of early milestones of motor, speech and cognitive development
History of early developments was recorded from the information provided by the parents about the child’s early development compared with their siblings or other children in the family or neighbours’ families.

4.6.2: Cognitive impairment and behavioural state on the day of diagnosis

Non-convulsive disorder also includes the child’s learning disability (delay or regression), which would be expressed by the parents as poor understanding, poor awareness about the surroundings, an inability to recognize parents or close relatives or not learning things as other children of the same age. School failure was not a common complaint of school aged children as the parents did not send them to school if they appeared to be delayed in learning things in the home.

4.7: Assessment of cognitive functions and behaviour

A formal psychological assessment was arranged for each child with the clinical psychologist using standardized psychological testing tools (see below). In addition, during the neurodevelopmental assessment (NDA), physicians assessed the child's behaviour, and cognitive level, level of understanding using the standard methodology appropriate for the age, i.e., ‘following simple commands’, ‘responding to call’, ‘following simple commands’, ‘drawing a man test’, ‘using building blocks’, ‘writing’, ‘solving simple mathematical problems’ and some tests of daily living.

4.7.1: Cognitive development on clinician’s judgment

Cognitive development was categorized as ‘impaired’ or ‘normal’ based on the clinician’s judgement. This was taken as the consensus diagnosis where IQ score was not available for the retrospective study (Chapter Five).
4.7.2: Cognitive development (Intellectual quotient or IQ)

Based on IQ test scores the cognitive development of each child was considered to be either 'impaired' or 'normal'. The Bayley Scales for Infant Development (Bayley 1993); Stanford-Binet Test (Huq 1996); Wechsler Intelligence Scales for Children, revised (Huq S.,1994; WISC-R, 1971); Independent Behaviour Assessment Scale (Munir, Zaman, & McConachie 1999): a test developed in Bangladesh for assessing adaptive behaviour of 2-9 year old children, were administered depending on the age of the child. The IQ score 70 was the cut off value, an IQ score of <70 was considered to be 'impaired'.

4.8: Assessment of child’s behaviour

4.8.1: Behaviour assessment by physician and the clinical child psychologist

A behavioural check-list, containing 5 questions for children under five years and 9 for over five years children was filled out by the physician (BSQ). In addition, there were questions in the MAF regarding the child’s behaviour from early infancy to the present date. Abnormal behaviour was recorded under the following categories: 'listless' when the child was apathetic or less responsive or extremely quiet; 'hyperactive or irritable child' was diagnosed when the child's activities fell into any of the following categories: crying often and easily, restless or overactive, constantly fidgeting, having with a short attention span, frequently changing moods, temper outbursts, explosive and unpredictable behaviour and distractibility or impulsiveness, all of which may characterise attention deficit disorder (APA, 1980).

Where some ambiguity of the child's behavioural pattern remained it was classified as 'uncertain' on the first visit assessment. This was later changed to a definite category during the subsequent visits by further assessing the child.
Behavioural assessment by the psychologist

Child behaviour problems were measured by the psychologist, using behavioural screening questionnaires appropriate for the age of the child.

BSID for 0-3 years
Richman's behavioural assessment questionnaire for 3 to 5 years (Richman, Graham, & Stevenson 1982).
Children's behavioural assessment questionnaire, Rutter, 1967; for 6 to 16 years old children (Rutter, Graham, & Yule 1970)
Conners' rating scales-revised for 6 to 16 years old children (Conners 1997b).

4.8.2: Adapted Richman’s behavioural assessment questionnaire for children aged 3 to 5 years (appendix: XI)

Child behaviour problem was measured using the version of Richman's behavioural assessment questionnaire for children aged 3 to 5 years (Richman, Graham, & Stevenson 1982) adapted for disabled children (Davis & Rushton 1991). The same questionnaire was used previously in BD in a study examining the effects of floods upon children (Durkin et al. 1993) and has been also used in diverse cultures (Richman, Graham, & Stevenson 1982). The total score range in this is 0-149.

4.8.3: Rutter scale of behavioural assessment for the middle age range children

Behaviour of children of middle age range was measured by the parental questionnaire, Rutter 1967, was designed to discriminate between different types of behavioural or emotional disorders. The questionnaire for parents was developed in parallel with similar questionnaire for teachers (Rutter 1967). The scale contains 26 brief statements concerning the child's behaviour, these are given a weight of 2 (certainly applied), 1 (applied somewhat, and 0 (does not apply). The scale differentiates neurotic (N) and antisocial (A.S) disorders. Children with a total score
of 9 or more are designated as showing some disorder. If ‘N’ score is greater than ‘AS’ score the children are designated neurotic, and if ‘AS’ is greater than ‘N’ the children are designated as antisocial. This scale had been used in BD for assessing the children’s behaviour for several years. This was also used in the RCT study in West Bengal to assess the behavioural side effect caused by AED (Pal et al. 1998d).

4.9: Introduction of Conners’ behavioural assessment questionnaire for mothers:

This is a useful test battery particularly in assessing behavioural problems in children from ages more than 5 to 16 years. This test has been applied in many of the studies to assess drug related behavioural disorders (Conners 1997).

The short version of the parental questionnaire (CPRS-R:S) for assessing the behavioural state of the child contains 27 questions. It takes not more than 15 minutes to complete.

Group A- questions are addressed to the oppositional character of the child (6 items)
Group B - the child’s cognitive or attention problem (6 items)
Group C- the child’s hyperactivity problem. (6 items)
Group D- the child’s ADHD index (12 items).

Total scores of each group are then plotted into the appropriate graph for the child’s age and sex to obtain the T-score and percentile. A T-score of more than 60 was considered as being a concern, and a score over 80 revealed a definite problem. The T-score before and after 12 months of treatment with either of the AEDs were compared in the RCT study population (Chapter Seven).
4.9.1: Reliability test and validity measure of Conners' short questionnaire for parents (CPRS-R:S)

This questionnaire was translated from English into Bangladesh by the epilepsy research team-members. We involved mothers to get the feedback from them about common understanding of the words used. The translated form was back-translated and revised before arriving at the final version. {The translated questionnaire was discussed within the team members first regarding the appropriate use of Bangla phrases for the English, and whether the question has the same meaning in Bangladesh. Changes were made where discrepancies were noted and then used among the parents of children without any impairment; their comments were taken into consideration.}

This modified questionnaire was administered among 20 mothers twice, at an interval of two weeks, for a reliability measure before using it on the children of the RCT group (Chapter Seven).

Table 4.2: Showing mean difference between the scores obtained on test 1 and test 2

<table>
<thead>
<tr>
<th></th>
<th>Mean diff. of T score.</th>
<th>St. Dev</th>
<th>St err. Mean( CI )</th>
<th>T</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>A- index</td>
<td>- .55</td>
<td>5.43</td>
<td>1.21(-3.09 to 1.99)</td>
<td>- .453</td>
<td>.656</td>
</tr>
<tr>
<td>B- index</td>
<td>-2.40</td>
<td>7.00</td>
<td>1.57(-5.68 to .88)</td>
<td>-1.533</td>
<td>.142</td>
</tr>
<tr>
<td>C- index</td>
<td>-.90</td>
<td>5.75</td>
<td>1.29(-3.59 to 1.79)</td>
<td>-.700</td>
<td>.492</td>
</tr>
<tr>
<td>D- index</td>
<td>-.95</td>
<td>3.63</td>
<td>.81(-2.65 to .75)</td>
<td>-1.169</td>
<td>.257</td>
</tr>
</tbody>
</table>

Test-retest reliability on 20 participants:

$T^2$ for time one and time two for each index revealed no significant difference suggesting ‘adequate test retest reliability’. It also shows the stability of parental responses over the two weeks period.
4.9.2: Concurrent validity measure

The Rutter test (Section 4.8.3) is a translated and validated questionnaire in the region. We used this as gold standard and administered it in 30 children with epilepsy. The Conners' questionnaires were administered in the same 30 children on a separate day. The total score obtained by administrating the Rutter scale and the score of the Conners' D- ADHD index were correlated by Pearson correlation co-efficient analysis. A very satisfactory correlation was found between the results obtained from the two tests administered to 30 participants. The Pearson correlation co-efficient test had a high positive correlation of .74, with 2-tailed significance, at < 0.01 level. The Pearson co-efficient was .46 with 2-tailed significance at <0.01 level with the sub-score of neurotic items and .59 with the same significance with the antisocial item sub-scores. We conclude from the above analysis that the concurrent validity measure of the tool recently translated into Bangla for the behavioural assessment has good correlation with the gold standard.

4.10: Investigations

4.10.1: Electroencephalograms (EEG) recording and findings

For the prospective study, at the initial consultation, each patient’s parents gave informed consent for the EEG study. EEG recordings were done promptly in this (prospective) group for two reasons: 1) to record the brain activities before starting treatment or within a short time after experiencing a recent seizure and 2) logistical reasons relating to distance of the family residence and the cost of travel (Section 3.2). The idea of doing the EEG within a short time of an attack is supported by one prospective study with 300 children and adult patients in Melbourne. Mark et al. assessed the diagnostic usefulness of early EEG, sleep-deprived EEG. They found a higher proportion of positive epileptiform discharges in the EEGs done early compared to those done later, (51% vs 34%) (Mark et al. 1996).
We used 16-channel analogue or 24-channel digital recordings with bipolar, longitudinal, transverse, average referential montages for both. Recording lasted for a minimum of 30 minutes, including eyes opened and closed, with intermittent photic stimulation recording for all children, and hyperventilation recording for 3 minutes in cooperative patients. An attempt was made to take both awake and sleep recordings for all the children. Sleep-deprived recordings were taken when suggested by the attending physician. For sleep-deprived tests, parents were advised to prepare the child for 3 days before the recording. This involved depriving the child of sleep for 3-4 hours daily for 3 days and waking them very early in the morning on the day of the test. The recording lasted for 40 minutes, or longer if needed. The electrodes were placed on the scalp according to the international 10-20 system of electrode placement.

4.10.2: EEG results were categorized as

(1) Normal; (2) abnormal with focal or generalised epileptiform discharges; (3) abnormal with non-epileptiform, background abnormality; (4) abnormal with both i.e., epileptiform discharges with abnormal background activities. The abnormal EEGs were re-categorized as with 'characteristic EEG pattern of dysfunction'.

Abnormalities of background activity: These are age dependant and non-epileptiform abnormal activities. They were again categorized according to the following types:

1. *Excessive slow waves (Delta waves):* paroxysmal, generalised, diffuse or focal dysrhythmic activity (delta waves, <4 c/s during fully awake state), which are slower than the expected background frequencies for the patient's age and state.

2. *Excessive beta wave activity:* more than 14 c/s activity (Beta wave) when more than expected amount of beta waves were present during the awake state.


4. *Asymmetry in background activity* or in response to external stimuli.
Epileptiform discharges: The presence of repeated spike wave discharges, either
generalised or focal is the specific feature of epileptiform discharges. These were
categorized as being either ‘present’ or ‘absent’. Positive results were categorized as
‘focal’ or ‘generalised’ according to their distribution in the recording.

Epileptiform discharges with abnormal background activity: These included focal
or generalised epileptiform discharges against an abnormal background in the EEG
tracing with a poverty of normal activity or reactivity to external stimuli. EEG traces were again examined for the presence or absence of the recognizable
abnormal patterns, which were categorized as:

1. ‘burst suppression pattern’;
2. ‘hypsarrhythmic pattern’;
3. ‘periodic complexes’;
4. ‘continuous spike wave complexes of sleep’;
5. characteristic pattern for ‘Lennox Gastaut Syndrome’.

4.10.3: Other investigations

Neuroimagings such as ultrasonogram, CT scan or MRI of the brain were arranged
when needed and when it was feasible (on the basis of clinical indication). Blood tests to ascertain the AED level were arranged for the RCT group and for others
when there was no response to drug therapy, despite prescribing a maximum dose.

Therapeutic level for phenobarbitone and carbamazepine: According to the WHO
recommendation the effective blood level for PB and CBZ are 15-20 micrograms /ml
and 4-10 mgm /litre respectively (Gastaut & Osontokun 1976).
4.11: Development of medical assessment form and training of the team workers

4.11.1: History record and medical assessment form (MAF) (Appendix-II)

A semi-structured questionnaire was developed based on the structure which had been used at the second stage for the epidemiological study on developmental disorders including epilepsy in children of 2-9 years of age in Bangladesh (Khan & Durkin 1995b),

The form had been constructed in 6 major parts:

Part 1. Child and family information

I. The child’s information: age, sex, date of birth, residence, parents’ chief complaints and duration of each.

II. Specific questions on seizure attacks to determine the age at onset of seizures; seizure type (partial, secondary generalised or primary generalised), seizure frequency, duration of each attacks, how that first started, if there was any evolution of seizure types, behaviour and schooling if of school age; past history regarding seizures; history of recurrent febrile seizures; any status epilepticus; and evidence of CNS infection.

III. Family history of similar diseases or other chronic illnesses or epilepsy.

IV. Information related to the pregnancy and previous obstetric histories of the mother, birth history and related problems and history during the neonatal period.

V. Developmental history during early infancy

VI. Past medical history particularly any history of hospital admission and reasons for taking medication or hospitalisation.

VII. Questions relating to any seizure attacks with associated fever or following a head injury; and history of taking AEDs or any other drugs daily over a long period. (3 months and longer).

VIII. Questions relating to parental attitudes and their understanding of seizures.
Part 2: Neurodevelopmental examination

I. Observation;

II. General examination including anthropometric examination;

III. Neurodevelopmental assessment: Gross motor, fine motor, vision, hearing, speech, and communation;

IV. Conclusion of the assessment

Part 3: Management form (Appendix III)

The epilepsy management included the following:

I. RCT criteria assessment;

II. Informed consent for participating in the study obtained from parents;

III. Parental counselling;

IV. Medical management with AEDs;

V. Developmental therapy, visual, hearing and speech stimulation for an already developed or impending disability;

VI. Parental education and counselling for patients with febrile seizures, advice on investigation;

VII. Advice on formal psychological and behavioural assessments;

Part 4: Follow up forms: A semi-structured form (Appendix-IV) was used for the first and then unstructured forms were used for the subsequent follow-ups.

Part 5: Summary form: This form was developed to compile a summary of the history and examination findings and the investigation results.

Part 6: Final follow-up forms: This was a structured form developed to compile the seizure and non-convulsive disorder related information and parents' perceptions (Appendix-VI). Information of the complaints on the final day and from the previous three months, information regarding attendance at the clinic; compliance; initial seizure(s) criteria, any evolution of seizure type(s); AEDs used, any change in the prescription and the reason; effects of prednisolone when used; parental perceptions of
their child's seizure and developmental condition at the beginning and at last follow-up, and the final comment of the physician etc. were collected in this form.

4.11.2: Socioeconomic status (SES) recording form (Appendix IX)

This was developed and used for the epidemiological study of childhood disability (Z. Sultana and Z Khan et al 1989) (Appendix IX) which includes information regarding the following:

- Family and residence
- Parental education
- Occupation
- Parent's awareness about, seizures and epilepsy
- Housing, water supply, toilet and sanitary conditions, family members in the house, and family possession of electronic equipment, animals, boats, land and rikshawa
- Family income
- Expenditure.

Definition of some points on the SES form

**Parental education:** Categorized as 'none', 'primary school', 'high school' or 'more than high school'.

Housing-condition categorized as:
1. kancha if the roof was made of hay and floor with mud;
2. semipacca if the roof was made of tin or brick, with tin walls and brick floor;
3. pacca if the roof, walls and floor were made of brick.

**Residences:** recorded as:
- 'urban' if regular automobile transportation, hospitals and emergency medicines were available nearby;
- 'rural' including suburban regions defined if these facilities were not available in the area.
Socio economic status was categorized according to the monthly family income. The family considered to have a 'very low income' when the monthly income was less than Taka 3000 (1 US Dollar = Taka 60), 'low income' when the income was between Taka 3000 and 5000, 'middle income' when it was above Taka 5000 to 10,000, and 'higher income' when it was more than Taka 10,000. Although the GNP per capita income of Bangladesh is USD 370, 1 US Dollar = 65 Taka; (UNICEF, 2001), a lower cut-off for income groups was considered as more than 24% of the Bangladeshi population earn less than 40% of the GNP.

Consanguinity was recorded to be positive when there was marriage between first-degree relatives, such as first cousins, and uncle-niece. Histories of marriage between second and third degree relatives were also recorded.

Parental perception about the seizure and epilepsy has been explored through the following questions (1) what do the family think of the seizure (Khich, or Khichuni or Jhatka) attacks; (2) what did family members or parents do, or where they went to get help the first time the child experienced these attacks and (3) where did they take their child for any other health problems?

4.11.3: Other data entry forms including psychological assessment form, EEG data entry form (Appendix XIII)

Simple leaflets for the family: two pages of A4 sized leaflets containing picture and information notes on seizures and epilepsy and how EEG is performed was prepared by the team in very simple Bangla. The information note was printed in two basic colours to make it attractive but cost-effective. This was done in collaboration with the EEG centre, and distributed to every parent and other family members. A hand made seizure record keeping diary was distributed with simple instructions to put a mark in case of large or small attacks. We advised them to bring the diary each time they came to the clinic (Appendix XVI).
4.12: Training of the PCP

A short training course for the primary health care physician (two weeks):
The primary care physician (PCP) holds MBBS and has been trained in general paediatric problems at the Bangladesh Institute of Child Health, Dhaka Shishu Hospital. A systematic course of training on child development and epileptology was conducted for the PCP at the Child Development and Neurology Unit by the researcher, involving other child neurologists, and developmental paediatricians.
The course curriculum for the primary care physician was as follows:

4.12.1: Practical training

Observation of the team activities at the CDC comprising of:
1. Attending the developmental assessment clinic, history taking; functional observation of the children; developmental assessment of motor, vision, hearing, speech, and communication skills; undertaking neurological examinations and taking part in discussions regarding the diagnosis and management plane for the children with multiple, severe disabilities.
2. Attending the psychological assessment session.
3. Attending the epilepsy clinic, developmental therapy and stimulation clinics.

4.12.2: Theoretical

Tutorials were arranged for the trainees:
1. Basic neurology highlighting its developmental aspects, and motor, visual, and hearing development for normal and deviated forms
2. Cerebral palsy;
3. Epilepsy (using the structured format)

3.1. Theory and clinical training:

a. seizure, epilepsy and epilepsy syndrome definitions;
b. classifications of seizures, epilepsy and epilepsy syndrome;
c. seizure semiology and clinical characteristics of commonly presented epilepsy and syndromes in children;
d. pathophysiology of epilepsy;
e. febrile seizures, and management;
f. central nervous system infection in children and its consequences;
g. basic principles of EEG and correlation with seizure semiology;
h. prognosis of childhood epilepsy.

3.2. Management:

a. basic principals of pharmacokinetics and pharmacodynamics of antiepileptic drugs;
b. diagnosis of seizures and epilepsy. Rational of choosing AED, and investigation for a child with epilepsy;
c. commonly available AEDs and their specific use in different types of epilepsy;
d. principals of drug prescription, importance of monotherapy, adverse effects of polytherapy, adequate dosages, and monitoring drug compliance;
e. monitoring the seizure rate, and the seizure diary;
f. management of acute seizure attacks in the community and in the hospital;
g. management of status epilepticus;
h. long term management, developmental therapy, and stimulation;
i. community empowerment by educating the parents and community, and re-enforcement for long term regular maintenance therapy; and
j. educating health workers
4.13: Training of the paediatric neurophysiologists

Two neurophysiologists had been trained first by the researcher, and then they were sent to the EEG department at Great Ormond Street Hospital for Children.

4.14: Training of the developmental therapist (DT)

Two developmental therapists were trained at the CDC for the prospective study. The same persons had been trained to complete the SES form and SRQ forms.

4.15: Record maintenance

The medical records were kept at the OPD and all of the team members were well motivated in maintaining them. The psychological assessment records and files were maintained at a separate location on the third floor. Medicines were stored and distributed on the third floor by another hospital staff who did not have direct knowledge of the study.

4.16: Patient recruitment site selection: description of the hospital in and outpatient departments. Rational for using a hospital site, particularly DSH

Dhaka Shishu Hospital (DSH)
The Bangladesh Institute of Child Health, Dhaka *Shishu* (Children's) Hospital, is a 350 bed national children's hospital, with an outpatient attendance of over 100,000 per year, mainly comprising of lower income families.

1. The *Shishu Bikash Kendro* (SBK), *Bangla* for Child Development Centre (CDC) is the out-patient wing of the Child Development and Neurology Unit of the hospital (Specialist OPD). The CDC was established in 1992 as the country’s first centre to provide a comprehensive service for children with neuro-developmental impairments and disabilities. The core team includes child health physicians, psychologists and developmental therapists. There is a weekly epilepsy clinic. Systematic record-keeping of histories, assessments, diagnosis and regular follow-ups involving a multidisciplinary team of professionals, is a key component of the work of this centre.

2. A non-specialist, general OPD was started in collaboration with a community service centre at the hospital premises. This community service was established in 1995 at the hospital entrance with the aim of providing a quick service to the nearby ‘slum’ population. We selected the site for enrolment of children with epilepsy and associated developmental disorders as a part of the community service. The primary physicians were responsible for treating the children and their mothers and other siblings for general health problems and seizure disorders.

**Logic behind this site selection**

a) Dhaka *Shishu* Hospital is the national hospital for children the vast majority of the patients come from the general population. Patients are self-referred or referred by physicians from primary care centres and from private practicing physicians.

b) CDC and its service is now well publicised among the professionals as well as community people. This happened through other parents and through radio, television programmes on child development and epilepsy.
c) We aimed at involving all seizure and epilepsy types, voluntary participation of the parents and the families and both doctor and self-referrals to the outpatient clinic were readily accepted.

d) There was very little provision within the community for investigation (EEG, & neuroimaging) and treatment of disadvantaged children with recurrent seizures.

e) We wanted to develop a practical problem-oriented treatment protocol based on the childhood epilepsy profile in this region. However, while accepting that this would not be a population-based study, we chose the national children's hospital as a development site for this, considering the availability of definite cases in a defined period of time.
Data-base creation and training of a data entry assistant:

1. patients’ information and clinical complaints on the first visit;
2. seizure information and past histories;
3. history of pregnancy and birth;
4. family history of any chronic illness and epilepsy;
5. history of initial developmental of the children including gross motor, fine motor, visual, hearing, speech and communication and cognitive skills;
6. general examinations;
7. neurodevelopmental examination findings;
8. summary of the previous information;
9. management files;
10. follow-up files;
11. psychological assessment files;
12. behavioural assessment file;
13. Conners assessment file;
14. Conners assessment pioneer study file
15. maternal stress assessment file;
16. investigation files; and
17. SES files.

About 700 variables were entered for 423 children’s and their family histories.
The data entry assistant was trained on the terms and questionnaire as the person was new to the medical terms, especially in the field of epilepsy and child development.
CHAPTER FIVE

5: The retrospective study

5.1: Introduction and background

Forty five percent of 130 million population in Bangladesh are under 18 years of age (UNICEF 2001) and epilepsy prevalence in this age group is also high in this region (Durkin, Leislie, Devidson, Hasan, Hasan, Khan, & Shrout 1992). The prevalence of childhood disabilities was about seven percent among the children aged 2-9 years (Durkin, Leislie, Devidson, Hasan, Hasan, Khan, & Shrout 1992; Khan & Durkin 1995). However, detailed information about childhood epilepsy is not available in this region. We aimed at compiling base-line information on epilepsy and associated disabilities of children below 15 years of age attending the national children’s hospital in Bangladesh. For this stage of the study, patients were identified from the first 1000 children who were sent for electroencephalography (EEG) at the first EEG service centre available for children in the country. The information was used in planning the prospective study. This chapter will present the methods, materials and results of the retrospective study.

5.2: Objectives of the study

The objectives of this study were to ascertain comprehensive baseline information regarding socio-demographic profiles, associated clinical factors, clinical presentation, epilepsy and EEG status of children with seizure disorders and to evaluate the best predictors of ‘seizure remission’ for planning an optimum service for children with epilepsy in Bangladesh.
5.2.1: Aims of the study

1. To ascertain the profile of childhood epilepsies (descriptive analysis of seizure disorder, i.e., onset, types, rate and severity, and their association with sociocultural factors, pregnancy and birth related factors, associated disabilities in a tertiary care setting in Bangladesh).

2. To identify the factors, which appear to be possible predictors of seizure remission.

5.3: METHODS AND MATERIALS

5.3.1: Study site

The study was conducted within the Shishu Bikash Kendro (SBK, Bangla for Child Development Centre) of the Dhaka Shishu (Children's) Hospital, which was attended primarily by the patients referred by the professionals from the same or other hospitals of the country (Section 4.16, point 1).

5.3.2: Study design

This was a retrospective study of children who were referred to an EEG service from the CDC, who had presented to the hospital with a seizure disorder and had been comprehensively assessed by a professional team of child neurologists and clinical child psychologists. Potential predictors of seizure outcomes were identified from clinical records, psychological assessments, EEG reports and other investigations, i.e., ultrasonograms (USG), CT scans or MRI of brain when available.
5.3.3: Study population

The initial patient selection was taken from the newly established EEG service centre (Section 3.8). The enrolment criteria for this study are listed below:

**Enrolment criteria:**

*a.* Children who had presented to the CDC, Dhaka Shishu Hospital with two or more seizures, and were being suspected of having epilepsy on clinical assessment;

*b.* Children who had been followed up regularly for at least one year in the Epilepsy Clinic of the CDC;

*c.* Children whose EEGs had been reported by trained paediatric neurophysiologists.

**Exclusion criteria:**

No active epilepsy

Follow-up period less than one year.

5.3.4: Follow-up period

**Children whose EEG had been done between May 1996 to October 1997.**

<table>
<thead>
<tr>
<th>Total period of follow up at the epilepsy clinic</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 months</td>
<td>8</td>
<td>5.3</td>
</tr>
<tr>
<td>13 months to 24 months</td>
<td>43</td>
<td>28.5</td>
</tr>
<tr>
<td>25 months to 36 months</td>
<td>34</td>
<td>22.5</td>
</tr>
<tr>
<td>37 months to 48 months</td>
<td>29</td>
<td>19.2</td>
</tr>
<tr>
<td>49 months and above</td>
<td>37</td>
<td>24.5</td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
<td>100.0</td>
</tr>
</tbody>
</table>

The mean and median period of follow-ups were 36.01 months and 32.83 months respectively
5.3.5: Assessment format

A review of the baseline clinical information, formal psychological assessment report, EEG reports, other investigations and follow-up records was carried out. If the information was insufficient, a further follow up review was undertaken by recalling the parents and child through either postal messages, telephone calls or home visits. Pre-coded form was filled out by the researcher for each child based on information collected (Appendix I). In this section a description of methods used for collection of information and for categorizing each variable is provided.

5.3.6: Socio-demographic information (Appendix IX)

This had been collected by a social worker of the CDC, which included information regarding the child's residence, family income, parental education, and consanguinity.

Socio-economic status: defined in Section 4.11.2
Residence of the child: this was recorded as being either urban or rural.
Consanguinity: defined in section 4.11.2.
Family history: defined in section 4.11.2.
Parental education: this was categorized as 'none', 'primary school', 'high school' or 'more than high school'.

5.3.7: Child Factors

Date of birth, sex of the child was recorded, and for the study purpose the age at which the EEG was done was taken to be the baseline age of the child.

History related to birth and the neonatal period:
History of perinatal asphyxia: (See Section 4.5.1)

History of neonatal seizures: (See section 4.5.2)

The history of neonatal seizures was obtained from the clear description of seizure attacks within 4 weeks of birth and/or from hospital discharge certificates produced by the family. (Section 4.5.2)

5.3.8: Variables used for seizure descriptions

This section describes the clinical interpretation and classification of seizures and its various aspects with working definitions, adapted for the analysis of the study.

Epilepsy definition and classification: see Section 4.3.
Malignant epilepsy syndromes: see Section 4.3, point 9.

Age at onset of seizures
The age at onset was recorded as the age when the first unprovoked seizures were reported by parents. It was recorded as a continuous variable in months. Neonatal seizures were not included in this variable.

Frequency of seizures at entry
Frequency of seizures were recorded as the number of attacks per day, per week or per month and/or per year at first presentation and considered as one continuous variable.

High rate of seizure attacks
One or more attack per week was defined as a 'high rate' of seizure in the child in contrast to those with lesser numbers of attacks, which was considered to be 'low rate'. Total seizure attacks were calculated as the number of seizures in a year.
Number of seizure types (Section 4.3.1, point 12)
If there was a history of more than one type of seizure during the first presentation or in the previous history (e.g. major attacks such as generalised tonic-clonic seizures interspersed with attacks of absences, head drops or reflex attacks) it was considered to be 'multiple' seizure types.

Preceding history of febrile seizures
If there was a history of recurrent seizures associated with febrile episodes prior to the development of unprovoked seizures, it was taken to be a 'positive history' of febrile seizures.

Family history of epilepsy
If there was a history of unprovoked seizures in first-degree and second-degree relatives (parents, siblings, or first cousins) it was considered to be a 'positive family history'.

5.3.9: Neurodevelopmental assessments (NDA)
NDAs were carried out by specialist child neurologists and developmental paediatricians working at the CDC. Follow-ups of each child also were done by the same team of medical professionals.

Diagnosis of neurodevelopmental impairments
The neurodevelopmental impairment was defined as 'non-convulsive disorders' that include motor and cognitive deficits found in the child. They were classified into the following categories:

Motor disorders
Motor disorders were rated as 'major motor disorders' when the child was dependent on the family members for his/her daily living activities, and 'minor motor disorders'
when there were abnormal neurological signs or weaknesses but the child was functioning independently.

**Cognitive impairments**

Cognitive impairments include the child's learning disability (delay or regression), which were categorized as 'normal' or 'impaired'.

**5.3.10: Assessment of cognitive functions and behaviour**

The cognitive development and behaviour of most children had been assessed by the psychologists using standardized psychological testing. Where such records were unavailable, the cognitive and behavioural state at first presentation was determined based upon the physician's NDA records. During the NDA physicians assess the child's behaviour and cognitive levels, levels of understanding using standard methods appropriate for the age (Section 4.7).

**Cognitive development (Intellectual quotient or IQ)**

This was based upon IQ test scores and/or the clinician's judgement and categorized as either 'impaired' or 'normal'. The IQ test and behavioural assessment tools are described in section 4.7. An IQ of <70 was considered to be 'impaired'.

**Behaviour**

Abnormal behaviour was recorded using the following categories: 'listless' when the child was apathetic, less responsive or extremely quiet; and 'hyperactive' or 'irritable child' when the child's activities fell into any of the following categories: crying often and easily, restless or overactive, constantly fidgeting, a short attention span, frequently changing moods, temper outbursts, explosive and unpredictable behaviour, distractibility or impulsivity (APA 1980). Where some ambiguity of the child's behavioural pattern remained it was classified as 'uncertain'.

5.3.11. Investigations

EEG

EEG was conducted on each child with a 16-channel paper and ink machine. Electrodes were placed according to the 10-20 international electrode placement system. Records were obtained while awake and asleep in most of the children. Sleep deprived recordings were obtained in cases when requested by the clinicians. The EEG data were assessed and reported by the specialist trained clinical child neurophysiologists.

EEG reports  Categorization explained in Section 4.10.2.

Other investigations

Information from brain ultrasonograms (USG), MRIs, CT Scans and other investigations were recorded where available.

5.3.12: Holistic management

At the CDC a multidisciplinary team approach is used to provide a holistic intervention programme for children with epilepsy. Apart from specific AED the caregivers, (usually parents) are also given advice on general cognitive stimulation and specific developmental therapy when necessary. The developmental therapy may include aspects from physiotherapy, occupational therapy and speech and language therapy against a developmental background and a management plan made for each child. This approach has been demonstrated to be beneficial to the overall well being and functional development of the child (Jahan 1996).

Previous history of AED treatment
The history of previous long-term drug intake for epilepsy (defined as regular/daily AED treatment for more than 3 months) before attending the epilepsy clinic was recorded to establish the treatment gap.

5.3.13: Follow-up information of the child and outcome measures

In this section the current status of various aspects of the child’s problems were reviewed from the follow-up medical and psychological records. The following aspects were recorded as measures of seizure outcome.

Outcome measure

Outcome was examined in two ways:
1. ‘Seizure remissions’ for which psychomotor developmental disability and or other seizure related factors are used as predictors.
2. A description of the phenotype of children with epilepsy, which included cognitive, behavioural and motor disabilities.

The following criteria were taken into consideration in measuring epilepsy outcomes:

Seizure remission

Seizure frequencies over the 3-month period before the last follow-up was taken from the medical records and the highest rate of seizure occurrence during this period of time was taken as the present seizure status.

Percentage of seizure reduction

The ‘percentage of seizure reduction’ was calculated by subtracting the rate of seizures during the last 3 months’ follow-up, from the rate of seizures recorded on the first visit to the epilepsy clinic.
Those children who had 100% reduction were categorized as having achieved 'seizure remission'. Those who had <100% reduction were categorized as having 'poor seizure remission'.

**Behaviour state on last visit**

Behaviour state on the final assessment day was recorded as either behaviour problems 'present' or 'absent' based on criteria described earlier.

**Motor disability on last visit**

Motor disabilities on last visit were recorded as 'present' or 'absent' on the last recorded visit and was based upon criteria described earlier.

**5.3.14: Potential predictors of seizure outcome**

The following seven clinical factors and one investigative factor were taken as independent variables (potential predictors of seizure outcome):

1. Age at onset of seizures: 'early onset’
2. 'Multiple seizure’ type
3. ‘High rate’ of seizures
4. 'Malignant' epilepsy syndromes
5. 'Positive family history’ of epilepsy
6. Associated ‘motor disability’
7. Associated cognitive impairment: ‘low IQ’
8. ‘Abnormal EEG’.

The EEG features were categorized as follows and were associated independently with seizure outcome:

1. Normal record
2. Abnormal record with only epileptiform discharges
3. Abnormal record with only non-epileptiform abnormality (abnormal activities in the background) and
4. Abnormal record with both epileptiform discharges and non-epileptiform abnormality.

5.3.14: Data Analysis

All information was entered into a pre-coded form (Appendix I). SPSS version 10.0 was used to analyse the data. Analysis of predictors of seizure outcomes was conducted. 'Poor seizure remission' was considered as the dependent variable.

Univariate analysis was done with each potential predictor. Odds ratios, confidence intervals and *p* values were calculated to show the magnitude of association between each factor and epilepsy outcome.

Multiple logistic regression was subsequently done using a stepwise backward logistic regression model. A variable was eliminated if the level of significance was more than 0.05.

The equation of the logistic regression model is as follows:

Probability (event) = 1/1+ e ^{-Z}.

When 

\[ Z = B_{0} + B_{1} \text{(MST)} + B_{2} \text{(HRTSZ)} + B_{3} \text{(MDIS)} + B_{4} \text{(LIQ)} + B_{5} \text{(SPSD)} + B_{6} \text{(FHOE)} + B_{7} \text{(AAONS)} + B_{8} \text{(ABNEEG)}. \]
5.4: RESULTS

5.4.1: Description of the study population

Age, sex and socio-demographic profile of the children (Table 5.1)

Median age at presentation was 3 years (range 3 months to 16 years). Only about 10% were less than 12 months of age. Most parents knew their child’s date of birth except for 11, whose ages were obtained to the nearest year. The male: female ratio was 1.8:1.

Residence
The majority of families, 65.6%, were from urban areas, and 34.4% were from rural areas. Of the total population, 70% were from the Dhaka division of BD (Fig 3.1 Map of BD showing six divisions).

Socio-economic status by family income (Section 4.11.2)
The majority of children came from ‘middle income’ and ‘higher income’ families; 31.1% were from the ‘lower-income’ group when ‘poor’ and ‘very poor income’ families were combined, 37.1% were from middle-income group and 31.8% from the higher-income group.

Consanguinity
Marriage between first-degree relative was recorded in 7.9% of parents. All were first cousins.

Parental education
Illiteracy was recorded in 9.9% mothers and 2.7% fathers, highlighting the disparity in basic education of mothers versus fathers, with the ratio of college education being 1.8 times higher in fathers.
Table 5.1: Demography of the study population.

<table>
<thead>
<tr>
<th>Items</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-12 mo</td>
<td>15</td>
<td>9.9</td>
</tr>
<tr>
<td>13 mo-3 yr</td>
<td>48</td>
<td>31.8</td>
</tr>
<tr>
<td>&gt;3yr-5 yr</td>
<td>39</td>
<td>25.8</td>
</tr>
<tr>
<td>&gt;5 yr-7 yr</td>
<td>24</td>
<td>15.9</td>
</tr>
<tr>
<td>&gt;7 years</td>
<td>25</td>
<td>16.6</td>
</tr>
<tr>
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<td>151</td>
<td>100.0</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>98</td>
<td>64.9</td>
</tr>
<tr>
<td>Female</td>
<td>53</td>
<td>35.1</td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
<td>100.0</td>
</tr>
<tr>
<td><strong>Residence</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban</td>
<td>99</td>
<td>65.6</td>
</tr>
<tr>
<td>Rural</td>
<td>52</td>
<td>34.4</td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
<td>100.0</td>
</tr>
<tr>
<td><strong>Socioeconomic status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very low income</td>
<td>25</td>
<td>16.6</td>
</tr>
<tr>
<td>Low income</td>
<td>22</td>
<td>14.6</td>
</tr>
<tr>
<td>Middle income</td>
<td>56</td>
<td>37.1</td>
</tr>
<tr>
<td>Higher income</td>
<td>48</td>
<td>31.8</td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
<td>100.0</td>
</tr>
<tr>
<td><strong>Consanguinity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>139</td>
<td>92.1</td>
</tr>
<tr>
<td>Present</td>
<td>12</td>
<td>7.9</td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
<td>100.0</td>
</tr>
<tr>
<td><strong>Maternal education</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>15</td>
<td>9.9</td>
</tr>
<tr>
<td>Primary level</td>
<td>36</td>
<td>23.8</td>
</tr>
<tr>
<td>SSC level</td>
<td>42</td>
<td>27.8</td>
</tr>
<tr>
<td>Above SSC</td>
<td>58</td>
<td>38.5</td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
<td>100.0</td>
</tr>
<tr>
<td><strong>Paternal education</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>4</td>
<td>2.7</td>
</tr>
<tr>
<td>Primary level</td>
<td>16</td>
<td>10.6</td>
</tr>
<tr>
<td>SSC level</td>
<td>29</td>
<td>19.2</td>
</tr>
<tr>
<td>Above SSC</td>
<td>102</td>
<td>67.5</td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Mo, month; yr, year, SSC, secondary school certificate.
5.4.2: Birth and past clinical history (table 5.2)

Birth history

Table 5.2 presents information on gestational age, history of perinatal asphyxia, and history relating to seizures in the child and the family. A history of (H/O) preterm delivery was found in 10 children (6.6%). A large proportion of the children, (46.4%), had a history of perinatal asphyxia.

Table 5.2: Clinical history of study population and family.

<table>
<thead>
<tr>
<th>Items</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>H/O preterm birth</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>141</td>
<td>93.4</td>
</tr>
<tr>
<td>Present</td>
<td>10</td>
<td>6.6</td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
<td>100.0</td>
</tr>
<tr>
<td><strong>H/O perinatal asphyxia</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>81</td>
<td>53.6</td>
</tr>
<tr>
<td>Present</td>
<td>70</td>
<td>46.4</td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
<td>100.0</td>
</tr>
<tr>
<td><strong>H/O Neonatal seizure</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>89</td>
<td>58.9</td>
</tr>
<tr>
<td>Present</td>
<td>62</td>
<td>41.1</td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
<td>100.0</td>
</tr>
<tr>
<td><strong>Family H/O epilepsy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>138</td>
<td>91.4</td>
</tr>
<tr>
<td>Present</td>
<td>13</td>
<td>8.6</td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
<td>100.0</td>
</tr>
<tr>
<td><strong>Family H/O febrile seizure</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>135</td>
<td>90.1</td>
</tr>
<tr>
<td>Present</td>
<td>15</td>
<td>9.9</td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
<td>100.0</td>
</tr>
<tr>
<td><strong>Previous H/O febrile seizure</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>114</td>
<td>75.5</td>
</tr>
<tr>
<td>Present</td>
<td>37</td>
<td>24.5</td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
<td>100.0</td>
</tr>
</tbody>
</table>
History of neonatal seizures
Two-fifths of the study population 41.1%, had experienced seizures in the neonatal period.

Family history of seizures
Family history of epilepsy was present in 8.6% of the population. A family history of febrile seizures was found in 9.9% of families.

Previous history of febrile seizures
This was present in about one quarter of the enrolled children.

5.4.3: Epilepsy profile (Table 5.3)
In table 5.3 a detailed description of age at onset, rates, types of seizures and epilepsy classification is presented.

Age at onset of seizure
More that half of the children had ‘early’ onset, of seizures (Section 4.3.1, point10). It should be noted that when compared with their age at presentation to the EEG services (Table 5.1) an EEG in 46.4% was performed much later.

Rate of seizures
The majority of the study children (97, 64.2%) had high rates of seizures (defined in section 4.3.1). When the numbers of attacks were calculated (Section 5.3.8), the mean and median number of seizure attacks per year was 1923.63 and 1095.00 respectively.

Seizure types
The majority (61.6 %) of the study population gave a history of ‘multiple seizure types’ on the first day of diagnosis. The total number of seizures was 291 in 151
children; 93 of them had multiple seizure types. The most frequent seizure type was myoclonic seizures (Table 5.3) on first presentation.

Epilepsy Classification (Table 5.3)
Based on the clinical information, the majority of children had generalised epilepsy (63.6%). Partial and secondary generalised epilepsy was diagnosed in 25.2%, while the epilepsy was unclassifiable in 11.2%.

Malignant epilepsy syndromes
Malignant epilepsy syndrome was diagnosed in 22 (14.6%) children. The breakdown is shown in Table 5.3.

Etiological classification of epilepsy
Ninety-two (61%) children had a diagnosis of symptomatic and cryptogenic epilepsy. Fifty-one of them had abnormality detected in their neuroimaging, and 41 children had clinical evidence of neurological deficit but no neuroimaging was not done in them. Idiopathic epilepsy was diagnosed in 59 children who had no such evidence of neurological deficit.
Table 5.3: Epilepsy profile

<table>
<thead>
<tr>
<th>ITEM</th>
<th>NUMBER</th>
<th>PERCENTAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at onset of seizure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early</td>
<td>85</td>
<td>56.3</td>
</tr>
<tr>
<td>Later</td>
<td>66</td>
<td>43.7</td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
<td>100.0</td>
</tr>
<tr>
<td>Rate of seizure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low rate</td>
<td>54</td>
<td>35.8</td>
</tr>
<tr>
<td>High rate</td>
<td>97</td>
<td>64.2</td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
<td>100.0</td>
</tr>
<tr>
<td>Seizure type(s)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple</td>
<td>93</td>
<td>61.6</td>
</tr>
<tr>
<td>Single</td>
<td>58</td>
<td>38.4</td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
<td>100.0</td>
</tr>
<tr>
<td>Seizure classification</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MC</td>
<td>63</td>
<td></td>
</tr>
<tr>
<td>GTCS</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td>GT</td>
<td>49</td>
<td></td>
</tr>
<tr>
<td>SPS/CPS</td>
<td>46</td>
<td></td>
</tr>
<tr>
<td>IS</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Unclassifiable</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>Secondary generalised sz.</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Absence</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Atonic</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>GCLLS</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Epilepsy type (clinical)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Generalised</td>
<td>96</td>
<td>63.6</td>
</tr>
<tr>
<td>Partial (SPS,CPS)</td>
<td>24</td>
<td>15.9</td>
</tr>
<tr>
<td>Secondary gen.</td>
<td>14</td>
<td>9.3</td>
</tr>
<tr>
<td>Unclassified</td>
<td>17</td>
<td>11.2</td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
<td>100.0</td>
</tr>
<tr>
<td>Malignant syndrome</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>129</td>
<td>85.4</td>
</tr>
<tr>
<td>Diagnosed syndrome</td>
<td>22</td>
<td>14.6</td>
</tr>
<tr>
<td>Infantile spasms</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Landau Kleffner syndrome</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Lennox Gastaut syndrome</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
<td>100.0</td>
</tr>
<tr>
<td>Etiological types</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Idiopathic</td>
<td>59</td>
<td>39.0</td>
</tr>
<tr>
<td>Symptomatic &amp; cryptogenic</td>
<td>92</td>
<td>61.0</td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Mo, months; mc, myoclonic; CTCS, generalised tonic-clonic seizures; GT, generalised tonic; IS, infantile spasms; SPS, simple partial seizures; CPS, complex partial seizures; sz, seizures.
5.4.4: Associated non-convulsive disorders (Table 5.4)

Co-existing impairments or disabilities i.e., motor, speech, cognitive and behavioural disorders are shown in Table 5.4

Motor disorders
Fifty-seven percent of the children had some degree of motor disorders i.e., major or minor (see section 5.3.IX). Signs of upper motor neurone lesion (e.g., exaggerated deep tendon reflexes, spasticity and persistence of primitive reflexes) were noted in 56 (37.1%) children. Signs of lower motor neuron lesion were found in 4 (2.6%) children.

Speech regression
Speech regression was found in 21 children (13.9%). Out of these eight had clinical diagnosis of Landau - Kleffner Syndrome.

Cognitive development
A formal psychometric test was performed in 106 (70.2%) children. A substantial number of children, (68.9%) had an IQ level of less than 70.

Cognitive development on physician's judgement
The physician’s assessment of the child’s cognitive developmental status was ‘impaired’ in 72.8% of the children.

It should be pointed out that the correlation between the ratios of children with delayed cognitive development on IQ testing and that of the physicians' clinical judgement, were significant with the Pearson correlation significance level < 0.01.
Behaviour problems

Thirty-nine children (25.8%) had normal behaviour recorded on first NDA, 72 (47.7%) had definite features of behavioural disorder and 40 (26.5%) children were categorised as 'uncertain' by the clinicians.

Table 5.4: Associated non-convulsive disabilities

<table>
<thead>
<tr>
<th>Items</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major motor disorder</td>
<td>62</td>
<td>41.00</td>
</tr>
<tr>
<td>Minor motor disorder</td>
<td>24</td>
<td>16.00</td>
</tr>
<tr>
<td>None</td>
<td>65</td>
<td>43.00</td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
<td>100.0</td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>110</td>
<td>72.8</td>
</tr>
<tr>
<td>Absent</td>
<td>41</td>
<td>27.2</td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
<td>100.0</td>
</tr>
<tr>
<td>IQ</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;70</td>
<td>73</td>
<td>68.9</td>
</tr>
<tr>
<td>&gt;70</td>
<td>33</td>
<td>31.1</td>
</tr>
<tr>
<td>Total</td>
<td>106</td>
<td>100</td>
</tr>
<tr>
<td>Behavioural state on clinical assessment:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperactive/irritable</td>
<td>59</td>
<td>39.1</td>
</tr>
<tr>
<td>Listless</td>
<td>13</td>
<td>8.6</td>
</tr>
<tr>
<td>Uncertain</td>
<td>40</td>
<td>26.5</td>
</tr>
<tr>
<td>Normal</td>
<td>39</td>
<td>25.8</td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
<td>100.0</td>
</tr>
</tbody>
</table>

5.4.5: EEG profile (Table 5.5)

Normal and abnormal EEG findings

EEG abnormalities were found in the 80.8% of children. This was sub-categorized into those who had epileptiform discharges with or without background abnormalities (61.6%), and those with non-epileptiform abnormal activity (19.2%), defined as
abnormal background activities (Section 4.10.2). Normal EEG features were noted in 29 (19.2%) children.

Table 5.5: Electroencephalographic (EEG) findings

<table>
<thead>
<tr>
<th>Item</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EEG</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal</td>
<td>122</td>
<td>80.8</td>
</tr>
<tr>
<td>Normal</td>
<td>29</td>
<td>19.2</td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
<td>100</td>
</tr>
<tr>
<td><strong>EEG features</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epileptiform disch.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Generalised</td>
<td>38</td>
<td>25.2</td>
</tr>
<tr>
<td>Localized</td>
<td>55</td>
<td>36.4</td>
</tr>
<tr>
<td>Abnormal background (NEAA)</td>
<td>29</td>
<td>19.2</td>
</tr>
<tr>
<td>Normal activities</td>
<td>29</td>
<td>19.2</td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
<td>100</td>
</tr>
<tr>
<td><strong>Abnormal EEG features</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epileptiform discharges</td>
<td>61</td>
<td>50.0</td>
</tr>
<tr>
<td>NEAA</td>
<td>29</td>
<td>23.8</td>
</tr>
<tr>
<td>Both</td>
<td>32</td>
<td>26.2</td>
</tr>
<tr>
<td>Total</td>
<td>122</td>
<td>100</td>
</tr>
</tbody>
</table>

Disch, discharges; epil, epilepsy; NEAA, non-epileptiform abnormal activities.
5.4.6: Neuroimaging profile (Table 5.6)

Seventy-nine children had some form of neuroimaging. Sixteen (10.6%) had USG, 46.6% had CT scans, and 9.9% had MRI of the brain performed. Of these, 64.5% had evidence of cerebral lesions.

Table 5.6: Neuroimaging reports

<table>
<thead>
<tr>
<th>Item</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuroimaging</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Done</td>
<td>79</td>
<td>52.3</td>
</tr>
<tr>
<td>Not done</td>
<td>72</td>
<td>47.6</td>
</tr>
<tr>
<td>USG</td>
<td>15</td>
<td>100.0</td>
</tr>
<tr>
<td>CT</td>
<td>70</td>
<td></td>
</tr>
<tr>
<td>MRI</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
<td></td>
</tr>
<tr>
<td>Abnormal</td>
<td>51</td>
<td>64.5</td>
</tr>
<tr>
<td>Normal</td>
<td>28</td>
<td>35.5</td>
</tr>
<tr>
<td>Total</td>
<td>79</td>
<td>100</td>
</tr>
</tbody>
</table>

USG, ultrasonogram; CT, computed topography; MRI, magnetic resonance imaging

5.4.7: Outcomes at one or more than one year’s follow-up

Seizure outcome (Table 5.8)

Percentage of seizure reduction

'Seizure remission' was recorded in 49.7%, while seizure reduction was partial (i.e. between >50- <100%) in 47 children (31.1%). In 29 children (19.2%), the seizures were refractory to treatment as there was <50% seizure reduction.
Table 5.7: Seizure outcome during the last follow up

<table>
<thead>
<tr>
<th>Item: Seizure outcome</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seizure reduction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;50% - &lt;100%</td>
<td>76</td>
<td>50.3</td>
</tr>
<tr>
<td>0-&lt;50%</td>
<td>47</td>
<td>31.1</td>
</tr>
<tr>
<td>100% seizure reduction</td>
<td>29</td>
<td>19.2</td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
<td>100</td>
</tr>
</tbody>
</table>

5.4.8: Baseline and follow-up AED status (Table 5.9)

Table 5.8 shows information about previous history of AED treatment on entry and at the last follow up.

Table 5.8: Baseline and follow-up 'AED' status

<table>
<thead>
<tr>
<th>AED status</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>No AED prior to entry at the CDC</td>
<td>85</td>
<td>56.3</td>
</tr>
<tr>
<td>On AED prior to entry at CDC</td>
<td>66</td>
<td>43.7</td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
<td>100</td>
</tr>
<tr>
<td>Current AED on last follow up</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single AED</td>
<td>115</td>
<td>76.2</td>
</tr>
<tr>
<td>Multiple AED</td>
<td>22</td>
<td>14.6</td>
</tr>
<tr>
<td>No medication</td>
<td>14</td>
<td>9.3</td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
<td>100</td>
</tr>
</tbody>
</table>

CDC, child developmental centre;
On the first day at the CDC (on entry): sixty-six children (43.7%) were on regular or irregular AED medication before presenting to the CDC.

On last follow-up: the majority of children were on single AEDs (76.2%). In 14 children, AEDs had been discontinued by the CDC physicians and the children remained seizure free.

Commonly used drugs were carbamazepine and valproic acid, one of which was been given to 36.5% of children. The next most common drugs were nitrazepam (14.6%) and clonazepam (13.1%).

5.4.9: Behaviour and motor problems at last follow-up (Table 5.9)

Table 5.9 shows the state of the child’s co-existing impairments and disorders on the last day of follow-up. Motor disability was present in 40.4% at last follow up, compared with 57% (Table 5.4) on the first day of assessment. The percentage of children who had behaviour problems at the last follow up was much less (30.5%) than what had been recorded at the first assessment (47.7%; Table 5.4). According to parents’ complaints, 12 children had behavioural problems, which were related to the AEDs. However, this was not found to be associated with any specific AED, and instead multiple drug use and over doses were suspected to be the cause.
Table 5.9: Motor disability and behavioural state on last follow-up day.

<table>
<thead>
<tr>
<th>Item</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor disability</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>90</td>
<td>59.6</td>
</tr>
<tr>
<td>Present</td>
<td>61</td>
<td>40.4</td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
<td>100</td>
</tr>
<tr>
<td>Behavioural state</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal behaviour</td>
<td>93</td>
<td>61.6</td>
</tr>
<tr>
<td>Abnormal behaviour</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Significant problem</td>
<td>24</td>
<td>15.9</td>
</tr>
<tr>
<td>Mild problem</td>
<td>22</td>
<td>14.6</td>
</tr>
<tr>
<td>Problem after starting AED</td>
<td>12</td>
<td>7.9</td>
</tr>
<tr>
<td>Total</td>
<td>151</td>
<td>100</td>
</tr>
</tbody>
</table>

5.4.10: EEG correlation

Correlation between clinical diagnosis and EEG (Table 5.11)

Based on only clinical information, 96 children (63.6%) were diagnosed with generalised epilepsy, and 38 children (25.2%) with partial epilepsy. When correlated with EEG features, the numbers of EEGs showing localized epileptiform discharges signifying partial epilepsy rose to 55 children (36.4%). EEG also identified two other categories with potentially important treatment and prognostic implications (a) twenty-nine (19.2%) children with background abnormal activities (non-epileptiform abnormal activity), and (b) twenty-nine children (19.2%) with no EEG abnormalities. Of those in the latter group, 65.5% had been diagnosed clinically to have generalised epilepsy, while 20.6% had partial epilepsy, and 13.8% had unclassified epilepsy on clinical diagnosis.
Table 5.10: Correlation between clinical diagnosis and EEG findings.

<table>
<thead>
<tr>
<th>Clinical diagnosis</th>
<th>Generalised epileptiform discharge</th>
<th>Localized epileptiform discharges</th>
<th>Non-epileptiform abnormal activity</th>
<th>No abnormality</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gen. Epilepsy</td>
<td>31</td>
<td>23</td>
<td>23</td>
<td>19</td>
<td>96</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>63.6</td>
</tr>
<tr>
<td>Partial epilepsy</td>
<td>5</td>
<td>22</td>
<td>5</td>
<td>6</td>
<td>38</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>25.2</td>
</tr>
<tr>
<td>Unclassified</td>
<td>2</td>
<td>10</td>
<td>1</td>
<td>4</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>11.2</td>
</tr>
<tr>
<td>Total</td>
<td>38 (25.2%)</td>
<td>55 (36.4%)</td>
<td>29 (19.2%)</td>
<td>29 (19.2%)</td>
<td>151 (100)</td>
</tr>
</tbody>
</table>

Gen, generalised.

Correlation between EEG features and seizure outcomes (Table 3.12):

Best outcomes, i.e. 100% seizure reduction, were seen in 75.9% of those children who had no EEG abnormalities. The next best outcomes were noted in those who had non-epileptiform abnormal activities on EEG, i.e., 48.3%.

Correlation between poor seizure remission and EEG features (Figure 5.1)

There was significant correlation between seizure remission and EEG feature when the EEG abnormalities were sub-categorized. Analysis showed Chi-square significance level at <0.001 with 2 degrees of freedom. Figure 5.1 shows an almost linear correlation between EEG findings and seizure remission, the best outcomes being with those having normal EEGs and worse in those with both epileptiform discharges and non-epileptiform abnormal activities.
Table 5.11: Correlation between EEG features and seizure outcome

<table>
<thead>
<tr>
<th>EEG- finding</th>
<th>Seizure remission (%)</th>
<th>Poor seizure remission (%)</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epileptiform discharges</td>
<td>32</td>
<td>29</td>
<td>61</td>
</tr>
<tr>
<td></td>
<td>52.5%</td>
<td>47.5%</td>
<td>100.0%</td>
</tr>
<tr>
<td>Background abnormality</td>
<td>14</td>
<td>15</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>48.3%</td>
<td>51.7%</td>
<td>100.0%</td>
</tr>
<tr>
<td>Both epileptiform discharges &amp;</td>
<td>7</td>
<td>25</td>
<td>32</td>
</tr>
<tr>
<td>Non-epileptiform abnormality</td>
<td>21.9%</td>
<td>78.1%</td>
<td>100.0%</td>
</tr>
<tr>
<td>Normal</td>
<td>22</td>
<td>7</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>75.9%</td>
<td>24.1%</td>
<td>100.0%</td>
</tr>
<tr>
<td>Total</td>
<td>75</td>
<td>76</td>
<td>151</td>
</tr>
</tbody>
</table>

Pearsons Chi-square value = 18.06 with two tailed significance <0.001
5.4.11: Predictors of seizure outcomes

Main effect model showing correlation between individual predictors and seizure outcomes (Table 5.12)

A list of potential predictors for epilepsy was provided in section 5.3.15. The dependent variable was encoded as seizure remission “0” and no remission “1”. The reference category was 'seizure remission', and 'poor seizure remission' was the event category.

A bivariate analysis with Pearson’s Chi-square test was performed to examine the relationship between seizure remission and each of the independent variables. p value was considered significant when it was 0.05 or less.
Table 5.12: Main effect model showing correlation between individual predictors and seizure outcome.

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Total frequency observed</th>
<th>Proportion of seizure remission</th>
<th>Odd ratio, limit with 95% CI, p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seizure type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple seizure</td>
<td>92</td>
<td>42.4</td>
<td>4.42 (2.07 - 9.57) 0.001</td>
</tr>
<tr>
<td>Single seizure</td>
<td>59</td>
<td>71.2</td>
<td></td>
</tr>
<tr>
<td>High rate of seizure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>97</td>
<td>44.3</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>54</td>
<td>70.4</td>
<td>3.38 (1.58 - 7.31) 0.005</td>
</tr>
<tr>
<td>Motor disability</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>86</td>
<td>45.3</td>
<td>2.08 (1.03 - 4.23) 0.027</td>
</tr>
<tr>
<td>Absent</td>
<td>65</td>
<td>64.6</td>
<td></td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>110</td>
<td>47.3</td>
<td>2.49 (1.11 - 5.70) 0.015</td>
</tr>
<tr>
<td>Absent</td>
<td>41</td>
<td>70.4</td>
<td></td>
</tr>
<tr>
<td>EEG report</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal</td>
<td>122</td>
<td>49.2</td>
<td>4.09 (1.53 - 12.11) 0.001</td>
</tr>
<tr>
<td>Normal</td>
<td>29</td>
<td>72.4</td>
<td></td>
</tr>
<tr>
<td>Age of onset</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early</td>
<td>85</td>
<td>51.8</td>
<td>1.14 (0.57 - 2.28) 0.689</td>
</tr>
<tr>
<td>Later</td>
<td>66</td>
<td>56.1</td>
<td></td>
</tr>
<tr>
<td>Malignant syndrome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>44</td>
<td>50</td>
<td>1.27 (0.59 - 2.73) 0.506</td>
</tr>
<tr>
<td>No</td>
<td>107</td>
<td>55.1</td>
<td></td>
</tr>
<tr>
<td>Family H/O epilepsy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>138</td>
<td>51.4</td>
<td>2.45 (0.64 - 11.37) 0.140</td>
</tr>
<tr>
<td>Present</td>
<td>13</td>
<td>76.9</td>
<td></td>
</tr>
</tbody>
</table>

H/O, history of
Five predictive variables showed significant correlation with 'poor seizure remission' independently.

**Multiple seizure types:** this had an independent association with seizure outcomes with an odds ratio of 4.42, 95% CI (2.07-9.57), \( p < 0.001 \). This suggests that a child with multiple seizure type has 4.42 times probability of 'poor seizure remission'.

**High rate of seizure:** 70.4% population with low rate seizure had seizure remission. Odds ratio 3.38, 95% CI (1.58-7.31), \( p < 0.005 \).

**Associated motor disorder:** 64.6% without this disability had seizure remission. Odds ratio 2.08, with 95% CI (1.03-4.23); \( p < 0.027 \).

**Cognitive impairment:** 70.7% without this impairment had seizure remission. Odds ratio 2.49, with 95% CI (1.11-5.70) \( p < 0.015 \).

**EEG feature:** when a normal or abnormal categorized EEG was correlated with seizure outcome, 72% of the children with normal EEG had seizure remission. Odds ratio 4.09, CI- (1.53-12.11); \( p < 0.001 \).

**Multivariate analysis between poor seizure remission and clinical, and EEG variables (Table 5.13)**

Multiple logistic regression model

Backward stepwise logistic regression analysis was performed for multiple analysis. Procedure of stepwise regression analysis: Using the above mentioned equation (see section 5.3.15), all the predictors were entered in the first step. The goodness of fit was 148.307, and model chi-square was 41.68. When all 8 predictors were associated
with the dependent variable, only the ‘multiple seizure types’ became the most significant predictor (p < 0.001).

The least significant variable was removed from the model in each step when p = 0.10.

The variable removed in step 2 was motor disability because the log likelihood decreased by less than 0.01 percent. The goodness of fit was 147.21, model chi-square 41.43.

The variable removed in step 3 was ‘age at seizure onset’. The goodness of fit 147.67, model chi-square 40.81.

The variable removed in step 4 was family history of epilepsy. The goodness of fit was 148.69, Model chi-square 38.76, improvement 2.05.

The variable removed in step no 5 was ‘malignant syndrome’. The goodness of fit was 147.96, model chi-square 36.31, improvement 2.44.

The variable removed in step 6 was high rate of seizure. The goodness of fit was 149.286, model chi-square 33.90, and improvement 2.41.

Three variables remain as significant predictors of poor seizure remission in the last step (Table- 5.14). These include the ‘multiple seizure type’, p <0.0001, ‘cognitive impairment’ p <0.011, and abnormal EEG, p value <0.012.
Table 5.13: Logistic regression model with interaction of independent variables and dependent variable.

<table>
<thead>
<tr>
<th>Independent variable</th>
<th>Chi-square</th>
<th>Coefficient</th>
<th>Odds ratio (C.I.)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Seizure types</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple</td>
<td>16.318 ***</td>
<td>1.549</td>
<td>4.42(2.07-9.57)</td>
</tr>
<tr>
<td>Single</td>
<td>0 R.C.</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>Cognitive impairment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>6.065 *</td>
<td>1.046</td>
<td>2.49(1.11-5.70)</td>
</tr>
<tr>
<td>Absent</td>
<td>0 R.C.</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>EEG report</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal</td>
<td>7.877 **</td>
<td>1.046</td>
<td>4.09(1.53-12.11)</td>
</tr>
<tr>
<td>Normal</td>
<td>0 R.C.</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>Model</strong></td>
<td>33.906 ***</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

R.C. reference category

* p <0.05,
** p <0.01
*** p <0.001
5.5: Conclusions and implications for future research

1. Among the five predictors independently related to the seizure outcome two are seizure related, two are associated non-convulsive disorders and the fifth one is an investigation finding. The association of the seizure characteristics and the non-convulsive disorders and their predictability of seizure outcome found in this stage of the study supports the concept that such readily available information could be used at an early stage to plan appropriate management of childhood epilepsies.

2. An abnormal EEG was significantly correlated with poor seizure outcome. EEG is therefore not only an investigative tool for supporting the diagnosis of epilepsy but might also have prognostic value in childhood epilepsy. The EEG also helped in making a more specific diagnosis of the seizures and in their classification. This may suggest that EEG services need to be developed at tertiary care levels of childhood epilepsy services.

3. The above findings justify the use of a multidisciplinary service for children with seizure disorders in Bangladesh; the purpose of such a service being to prevent non-convulsive disorders in childhood epilepsy.

4. The chief limitations of the study were: (a) it was a retrospective study, and therefore information was often incomplete; (b) many relevant socio-economic and cultural factors could not be obtained; (c) all children were referred from the general OPD of the hospital only when their seizures were difficult to control and represented the tertiary end of the spectrum; (d) there was an overrepresentation of middle-class families, and therefore not representative of the general population of Bangladesh.

5. Further research should be prospective and should take into account the high proportion of low-income families in the population and more putative risk factors should be included. Attitudes, maternal stress, economics of treatment and compliance need to be assessed together with a comprehensive psychological and
behavioural assessment of all enrolled children. Attempts should be made to enrol the children at early stage of their seizure disorder, and EEG should be recorded within a short time of first presentation. The study should also be able to suggest the levels of medical and paramedical personnel who need to be trained to provide optimum services at the primary and secondary health care centres and should provide guidelines for a well-designed curriculum for them.
CHAPTER SIX

6: The prospective study

6.1: Introduction and background of this stage

The previous chapter (Chapter Five) demonstrated the epilepsy profile in children attending a special centre in which the population was biased towards the severe end of the spectrum. Predictors of ‘poor seizure remission’ were identified, and the need for a prospective study was discussed. The present chapter describes that prospective study, performed on children with epilepsy attending a community centre and on children who were attending a special centre at the national paediatric hospital (Section 4.14).

Methods and materials

6.2: Aims of this stage of study

1. To validate the model of clinical predictors of seizure outcome and see if there was any additional role for EEG information. (See potential predictors in Section 5.3.15)
2. To identify the proportion of newly diagnosed children with epilepsy needing long-term medical follow-up.
3. To identify the epilepsy treatment gap (Section 2.9.1) among the population studied.
4. To test the hypothesis that i) 70% of the newly diagnosed epilepsy patients (without any major risk factors) become seizure free with appropriate treatment after 1 year and ii) that in those with one or more associated risk factors, seizure freedom will be 20-30% or less.
6.3: Study design

6.3.1: Sample size

We decided to recruit a total of 400 patients for the prospective study.

Power calculation

For 95% power, 5% significance value and assuming that 70% of the newly diagnosed with no associated disabilities have seizure remission and that this falls to at least 50% or less in those with associated disabilities, the sample size for this study was calculated using the formula below.

One sample formula: \( n > (Z_\alpha + Z_\beta)^2 \left\{ \pi_1(1 - \pi_1) + \pi_2(1 - \pi_2) \right\}/\delta^2 \)

When, \((Z_\alpha + Z_\beta)^2 = 12.99\) for 95% power at 5% significance level.

\[
\begin{align*}
n &> 12.99 \left( 0.70 \times 0.30 + 0.50 \times 0.50 \right) / 20^2 \\
&> 12.99 \times (0.21 + 0.25) / 400 \\
&> 12.99 \times 0.46 / 400 \\
&> 0.03198 \times 400 \\
&> 12.79 \\
&\geq 150 \\
\end{align*}
\]

Total 300

But associated disability and no associated disability were expected to be equal sized groups. This occurs in the ratio approximately 2:1 as identified in retrospective study.

A total sample size needs to be increased to

\[
\begin{align*}
&2 \times 150 \times 3^2 / 8 \\
&= 9 \times 150 / 4 \\
&= 9 \times 37.5 \\
&n \geq 338 \\
\end{align*}
\]

Allowing for 20% drop out the sample size required was approximately 400

6.3.2: Inclusion criteria

Eligible patients were from 2 months to 15 years of age.
Seizure type: children with all types of seizures and epilepsy were included. Cases with recurrent typical and atypical febrile seizures were recorded separately.

Previous treatment: a detail drug history was entered for children who had been treated previously with AEDs. If there was a history of AED treatment for a period of three months or more, this was recorded as a positive past history of AED medication.

6.3.3: Exclusion criteria

Acute cases of meningitis or encephalitis, diagnosed or suspected by the attending doctor, a single episode of status, and 2 or more seizures within 24 hours were not included.

6.3.4: Preparation

A medical assessment form (Section 4.11.1, Appendix II) was prepared for the prospective study, which is described in section 4.11.1.

The Conners’ Parental Assessment Questionnaire (Appendix-X) was translated into Bangla. This is described in section 4.9. Reliability and concurrent validity measure of the translated Conners’ Parental Assessment questionnaire are described in section 4.9.1 and 4.9.2.

An adapted Richman child behaviour assessment questionnaire was used for 3 to 5 years aged children (Section 4.8.2, Appendix XI) (Davis & Rushton 1991).

The Rutter behaviour assessment questionnaire (Rutter 1967) was used for children aged 6 years and above (Section 4.8.3 and Appendix: XII)

6.4: Patient recruitment

Following approval of the protocol by the Research Ethics Committee of Great Ormond Street Hospital for children and the Institute of Child Health London and the
Ethical Review Committee (ERC) of Bangladesh Institute of Child Health (BICH), patients were recruited over 6 months and followed up for 12 months. Patients were recruited from two sources, and were followed up regularly for 12 months.

One source was a newly opened general outpatient department (OPD) (Section 4.14). It was expected that the patients of this group would be more representative of the general population, would have newly diagnosed epilepsy and that associated motor and cognitive disabilities would be less frequent. A second source of the patient recruitment was the epilepsy clinic at CDC (specialist OPD) (Chapter Four, Section 4.14), excluding those who were enrolled in the retrospective study (Chapter Five). Children in this group were expected to be more severely affected and likely to have multiple disabilities.

Patient referral at the research centre

**Referral to the non-specialist OPD**

1. Self-referral.
2. Referred by the general OPD doctors often when the child had presented with other health problems and later it was found that the child had a history of unprovoked or provoked seizure attacks.
3. By the emergency medical officer after managing an acute attack.

**Referral to the CDC**

1. From the in patients department (IPD) of the same hospital: children who were admitted to any unit with acute, prolonged seizures or epilepsy with loss of functional skill or repeated unprovoked seizures were referred to the CDC after the acute management.
2. From other private or Government run hospitals.

**6.5: Medical and non-medical personnel involved**
Primary care physicians (PCP), clinical child psychologists (CCP), developmental therapists (DT), clinical neurophysiologists (NP), EEG technicians and research assistants.

6.6: Commencing the study

6.6.1: Training the team workers (Section 4.12)

A. The Primary care physician (PCP) was responsible for the following: history taking with a structured questionnaire, conducting general and neurodevelopmental assessment (NDA), grading the disability using the WHO guide lines (Appendix XV), making a preliminary diagnosis of seizures and epilepsy and other associated problems, AEDs and prescribing them according to the dose guide (Appendix VIII), making a short and long-term management plan and contacting a neurologist at the CDC or SHB in case of any confusion in diagnosis or drug selection. The PCP was also responsible for guiding the therapist in prescribing developmental therapy, educating and re-enforcing the parents about epilepsy and the importance of regular drug intake, showing parents the use of the seizure diary and arranging for a psychological and behavioural assessment tests on the first day or during the second visit within two week’s time. An EEG recording was performed including other investigations as appropriate and regular follow-up was planned.

B. Examination of the child: both the general and neurodevelopmental examinations were carried out following a standard protocol (Egan 1990). During the NDA, physicians assessed the child’s behaviour and cognitive level and level of understanding using standard methodology appropriate for the age (Section 4.7).

C. The developmental therapist (DT) was responsible for the following: the DT explained the theoretical aspect of developmental therapy to the family, gave hands-on demonstrations to them using a dummy baby; this was followed by the physical therapy, visual, hearing, and cognitive stimulation for the child. S/he agreed a short-term, and a long-term goal for the child’s functional development, and fixed the
follow-up dates on discussion with the physician and the family. The DT took the
body measurements of the child during each visit and was responsible for exchanging
the contact address with families, such as mailing address, telephone numbers of the
parents and/or other relatives and/or friends to ensure the source of contact with them.
She was also responsible for filling out the SES and SRQ forms.

D. The psychologist was responsible for the following: conducting a baseline
psychological assessment, filling out the psychological data entry forms, conducting
behavioural assessment of the child using questionnaires appropriate to the child’s age,
(See below, section 6.6.4), making an appointment for the second test on discussion
with other members of the team and the family. In addition the psychologist was
responsible for educating parents about the cognitive stimulation of their child.

6.6.2: On arrival

At the initial consultation each patient’s parents gave informed consent to participate
in the research. The families were informed of the investigations the child might go
through during the follow up period and asked for their consent.
A detailed history (including the family, pre-, peri-, and post-natal, early
developmental and seizures histories) was obtained and examination of the child and
management planning was carried out by the PCP, DT and psychologist. The
researcher met the team-members daily to discuss and review the completed MAF
(Appendix II), diagnosis and management plan. At the initial stage each MAF was
checked by the researcher (first 50 MAFs) later random checking of every 4th MAF
was continued up to the last patient. Where there was any confusion or ambiguity
noticed regarding the diagnosis or management, the next visit was then arranged with
SHB.

6.6.3: Psychological evaluation
Psychological and behavioural assessment tests were done on the first presentation when possible, or with an appointment according to the parent’s convenience for each child. A second behavioural assessment was arranged after 11-12 months of treatment.

Each MAF was reviewed by SHB along with the team members.

IQ test

1. The Bayley Scale of Infant Development (BSID) (Bayley 1993) for 1 month to 42 month old children. (2 month to 3 year old children for this study)

6.6.4: Behavioural assessment

The behavioural assessment tools used are mentioned in Section 4.8.

6.6.5: Sociodemographic (SES) form (Section 4.11.2, Appendix-IX)

The SES forms were filled-out by the DT after the family had visited the clinic 2 to 3 times. We took this opportunity to try to make them feel at ease while giving the information to us.

6.6.6: Family inventory SRQ (Appendix XIII)

We assessed maternal stress with a 20-item Self-Report Questionnaire (SRQ, 20 item yes/no version; Harding et al.1980), adapted from the General Health Questionnaire, and validated through use in a number of developing countries. Mari and Williams
(1985) give a cut off point for psychiatric morbidity >7 (sensitivity 83%, specificity 80%, total score range 0-20). The same SRQ has been used in one study in BD to identify the predictors of stress in mothers of children with cerebral palsy (Riaz & Khan 1999).

In our study, out of 287 of the mothers who filled up the SRQ forms, 183 mothers’ total score was recorded more than 7, indicating potential maternal psychiatric morbidity in 63.8%. This is higher than that found in mothers of children with cerebral palsy.

6.6.7: Ensuring drug availability, emergency management, compliance, seizure record keeping and educating the parents about epilepsy

A. Ensuring drug availability

We developed methods to try to ensure that the medicine supply to the parents particularly when the family came from remote areas, failed to attend clinic or when the family temporarily moved. (i) Certain medicines were supplied by the clinic (PB, CBZ), (ii) the rest were arranged through a reputable pharmacy which kept the commonly used AEDs at their stores, iii) the clinic also provided the medicine for some patients in the non-RCT group based upon the information obtained in the socio economic questionnaire and the family situation.

B. Emergency management; guidance for the parents

1. Parents were informed about the seizures and their consequences. In cases of a prolonged major attack, we advised the parents to go to the nearest primary health complexes or to the nearest practicing physician for appropriate management. The instructions for emergency management of such prolonged attacks were outlined in the general information given to the family at the time of the prescription.
2. Specific instructions for the parents to follow during a major acute attack were written in simple Bangla, so that any family member, friend of the family or neighbour could read them and remind the parents what to do in case of emergency.

3. When children experienced frequent major attacks we supplied their parents a tube used for per rectal medication, a 5cc syringe and an ampoule of injectable Diazepam and advised to keep this at home for emergency use or with them when they travel. Parents were shown how to use per-rectal diazepam during hospital stays or at the emergency management area, as suggested by a recent study (Rossi et al. 1989b).

4. Parents were asked to contact the nearest primary health complex (THC) first for the immediate management of status epilepticus and then to contact the epilepsy team or to bring the child to the Dhaka Shishu Hospital. Patients were also carried to the DSH by ambulance when available.

5. Compliance was ensured by verbal enquiry and tablet counting in all cases. Assessment of blood level was carried out on one occasion, without previous warning of parents mainly for the RCT group (Chapter Seven).

C. Parents and family education about epilepsy, and seizure attack, and information about EEG recording was provided

Parental education and home management of major seizure attacks are found to be effective in some studies irrespective of educational level (Huang, Liu, & Huang 1998d; Ling 2000b; Parmar, Sahu, & Bavdekar 2001b; Rossi et al. 1989e). Based on the findings from other studies we started to develop simple methods to educate the parents, family members and the child about epilepsy. A pictorial description of the brain, disease process and how an EEG is done were demonstrated to the patients and other family members (Appendix: XVII). They were informed about the seizures, their consequences and what to do during a seizure attack and how to manage a major seizure attack. Parents and the family were reminded about acute management on each visit. A hand-made seizure record diary (Appendix XVI) was supplied with instructions on how to use it, and they were asked to bring this to each visit.
D. Family and Parents’ first reaction, existing knowledge about epilepsy or seizure attacks

There were two direct questions to explore the parents’ awareness and knowledge about seizure attacks and another indirect question to support the answer to these (Last two questions in section II in MAF, Appendix II and question 9 in SES form, Appendix: IX).

6.6.8: Attendance compliance and managing other problems

Through epilepsy education the parents and other family members were informed on the importance of follow up, AED introduction and maintenance therapy. If the child had severe epilepsy with multiple disabilities and travelled a long distance, the child was hospitalised to treat any other acute illness, to initiate and stabilize the AED dose and to start the stimulation therapy. If families were reluctant to stay at the hospital, they were requested to stay with friends or relatives and come to the clinic at 2-3 day intervals until stabilization of the AED dosage. During the first visit we told the parents to feel free to contact the team members at any time other than the appointment date. In situations when the child or mother had another illness and was not able to attend the clinic, father or other family member was advised to come with the advice paper and the seizure record-keeping diary.

6.6.9: Follow up record

First follow-up was arranged 2 weeks after the first prescription of AED and subsequent follow-ups were at an interval of 1-3 months according to the seizure condition and distance of the family residence.

First follow up: we intended to review each child after two weeks of starting the AED. However, when this was not possible, we advised increasing the dose to the
maintenance level in the same prescription with instruction for turning of increase depending on seizure control. For example if seizures were controlled significantly we advised maintaining the dose at the level at which the seizures stopped and if not to increase the dose to the top end of the dose range at intervals of 2 weeks. If parents found that the child appeared too drowsy for more than one week, we advised them to reduce the dose to the previous level. An explanation of the doses and their relation to seizure control and alertness of the child was given to the parents. Once the seizures were controlled follow-ups were arranged depending on the distance of family residence and the family’s level of anxiety.

Visit compliance: the researcher checked the appointment diary at the beginning and end of each day clinic. When an appointment was missed and the family did not make any contact in 2 weeks to one month’s time after an appointment date, we tried to make contact over the telephone if there was a contact number or sent a letter with an appointment date, giving enough time for the letter to arrive, and for the family to prepare for travel. We provided the fare depending on the SES information provided. At first we did not give any indication that we could provide the transportation cost for the mother and child, thinking that it may cause huge cost problems. We also considered the issue that if we provided all the costs we might produce an expectation that could not be sustained.

When there was no answer to the first letter, we sent a second, and third letter with a request for the family to contact us. After this we were only able to arranged for home visits within Dhaka city.

6.6.10: EEG recording and interpretation: (Section 6.10.6)

The EEG recordings were conducted by the trained-technicians (Section 4.10.1). The EEG findings are described in Section 4.10.2.
An inter-observer reliability study
The EEGs were reported twice, first by a paediatric neurophysiologist trained
specifically for the project being blind to the patients’ information and then by myself,
having knowledge of the rest of the data. In cases where disagreements arose, a third
opinion was sought from Dr. Boyd, London.
The data of the EEG features were collected in the data entry form (Appendix: VII).

6.6.11: Other investigations

Neuroimagings and blood tests for AED levels were arranged by the attending
physician when required (Section 4.10.3).

6.6.12: Management

At the community service centre (OPD), a multidisciplinary team approach was used
to provide a holistic intervention programme for children with epilepsy. Apart from
specific AEDs (Appendix-VIII), the care-givers (usually parents) were also given
advice on general cognitive stimulation and specific developmental therapy when
necessary. In addition, we also arranged a parental counselling and education
programme to discuss simple information about epilepsy and seizure attacks, and
answered questions asked by the families for example: ‘if epilepsy is treatable’, ‘if it is
a communicable or hereditary problem’, ‘if their children can eat everything’, ‘if they
can go to school’ etc. A seizure record diary (Appendix-XVI) was distributed to each
family.

AED treatment was given following the standard treatment procedure for specific
epilepsy and epilepsy syndrome and availability of the drugs (Aicardi 1994a; Neville
1997)

In the case of poorly controlled seizures, the dose was increased up-to the highest
recommended dose. If ‘treatment failed’ defined as the seizure rate not reduced to
50% of the entry rate after 3 months on full dose, then a second drug was added. The
combination was maintained if significant seizure control was achieved. If in the event
the second drug also failed to reduce seizures, a third suitable drug was introduced at a
dlow dose and one of the two drugs, which seemed to be least effective according to the
parents description and physicians judgment, was weaned off and the combination of
two was continued. If seizures were controlled best with the combination of the three
AEDs without producing side-effects then this combination was maintained.
The history of ‘previous AED(s)’ was recorded and the previously taken drug was
continued if it was seen that the drug was appropriate for the epilepsy diagnosed and
the dose was adjusted. Otherwise the appropriate drug was administered.
A list of AEDs with doses and how to shift or add a second drug was prepared for the
PCP to follow (Appendix VIII and management plan form Appendix III).
This drug-protocol was different from the drug treatment for the RCT eligible group,
which is described in chapter seven.

6.7: Follow-up information

The numbers of seizure episodes since the previous follow up dates including any
other health problems were noted during each visit. Complaints of any side effects
caused by AEDs were checked by the drug side effect checklist in the follow-up form
(Appendix-III) and recorded during each visit. Drugs and doses were adjusted
according to the rate of seizure control and recent body weight. Evaluation of seizures
and re-assessment of the child’s functional ability, cognitive and behavioural state
were conducted and recorded by the team after one year’s treatment.

6.8: Epilepsy outcome measures

The following criteria were taken into consideration in measuring seizure outcomes:

6.8.1: Seizure remission

Seizure outcome and remission are described in the Section 4.3.1 point 18.
6.8.2: Behaviour state on last visit

Behaviour state was recorded as either behaviour problems ‘present’ or ‘absent’ based on criteria described earlier (Section 4.9.2).

Behavioural state after regular treatment for the RCT group were assessed according to the protocol described in chapter seven (Section 7.3).

6.8.3: Motor disability on last visit

Information on last NDA were coded as ‘normal’, ‘mild’, ‘moderate’ and ‘severe’ (Section 4.6.1).

6.8.4: Cognitive assessment on last visit

A second IQ test was conducted at the end of 12 months treatment.

6.8.5: Parental perception

At one-year follow-up, parents were asked about their perception on

1. Functional state during the last three months.
2. Understanding abilities compared to that of before treatment.

The information were categorized as

1. Excellent: parents were very satisfied
2. Good: there is significant improvement after treatment parents are quite satisfied
3. Fair: there is some improvements, parents are fairly satisfied
4. Hopeful: no obvious improvement but parents are hopeful
5. Hopeless: not improved and parents feel hopeless
6. Very unsatisfied; deteriorated condition.
6.9: Data Analysis

6.9.1: Reliability measure for the Conners' short parental questionnaire. Paired sample t-test ($T^2$) for time one and time two test scores for each index were carried out.

6.9.2: A concurrent validity measure test was done with the raw scores obtained by the Conners' assessment tool correlated with the total score and sub-scores obtained by gold standard (the Rutter test) using Pearson correlation co-efficient test with 2 tailed significance level.

6.9.3: K- statistics for two raters (Fleiss 1981; Landis & Koch 1977) were used as a measure of inter-rater agreement. As suggested by Landis and Koch (Fleiss 1981; Landis & Koch 1977), the strength of agreement was considered 'very good': $k >.81$, 'good': $k$ being $0.61 - 0.80$, and 'moderate': $k .41 - 0.60$.

6.9.4: Univariate analysis was done with each potential predictor. Odds ratios, confidence intervals, and p-values were calculated to show the magnitude of association between each factor and seizure outcome.

6.9.5: Multiple logistic regression tests were subsequently done using all entered, stepwise forward, and stepwise backward logistic regression model. A variable was eliminated if the level of significance was $>0.05$. The equation of the logistic regression model is as follows:

$$\text{Probability (event)} = 1 / 1 + e$$

When $Z = B_0 + B_1 \text{(NOS)} + B_2 \text{(RTOSZ)} + B_3 \text{(NMDIS)} + B_4 \text{(MRTD)} + B_5 \text{(SPSYND)} + B_6 \text{(FHOEP)} + B_7 \text{(AAONS)} + B_8 \text{(ABNEEG)}$. 
6.10: RESULTS

6.10.1: Description of the study population

Table 6.1: Patient overview

<table>
<thead>
<tr>
<th></th>
<th>OPD+CDC</th>
<th>%</th>
<th>OPD</th>
<th>%</th>
<th>CDC</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patient recruited</td>
<td>423</td>
<td>100.0</td>
<td>250</td>
<td>59.1</td>
<td>173</td>
<td>40.9</td>
</tr>
<tr>
<td>Non-febrile sz.since beginning</td>
<td>324</td>
<td>76.6</td>
<td>175</td>
<td>70.0</td>
<td>149</td>
<td>84.9</td>
</tr>
<tr>
<td>Evolved from febrile seizure</td>
<td>66</td>
<td>15.6</td>
<td>48</td>
<td>19.2</td>
<td>18</td>
<td>10.4</td>
</tr>
<tr>
<td>Diagnosed febrile seizures</td>
<td>33</td>
<td>7.8</td>
<td>27</td>
<td>10.8</td>
<td>6</td>
<td>4.6</td>
</tr>
</tbody>
</table>

Sz, seizure.

Patient overview: (Flow chart-6.1)
A total of 423 children were recruited, among them 390 children had epilepsy, and 33 had febrile seizures. Among the 390 children, 324 had a history of having non-febrile seizures from the beginning of their illness, and 66 had history of recurrent febrile seizures before they had unprovoked seizures, and categorized as ‘evolved epilepsy’ (Section 4.3). Out of 390 children with a primary diagnosis of epilepsy, 319 could be followed up for one year, and 71 could not be traced.

66 children with ‘evolved epilepsy’
Among 66 children identified as ‘evolved epilepsy’ the male female ratio was 1.2: 1, and 2.6% had multiple seizure types. Associated motor disability was present in 15%, and low IQ in 31%. Perinatal asphyxia, neonatal seizures, and CNS infection was recorded in 11(16.7 %). Forty- four children had more than 5 febrile seizures, 53% had an initial febrile seizure before 12 months of age. A family history of febrile seizures or epilepsy was recorded in 20(30.3%). Out of these 66 children, 57 (86.4%)
could be followed and 36 (63.2%) among them were on ‘seizure remission’ at 12 months follow up. EEG abnormalities were detected in the majority (59%).

33 children with febrile seizures
The median age at presentation among the 33 children with febrile seizures was 2 years, interquartile range 1.5 years. The male to female ratio was 10:1, motor and cognitive impairments were noted in 4(12.1%), and 3(9.1%) respectively. A history of perinatal asphyxia, neonatal seizures or prolonged seizures was present in 7 (21%). Seven children had more than 5 episodes, 81% had less than 5 episodes and the majority had 1-2 seizures. A family history of febrile seizures or epilepsy was present in 30%.

Follow-up result
Three children (9.1%) evolved into epilepsy (defined as 2 or more unprovoked seizures). Two children had developed non-febrile seizures during the follow up period, one child had an episode of viral encephalitis with loss of developmental skills and frequent non-febrile seizures, poorly responsive to AEDs and a later blood test revealed antibody positive for CMV IgM. All of them had had motor and cognitive impairments since early infancy.
During follow-ups of these cases (febrile seizures), AED was started in 10 children. Seven had been on AEDs from before and the medication was tapered off in five.
Figure 6.1: FLOW CHART OF THE STUDY- POPULATION

423 children recruited from April 2001 – October 2001, 250 at OPD, 173 at CDC

Epilepsy as 1st diagnosis in 390

319 followed up for >12mon.
71 lost to follow-up

Seizure outcome

Total seizure remission in 168 (52.7%)
Significant (>80%) reduction 47 (14.7%)
Some (>50%) reduction 44 (13.8%)
Minor (<50%) reduction 60 (18.8%)

Seizure outcome in

Those without non-convulsive disorder

Total remission in 76.9%
Significant reduction 10.3%
Some reduction 13%

With non-convulsive disorder, single or both motor & cognitive

Seizure remission 40.3%
Significant reduction 15.6%
Some reduction 15.6%
<30% reduction 28.4%

Febrile seizure only, initial diagnosis in 33

22 followed up, 11 lost

5 had > 2 episodes in 1 month
2 developed epilepsy
2 + myoclonic seizures & dev.delay
1 had severe dev. delay and atypical febrile seizures.
6.10.2: Family criteria (Table 6.2)

SES, residence, housing, family size

The majority of the total population (about 60%) came from lower income, nuclear families; 61.8% in the community (OPD) group and 38.2% in the CDC group. Over 61% came from rural residences with more than 77% of them from the Dhaka division. Over 40% of families had ‘kancha’ houses, 30.7% had ‘semi pacca’ houses, and 28.9% had ‘pacca’ houses. The majority of the families had shared toilets. Deep wells were the source of drinking water for the majority (44%), 31% had tap water, and 25% used surface water from a shallow well or pond and river water. The median number of rooms including the kitchen was 2 and the median number of adults living in a house was 2. A large number of families (47.8%) had one child (patient), about 29% of families had 2 children including the patient and 23% of families had 3 or more children. A history of sibling death from any cause was recorded in 13.7% population. Over 60% of the mothers and 65.5% fathers had a minimum primary level of literacy. Fifteen percent of mothers and 26% of the fathers had above secondary school level of education.
Table 6.2: Family criteria, SES

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>%</th>
<th>OPD</th>
<th>%</th>
<th>CDC</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Family type</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Nuclear</td>
<td>247</td>
<td>58.4</td>
<td>134</td>
<td>53.6</td>
<td>113</td>
<td>65.3</td>
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<tr>
<td>Joint</td>
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<td>41.6</td>
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<td>46.4</td>
<td>60</td>
<td>34.7</td>
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<tr>
<td><strong>Consanguinity</strong></td>
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<td></td>
</tr>
<tr>
<td>Positive</td>
<td>16</td>
<td>3.8</td>
<td>7</td>
<td>2.8</td>
<td>9</td>
<td>5.2</td>
</tr>
<tr>
<td><strong>Residence</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>259</td>
<td>61.2</td>
<td>156</td>
<td>62.4</td>
<td>103</td>
<td>59.5</td>
</tr>
<tr>
<td>Urban</td>
<td>164</td>
<td>38.8</td>
<td>94</td>
<td>37.6</td>
<td>70</td>
<td>40.5</td>
</tr>
<tr>
<td><strong>Monthly income</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower</td>
<td>251</td>
<td>58.3</td>
<td>155</td>
<td>62.0</td>
<td>96</td>
<td>55.5</td>
</tr>
<tr>
<td>Middle</td>
<td>154</td>
<td>36.4</td>
<td>83</td>
<td>33.2</td>
<td>71</td>
<td>41.1</td>
</tr>
<tr>
<td>Higher</td>
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<td>12</td>
<td>4.8</td>
<td>6</td>
<td>3.4</td>
</tr>
<tr>
<td><strong>Maternal education</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-literate</td>
<td>165</td>
<td>39.0</td>
<td>95</td>
<td>38.0</td>
<td>70</td>
<td>40.5</td>
</tr>
<tr>
<td>Primary level</td>
<td>132</td>
<td>31.2</td>
<td>82</td>
<td>32.8</td>
<td>50</td>
<td>28.9</td>
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<tr>
<td>SSC</td>
<td>61</td>
<td>14.4</td>
<td>41</td>
<td>16.4</td>
<td>20</td>
<td>10.6</td>
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<tr>
<td>HSC</td>
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<td>9.0</td>
<td>24</td>
<td>5.6</td>
<td>14</td>
<td>4.0</td>
</tr>
<tr>
<td>Bachelor &amp;Graduate</td>
<td>27</td>
<td>6.4</td>
<td>8</td>
<td>7.2</td>
<td>19</td>
<td>11.0</td>
</tr>
<tr>
<td><strong>Paternal education</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>146</td>
<td>34.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary</td>
<td>109</td>
<td>25.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSC</td>
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<td>12.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HSC</td>
<td>44</td>
<td>10.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bachelor &amp;Graduate</td>
<td>71</td>
<td>16.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>423</td>
<td>100</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

General information on the parents' reaction when the child had first major seizure and existing knowledge about the seizures and epilepsy
(Section 6.6.7, point D)
The answers to the two questions related to parents' existing knowledge were categorized as following:
Table 6.2.1: Parents’ first reaction after a major seizure attack:

Q. Where did you go first to get help?

<table>
<thead>
<tr>
<th>Option</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>To a private practising primary physician (PCP)</td>
<td>151</td>
</tr>
<tr>
<td>To the hospital / Primary health complex</td>
<td>122</td>
</tr>
<tr>
<td>To a community health workers</td>
<td>31</td>
</tr>
<tr>
<td>To the religious people/Fakir for ‘tabeej’ or ‘panipora’</td>
<td>86</td>
</tr>
<tr>
<td>To the traditional healers</td>
<td>254</td>
</tr>
<tr>
<td>None</td>
<td>5</td>
</tr>
</tbody>
</table>

Over 87% of the families had gone to the traditional healers (Kabiraj, religious person) before and after starting AEDs treatment.

The traditional healers’ usual practices of treating seizures

The samams and kabiraj treat with one or a combination of the following: herbal medicine, burns a spot on the forehead with a heated rod, places a very young baby on earth with a circle of fire around it, beats the person with his ‘holy stick’ with belief that it was treating the evil spirit and/or ‘jhar-fuk’ which means the healer blows on the person with epilepsy, reciting his magic words. The Religious people usually provides ‘tabeej’ to be tied on the person’s hand or feet or use as a pendant, or ‘panipora’ or holy water for the patient to drink.

Parents’ existing knowledge of seizures/epilepsy

Q. Do you have any idea about the problem, ever heard about epilepsy/ mrigi rogi?

Why it occurs to some people?

Table 6.2.2: Parents' existing knowledge of seizures and epilepsy:

<table>
<thead>
<tr>
<th>Reason</th>
<th>On first visit</th>
<th>After epilepsy education</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Bad wind or evil spirit</td>
<td>193</td>
<td>0</td>
</tr>
<tr>
<td>2. Don't know</td>
<td>164</td>
<td>94</td>
</tr>
<tr>
<td>3. Chronic illness (mrigi rogi)</td>
<td>56</td>
<td>225</td>
</tr>
<tr>
<td>4. Psychological problem (mathakharap)</td>
<td>10</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>423</td>
<td>319</td>
</tr>
</tbody>
</table>
Most of the parents’ asked, whether seizures or epilepsy are contagious or not, and hereditary or not. One hundred and ninety-three (45.6%) parents believed that epilepsy is a ‘sacred’ disease, 38.8% parents did not know about epilepsy and/or never have heard about it.

Only 13.2% of the parents believed that epilepsy (mrigi rog in Bangla) is a chronic illness, 2.3% believed that it is a psychological problem.

The same questions were asked after educational induction when 70.5% accepted that epilepsy is a chronic illness, 29.5% said they did not know or probably a sacred disease.

Question asked to the family: where do you take your child for any other illness, or who treats other general illnesses or where did you take your child during the last illness?

Thirty six percent of parents said that they took the advice of the nearest practising doctor at the market place, 25% from the community health workers who are trained for diarrhoeal diseases and respiratory tract infections, 20% informed they went to the district hospital for their children’s last illness, 8.7% went to the thana health complex (primary health care centres). Only 7% took the advice of ‘traditional healers’ while more than 80% did so for their child’s seizure problem with the belief that it is an evil spirit causing the attacks.

6.10.3: Pregnancy and birth related problems (Table 6.3)

Place of birth

Over 65% of the births took place at home with the help of a traditional birth attendant or family members. Another 33 (7.8%) labours started at home with help from the traditional birth attendants (TBAs) but ended up at hospital by assisted delivery due to prolonged, obstructed second stage of labour.

Mode of delivery

The majority were normal vaginal deliveries. Assisted deliveries by forceps or caesarean section occurred in 17.5% of deliveries.
Estimated gestational age
Preterm delivery was recorded in 6.1%, and 85% were full-term babies.

Antenatal check ups, maternal age and medical problem during the pregnancy
Over one third of the population had anti-natal check ups, and another 32.5% had visited the primary health centres at least twice for vaccination against tetanus and they had blood pressure, oedema and pallor check ups. Thirty six percent had never had a health check ups but had been vaccinated against tetanus during their pregnancy. Maternal median-age during the related pregnancy was 23 years, the youngest age being 14 years, 39 of the mothers were between 14 to 18 years of age during the related pregnancy.

Any problems detected during the pregnancy
Medical problems such as diabetes or high blood pressure were detected in 10.4%, 11.1% of the mothers were suspected to have suffered from german measles or other viral infections during their first trimester. About 2% reported taking an abortificient and another 2% had suffered psychosocial problems. Accidental or non-accidental injury during the third trimester was reported in 5 mothers. A poor obstetric history (Section 4.5.3) was recorded among 97 (22.9%) mothers.

These data may help to plan antenatal care in the community in collaboration with EPI programme as it was identified from this study that more than 63% of the mothers were aware of birth related tetanus in the new-born and voluntarily went to the EPI centre for prevention. Antenatal care and birth by a trained traditional birth attendant (TTBA) may help to reduce the preventable childhood epilepsy, which are caused by pre-, peri-, and post-natal problems.
Table 6.3: Pregnancy and birth related information (Total- 423)

<table>
<thead>
<tr>
<th>Items</th>
<th>Total</th>
<th>%</th>
<th>OPD</th>
<th>%</th>
<th>CDC</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Place of birth</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Home</td>
<td>277</td>
<td>65.5</td>
<td>178</td>
<td>72.2</td>
<td>99</td>
<td>57.2</td>
</tr>
<tr>
<td>Hospital</td>
<td>146</td>
<td>34.5</td>
<td>72</td>
<td>28.8</td>
<td>74</td>
<td>42.8</td>
</tr>
<tr>
<td>Total</td>
<td>423</td>
<td>100</td>
<td>250</td>
<td>100</td>
<td>173</td>
<td>100</td>
</tr>
<tr>
<td>2. Mode of delivery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>348</td>
<td>82.5</td>
<td>220</td>
<td>88.0</td>
<td>128</td>
<td>73.8</td>
</tr>
<tr>
<td>El. C/S</td>
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<td>11.8</td>
<td>22</td>
<td>8.8</td>
<td>28</td>
<td>16.2</td>
</tr>
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<td>Em. C/S</td>
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<td></td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Forceps</td>
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<td></td>
<td>5</td>
<td></td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>423</td>
<td>100</td>
<td>250</td>
<td>100</td>
<td>173</td>
<td>100</td>
</tr>
<tr>
<td>3. Labour assisted by</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TBA</td>
<td>209</td>
<td>49.4</td>
<td>127</td>
<td>50.8</td>
<td>82</td>
<td>47.4</td>
</tr>
<tr>
<td>F. member</td>
<td>64</td>
<td>15.1</td>
<td>48</td>
<td>19.2</td>
<td>16</td>
<td>9.2</td>
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<tr>
<td>Dr. /nurse</td>
<td>150</td>
<td>35.5</td>
<td>75</td>
<td>30.0</td>
<td>75</td>
<td>43.4</td>
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<tr>
<td>4. Gestational age</td>
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<td>Full-term</td>
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<td>84.9</td>
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<td>16</td>
<td>9.2</td>
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<td>0.8</td>
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<td>2.9</td>
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<td>31</td>
<td>7.3</td>
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<td>9.2</td>
<td>8</td>
<td>4.6</td>
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<tr>
<td>Total</td>
<td>423</td>
<td>100</td>
<td>250</td>
<td>100</td>
<td>173</td>
<td>100</td>
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<td>5. A/N check-ups</td>
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<tr>
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<td>37.6</td>
<td>59</td>
<td>34.1</td>
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<td>Regular</td>
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<td>77</td>
<td>30.8</td>
<td>56</td>
<td>32.4</td>
</tr>
<tr>
<td>Total</td>
<td>423</td>
<td>100</td>
<td>250</td>
<td>100</td>
<td>173</td>
<td>100</td>
</tr>
<tr>
<td>6. Pregnancy problem</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>None</td>
<td>310</td>
<td>73.3</td>
<td>193</td>
<td>77.2</td>
<td>117</td>
<td>67.6</td>
</tr>
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<td>Medical</td>
<td>44</td>
<td>10.4</td>
<td>20</td>
<td>8.0</td>
<td>24</td>
<td>13.9</td>
</tr>
<tr>
<td>Susp. IUI.</td>
<td>47</td>
<td>11.1</td>
<td>25</td>
<td>10.0</td>
<td>22</td>
<td>12.7</td>
</tr>
<tr>
<td>Abortifcient</td>
<td>8</td>
<td>1.9</td>
<td>5</td>
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</tr>
<tr>
<td>Psychosocial</td>
<td>9</td>
<td>2.1</td>
<td>5</td>
<td></td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Accident</td>
<td>5</td>
<td></td>
<td>2</td>
<td></td>
<td>3</td>
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<td>Total</td>
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<td>250</td>
<td>100</td>
<td>173</td>
<td>100</td>
</tr>
<tr>
<td>7. Maternal age at preg.</td>
<td>Mean, Median, (min.&amp;max.) Range in years</td>
<td>23.79, 23, (14 &amp; 40), 28</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Obstetric history</td>
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<tr>
<td>Abortion</td>
<td>70</td>
<td>16.5</td>
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<td>14.4</td>
<td>34</td>
<td>19.7</td>
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<tr>
<td>Stillbirth</td>
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<td>11</td>
<td>4.4</td>
<td>11</td>
<td>6.4</td>
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<tr>
<td>IUD</td>
<td>5</td>
<td>1.2</td>
<td>4</td>
<td>1.6</td>
<td>1</td>
<td>0.6</td>
</tr>
<tr>
<td>Total</td>
<td>97</td>
<td>22.9</td>
<td>51</td>
<td>20.4</td>
<td>46</td>
<td>26.6</td>
</tr>
</tbody>
</table>

El, elective; em, emergency; C/S, caesarean section; TT inj, tetanus toxoid injection;
susp, suspected; IUI, intra-uterine infection; IUD, intra-uterine death, preg, pregnancy.

Pre-term= birth >3 wks earlier than EDD; Post-term= birth >2wks later than EDD.
History of past events as a clue to an early cerebral lesion

Table 6.3.1: History of Event(s) associated (N = 423)

<table>
<thead>
<tr>
<th>Events</th>
<th>Total (423) %</th>
<th>OPD(250) %</th>
<th>CDC(173) %</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>129 30.5</td>
<td>89 35.6</td>
<td>40 23.1</td>
</tr>
<tr>
<td>P.A</td>
<td>165 39.0</td>
<td>82 32.8</td>
<td>78 45.7</td>
</tr>
<tr>
<td>N.S</td>
<td>132 31.2</td>
<td>61 24.4</td>
<td>71 41.0</td>
</tr>
<tr>
<td>P.A + N.S</td>
<td>85 20.1</td>
<td>46 18.4</td>
<td>40 23.1</td>
</tr>
<tr>
<td>CNS infection</td>
<td>29 6.9</td>
<td>13 5.2</td>
<td>15 8.7</td>
</tr>
<tr>
<td>Head injury</td>
<td>7 1.7</td>
<td>6 2.4</td>
<td>1 .6</td>
</tr>
</tbody>
</table>

In children who were followed-up (319)

| P.A              | 119 37.3 |
| Epilepsy type    |          |
| Symptomatic      | 67 56.3  |
| Cryptogenic      | 28 23.5  |
| Idiopathic       | 24 20.2  |

| N.S              | 110 34.5 |
| Epilepsy type    |          |
| Symptomatic      | 65 59.0  |
| Cryptogenic      | 28 25.5  |
| Idiopathic       | 17 15.5  |

P.A, perinatal asphyxia; N.S, neonatal seizure; CNS, central nervous system.

History of perinatal asphyxia, neonatal seizures

These have been defined elsewhere (Section 4.5.1 and 4.5.2)

Difficult, prolonged labour followed by perinatal asphyxia was recorded in 165 (39%) of the children, which was more frequent in the CDC group (45.7%) compared to 32% in the community group. More than half had hospital evidence of severe asphyxia. Others did not have hospital management but the history was suggestive of having perinatal asphyxia.

History of neonatal seizures

Positive history of neonatal seizure was recorded in 29% of the total population, which again was more frequently noted in the CDC group (42%).

Epilepsy type and seizure outcome after treatment

80% of the children who had positive history of perinatal asphyxia and 84% who had positive history of neonatal seizures had had diagnoses of symptomatic and cryptogenic epilepsy. After one year’s regular treatment 47.1% of the children with
perinatal asphyxia and 44.5% of the children with neonatal seizures had ‘seizure remission’.

6.10.4: Epilepsy profile

Child and seizure related profile (Table 6.4)

Age at presentation
Two thirds of the population were less than 3 years of age at first presentation. Median age at presentation was 22 months, which was a little higher (26 months) in the community group than in the CDC group (15 months). Gender distribution was 2.2:1 in the total population, which was 3.2:1 in CDC group.

Age at seizure onset
The median age at onset of epileptic seizures was 8 months in the total population, 12 months in the community group and 5 months in the CDC group. Over 71% of the CDC children had an ‘early age of seizure onset’ (Section 4.3.1, point 10). Over 50% of them had started seizures during early infancy period before 4 months of age (66 out of 124). In the total population 118 children had started seizures before 3-4 months of age. (Table 6.4)

Seizure types
Children with a ‘single seizure type’ were greater in number than those with ‘multiple seizure types’. Among the whole population 28.4 % had multiple seizures types and among the 319 children with epilepsy who had been followed up for one year 32.3% had multiple seizure types.

Seizure frequency
This was high in all groups. High rates of seizures were recorded in the whole population. Among the 390 children, high rate of seizure was recorded in 73.8% and this was recorded in 75.5% among the 319 children.
Family history of epilepsy

This was noted in 7.1% population when first-degree relatives were counted and 13.5% when the history for second and third degree relatives were taken into account.

Table 6.4: Child and Seizure related information

<table>
<thead>
<tr>
<th>Information</th>
<th>Total</th>
<th>%</th>
<th>OPD</th>
<th>%</th>
<th>CDC</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Age at presentation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2mo-1yr</td>
<td>145</td>
<td>34.3</td>
<td>72</td>
<td>28.8</td>
<td>73</td>
<td>42.2</td>
</tr>
<tr>
<td>&gt;1yr-3yr</td>
<td>134</td>
<td>31.7</td>
<td>78</td>
<td>31.2</td>
<td>58</td>
<td>33.5</td>
</tr>
<tr>
<td>&gt;3-5 yr</td>
<td>50</td>
<td>13.7</td>
<td>33</td>
<td>15.2</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>&gt;5-7 yr</td>
<td>37</td>
<td>9.5</td>
<td>20</td>
<td>12.6</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>&gt;7-10 yr</td>
<td>32</td>
<td>8.1</td>
<td>20</td>
<td>13.9</td>
<td>28</td>
<td>17</td>
</tr>
<tr>
<td>&gt;10-13 yr</td>
<td>19</td>
<td>4.8</td>
<td>16</td>
<td>10.5</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>&gt;13-15 yr</td>
<td>3</td>
<td>0.8</td>
<td>3</td>
<td>1.9</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mean, median, IQR(in mo)</td>
<td>37.61</td>
<td>22</td>
<td>44.54</td>
<td>26</td>
<td>27.60</td>
<td>15</td>
</tr>
<tr>
<td>2. Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>289</td>
<td>68.3</td>
<td>157</td>
<td>62.8</td>
<td>132</td>
<td>76.3</td>
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<tr>
<td>Female</td>
<td>134</td>
<td>31.7</td>
<td>93</td>
<td>36.2</td>
<td>41</td>
<td>23.7</td>
</tr>
<tr>
<td>3. Age at onset</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early</td>
<td>257</td>
<td>60.8</td>
<td>122</td>
<td>48.8</td>
<td>124</td>
<td>71.7</td>
</tr>
<tr>
<td>After 12 mo</td>
<td>166</td>
<td>39.2</td>
<td>128</td>
<td>51.2</td>
<td>49</td>
<td>28.3</td>
</tr>
<tr>
<td>Mean, med, IQR in mo.</td>
<td>22.47</td>
<td>8</td>
<td>29.21</td>
<td>12</td>
<td>13.97</td>
<td>5</td>
</tr>
<tr>
<td>4. Seizure type</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>303</td>
<td>71.6</td>
<td>203</td>
<td>81.2</td>
<td>98</td>
<td>56.6</td>
</tr>
<tr>
<td>Multiple</td>
<td>120</td>
<td>28.4</td>
<td>47</td>
<td>18.8</td>
<td>75</td>
<td>43.4</td>
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<td>5. Seizure rate</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>High</td>
<td>290</td>
<td>68.6</td>
<td>154</td>
<td>61.6</td>
<td>136</td>
<td>78.6</td>
</tr>
<tr>
<td>Low</td>
<td>133</td>
<td>31.4</td>
<td>96</td>
<td>37.4</td>
<td>37</td>
<td>21.4</td>
</tr>
<tr>
<td>6. H/O febrile seizures</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>357</td>
<td>84.4</td>
<td>201</td>
<td>80.4</td>
<td>155</td>
<td>89.6</td>
</tr>
<tr>
<td>Present</td>
<td>66</td>
<td>15.6</td>
<td>49</td>
<td>19.6</td>
<td>18</td>
<td>10.4</td>
</tr>
<tr>
<td>7. Family H/O epilepsy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st degree</td>
<td>30</td>
<td>7.1</td>
<td>18</td>
<td>7.2</td>
<td>12</td>
<td>6.9</td>
</tr>
<tr>
<td>1st, &amp; 2nd degree</td>
<td>57</td>
<td>13.5</td>
<td>37</td>
<td>14.8</td>
<td>20</td>
<td>11.6</td>
</tr>
</tbody>
</table>

Early, at or before 12 mo. age; mo, month; IQR, interquartile; med, median.
Seizure classification
More than one third of the population had generalised tonic-clonic seizures. The next commonest seizure type was myoclonic seizures followed by generalised tonic seizures (Table 6.4). About 8% of the children had 3 types of seizure at first presentation.

Epilepsy classification
Primary generalised epilepsy was diagnosed in 67%, partial and secondarily generalised epilepsy in 26.4% and 6.4% remained unclassifiable when classification was based on the clinical history at first presentation. Subsequent classification was based on clinical history and EEG findings, which gave a 14.4% increase in partial epilepsy (Table-6.5); 17.7% of those with primary generalised epilepsy diagnosed on the basis of clinical information had focal epileptiform discharges on EEG (Table 6.7), 4.9% remained unclassifiable.

Etiological classification
Based on the clinical history, examination findings and available investigations, an ‘idiopathic’ epilepsy was diagnosed in 162 (38.3%), definite ‘symptomatic and cryptogenic’ epilepsy was diagnosed in 240 (56.70%) who had clinical or investigative evidence of cortical damage. A small proportion was initially diagnosed as ‘remote symptomatic’ having had definite history of cerebral insult (CNS infection, head injury, perinatal asphyxia or neonatal seizures) but had not yet developed any clinical sign or had had neuroimaging (21, 5%). Later at 6 months follow up 3 among the remote symptomatic epilepsy children had been lost to follow up and 18 either developed evidence of cerebral damage or attained normal development and were categorized accordingly (Table 6.5). Among the children followed up for 12 months, a subsequent diagnosis was made based upon the clinical information and diagnostic evidences in which diagnosis of symptomatic and cryptogenic epilepsy was made in 64.6% and idiopathic epilepsy in 35.4%.
Table 6.5: Classification of seizures and epilepsies

<table>
<thead>
<tr>
<th>Items</th>
<th>Total</th>
<th>%</th>
<th>OPD</th>
<th>%</th>
<th>CDC</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Seizures</strong></td>
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<tr>
<td>GTCS</td>
<td>163</td>
<td>38.5</td>
<td>106</td>
<td>42.4</td>
<td>57</td>
<td>32.9</td>
</tr>
<tr>
<td>MC</td>
<td>141</td>
<td>33.3</td>
<td>56</td>
<td>22.4</td>
<td>85</td>
<td></td>
</tr>
<tr>
<td>GT</td>
<td>109</td>
<td>15.8</td>
<td>49</td>
<td>19.6</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>IS</td>
<td>80</td>
<td>18.9</td>
<td>24</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPS/ CPS</td>
<td>54</td>
<td>12.8</td>
<td>33</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multifocal sz</td>
<td>28</td>
<td>6.6</td>
<td>22</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GCL</td>
<td>24</td>
<td>5.7</td>
<td>7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absence (typical)</td>
<td>6</td>
<td>1.4</td>
<td>3</td>
<td>1.2</td>
<td>3</td>
<td>1.7</td>
</tr>
<tr>
<td>Atonic</td>
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<td>0.9</td>
<td>1</td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>2. Epilepsy (clinical)</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>P. generalised</td>
<td>255</td>
<td>65.4</td>
<td>144</td>
<td>64.3</td>
<td>111</td>
<td>66.9</td>
</tr>
<tr>
<td>S. generalised</td>
<td>56</td>
<td>14.4</td>
<td>40</td>
<td>17.9</td>
<td>16</td>
<td>9.6</td>
</tr>
<tr>
<td>Partial</td>
<td>40</td>
<td>10.3</td>
<td>25</td>
<td>11.2</td>
<td>15</td>
<td>9.0</td>
</tr>
<tr>
<td>Mixed partial&amp;gen.</td>
<td>39</td>
<td>10.0</td>
<td>15</td>
<td>6.6</td>
<td>24</td>
<td>14.5</td>
</tr>
<tr>
<td>Total</td>
<td>390</td>
<td>100</td>
<td>224</td>
<td>100</td>
<td>166</td>
<td>100</td>
</tr>
<tr>
<td>Epilepsy (clinical&amp;EEG)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Generalised</td>
<td>205</td>
<td>52.6</td>
<td>117</td>
<td>52.2</td>
<td>88</td>
<td>53.0</td>
</tr>
<tr>
<td>Partial &amp; S. gen.</td>
<td>165</td>
<td>42.3</td>
<td>99</td>
<td>44.2</td>
<td>66</td>
<td>39.8</td>
</tr>
<tr>
<td>Unclassified</td>
<td>20</td>
<td>5.2</td>
<td>8</td>
<td>3.6</td>
<td>12</td>
<td>7.2</td>
</tr>
<tr>
<td>Total</td>
<td>390</td>
<td>100</td>
<td>224</td>
<td>100</td>
<td>166</td>
<td>100</td>
</tr>
<tr>
<td><strong>Etiological</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Idiopathic</td>
<td>135</td>
<td>34.6</td>
<td>105</td>
<td>46.9</td>
<td>30</td>
<td>18.1</td>
</tr>
<tr>
<td>Sympt.&amp;crypt.</td>
<td>236</td>
<td>60.5</td>
<td>103</td>
<td>46.0</td>
<td>113</td>
<td>80.1</td>
</tr>
<tr>
<td>Remote sympt.</td>
<td>19</td>
<td>4.9</td>
<td>16</td>
<td>7.1</td>
<td>3</td>
<td>1.8</td>
</tr>
<tr>
<td>Total</td>
<td>390</td>
<td>100</td>
<td>224</td>
<td>100</td>
<td>166</td>
<td>100</td>
</tr>
</tbody>
</table>

P. gen, primary generalised; S. gen, secondary generalised; sympt, symptomatic; crypt, cryptogenic.
Table 6.6: Diagnosis of ‘malignant epilepsy syndrome’ in 390 & 319 children

<table>
<thead>
<tr>
<th>M.E.S</th>
<th>Total</th>
<th>%</th>
<th>OPD</th>
<th>%</th>
<th>CDC</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. M.E.S in 390 children</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None diagnosed</td>
<td>269</td>
<td>69.0</td>
<td>173</td>
<td>77.2</td>
<td>96</td>
<td>57.8</td>
</tr>
<tr>
<td>Diagnosed</td>
<td>121</td>
<td>31.0</td>
<td>51</td>
<td>22.8</td>
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<td>42.2</td>
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<tr>
<td>Total</td>
<td>390</td>
<td>100</td>
<td>224</td>
<td>100</td>
<td>166</td>
<td>100</td>
</tr>
<tr>
<td>I.S</td>
<td>80</td>
<td>66</td>
<td>36</td>
<td>70.6</td>
<td>45</td>
<td>64.3</td>
</tr>
<tr>
<td>M.C.E</td>
<td>27</td>
<td>22.3</td>
<td>12</td>
<td>23.5</td>
<td>16</td>
<td>22.9</td>
</tr>
<tr>
<td>L.G.S.</td>
<td>11</td>
<td>9.0</td>
<td>3</td>
<td>5.9</td>
<td>8</td>
<td>11.4</td>
</tr>
<tr>
<td>L.K.S.</td>
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<td>0.8</td>
<td>0</td>
<td>1.4</td>
<td></td>
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</tr>
<tr>
<td>Total</td>
<td>121</td>
<td>100.0</td>
<td>51</td>
<td>100.0</td>
<td>70</td>
<td>100.0</td>
</tr>
</tbody>
</table>

2. M.E.S in 319 children

<p>| | | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>223</td>
<td>69.9</td>
<td>136</td>
<td>77.7</td>
<td>87</td>
<td>60.4</td>
</tr>
<tr>
<td>Diagnosed</td>
<td>96</td>
<td>30.1</td>
<td>39</td>
<td>22.3</td>
<td>57</td>
<td>39.6</td>
</tr>
<tr>
<td>Total</td>
<td>319</td>
<td>100</td>
<td>175</td>
<td>100</td>
<td>144</td>
<td>100</td>
</tr>
</tbody>
</table>

EEG characteristic pattern in 319

<p>| | | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypsarrhythmia</td>
<td>34</td>
<td>58.6</td>
<td>14</td>
<td>60.9</td>
<td>20</td>
<td>57.1</td>
</tr>
<tr>
<td>LGS like pattern</td>
<td>10</td>
<td>18.2</td>
<td>2</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Burst suppression</td>
<td>7</td>
<td>12.1</td>
<td>3</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PLED</td>
<td>5</td>
<td>8.6</td>
<td>3</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CSWS</td>
<td>2</td>
<td>3.4</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Char.EEG pattern</td>
<td>58</td>
<td>18.2</td>
<td>23</td>
<td>13.1</td>
<td>35</td>
<td>21.7</td>
</tr>
</tbody>
</table>

Malignant epilepsy syndrome; IS, infantile spasms; MCE, myoclonic encephalopathy; LGS, Lennox Gastaut syndrome; LKS, Landau Kleffner syndrome; PLED, periodic lateralized epileptiform discharges; CSWS, continuous spike wave of slow sleep; char, characteristic.

Malignant epilepsy syndrome (Table 6.6)

A malignant epilepsy syndrome was diagnosed on first presentation in 31% of the 390 children with first diagnosis of epilepsy. The majority were diagnosed with infantile spasms and myoclonic encephalopathy, followed by Lennox-Gastaut syndrome. Among the 319 children followed up for one year 96(30.1%) were clinically diagnosed as having a malignant epilepsy syndrome. Recognisable characteristic patterns (Section 4.10.2) in EEG were diagnosed in 58 (18.2%), which was more frequently
found in CDC group, 21.7%. Twenty-five in this group of patients were lost to follow up (Table 6.6).

Table 6.7: Correlation between epileptiform discharges in EEG & clinical diagnosis in 319 patients

<table>
<thead>
<tr>
<th>Epileptiform discharges</th>
<th>Clinical diagnosis of epilepsy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Generalised</td>
</tr>
<tr>
<td>Generalised discharges</td>
<td>40</td>
</tr>
<tr>
<td>Focal or multifocal Discharges</td>
<td>75 (17.7%)</td>
</tr>
<tr>
<td>No discharges</td>
<td>92</td>
</tr>
<tr>
<td>Total</td>
<td>207</td>
</tr>
</tbody>
</table>

17.7% of the initially diagnosed primary generalised epilepsies were later diagnosed as partial epilepsy on the basis of EEG findings.

6.10.5: Non-convulsive disorders (Table 6.8)

More than half of the total population had either mild to severe motor disorder and/or cognitive impairment at first presentation. About three quarters of the CDC population had associated non-convulsive disorders when less than half of the newly diagnosed (OPD) population were positive for associated impairments.
Table 6.8: Associated non-convulsive disorders (Total 423)

<table>
<thead>
<tr>
<th>Disorders</th>
<th>Total</th>
<th>%</th>
<th>OPD</th>
<th>%</th>
<th>CDC</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Any disorder</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>242</td>
<td>57.2</td>
<td>113</td>
<td>45.2</td>
<td>129</td>
<td>74.6</td>
</tr>
<tr>
<td>Absent</td>
<td>181</td>
<td>42.8</td>
<td>137</td>
<td>54.8</td>
<td>44</td>
<td>25.4</td>
</tr>
<tr>
<td>Total</td>
<td>423</td>
<td>100</td>
<td>250</td>
<td>100</td>
<td>173</td>
<td>100</td>
</tr>
<tr>
<td><strong>2. Motor disorder</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>67</td>
<td>15.8</td>
<td>34</td>
<td>13.6</td>
<td>33</td>
<td>19.1</td>
</tr>
<tr>
<td>Moderate</td>
<td>15</td>
<td>5.2</td>
<td>5</td>
<td>2.0</td>
<td>10</td>
<td>5.8</td>
</tr>
<tr>
<td>Severe</td>
<td>137</td>
<td>32.4</td>
<td>58</td>
<td>23.2</td>
<td>79</td>
<td>45.7</td>
</tr>
<tr>
<td><strong>3. Cogn.imp.(clinic.jud)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>230</td>
<td>54.4</td>
<td>109</td>
<td>43.6</td>
<td>121</td>
<td>69.9</td>
</tr>
<tr>
<td>Absent</td>
<td>177</td>
<td>41.8</td>
<td>136</td>
<td>54.4</td>
<td>41</td>
<td>23.7</td>
</tr>
<tr>
<td>Uncertain</td>
<td>16</td>
<td>3.8</td>
<td>5</td>
<td>2.0</td>
<td>11</td>
<td>6.4</td>
</tr>
<tr>
<td>Cognitive imp.(IQ)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;70</td>
<td>258</td>
<td>61.0</td>
<td>123</td>
<td>49.2</td>
<td>135</td>
<td>78.0</td>
</tr>
<tr>
<td>&gt;70</td>
<td>165</td>
<td>39.0</td>
<td>127</td>
<td>50.8</td>
<td>38</td>
<td>22.0</td>
</tr>
<tr>
<td>Total</td>
<td>423</td>
<td>100</td>
<td>250</td>
<td>100</td>
<td>173</td>
<td>100</td>
</tr>
</tbody>
</table>

In 319 children

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>%</th>
<th>OPD</th>
<th>%</th>
<th>CDC</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>108</td>
<td>33.9</td>
<td>82</td>
<td>46.9</td>
<td>26</td>
<td>18.0</td>
</tr>
<tr>
<td>Any disorder</td>
<td>211</td>
<td>66.1</td>
<td>93</td>
<td>53.1</td>
<td>118</td>
<td>82.0</td>
</tr>
</tbody>
</table>

Motor disorder

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>%</th>
<th>OPD</th>
<th>%</th>
<th>CDC</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>148</td>
<td>46.4</td>
<td>43</td>
<td>24.6</td>
<td>105</td>
<td>72.9</td>
</tr>
<tr>
<td>Absent</td>
<td>171</td>
<td>53.6</td>
<td>132</td>
<td>75.4</td>
<td>39</td>
<td>27.1</td>
</tr>
</tbody>
</table>

Cogn. imp.

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>%</th>
<th>OPD</th>
<th>%</th>
<th>CDC</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>192</td>
<td>60.2</td>
<td>86</td>
<td>49.1</td>
<td>106</td>
<td>73.6</td>
</tr>
<tr>
<td>Absent</td>
<td>127</td>
<td>39.8</td>
<td>89</td>
<td>50.9</td>
<td>38</td>
<td>26.4</td>
</tr>
<tr>
<td>Total</td>
<td>319</td>
<td>100</td>
<td>175</td>
<td>100</td>
<td>144</td>
<td>100</td>
</tr>
</tbody>
</table>

Cogn, cognitive; imp, impairment; clinic.jud, clinician's judgement; IQ, intelligence quotient; chil, children.

The majority (70.5%) of the CDC group had an associated motor disorder and this was present in 38.8% of the OPD population at first presentation.

Cognitive impairment was more frequently observed non-convulsive disorder, but the majority had both motor and cognitive impairments. More than one third of the population had visual and hearing impairments in addition to psychomotor disability on first day of assessment.
Consensual diagnosis of cognitive impairment

The PCP's diagnosis of cognitive impairment based on the clinical judgment was correlated with the categorized result of the formal IQ test done by the psychologist, which shows significant chi square correlation with two tailed significance level < 0.01, odds ratio 3.08, CI 2.47, to 3.85.

Table 6.9: Correlation between cognitive impairment diagnosed on clinical judgment and on IQ test

<table>
<thead>
<tr>
<th>Based on clinical judgment</th>
<th>Based on IQ score</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&gt;70</td>
<td>&lt;70</td>
<td>Total</td>
</tr>
<tr>
<td>Seem age appropriate</td>
<td>94</td>
<td>19</td>
<td>113</td>
</tr>
<tr>
<td>% Total</td>
<td>29.5%</td>
<td>6.0%</td>
<td>35.4%</td>
</tr>
<tr>
<td>Poor for the age</td>
<td>27</td>
<td>164</td>
<td>191</td>
</tr>
<tr>
<td>% Total</td>
<td>7.8%</td>
<td>52.0%</td>
<td>59.9%</td>
</tr>
<tr>
<td>Uncertain</td>
<td>6</td>
<td>9</td>
<td>15</td>
</tr>
<tr>
<td>% Total</td>
<td>1.9%</td>
<td>2.8%</td>
<td>4.7%</td>
</tr>
<tr>
<td>Total</td>
<td>127</td>
<td>192</td>
<td>319</td>
</tr>
<tr>
<td>% Total</td>
<td>39.8%</td>
<td>60.2%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Pearson chi-square is significant at < 0.01 level (2 tailed)
6.10.6: Investigation (Table 6.10)

**EEG**

EEG was performed in 383 patients; 40 children were not brought for the test or could not be traced for follow-up. One third of these children (118, 30.8%) had a normal EEG record for the age and state of the child of which 78% were in the OPD group. Among the total EEGs, about 70% had abnormal features in the recording.

*When the EEG findings were categorized (Section 4.10.1)*

Over one third (119, 31.1%) of the abnormal records revealed both epileptiform discharges and background abnormal activities. Among the rest 88 (23%) children had only epileptiform discharges and 58 (15.1%) (62% of these from CDC) had only background abnormality but no epileptiform discharges. Abnormal background activities were found among 179 children of which, 60% were from CDC group. Among the records with abnormal background activities 68(17.8) revealed characteristic EEG pattern with poverty of normal rhythmic activities in the background.

*Inter-rater agreement test (Section 6.6.10)*

The inter-rater reliability of the two neurophysiologists’ reports on 383 EEGs was tested. The un-weighted kappa measure of agreement between the two neurophysiologists’ reports was 0.93 ($k = 0.93$), which according to standard interpretation is ‘very good’ (Landis & Koch 1977). This $k$ value was obtained when normal or abnormal EEG, presence or absence of epileptiform discharges or background abnormality were considered.

The same statistical measure was used for testing the agreement on the presence or absence of characteristic EEG pattern. The kappa measure was 0.64, which according to standard interpretation was ‘good’ ($k = 0.64$). Although there was no major difference of opinion about the presence or absence of the abnormal activities, the issue whether they constitute the diagnosis of specific pattern or not produced differences of opinion.
Table 6.10: Investigation and findings

<table>
<thead>
<tr>
<th>Tests</th>
<th>Total</th>
<th>OPD</th>
<th>CDC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>1. EEG</td>
<td></td>
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</tr>
<tr>
<td>Normal</td>
<td>118</td>
<td>92</td>
<td>26</td>
</tr>
<tr>
<td>Abnormal</td>
<td>265</td>
<td>130</td>
<td>135</td>
</tr>
<tr>
<td>Not done</td>
<td>40</td>
<td>28</td>
<td>12</td>
</tr>
<tr>
<td>Total</td>
<td>423</td>
<td>250</td>
<td>173</td>
</tr>
<tr>
<td>Only epil.disch</td>
<td>88</td>
<td>55</td>
<td>33</td>
</tr>
<tr>
<td>Only back.abn.</td>
<td>58</td>
<td>22</td>
<td>36</td>
</tr>
<tr>
<td>Both</td>
<td>119</td>
<td>53</td>
<td>66</td>
</tr>
<tr>
<td>Total</td>
<td>383</td>
<td>222</td>
<td>161</td>
</tr>
<tr>
<td>Epil.disch.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>176</td>
<td>114</td>
<td>62</td>
</tr>
<tr>
<td>Present</td>
<td>207</td>
<td>108</td>
<td>99</td>
</tr>
<tr>
<td>Total</td>
<td>383</td>
<td>222</td>
<td>161</td>
</tr>
<tr>
<td>Type of discharges</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Focal</td>
<td>100</td>
<td>62</td>
<td>38</td>
</tr>
<tr>
<td>Generalised</td>
<td>52</td>
<td>25</td>
<td>27</td>
</tr>
<tr>
<td>Multifocal</td>
<td>46</td>
<td>20</td>
<td>26</td>
</tr>
<tr>
<td>Gen. &amp; focal</td>
<td>9</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>207</td>
<td>108</td>
<td>99</td>
</tr>
<tr>
<td>Background activity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>204</td>
<td>147</td>
<td>55</td>
</tr>
<tr>
<td>Abnormal</td>
<td>179</td>
<td>75</td>
<td>106</td>
</tr>
<tr>
<td>Total</td>
<td>383</td>
<td>222</td>
<td>161</td>
</tr>
<tr>
<td>2. Neuroimaging reports</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal</td>
<td>131</td>
<td>53</td>
<td>78</td>
</tr>
<tr>
<td>Normal</td>
<td>56</td>
<td>41</td>
<td>15</td>
</tr>
<tr>
<td>Tests done</td>
<td>187</td>
<td>94</td>
<td>93</td>
</tr>
<tr>
<td>Abnormalities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrophy</td>
<td>76</td>
<td>28</td>
<td>48</td>
</tr>
<tr>
<td>Hydrocephalus</td>
<td>12</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Nonspecific</td>
<td>15</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Ischemic damage</td>
<td>11</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Leukomalacia</td>
<td>7</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Lissencephaly</td>
<td>5</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Tuberous sclerosis</td>
<td>5</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>131</td>
<td>53</td>
<td>78</td>
</tr>
</tbody>
</table>

Epil.dich, epileptiform discharges; back.abn., background abnormalities.
Table 6.11: Comparison of EEG reports by two reporters, NP1 was blind to the patients’ information and NP2 was aware of the patients’ information.

<table>
<thead>
<tr>
<th>EEG features</th>
<th>Neurophysiologist (NP1)</th>
<th>Neurophysiologist(NP2)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Normal record</td>
<td>123</td>
<td>32.1</td>
</tr>
<tr>
<td>Only epil.disch.</td>
<td>92</td>
<td>24.0</td>
</tr>
<tr>
<td>Only backg.abn.</td>
<td>53</td>
<td>13.8</td>
</tr>
<tr>
<td>Both present</td>
<td>115</td>
<td>30.1</td>
</tr>
<tr>
<td>Total</td>
<td>383</td>
<td>100</td>
</tr>
</tbody>
</table>

Epil.disch, Epileptiform discharges; backg.abn. background abnormality.

**Neuroimaging**

Some form of neuroimaging (USG, CT, MRI of brain) was done in 187 (44.2%) children of which, 70% were abnormal. The abnormal imaging reports comprised from most common cerebral atrophy, hydrocephalus, non-specific abnormality, ischemic damage, leukomalacia, lissencephaly and tuberous sclerosis (Table 6.10).

**6.10.7: Outcome (Table 6.12)**

**Seizure outcome**

‘Seizure remission’ was found in 168 (52.7%) of the whole population, 61.7% in OPD group and 41.7% in the CDC group. Another 19.4% had more than 50% seizure reduction and 6.6% >30 % sz reduction, 18.8% had < 30% seizure reduction. Two patients died, one 6 months and other 17 months after starting regular treatment, both had very early onset multiple type of seizures with severe developmental delay, and seizures were poorly controlled. However, the exact cause of death was unknown.

**Seizure remission in the patients without associated non-convulsive disorder**

Motor and cognitive functions were recorded as age appropriate in 108 (33.9%) children. Seizure remission occurred in 76.9%, 80.5% and 65.4% in the whole, newly
Seizure remission in children with non-convulsive disorders
Among 319 children, 211 (66.1%) had one or both of the disorders present on the day of diagnosis and of these 40% had 'seizure remission' 54-65% had no seizure remission. Of the latter 28.4% had no recognizable seizure control (0-<30%) (Table 6.12).

Seizure remission in children with malignant syndromes
The majority (58.3%) among total 96 children diagnosed as malignant syndrome (MS) had poor seizure remission. Similarly the majority (66.7%) of 57 children diagnosed as MS in the CDC group had poor seizure remission. In the OPD group 53% among 39 children with this diagnosis had seizure remission.
Table 6.12: Seizure outcome after regular AED treatment

<table>
<thead>
<tr>
<th>Sz. Outcome</th>
<th>Total</th>
<th>%</th>
<th>OPD</th>
<th>%</th>
<th>CDC</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. In all children</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sz. remission</td>
<td>168</td>
<td>52.7</td>
<td>108</td>
<td>61.7</td>
<td>60</td>
<td>41.7</td>
</tr>
<tr>
<td>Poor sz. rem.</td>
<td>151</td>
<td>47.3</td>
<td>67</td>
<td>38.3</td>
<td>84</td>
<td>58.3</td>
</tr>
<tr>
<td><strong>Sz. reduction rate</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100%</td>
<td>168</td>
<td>52.7</td>
<td>108</td>
<td>62.3</td>
<td>60</td>
<td>41.7</td>
</tr>
<tr>
<td>80-99%</td>
<td>47</td>
<td>14.7</td>
<td>24</td>
<td>13.7</td>
<td>23</td>
<td>16.0</td>
</tr>
<tr>
<td>50-79%</td>
<td>23</td>
<td>7.2</td>
<td>9</td>
<td>5.1</td>
<td>14</td>
<td>9.0</td>
</tr>
<tr>
<td>30-49%</td>
<td>21</td>
<td>6.6</td>
<td>10</td>
<td>5.7</td>
<td>11</td>
<td>7.6</td>
</tr>
<tr>
<td>&lt;30%</td>
<td>60</td>
<td>18.8</td>
<td>23</td>
<td>13.2</td>
<td>37</td>
<td>25.7</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>319</td>
<td>100</td>
<td>175</td>
<td>100</td>
<td>144</td>
<td>100</td>
</tr>
</tbody>
</table>

| **2. Without non-conv. dis.** |       |      |     |      |     |      |
| Seizure rem. | 83    | 76.9 | 66  | 80.5 | 17  | 65.4 |
| Poor sz. rem. | 25    | 23.1 | 16  | 20.5 | 9   | 34.6 |
| **Sz. reduction rate** |       |      |     |      |     |      |
| 100% | 83   | 76.8 | 66  | 80.5 | 17  | 65.3 |
| 80-99% | 16  | 14.8 | 10  | 12.2 | 6   | 23.1 |
| 50-79% | 6   | 5.6  | 4   | 4.9  | 2   | 7.7  |
| 30-49% | 3   | 2.8  | 2   | 2.4  | 1   | 3.9  |
| <30%  | 0    | 0    | 0   | 0    | 0   | 0    |
| **Total** | 108 | 100.0 | 82  | 100  | 26  | 100  |

| **3. With non-conv. dis.** |       |      |     |      |     |      |
| Sz. reduction |       |      |     |      |     |      |
| 100% | 85   | 40.3 | 43  | 46.2 | 42  | 35.6 |
| 80-99% | 33  | 15.6 | 17  | 18.3 | 16  | 13.6 |
| 50-79% | 15  | 7.1  | 3   | 3.2  | 12  | 10.2 |
| 30-49% | 18  | 8.5  | 8   | 8.6  | 10  | 8.5  |
| <30%  | 60   | 28.4 | 22  | 23.7 | 38  | 32.1 |
| **Total** | 211 | 100  | 93  | 100  | 118 | 100  |

| **4. With malg. synd.** |       |      |     |      |     |      |
| Seizure rem. | 40    | 41.7 | 21  | 53.8 | 19  | 33.3 |
| Poor sz. rem. | 56    | 58.3 | 18  | 46.2 | 38  | 66.7 |
| **Total** | 96   | 100  | 39  | 100  | 57  | 100  |

Chil, children; non-conv. dis, non-convulsive disorder; malg. synd, malignant syndrome; Sz. Rem, seizure remission;

Among the population with both motor and cognitive impairment present 31.2% had seizure remission (30.6% in OPD and 31.5% in CDC group) (Table-6.13).
Table 6.13: Seizure outcome in children having severe neurological deficit

Disability = motor & cognitive

<table>
<thead>
<tr>
<th>Seizure outcome</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seizure remission</td>
<td>41</td>
<td>31.0</td>
</tr>
<tr>
<td>Poor sz. remission</td>
<td>90</td>
<td>69.0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>132</strong></td>
<td><strong>100</strong></td>
</tr>
<tr>
<td>Sz. reduction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>80-99%</td>
<td>19</td>
<td>14.4</td>
</tr>
<tr>
<td>50-79%</td>
<td>14</td>
<td>11.2</td>
</tr>
<tr>
<td>30-49%</td>
<td>12</td>
<td>8.8</td>
</tr>
<tr>
<td>&lt;30%</td>
<td>46</td>
<td>34.4</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>132</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>

Table 6.14: Description of children who had poor seizure remission: Number 151

<table>
<thead>
<tr>
<th>Age at presentation</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 mo- 1 yr</td>
<td>60</td>
<td>39.7</td>
</tr>
<tr>
<td>&gt;1 - 3 yrs</td>
<td>43</td>
<td>28.5</td>
</tr>
<tr>
<td>&gt;2 - 5 yrs</td>
<td>18</td>
<td>11.9</td>
</tr>
<tr>
<td>&gt;5 - 7 yrs</td>
<td>16</td>
<td>10.6</td>
</tr>
<tr>
<td>&gt; 7 yrs</td>
<td>14</td>
<td>9.3</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>103</td>
<td>68.2</td>
</tr>
<tr>
<td>Female</td>
<td>48</td>
<td>31.8</td>
</tr>
<tr>
<td><strong>Seizure type</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>80</td>
<td>53.0</td>
</tr>
<tr>
<td>Multiple</td>
<td>71</td>
<td>47.0</td>
</tr>
<tr>
<td><strong>Seizure rate</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>124</td>
<td>82.1</td>
</tr>
<tr>
<td>Low</td>
<td>27</td>
<td>17.9</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diagnosis &amp; associated non-convulsive disorders</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant syndrome</td>
<td>56</td>
<td>37.1</td>
</tr>
<tr>
<td>Motor disability</td>
<td>95</td>
<td>62.9</td>
</tr>
<tr>
<td>IQ &lt; 70</td>
<td>118</td>
<td>78.1</td>
</tr>
<tr>
<td><strong>EEG</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal</td>
<td>125</td>
<td>82.8</td>
</tr>
<tr>
<td>Normal</td>
<td>26</td>
<td>17.2</td>
</tr>
<tr>
<td><strong>Background abn</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Background abn</td>
<td>26</td>
<td>17.2</td>
</tr>
<tr>
<td>Epileptiform disch</td>
<td>32</td>
<td>21.2</td>
</tr>
<tr>
<td>Both</td>
<td>67</td>
<td>44.4</td>
</tr>
</tbody>
</table>

In the newly diagnosed OPD children, 67 (38.3%) had poor seizure remission and of these, 46 (68.7%) had IQ less than 70 and 29 (43.3%) had motor disorder. The follow-up IQ test shows 76% had IQ less than 70, motor functional assessment on last follow up was improved in 4 children who had mild disability at entry (Table-6.15).
Table 6.15: Non-convulsive disorders in 67 OPD patients with poor seizure remission before and after treatment.

<table>
<thead>
<tr>
<th>Non-convulsive disorders</th>
<th>At entry %</th>
<th>last follow-up %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>24</td>
<td>28</td>
</tr>
<tr>
<td>Mild</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Moderate</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Severe</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Cognitive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IQ&lt; 70</td>
<td>46</td>
<td>51</td>
</tr>
<tr>
<td>Malignant syndrome</td>
<td>18</td>
<td>26.9</td>
</tr>
<tr>
<td>No neurodisability</td>
<td>17</td>
<td>25.4</td>
</tr>
</tbody>
</table>

6. 10.8: Predictors of seizure outcome

A list of potential predictors for seizure remission was presented in chapter five, section 5.3.15. The dependent variable was encoded as seizure remission “0” and no remission “1”. The reference category was 'seizure remission', the event category was 'poor seizure remission'. A univariate analysis with pearson’s chi-square test was performed to examine the independent relationship between the seizure remission and the independent predictors. P-value was considered significant, if it was 0.05 or less.

Univariate correlation with total population (Table 6.16)

Seven factors became significantly correlated with the 'poor seizure remission'. Only a family history of epilepsy had no significant correlation when tested with the whole population (319, newly diagnosed 175 + CDC group 144), (Group I). The factors which had independently significant correlation with the ‘poor seizure remission’ were i)malignant syndrome, ii) ‘associated motor disorder, iii) associated low IQ, iv) multiple types of seizure, v) high rate of seizure, vi) early onset epilepsy, and vii) abnormal EEG.
Table 6.16: Univariate analysis to see the main effect of predictors with seizure outcome.

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Poor seizure remission</th>
<th>Total</th>
<th>Odds ratio</th>
<th>95% Confidence interval</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>Yes</td>
<td></td>
<td>Lower limit</td>
<td>Upper limit</td>
</tr>
<tr>
<td>1. Malignant syndrome</td>
<td>133</td>
<td>90</td>
<td>223</td>
<td>2.575</td>
<td>1.571</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>Yes</td>
<td>35</td>
<td>61</td>
<td>96</td>
</tr>
<tr>
<td>2. Motor disorder</td>
<td>115</td>
<td>56</td>
<td>171</td>
<td>3.682</td>
<td>2.315</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>Yes</td>
<td>53</td>
<td>95</td>
<td>148</td>
</tr>
<tr>
<td>3. Low IQ</td>
<td>94</td>
<td>33</td>
<td>127</td>
<td>4.542</td>
<td>2.778</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>Yes</td>
<td>74</td>
<td>118</td>
<td>192</td>
</tr>
<tr>
<td>4. Family history of epilepsy</td>
<td>158</td>
<td>137</td>
<td>295</td>
<td>1.615</td>
<td>.659</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>Yes</td>
<td>10</td>
<td>14</td>
<td>24</td>
</tr>
<tr>
<td>5. Multiple seizures</td>
<td>136</td>
<td>80</td>
<td>216</td>
<td>3.772</td>
<td>2.287</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>Yes</td>
<td>32</td>
<td>71</td>
<td>108</td>
</tr>
<tr>
<td>6. High rate of seizure</td>
<td>54</td>
<td>24</td>
<td>78</td>
<td>2.506</td>
<td>1.456</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>Yes</td>
<td>114</td>
<td>127</td>
<td>241</td>
</tr>
<tr>
<td>7. Early onset of seizure</td>
<td>81</td>
<td>47</td>
<td>128</td>
<td>2.060</td>
<td>2.649</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>Yes</td>
<td>87</td>
<td>104</td>
<td>191</td>
</tr>
<tr>
<td>8. Abnormal EEG</td>
<td>73</td>
<td>25</td>
<td>98</td>
<td>3.879</td>
<td>2.261</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>Yes</td>
<td>95</td>
<td>126</td>
<td>221</td>
</tr>
<tr>
<td>Total</td>
<td>168</td>
<td>151</td>
<td>319</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 6.17: Multiple logistic regression analysis with 7 potential predictors

<table>
<thead>
<tr>
<th>Analysis Done</th>
<th>Independent variables</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Backward Stepwise Logistic Regression</td>
<td>Low IQ</td>
<td>3.126</td>
<td>1.746</td>
<td>5.59</td>
</tr>
<tr>
<td></td>
<td>Multiple seizure type</td>
<td>3.035</td>
<td>1.731</td>
<td>5.324</td>
</tr>
<tr>
<td></td>
<td>Motor disorder</td>
<td>1.813</td>
<td>1.047</td>
<td>3.140</td>
</tr>
</tbody>
</table>

*Predicted probability of membership for ‘poor seizure remission’. Contrast set at indicator, reference category first (when yes =1, no=0)

* Multiple logistic model excludes EEG.

* History of perinatal asphyxia, neonatal seizure did not cause any significant change when entered all.

Table 6.18: Multiple logistic regression analysis of predictors when EEG entered in-to the model

<table>
<thead>
<tr>
<th>Analysis Done</th>
<th>Variables entered</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Backward Stepwise Logistic Regression</td>
<td>Low IQ</td>
<td>2.915</td>
<td>1.611</td>
<td>5.274</td>
</tr>
<tr>
<td></td>
<td>Multiple seizure type</td>
<td>2.516</td>
<td>1.412</td>
<td>4.483</td>
</tr>
<tr>
<td></td>
<td>Motor disorder</td>
<td>1.718</td>
<td>0.982</td>
<td>3.005</td>
</tr>
<tr>
<td></td>
<td>Abnormal EEG</td>
<td>2.346</td>
<td>1.245</td>
<td>4.418</td>
</tr>
</tbody>
</table>

Multiple logistic regression analysis: (Table-6.17)
When multiple logistic regression analysis was done with 7 predictive factors excluding EEG, following three were the most significant predictors of poor seizure remission:

1. ‘Low IQ’ with odds ratio: 3.126, 95% CI 1.74 to 5.59, p value <0.001.
2. ‘Multiple seizure type’, with odds ratio 3.03, CI 1.73 to 5.32, and p value < 0.001
3. ‘Motor disorder’, with odds ratio 1.81, CI 1.047 to 3.140 and p value < .04.

No significant change was noted when EEG entered into the model. However, small change was noted with the p value of motor disorder, but this is non-significant, i.e. point estimate and confidence intervals are very similar. EEG had independent association with p 0.008; odds ratio 2.346; and CI 1.245 to 4.418. EEG did not affect other predictors in the model. Individual factors were entered into the model to see their effect on the estimate for EEG feature. There was no significant association found between EEG and other clinical factors when correlated with seizure outcome.

Table 6.19: Sensitivity and specificity of the predictors

<table>
<thead>
<tr>
<th>Prevalence of poor seizure remission, positive &amp; negative predictive value of the predictors</th>
<th>In total population</th>
<th>OPD</th>
<th>CDC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple seizure type:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>0.47</td>
<td>0.32</td>
<td>0.58</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.80</td>
<td>0.85</td>
<td>0.73</td>
</tr>
<tr>
<td>Motor disorder</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>0.63</td>
<td>0.43</td>
<td>0.79</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.68</td>
<td>0.87</td>
<td>0.35</td>
</tr>
<tr>
<td>Low IQ</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>0.78</td>
<td>0.69</td>
<td>0.86</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.56</td>
<td>0.63</td>
<td>0.43</td>
</tr>
<tr>
<td>Presence of any disability</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>0.83</td>
<td>0.75</td>
<td>0.64</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.49</td>
<td>0.60</td>
<td>0.28</td>
</tr>
</tbody>
</table>
Chart 6.2: Correlation between poor seizure remission and EEG features

![Chart showing the correlation between poor seizure remission and EEG features. The x-axis represents EEG features (Normal EEG, abnormal background only, epileptic discharge only, both) and the y-axis represents poor seizure remission. The line graph indicates an increasing trend in poor remission with more complex EEG features.]
6.10.9: Motor functional outcome

After a comprehensive management including medical treatment and developmental therapy, it was reported by the parents that the child’s alertness, understanding and functional ability started to improve. The parents’ opinion regarding their child’s functional abilities before and after treatment was obtained by a third person who did not have a direct involvement in the study. Motor function was re-assessed by the physician at the end of one year’s follow up.

Table 6.20: Parent’s perception about the child’s functional development after one year’s treatment

<table>
<thead>
<tr>
<th>Comments from parents</th>
<th>Motor function</th>
<th>Understanding</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Child is doing well</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very satisfied</td>
<td>150 (47.3)</td>
<td>127 (40.1)</td>
</tr>
<tr>
<td>2. Significant improvement</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quite satisfied</td>
<td>30 (9.5)</td>
<td>55 (17.4)</td>
</tr>
<tr>
<td>3. Some improvement</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fairly satisfied</td>
<td>45 (14.2)</td>
<td>47 (14.8)</td>
</tr>
<tr>
<td>4. No improvement but</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hopeful</td>
<td>35 (11.0)</td>
<td>30 (9.5)</td>
</tr>
<tr>
<td>5. No improvement and feeling</td>
<td></td>
<td></td>
</tr>
<tr>
<td>hopeless about functional dev</td>
<td>38 (12.0)</td>
<td>40 (12.6)</td>
</tr>
<tr>
<td>6. Deteriorated</td>
<td>19 (6.0)</td>
<td>18 (5.7)</td>
</tr>
<tr>
<td>Total</td>
<td>317 (100.0)</td>
<td>317 (100.0)</td>
</tr>
</tbody>
</table>

According to parents’ opinion functional developmental of 82 children had improved compared with before treatment. With parents feeling very satisfied, or fairly satisfied. Thirty-eight children had no improvement and parents felt hopeless, and 19 patients had deterioration of their functional ability.

According to physician’s assessment 63 children had improved in their motor functions. Sixteen children had deteriorated compared with the assessment results from the first day. These were overlapping with the parents’ assessment, however,
those who had some improvement according to parents’ opinion were not recorded as improved by the physician.

Table 6.21: Motor functional state after one year’s treatment (assessed by the PCP)

<table>
<thead>
<tr>
<th>Motor disability</th>
<th>At first day of assessment</th>
<th>At last follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>171</td>
<td>161</td>
</tr>
<tr>
<td>Mild</td>
<td>17</td>
<td>11</td>
</tr>
<tr>
<td>Moderate</td>
<td>19</td>
<td>38</td>
</tr>
<tr>
<td>Severe</td>
<td>135</td>
<td>107</td>
</tr>
<tr>
<td>Total</td>
<td>319</td>
<td>317</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cognitive impairment</th>
<th>At first day of assessment</th>
<th>At last follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>127</td>
<td>124</td>
</tr>
<tr>
<td>Mild</td>
<td>26</td>
<td>18</td>
</tr>
<tr>
<td>Moderate</td>
<td>31</td>
<td>50</td>
</tr>
<tr>
<td>Severe</td>
<td>135</td>
<td>125</td>
</tr>
<tr>
<td>Total</td>
<td>319</td>
<td>317</td>
</tr>
</tbody>
</table>

| Expired             | 2                         |

Total 319

6.10.10: Treatment

AEDs, Present medication

Over 32% of the patients were on phenobarbitone therapy at the one year’s follow-up. The next most common AED used was sodium valproate (25.1%), then carbamazepine (24.5%) followed by nitrazepam. Polytherapy was needed as maintenance in 83 (26.6%) children.

A response to a single drug (total or significant seizure control achieved by the AED started at the beginning of the study) was noted in 95 (29.8%) children. A second or additional AEDs were used in 180 and 44 children respectively. The time gap between parents recognized the repeated attacks and starting regular AED was a mean 15 months and median 7 months.
Table 6.22: Present medication (319 patients)

<table>
<thead>
<tr>
<th>AEDs</th>
<th>Total</th>
<th>%</th>
<th>OPD</th>
<th>CDC</th>
</tr>
</thead>
<tbody>
<tr>
<td>PB</td>
<td>103</td>
<td>32.3</td>
<td>62</td>
<td>29</td>
</tr>
<tr>
<td>CBZ</td>
<td>78</td>
<td>24.5</td>
<td>49</td>
<td>28</td>
</tr>
<tr>
<td>VPA</td>
<td>80</td>
<td>25.1</td>
<td>32</td>
<td>59</td>
</tr>
<tr>
<td>NTZ</td>
<td>72</td>
<td>22.6</td>
<td>43</td>
<td>58</td>
</tr>
<tr>
<td>CLZ</td>
<td>17</td>
<td>5.3</td>
<td>11</td>
<td>18</td>
</tr>
<tr>
<td>CLB</td>
<td>15</td>
<td>4.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PHT</td>
<td>10</td>
<td>3.1</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>LTZ</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Topiramet</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Poly therapy during the last follow-up in 83 (26.6%)

Time gap to start regular treatment in months

Mean, median, IQR

\[
\begin{array}{ccc}
15, 7, 15 & 16, 7, 15 & 13, 7, 15
\end{array}
\]

Compliance

During follow-ups based on the seizure diary information, verbal inquiry, and drug strip counting 33 (8.5%) children were identified as having poor compliance. This was strongly related to poor financial condition in most of the cases.

A short course of prednisolone (PD)

A short course of PD (for 4-6 weeks) was prescribed in 137 children. PD was introduced to the children who had been newly diagnosed with IS, epileptic encephalopathy and myoclonic encephalopathy. This was introduced and the previous AED was tapered off in those who had been treated before with other AEDs such as PB or CHZ or VPA without seizure control at the highest level of the drug.

The effect of PD treatment was noted after 2 weeks of treatment. Eighty (58.4%) children had total, significant or some seizure control within 2 weeks of PD therapy, termed as “early positive response to PD”, 19% had no remarkable change of seizure attacks and 10% had increased seizures. Three children (2.2%) had severe side effects, as parents complained of excessive continuous cry and marked restlessness, after starting PD and other were lost to follow up (Table 6.24, Chart 6.2).
Table 6.23: Response to prednisolone treatment after two weeks (Number 137)

<table>
<thead>
<tr>
<th>Response after 2 wks</th>
<th>Total</th>
<th>OPD</th>
<th>%</th>
<th>CDC</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sz stopped in 2 wks</td>
<td>35</td>
<td>17</td>
<td>28.3</td>
<td>18</td>
<td>23.4</td>
</tr>
<tr>
<td>Significant-some red.</td>
<td>45</td>
<td>18</td>
<td>13.3</td>
<td>27</td>
<td>18.2</td>
</tr>
<tr>
<td>No change</td>
<td>26</td>
<td>11</td>
<td>18.3</td>
<td>15</td>
<td>19.5</td>
</tr>
<tr>
<td>Increased</td>
<td>15</td>
<td>5</td>
<td>8.3</td>
<td>10</td>
<td>13.0</td>
</tr>
<tr>
<td>Severe side effect</td>
<td>3</td>
<td>1</td>
<td>1.7</td>
<td>2</td>
<td>3.0</td>
</tr>
<tr>
<td>Lost to fu after prescribed</td>
<td>13</td>
<td>9</td>
<td>15.0</td>
<td>5</td>
<td>6.5</td>
</tr>
</tbody>
</table>

Fu, follow-up; red, reduction.

Table 6.24: Seizure outcome at the final follow up in 137 children treated with short course of PD at the beginning.

<table>
<thead>
<tr>
<th>Effect of PD-therapy at 2wk</th>
<th>Seizure outcome at 1 year follow up</th>
<th>None</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&gt;50% sz.red.</td>
<td>&lt;50% sz.red.</td>
<td></td>
</tr>
<tr>
<td>Positive response to PD therapy</td>
<td>64</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td>No response</td>
<td>9</td>
<td>7</td>
<td>41</td>
</tr>
<tr>
<td>Total</td>
<td>73</td>
<td>12</td>
<td>52</td>
</tr>
</tbody>
</table>

PD, prednisolone; wk, week; sz.red., seizure reduction.

Chart 6.3: initial response to prednisolone treatment among 137 children

<table>
<thead>
<tr>
<th>sz.stopped</th>
<th>significantly improved</th>
<th>none</th>
<th>increased</th>
<th>severe side effects</th>
<th>Lost to FU</th>
</tr>
</thead>
<tbody>
<tr>
<td>35</td>
<td>45</td>
<td>26</td>
<td>15</td>
<td>3</td>
<td>13</td>
</tr>
</tbody>
</table>
Table 6.25: History of previous AED treatment and time gap

<table>
<thead>
<tr>
<th>History of</th>
<th>Total</th>
<th>%</th>
<th>OPD</th>
<th>%</th>
<th>CDC</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prev. AED</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>294</td>
<td>75.4</td>
<td>194</td>
<td>86.6</td>
<td>100</td>
<td>60.2</td>
</tr>
<tr>
<td>Yes</td>
<td>96</td>
<td>24.6</td>
<td>30</td>
<td>13.4</td>
<td>66</td>
<td>39.8</td>
</tr>
<tr>
<td>Total</td>
<td>390</td>
<td>100</td>
<td>224</td>
<td>100</td>
<td>166</td>
<td>100</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time gap to start regular treatment in months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
</tr>
<tr>
<td>Median</td>
</tr>
<tr>
<td>Maximum gap</td>
</tr>
<tr>
<td>Skeweness (st error)</td>
</tr>
</tbody>
</table>

H/O, history of; prev, previous; AED, antiepileptic drug; treat, treatment.

**Previous history of Antiepileptic medication**

About one fourth of the total population was on AED treatment before enrolled in the study and another 7.6% (26 in total, 8 in OPD and 24 in CDC) children had a history of taking AEDs irregularly or for a brief period.

**Time gap to start regular treatment**

The seizure frequency at the time of diagnosis was found to have significant correlation with time gap between the first unprovoked seizure and starting the appropriate treatment, with $p < .01$, OR 0.983, CI (0.974 - 0.993).
6.11: Discussion

This section of chapter six will discuss the findings of the prospective study and will compare the results of two groups of patients (OPD & CDC). It will also discuss and compare the findings of retrospective study.

6.11.1: Febrile seizures and subsequent epilepsy

Evolved epilepsy cases (66) and febrile seizures cases (33)

Recurrent febrile seizures before non-febrile seizures occurred in a proportion of children who had been diagnosed as ‘evolved epilepsy’ (16.9%) in 390 children. In the retrospective study population previous history of febrile seizures was recorded in 24.5%. The majority of them had frequent episodes of febrile seizures and some had more than 2 episodes in one month even when the child was on regular AED treatment.

Febrile seizures are a frequently occurring seizure condition in children, but no accurate incidence rate is known in BD. The estimated prevalence is 50.6 per 1000 in one study among 2-9 year aged children (Durkin, Leislie, Devidson, Hasan, Hasan, Khan, & Shrout 1992).

In our experience with 1000 EEGs from Dhaka city (Poster presentation at OSET congress meeting in Birmingham, 1999), 179 in 1000 children referred for EEG had febrile seizures (Table 3.4, Chapter Three), and 8% of them had non-febrile episode in addition.

The frequency of febrile seizure attacks may indicate the poor management of fever, as 66.9% in the prospective study group and 23% of the first 1000 EEG group gave a history of 5 or more episodes before they had non-febrile seizure attacks.

Among the children who had febrile seizures at the first diagnosis day (n=33)

During one year’s follow up period a comparable proportion of evolution was reported in this prospective study. In different hospital and population based studies, 4.3 to 9.9% of children with initial febrile seizures have been found to develop subsequent epilepsy (Konishi et al. 1990; Seki, Yamawaki, & Suzuki 1981; Tsuboi & Okada
Febrile seizures have been identified to be one of the important risk factors for epilepsy in population based studies (Danesi 1983; Durkin et al. 1992; Tsuboi & Okada 1985). One case control study in Nigeria has demonstrated that children with more than one episode of febrile seizures have an increased risk of developing epilepsy (Ogunniye et al. 1987).

Long-term outcome of these children with a preceding history of febrile seizure and correlation with the development of specific types of epilepsies (complex partial epilepsy with mesial temporal sclerosis) needs to be studied.

6.11.2: Characteristics of the study population in the context of SES of the country

1. Socio-economic demography

Monthly income, housing, and drinking water supply: the prospective study was more representative of Bangladeshi population because the majority of them came from lower income and rural areas with a poor standard of living in *kancha* or *semipakka* houses sharing a common bathroom, and kitchen with other families.

In the retrospective study one-third of the population represented lower-income families, while the majority came from middle-income families and from the urban area. The reasons for this were:

1. these patients were identified from the first 1000 EEGs done at a privately run clinic (started for the first time in the country).
2. data were collected from a specialist centre, where patients are seen on an appointment basis on referral from other centres or private practitioners and therefore direct access for the poorest was often limited.
3. in BD, other than cost of travel cultural barriers also hinder the mothers from travelling independently to service centres (McConachie et al. 2001).
4. the service providers' negative behaviour and attitude acts as another barrier to the poorest in making use of hospital services as has been demonstrated in a very poor population adjacent to Dhaka Shishu Hospital (Khan 1998).
These barriers can be overcome by establishing more community-based links with the hospital services and with attitudinal changes of the service providers. This has been shown within the CDC which has utilized known epidemiological methodologies (Zaman, Khan, Islam, Banu, Dixit, Shrout, & Durkin 1990) to establish a door-to-door surveillance of impairments and disabilities within a community and by establishing a separate community service to provide outpatient services not only to neurologically impaired children, but also their siblings and neighbours. This has resulted in optimum utilization of services by this community (Khan et al. 1997; Khan 1998).

2. The rate of consanguinity

Consanguineous marriage was recorded in a lower proportion in the prospective (3.8%) compared to the retrospective (7.9%) study population. The rate found in the retrospective population was comparable with that found in one population based study (10%) in Bangladesh (Durkin, Khan, Davidson, Zaman, & Stain 1993). When compared with international studies, the rate of consanguineous marriage is much less than in other regional countries such as in Pakistan (Durkin, Hasan, & Hasan 1998). The lower rate of consanguinity in the prospective group is most likely to be due to changing social and family attitudes; the fact that the younger generation is less dependent on land and family properties, an increase in family diversity and the spread of families to different regions of the country.

Consanguinity was found to be a high risk factor for cognitive disabilities in Bangladesh (Durkin, Khan, Devidson, Huq, Rasul, & Zaman 2000). This feature also needs to be further studied to determine its effects on seizure prevalence, diagnosis, and outcomes.

3. Maternal age

The median maternal age during related pregnancy was 23 years, however, the minimum age was 14 years. Early marriage and early pregnancy is much reduced in last decade in BD but still occurs in the rural community.
4. Improvement in female literacy

Bangladesh had made a significant progress in female education and female empowerment in last 15 years, which has directly influenced the family size (birth rate 2.6, UNICEF) and maternal literacy. Parents’ concern and demand for a higher quality of life for their children has increased compared with one decade ago. When the key care-providers of the children are mothers the basic literacy skills and education may have long-term implications for the child and family. In one study of mothers with disabled children in BD Mobarak et al. have shown that more literate and educated mothers are better able to cope with stress (Mobarak et al. 2000). Non-literate and poor rural mothers of children with cerebral palsy were found to be at high risk (>35%) of psychiatric morbidity. Furthermore, when intervention of developmental stimulation therapy was provided for these same children, after two years the mothers felt an increase in formal support (professionals) but none in informal support (family, closest neighbours etc.) (McConachie et al, 2001). Further study needs to be made to correlate family background, parental education and available resources and stress in the basic care-provider of children with epilepsy.

5. Educating the family about epilepsy and home management of seizures: parental knowledge measured before and after education (Section 6.10.2)

The majority of the family members had either no knowledge or a wrong idea about seizures and epilepsy and this was greatly changed to an appropriate knowledge level after an epilepsy education (Section 6.10.2, Table 6.2.2). Home management of febrile and no-febrile seizures by per rectal diazepam was well conducted by many parents. The seizure record diary was also a successful introduction to this population. Initially, many parents would forget to bring the diary to each follow-up day, although they were able to keep the records irrespective of the literacy rate. The majority of the parents (68%) were able to show their recorded diary more than 3 times during the follow up period. This information, however, is not enough on which to comment further. More systematically collected information is required, using a set of validated
questionnaires to gain knowledge of the existing attitudes and practices relating to epilepsy among the population.

6.11.3: Pregnancy and birth related problems as potential risk factors

The recorded rate of preterm delivery was higher in both retrospective (6.6%) and prospective (6.1%) population in this study compared to that of one population based study in Bangladesh (2.2%) (Durkin, Khan, Devidson, Huq, Rasul, & Zaman 2000). Birth weight: In the prospective study 9.5% had smaller and 2.6% had bigger than usual sized infants at birth. Durkin et al. also shows the prevalence of low birth weight (LBW) in 10%. Other studies have found the incidence of LBW babies to be high in Bangladesh. In one study in urban poor and middle class communities, the incidence of LBW ranges from 48% to 73% of primigravidae (Nahar, Afroza, & Hossain 1998). However, the incidence of full-term LBW compared to preterm LBW is much higher in Bangladesh. The reasons may be several. Firstly, the validity of the mother’s history could be questioned because pregnancy and child records at delivery are almost non-existent. In Bangladesh only 26% of pregnant women are given any form of antenatal check-up by a health worker (UNICEF, 2000). Birth records are also not kept as 85% deliveries occur at home attended mostly by untrained birth attendants (Durkin, Khan, Devidson, Huq, Rasul, & Zaman 2000). Secondly perinatal and neonatal mortality rates are high so that many preterm and low birth weight children do not survive infancy.

The risk for seizures and other neurological impairments posed by maternal age, malnutrition and other social risk factors, levels of antenatal care, gestational age and birth-weight needs further study.

In the prospective study the majority of deliveries took place at home assisted by traditional birth attendants or family members. Among the hospital or clinic deliveries another proportion had tried at home first and were taken to hospital with prolonged, complicated second stage of labour.
1. Antenatal check up

An interesting finding was noted that a large number of mothers had visited the health centres at least twice to get the tetanus vaccine, despite antenatal care being very poor in Bangladesh (26%, UNICF, 2000). About one third of our population had antenatal check-ups during their pregnancy. This may reflect the positive effect of nuclear families on this study population because the traditional social and family practice means elderly family members are against medical intervention during pregnancy insisting that the baby is born at home, even after regular check-ups.

2. High-risk pregnancy, perinatal asphyxia and neonatal seizures

Medical, psychosocial, or accidental problems were recorded in approximately one-third of the prospective study population and such information was not available in the retrospective group. However, this was recorded more frequently (33%) in the CDC group compared to 23% the community (OPD) group.

A history of perinatal asphyxia and neonatal seizures was very high (46% and 41%) both in the retrospective group and in the CDC group of prospective population. These were comparatively less (32% and 24%) in the community (OPD) group.

Perinatal asphyxia and neonatal seizures might be a reflection of problems arising in utero as well as those arising during delivery. Intrauterine growth retardation (IUGR), intrauterine infections, and toxaeamias of pregnancy etc. are very common problems in developing countries. There are very few studies, which have correlated such problems with seizure disorders in these countries. One study (Zareen, MPhil thesis 1995) showed that children coming to the CDC had much higher antibody titres for rubella, cytomegalovirus and toxoplasma compared with normal controls. Another study has shown that children with a history of birth asphyxia were five times more at risk of developing cerebral palsy than those who did not have such a history (Jahan, FCPS thesis 1995). In the North America collaboration study, low Apgar score, neonatal abnormal signs and neonatal seizures within the first days of life incurred a 55% risk of developing chronic disability and a 70% chance of death or disability (Ellenberg & Nelson 1988). However, our arbitrary definition of perinatal asphyxia
(Section 4.5.1) did not require a definite neonatal encephalopathy, which has been suggested by the US national collaborative perinatal project (Ellenberg and Nelson 1988) to have the major predictive power of later developing cerebral palsy and other disabilities in children (op.cit.). The highest rate of cerebral palsy in term infants was detected in those who had the combination of low Apgar scores, neonatal signs and neonatal seizures, which comprises neonatal encephalopathy (Ellenberg and Nelson 1988, Nelson and Emery 1993). Significant direct correlation between perinatal complications and epilepsy was found in studies from India and South Africa (Hackett, Hackett, & Bhakta 1997; Leary & Morris 1998).

The percentage of perinatal complications found in our study are comparable with that of South African child-hospital based study (Leary & Morris 1998). Findings from these studies (see section 2.5) including ours are suggestive of possible preventive measures within the community people to reduce perinatal morbidity.

6.11.4: Family history of epilepsy

**Comparable proportion of children with family history of epilepsy**

A positive family history of epilepsy was recorded in 8.6% of the retrospective, and in 7.1% of the prospective population in our study. This was present in 13.5%, when a history from the second-degree relatives was counted. A similar frequency of epilepsy in the first degree relatives was found (5.2% to 8.9%) in prevalence and pattern studies done in Kashmir, India (Durkin, Leislie, Devidson, Hasan, Hasan, Khan, & Shrout 1992; Koul, Razadan, & Motta 1988). In Bangalore, India Satishchandra et al. 1996, recorded a history of epilepsy in first or second-degree relatives in 13.7% of their survey patients.

6.11.5: Child characteristics

Age at presentation: an earlier age at presentation was recorded in the prospective population compared with that of the retrospective group. The majority of the children
were below 3 years of age (66%), and more than half were up-to 12 months of age, compared with the retrospective study where only 23.9% were up-to 12 months of age. The majority of both populations had the onset of their first unprovoked seizures at or before 12 months of age. This probably indicates the parents’, increasing concern about their child’s problem and the availability of a service.

Gender bias towards male: the gender discrimination was slightly less in the OPD group but increased in the CDC group, compared with those in retrospective study. The most striking difference was noted in the 33 children diagnosed as febrile seizures on entry day, where 30 were male and only 3 were female. The gender discrepancy in this group is very remarkable, compared with the data we found from the first 1000 EEGs, where male female ratio was 2.8:1 in the children with febrile seizures. This shows a marked discrimination against the female child especially in the low-income group of population. An acute seizure attack in female child and such an attack in a male child are probably not given equal importance so far as the need for medical treatment is concern. It was seen in many cases, especially in idiopathic epilepsy, that a female child would be brought to the hospital when the question of marriage arises (personal experience). Social bias towards the male-child has been found in most community and hospital settings in Bangladesh and families are more willing to spend limited resources on a boy (Koenig & D'Souza 1986; Mosaddeque & Glass 1988; Stanton & Clemens 1988). This is probably more prominent in any acute condition, however no data were available to compare this finding in children with febrile seizures.

Gender equity of access can only be developed in community based services where families are motivated to come (by a key member of the community) and where accessibility is not a problem or in a hospital clinic which has links with the community (Khan, Begum, Hussain, & Begum 1997).

6.11.6: Epilepsy profile and associated non-convulsive disorders
1. Seizures and Epilepsy classification

**Generalised epilepsy was highest in clinical presentation:** The seizure type and epilepsy classification had been based on the international classification of seizure disorder (ILAE 1981a; ILAE 1989). There have been certain limitations in using the complete classification criteria of ILAE as it was not possible to obtain neuroimaging in suspected cases of cryptogenic or symptomatic epilepsy syndrome.

Taking this into consideration, we used a simpler classification based on the major categories of the international classification of seizure and epilepsy syndrome to make it easier to use (Neville 1997). Based on the clinical information and EEG findings a realistic and user-friendly classification was adapted for this study (Chapter Four, Table 4.4.1).

**Primary generalised epilepsy** was diagnosed in a majority of both the retrospective and prospective groups (above 63%).

**Malignant epilepsy syndrome** was diagnosed at two times the rate in the prospective group compared to the retrospective group, which was again more frequently diagnosed in the CDC group compared with the community (OPD) group.

**Symptomatic and cryptogenic epilepsy** on aetiological classification: symptomatic and cryptogenic epilepsies were diagnosed in more than half (56%) of the total prospective population and more frequent in the CDC population (78%) compared with that of community population (42%).

Out of 390 children in whom epilepsy was the first diagnosis (excluding febrile seizures) 69.8% had been diagnosed as symptomatic and cryptogenic epilepsy (35.1% generalised and 26.2% localization related). Among the retrospective group 61% were categorized as having symptomatic and cryptogenic epilepsy.

This study’s findings were compared with those of other studies. One hospital based study in children which included situation related seizures (Aydinli et al. 1996), febrile seizures and isolated seizures or isolated status epilepticus, symptomatic and
cryptogenic epilepsy was diagnosed in 52.38% of the population (26.2 and 26.18 were categorized as generalised and localization related epilepsy respectively). This is comparable with the result found in our study group (56.7%) when febrile seizure cases were included.

In one population based study carried out among children and adolescents in Estonia (Beilmann & Talvik 1999) symptomatic and cryptogenic epilepsies is diagnosed in 62.7% (43% localization related and 19.7% generalised). They included only the predefined epilepsy cases (2 or more seizures unprovoked). The total incidence of this category in the study is comparable with a 7% higher incidence in our prospective group when only the non-febrile seizure cases (69.6%) were included.

The reasons for the higher incidence of the symptomatic and cryptogenic category in our study population may be:

1. Most of the patients were of early child age.
2. People came as patients, so it can be presumed that most of the cases would be at the severe end of the spectrum.
3. Given the population background with a high level of poverty, malnutrition, poor antenatal, perinatal care and frequent infection among the early aged children it could be postulated that the incidence of cerebral damage in the younger children is increased.

In most of the population and hospital based studies localization related symptomatic and cryptogenic epilepsy has been the most prevalent (Ohtsuka et al. 1993; Oka et al. 1995; Osservatorio 1996), except in one study done in the UK (Manford et al. 1992). This population based British national general practice study of epilepsy found only 29.7%, which is comparable with our findings of 25% for localization related symptomatic and cryptogenic epilepsy cases.

Identification of the anatomical lesion in the brain, which is the source of seizures is difficult in a resource-limited setting. Our classification was done using a broader approach, mostly based upon the clinical information, physical examination, EEG and some of the neuroimagings.
2. Seizure history

Multiple types of seizures were noted amongst two-thirds (61.6%) of the retrospective group and about one-third of the prospective group, which was again higher (about 50% more) in the CDC group. This is comparable with one study in Finland (Keranen, Sillanpaa, & Riekkinen 1988).

High rate of seizures: a high rate of seizures was recorded in the same number of the population of both the retrospective and prospective groups.

Age at seizure onset: ‘early’ onset was recorded in a slightly higher population among the prospective group (60.8%) compared with the retrospective group (56.3%), which was again higher (71.7%) in the CDC group.

Associated motor disorders: this was less commonly noted in the community (OPD) group compared with that of the prospective CDC and retrospective CDC group. Again a severe form of associated motor disorder was noted in 45% of the prospective CDC group and 41% of the retrospective study.

Associated cognitive impairment: similarly this was more frequently noted (70%) among the CDC population both in the retrospective, and prospective study. This was noted amongst 43% in the community (OPD) group. One interesting finding here was that the diagnosis of cognitive impairment on clinical judgment had a good correlation with that of formal IQ assessment.
6.11.7: Epilepsy management

1. **Parental knowledge, attitude assessment and education intervention program**
   
   The programme may help to improve the compliance and allay family concerns and anxiety. We used this intervention programme with all parents and the family. We wanted the parents to become familiar with the drug doses in relation to seizure control, body weight, other illness and excessive drowsiness.
   
   We trained parents in how to use rectal diazepam and supplied the syringe, tube and injections when it was needed. The aim was to change their negative attitude, to improve their confidence and to achieve the best compliance. This kind of educational program was found to be acceptable and effective in other studies done with parents and families with febrile convulsive children. (Huang, Liu, & Huang 1998; Ling 2000; Rossi et al. 1989; Ventura et al. 1982)

2. **Treatment of febrile seizures and major seizure attacks, home management, and parental training:** a survey among the families with children who had experienced febrile seizures suggests that parents’ fear of fever and seizures is the major problem with serious negative consequences affecting daily family life but which concerns, could be reduced by educating parents. Parents’ poor knowledge, negative attitude, anxiety and inadequate first-aid measure towards febrile convulsions are shown to be improved by an education intervention programme (Huang, Liu, & Huang 1998; Ling 2000; Parmar, Sahu, & Bavdekar 2001; Rossi et al. 1989).

   **Home management:** parental education/training of managing a major attack by rectal diazepam proved to be acceptable and effective among more than 80% of the parents irrespective of their educational level (Huang, Liu, & Huang 1998; Ling 2000; Rossi et al. 1989; Ventura, Basso, Bortolan, Gardini, Guidobaldi, Lorusso, Marinoni, Merli, Messi, Mussi, Muner, Patamia, Rabusin, Sacher, & Ulliana 1982).

3. **AED history before entry to the study in the children with epilepsy:** a remarkable numbers of children in the retrospective group were already on AEDs before coming to the specialist epilepsy clinic (CDC) (43.7%), whilst this was noted in
only 24.6% of the total prospective population. Both are comparable with other studies; for example in India where 46% of the study group had received AEDs before they had been randomized (Pal et al. 1998a) and in other developing countries the percentage ranges from 6 to 26% (Feksi, Kaamugisha, Sander, & Gatiti 1991; Pal et al. 1998a; Shorvon & Farmer 1988).

4. Time gap between first recognized seizures and starting of regular AED treatment: the mean and median time gap recorded was higher in the retrospective population compared with that of prospective study population, which were 30 and 23 months in retrospective and 15 and 7 months in the prospective population.

5. Treatment Gap: in the patients with epilepsy in the prospective study, the treatment gap (the percentage of patients who warrant treatment but are not receiving it) was 86.6% in the non-specialist centre (OPD) population.

6. Other aspect of HO of previous AED medication: although 273 (64.5%) families went to the medical centres when their children had a major attack, only a small proportion of children had regular AED treatment for more than 3 months, and another small proportion (32) of children had irregular AEDs for less than 3 months. The majority families used traditional healers. There may be multiple reasons for this. The most important one in my opinion is that the parents did not have proper guidance and knowledge about and confidence in medical treatments. The practical picture of a primary care centre in BD is that children are the major patient population, with the most common problems being RTI and ENT problems and GIT problem. Primary care physicians usually have little interest or time to offer to the children with epilepsy or with developmental problems mainly due to lack of any training in this particular field.

A diagram based explanation of the disease process to the parents was seen to be helpful in highlighting the cause of their problem and once the parents were informed about the disease they became more confident in the medical treatment and accept to use regular medication even at the cost of selling their valuables (personal experience).
When the same question was asked after one year’s treatment, majority replied that they now think it is a chronic illness 225 (70%), 94 of the families had doubt.

From the above comparison, we can conclude:

a. High-risk prognostic features were more common among the population attending the special centre.

b. That patients seeking medical help were those with high rates of seizures in both groups, who came to hospital only when it went beyond any traditional treatment and severely affected the family who were witnessing the frequent seizures. Other explanations may be that they did not know if there was any medical treatment or there was a lack of training and experience of primary care physicians at primary care hospitals where they attended first time.

c. A diagnosis of ‘malignant epilepsy syndrome’ was more frequent in the prospective group. Parents’ awareness, service availability and the care-providers’ awareness may be the reason for this.

6.11.8: Outcome

Seizure outcome after one year’s treatment: with such poor prognostic features associated a good outcome was found in 52.7% of the whole prospective population, which was more frequent in the community group (61.7%). The rate of seizure remission was higher among the prospective study population compared with that of the (49.7%) retrospective study population.

Seizure remission rate in the population without any sign of neurological deficit: seizure remission was found among 76.9% of the whole prospective group, which was higher in the community group (80%) who did not have any sign of cerebral lesions. The remission rate in the CDC group was 35% among those who had associated neurological deficit (non-convulsive disorder).

Comparison with other studies: this is discussed in Chapter Eight.
6.11.9: Predictors of ‘poor seizure remission’

Presence of multiple seizure types, associated cognitive impairment, and motor disorder on first presentation were significantly associated with poor seizure remission. When the investigative variable, abnormal EEG, was entered it did not affect the model of predictors. Abnormal EEG was strongly associated with poor seizure remission both in the retrospective and the prospective groups. In addition when correlated with subcategories of EEG features there is a linear correlate observed i.e., normal EEG with the best seizure prognosis, and abnormal EEG with the presence of both 'epileptiform discharges and background abnormality' had the worse prognosis (fig-5.6 & fig-6.1).

6.11.10: Role of EEG and other investigations in diagnosing epilepsy and identifying preventable causes of epilepsy.

EEG recording: (Chapter Four section 4.10.1)

In the retrospective study EEGs were done after a period of getting treatment (not recorded) and the mean time gap between the first seizure and EEG recording was 30 months (15 months in prospective group). This is because there was no EEG service for the children before 1996 in Bangladesh. A prompt EEG recording was arranged for each child of the prospective study population on the day of first diagnosis or within two weeks. Although this was done mainly for logistic reason however, Mark et al.(1996) have suggested that early EEG (ideally done within 24 hours of seizures) is more useful in the finding epileptiform abnormalities (51%) than later EEG (34%) (Mark, Mark, Graeme, Gregory & Mervyn 1996).
EEG findings

1. Abnormal EEGs were identified more frequently among the retrospective group and the CDC group (over 80%), which was less than 60% in the OPD group. However, abnormal EEGs were reported among 70% of the whole prospective study population. This difference is probably because more symptomatic epilepsy cases with cerebral lesions were represented at the specialist centre:
   a. The median age of seizure onset was 10 months while median age of EEG recorded was 3 years in the retrospective study population.
   b. The median ages and age of EEG recordings were 8 and 22 months in the prospective population, 12 and 26 months in community group and 5 and 15 months in the CDC group.

2. EEG aided in making a more specific diagnosis: EEG showing definite epileptiform discharges, helped to diagnose definite epilepsy in 61.5% of the children in the retrospective group and 54% in the prospective group and even within this group of children certain specific epilepsies were either newly diagnosed or confirmed. For example, a diagnosis of focal epilepsy increased in substantial numbers of children (11% in the retrospective study and 14% in the prospective study) in whom the initial diagnosis was generalised seizures based on the description of the attacks. The findings can be compared to another study done in Bolivia (Nicoletti et al, 1999). Nicoletti et al conducted a population based study where they found the diagnosis of a large number of generalised seizure type (19.3%) had changed to partial seizure when the electroclinical diagnosis was considered. This finding may have had important implications for the child. It provided a valuable diagnostic and prognostic message for the attending physicians.

The diagnosis of ‘malignant epilepsy syndromes’ were confirmed by EEG in a large group i.e., 14.5% among the retrospective group and in 14.6% in the prospective group having a recognizable characteristic EEG pattern.

EEG also helped to differentiate children with other non-epileptiform abnormalities in their cerebral function in another proportion of children i.e., 29 (19.2%) in the retrospective group and 58 (15.1%) in the prospective population. A preliminary
Diagnosis of active focal or generalised cerebral lesion could possibly be identified from the characteristic non-epileptiform abnormalities in the EEGs and may be suggestive of further investigation for specific cases in a limited resource situation. However, this needs further investigation.

Neuroimaging revealed structural abnormality in a large number of children:

Neuroimaging including USG, CT scan and MRI of the brain was performed in 44.2% of the prospective population, and was abnormal in 51 children (33.8% of 151) of retrospective and 131 children (31.9% of 319) of prospective population. It again reflects the nature of the study population most of whom were at high risk for neurological damage. However, it needs to be mentioned here that MRI and CT scan services could only be used in selected children mainly due to costs of establishing the base services and maintenance and cost to the family. The cost of EEG, when compared to that of CT and MRI, is about one-third. The cost-benefit ratio of the two types of investigations needs to be further evaluated.
CHAPTER SEVEN

7: A randomized controlled trial of phenobarbitone and carbamazepine monotherapy in children with epilepsy in Bangladesh

7.1: Introduction

Control of seizures without intolerable side-effects is the goal of AED therapy (US government 1977). The requirements for a successful and sustainable treatment programme are:

1. The target group should be easily identified.
2. The drug should stop seizures in a useful proportion.
3. The drug should have a low rate of side effects, particularly of behavioural complications.
4. The prescribed drug should be affordable as well as effective.

Phenobarbitone, (Gastaut & Osontokun 1976; WHO 1990) is recommended by the WHO as the first line AED for most seizure and epilepsy types in developing countries mainly because of its low production cost. However its use is controversial with several studies showing increased behavioural side-effects compared with other AEDs or with no treatment (de Silva, Mac Ardle, McGowan, Hughes, Stewart, Neville, Johnson, & Reynolds 1996; Vining, Mellits, Dorsen, Carpay, Craldo, Quaskey, Spielberg, & Freeman 1987; Wolf & Forsyth 1978). However, other authors found no significant behavioural side-effects caused by daily use of phenobarbitone in children (Feksi, Kaamugisha, Sander, & Gatiti 1991; Pal et al. 1998a; Wendy 1987). CBZ was the most commonly used AED used in the epilepsy clinic (Section 5.4.8) and is recommended by the WHO for all types of epileptic seizures except typical absences. We therefore decided to conduct a study to assess the drug efficacy and compare the
behavioural side-effects produced by PB and CBZ monotherapy in children with epilepsy as part of the process of developing an effective management plan for children with epilepsy in BD.

7.2: Study design and setting

The double-blind randomized controlled study was conducted within the Dhaka Shishu Hospital (Section 4.14). Patients were recruited for six months (Section 6.4).

7.2.1: Site of patient recruitment

Patients were recruited from a non-specialized OPD which was established by SHB for this research project in collaboration with a community service centre on the hospital premises (Section 4.14).

7.2.2: Patients

The study included children who were between the ages of 2 to 15 years, with ‘active epilepsy’ which included unprovoked generalised tonic-clonic seizures and partial or secondary generalised tonic-clonic seizures.

Children were excluded if they were less than 2 years of age, had absence, myoclonic or severe malignant epilepsy or had major non-convulsive neurodisabilities (Section 4.6) or if they were already on regular antiepileptic medication.

7.2.3: Sample size

On the basis of previous studies showing adverse side effects of PB, we hypothesized that there would be a 25% excess of behavioural side effects with the PB group compared with the CBZ group with a predicted incidence of CBZ side effect of 15%. For 80% power at 5% significance 46 subjects were required in each treatment group (using the one sample formula for power calculation).
One sample formula: \( n > (Z_{\alpha} + Z_{\beta})^2 \left( \pi_1(1 - \pi_1) + \pi_2(1 - \pi_2) \right) / \delta^2 \)
\[
n > 7.849 \left( \frac{40.60 + 15.85}{25} \right)^2
\]
\[
7.849 \times 5.88 = 46 \text{ patients were required in each group}
\]

Allowing for a 20% drop out rate (unpublished data from CDC), we intended to enrol 54 patients into each treatment group. Therefore required sample was approximately 108.

A detailed history of seizures and other neurodevelopmental problems, pregnancy, birth related problems, milestones of early development, immunisation and family history were obtained from patients, parents and other family members. A history of socio-economic status and maternal stress was completed during subsequent visits. An electroencephalogram (EEG) was carried out on each child, and plans for other investigation were made if needed.

7.2.4: Diagnosis and classification of active epilepsy

Diagnosis of epilepsy and their classifications were based on the previously mentioned method (Section 4.4).

7.2.5: Associated non-convulsive disabilities (Section 4.6)

The non-convulsive disabilities included both motor disorders and cognitive impairments. We included those children with mild motor disorders defined as having signs of motor deficit but capable of performing daily living activities independently with or without some limitation (Section 4.6.1). Cognition was defined as ‘normal’ if IQ score was 70 and above, and ‘impaired’ if it was less than 70.
7.2.6: Neurodevelopmental assessment (NDA) and behavioural state at randomization, and after 12 months of AED treatment

Both a general and central nervous system (CNS) examination, and functional neurodevelopmental assessment (NDA) were carried out on the first visit following a standard protocol (Section 6.6.1, point B). The psychological and behavioural assessment tools used are described in Section 4.7, and 4.8. A second behavioural assessment was conducted after 12 months of regular treatment or at the time of drug withdrawal. Our behavioural assessment instruments were adapted and validated in the same region using the local language (Section 4.8 and 4.9).

7.2.7: Seizure outcome

Seizure outcome was recorded as percentage of seizure reduction and then categorized as ‘seizure remission’ or ‘no seizure remission’ (Point 18 in Section 4.3.1).

7.2.8: Simple randomization

Fifty-four papers with drug A (phenobarbitone), and other 54 papers with drug B (carbamazepine) written on them were folded twice and sealed each in an envelope. The 108 sealed envelopes were shuffled and then kept under lock and key by the researcher. Once the child had fulfilled the RCT enrolment criteria consent was obtained from the parent, and an envelope was picked up by a reliable person who did not have any part in the research work.

For practical and ethical reasons the treating physician was aware of the treatment drug. Other research assistants, i.e., the psychologist, therapist and the researcher were blind to the treatment. The researcher was only made aware during the data analysis. Drugs were supplied by the clinic. We developed methods of ensuring the medicine supply if the family failed to attend clinic or temporarily moved. Depending on the family needs and distance from the clinic, either sufficient numbers of tablets were supplied or any of the family members were able to collect the medicine, or parents
would buy the medicine from the nearest pharmacy, then the clinic would refund on presentation of receipts and tablet strips.

Compliance was ensured by verbal reply and by counting the remaining tablets. Blood tests for detection of drug levels were carried out on one occasion without a previous warning to the parents.

Participants were supplied with a hand-made seizure diary (Appendix XVI), in which they were trained to record the events by putting a mark or a dot for a major or a minor attack.

Patients were reviewed at two weeks, one month, three month, or six-month intervals depending on the therapeutic response and distance of the family residence. During each visit the physician recorded their immediate complaints and the number of seizure attacks or rate of seizures since the last visit. The AED dose was calculated and adjusted with the rate of seizure control and recent body weight of the child. The list of side-effects was checked at each visit.

7.2.9: Drugs and doses

Phenobarbitone was available as 30mg tablets in strips, and carbamazepine as 200mg in strips. Treatment was started with a low, weight-related dose and was increased after 2 weeks following the WHO recommendation (Gastaut & Osontokun 1976a).

Phenobarbitone was started at 1.5 mg/kg/day taken in two divided doses and the maintenance dose was 3 mg/kg. Carbamazepine was started at 5mg/kg daily and increased to 10 mg/kg in 2 weeks then 16 mg/kg after another 2 weeks as a maintenance dose. A maximum of 4 mg/kg per day for phenobarbitone and 20 mg/kg per day for carbamazepine was allowed until effective seizures control was achieved.

If seizures were not controlled, despite the full dose and blood level results being within a therapeutic level, treatment was changed to the other study drug while the previous one was weaned. If seizure control was achieved while weaning the previous drug and increasing the new drug the combination was maintained (WHO & author’s previous experience). If none of the trial drugs were effective or there was complaint
of unacceptable side effect from both the trial drugs a third suitable AED was introduced. However, when a patient had to change the randomised drug s/he was withdrawn from the trial and recorded as 'drug failed'.

All participants were followed up for a minimum of 12 months after randomization.

7.2.10: Outcome measures

The main outcome measure was behavioural side effects recorded as either complaints from the parents (check list, Appendix III) of hyperactivity, irritability and aggressiveness or a behavioural assessment score compared with the score before starting treatment. Formal behavioural assessment scores were reported as continuous variables.

Parental impressions of any change of their children’s behaviour after starting the AED treatment were categorized as ‘deteriorated’, ‘unchanged’ or ‘improved’ compared to before treatment. To assess the drug efficacy, the following data were collected: (1) date of treatment allocation; (2) time to first seizure post randomisation; (3) time to treatment withdrawal due to adverse effects and (4) date of last follow-up.

7.2.11: Analysis

The analysis was based on the policy of intention to treat. The primary aim of the analysis was to compare the drug side effects. Parametric, independent sample t-tests and nonparametric, Mann Whitney tests were used to measure the difference of behavioural side effects. Paired sample t-tests were done to compare the difference of behavioural assessment scores before and after treatment within the trial groups.

The drug efficacy was compared using the time to first seizure after randomization as the primary data. The Kaplan-Meier test was applied to the time from randomization to first date of seizure or to the date of last follow-up when there was no recorded seizure after randomization. Behaviour outcome were analysed, both unadjusted and adjusted for motor disorder and cognitive impairment. The Cox-regression test was performed to analyse correlation of age, sex, presence or absence of motor disability and cognitive impairment with the outcome behavioural problem.
Figure - 7.1 Trial profile:

423 children recruited with seizure disorders

108 eligible for RCT

54 assigned phenobarbital

Followed up 12 months
42 for seizure outcome
40 for behavioural outcome

14 withdrawn
12 lost to follow up
2 changed trial drug for poor seizure control.

42 continued PB

54 assigned carbamazepine

Followed up 12 months
49 for seizure outcome
45 for behavioural outcome

9 withdrawn
5 lost to follow up
4 changed trial drug for poor seizure control

45 continued CBZ
7.3: Results

Of the 108 patients eligible for the drug trial, 91 (84.3%) children were followed up and continued the regular treatment. Sixty-one (67.0%) children came to the clinic regularly, 30 (33%) needed recall by letter, telephone and/or home visit before the final follow-up at one year. Seventeen patients (15.7%) were untraced.

Of the 91 children, 6 had to change drugs due to poor seizure control or the occurrence of other seizure types for example, myoclonic seizures. Eighty-five children (40 in PB & 45 in CBZ group) continued with the drug trial for 12 months.

The family characteristics are shown in Table 7.1. The majority of children came from poor and middle class families in rural area. Most of the families travelled from rural residences, and sometimes from remote countryside by foot, bus, boat or train, involving great effort and often hardship. Minimum and maximum transportation cost for each visit were taka 20 and taka 5000. Maternal illiteracy was recorded in 40% of the families.

7.3.1: Child characteristics, seizure and epilepsy profiles (Table 7.1)

Age and sex
Although the male/female ratio was 1.3:1 in the whole population, more girls than boys were allocated to CBZ. Median age at randomisation and median age of seizure onset were higher in the CBZ group (Table 7.1).

Age at onset, seizure and epilepsy classification at randomisation
Over 80% of the children had their first seizure after 1 year of age. Generalised tonic clonic seizures were more prevalent in the PB group whilst partial and secondary generalized seizures were higher in the CBZ group. Seizure rate and the median
number of seizures during the previous year increased in the PB group. Idiopathic epilepsy was diagnosed in 73% of the children.

Mean and median duration of epilepsy increased by 6 months in the CBZ group. Ten or more episodes of seizures in previous year were recorded in 66.6% of the PB and 66.1% of CBZ group (Table 7.1). This was recorded in 63.9% of the whole population.

The treatment gap was 77.8%. About three quarters of the children had never had daily, long-term (AED) treatment, while the remainder had had daily AED treatment for a minimum of 3 months, prescribed by a physician. Associated non-convulsive disorders i.e., neurodevelopmental disorders were similar in both trial groups (Table 7.1). Seven in the CBZ and three in the PB group had a family history of epilepsy.

A cognitive state (IQ) within normal limits was recorded in 74 (68.5%). Behavioural assessment scores before treatment were within normal limits in 43 on both groups and problems were detected in 22 (11 in both groups, Table 7.1).
Table 7.1: Randomized subjects: family and child characteristics \((n = 108)\)

<table>
<thead>
<tr>
<th>Items</th>
<th>PB(%)</th>
<th>CBZ (%)</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Family type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nuclear</td>
<td>33 (61.1)</td>
<td>35 (64.8)</td>
<td>68 (62.9)</td>
</tr>
<tr>
<td>Joint</td>
<td>21 (38.9)</td>
<td>19 (35.2)</td>
<td>40 (37.1)</td>
</tr>
<tr>
<td>2. Residence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>35 (64.8)</td>
<td>32 (59.3)</td>
<td>67 (62)</td>
</tr>
<tr>
<td>Urban</td>
<td>19 (35.2)</td>
<td>22 (40.7)</td>
<td>41 (38)</td>
</tr>
<tr>
<td>3. SES by monthly income</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower income</td>
<td>20 (37.0)</td>
<td>33 (61.1)</td>
<td>53 (49.0)</td>
</tr>
<tr>
<td>Middle income</td>
<td>32 (59.3)</td>
<td>13 (24.1)</td>
<td>45 (41.7)</td>
</tr>
<tr>
<td>Higher income</td>
<td>2 (3.7)</td>
<td>8 (14.8)</td>
<td>10 (9.3)</td>
</tr>
<tr>
<td>4. Age at present (mo.)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>7 (13.0)</td>
<td>5 (9.3)</td>
<td>12 (11.1)</td>
</tr>
<tr>
<td>25-60</td>
<td>23 (42.6)</td>
<td>21 (38.9)</td>
<td>44 (42.6)</td>
</tr>
<tr>
<td>61 &amp; above</td>
<td>24 (44.4)</td>
<td>28 (51.8)</td>
<td>52 (46.3)</td>
</tr>
<tr>
<td>Total</td>
<td>54 (100)</td>
<td>54 (100)</td>
<td>108 (100)</td>
</tr>
<tr>
<td>Mean median (IQR) in years</td>
<td>5.3, 4.1, (5.7)</td>
<td>6, 5.5, (6.3)</td>
<td>5.7, 4.7, (6.3)</td>
</tr>
<tr>
<td>5. Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>37 (68.5)</td>
<td>24 (44.4)</td>
<td>61 (56.5)</td>
</tr>
<tr>
<td>Female</td>
<td>17 (31.5)</td>
<td>30 (55.6)</td>
<td>47 (43.5)</td>
</tr>
<tr>
<td>6. Age at onset</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>After 12 mo</td>
<td>41 (75.9)</td>
<td>46 (85.7)</td>
<td>87 (80.6)</td>
</tr>
<tr>
<td>Early</td>
<td>13 (24.1)</td>
<td>8 (14.8)</td>
<td>21 (19.4)</td>
</tr>
<tr>
<td>Total</td>
<td>54 (100)</td>
<td>54 (100)</td>
<td>108 (100)</td>
</tr>
<tr>
<td>Mean, med., IQR in yr.</td>
<td>3.4, 2.4, (4.7)</td>
<td>4.1, 3, (4.8)</td>
<td>3.8, 2.7, (4.8)</td>
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<tr>
<td>7. Epilepsy classified</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gen.</td>
<td>29 (53.7Z)</td>
<td>22(40.7)</td>
<td>51 (47.2)</td>
</tr>
<tr>
<td>Partl.</td>
<td>25 (46.3)</td>
<td>32 (59.3)</td>
<td>57 (52.8)</td>
</tr>
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<td>8. Seizure type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>49 (90.7)</td>
<td>49 (90.7)</td>
<td>98 (90.7)</td>
</tr>
<tr>
<td>Multi.</td>
<td>5 (9.3)</td>
<td>5 (9.3)</td>
<td>10 (9.3)</td>
</tr>
<tr>
<td>9. Seizure rate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>32 (59.3)</td>
<td>34 (63.0)</td>
<td>66 (61.1)</td>
</tr>
<tr>
<td>High</td>
<td>22 (40.7)</td>
<td>20 (37.0)</td>
<td>42 (38.9)</td>
</tr>
<tr>
<td>10. Seizure frequency</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily sz.</td>
<td>14 (25.9)</td>
<td>15 (27.8)</td>
<td>29 (26.9)</td>
</tr>
<tr>
<td>Weekly, &lt;1/ld</td>
<td>8 (14.8)</td>
<td>5 (9.3)</td>
<td>13 (12.0)</td>
</tr>
<tr>
<td>Mo.ly, &lt;1/wk</td>
<td>21 (38.9)</td>
<td>23 (42.6)</td>
<td>44 (40.7)</td>
</tr>
<tr>
<td>Yearly, &lt;1/mo</td>
<td>11 (20.4)</td>
<td>11 (20.4)</td>
<td>22 (20.4)</td>
</tr>
<tr>
<td>11. Etiological classification</td>
<td></td>
<td></td>
<td></td>
</tr>
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<td>12. Duration of epilepsy</td>
<td>1 year</td>
<td>&gt;1-2</td>
<td>&gt;2-3</td>
</tr>
<tr>
<td>--------------------------</td>
<td>--------</td>
<td>------</td>
<td>------</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>40 (74.1)</td>
<td>31 (57.4)</td>
<td>71 (65.7)</td>
</tr>
<tr>
<td>Sympt.</td>
<td>14 (25.9)</td>
<td>23 (42.6)</td>
<td>37 (34.3)</td>
</tr>
</tbody>
</table>

Mean, med., (IQR) in mo. | 19, 13, (18) | 25, 16, (30) | 22, 15, (24) |

<table>
<thead>
<tr>
<th>19. Previous H/O AED</th>
<th>Absent</th>
<th>Present</th>
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<td>Absent</td>
<td>42 (77.8)</td>
<td>12 (22.2)</td>
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<td>Present</td>
<td>40 (74.1)</td>
<td>14 (25.9)</td>
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<table>
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<tr>
<th>13. Number of sz.(prev. yr)</th>
<th>&lt; 10</th>
<th>10-20</th>
<th>&gt;20</th>
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<tr>
<td>Absent</td>
<td>18 (33.3)</td>
<td>15 (27.8)</td>
<td>21 (38.9)</td>
</tr>
<tr>
<td>Present</td>
<td>21 (38.9)</td>
<td>18 (33.3)</td>
<td>39 (36.1)</td>
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<th>20. Motor disability</th>
<th>Absent</th>
<th>Present</th>
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<td>Absent</td>
<td>45 (83.3)</td>
<td>9 (16.7)</td>
</tr>
<tr>
<td>Present</td>
<td>45 (83.3)</td>
<td>9 (16.7)</td>
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<th>21. Cognitive impairment</th>
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<td>Absent</td>
<td>37 (68.5)</td>
<td>17 (31.5)</td>
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<tr>
<td>Present</td>
<td>37 (68.5)</td>
<td>17 (31.5)</td>
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<th>22. Pre-exist. bh. problem</th>
<th>Absent</th>
<th>Present</th>
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<tbody>
<tr>
<td>Absent</td>
<td>43 (79.6)</td>
<td>11 (20.4)</td>
</tr>
<tr>
<td>Present</td>
<td>43 (79.6)</td>
<td>11 (20.4)</td>
</tr>
</tbody>
</table>

Sz: seizures; H/O, history of; bh, behaviour; mo, month; yr, year; wk, week; medn, median; gen, generalised; partl, partial; multi, multiple; prev, previous; pre-exist, pre-existing
7.3.2: Outcome

No change of behaviour was reported in 70%, and improved behaviour and/or attention was noted in 16 (18.8%) children. Excessive restlessness and hyperactivity was reported in 10 (11.8%) after regular AED treatment for 1 year (Table 7.2).

The mean difference between the behavioural assessment score before and after treatment is showed in Table 7.3. A significant behavioural improvement was noted in paired t-test after regular AED treatment ($p$ value $<0.02$, 95% CI (1.29, 9.05) in PB, and $p$ value $<0.05$, 95% CI (0.65, 7.15) in CBZ group among the 3 to 5 years old children.

Mean, median, and range of behavioural outcome scores show no significant difference between the two trial groups, and there is no significant difference in mean behavioural outcome scores between the two groups by independent t-test (Table 7.4). There was no association between the outcome behaviour and age, sex, motor disability, cognitive developmental delay, antiepileptic drugs or pre-existing behavioural problems by multiple logistic regression analysis (Table 7.5).

One patient withdrew from the trial after four months due to severe headaches and aggressive outbursts (CBZ). Occasional severe headaches were reported in another patient in the CBZ group. Among other side effects, 3 in PB group and 1 in CBZ group had complained of sleep disturbance at the initiation of the treatment. One parent wanted to avoid the morning dose of PB because of excessive irritability. Gastrointestinal disturbances were reported in 4 in the PB group. Worsening of seizures was noted in 3 patients, 1 in PB and 2 in CBZ group and a third AED (valproic acid and nitrazepam) had to be added.

There was no evidence of association between behavioural problems and antiepileptic drug used, age, sex, and associated neurodisability, or pre-existing behavioural problems revealed by multiple logistic regression analysis (Table 7.5 and Table 7.6).
7.3.3: Seizure outcome and Blood levels

Three children in the PB group and four in the CBZ group discontinued the drug for more than 7 days for various reasons, for example they went to their village, and ran out of drug supply and started homeopathic treatment. Four patients had status epilepticus while off the medication (2 in each group), 3 within 7-10 days and 1 after 30 days of drug withdrawal. All were admitted to the hospital and all restarted treatment. Blood level of AED was tested once during the follow-up in 85 children. One child had below the therapeutic level, five showed blood level towards the lower limit other showed the blood level of AEDs within the therapeutic limit on a single blood test.

**Seizure remission:** A six-month to one-year seizure free period was recorded in 53 (58.2%); another 18 children (19.8%) were seizure free during the last three months at 1 year’s follow-up. At 1 year, ‘seizure remission’ (defined as 100% seizure reduction during the last 3 months of follow up period, see Section 4.3.1-18) was achieved in 71 (78%), 11% had more than 80% seizure reduction and another 11% had achieved 50-80% seizure reduction (Table 7.2).

The log rank test including 91 patients, mean survival time in PB group was 102 days with 95% CI 66.68, 137.36, and 73.71 days with 95% CI 42.85, 104.57 in the CBZ group (Table 7.7). The Kaplan-Meier curve for patients with phenobarbitone and carbamazepine is shown in figure 7.1, indicating that there is no difference in efficacy between the two drugs.
Table 7.2: Description of 91 children and outcome at 1 year

<table>
<thead>
<tr>
<th>Description</th>
<th>PB(%)</th>
<th>CBZ</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Age in mo.</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>6</td>
<td>4</td>
<td>10 (10.9)</td>
</tr>
<tr>
<td>25-60</td>
<td>20 (47.6)</td>
<td>20 (40.0)</td>
<td>40 (44.0)</td>
</tr>
<tr>
<td>&gt;60</td>
<td>16 (38.1)</td>
<td>25 (51.0)</td>
<td>41 (45.1)</td>
</tr>
<tr>
<td>Total</td>
<td>42 (100)</td>
<td>49 (100)</td>
<td>91 (100)</td>
</tr>
<tr>
<td><strong>2. Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>31 (73.8)</td>
<td>20 (40.8)</td>
<td>51 (56.0)</td>
</tr>
<tr>
<td>Female</td>
<td>11 (26.2)</td>
<td>29 (54.2)</td>
<td>40 (44.0)</td>
</tr>
<tr>
<td><strong>3. Behavioural outcome</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No change</td>
<td>28 (70.0)</td>
<td>31 (68.9)</td>
<td>59 (69.4)</td>
</tr>
<tr>
<td>Improved</td>
<td>8 (20.0)</td>
<td>8 (17.8)</td>
<td>16 (18.8)</td>
</tr>
<tr>
<td>Tol. prob.</td>
<td>3 (7.5)</td>
<td>3 (6.7)</td>
<td>6 (7.1)</td>
</tr>
<tr>
<td>Intol. prob.</td>
<td>1 (2.5)</td>
<td>3 (6.7)</td>
<td>4 (4.7)</td>
</tr>
<tr>
<td><strong>4. Seizure outcome at 1 year</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sz free during</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>last 3 mo</td>
<td>32 (76.2)</td>
<td>39 (79.6)</td>
<td>71 (78)</td>
</tr>
<tr>
<td>last 6 mo</td>
<td>19 (45.3)</td>
<td>37 (55.1)</td>
<td>46 (50.5)</td>
</tr>
<tr>
<td>12 mo</td>
<td>3 (7.1)</td>
<td>4 (8.2)</td>
<td>7 (7.7)</td>
</tr>
<tr>
<td><strong>5. Percentage of sz. reduction during last 3mo</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100%</td>
<td>32 (76.2)</td>
<td>39 (79.6)</td>
<td>71 (78.0)</td>
</tr>
<tr>
<td>80-99%</td>
<td>5 (11.9)</td>
<td>5 (10.2)</td>
<td>10 (11.0)</td>
</tr>
<tr>
<td>50-79%</td>
<td>2 (4.8)</td>
<td>3 (6.1)</td>
<td>5 (5.5)</td>
</tr>
<tr>
<td>&lt;50%</td>
<td>5 (11.9)</td>
<td>2 (4.1)</td>
<td>5 (5.5)</td>
</tr>
<tr>
<td>Total</td>
<td>42 (100)</td>
<td>49 (100)</td>
<td>91 (100)</td>
</tr>
<tr>
<td><strong>6. Distribution of outcome behavioural problem</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>3</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Male</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;3 years</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>3-5 years</td>
<td>0</td>
<td>5*</td>
<td>5</td>
</tr>
<tr>
<td>&gt;5 years</td>
<td>3</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>With motor dis.</td>
<td>0</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>With cogn. imp.</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Pre-ex. bh. prob.</td>
<td>1</td>
<td>2*</td>
<td>3</td>
</tr>
<tr>
<td>Tolerable</td>
<td>3</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Intolerable</td>
<td>1</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

Pre-ex, pre-existing; bh, behaviour; imp, impairment; sz.rem, seizure remission; Tol.prob, tolerable behavioural problem
Table 7.3: Mean differences between behavioural tests scores before and after treatment: Paired $t$- test.

<table>
<thead>
<tr>
<th>Tests applied</th>
<th>PB group</th>
<th>$p$</th>
<th>CBZ group</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conner’s ADHD index</td>
<td>3.75 (-4.49, 11.99)</td>
<td>.348</td>
<td>2.64 (-64, 5.92)</td>
<td>.109</td>
</tr>
<tr>
<td>Richman</td>
<td>5.15 (1.25, 9.05)</td>
<td>.012</td>
<td>3.90 (.65, 7.15)</td>
<td>.021</td>
</tr>
<tr>
<td>BSID</td>
<td>-2.83 (-7.16, 1.49)</td>
<td>.153</td>
<td>1.25 (-6.26, 8.76)</td>
<td>.633</td>
</tr>
</tbody>
</table>

Difference, (95% confidence interval), $p$ value

Table 7.4: Independent $t$-test difference in mean behavioural outcome score between phenobarbitone and carbamazepine group.

<table>
<thead>
<tr>
<th>Tests applied</th>
<th>Difference (mean)</th>
<th>CI</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conner’s ADHD index</td>
<td>-0.24</td>
<td>-10.16, 9.67</td>
<td>.96</td>
</tr>
<tr>
<td>Richman</td>
<td>.95</td>
<td>.783, 13.53</td>
<td>0.16</td>
</tr>
<tr>
<td>BSID</td>
<td>-12.08</td>
<td>-43.58, 19.41</td>
<td>0.501</td>
</tr>
</tbody>
</table>
Table 7.5: Main effect model showing correlation between outcome behavioural problem and individual variables

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total frequency</th>
<th>N with bh.Prob.</th>
<th>Odds ratio 95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Drug</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PB</td>
<td>39</td>
<td>4</td>
<td>1.385 (.361, 5.308)</td>
<td>.635</td>
</tr>
<tr>
<td>CBZ</td>
<td>46</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Age in yr.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-5</td>
<td>46</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;5</td>
<td>39</td>
<td>5</td>
<td>.998 (.982, 1.014)</td>
<td>.799</td>
</tr>
<tr>
<td>3. Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>48</td>
<td>3</td>
<td>3.383 (.825, 3.875)</td>
<td>.086</td>
</tr>
<tr>
<td>Female</td>
<td>37</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. IQ</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 70</td>
<td>57</td>
<td>7</td>
<td>.982 (.955, 1.009)</td>
<td>.191</td>
</tr>
<tr>
<td>&lt;70</td>
<td>28</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Motor disability</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>71</td>
<td>9</td>
<td>2.493 (.559, 11.132)</td>
<td>.231</td>
</tr>
<tr>
<td>Present</td>
<td>14</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Pre-exist. bh.prob</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>68</td>
<td>8</td>
<td>1.000 (.192, 5.205)</td>
<td>1.00</td>
</tr>
<tr>
<td>Present</td>
<td>17</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>85</td>
<td>10</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

N, number; PB, phenobarbitone, CBZ, carbamazepine, bh, behaviour,
Table 7.6: Multiple logistic regression model for outcome behavioural problems

<table>
<thead>
<tr>
<th>Variables</th>
<th>Odds ratio (95% CI) for behavioural problems</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. PB vs CBZ</td>
<td>1.184 (0.283, 4.953)</td>
</tr>
<tr>
<td>2. Age at presentation</td>
<td>0.997 (0.979, 1.015)</td>
</tr>
<tr>
<td>3. Male vs Female</td>
<td>3.407 (7.87, 14.746)</td>
</tr>
<tr>
<td>4. IQ=&gt;70 vs&lt;70</td>
<td>0.815 (0.164, 4.055)</td>
</tr>
<tr>
<td>5. Motor disability</td>
<td></td>
</tr>
<tr>
<td>Absent vs present</td>
<td>2.110 (.417, 10.685)</td>
</tr>
<tr>
<td>6. Bh problem</td>
<td></td>
</tr>
<tr>
<td>Absent vs present</td>
<td>1.121 (.196, 6.395)</td>
</tr>
</tbody>
</table>

Bh, behavioural
Table 7.7: Survival time difference adjusted and non-adjusted (by Cox-regression)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Survival time</th>
<th>Standard error</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted with other disability</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phenobarbitone</td>
<td>102</td>
<td>18.03</td>
<td>66.68, 137.36</td>
</tr>
<tr>
<td>Mean survival time</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>73.71</td>
<td>15.74</td>
<td>42.85, 104.57</td>
</tr>
<tr>
<td>Mean survival time</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted with other disability</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phenobarbitone</td>
<td>122</td>
<td>31.61</td>
<td>60.26, 161.04</td>
</tr>
<tr>
<td>Mean survival time</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>72.56</td>
<td>37.48</td>
<td>0.00, 46.04</td>
</tr>
<tr>
<td>Mean survival time</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure- 7.1: Kaplan-Meier cumulative seizure curve for patients with PB & CBZ

Survival Functions

Kaplan-Meier curve showing seizure-free interval. Drug A, phenobarbitone
Drug B, carbamazepine
7.4: Discussion

In this trial we found no significant difference in behavioural side effects between the PB and CBZ groups using objective, masked assessments and parental reporting. In a study designed to find at least a 25% difference at 5% level, ten children showed deterioration of behavioural state of which four were in the PB group and six in the CBZ group. Intolerable behavioural problems were reported more frequently in the CBZ than in the PB group. Among other side effects, sleep disturbance and gastrointestinal problems were more frequently reported in the PB group. By contrast headache and worsening of seizures (defined as increased the existing seizure type or evolving to myoclonic type of seizures) were more frequently reported in the CBZ group. However there was no statistically significant difference between the two groups in respect to side effects. We found significant improvement in behaviour after regular treatment in 16 (18.8%) children (8 in each group). This probably reflects removal of the burden of frequent seizures improving quality of sleep and/or feeding and reducing irritability.

Studies supporting of this finding
Our results support the findings of studies in Kenya and in India, where the authors have found no severe behavioural side effects with PB (Feksi, Kaamugisha, Sander, & Gatiti 1991; Pal et al. 1998a; Wendy 1987). The population characteristics are similar in those two developing countries with high rates of seizures (op.cit.). Wendy et al. examined the trial in the US on children with partial seizures (Wendy 1987). They also have found no difference in terms of behavioural or cognitive effects between the two drug trial groups.

Studies not supportive of this finding
In the UK mono-therapy trial, de Silva and co-workers studied four AEDs (PB, CBZ, PHT, and VPA) to compare their efficacy and side-effects (de Silva, Mac Ardle,
McGowan, Hughes, Stewart, Neville, Johnson, & Reynolds 1996). The authors stopped the PB assignment when 6 out of the first 10 children given this drug had to change because of carers’ reports of unacceptable behavioural side effects. This was on the basis of widespread views of such effects on children in the UK, so that continued medical and parental cooperation in the study of the other drugs necessitated the withdrawal of PB. No standardised behavioural assessment tool was used, however.

Wolf and Forsyth (1978) in another study from Los Angeles (Wolf & Forsyth 1978) have reported marked behavioural problems in children treated with PB compared with those with no therapy. The background of their study differs from other trial studies mentioned before in some ways: (i) patient selection was of children with febrile seizures, in which pre-existing neurodisability would be low and the children were relatively younger, (ii) side-effects were not compared with those of another AED and (iii) there was no formal measuring scale.

My personal inclination is to say that there is a clear bias in patient selection in Wolf and Forsyth’s study and in de Silva et al’s study. The AEDs have effects on alertness, mood and memory, which also might be the result of the disease process. As shown in Wolf and Forsyth’s study, a percentage of children who were not treated also developed hyperactivity during follow-up. It is therefore important to consider the intrinsic factors, which would include seizure types and severity. This can be justified by the fact that the children in the other three studies, which did not find any difference between the trial groups in their populations, were all diagnosed with epilepsy.

In the North American “cross-balanced randomized controlled trial study” of PB vs VPA using 28 children of normal intelligence with relatively mild seizure disorders, the authors found only marginal difference in hyperactivity between the two drugs (Vining, Mellits, Dorsen, Carpay, Citaldo, Quaskey, Spielberg, & Freeman 1987).

Two studies (Wendy 56-60; Vining, Mellits, and Dorsen 165-74) from developed countries undertook the trial in epileptic children and have found no remarkable difference in hyperactivity between the trial drugs i.e., PB vs CBZ or PB vs VPA.
Although the total numbers are not large, the accumulated findings from these studies and clinical experience suggests that behavioural side effects are reported less often in countries with limited resources than in more affluent countries.

**Age, sex and seizure criteria of this study population compared with other studies and seizure remission rates**

Age at randomisation, the seizure characteristics and associated prognostic features, i.e., age at first seizure, total number of seizures before starting appropriate treatment and associated non-convulsive disorders in our study population were unlike the study population in developed countries. However proportions of seizure types were comparable with those in the UK and Indian studies.

A small proportion of our population had given a previous history of daily AED intake. This figure is comparable with that found in other developing countries (Pakistan, Ecuador, and Kenya) where 6-26% were on regular medication (Shorvon et. al. 1988; Feksi, Kaamugisha, Sander, & Gatiti 1991).

The population we studied was from a mixed rural and urban population and was approximately representative of the population of the country. The seizure and epilepsy related characteristics were comparable with other studies in countries with limited resources and some were comparable to those of the UK study.

Medium term seizure remission rate in this study was comparable to that found in developed countries and there was no difference in efficacy between PB and CBZ. The seizure remission rate in other studies varies from 67% to 73% (Feksi, Kaamugisha, Sander, & Gatiti 1991; Placencia, Sander, Shorvon, Roman, Alarcon, Bimos, & Cascante 1993; Shorvon & Farmer 1988).

Feksi in Kenya included both a child and adult group. Their population had similar background of high seizure frequency and time gap between the onset of seizures and starting appropriate treatment. Fifty three percent of the patients were seizure free in the 6 to 12 month follow-up period and this was 50.5% in our study.
Wendy (1987) studied PB trial in the children with partial seizures in the USA and 66.7% of them were seizure free after one year of treatment (78% in our study). In the Northern Ecuador study (Placencia et al., 1993) 65% were seizure-free at 6 months follow-up and 72.7% at 1 year’s follow-up (78% in our study). In the UK study (de Silva et al., 1996) 73% of the total population achieved one-year seizure remission at 3 years.

We found no significant difference in mean, median and range of IQ scores before and after one year of treatment. Treatment was effective because despite 63% of the children having more than 10 seizures during the previous year, 30% more than 10 seizures during the previous month and 57% having more than one year’s time gap before starting regular treatment so that 78% of children had total seizure reduction and another 11% had more than 80% seizure reduction after one year of treatment. We therefore recommend that PB is an effective and acceptable AED in the setting of rural and urban childhood population in Bangladesh.
CHAPTER EIGHT

8. Discussion and implications of the results

8.1: introduction

This study aimed to describe the profile of childhood epilepsy and associated disabilities in BD, to identify predictors of seizure outcome from the information available on first day of diagnosis, and to compare the behavioural side effects of two commonly used AEDs. This chapter will discuss the implications of the study findings for countries with limited resources and will consider the limitations of the study and evaluate the validity of the predictors of seizure remission. Finally, possible directions for future work will be considered.

8.2: Results and their implications

8.2.1: Epilepsy profile and service development

The epilepsy profile has already been described (Section 6.10.4) and discussed (Section 6.11.6). Unfortunately there is only a few studies on the detailed epilepsy profiles and even less studies on the treatment and outcome of seizures in populations with limited resources that lack structured services. Some simple treatment models have been suggested from studies in Africa and northern Ecuador. However, their sustainability is uncertain, because although initially successful the programs stopped after the people who had established them moved away (Feksi, Kaamugisha, Sander, & Gatiti 1991; Palencia et al. 1981). These examples have therefore more similarities with failing vertical interventions such as those associated with malaria or trypanosomiasis (Unger & Killingworth 1986), than with the community based approach that they were trying to adopt.
In keeping with WHO recommendations, the background, setting, and the results of this study are supportive of epilepsy services being integrated into general primary care services with close links between primary, secondary and tertiary centres to ensure sustainability.

8.2.2: Significant predictors of seizure outcomes

Multiple seizure types, a high rate of seizures, early onset of seizures, malignant epilepsy syndromes, associated motor disability, low IQ and abnormal EEG were strongly associated with ‘poor seizure remission’ as identified by univariate analysis. On multiple logistic regression, multiple seizure type ($p < 0.001$), low IQ ($p < 0.001$), and motor disorder ($p < 0.04$) independently had a significant association with poor seizure remission when the clinical predictors were entered into the model (Section 6.10.8). ‘Abnormal EEG feature’ was another strong independent predictor ($p < 0.01$) of seizure outcome when entered into the multiple logistic regression model without any significant effect on the estimate of other clinical predictors in the model (Section 6.10.8, Table-6.18).

‘Low IQ’, and ‘multiple seizure types’ remain the most significant predictors of poor seizure prognosis when controlled by all potential predictors in our study. With stepwise logistic regression, the last step in the model contains another significant predictor - ‘motor disability’.

The predictors of poor seizure remission identified in this study are comparable with several studies done elsewhere. For example, the presence of cognitive impairment during first diagnosis was found to be associated with poor seizure remission in almost all the studies performed in children, e.g., Berg (1996), Brorson and Wranne (1987), Sillanpaa (1993), Camfield (1993), Anneger (1979) (Table 2.1 in Section 2.11.1).

‘Motor disability’ has had a similar strong association with seizure outcome in the literature, except in Camfield et al’s paper (op.cit.) where only selected seizure types and age groups were studied.
The motor and cognitive impairments are readily available signs at the time of diagnosis, but other clinical factors are often identified as predictors of seizure outcome in different combinations (Section 2.11.1, Table 2.1) such as seizure types, rate or number of seizures before starting treatment, status epilepticus and age at onset (Annegers, Hauser, & Elveback 1979; Arts et al. 1999; Berg, Hauser, & Shinnar 1995; Brorson & Wranne 1987; Camfield, Camfield, Gordon, Smith, & Dooley 1993; Casetta, Granieri, Monetti, Gilli, Tola, Paolino, Govoni, & Lezzi 1999; Wakamoto, Hideo, Masatoshi, & Takehiko 2000). EEG features were also considered in a few studies (Ko & Holmes 1999; Shafer, Hauser, Annegers, & Klass 1988).

The accumulated evidence from this and other studies is that the common denominator of poor seizure outcome in childhood epilepsy is the presence of some kind of brain-damage or structural abnormality. This is the case whether expressed as symptomatic or remote symptomatic epilepsy, the presence of neurological abnormalities at examination (identified as motor, and/or cognitive impairments).

Other frequently reported predictors of poor seizure outcome are the presence of multiple seizure type, high initial seizure frequency and early onset of seizures (Table 2.1). Among these three characteristics of seizures, multiple seizure types and high initial seizure frequency are found to be associated with poor seizure remission in many of the studies (op.cit). 'Multiple seizure types' is more an independent factor compared to 'initial seizure frequency'. The latter can be influenced by a number of factors, such as treatment, time gap (Section 4.5.10) and type of seizures such as infantile spasms, tonic and myoclonic seizures are mostly with higher frequency from the onset compared to other types of seizures.

In our study, the seizure rate at the time of diagnosis had a significant correlation with treatment time gap indicating that the more frequent the seizure rate the less was the time gap (Section 6.10.10). It was evident from our data that, parents seek medical help more readily in case of frequent seizures and that once medical treatment is established seizures are more likely to be controlled. On the other hand less frequently occurring major attacks or multiple seizure types with less frequent major attacks might delay appropriate treatment.
'Age of onset' was significantly correlated with seizure outcome when both the continuous or categorized variables were correlated independently, however, this lost its significance in the multiple logistic regression when associated with other factors in our study. Most of the children with 'early age of onset' also had high rates and multiple types of seizures. We explored this by entering individual factors into the model, examining their effect on the estimate for early age at seizure onset and found that early age at onset had direct co-relations with 'malignant epilepsy syndrome' and with 'multiple seizure type'.

In other studies age at onset is variable. In Berg et al.'s (1996) study, onset between 5-9 years was found to be associated with seizure remission, while in Camfield et al.'s (1991) study this was the case with children who had their first seizure before 12 years of age. However this was not confirmed by Sillanppa et al.'s (1995) study as very few of the Finnish cohort of children had their first seizure after the age of 12 years.

Chawla et al. have identified early age at onset as a predictor of poor seizure remission (Chawla et al. 2002) (Section 2.11.1). The OR and 95% CI, however, indicate a small sample in their study. In our study, age at onset before 1 year and myoclonic/infantile seizures, two variables, which have been identified as independent predictors of seizure outcome in Chawka's study, had a shared correlation with multiple seizure types.

'Malignant epilepsy syndromes' had a strong independent association with poor seizure outcome in our study. This factor lost significance when correlated with other factors. We explored why this was the case by entering individual factors into the model, examining their effect on the estimate for 'malignant syndrome'. It appeared that the factors characteristic of 'malignant syndrome', especially low IQ, motor disorder and multiple seizure types were important predictors of seizure outcome regardless of that diagnosis.

'Status epilepticus' was identified as one important predictor of seizure outcome in some of the previous studies (Silanppa (1993), Berg (1996)). However, the data in
Berg's study reveals that this was found in children who had remote symptomatic epilepsy or signs of brain damage. It is therefore evident that the significant predictors of seizure outcome identified in our study i.e. low IQ, motor disorder, multiple seizure types at diagnosis are supported by most of the previous studies, allowing for differences in emphasis.

Abnormal EEG was another important prognostic factor found in our study. Few previous studies have considered EEG features as a prognostic predictor (Table 2.1) and our study used similar categories of EEG features (Section 4.10.2). However, for multiple logistic regression analysis we used only a major dichotomy - normal or abnormal EEG features - as a potential predictor, which then showed a strong independent correlation with seizure outcome (Section 6.10.8). In addition, there was a linear correlation with subcategories of abnormal EEG features. Children with both 'epileptiform activities and non-epileptiform abnormalities' in the EEG had a worse prognosis compared to those with either abnormality alone or with no EEG abnormality (Chart 6.1).

Seizure remission was defined differently in various studies; however, the initial response to medical therapy and the short-term and/or medium-term seizure outcome are valuable provisional indicators of long-term seizure remission and are supported by Dutch and Japanese studies (Arts et al. 1999; Wakamoto, Hideo, Masatoshi, & Takehiko 2000).

In our study 52.7% of the whole population had 'seizure remission'; children in the non-specialized OPD group had a better outcome compared to that of the specialized centre (CDC) group (Section 6.10.7). This finding is comparable with results from other countries, including those with limited resources (Section 2.10.3). Brorson and Wranne (1987) suggest that among those children with neurological deficits, the annual remission rate was high only during the first years after onset, subsequently falling to 3% per year (Brorson & Wranne 1987). This may explain why the seizure remission rate in the CDC group of our population is less compared with those in the OPD group.
The better response to a comprehensive management in the OPD population suggest that community-integrated services are more useful where the early detection of the condition and establishment of appropriate management are possible, and that this may prevent further neurological impairments and secondary educational and social problems.

The patients recruited from non-specialized (OPD) centre were fairly representative of the general population in terms of socio-economic status though some selection bias undoubtedly remains. More severe epilepsies are represented in the whole population, but there are no other data to compare this profile with the general community as a whole.

Seizure remission was good when there was no associated motor or cognitive disability present (Table 6.12). Among the children who had associated non-convulsive disorders, seizure remission was achieved in 35.6 to 40.3%, and was faster in the OPD group. Epilepsies in the CDC group were longstanding and had more severe grade of non-convulsive disorders. A large proportion of this group was on AED treatment before entering in the study. Our result was comparable with the findings of a U.S. study (Annegers et al. 1979) where the authors differentiated the seizure outcomes amongst the two groups with and without associated neurological deficits after 15 years of observation (Section 2.11.1).

Two immediate important messages emerged from the above discussion: non-specialized service for childhood epilepsy is more useful and early commencement of treatment help to prevent further disability and reduce the family burden.

A pilot study in India advocated a short-term training for PCP (Section 4.12) to improve compliance and follow up care in their ‘epilepsy control programme’. However, they did not focus on childhood epilepsy and associated disabilities. These were emphasised in the intense training for our prospective study however, the effectiveness of this is yet to be studied.
Our study population included children with all types of epilepsy and associated neurodevelopmental disorders regardless of underlying cause and severity, which is an appropriate model of epilepsy service in a country with limited resources like BD. By exploring the epilepsy profile at a specialized and at a non-specialized centre we are able to provide a more comprehensive picture of the problem. In addition to that, we explored the potential preventable risk factors of early onset epilepsy and associated neurodevelopmental disorders (Section 6.11.3; Table-6.3.1). Over 60% of the children who had poor seizure remission had history of perinatal asphyxia and/or neonatal seizures. Early identification of high-risk pregnancies and arranging for their delivery at the health care centres or hospitals, ensuring normal deliveries by trained traditional birth attendants will together reduce a large number of early onset epilepsy and neurological disabilities in rural children. With the increasing rate of female literacy this will be easier to achieve at the present time in BD.

In the total population, 87(22.3%) (Section 6.10.1; Table-6.1) had a previous history of febrile seizures or meningitis/encephalitis. Given the background of low living standard and malnutrition among the under five year old children, frequent infection at this age group is very common in BD. Strategies to address these important issues must be taken into account in any programme to reduce early childhood epilepsy.

We considered the need not only for an appropriate treatment guide for the epilepsy service provider but also for the education of the patients and the family members in our study. Assessment of the existing knowledge and attitudes towards epilepsy in the population is an important step to providing a successful long-term management programme. The findings (Section 6.10.2) regarding the families’ existing knowledge about epilepsy in this study provide important background data, based on which an educational program can be developed for the general population in this region. This however, needs further investigation in general population. In addition, we provided parental education on epilepsy and non-convulsive disorders, the data after follow-ups (Table 6.2.2) proves the positive effect of such educational programme. Our experience in this regard is supportive of other studies on parental education (Section 6.6.7. point c).
We therefore suggest that a comprehensive management programme for the children with epilepsy and non-convulsive disorders should include an education intervention programme for the population.

The remarkable gender discrimination observed in this study reflects common social practices in this region as parents are expected to spend their limited resources on the male child. This was particularly demonstrated (male female ratio 10:1) in the children with febrile seizures. However, there was no male-female difference seen in the prevalence study among the urban and rural population (Durkin et al. 1992).

Most of the studies from the developing and developed countries, which examined the seizure outcome in children, reported median age at onset of seizures from 2.5 to 6 years. Our population showed a much earlier age of onset, which was 8 months (Section 6.10.4). This was also seen in the seizure characteristics, which revealed that frequency and number of seizures before starting treatment was very high in our population and comparable to studies in other developing countries (Feksi, Kaamugisha, Sander, & Gatiti 1991; Placencia et al. 1993). The severity of seizure-disorder and associated motor and/or cognitive impairment were also higher in the CDC group when compared between the two groups in our study population (Table 6.4).

Although the estimated prevalence of febrile seizures in Bangladesh is high, no association between the febrile seizures and epilepsy is noted (Durkin, Leislie, Devidson, Hasan, Hasan, Khan, & Shrout 1992). A remarkable proportion of children in the newly diagnosed epilepsy group had history of recurrent febrile seizures. However associated factors recorded in this group are suggestive of different pathophysiology of febrile seizures evolving to non-febrile seizures (Section 6.10.1). The incidence rate of evolving non-febrile seizures is comparable with other long-terms studies (Konishi et al. 1990; Seki, Yamawaki, & Suzuki 1981; Tsuboi, Endo, & Iida 1991). Associated factors in these children are also comparable to those found in one study of febrile seizures with a long-term follow-up which identified risk factors for developing non-febrile seizures in children (Tsai & Hung 1995).
A proportion of our study population were treated with a short course of prednisolone on appropriate indication (Section 6.10.10). The analysis of the data provides two pieces of information: (i) a large proportion of these cases were inappropriately treated with AEDs before entering to this study; (ii) early response to prednisolone therapy has a prognostic value with significant positive correlation between the early response and seizure reduction after one year (Table 6.23 & 6.24).

A comparable proportion of population gave a history of previously AED treatment (Table 6.25), this data is adding information to the previous studies in developing countries. Among the children with a primary diagnosis of epilepsy, about a quarter gave a history of taking AEDs for more than 2 months, although only 44 of them were taking regular medicine on the day of assessment. The treatment gap (Section 2.10.1) was 88.7%. Because this assessment includes only those children who came for medical care voluntarily, the true figure for the population in this region may be even higher.

Difficulties with behaviour and emotion are more marked and common in epilepsy compared to other chronic conditions in children such as diabetes (Davies, Heyman, & Goodman 2003). The various ways that cognitive function is affected in children with epilepsy are discussed in section 2.6. In Sillanpaa et al’s study over 49% of the children with epilepsy had a learning disability (Sillanpaa 1993). Our population seemed more vulnerable with 61% with cognitive impairment (Section 6.10.5), which is likely to be significantly related to the poor pre-, peri-, and post-natal care. However the proportion of children with cognitive impairment in the OPD group (49.2%) was comparable with that of Silanapaa’s group (op.cit.). This high rate of cognitive impairment among the children with epilepsy highlights the need for special education in this region.

As discussed above (Section 7.4), the behavioural side effects of PB treatment in particular have been examined both in countries with limited resources and in developed countries. There were no significant behavioural side effects compared to the CBZ group in our study (Section 7.3.2).
Given the importance of EEG as an independent predictor, the establishment of paediatric neurophysiology services would be another key component to the success of a paediatric epilepsy service. Although, Senanayake and Roman (1993) (Senanayake & Roman 1993) reported from Sri Lanka that EEG was not necessary for the diagnosis of epilepsy in children; they did not consider short- or long-term outcomes. The results of the present study emphasize the need for non-invasive diagnostic tools such as EEG as an essential part of any epilepsy services at the tertiary level in developing countries. Binnie (1999) recommends that EEG is of crucial importance for answering the specific, clearly defined questions which commonly arise in the management of seizure disorders (Binnie 1999). In our setting the EEG appears to offer improved classification of seizures and epilepsy (Section 6.11.10), rationalization of selection of cases for neuroimaging and confirmation/supporting evidence of continuing need for AEDs, all at comparatively low cost.

8.3: Conclusion

The clinical predictors of seizure outcome validated by this study are strong evidence that the presence or absence of certain clinical factors at first diagnosis can predict the medium-term seizure outcome. Current knowledge suggests that early identification of epilepsy in children and establishment of appropriate treatment should start as soon as possible with an aim to prevent further neurodisability. Our study suggests that it will be feasible to develop an appropriate treatment guide for childhood epilepsy and associated disabilities for a country with limited resources. This study also found that phenobarbitone is effective for generalised tonic-clonic, partial and secondary generalised type of seizures in children without producing unacceptable behavioural problems when compared to carbamazepine. This supports the WHO strategy of low-cost epilepsy control programme for the countries with limited resources. These data provide additional perspectives for counselling patients and their families and help the professionals in the early selection of subjects for intensive follow-up and
more extensive investigation. The present study also supports that a holistic approach to the assessment and management of children with epilepsy and associated impairments is required. Such a service is best delivered by a “multidisciplinary approach” with a particular role for developmental therapists, special education teachers, and psychologists. The results show that even with a short training period, a comprehensive epilepsy service can be delivered by a non-specialist team in a setting with limited resources which should, however, include provision for first line investigations such as EEG.

Building upon the experiences from other studies in similar settings, priority must now be given to the sustainability of any epilepsy programme. A close link between the primary, secondary and tertiary centres will be an essential component. This can be achieved by integrating the epilepsy service with the governmental primary health care centres and with community based rehabilitation services (CBR), which have already been started in the rural and urban areas in Bangladesh as non-government organizations.
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APPENDIX: I

CDC EPILEPSY- RESEARCH, RETROSPECTIVE STUDY DATA
ENTRY FORM

1. Name of the child ..........................  CDC M no:------   RID No: ------
   DOB ---/--/---  SES no:----  ----  EEG No:------
age --- Y ---Mo  sex ----
DO first visit at CDC ---/--/---
Last visit on  ---/--/---  total number followed up: ___

Parents' Ma --------------------------------, Baba ---------------------------
Address :
Phone number:
Urban [ ] Rural [ ]

2. Clinical diagnosis :

3. C/O (on the first day at CDC)
   Seizure 1.-----------------------
   Neurological(motor) 2.-----------------------
   Cognitive 3.-----------------------
   Behavioural problem 4.-----------------------
   Other 5.-----------------------

4. H/O

   Consanguinity : Marriage between first degree relative?
   Epilepsy in first degree relatives
   F/H of febrile convulsion
   Preceding febrile convulsion
   Meningitis
   Encephalitis
   Status epilepticus (before entry / during follow up period)
   Head injury
   Preterm birth
   Perinatal asphyxia
   Neonatal seizure
   Kernicterus
   Recurrent infection during follow up period
   Socioeconomic status (very poor=1,poor=2, middle income group=3
   higher inc.gr=4)

Parental education: (none= 1, primary=2, secondary=3, >secondary level=4)
   Mother: [ ] father : [ ]
5. Seizure evaluation (on first visit at the epilepsy centre):

Age of first unprovoked seizure (age in months)

Seizure frequency (number of seizure/day, wk, mo/year)

High rate of seizure (1/wk) y/n

Seizure type: (GTCs, GTs, MC, IS, Clonic, Atonic, Absence, simple partial, complex partial, secondarily generalised seizure, unclassified)

Single seizure (y/n)  Multiple seizure (y/n)

Epilepsy type (generalised, partial, secondarily generalised, Unclassified, reflex)

Specific syndrome (IS, WS, LGS, LKS, MC encephalopathy)

6. Findings on examination:

Sign of UMN lesion? (y/n)

Sign of LMN lesion?

Motor disorder: (major=1; mild=2; none=3)

Mental state (retarded = 1; normal = 2; uncertain = 3)

Psychological assessment report (IQ=)

Behavioural state (hyperactive/irritable=1, doped/drowsy/less responsive=2; uncertain=3; normal=4)

7. AED started on: ---/----/----

AED Present previous

(if AED changed at CDC, please mention why changed)

Date of last seizure ---/----/----

Is the child seizure free now? (y/n)

Time taken to become seizure free (in months)

8. EEG study finding: description of the report

Electro clinical diagnosis: EEG feature compatible with

8.1. Other investigation done? (if yes please write the major finding)

USG: (Y/N)

CT scan of brain:
9. Follow up records:

Last day of follow up: --- / --- / ---
Seizure frequency during 3 months time before the last follow up day:
(number of attacks per day, per wk, per mon, per yer.) /d / wk /mo /yr

Seizure types during the last follow up
Is the child seizure free? (Y/N)
Seizure free for (in months)
Motor functional development (delayed =1, normal =2)
Cognitive assessment report after intervention
Behavioural problem (Y/N)

Date:
APPENDIX: II

EPILEPSY RESEARCH IN CHILDREN: MEDICAL-ASSESSMENT FORM (MAF)

Section I

(A.) Patient’s name ___________________________ sex __________
Mother: ___________________________
Father: ___________________________
Address: Village: ___________________________ P/O: __________________________ Thana ___________________________
District: ___________________________

Date of examination: ————/ ————/ ————
Date of birth: ————/ ————/ ————
Present age: ——— yr ——— mo
Tel.ph.no ————

Location of examination: (1=D.S.H. OPD, 2=CDC) Examiner’s initials ————

Informant(s):
Mother=1, Father=2, grand parents = 3, sibling = 4, other relatives = 5, self =6

Instructions:
Part I: Please administer semi-structured interview. Ask all the questions specified in this form. Use local terminology if necessary to ensure that the informant understands the question. Please ask the informant to show you the seizure attacks by acting. Be sure to answer all questions. Most should be answered by writing the code or putting tick mark in the space provided. Some of the question require a brief answer in words.

Part II: please read the management part and the follow up part carefully before you advise.

(B) PRESENTING COMPLAINTS:

Parents’ concern on first visit: (please ask the parents)

Q. What are the main reasons you brought your child to the doctor for?

Related to:
1. Seizure

2. motor/functional dev.

3. vision/hearing

4. cognition/behaviour

5. other(specify) Please ask the parents the following questions.

Q. When your child was alright?

1= was never alright, has seizure since birth (when there was no sz-free period after neonatal sz. in other cases, consider the neonatal sz. a separate event )

2= Never alright, did not have seizure but other related to development

3= Was alright up-to the age ——— years ——— months

Q. When you noticed the first seizure (after the neonatal period)?

Q. First unprovoked seizure on ——— years ——— months ——— days of age

age of onset after 12 months of age =1, before 12 mo. Age=2
Please ask the parents to show you the exact events that occur to their child.

Q. Onset: 
always partial = 1, always generalized = 2, mixed focal and generalized = 3,
multifocal = 4, uncertain = 5

Q. Seizures associated with:
Vocalization = 1, screaming = 2, fear = 3, Hallucination = 4
sensory symptom or automatism = 5, Aura = 6, none = 7

Q. Usual time of the episodic attacks? (Relation with the child's state) eg.
1 = During sleep, 2 = in awake state, 3 = while playing, 4 = just on awakening,
5 = after physical or mental exhaustion, 6 = no such relation

Q. Is there any provoking factor?
1 = Flickering light, 2 = TV/ VDO game, 3 = touch, 4 = sudden noise, 5 = mental/physical exhaustion,
6 = none, 9 = other (specify)

Q. Duration, frequency. Please mention the duration of attacks separately if there are multiple types
seizures. How frequently they occur? Please start asking the parents from per day to per year.

Seizure type | age at onset | duration | frequency
-------------|-------------|----------|-------------
type 1. | | | |
type 2. | | | |
type 3. | | | |

Q. Single or multiple type of seizure attacks:
Single seizure type = 1, Multiple seizure type = 2, uncertain = 3

Q. Seizure rate:
Freq. of minor attacks (nc Jerks, muscle spasms, absences, head drops)
less than 1/Week = 1, 1 or more/week = 2, uncertain = 3

Frequency of major attacks (Gen tonic, GTC, atonic)
less than one per week =1, 1 or more/Week = 2, Uncertain =3

Q. What happens after recovery from each attack?
1 = starts doing what s/he was doing before, 2 = sleeps for a long time, 3 = recovers with vomiting
4 = complains of headache, 5 = develops weakness of limbs, 6 = temporary loss of speech
7 = other (specify) 8 = none

A COMPLETE DESCRIPTION OF THE SEIZURE ATTACKS:
(nonconvulsive episodes, sudden behavioural change, sudden fear, cry, flickering of fingers during sleep,
frequent fall, fidgety, sudden restlessness, screaming, head drop, head jerk, reflex seizure, flushed face in
children, all the episodic attacks should be written in language.)

---

Seizure type (s) from beginning to present state. (evolution)
Initial episodes: seizure type -------- frequency --------- duration -----------
Subsequent episodes: Sz type ------- frequency --------- duration -----------
Present episode: Sz type --------- frequency --------- duration -----------

change of seizure type at entry present = 1, no such change = 2, uncertain = 3

Q. Associated impairment or disability?: Absent = 1, present = 2

If there is other problem, please mention the age of the child when parents noticed them
Any problem with age when first noticed

- Gross motor (head control / Sitting / Standing / Walking)
- Fine motor (Hand use)
- Vision (does not look at things, no social smile)
- Hearing (no response to call or sound)
- Speech (developmental delay or regression)
- Poor understanding comparing with children of same age
□ Behaviour (problem since birth or sudden onset)
Other (specify) ________________________________________________________________

Q. Is there any correlation between the above mentioned problems and the child’s seizure?
problem(s) is/are influenced by seizure frequency and severity = 1, no such relation = 2, uncertain = 3

If the child is of school age (5 years or above)
Q. Does the child go to school? If not why? (yes = 1, no = 2)
□ Yes, goes to a regular school = 1, yes goes to a special school = 2
□ No does not go to school because of:
1 = epilepsy, 2 = motor developmental delay, 3 = both 1+2, 4 = poor cognition, 5 = behavioural problem
6 = 3+4+5, 7 = parents are not aware of sending the child to school, 8 = not yet achieved
9 = other (specify) ________________________________________________________________

Q. During the past month has the child been limited in school work or activities with friends due to:
not applicable = 8
Emotional / behavioural difficulties?

□ No = 1 somewhat limited = 2 very limited = 3
Problem with recurrent seizure attacks?

C. Family history
Q. With who the child leaves most of the time?
Parents = 1, Aunt / uncle = 2, grand parents = 3, other relatives = 4, joint family = 5

Q. Consanguinity: were the child’s parents related before marriage?
(no = 0: yes, as first cousins = 1, 2nd cousins = 2, as uncle and niece = 3,
no, but grand parents were 1st cousins = 5, no but grand parents were 2nd cousins = 6)

Q. How many brothers and sisters does the child have? ----- older ----- younger, none = 8
Q. Is there any history of sibling death, (No =, Yes = 2)
If yes mention the cause? ________________________________

D. Family history of medical Conditions
Please indicate whether any relatives of the child have a history of any of the following medical Conditions. Check all that apply:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Sibling</th>
<th>Mother</th>
<th>Father</th>
<th>Other relative (specify)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergies</td>
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<tr>
<td>Asthma</td>
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<td>Attention problems</td>
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<tr>
<td>Behavioural or psychiatric problem</td>
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<tr>
<td>Cerebral palsy</td>
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<td>Developmental disability</td>
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<td>Epilepsy</td>
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<td>Febrile seizure</td>
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<td>Learning disability</td>
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<td>Speech delay</td>
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<tr>
<td>Other disabilities or conditions</td>
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</tbody>
</table>

Q Has Family history of febrile seizure = 1, F.H. of epileptic seizure = 2, other = 3, None = 4

E. Mother’s Pregnancy History:
Maternal age during pregnancy: _______ years
Q. Was she on Antinatal check up? (yes on regular check up = 1, yes but irregular = 2, not at all = 3)
Q. How many times have you been pregnant, including miscarriages and abortion? _______
Q. Is there any H/O abortion=1, stillbirth =2, IUD=3, none=8
please put a tick mark if there is positive history of the following

H/O maternal illness:
  a) High blood presser (m)
  b) Diabetes during pregnancy or before(m)
  c) Pre-eclampsia (m)
  d) Seizure (m)
  e) Fever during the pregnancy(1st,2nd trim)
  f) J. Measles during the pregnancy
  g) Accident/physical trauma
  h) Psychological disturbance
  i) Taking abortificiant during pregnancy period
  j) Threatened abortion
  k) Other (specify) ----------------------------------
  o
  c
  d
  h)
  i)

F. Perinatal/birth history:
Q. Where was the child born? (Home =1, Hospital=2, clinic = 3, other = 4) 
Q. Was the baby born at full term(9 months)?
  Yes = 1, no >3 wks earlier=2, no >2 weeks later =3, Unknown = 4
Q. How long was the labour?(2nd stage) ______hrs. (within normal limit=1, prolong =2, uncertain=3)
Q. Who assisted in delivering the baby?
  Trained midwife/TBA=1, untrained TBA=2, family member=3, doctor=4, other=5 (specify),
Q. Mode of delivery: N. V. D. =1, assisted with forceps/vacume = 2, By LUCS = 3
Q. H/O difficult labour? No =1, prolong 2nd stage of labour with head obstructed =2
Q. Did the baby cry immediately?
  yes = 1, no but in <5 minutes = 2, after >5 minutes = 3, after a few days = 4, unknown = 5
Q. What was the baby's skin colour after birth? pink = 1, white or pale =2, blue or black =3
Q. Movement at birth: (normal=1, limp/did not move=2, almost like a dead baby=3)
Q. Did the birth attendant had to do anything to make the baby cry?
  no=0, yes =1, unknown = 2, had to be hospitalized for resuscitation = 3
  If yes explain what____________________________________________________________
Q. Had no asphyxia=1, history suggestive of P/A =2, had definite p/a=3, Uncertain=4
Q. How big was the baby? (about the size of most babies =1, smaller than most babies =2, bigger than most babies =3, uncertain = 4)
Q. What was the birth weight of the baby in grams? _____________________gms. Unknown =0
  Birth weight: within normal limit=1, LBW=2, VLBW=3, Unknown =5

Comment on perinatal history:
1=Full term normal delivery no P/A, 2=preterm ND with no P/A, 3=definite P/A with FT Vaginal
delivery, 4=preterm VD with P/A, 5=FTCS with P/A

G. Neonatal history:
Q. Did the baby have any difficulties during the first four wks?
  no=1, yes=2, unknown = 3
Q. If yes, what difficulties?  
  1=Difficulty in breathing, 2=poor cry, 3=poor feeding, 4=excessive cry, 5=poor sleep,
  6=n. seizure, 7=n. sepsicemia, 8=n. meningitis, 9=jaundice/kernicterus, not physiological
  10=other (specify)

H. Nutritional History:
Q. For how long was the child fed breast milk only? ____________mo. of age -
Q. At what age was solid food introduced? ____________________mo of age
  Undernurished child = 1, well nourished child = 2, Uncertain = 3

I. Developmental history:
As an infancy:
  No yes don't know
Does / did the child enjoy cuddling? □ □ □
Is / was the child irritable, crying excessively? □ □ □
Does / did the child sleep less because of restlessness or excessive cry or waking up easily? □ □ □

as a Toddler (2 to 5 yrs)
is / was the child engaged in frequent head banging? □ □ □
Does/did the child seem to have more injuries than most other children? □ □ □

Q. At what age the child did the following? (please record the period in months)
milestone of development within normal limit = 1, delayed = 2, not yet reached = 8, don't know = 4

smiled at ------------------ mo age □
rolled over at ------------------ mo age □
head controlled at ------------------ mo age □
crawling at ------------------ mo □
standing with support at ------------------ mo □
Independent standing at ------------------ mo □
walking at ------------------ mo □
running at ------------------ mo □

Comment: Milestone of development
Achieved at appropriate age = 1, delayed = 2, uncertain = 5. Not yet reached = 8.

J. The child's past medical history:
Immunization history: refer to the child's immunization record if the mother brings with her.

Q. Has the child ever immunized for the following diseases?
1) polio: ------ doses, 2) DPT: ------ doses, 3) TT: ------ doses, 4) BCG: ------ doses, 5) measles: ------ doses.
Immunization complete = 1, incomplete = 2, not yet reached = 8, not given at all = 3

Q. Has the child ever had any of the following disease?
Diagnosis age of event diagnosis age of events
(1) meningitis: ------------------ (3) Status epilepticus: ------------------
(2) encephalitis: ------------------ (4) Febrile seizures: ------------------
(5) None

Total episodes of febrile seizures ----------- first at ------------------ mo last at ------------------ mo age

Q. Atypical febrile seizure? Describe ____________________

Q. Has the child ever lost consciousness or had convulsion after an incidence of a head injury?
no = 1, yes within 24 hours = 2, 24 hrs to 1 wk time = 3, 1 wk to 1 mo time = 4, after 1 mo = 5

Q. Has the child had tuberculosis? (No = 1, yes = 2, unknown = 9)

Q. Has the child ever lost consciousness or had convulsion after an incidence of a head injury?
no = 1, yes within 24 hours = 2, 24 hrs to 1 wk time = 3, 1 wk to 1 mo time = 4, after 1 mo = 5

Q. Has the child been hospitalized for an overnight or more? (No = 1, yes = 2, unknown = 9)

If yes, please mention how many times, at what age and reason for admission/diagnosis

diagnosis age or date diagnosis
status epilepticus ------ pneumonia
meningitis/ encephalitis ------ Severe Diarrhoea
febrile convulsion ------ other

Q. Did the child have any surgery? 1= V-P shunt, 2= Other brain surg,
3= other general surg (specify), None = 4

Q. Does the child has a previous diagnosis of any of the following?
1= Down syndrome, 2= cong. Hypothyroidism, 3= Neurometabolic disorder, 4= Cognitive impairment/ MR.
5 = Learning disability, 6 = None

K. History of Medication

Q. Does your child take any medications regularly (every day) for any of the following?
No = 1, yes = 2

<table>
<thead>
<tr>
<th>Medication Type</th>
<th>Since</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seizure or epilepsy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thyroid disorder</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Section II

Evaluation of seizure on the first visit at the Epilepsy clinic:

Type of seizure | age of onset of the particular type | frequency of attacks

- I.S.
- Myoclonic seizure
- Generalized clonic seizure
- Generalized tonic seizure
- Generalized tonic clonic seizure
- Atonic seizure
- Absence seizure
- Simple partial seizure
- Complex partial seizure
- Secondary generalized seizure
- Not clear SPS/CPS
- Reflex seizure on sound
- Reflex seizure on touch
- Seizure on photic stimulation
- Unclassifiable seizure

(unclsz.-includes those where classification is not possible because of inadequate information, or in hitherto described categories, i.e. rhythmic eye movement, chewing and swimming movement).

Minor attacks: (discrete jerks, mild head drop, absences, group of muscle twitching, finger flickering):

<table>
<thead>
<tr>
<th>Frequency</th>
<th>duration</th>
<th>low rate of sz. = 1, high rate = 2</th>
</tr>
</thead>
</table>

Major attacks (big attacks which are sustained, GT, GTC, GCL):

<table>
<thead>
<tr>
<th>Frequency</th>
<th>duration</th>
<th>low rate of sz. = 1, high rate = 2</th>
</tr>
</thead>
</table>

Total number of attacks since first seizure: ____________
Total number of seizures in last year: ____________
Total number of seizures in last month: ____________

Parents' attitude towards their child's problem:

Q. What did the parents do when they first noticed major seizure attacks?
(went to hospital = 1, a primary health physician = 2, a community health worker = 3, Kobiraz = 4, religious people/mowlana for tabiza/pani-pora = 5, other = 6, none = 7)

Q. What is the parents' idea/knowledge about the Mrigi rog/ Epilepsy/ convulsions? (a chronic organic illness = 1, psychological illness = 2, unnatural/jeen-bhut/algा bаtаsh = 3, don't know = 5)

Other (specify) __________________________________________________________________________________

Section III

Neurodevelopmental examination

A. Observation of function:

Please get friendly with the child and the attendant. Give the child a toy for below 2 yrs of age or a pencil and paper/cubes for above, observe the posture, manipulation, movement, response, vision, hearing ability, expression, and speech. Rate the child in the following areas after observing the tasks:

code: pass = 1, fail = 2, uncertain = 3, no response = 4

- Gross motor
- Fine motor
- Speech (motor)
- Speech (language)
additional comment on observation of function of the child:

B. Physical examination (General)

Anthropometry:

<table>
<thead>
<tr>
<th>Child</th>
<th>Mother</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height: ___ cm</td>
<td>Height: ___ cm</td>
</tr>
<tr>
<td>Weight: ___ kg</td>
<td>Weight: ___ kg</td>
</tr>
<tr>
<td>OFC: ___ cm</td>
<td>OFC: ___ cm</td>
</tr>
<tr>
<td>MAC: ___ cm</td>
<td>MAC: ___ cm</td>
</tr>
</tbody>
</table>

Neuromotor status:
- within normal limits = 1
- malnourished = 2
- severely malnourished = 3
- uncertain = 4

Head size and shape:
- normocephalic = 1
- microcephalic = 2
- macrocephalic = 3
- dolicocephalic = 4
- other abnormal shape = 5

Anterior Fontanelle:
- open, normal = 1
- open, abnormal = 2
- closed, normal = 3
- closed, abnormal = 4
- bulged = 5

Any overt dysmorphism?: (absent = 1, present = 2, uncertain = 3)

Facial deformity (specify) __________________________

Other deformity (specify) ____________________________________________________________

Compatible with any genetic Syndrome? (Specify): _____________________________

General appearance:

- Alert
- Apprehensive
- Playful
- Nonresponsive
- Irritable
- Hyperactive/restless
- Doped/poor response
- Other (specify)

Hair:
- Brittle/discolored
- Sparse
- Normal

Skin:
- Hyperpigmented
- Cafe au lait spot
- Normal

Eyes:
- Ptosis
- Nystagmus
- Squint
- Cataract
- Conjunctivitis
- Conjunctival xerosis
- Xerophthalmia
- Normal eye

Mouth:
- Drooling
- Gum bleeding
- Dental caries
- Hair lip
- Cleft palate
- High arched palate
- Normal mouth

Social interaction:
1. Eye contact with examiner and interact either by language or play
2. Eye contact present but does not interact
3. No eye contact but plays on own
4. No eye contact and no interaction, no play on own but attends to other visual or auditory stimuli
5. Visually not fixate but responds to auditory stimuli
6. Visually not fixate but responds to auditory stimuli
7. Other (specify)
8. Cannot assess (specify)

Comment on general examination: 1 = normal, 2 = abnormal (specify)

Attention span:
- Poor attention span = 1
- Normal attention span = 2
- Uncertain = 3

Behavioural state:
Q. Does your child have any problem with behaviour? If yes, for how long?

Codes: no = 1, yes since developing age = 2, recent onset = 3, uncertain = 4

Is he/she very restless, hyperactive? ________
- acts very aggressively to other people?
- acts extremely withdrawn and shy?
- shows odd repetitive movement?
- Head banging?
- Day or night wet/soiling?

If other, list problems: ____________________________________________
Comprehension and understanding:

Q. Does the child understand direction and situations as well as other children of the same age?
Yes = 1  No = 2 (Describe)

Understanding or cognitive state of the child:
seems age appropriate = 1, poor for the age = 2, uncertain = 4

Level of understanding or Cognitive assessment (clinician's judgement during observation):
Seems age appropriate = 1, seems poor for the age of the child = 2, Uncertain = 3

POSTURE OF WHOLE BODY:

Head control:
Normal posture - 1, unable to perform normal posture in any case - 2

Arm posture ........................................ - .. Rt.  Lt.
1-normal, 2-flexor posture, 3-Extensor posture, 4-clenched fist, 5-other (specify)

Reaching for object on lap
1-overcome posture, reaches object, 2-overcome posture tries to reach object
3-makes no motion towards object, 8-not yet reached the age

Grasping for object
1-normal grasp, 2-palmer grasp, 3-Ulner grasp, 4-very weak grasp, 5-does not grasp, not yet achieved=8

Picking up the pellet
1-picks up with both thumb and forefingers, 2-picks up with several fingers opposed to thumb,
3-scoops into palm, 4-touches but does not pick it up, 5-makes no movement toward pellet
not yet reached the age=8

COMMENT:
1=Normal body posture 4=Abnormal body posture
2=Normal arm posture 5=Abnormal arm posture
3=Normal hand function 6=Abnormal hand function

G. Spontaneous motor activity

Four limbs during spontaneous movement
1-active symmetric, 2-asymmetric > on right; 3-Asymmetric > on left,
4-no spontaneous movement, 9-Not in state

Crawling, sitting and walking: (1-child does item, 2-attempt to do, 3-child does not do item, 8-not yet reached)

Side to side movement Pulls to stand
Rolling on bed Stands with support
Commando crawling Stands alone for a few minutes
Independent crawling Takes a few steps without support
Sits with support Independent walking
Sits independently running and climbing stairs

Abnormal movement (Codes 1=none; 2=on right side only; 3=on left side only; 4=on both sides)

Limb dystonia ........................................
Limb tremors ........................................
Spontaneous ........................................
Induced ...........................................

Chorea ............................................
Athetosis ...........................................
Tics .............................................

GAIT TASKS
Have child walk 6' away from examiner and walked back, repeat observing from side.
<table>
<thead>
<tr>
<th>Task</th>
<th>Rt</th>
<th>Lt</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stands on one foot for at least 10 seconds</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hops on one foot for at least 6 times</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walks on toes on command for 6' or more</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walks on heels on command for 6' or more</td>
<td></td>
<td></td>
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<tr>
<td>Tandem walk on command 6' or more</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>BALANCE</strong> (with eyes open, stand with feet together, where stands stable for 10 seconds)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-stable; 2-Unstable; 9-cannot stand. If 1-complete [Romberg test] if 2 or 9 skip</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Romberg test</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(1-does not sway or step off, 2-sways but does not step off, 3-steps off, 9-can’t assess explain)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Finger-to-nose test (test on six excursions)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of excursions off target</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of excursions with ataxia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coordination: normal =1, poor =2, can not performe=3(explain)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not yet reached to test=8</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>COMMENT</strong>: On motor examination:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mobility:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1= Normal gait/ functioning for the age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2= Not normal but ambulant, no aids, independent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3= Ambulant with aids, independent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4= Ambulant with aids, limited</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5= Not ambulant, special chair/sitting</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6= Not ambulant, bed ridden</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hand function(observations and examination of function)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1= Normal functioning</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2= Mild impairment but functioning independently</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3= Moderate impairment performs daily living activity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4= Marked impairment no daily living activities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5= No useful function</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>C. SYSTEMIC EXAMINATION</strong>:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is there any abnormality on examination of the following? if yes specify</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lungs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genitalia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spleen</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>D. NEUROLOGICAL EXAMINATION</strong>:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Examination of the cranial nerves:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intact all the cranial nerves? Yes =1, no =2, If 2 please specify</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscle Tone and Strength</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper extremity (TONE)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1=normal, 2=reduced, 3=increased</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strength</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1=normal, 2=weak proximal only, 3=weak distal only, 4=weak proximal and distal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-other (specify)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9-cannot assess (explain)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower extremity: Tone:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1=normal, 2=reduced, 3=increased</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strength</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1=normal, 2=weak proximal only, 3=weak distal only, 4=weak proximal and distal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-other (specify)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9-cannot assess (explain)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reflexes:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jaw jerk</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
I-no reflex elicited, 2-muscle contraction, 3-muscle contraction accompanied by clonus (exaggerated)

**Biceps Jerk (upper limb)**

<table>
<thead>
<tr>
<th>Rt</th>
<th>Lt</th>
</tr>
</thead>
</table>

I-no reflex elicited, 2-muscle contraction, 3-muscle contraction accompanied by clonus (reflex asymmetry: 1=no, 2=yes on right, 3=yes on left)

**Knee jerks (same code)**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
</table>

**Ankle jerks (same code)**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
</table>

**Ankle clonus**

1=absent, 2=transient clonus, 3=sustained cl, 4=sponataneous clonus

**Plantar response**

flexor=1, extensor=2, uninformative two trials (equivocal)=3

Special issues: For <3 years and those who can not follow C or E chart do the functional assessment:

**Functional assessment:**

<table>
<thead>
<tr>
<th>rt eye</th>
</tr>
</thead>
</table>

1-Fixing and following object; 2-Fixing and following face
3-Fixing and following a bright light only; 4-No fixing or following at all
9-Can't be examined (specify)

**Visual acuity:**

For 3-15 year-olds who can follow C or E chart instructions use Landolt C chart.

Otherwise use the E chart

code:

<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
</tr>
</thead>
</table>
| 6/6 or better (20/20 or better) | 6/9 or better (20/30 or better) | 6/18 or better (20/70 or better) | 6/60 or better (20/200 or better) | 6/61 or light perception (20/201 thru light perception) | No light perception | Unstable | Age <3 yrs. | Cannot be assessed because child is blind, could not follow instructions or other (specify)

If vision is impaired, determine:

was the parent/guardian aware of the child's vision impairment?

yes=1, no=2

**Fundoscopic examination:**

| rt eye |

Normal fundus =1, feature of optic atrophy present=2, other abnormality in the fundus (specify)

**Retinoscopic examination:**

(for selected cases)

<table>
<thead>
<tr>
<th>retinal abnormality</th>
</tr>
</thead>
<tbody>
<tr>
<td>cortical blindness</td>
</tr>
</tbody>
</table>

**Hearing screen (screen at 20 dbHL):**

Functional assessment: (can locate origin of sound =1, cannot hear at all =2, Uncertain =3

Audiometric test result: (1=pass, 2=fail)

Cannot assess because child- 7=cannot hear (deaf) 8-could not follow instructions

9-othe reason (specify)

If hearing is impaired determine:

Was the parent/guardian aware of the child's hearing impairment? (yes=1, no=2)

Please specify if the child has any of the following (put tick mark in the box):
Any soft neurological sign (sns)
Sign of cranial nerve lesion (socnl)
Sign of lower motor neuron lesion (sollmnl)
Sign of upper motor neuron lesion (soumnl)
Nonspecific motor delay (nsmd)
Motor deve. regression (mregs)
Visual impairment (vimp)
Hearing impairment (himp)
Speech and communication problem (spdel)

comment:
seizure started before 12 mo: 1d after 12 months
l=none, 2=mild, 3=moderate, 4=severe
Motor developmental delay: for developmental regression
l=none, 2=mild, 3=moderate, 4=severe
hearing problem since birth: for normal hearing
l=none, 2=mild, 3=moderate, 4=severe
Visual problem since birth: for normal vision
l=none, 2=mild, 3=moderate, 4=severe
Speech delay (expressive): for normal speech
l=none, 2=mild, 3=moderate, 4=severe
Cognition delayed development: for normal cognition
l=none, 2=mild, 3=moderate, 4=severe
Behavioural problem since developing age
l=none, 2=mild, 3=moderate, 4=severe
Behavioural problem recent onset
APPENDIX: III

Section V: Management plan sheet

1. Epilepsy? Yes □ No □ Don’t know □

2. Clinical diagnosis: ________________________________ □ □ □ □

Plan of management:

3. Check eligibility criteria:
   □ Age: 2-15 years
   □ Correct seizure type (generalized except absence and myoclonic; partial, secondarily generalized)
   □ Did not have regular treatment for epilepsy
   □ Static neurology
   □ No contra-indication (leaver disease)
   □ No behavioural disorder before
   □ No significant cognitive impairment

   Action: (if the eligibility criteria fulfils then follow this, if not go to number 8)

4. Counselling
   Treat out of trial
   Investigation
   Randomise

5. RANDOMISATION GROUP
   age
   type of seizure

6. RANDOMISATION RESULT (drug A or drug B) _________

7. Start AED
   Phenobarbital ( mg/kg) Carbamazepine ( mg/kg)
   Actual dose prescribed:
   Number of tablets given:

8. ANTIEPILEPTIC DRUGS (for others than RCT group)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Starting dose/kg/day</th>
<th>Maximum/kg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenobarbitone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phenytoin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbamazepine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valproic acid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clobazam</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nitrazepam</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clonazepam</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lamotrigine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prednisolone/ACTH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
9. Previous history of antiepileptic medication

First started on--------

Time gap between the seizure onset and starting of medication-------

Number of seizures before starting the regular medication :----------

10. Parental counselling
11. developmental therapy
12. special schooling
13. Other
14. Investigation:
   □ EEG -------------------------------

   □ USG of brain (normal= 1, abnormal = 2, Atrophy =3, hydrocephalus =4, other ----------

   □ CT scan of brain(normal= 1, abnormal = 2, Atrophy =3, hydrocephalus =4, other -------

   □ MRI of brain: -----------------------

   □ Biochemistry: ----------------------

   □ Other : ---------------------------

15. follow up date: -------------------------

Plan things to assess on the follow-up day

1st follow up 2 weeks after starting the AED then f/u at one to 3 months interval according the progress of the patient's condition.

During each f/u time, please record the following
1. any new different complaint
2. evolution of seizure: type, frequency, intensity of seizure
3. motor/functional state
4. visual/hearing/speech/cognitive state/alertness/behavioural state.
5. Fix a goal and change it according the present state.
APPENDIX: IV: Follow-up form

Section VI.

Follow up form

Follow up number 1st, 2nd, 3rd, 4th, 5th, 6th, 7th etc. __________

Date ----/--/--
Age: ----- years ------ months Weight of the child: ------ Kg.

1. Any complaint Other than seizure?

2. When had the first seizure after starting the AED

3. Seizure evaluation: Is there any evolution of seizure since started the AED?

   Number or Frequency, date and type of seizures since last visit:

   Type of seizure: 1. ----------------- 2. ----------------- 3. ----------------- 4-----------------

   Frequency: (number of episodes / day, week, / month or / year)

   Minor attacks: ------/ day , ------/ week , ------/ month , ------/ year none
   Major attacks ------/ day , ------/ week , ------/ month , ------/ year none

If no attacks, then when stopped after starting AED? Within 2 wks =1, 4 wks =2, after 6 wks.

Total attacks in previous month (write the number) ------------

Date of last attack --/--/--

4. Examine the child for anemia, jaundice, rickets, skin, face, gums, gait, co-ordination, tremor

5. Look for the drug side effect: action

   Side effect of antiepileptic drug:

   Drowsiness, sleepiness reversible, reassess in one month
   Nausea/anorexia reversible, reassess in one month
   Sedation reversible, reassess in one month
   Sleep disturbance reversible, reassess in one month
   Acne continue if tolerable
   Agitation continue if tolerable
   Dizziness continue if tolerable
   depression/mood disturbance continue only if tolerable
   Doped continue only if tolerable
hyperactive
temper tantrums, aggression
Lethargy
Hirsutism
Uncertainty when walking
Diarrhoea
Shaking, trembling
Abdominal dyscomf ort
increased of appetite
everseous drooling
skin rash
gum bleeding, hyperplasia
Lupus syndrome/ joint pains
Stevens-Johnson Syndrome
Osteoalacia/rickets
Neuropathy
Megaloblastic anaemia
Ataxia or nystagmus
Hepatitis
Neuropathy
Ataxia or nystagmus
continue only if tolerable
continue only if tolerable
continue only if tolerable
continue only if tolerable
continue only if tolerable
continue only if tolerable
continue only if tolerable
continue only if tolerable
discontinue drug gradually
discontinue drug gradually
discontinue drug gradually
discontinue drug gradually
discontinue drug gradually
discontinue drug gradually
discontinue drug gradually
discontinue drug gradually

6. Reported compliance
Blood level of drug done? (1 month, 6 months, end)

Blood level of the AED ----- 

7. Seizure responded to AED ? (yes =1, no =2)
If not, what is the reason do you think?
(Wrong drug / low dose / drug side effect / poor compliance / other )

8. Other advice :
   Developmental therapy
   Special schooling
   Stimulation

9. Reinforce counseling, educate the parents and the child about the illness:
   Epilepsy is a chronic condition like Diabetes, Asthma)
   Not a psychiatric condition, often benign
   Aims of the treatment
   Possible side effects of drug
   Probable duration of treatment
   Consequence of sudden withdrawal
   First-aid/ emergency management
   Restrictions

10. Result:
Name of the AED: ___________________________
Continue treatment with the same AED □
Increase / adjust the dose □
Change to another drug □ State reason
Stop treatment □ State reason

Adjusted dose of AED: ------- mg/kg /day

-sighed:-----------------

How to increase the dose of AED: Starting dose  Maintenance dose  Highest dose
Phenobarbital  1.5 mg/kg/d  3 mg /kg/  5 mg /kg/d
Carbamazepine  4-5mg/kg/d  10-16 mg/kg/d  20 mg/kg/d

Failed treatment: Defined as seizures occurring not controlled 50%, after 3 months on full dose.

Instructions for changing AED
Introduce new drug at half normal dose for two weeks, do not reduce old drug
Then increase new drug to normal dose for two weeks
Next reduce old drug dose to alternate day for two weeks
Finally stop the old drug

Instructions for withdrawing AED completely
Reduce dose by half for two months
Then reduce dose to alternate day for one month
Finally stop
APPENDIX: V: Summary form

Pt's ID no ___________

Section IV

Summary sheet: Complete for all children, for each type of problem listed below, indicate whether you think impairment is present or not. If impairment is present indicate the diagnosis and the degree of disability (WHO proceeding manual, 1987), whether or not the child need long term treatment including AED, developmental therapy, rehabilitation, special schooling, and or other therapy

Clinical diagnosis:

I. Epilepsy type:  II. Syndrome type:  III. Etiological type:  IV. Number of sz type
1 = generalized  1 = west syndrome  1 = Idiopathic  1 = single seizure type
2 = partial  2 = Infantile spasm  2 = cryptogenic  2 = multiple seizure type
3 = secondary gen.  3 = LKS,  4 = LGS,  3 = Remote symptomatic  3 = uncertain
4 = mixed partial and gen.  5 = Myoclonic encephalopathy  4 = Symptomatic  1 = None
5 = unclassifiable  5 = Uncertain  5 = Uncertain

VI. Age at onset of epileptic seizure:

in months ________

1 = after 12 mo. age  2 = before 12 mo. age

VII. Event associated

1 = none  2 = prenatal
3 = perinatal asphyxia  4 = neonatal seizure
5 = CNS infection  6 = head injury
7 = recurrent febrile seizure

VIII. Family h/o epilepsy

1 = none  2 = parents
3 = sibling  4 = grand parent
5 = cousin/aunt/uncle  6 = other

IX. F.H. of febrile seizure

1 = none  2 = parents
3 = sibling  4 = grand parent
5 = cousin/aunt/uncle  6 = other

X. Associated Imp.

Motor impairment

No  Yes

Gross motor

No  Yes

Fine motor

No  Yes

Visual impairment

No  Yes

Hearing impairment

No  Yes

Cognition (physician's judgment)

No  Yes

Cognition (joint decision)

No  Yes

Associated impairment

Diagnosis

Severity grading (WHO, 1988) Treatment needs for

1 = none  2 = mild
3 = moderate  4 = severe
5 = uncertain  6 = other

Bchavi. disorder

No  Yes
MAF summary page no-1

| Pt's ID no: |  |  |
|------------|  |  |

phys. judge: No Yes

Behavi. disorder: No Yes

(Joint deci): No Yes

Seizure disorder: No Yes

Other disorder: No Yes

EEG finding: date of test: -----/------/------

<table>
<thead>
<tr>
<th>Background activity</th>
<th>Epileptiform discharges(B)</th>
<th>Specific pattern ©</th>
</tr>
</thead>
<tbody>
<tr>
<td>1=normal</td>
<td>1=gen.epil discharges</td>
<td>1=Hypsarrhythmic</td>
</tr>
<tr>
<td>2=excess gen. slow w</td>
<td>2=focal epil discharges</td>
<td>2=burst suppression</td>
</tr>
<tr>
<td>3=excess loc. slow w</td>
<td>3=multifocal epil.disch</td>
<td>3=PLED</td>
</tr>
<tr>
<td>4=diffuse slow w</td>
<td>4=lateralized epil.disch.</td>
<td>4=CSWSS</td>
</tr>
<tr>
<td>5=excess gen.beta w</td>
<td>5=no epil.discharges</td>
<td>5=none</td>
</tr>
<tr>
<td>6=excess loc.beta w</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7=mix beta,theta,delta w</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8=asymmetric amplitude</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9=other(specify)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Overall comment:

Compatible with any specific clinical diagnosis? _____________________________

Normal study? _____________________________

USG of brain:

<table>
<thead>
<tr>
<th>CT scan of brain</th>
<th>MRI of brain</th>
<th>TORCH screen.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1=not done</td>
<td>Same</td>
<td>1= not done</td>
</tr>
<tr>
<td>2=normal study</td>
<td></td>
<td>Antibody +ve for</td>
</tr>
<tr>
<td>3=abn.atropsy</td>
<td></td>
<td>2=Toxopl. Positve</td>
</tr>
<tr>
<td>4=hydrocephalus</td>
<td></td>
<td>3=Rubella</td>
</tr>
<tr>
<td>5=nonspecific abno.</td>
<td></td>
<td>4=cytom.V</td>
</tr>
<tr>
<td>6=ischemic damage</td>
<td></td>
<td>5=Herpis symp</td>
</tr>
<tr>
<td>7=agenesis</td>
<td></td>
<td>6=none</td>
</tr>
<tr>
<td>8=leukomalacia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9=leisencephaly/cong anomaly</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Blood test for drug level:

Other (specify):
APPENDIX: VI: Final assessment form

Final follow up form

Name of the child: ____________________________

Age: _______ months
Sex: _______

Weight: ______ kg
OFC 1: ______ cm
OFC 2: ______ cm
OFC 3: ______ cm

Diagnosis: ____________________________
List of problems:

Pt's ID: ____________ Date last FU: ___/___/___

Date of first visit: ___/___/___
Date of EEG done: ___/___/___

Psychological ID: ____________ EEG repeat test done? : ______

(No=1, yes by us=2, yes by other=3)

Total visit: ____________

Date of last seizure: ___/___/___

Entry sz frequency: ___/___/___
Present sz frequency: ___/___/___

Sz remission? ___________________% of remission ____________

(time taken for significant or total remission after starting regular AED)
(REMI : ______)

Evolution during last 12 months follow up period?
None=1, evolved into different seizures type=2, uncertain=3.

Did the child had frequent infection during last follow up period?: ______
If more in one month=1, once in 2-3 months=2, once in 6 months=3, once in while=4, none=5

Did the child had status epilepticus during follow up period? If yes how many times?

<table>
<thead>
<tr>
<th>Seizure type:</th>
<th>at entry:</th>
<th>6mo</th>
<th>at last FU:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>single=1, multiple=2</td>
</tr>
<tr>
<td>Rate:</td>
<td></td>
<td></td>
<td>1=low, 2=high</td>
</tr>
<tr>
<td>Epilepsy type:</td>
<td></td>
<td></td>
<td>codes 1 through 6, summ sheet</td>
</tr>
<tr>
<td>Syndrome type:</td>
<td></td>
<td></td>
<td>codes summary sheet</td>
</tr>
<tr>
<td>F/H/O feb sz.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F/H/O epilepsy:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H/O status ep:</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Impairment grading: 1=none, 2=mild, 3=mod, 4=severe, 5=uncertain
Final follow up form

Name of the child: ____________________________

Age: _______ months

Sex: □

Weight: ______ kg

OFC 1: ______ cm

OFC 2: ______ cm

OFC 3: ______ cm

Diagnosis: ___________________________________________________________________

List of problems:

Date of last seizure: __________ / ______ / ______

Entry sz frequency: __________ / ______ / ______ / Year

Present sz frequency: __________ / ______ / ______ / Year

Sz remission? __________

% of remission __________

REMI: □

(1=total remission, 2= significant rem, 3=some rem, 4= minor remission, 5= none, 6= increased)

Evolution during last 12 months follow up period? □

None=1, evolved into different seizure type=2, uncertain=3.

Did the child had frequent infection during last follow up period?: □

1= more in one month=1, once in 2-3 months=2, once in 6 months=3, once in while=4, none=5

Evolution during last 12 months follow up period? □

Did the child had status epilepticus during follow up period? If yes how many times?

Seizure type: □

Rate: □

Epilepsy type: □

Syndrome type: □

F/H/O feb sz. □

F/H/O epilepsy: □

H/O status ep: □ during follow up period

Impairment grading: 1=none, 2=mild, 3=mod, 4=severe, 5=uncertain)

Pt's ID: __________

Date of first visit: __________ / ______ / ______

Date of EEG done: __________ / ______ / ______

Psychological ID: __________

EEG repeat test done?: □

Date last FU: __________ / ______ / ______

Date of last seizure: __________ / ______ / ______

Entry sz frequency: __________ / ______ / ______ / Year

Present sz frequency: __________ / ______ / ______ / Year

Sz remission? __________

% of remission __________

REMI: □

(1=total remission, 2= significant rem, 3=some rem, 4= minor remission, 5= none, 6= increased)

Evolution during last 12 months follow up period? □

None=1, evolved into different seizure type=2, uncertain=3.

Did the child had frequent infection during last follow up period?: □

1= more in one month=1, once in 2-3 months=2, once in 6 months=3, once in while=4, none=5

Did the child had status epilepticus during follow up period? If yes how many times?

Seizure type: □

Rate: □

Epilepsy type: □

Syndrome type: □

F/H/O feb sz. □

F/H/O epilepsy: □

H/O status ep: □ during follow up period

Impairment grading: 1=none, 2=mild, 3=mod, 4=severe, 5=uncertain
Motor functional development
Vision at entry
Hearing at entry
Behaviour
Cognition

at entry: [ ] [ ] [ ] [ ]
at last FU: [ ] [ ] [ ] [ ]

IQ 1: [ ]
IQ 2: [ ]

Anitiepileptic drug history in last one year:

<table>
<thead>
<tr>
<th>AED 1</th>
<th>Starting date</th>
<th>Age at starting</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>yr. mo</td>
</tr>
<tr>
<td>AED 2</td>
<td></td>
<td>yr. mo</td>
</tr>
<tr>
<td>AED 3</td>
<td></td>
<td>yr. mo</td>
</tr>
<tr>
<td>AED 4</td>
<td></td>
<td>yr. mo</td>
</tr>
</tbody>
</table>

Prednisolone effect: 1=sz.stoppe, 2=significantly improved in 2 wk., 3=some improved in 2 wks time
4=sz 0 in 4 wks time, 5= no change, 6= increased, 8=N.A

PEFF: [ ]

Why changed AED?

Blood level of AED:

Drug level:

Any evidence of drug side effect? [ ] [ ] [ ] Dose:

Present AED:

Compliance: Stopped medication for 7 days or more than that at one stretch? If yes, Why?

Parents' perception: (describe condition of their child before and after 12 mo treatment)

codes: sz=0 / other, age appropriate=1, improved significantly=2, some improvement=3,
no improvement but has hope=4, none=5, increased or deteriorated condition=6)

Seizure [ ] understanding/learning ability [ ] Function [ ]

Behaviour [ ] Other [ ]

Comment:
APPENDIX: VII

**EEG data entry form:**

<table>
<thead>
<tr>
<th>EEG no</th>
<th>RID no</th>
<th>Date -/---/---</th>
<th>sex: (M=1 F=2)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

D.O.B -/---/--- age: ---Y--- M Corrected age (in case of neonate) ------ weeks

Ma ----------------------------------------------- Baba -------------------------------------

Address: H. no---- Rd.no ----- area -------------- village----------------

Thana ---------------- District ------------------- area code ----------------

Phone: Residential status: Urban = 1 / suburb = 2 / rural = 3

<table>
<thead>
<tr>
<th>Referral details:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Referred by:</td>
<td>Hospital</td>
</tr>
<tr>
<td>Hospital Reg.no</td>
<td>Private clinic/chamber</td>
</tr>
<tr>
<td>Question asked by the clinician:</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parents’ concern:</th>
<th>1.</th>
<th>2.</th>
<th>3.</th>
<th>4.</th>
</tr>
</thead>
</table>

Seizure detail:

<table>
<thead>
<tr>
<th>Seizure typ</th>
<th>Age of onset in months</th>
<th>Frequency at the beginning</th>
<th>Frequency at present</th>
<th>Date and type of last attack</th>
</tr>
</thead>
<tbody>
<tr>
<td>GTC</td>
<td>-/d.---/w--/m--/y</td>
<td>-/d.---/w--/m--/y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GT</td>
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<tr>
<td>GC</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>MC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absence</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondarily gener.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mixed gen+partial</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reflex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Photosensitive</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atypical febrile sz.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other (specify)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

History or recurrent febrile seizure: total episodes

Family history of febrile seizure: sibling/parents/ cousins/ uncle or aunt/grand parents

Family history of epilepsy: sibling/parents/ cousins/ uncle or aunt/grand parents
### Prenatal Problem
- Maternal high blood pressure: 1
- Diabetes: 2
- PET: 3
- History of taking abortificient: 4
- None: 5

### Perinatal History
- Place of delivery: Home: 1, Hospital: 2
- Gestational age: Full term (9 mo): 1, Preterm (<8 mo): 2, Post term (9m +2 wks): 3

### H/o asphyxia
- Prolong 2nd stage of labour?:
- Cried more than 5 minutes after birth?:
- Definite h/o birth asphyxia?: None: 1, if any of the 3 present: 2

### Neonatal History
- H/o seizure: 1, Jaundice (not physiological): 2, Septicemia: 3

### Milestone of Development
- Age appropriate: 1, Delayed: 2, Regressed: 3, Uncertain: 4

### Motor Function (Present Ability)

### Cognitive State (Describe if No Test Done)

### Current Medication (AED)

### How many times the child was hospitalized with seizure?

### EEG Information
- Any typical event during recording?: Y/N

### Patients State during the Test
- Awake: Yes
- Alert: Yes
- Cooperative: Yes
- Non-cooperative: Yes
- Drowsy: Yes
- Sleeping: Yes
- Irritable: Yes
-Unable to follow command: Yes

### Activating Process Used
- Photic stimulation: Yes
- Hyperventilation: Yes
- Sleep: Yes
- Touch: Yes

### Any seizure provoked by activating process?: Y/N

### EEG Report

#### 1. Background Activity
- Normal for the age and state of the child: Yes

#### 2. Background Activity: Abnormal (for the age and state) with presence of
- Excessive slow wave activity (delta w): Yes
- Excessive fast (beta) wave activity: Yes
- Excessive Theta wave activity: Yes
- Mixed abnormal activity: Yes

#### 3. Abnormal with presence of
- Bursts of epileptiform discharges: Yes
- Spike wave complexes/spikes: Yes
- Sharp waves: Yes

#### 4. Abnormal with recognisable abnormal EEG pattern:
- Burst suppression pattern: Yes
- Hypsarrhythmic pattern: Yes
- PLED: Yes
- Other (specify):
5. Cerebral reactivity to activating process: normal Epl. discharge. Other aypi.

<table>
<thead>
<tr>
<th>Process</th>
<th>Normal</th>
<th>Other aypi.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Photic stimulation</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Hyperventilation</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Sleep</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Tactile stimulation</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Eye closure</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

5. Overall Comment: suggestive electroclinical diagnosis
<table>
<thead>
<tr>
<th>Drugs</th>
<th>Indication</th>
<th>Starting dose</th>
<th>Total daily dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenobarbitone (PB)</td>
<td>Generalised, partial seizures.</td>
<td>1.5</td>
<td>3-5</td>
</tr>
<tr>
<td>Carbamazepine (CBZ)</td>
<td>Partial, generalised.</td>
<td>4 to 5</td>
<td>10-20</td>
</tr>
<tr>
<td>Phenytoin (PHT)</td>
<td>Generalised, partial.</td>
<td>3 to 4</td>
<td>8-10</td>
</tr>
<tr>
<td>Sodium Valproate</td>
<td>Primary gen. Epilepsies, MC, Generalised &amp; partial sz.</td>
<td>10</td>
<td>20-50</td>
</tr>
<tr>
<td>Valproic acid (VPA)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nitrazepam (NTZ)</td>
<td>Infantile spasms, Myoclonic epilep.</td>
<td>&lt;0.1</td>
<td>0.150-0.500</td>
</tr>
<tr>
<td>Clonazepam (CLZ)</td>
<td>all spec. MC.epil., LGS</td>
<td>0.05</td>
<td>0.05-0.3</td>
</tr>
<tr>
<td>Clobazam</td>
<td>all forms, development of tolerance is frequent</td>
<td></td>
<td>0.25-1.0</td>
</tr>
<tr>
<td>Diazepam</td>
<td>Mainly status epilepticus (SE)</td>
<td>0.25 -1.5 mg/kg</td>
<td>0.1 -0.3 mg/kg I.v.</td>
</tr>
<tr>
<td>Ethosuximide (ETH)</td>
<td>Absences epilepsy</td>
<td>0.25 -0.5 mg/kg p/r</td>
<td>20-40 mg/kg</td>
</tr>
<tr>
<td>Lamotrigine (LTZ)</td>
<td>Partial &amp; secondary gen sz. primary gen. &amp; myoclsz.</td>
<td>1-2 mg</td>
<td>5-20 mg/kg</td>
</tr>
<tr>
<td></td>
<td>refractory absences, LGS</td>
<td></td>
<td>0.1 - 5 mg/kg for</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>children receiving</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>sodium valp.</td>
</tr>
<tr>
<td>ACTH</td>
<td>IS, LGS, sever myoclonic epilep.</td>
<td></td>
<td>0.1 - 10 IU/kg</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>Same as ACTH</td>
<td>1 - 2 mg/kg</td>
<td></td>
</tr>
</tbody>
</table>
SOCIOECONOMIC STATUS ASSESSMENT FORM (SES)  ID number ________

Child's Name ___________________________________________  date of birth: __/__/__
Mother's Name_________________________________________  age: ___yrs. ___mo.
Father's Name_________________________________________  Sex: M=1, F=2

Residential status: Urban=1, suburban=2, rural=3

Address: Village ____________________________  Thana  ______________________
          P.O: ____________________________  District _________________________
          Division ____________________________  H no: ______  R no: ______
          Phone no: ____________________________

Informant(s): Mother-1, Father-2, child's grand parents-3, sibling-4, self-5, other relatives-6

A. Please provide the following information about the child’s parents

Mother  Father

1. Age:                   

2. Highest level of education completed
   ☐ Primary school
   ☐ S.S.C.
   ☐ College
   ☐ H.S.C.
   ☐ Bachelor degree
   ☐ Graduate/Professional degree

3. Occupation of the parents:
   ☐ Agriculture/Fishing
   ☐ Business/trader
   ☐ Daily wage earner/
   ☐ Service
   ☐ Self employee
   ☐ Unskilled worker
   ☐ Professional
   ☐ Mainly un-employed
   ☐ Other

4. Do you/your family have own land property? if yes how much
   ☐ Has own land
   ☐ Has land inherited from parents
   ☐ No land but good Bank balance
   ☐ Land less, depends on daily/monthly income

B. Health care:

5. Who pay for your child’s health care?
   ☐ Father/mother  ☐ Grand father  ☐ other family members(specify)  ☐ health care center  ☐ other(specify)

6. What is your child’s treatment cost for this specific illness?
   For regular medication per month Tk. __________  Transport cost at the health care center Tk. __________
   Cost for the investigation Tk. ___________  Other (specify) ______________________________

7. How much have you already spent for treatment of this specific problem? _________

   which way? _________

8. Where do you take your child for any common illness?
   ☐ District Hospital  ☐ Thana health complex  ☐ nearest practicing doctor
   ☐ Village doctor  ☐ Kabiraz/ozha/fakir  ☐ religious people  ☐ other(specify)
APPENDIX: IX: SES form

SES Form

Patient's ID __________

9. Where did you take your child for this specific illness for the first time?  
   1=District Hospital, 2=Thana health complex, 3=nearest practicing doctor, 4=Village doctor,  
   5=Kabiraz/ozha/fakir, 6=religious people, 7=other(specify)

10. What do you think about the attacks of your child?  
   1=A sacred disease, 2=mental disease, 3=communicable disease, 4=not treatable, 5=disease which needs  
      medical treatment like chronic disease like asthma, hypertension, diabetes, 6=Don’t know, 7=other(specify)

11. What is your expectation in this regard? ________________________________

C. Housing

12. Which best describes where your child leaves?  
   1=house family owns, 2=family rents, 3=stay with relatives/friends, 4=rented house at the slum  
   5=other(specify)

13. Which your house fall in?  
   1=Pacca house (roof, floor and wall made of brick and cement), 2=semi-pacca, 3=Kancha(no brick or ce

14. Number of rooms in the house/apartment (not including bathroom/kitchen) __________

15. Number of people living there most of the time: _______, Adults _______ Children _______

16. Do you have following at your house?  
   regular electricity □ radio □ television □ VCR □ Computer □ telephone □ Fridge □

17. What is the source of drinking water?  
   1=Wasa supply, 2=deep tube well, 3=surface well, 4=pond / river, 5=Other, specify

18. What type of toilet do your family members use?  
   1=Modern toilet, 2=Private semi pacca or kancha for the single family, 3=Common toilet sharing with  
      other families in the community, 4=none, 5=other(specify)

19. Do any one of your family member has some of the following?  
   Motor car □ Bicycle □ Boat □ Cart □ Cow or other cattle □ Computer □
   Rikshaw □ Shallow tube well □

D. Income

20. What is/are the source of your family's income? Check all that apply  
   1=Employment, 2=other property(specify), 3=daily income, 4=other, 5=do not know

21. In which category your family monthly income and expenditure fall?  

   Monthly income:  
   □ Tk under 3000 month  
   □ Tk. 3000 to 5000 / month  
   □ Tk. >5000 to 10,000 / mo  
   □ Tk. >10,000 to 20,000/ mo  
   □ Tk.>20,000 to 40,000/mo  
   □ Tk.>40,000 to 60,000/mo  
   □ Tk.>60,000 to 80,000/mo  
   □ More than 80,000

   Expenditure  
   daily exp. for food tk. _______  
   monthly expenditure tk. _______  
   monthly exp. for other purpose tk. _______
Conners' Parent Rating Scale - Revised (S)

<table>
<thead>
<tr>
<th>Questions</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Inattentive, easily distracted</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Angry and resentful</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Difficulty doing or completing homework</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Is always 'on the go' or acts as if driven by a motor</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Short attention span</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Argues with adults</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Fidgets with hands or feet or squirms in seat</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Fails to complete assignments</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. Hard to control in malls or while grocery shopping</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. Messy or disorganized at home or school</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11. Loses temper</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12. Needs close supervision to get through assignments</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13. Only attends if it is something he/she is very interested in</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Instructions: Below are number of common problems that children have, please rate each item according to your child's behavior in the last month. For each item, ask yourself, "How much of a problem has this been in the last month?" and circle the best answer for each one. If none, not at all, seldom or very infrequently, you would circle 1 or 2 for ratings in between. Please respond to each item.

0 = not at all true, seldom
1 = Just a little true, occasionally
2 = Pretty much true, often, quite a bit
3 = Very much true, very often, very frequently
### APPENDIX: X

<table>
<thead>
<tr>
<th>Questions</th>
<th>0 = not at all true, seldom</th>
<th>1 = Just a little true, occasionally</th>
<th>2 = Pretty much true, often, quite a bit</th>
<th>3 = Very much true, very often, very frequently</th>
</tr>
</thead>
<tbody>
<tr>
<td>14. Runs about or climbs excessively in situations where it is inappropriate</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>15. Distractibility or attention span a problem</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>16. Irritable</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>17. Avoids, expresses reluctance about, or has difficulties engaging in tasks that require sustained mental effort (such as schoolwork or homework)</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>18. Restless in the &quot;squirming&quot; sense</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>19. Gets distracted when given instructions to do something</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>20. Actively defies or refuses to comply with adults' requests</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>21. Has trouble concentrating in class</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>22. Has difficulty waiting in lines or awaiting turn in games or group situations</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>23. Leaves seat in classroom or in other situations in which remaining seated is expected</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>24. Deliberately does things that annoy other people</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>25. Does not follow through on instructions and fails to finish school work, chores or duties in the workplace (not due to oppositional behavior or failure to understand instructions)</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>26. Has difficulty playing or engaging in leisure activities</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>27. Easily frustrated in efforts</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Score obtained</th>
<th>T-score</th>
<th>percentile</th>
<th>Impression</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
APPENDIX: XI: Children’s behavioural assessment questionnaire
Adapted from Richman’s behavioural screening questionnaire

Child’s ID □ □ □ □

Bangladesh Protibondhi Foundation
Adapted Behaviour Screening Questionnaire (BPF), May 1993.

Child’s ID Number ................................................................. □ □ □ □ ID

BEHAVIOUR PROBLEMS RECORD SHEET

1. (a) Poor behavior in school lesson........................................... □ BS 2
   (b) Trouble with peers........................................................... □ BS 3

2. Jokes and teasing others........................................................ □ BS 4

3. (a) Refuses to do homework ................................................ □ BS 5
   (b) Refuses to do the housework .......................................... □ BS 6
   (c) Refuses to go to school ................................................ □ BS 7

4. (a) Aggression ..................................................................... □ BS 8

5. (a) Frightened ..................................................................... □ BS 9
   (b) Frightened ..................................................................... □ BS 10

Page 1 of 5
শুধুমাত্র

৫।  (ক) যুবাকের ব্যবহার ..........................................................□ - Total Score এ অন্তর্ভুক্ত BS 11

(খ) বিভাগ যাওয়া/ যুবকে যাওয়া ..........................................................□ BS 12

রাতে মসজিদে মন্দির চলা ..........................................................□ BS 13

(গ) বাবা- মায়ের সঙ্গে যুবক ..........................................................□ BS 14

ভাই-বোনদের সঙ্গে যুবক/ পরিবারের অন্য সদস্যদের সঙ্গে যুবক ..........................□ BS 15

অভ্যন্তর

নিম্নের নিয়ে কামড়ানো ..........................................................□ BS 16

৬। মাথা কোটা অথবা মাথা ঢোকা ..........................................................□ BS 17

শরীর পোশাক ..........................................................□ BS 18

যুবকের মত প্রতিক্রিয়া উদ্যোগে দেব পিট পিট করা, মুখ ঢালা, দাঁত নিউনিট করে,

ঢেট ঢাটা অথবা বিষ্ণু মূখ্যা ..........................................................□ BS 19.

চুল টেনে উঠান, চুল ঢালা, মুখ, ঢুক অথবা থোটা ..........................................................□ BS 20

মুখে আঘাত অথবা অঘাত মূখ্যা ..........................................................□ BS 21

বন্ধ কামড়ানো ..........................................................□ BS 22

বিক্রিয়া শুরু করা, উদ্যোগের গোর্ণ করা, মৌলিক চোখে চোখ দেওয়া,

অবিচ্ছিন্ন বিক্রিয়া করে চাপা মুখ হানা অথবা মেশাক মত হানা ..........................................................□ BS 23

খেয়াল পুষ্পিত জিনিস ধারণ করা ..........................................................□ BS 24

নিজের বৌদ্ধ নিয়ে খেলা করা ..........................................................□ BS 25

অন্যান্য ..........................................................□ BS 26
বিশুদ্ধতার আচরণ

$1$ গৌরব চলে না বা গৌরব চলে যায়না চেক করা ............................................... ☐ BS 27

$2$ প্রথা .............................................................. ☐ BS 28

$3$ গার্হস্থল ও প্রাপ্ত ভাঙ্গনামাটি করা .............................................................. ☐ BS 29

$4$ চিকিৎসা এবং / সীমাবদ্ধ আচরণ করো .............................................................. ☐ BS 30

$5$ অন্যান্য তথ্য অভিন্ন তথ্যগুলি নিয়ে নেয়া (রিও নম্বর) .............................................................. ☐ BS 31

অভিন্নতার গার্হস্থল বা বাংলা গাবুল আঁকে বা অপ্রত্যাশিতা হয় .............................................................. ☐ BS 32

$6$ অন্যান্য তথ্য অভিন্ন তথ্যগুলি নিয়ে নেয়া (রিও নম্বর) .............................................................. ☐ BS 33

$7$ গার্হস্থল বা বাংলা গাবুল আঁকে বা অপ্রত্যাশিতা হয় .............................................................. ☐ BS 34

$8$ অন্যান্য তথ্য অভিন্ন তথ্যগুলি নিয়ে নেয়া (রিও নম্বর) .............................................................. ☐ BS 35

$9$ গার্হস্থল বা বাংলা গাবুল আঁকে বা অপ্রত্যাশিতা হয় .............................................................. ☐ BS 36

$10$ অন্যান্য তথ্য অভিন্ন তথ্যগুলি নিয়ে নেয়া (রিও নম্বর) .............................................................. ☐ BS 37

$11$ গার্হস্থল বা বাংলা গাবুল আঁকে বা অপ্রত্যাশিতা হয় .............................................................. ☐ BS 38

$12$ অন্যান্য তথ্য অভিন্ন তথ্যগুলি নিয়ে নেয়া (রিও নম্বর) .............................................................. ☐ BS 39

$13$ কার্যক্ষেপ.............................. ☐ BS 40

$14$ ব্যক্তি.............................. ☐ BS 41

$15$ মনোযোগ.............................. ☐ BS 42

$16$ মনোযোগের আবেদনের চেষ্টা.............................. ☐ BS 43

$17$ অবনিভাূতা.............................. ☐ BS 44

$18$ মেয়াদ.............................. ☐ BS 45

Page 3 of 5  14 May 1993
১৪ বাতিক গাত্র আচরণ/ নিষিদ্ধ ভাবে বাধা করার প্রবণতা 

১৫ ভা / জিভি 

ক্রুদ্ধ ........................................................................................................... BS 48
বিভাল ............................................................................................................. BS 49
অনান্য .......................................................................................................... BS 50
জল / লীল প্রতি ............................................................................................... BS 51
বাঁধ / ভোয়ে শব্দ ...................................................................................... BS 52
অন্তরার ......................................................................................................... BS 53
অপরিচিত ব্যক্তি ...................................................................................... BS 54
(গাছি, বাগ, টেল, এলস ফি তার কাছে পরিচিত)?
পানি ................................................................................................................. BS 55
চুলকাটা ........................................................................................................ BS 56
ভাজর ................................................................................................................. BS 57
গাছ .................................................................................................................... BS 58
টেলিফেন্স ..................................................................................................... BS 59
অন্যান্য অনুমতি করে নিয়ন্ত্রণ ................................................................ BS 60

১৬ ওইরোসের সাথে সম্পর্ক 

১৭ সমবায়সের সাথে সম্পর্ক 

১৮ অনামিকা / সমবায়সের সাথে সম্পর্কের কেন্দ্র সমস্যা
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>☐ ☐ ☐ ☐ BS 63</td>
</tr>
<tr>
<td>☐ ☐ ☐ ☐ BS 64</td>
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<tr>
<td>☐ ☐ ☐ ☐ BS 65</td>
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<td>☐ ☐ ☐ ☐ BS 75</td>
</tr>
<tr>
<td>☐ ☐ ☐ ☐ BS 76</td>
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</table>
APPENDIX: XII: Children's behaviour questionnaire, Rutter. 1967

<table>
<thead>
<tr>
<th>Question</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Your child is often restless.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Your child is often quiet.</td>
<td></td>
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<tr>
<td>3. Your child is often irritable.</td>
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<td>4. Your child is often smiling.</td>
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<td>5. Your child is often lazily busy.</td>
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<tr>
<td>6. Your child is often sitting still.</td>
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<tr>
<td>7. Your child is often playing.</td>
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</table>

Note: The table above represents a questionnaire used to assess children's behavior. Each question is scored on a scale from 0 to 4, with higher scores indicating more problematic behavior. The scores can be used to identify children who may need additional support or further evaluation.

Name of child ..................................................
Date of birth ............................................. Date of this record ..............................

School ......................................................

Below are a series of descriptions of behaviour often shown by children. After each statement are three columns: "Doesn't Apply", "Applies Somewhat", and "Certainly Applies". If the child definitely shows the behaviour described by the statement place a cross under "Certainly Applies". If the child shows the behaviour described by the statement but to a lesser degree or less often place a cross under "Applies Somewhat". If, as far as you are aware, the child does not show the behaviour place a cross under "Doesn't Apply".

Please put one cross against EACH statement. Thank you.

<table>
<thead>
<tr>
<th>Statement</th>
<th>Doesn't Apply</th>
<th>Applies Somewhat</th>
<th>Certainly Applies</th>
<th>For Office use only</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Very restless. Often running about or jumping up and down. Hardly ever still</td>
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<tr>
<td>2. Travels from school</td>
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<tr>
<td>3. Squinty, fidgety child</td>
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<tr>
<td>4. Often destroys own or others' belongings</td>
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<tr>
<td>5. Frequently fights with other children</td>
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<tr>
<td>6. Not much liked by other children</td>
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<tr>
<td>7. Often worried, worries about many things</td>
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<tr>
<td>8. Tends to do things on his own - rather solitary</td>
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<tr>
<td>9. Irritable, is quick to &quot;fly off the handle&quot;</td>
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<tr>
<td>10. Often appears miserable, unhappy, fearful or distressed</td>
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<tr>
<td>11. Has twitches, mannerisms or tics of the face or body</td>
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<tr>
<td>12. Frequently sucks thumb or finger</td>
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<tr>
<td>13. Frequently bites nails or fingers</td>
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<tr>
<td>14. Tends to be absent from school for trivial reasons</td>
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<tr>
<td>15. Is often disobedient</td>
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<tr>
<td>16. Has poor concentration or short attention span</td>
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<tr>
<td>17. Tends to be fearful or afraid of new things or new situations</td>
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<tr>
<td>18. Fussy or over-particular child</td>
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<tr>
<td>19. Often tells lies</td>
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<tr>
<td>20. Has stolen things on one or more occasions</td>
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<tr>
<td>21. Has wet or soiled self at school this year</td>
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<tr>
<td>22. Often complains of pains or aches</td>
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<tr>
<td>23. Has had tears on arrival at school or has refused to come into the building this year</td>
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<tr>
<td>24. Has a stutter or stammer</td>
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<tr>
<td>25. Has other speech difficulty</td>
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<tr>
<td>26. Gullies other children</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Name</td>
<td>Sex</td>
<td>Age</td>
<td>Psy.</td>
<td>Dated</td>
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<td>------</td>
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</tr>
</tbody>
</table>

**INDEPENDENT BEHAVIOUR ASSESSMENT SCALE (IBAS)**

<table>
<thead>
<tr>
<th>TOILETING</th>
<th>SCORE</th>
<th>DRESSING</th>
<th>SCORE</th>
<th>SELF-CARE</th>
<th>SCORE</th>
<th>DOMESTIC SKILL</th>
<th>SCORE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. পাটি হাজি গলা খুলিয়ে রাখেন।</td>
<td>1. বাড়ি পড়তে এবং খানতে সরামাতা করাও।</td>
<td>1. শীত শরীরে সরামাতা করা।</td>
<td>1. শিক্ষা পেতে যান। (পশ্চাৎ)</td>
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<tr>
<td>2. মল মুক্ত ভাবে করেন।</td>
<td>2. নিজের বলে রাখতে পারেন।</td>
<td>2. মূত্র আর্নিতা, এবং কাঁচ পানীয় গ্রহন।</td>
<td>2. শিক্ষা খুলে রাখেন।</td>
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<tr>
<td>3. ভিতর থেকে খুলিয়ে রাখেন।</td>
<td>3. সাত্রে কাঁচ মুক্ত করেন। (প্রথম/পশ্চাৎ)</td>
<td>3. মূত্র/পিউরে উঠে যাতে পানীয় গ্রহন করেন।</td>
<td>3. উদ্যোগের সমস্ত মাজার হয়ে পড়ে।</td>
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<tr>
<td>4. ব্যবক্তি থেকে খুলিয়ে রাখেন।</td>
<td>4. নিজের হাতে রাখেন।</td>
<td>4. মূত্র দুই উড় রাখেন। নিজের থেকে।</td>
<td>4. এক্ষেত্রে নিজের পাতায় মাজা করে।</td>
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<tr>
<td>5. ধাও রাখতে পারেন।</td>
<td>5. তৈরি করে নেন। নিজের থেকে।</td>
<td>5. মূত্রপিউরে নিজের নিজের মাজা।</td>
<td>5. মাজার/পিউরের মাজা অপরাজেয় হয়।</td>
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<tr>
<td>6. ব্যবহার থেকে খুলিয়ে রাখেন।</td>
<td>6. সাত্রে কাঁচ মুক্ত করেন। (প্রথম/পশ্চাৎ)</td>
<td>6. মূত্র দুই উড় রাখেন।</td>
<td>6. ধাও এর সময় শরীরের পার্থিব নিষ্ঠ।</td>
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<tr>
<td>7. মুক্ত করে দুই মুক্ত করেন।</td>
<td>7. কিন্তু পেয়ে যান। নিজের থেকে।</td>
<td>7. শরীরের দুই মুক্ত যে।</td>
<td>7. মূত্র/পিউরের দুই মাজা করে।</td>
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<tr>
<td>8. নিজের শরীর থেকে খুলিয়ে রাখেন।</td>
<td>8. সাত্রে কাঁচ মুক্ত করেন।</td>
<td>8. মূত্রপিউরে নিজের নিজের মাজা।</td>
<td>8. মূত্রপিউরের মাজা অপরাজেয় হয়।</td>
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<tr>
<td>10. মুক্ত করেন।</td>
<td>10. মূত্র দুই উড় রাখেন।</td>
<td>10. মূত্র দুই উড় রাখেন।</td>
<td>10. মূত্র দুই উড় রাখেন।</td>
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<td>11. তৈরি করে। নিজের থেকে।</td>
<td>11. মূত্র দুই উড় রাখেন।</td>
<td>11. মূত্র দুই উড় রাখেন।</td>
<td>11. মূত্র দুই উড় রাখেন।</td>
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<tr>
<td>12. তৈরি করে। জলপানি।</td>
<td>12. মূত্র দুই উড় রাখেন।</td>
<td>12. মূত্র দুই উড় রাখেন।</td>
<td>12. মূত্র দুই উড় রাখেন।</td>
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<tr>
<td>13. তৈরি করে। শরীরের পায়ে মাজা।</td>
<td>13. মূত্র দুই উড় রাখেন।</td>
<td>13. মূত্র দুই উড় রাখেন।</td>
<td>13. মূত্র দুই উড় রাখেন।</td>
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<td>15. তৈরি করে। মূত্র দুই উড় রাখেন।</td>
<td>15. মূত্র দুই উড় রাখেন।</td>
<td>15. মূত্র দুই উড় রাখেন।</td>
<td>15. মূত্র দুই উড় রাখেন।</td>
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<td>16. তৈরি করে। মূত্র দুই উড় রাখেন।</td>
<td>16. মূত্র দুই উড় রাখেন।</td>
<td>16. মূত্র দুই উড় রাখেন।</td>
<td>16. মূত্র দুই উড় রাখেন।</td>
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<td>17. তৈরি করে। মূত্র দুই উড় রাখেন।</td>
<td>17. মূত্র দুই উড় রাখেন।</td>
<td>17. মূত্র দুই উড় রাখেন।</td>
<td>17. মূত্র দুই উড় রাখেন।</td>
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<td>18. তৈরি করে। মূত্র দুই উড় রাখেন।</td>
<td>18. মূত্র দুই উড় রাখেন।</td>
<td>18. মূত্র দুই উড় রাখেন।</td>
<td>18. মূত্র দুই উড় রাখেন।</td>
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<td>19. তৈরি করে। মূত্র দুই উড় রাখেন।</td>
<td>19. মূত্র দুই উড় রাখেন।</td>
<td>19. মূত্র দুই উড় রাখেন।</td>
<td>19. মূত্র দুই উড় রাখেন।</td>
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<td>20. তৈরি করে। মূত্র দুই উড় রাখেন।</td>
<td>20. মূত্র দুই উড় রাখেন।</td>
<td>20. মূত্র দুই উড় রাখেন।</td>
<td>20. মূত্র দুই উড় রাখেন।</td>
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</tbody>
</table>

**TOTAL SCORE**

**RS**  | **RS**  | **RS**  | **RS**  | **RS**

**MOTOR SK**  | **RS**  | **SOCIAL SK**  | **RS**  | **COMM SK**  | **RS**  | **DAILY LSK**  | **RS**
APPENDIX: XV

Severity grading for the disabilities during the medical assessment
(WHO, 1980) rating of 1=no disability, 2=mild, 3=moderate, 4=severe

Seizure
Mild: Two to four seizure in the past year
Moderate: One or more than one seizure per month
Severe: One or more than one seizure per week

Movement
None: No movement disability; the child is functioning age appropriately, without
any sign of neurological damage
Mild: Weak grasp, can use hands for most purposes, can stand without support, may
may need help in climbing steep steps, but able to do daily living activities.
Moderate: Difficulty in holding implements, dressing, needs support to sit upright,
can move around with substantial help.
Severe: Unable to walk, no function of hands except to point.

Hearing
Mild: A 20 to 40 Db loss of hearing in the best ear, difficulty in hearing but able to
to manage with or without a hearing aid.
Moderate: A 41 to 70 Db loss of in the best ear, difficulty in hearing even with a hearing aid.
Severe: More than 70 Db loss in the best ear, no useful hearing.

Vision
Mild: Can see the chart through a pin-hole, correctable vision loss.
Moderate: vision loss of 20/60 feet or 6/18 m, not correctable, but can get about with a cane
Severe: Visual acuity worst than 6/60, only light perception.

Speech
Mild: Speaks and is understood, but can get across only basic ideas.
Moderate: Understood with difficulty, gets only basic needs across.
Severe: Either no speech, or can not understood by others.

Cognition
Mild: Slow in cognition, no accompanying motor, speech deficit or delay in milestone.
Moderate: Some delay in attaining growth milestone, difficulty in speech as well as moderate
cognitive deficit.

Severe: With fine motor deficits, delay in speech and in attaining growth milestones,
as well as with a significant cognitive deficit.

**Behaviour**

**Mild**: Recent onset of abnormal behaviour, which is opposite to the particular child's usual behavioural state (irritability, restlessness, hyperactive, imperative, or very quiet, unusually shy, sleepy behavioural state otherwise normal milestone of development, age appropriate cognitive development.

**Moderate**: Abnormal behaviour; inappropriate for the age, some delay in attaining milestone, speech and communication problem recently started or since developing age.

**Severe**: Behavioural problems from developing age; unaware of surrounding, unable to communicate; poor cognition. Severe gross and fine motor deficits.
APPENDIX: XVI  Seizure Record Diary for parents

Please put a mark ( ) for one seizure attack, when you or anyone of your family members notice one attack or the child says that s/he had an attack.

<table>
<thead>
<tr>
<th>Date</th>
<th>Morning</th>
<th>Afternoon</th>
<th>Night</th>
<th>Additional info.</th>
<th>Doctor's com.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/1/1</td>
<td>11:00</td>
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<tr>
<td>1/2/1</td>
<td>11:00</td>
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<tr>
<td>1/3/1</td>
<td>11:00</td>
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<tr>
<td>1/4/1</td>
<td>11:00</td>
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</table>

Additional info: Sleeps less

Doctor's comments:
APPENDIX: XVII

ধন ঘন ফিচুনী বা এ্যলিপসি সম্পর্কে সাধারণ কিছু তথ্য:

শীতের উচ্চতায় বা জ্বরের সাথে ফিচুনী (Febrile Convulsion)

নিঃশর বয়স ৬ মাস থেকে ৭ বছর বয়স পর্যন্ত জ্বর তৃষ্ণ সময় ফিচুনী হতে পারে। এটি মৃদুফোগ বা এ্যলিপসি নয়। জ্বর হলে ধন ঘন শরীরের স্পষ্ট করেন, মাঝারি পানি চানুন এবং ডায়রের প্রমাণ অনুযায়ী উপস্থাপন। তথে ফিচুনীর স্বাভা ১০-১৫ মিনিটের নেশী হলে দেহি না করে ফিচুকে হস্তপাতালে নিন।

ফিচু ছাড়া ধন ঘন ফিচুনী: (Epilepsy)

মৃদু ফোগ বা এ্যলিপসির উপপর হলকড় হয় বা এ্যলিপসি। এর প্রকাশ বিভিন্ন রকম হতে পারে, এক্ষণে সারা শরীরের বা শরীরের কেন্দ্র অংশ বিশেষ জ্বরে ফিচুনী হতে পারে।

সারা শরীর স্নাত হলে উপপরি বকানুনি সহকারে মৃদু ফোগে উড়া যাওয়া, ধন ঘন পড়ে দিয়ে আমতা যাওয়া, ক্রমকুলুফত্রের জন্য নির্ধারণ করা হয় বা মাঝারি বকানুনি হওয়া, ধরা পালন হঠাৎ ও ধন ঘন ফিচু প্রাপ্ত হওয়া ইত্যাদি এ্যলিপসির কিছু লক্ষণ।

আপনার পিঁপড় এর সর্বকালে জ্বর হলে একটি অতিস্ত চিকিৎসকের প্রামাণ্য নিন।

চিকিৎসক আলোচনার বাচ্চার এবং পরিবারের বিজ্ঞান ইতিবাচ অনুভুম পর প্রায় নিযুক্ততাতে তার এখনের কিছু পরিকল্পনা করতে উপদেশ দিন। ইতিবাচক চিকিৎসার বাচ্চার ক্রিয়াবর্ধনের বেশি যা স্নাত পোস্ট তার সাধারনের সমন্ধে।

ক্রমে বন্ধরের নিম্ন হল পারে, তাস সাধারণ জ্বরিপ হলে যার প্রায় শক্তিকরা ৭৫ ভাগ ফিচুনী প্রাপ্ত অবস্থায় হয়। বালমেকে জ্বরেরকালের প্রায় শক্তিকরা ৪৫ ভাগ প্রাপ্ত (১৮ বছরের নিজ)। ধন ঘন ফিচুনী প্রাপ্তের জ্বর সাধারণ সময়।

চিকিৎসার প্রায় ২-৩ বছর বয়স শিশুর নিয়ন্ত্রণ করা একটি জ্বরিপ শেষে হয় এবং প্রতি ১০০০ শিশুর মধ্যে ৮ থেকে ৯ জনের এ্যলিপসি রয়েছে।

আলোচনা:

- এটি এসময়, উচ্চ রক্তচাপ বা ডায়রের মতই শরীরের একটি ক্রিয়া অবস্থা যা।
- এর সচিব ডায়রেনেশন, কালি নিউর ও তার চিকিৎসার ফলে সম্পূর্ন অভাজক ও সুষু জীবন বায়ন করা যায়।
- এ্যলিপসি এপন অফ ইন্ডিয়া উচ্চস্তর কিছু নয়।
- এ্যলিপসি হ্রোয়াচ রোগ নয়।

আপনার পিঁপড় এ্যলিপসি হলে ধরকে তাকে নিরস্ত রোগ দায়ে এবং তার চিকিৎসকের সাথে নিয়ন্ত্রিত বোঝায় রাখুন।
APPENDIX: XVII  EEG related information for parents

**APENDIX: XVII  EEG related information for parents**

**নিজের ইতিহাস (EEG) পরীক্ষার জন্য প্রযোজনীয় তথ্য:**

ইতিহাস এক ধরনের নতুন- ইনডেন্সিয় পরীক্ষা পদ্ধতি, যার সূচনার অভ্যমানে কোন কিছু হয়নি তাদের প্রশ্নের সম্ভাবনায়। এ পরীক্ষা কোন প্রত্যেক তথ্য বা কোন ধরনের চিকিৎসা দেহের বিভিন্ন সময় সম্পন্ন করা।। অনুসারে তাদের পাত্রকলাপ এ পরীক্ষার সাথে সংশ্লিষ্ট হয়।

অন্তঃপুষ্টক ২.২.৩. কেন্দ্র আসার পূর্ব নিয়নিষ্ঠিত নির্দেশনা সম্পূর্ণ অনুসরণ করুন।

1. যারা অবধি শয্যাপূর্ব সিজা যেন একটি চল চলে যায়। এর ফলে কোন ধরনের তৈরি পর্যন্ত চলে যায়।
2. করা ব্যাপার, সম্পূর্ণ এক পর্যায়ে চলা যায়।
3. দীর্ঘমেয়াদী পাত্র পরিবেশ কিনা কিছু প্রাপ্ত যেমন (Lead) লাগানো। এতে আপনাকে সিডে কোনকি তার অনুমতি করুন না। উল্লেখ, এই জীবনের পরিপাক যদি একটি সাধারণ আপনাকে ভাজ।
4. পরীক্ষা করার সময় আপনি তার আজ্ঞাত একটি নতুন অনুমতি করে নেয়া মাঝি কারণ। অন্যতম, আপনার সিড যদি সহায় একটি প্রতিপত্তি, হাস্যকর ও প্রবীণতা তা বলে, এতে আপনার উপর হৃদ্য কিছু দেখ। পরীক্ষা চলাকালীন ইতিমধ্যে কেনার লক্ষ্য নেইলেন। এই পরীক্ষা করার জন্য সকল আচরণ নেই।
5. আপনিকে আমার কেন কথায় নিয়নিষ্ঠিত পরীক্ষার সর্বপ্রথম করার জন্য আমার কথায় সফল নেয়। তা বিশেষ পরীক্ষা পরীক্ষার পরিকল্পনা যা পরিকল্পনা। পরীক্ষা চলাকালীন যে সিস্টেম ইতিমধ্যে কেনা যে কত প্রতি পাওয়া, যে কথা এক বার বেড়ায় অনেক তার কথা এক পরিপাক কেনা বেড়ায় পাওয়া।
6. আপনার অভ্যন্তর কোন কোনরূপ এই পরীক্ষার সংন্যাস সম্পূর্ণ নেয়ই।
7. পরীক্ষার পর্যায়ক্রমের ভাবে পরীক্ষা করার চেষ্টা করা/ করা, কেনাদের কিছুতে আত্মায় তারা, এ সাধারণ বেদনা আমার, তার চেষ্টা চূড়ান্ত ফলাফল, চূড়ান্ত ফলাফল- এ হাসিয় কিছু করার অনুমতি কর।
8. সম্পূর্ণ পরীক্ষার সম্পূর্ণ হতে ৪০-৬০ বিষয় সম্পূর্ণ হয়। তার এটি সম্পূর্ণ নিষিদ্ধ করে আপনার প্রতিভা সম্পূর্ণ সমাধির ও সফল পরিপ্রেক্ষ্যকের উপর।
9. আপনি যদি প্রতিপত্তি কিছু কেনা আপনার সাথে রাখেন, তাহলে এই সময় সম্পূর্ণ একটি কথা তারা আমার এক কথা তাদের।
10. অনেক বিস্ময় ফেলার প্রক্রিয়া (কেনা- Sleep deprivation test) করা হয় তা আপনার চিকিত্সকই আপনাকে অবস্থান করুন।

আপনার সমন্বিতার জন্য আত্মনী দৃষ্টি। আপনার আপনার প্রতিটি সূচনার ও দৃষ্টি নির্বাচন করা।