Childhood epilepsy in Bangladesh:

Clinical profile, predictors of outcome and randomized controlled trial of efficacy and side effects of drug treatment.

by

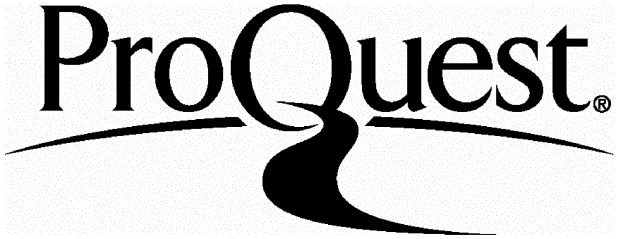
Selina Husna Banu

Neurosciences Unit

Institute of Child Health, London

2003

Thesis submitted for the Degree of Doctorate of Philosophy in the faculty of Medicine University College London.



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 multi-disciplinary 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.

TABLE OF CONTENTS

ABSTRACT **2**

TABLE OF CONTENTS **4**

LIST OF TABLES **11**

LIST OF FIGURES **13**

INDEX OF APPENDICES **14**

INDEX OF ABBREVIATIONS **15**

ACKNOWLEDGEMENTS **16**

CHAPTER ONE **17**

1: ELEMENTS OF THE STUDY 17
1.1.1: OVERVIEW OF THE THESIS 17
1.1.2: BROADER AIM OF THE STUDY 17
1.1.3: CHAPTER CONTENTS 17
1.2: THE CANDIDATE'S ROLE IN THIS STUDY 20
1.2.1: BACKGROUND PREPARATION 20
1.2.2: PREPARATION OF THE ENTRY FORMS AND TRAINING FOR THE PERSONNEL 20
1.2.3: PROCEDURE 21
1.2.4: DATA STORAGE AND ANALYSIS 22

PART ONE **23**

BACKGROUND TO THE STUDY 23

CHAPTER TWO **27**

2.1: INTRODUCTION 27
2.2: EPIDEMIOLOGY 27
2.3: EPILEPSY CLASSIFICATION 28
2.4: CHILDHOOD EPILEPSY AND ASSOCIATED NON-CONVULSIVE NEUROLOGICAL DISORDERS 29
2.5: PREGNANCY AND BIRTH-RELATED PROBLEMS AND EPILEPSY 30
2.6: INTERRELATIONSHIP BETWEEN EPILEPSY, MOTOR DISORDER AND COGNITIVE IMPAIRMENT 31

2.7: AEDs AS A CAUSE OF BEHAVIOURAL SIDE-EFFECTS 32
2.8: AVAILABILITY OF FIRST LINE AEDs, AND NEW ANTIEPILEPTIC MEDICATIONS IN BANGLADESH 33
2.9: EPILEPSY TREATMENT GAP IN DEVELOPING COUNTRIES, AND SEIZURE OUTCOME 34
2.9.1: Treatment gap *34*
2.9.2: AED selection, developed and developing countries *34*
2.9.3: Seizure remission and treatment gap *35*
2.9.4: Prognosis and response to treatment (based upon the syndromic classification) *36*
2.10: BEST PRACTICES AND PREDICTORS OF SEIZURE REMISSION: LESSONS LEARNT FROM DEVELOPED COUNTRIES 36
2.10.1: Clinical factors as predictors of seizure remission *37*
2.10.2: EEG as a predictor of seizure remission *39*

CHAPTER THREE **42**

3.1: INTRODUCTION 42
3.2: GEOGRAPHICAL AND SOCIAL ASPECTS OF BANGLADESH 42
3.3: EPIDEMIOLOGY OF CHILDHOOD DISABILITIES AND SEIZURE DISORDERS IN BANGLADESH AND OTHER DEVELOPING COUNTRIES 43
3.4: MULTIDISCIPLINARY CHILD DEVELOPMENT AND NEURODISABILITY SERVICES IN BANGLADESH: A NEW DIMENSION TO CHILD HEALTH 46
3.5: DEVELOPING EEG SERVICES IN BANGLADESH 48
3.6: SOCIAL AND PUBLIC HEALTH CONCERNS RELATING TO CHILDHOOD EPILEPSY IN DEVELOPING COUNTRIES 49
3.7: DEVELOPING EPILEPSY SERVICES FOR CHILDREN IN A COUNTRY WITH LIMITED RESOURCES 51
3.8: EXPERIENCE WITH FIRST 1000 EEGs 52

PART TWO **56**

BACKGROUND OF PART TWO 56

CHAPTER FOUR **57**

4.1: INTRODUCTION 57
4.2: METHODS AND MATERIAL 57
4.3: DEFINITIONS 58
4.3.1: Definitions related to seizures and epilepsy *58*
4.4: CLASSIFICATION OF EPILEPSIES AND EPILEPSY SYNDROMES 61
4.5: PREGNANCY AND BIRTH RELATED RISK FACTORS AND PAST MEDICAL HISTORIES DEFINED 65
4.5.1: History of perinatal asphyxia *65*
4.5.2: Any problems during the neonatal period and history of neonatal seizures *66*
4.5.3: Previous obstetric history *66*
4.5.4: Preceding history of febrile seizures *66*

4.5.5: Family history of epilepsy *66*
4.5.6: Previous history of CNS infection *67*
4.5.7: History of significant head injury *67*
4.5.8: History of status epilepticus before entry *67*
4.5.9: Previous history of AED treatment *67*
4.5.10: Time gap *67*
4.5.11: Treatment gap *68*
4.6: NON-CONVULSIVE DISORDERS 68
4.6.1: Motor disorder *68*
4.6.2: Cognitive impairment and behavioural state on the day of diagnosis *69*
4.7: ASSESSMENT OF COGNITIVE FUNCTIONS AND BEHAVIOUR 69
4.7.1: Cognitive development on clinician's judgment *69*
4.7.2: Cognitive development (Intellectual quotient or IQ) *70*
4.8: ASSESSMENT OF CHILD'S BEHAVIOUR 70
4.8.1: Behaviour assessment by physician and the clinical child psychologist *70*
Behavioural assessment by the psychologist *71*
4.8.2: Adapted Richman's behavioural assessment questionnaire for children *71*
4.8.3: Rutter scale of behavioural assessment for the middle age range children *71*
4.9: INTRODUCTION OF CONNERS' BEHAVIOURAL ASSESSMENT QUESTIONNAIRE FOR MOTHERS: 72
4.9.1: Reliability test and validity measure of Conners' short questionnaire for parents (CPRS-R:S) *73*
4.9.2: Concurrent validity measure *74*
4.10: INVESTIGATIONS 74
4.10.1: Electroencephalograms (EEG) recording and findings *74*
4.10.2: EEG results were categorized as *75*
4.10.3: Other investigations *76*
4.11: DEVELOPMENT OF MEDICAL ASSESSMENT FORM AND TRAINING OF THE TEAM WORKERS 77
4.11.1: History record and medical assessment form (MAF) *77*
4.11.2: Socioeconomic status (SES) recording form (Appendix IX) *79*
4.11.3: Other data entry forms including psychological assessment form, EEG data entry form (Appendix XIII) *80*
4.12: TRAINING OF THE PCP 81
4.12.1: Practical training *81*
4.12.2: Theoretical reaching *81*
4.13: TRAINING OF THE PAEDIATRIC NEUROPHYSIOLOGISTS 83
4.14: TRAINING OF THE DEVELOPMENTAL THERAPIST 83
4.15: RECORD MAINTENANCE 83

4.16: PATIENT RECRUITMENT SITE SELECTION: DESCRIPTION OF THE HOSPITAL IN AND OUTPATIENT DEPARTMENTS. RATIONAL FOR USING A HOSPITAL SITE, PARTICULARLY DSH 83
Dhaka Shishu Hospital (DSH) *83*
Logic behind this site selection *84*

CHAPTER FIVE **87**

5: THE RETROSPECTIVE STUDY 87
5.1: INTRODUCTION AND BACKGROUND 87
5.2: OBJECTIVES OF THE STUDY 87
5.2.1: Aims of the study *88*
5. 3: METHODS AND MATERIALS 88
5.3.1: Study site *88*
5.3.2: Study design *88*
5.3.3: Study population *89*
5.3.4: Follow-up period *89*
5.3.5: Assessment format *90*
5.3.6: Socio-demographic information (Appendix IX) *90*
5.3.7: Child Factors *90*
5.3.8: Variables used for seizure descriptions *91*
5.3.9: Neurodevelopmental assessments *92*
5.3.10: Assessment of cognitive functions and behaviour *93*
5.3.11. INVESTIGATIONS 94
5.3.12: Holistic management *94*
5.3.13: Follow-up information of the child and outcome measures *95*
5.3.14: Potential predictors of seizure outcome *96*
5.3.14: Data Analysis *97*
5.4: RESULTS 98
5.4.1: Description of the study population *98*
5.4.2: Birth and past clinical history *100*
5.4.3: Epilepsy profile *101*
5.4.4: Associated non-convulsive disabilities *104*
5.4.5: EEG profile *105*
5.4.6: Neuroimaging profile *107*
5.4.7: Outcomes at one or more than one year's follow-up *107*
5.4.8: Baseline and follow-up AED status *108*
5.4.9: Behaviour and motor problems at last follow-up *109*
5.4.10: EEG correlation *110*
5.4.11: Predictors of seizure outcomes *113*

5.5: Conclusions and implications for future research *118*

CHAPTER SIX **120**

6: THE PROSPECTIVE STUDY 120

6.1: INTRODUCTION AND BACKGROUND OF THIS STAGE 120

METHODS AND MATERIALS 120

6.2: AIMS OF THIS STAGE OF STUDY 120

6.3: STUDY DESIGN 121

6.3.1: Sample size *121*

6.3.2: Inclusion criteria *121*

6.3.3: Exclusion criteria *122*

6.3.4: Preparation *122*

6.4: PATIENT RECRUITMENT 122

6.5: MEDICAL AND NON-MEDICAL PERSONNEL INVOLVED 123

6.6: COMMENCING THE STUDY 124

6.6.1: Training the team workers *124*

6.6.2: On arrival *125*

6.6.3: Psychological evaluation *125*

IQ test *126*

6.6.4: Behavioural assessment *126*

6.6.5: Sociodemographic (SES) form *126*

6.6.6: Family inventory SRQ (Appendix XIII) *126*

6.6.7: Ensuring drug availability, emergency management, compliance, seizure record keeping and educating the parents about epilepsy *127*

6.6.8: Attendance compliance and managing other problems *129*

6.6.9: Follow up record *129*

6.6.10: EEG recording and interpretation *130*

6.6.11: Other investigations *131*

6.6.12: Management *131*

6.7: FOLLOW-UP INFORMATION 132

6.8: EPILEPSY OUTCOME MEASURES 132

6.8.1: Seizure remission *132*

6.8.2: Behaviour state on last visit *133*

6.8.3: Motor disability on last visit *133*

6.8.4: Cognitive assessment on last visit *133*

6.8.5: Parental perception *133*

6.9: DATA ANALYSIS 134

6.10: RESULTS 135

6.10.1: Description of the study population *135*
6.10.2: FAMILY CRITERIA 138
6.10.3: Pregnancy and birth related problems *141*
6.10.4: Epilepsy profile *145*
6.10.5: Non-convulsive disorders *150*
6.10.6: Investigation *153*
6.10.7: Outcome *155*
6. 10.8: Predictors of seizure outcome *159*
6.10.9: Motor functional outcome *164*
6.10.10: Treatment *165*
6.11: DISCUSSION 169
6.11.1: Febrile seizures and subsequent epilepsy *169*
6.11.2: Characteristics of the study population in the context of SES of the country *170*
6.11.3: Pregnancy and birth related problems as potential risk factors *173*
6.11.4: Family history of epilepsy *175*
6.11.5: Child characteristics *175*
6.11.6: Epilepsy profile and associated non-convulsive disorders *176*
6.11.7: Epilepsy management *180*
6.11.8: Outcome *182*
6.11.9: Predictors of 'poor seizure remission' *183*
6.11.10: Role of EEG and other investigations in diagnosing epilepsy and identifying preventable causes of epilepsy *183*
6.11.11: EEG recording: *183*
6.11.12: Neuroimaging revealed structural abnormality in a large number of children: *185*

CHAPTER SEVEN **186**

7: A RANDOMIZED CONTROLLED TRIAL OF PHENOBARBITONE AND CARBAMAZEPINE MONOTHERAPY IN CHILDREN WITH EPILEPSY IN BANGLADESH 186
7.1: INTRODUCTION 186
7.2: STUDY DESIGN AND SETTING 187
7.2.1: Site of patient recruitment *187*
7.2.2: Patients *187*
7.2.3: Sample size *187*
7.2.4: Diagnosis and classification of active epilepsy *188*
7.2.5: Associated non-convulsive disabilities *188*
7.2.6: Neurodevelopmental assessment and behavioural state at randomization and after12 months of AED treatment *189*
7.2.7: Seizure outcome *189*

7.2.8: Simple randomization *189*
7.2.9: Drugs and doses *190*
7.2.10: Outcome measures *191*
7.2.11: Analysis *191*
7.3: RESULTS 193
7.3.1: Child characteristics, seizure and epilepsy profiles *193*
7.3.2: Outcome *197*
7.3.3: Seizure outcome *198*
7.4: DISCUSSION 204

CHAPTER EIGHT **208**

8. DISCUSSION AND IMPLICATIONS OF THE RESULTS 208
8.1: INTRODUCTION 208
8.2: RESULTS AND THEIR IMPLICATIONS 208
8.2.1: Epilepsy profile and service development *208*
8.2.2: Significant predictors of seizure outcomes *209*
8.3: CONCLUSION 217

BIBILIOGRAPHY **219**

LIST OF TABLES

TABLE 2.1: IDENTIFIED PREDICTORS OF SEIZURE OUTCOME IN OTHER STUDIES 41
TABLE 3.1: ESTIMATED PREVALENCE OF DISABILITIES PER 1000 IN 2 TO 9 YEAR-OLD CHILDREN IN BANGLADESH. 44
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) 45
TABLE-3.3: CLINICAL PROFILE OF 1000 CHILDREN REFERRED FOR EEG: 54
TABLE 3.4: SALIENT FEATURES OF THE 179 CHILDREN WHO PRESENTED WITH FEBRILE-CONVULSION 54
TABLE 3.5: ABNORMAL EEG FINDINGS IN CHILDREN WHO PRESENTED WITH FEBRILE SEIZURES 55
TABLE 4.1: CLASSIFICATION OF SEIZURES AND EPILEPSIES ADAPTED FROM THE ILAE CLASSIFICATION 63
TABLE 4.2: MEAN DIFFERENCE BETWEEN THE SCORES OBTAINED ON TEST 1 AND TEST 2 73
TABLE 5.1: DEMOGRAPHY OF THE STUDY POPULATION. 99
TABLE 5.2: CLINICAL HISTORY OF STUDY POPULATION AND FAMILY 100
TABLE 5.3: EPILEPSY PROFILE 103
TABLE 5.4: ASSOCIATED NON-CONVULSIVE DISABILITIES 105
TABLE 5.5: ELECTROENCEPHALOGRAPHIC (EEG) FINDINGS 106
TABLE 5.6: NEUROIMAGING REPORTS 107
TABLE 5.7: SEIZURE OUTCOME DURING THE LAST FOLLOW UP 108
TABLE 5.8: BASELINE AND FOLLOW-UP 'AED' STATUS 108
TABLE 5.9: MOTOR DISABILITY AND BEHAVIOURAL STATE ON LAST FOLLOW-UP DAY 110
TABLE 5.10: CORRELATION BETWEEN CLINICAL DIAGNOSIS AND EEG FINDINGS 111
TABLE 5.11: CORRELATION BETWEEN EEG FEATURES AND SEIZURE OUTCOME 112
TABLE 5.12: MAIN EFFECT MODEL SHOWING CORRELATION BETWEEN INDIVIDUAL PREDICTORS AND SEIZURE OUTCOME 114
TABLE 5.13: LOGISTIC REGRESSION MODEL WITH INTERACTION OF INDEPENDENT VARIABLES AND DEPENDENT VARIABLE 117
TABLE 6.1: PATIENT OVERVIEW 135
FIGURE 6.1: FLOW CHART OF THE STUDY- POPULATION 137
TABLE 6.2: FAMILY CRITERIA, SES 139
TABLE 6.2.1: PARENTS' FIRST REACTION AFTER A MAJOR SEIZURE ATTACK 140
TABLE 6.2.2: PARENTS' EXISTING KNOWLEDGE ABOUT EPILEPSY : 140
TABLE 6.3: PREGNANCY AND BIRTH RELATED INFORMATION 143
TABLE 6.3.1: HISTORY OF EVENT(S) ASSOCIATED 144

TABLE 6.4: CHILD AND SEIZURE RELATED INFORMATION 146
TABLE 6.5: CLASSIFICATION OF SEIZURES AND EPILEPSIES 148
TABLE 6.6: DIAGNOSIS OF 'MALIGNANT EPILEPSY SYNDROME' IN 390 & 319 CHILDREN 149
TABLE 6.7: CORRELATION BETWEEN EPILEPTIFORM DISCHARGES IN EEG & CLINICAL DIAGNOSIS IN 319 PATIENTS 150
TABLE 6.8: ASSOCIATED NON-CONVULSIVE DISORDERS 151
TABLE 6.9: CORRELATION BETWEEN COGNITIVE IMPAIRMENT DIAGNOSED ON CLINICAL JUDGMENT AND ON IQ TEST 152
TABLE 6.10: INVESTIGATION AND FINDINGS 154
TABLE 6.11: COMPARISON OF EEG REPORTS BY TWO REPORTERS 155
TABLE 6.12: SEIZURE OUTCOME AFTER REGULAR 'AED' TREATMENT 157
TABLE 6.13: SEIZURE OUTCOME IN CHILDREN HAVING SEVERE NEUROLOGICAL DEFICIT 158
TABLE 6.14: DESCRIPTION OF CHILDREN WHO HAD POOR SEIZURE REMISSION: NUMBER 151 158
TABLE 6.15: NON-CONVULSIVE DISORDERS IN 67 OPD PATIENTS WITH POOR SEIZURE REMISSION BEFORE AND AFTER TREATMENT 159
TABLE 6.16: UNIVARIATE ANALYSIS TO SEE THE MAIN EFFECT OF PREDICTORS WITH SEIZURE OUTCOME. 160
TABLE 6.17: MULTIPLE LOGISTIC REGRESSION ANALYSIS WITH 7 POTENTIAL PREDICTORS 161
TABLE 6.18: MULTIPLE LOGISTIC REGRESSION ANALYSIS OF PREDICTORS WHEN EEG ENTERED IN-TO THE MODEL 161
TABLE 6.19: SENSITIVITY AND SPECIFICITY OF THE PREDICTORS 162
TABLE 6.20: PARENT'S PERCEPTION ABOUT THE CHILD'S FUNCTIONAL DEVELOPMENT AFTER ONE YEAR'S TREATMENT 164
TABLE 6.21: MOTOR FUNCTIONAL STATE AFTER ONE YEAR'S TREATMENT 165
TABLE 6.22: PRESENT MEDICATION 166
TABLE 6.23: RESPONSE TO PREDNISOLONE TREATMENT AFTER TWO WEEKS 167
TABLE 6.24: SEIZURE OUTCOME AT THE FINAL FOLLOW UP IN 137 CHILDREN TREATED WITH SHORT COURSE OF PD AT THE BEGINNING. 167
TABLE 6.25: HISTORY OF PREVIOUS AED TREATMENT AND TIME GAP 168
TABLE 7.1: RANDOMIZED SUBJECTS: FAMILY AND CHILD CHARACTERISTICS 195
TABLE 7.4: INDEPENDENT *T*-TEST DIFFERENCE IN MEAN BEHAVIOURAL OUTCOME SCORE BETWEEN PHENOBARBITONE AND CARBAMAZEPINE GROUP 200
TABLE 7.5: MAIN EFFECT MODEL SHOWING CORRELATION BETWEEN OUTCOME BEHAVIOURAL PROBLEM AND INDIVIDUAL VARIABLES 201
TABLE 7. 6: MULTIPLE LOGISTIC REGRESSION MODEL FOR OUTCOME BEHAVIOURAL PROBLEMS 202
TABLE 7.7: SURVIVAL TIME DIFFERENCE ADJUSTED AND NON-ADJUSTED 203

LIST OF FIGURES

FIGURE 3.1: MAP SHOWING THE AREAS, WHERE COMPREHENSIVE SERVICE FOR THE DISABLED CHILDREN ARE DISSEMINATED ----------47

FIGURE 3.2: INCIDENCE OF DEVELOPMENTAL DISABILITIES AT SISHU BIKASH KENDRO, DHAKA SHISHU HOSPITAL IN 4100 CHILDREN 1992- 1998----------48

FIGURE 3.3: FLOW CHART OF FIRST 1000 CHILDREN REVIEWED FROM THE EEG CENTRE TO LAST FOLLOW-UP----------53

FIGURE 5.1: CORRELATION BETWEEN POOR SEIZURE REMISSION AND EEG FETURES----------113

FIGURE 6.1: FLOW CHART OF THE STUDY POPULATION----------137

FIGURE 6.2: CORRELATION BETWEEN POOR SEIZURE REMISSION AND EEG FEATURE IN THE PROSPECTIVE GROUP----------163

FIGURE 6.3 : INITIAL RESPONSE TO PREDNISOLONE TREATMENT AMONG 137 CHILDREN----------167

FIGURE 7.1: TRIAL PROFILE:----------192

FIGURE 7.2: KAPLAN-MEIER CUMULATIVE SEIZURE CURVE FOR PATIENTS WITH PB & CBZ----------203

INDEX OF APPENDICES

Appendix I :	Retrospective study data entry form
Appendix II :	Medical Assessment form
Appendix III:	Management form
Appendix IV:	Follow up form
Appendix V:	Summary form
Appendix VI:	Final assessment form
Appendix VII:	EEG data entry from
Appendix VIII:	Antiepileptic drugs and doses
Appendix IX:	Socio-economic status form (SES)
Appendix X:	Conners' behavioural assessment questionnaire
Appendix XI:	Richman behavioural assessment questionnaire
Appendix XII:	Rutter behavioural assessment questionnaire
Appendix XIII:	Maternal stress assessment questionnaire
Appendix XIV:	Independent behaviour assessment scale (IBAS)
Appendix XV:	WHO disability grading
Appendix XVI:	Seizure record diary
Appendix XVII:	Parental education

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

ACKNOWLEDGEMENTS

This study is dedicated to the children of Bangladesh who need more care for our better future.
I am grateful to my supervisors Professor Brian Neville, Dr. Stewart Boyd and Professor Naila Z. Khan who have guided me and provided support throughout. I extend my special thanks to the British Council for providing the financial support for the whole project and the course.

I am grateful to Dr.Anthony Johnson, Dr. Abbas Bhuiya and Dr. Angie Wade, for their support in statistical analysis. I wish to express my special thanks to Dr. Moshrat Jahan, Dr. Mahmuda Hussain, Dr. Anisa Jahan, Ms. Monwara Parveen, Ms.Umme Kulsum, Ms. Rumana Mahfuz, Ms. Regina Parveen and Abid Hossain for helping me all the way during the data collection. I am also very grateful to the Dhaka Shishu Hospital authority for giving logistic supports.
My thanks must extend for Dr.Humaira Islam, Dr. Jahangir Alam, and Dr. Jalaluddin for supporting us in doing the investigations for the children.
Very special thanks to all the children and their families, without their co-operative participation this work would never be performed.

I wish to acknowledge the understanding and tolerance of my family members, my parent in laws, my husband Parvez and my two daughters Mahpara and Fairuz. I am grateful to my parents and all my friends whose inspiration meant a lot during this work. Finally, my heartiest gratitude to my late brother whose love and support had always been with me till the last day of his life.

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.

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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). Canger 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

controversial and unclear in some studies (Aicardi 1994b; Manford et al. 1992; Murthy & Yangala 2000; Murthy, Yangala, & Srinivas 1998; Rinaldi et al. 2000).
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, & Sackellares 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.

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 (Farewell 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 & Brodie 2000; de Silva., Mac Ardle, & McGowan 1996; Matson et al. 1985). Among

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

studies (Arts et al. 1999; Berg et al. 2001; Berg, Hauser, & Shinnar 1995; Brorson & Wranne 1987; de Silva., Mac Ardle, & McGowan 1996; Hauser et al. 1996).

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 2.1: Identified predictors of seizure outcome in other studies

Authors	Year	Country	Study design	Poor sz. remission significantly influenced by the presence or absence of the following
Camfield et al.	1993	Nova Scotia, Canada	Child age study of follow-up data. Retrospective	Age at onset; low IQ; neonatal seizures, number of sz. before treatment in MVA, EEG in UVA.
Sillanpaa et al.	1995	Turku, Finland	Validation of the scoring system. Retrospective	Low IQ, neonatal seizures, number of sz. before treatment.
Sillanpaa et al.	1993	Turku, Finland	Long term (30 years) follow-up of incidence cohort	N.D, high initial seizure rate, SE, poor short-term effects of AED therapy.
Berg et al.	1996	New York, U.S.A.	Case-control study. Retrospective	Remote symptomatic epilepsy, I.S., age at onset, S.E.
Berg et al.	2001	Connecticut, U.S.A.	Prospective community based study	Symptomatic epilepsy, FHO epilepsy, sz. Frequency, EEG slowing.
Wakamoto et al.	2000	Japan	Childhood onset epilepsy, in 20 years or older. Retrospective	Low IQ, sz. Frequency, SE, early response to therapy.
Casetta et al.	1999	Copparo, Italy	Case-control Community based	Remote symptomatic epilepsy (mostly represented by perinatal injury); sz. frquency, age at onset (not confirmed in all age group)
Annegers et al.	1979	Minnesota, U.S.A.	Retrospective and Long-term follow-up	Neurological deficits, remote symptomatic epilepsy, partial epilepsy, adult onset epilepsy.
Arts et al.	1999	The Netherlands	Prospective, in children such an outcome	Symptomatic epilepsy, number of sz. before treatment, sz. types.
Tae-Sung Ko et al.	1999	Boston, U.S.A.	Retrospective, in children followed up for 2 years.	Symptomatic epilepsy, early age at onset, sz. Types, EEG: diffuse slowing, focal spike and wave activity
Shafer et al.	1988	Minnesota, U.S.A.	Retrospective.	Early brain damage, GTCS, abnormal first EEG
Brorson And Wranne	1987	Sweden	Retrospectively traced 12 years followed up	ND; low IQ; sz. frequency.
Chawla et al.	2002	India	Case control study in children	N.D., age of onset before 1year, MCS/IS, remote symptomatic epilepsy.

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 under18 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.

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

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)

Prevalence	Bangladesh	Jamaica	Pakistan
Neonatal seizures	8.4 (5.6-11.2)	0.9 (0.4-1.3)	13.0 (9.4-16.7)
Febrile seizures	50.6 (43.7-57.5)	10.9 (2.6-19.3)	62.8 (54.8-70.9)
Provoked seizures	57.7 (50.5-65.0)	11.8 (3.5-20.2)	70.4 (61.9-78.9)
Unprovoked sz.[a]	8.7 (6.7-11.3)	6.3(0.3- 12.2)	17.8 (10.9- 24.7)
Epilepsy	6.5 (2.2-10.6)	5.8 (0.0-11.7)	15.5 (9.6-21.4)
Active epilepsy[b]	5.8 (1.6-10.1)	5.2 (0.0-11.1)	12.4 (6.6-18.2)
Any seizure history	68.3 (60.5-76.1)	17.7 (12.4-22.9)	91.2 (82.2-101.2)

Information taken from (Durkin, Leislie, Devidson, Hasan, Hasan, Khan, & Shrout 1992).

*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

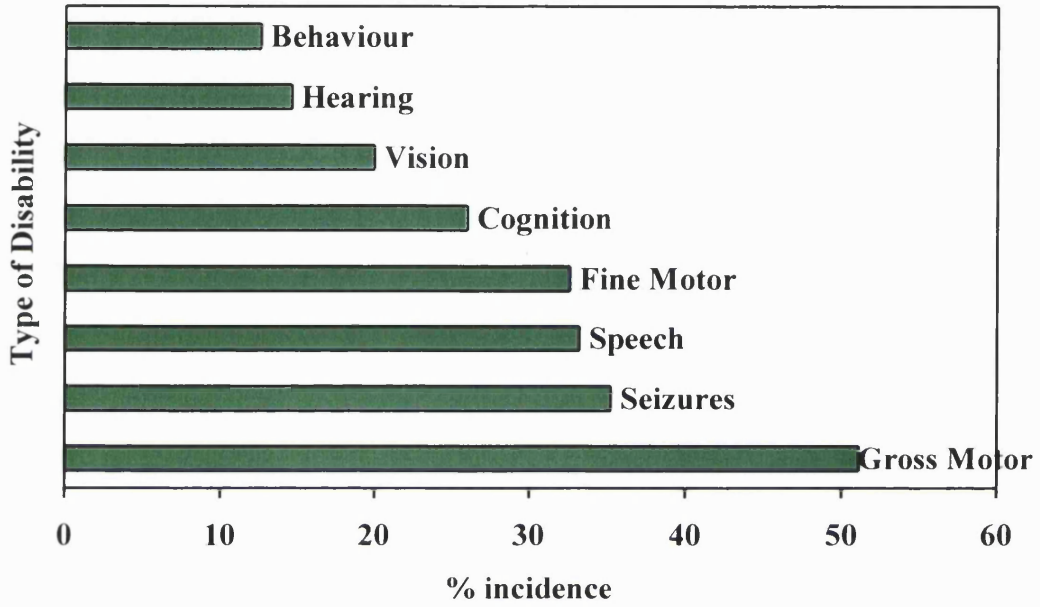
In 1992 a Child Development and Neurology centre (CDC) was established for the first time in the country within a 350 bed national hospital for children, the Dhaka *Shishu* (Children's) Hospital (DSH). The aim was to provide a comprehensive, multidisciplinary service for children presenting with both 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.

■ SHISHU BIKASH (CHILD DEVELOPMENT) NETWORK

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. In1996 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 cysticercosis, 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 Helath 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

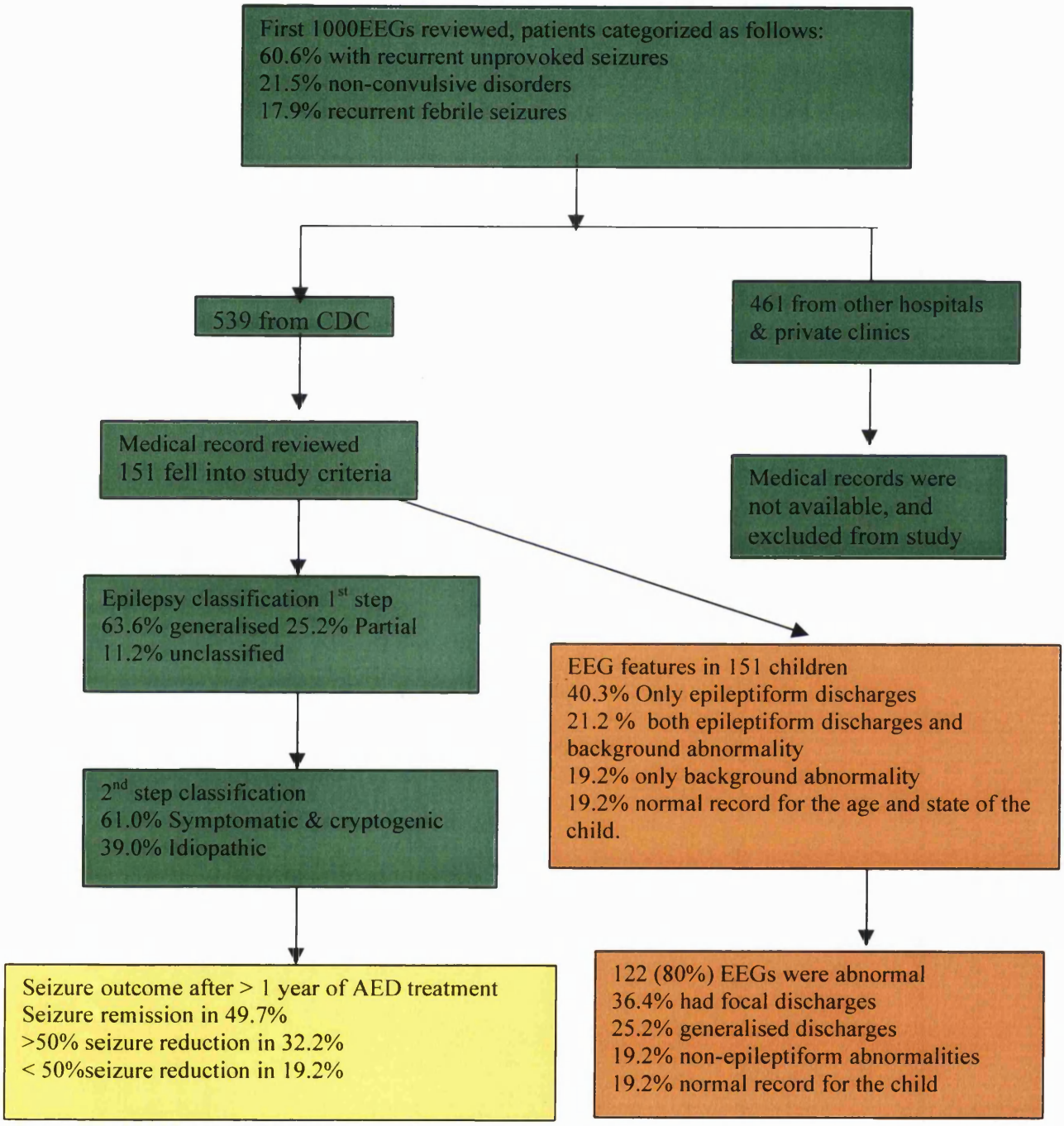


Table-3.3: Clinical profile of 1000 children referred for EEG:

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

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

Age in years	n =179	%
<2-4 years	114	63.7
>4-7 years	65	36.3
Total	179	100.0
Sex		
Male	132	73.7
Female	47	26.3
Total	179	100.0
Number of febrile convulsions		
1-2	69	38.5
3-5	69	38.5
>5	41	23.0
Total	179	100.0
Non-convulsive disorders *		
Absent	145	81.0
Present	34	19.0
History of non-febrile seizure present	15	8.0
AED history		
None	98	54.7
On long-term AEDs	81	45.3
Total	179	100.0

* Defined in section 4.6

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

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

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 epilepiform 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 eilepticus 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.I: 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
Richmans 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 Richmans 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 *Bangla* 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

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

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-sore 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 dysrrhythic 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.

3. Mixed runs of delta and beta wave activity with gross poverty of normal rhythmic activity.

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 are15-20 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 el 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 rikshowa
- 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. Independent history taking and assessment of the patient handling under direct supervision and assessment of the physician.

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:

17 Data base files were made on:

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 under18 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.

Total period of follow up at the epilepsy clinic

	Number	Percent
12 months	8	5.3
13 months to24 months	43	28.5
25 months to 36 months	34	22.5
37 months to 48 months	29	19.2
49 months and above	37	24.5
Total	151	100.0

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 care givers, (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 + B1 (MST) + B2 (HRTSZ) + B 3 (MDIS) + B 4 (LIQ) + B 5 (SPSD) + B6 (FHOE) + B 7 (AAONS) + B8 (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.

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

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.

Items	Number	%
H/O preterm birth		
Absent	141	93.4
Present	10	6.6
Total	151	100.0
H/O perinatal asphyxia		
Absent	81	53.6
Present	70	46.4
Total	151	100.0
H/O Neonatal seizure		
Absent	89	58.9
Present	62	41.1
Total	151	100.0
Family H/O epilepsy		
Absent	138	91.4
Present	13	8.6
Total	151	100.0
Family H/O febrile seizure		
Absent	135	90.1
Present	15	9.9
Total	151	100.0
Previous H/O febrile seizure		
Absent	114	75.5
Present	37	24.5
Total	151	100,0

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 naeuroimaging 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

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

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 in106 (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

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

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

Item	Number	%
EEG		
Abnormal	122	80.8
Normal	29	19.2
Total	151	100
EEG features		
Epileptiform disch.	93	61.6
Generalised	38	25.2
Localized	55	36.4
Abnormal background (NEAA)	29	19.2
Normal activities	29	19.2
Total	151	100.0
Abnormal EEG features		
Epileptiform discharges	61	50.0
NEAA	29	23.8
Both	32	26.2
Total	122	100

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

Item	Number	Percent
Neuroimaging		
Done	79	52.3
Not done	72	47.6
USG	15	
CT	70	
MRI	15	
Total	151	100.0
Abnormal	51	64.5
Normal	28	35.5
Total	79	100

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

Item: Seizure outcome	Number	%
Seizure reduction	76	50.3
>50%- <100%	47	31.1
0-<50%	29	19.2
100% seizure reduction	75	49.7
Total	151	100

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

AED status	Number	Percentage
No AED prior to entry at the CDC		
On AED prior to entry at CDC	85	56.3
	66	43.7
Total	151	100
Current AED on last follow up		
Single AED	115	76.2
Multiple AED	22	14.6
No medication	14	9.3
Total	151	100

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.

Item	Number	Percentage
Motor disability		
Absent	90	59.6
Present	61	40.4
Total	151	100
Behavioural state		
Normal behaviour	93	61.6
Abnormal behaviour	58	38.4
Significant problem	24	15.9
Mild problem	22	14.6
Problem after starting AED	12	7.9
Total	151	100

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.

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

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)

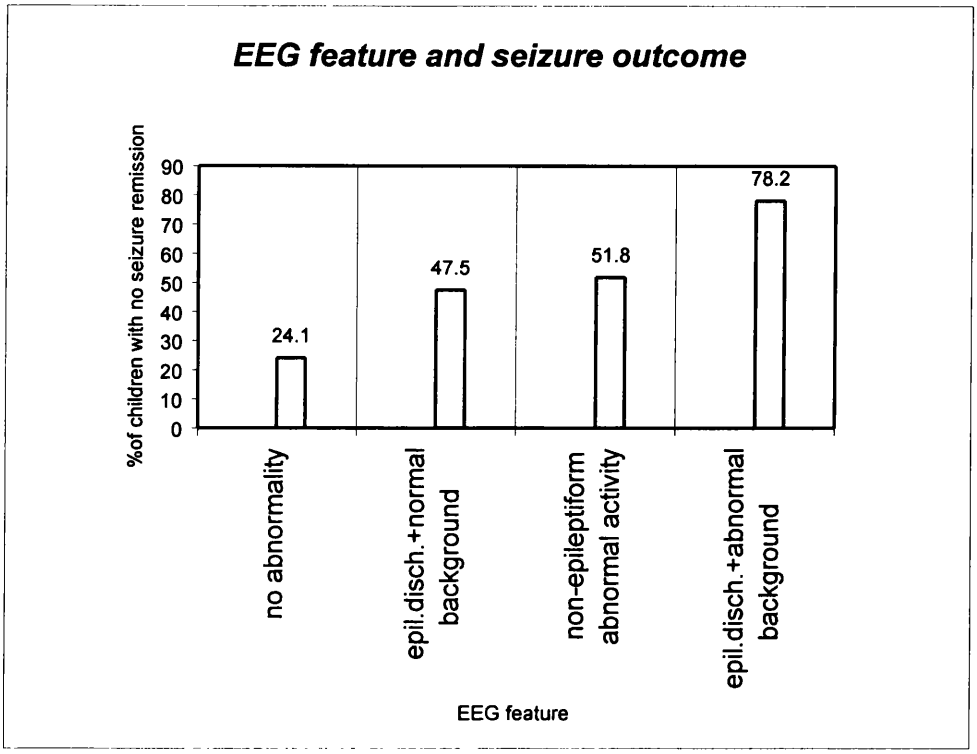
There was significant correlation between seizure remission and EEG feature when the EEG abnormalities were sub-categorized. Analysis showed Chi-square significance level at <0.001 with 2 degrees of freedom. Figure 5.1 shows an almost linear correlation between EEG findings and seizure remission, the 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

EEG- finding	Seizure remission (%)	Poor seizure remission (%)	Total (%)
Epileptiform discharges	32 52.5%	29 47.5%	61 100.0%
Background abnormality	14 48.3%	15 51.7%	29 100.0%
Both epileptiform discharges & Non-epileptiform abnormality	7 21.9%	25 78.1%	32 100.0%
Normal	22 75.9%	7 24.1%	29 100.0%
Total	75	76	151

Pearsons Chi-square value = 18.06 with two tailed significance <0.001

Fig-5.1: Correlation between poor seizure remission and EEG feature.



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.

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

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 and odds ration 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 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.

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

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: $n > (Z_\alpha + Z_{2\beta})^2 \{\pi_1(1-\pi_1) + \pi_2(1-\pi_2)\}/\delta^2$

When, $(Z\alpha + Z2\beta)^2 = 12.99$ for 95% power at 5% significance level.

$n > 12.99\ (70.30 + 50.50) / 20^2$

150 per group

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

$2.150.3^2/8$

$= 9 \times 150/4$

$= 9 \times 37.5$

$n \geq 338$

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

6.3.2: Inclusion criteria

Eligible patients were from 2 months to15 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 bellow, 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)
2. Independent Behaviour Assessment Scale (IBAS)(Munir, Zaman, & McConachie 1999) (3 to 6 year of children).
3. Wechslar Intelligence Scales for children Revised (WISC-R) (Huq 1994; WISC-R 1971) (6 to 16 year old children).

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 low 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.
3. Behavioural state comparing 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:

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

When Z = B 0 + B1 (NOS) + B2 (RTOSZ) + B 3 (NMDIS) + B 4 (MRTD) + B 5 (SPSYND) + B6 (FHOEP) + B7 (AAONS) + B8 (ABNEEG).

6.10: RESULTS

6.10.1: Description of the study population

Table 6.1: Patient overview

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

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

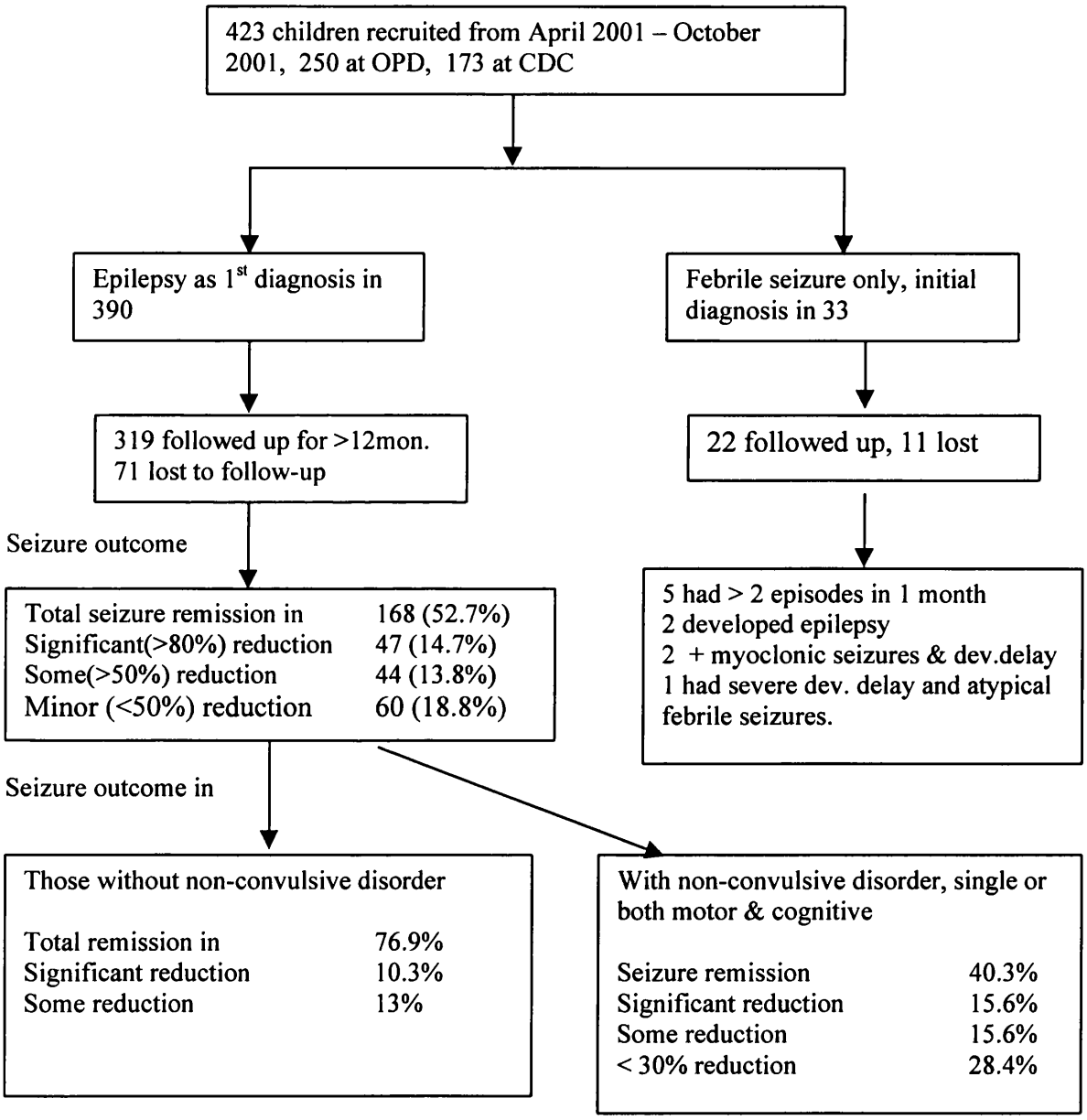
The median age at presentation among the 33 children with febrile seizures was 2 years, interquartile range 1.5 years. The male to female ratio was 10:1, motor and cognitive impairments were noted in 4(12.1%), and 3(9.1%) respectively. A history of perinatal asphyxia, neonatal seizures or prolonged seizures 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



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

	Total	%	OPD	%	CDC	%
Family type						
Nuclear	247	58.4	134	53.6	113	65.3
Joint	176	41.6	116	46.4	60	34.7
Consanguinity						
Positive	16	3.8	7	2.8	9	5.2
Residence						
Rural	259	61.2	156	62.4	103	59.5
Urban	164	38.8	94	37.6	70	40.5
Monthly income						
Lower	251	58.3	155	62.0	96	55.5
Middle	154	36.4	83	33.2	71	41.1
Higher	18	4.2	12	4.8	6	3.4
Maternal education						
Non-literate	165	39.0	95	38.0	70	40.5
Primary level	132	31.2	82	32.8	50	28.9
SSC	61	14.4	41	16.4	20	15.6
HSC	38	9.0	24	5.6	14	4.0
Bachelor &Graduate	27	6.4	8	7.2	19	11.0
Paternal education						
None	146	34.5				
Primary	109	25.8				
SSC	53	12.5				
HSC	44	10.4				
Bachelor &Graduate	71	16.8				
Total	423	100				

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?

To a private practising primary physician (PCP)	151
To the hospital / Primary health complex	122
To a community health workers	31
To the religious people/*Fakir* for *'tabeej'* or *'panipora'*	86
To the traditional healers	254
None	5

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 rog*? Why it occurs to some people?

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

	On first visit	After epilepsy education
1. Bad wind or evil spirit	193	0
2. Don't know	164	94
3. Chronic illness (*mrigi rog*)	56	225
4. Psychological problem (*mathakharap*)	10	7
Total	423	319

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 (m*rigi 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.

Antinatal 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 to18 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)

Items	Total	%	OPD	%	CDC	%
1. Place of birth						
Home	277	65.5	178	72.2	99	57.2
Hospital	146	34.5	72	28.8	74	42.8
Total	423	100	250	100	173	100
2. Mode of delivery						
Normal	348	82.5	220	88.0	128	73.8
El. C/S	50	11.8	22	8.8	28	16.2
Em. C/S	12		3		9	
Forceps	13		5		8	
Total	423		250		173	
3. Labour assisted by						
TBA	209	49.4	127	50.8	82	47.4
F. member	64	15.1	48	19.2	16	9.2
Dr. /nurse	150	35.5	75	30.0	75	43.4
4. Gestational age						
Full-term	359	84.9	215	86.0	144	83.2
Pre-term	26	6.1	10	4.0	16	9.2
Post-term	7	1.7	2	0.8	5	2.9
Unknown	31	7.3	23	9.2	8	4.6
Total	423	100	250	100	173	100
5. A/N check-ups						
Never	153	36.2	94	37.6	59	34.1
TT inj.	137	32.4	79	31.6	58	33.5
Regular	133	31.4	77	30.8	56	32.4
Total	423	100	250	100	173	100
6. Pregnancy problem						
None	310	73.3	193	77.2	117	67.6
Medical	44	10.4	20	8.0	24	13.9
Susp. IUI.	47	11.1	25	10.0	22	12.7
Abortificient	8	1.9	5		3	
Psychosocial	9	2.1	5		4	
Accident	5		2		3	
Total	423		250		173	
7. Maternal age at preg.						
Mean, Median, (min.&max.) Range in years			23.79, 23, (14 & 40), 28			
8. Obstetric history						
Abortion	70	16.5	36	14.4	34	19.7
Stillbirth	22	5.2	11	4.4	11	6.4
IUD	5	1.2	4	1.6	1	0.6
Total	97	22.9	51	20.4	46	26.6

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)

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

Information	Total	%	OPD	%	CDC	%
1. Age at presentation						
2mo-1yr	145	34.3	72	28.8	73	42.2
>1yr-3yr	134	31.7	78	31.2	58	33.5
>3-5 yr	50		33		17	
> 5-7 yr	37		20		17	
>7-10 yr	32		28		4	
>10-13 yr	19		16		3	
>13-15 yr	3		3		0	
Mean, median, IQR(in mo)	37.61, 22, (2-44)		44.54, 26, (2-55)		27.60, 15, (2-28)	
2. Sex						
Male	289	68.3	157	62.8	132	76.3
Female	134	31.7	93	37.2	41	23.7
3. Age at onset						
Early	257	60.8	122	48.8	124	71.7
After12 mo	166	39.2	128	51.2	49	28.3
Mean, med, IQR in mo.	22.47, 8, (1-27)		29.21, 12, (1-37)		13.97, 5, (1-16)	
4. Seizure type						
Single	303	71.6	203	81.2	98	56.6
Multiple	120	28.4	47	18.8	75	43.4
5. Seizure rate						
High	290	68.6	154	61.6	136	78.6
Low	133	31.4	96	38.4	37	21.4
6. H/O febrile seizures						
Absent	357	84.4	201	80.4	155	89.6
Present	66	15.6	49	19.6	18	10.4
7. Family H/O epilepsy						
1st degree	30	7.1	18	7.2	12	6.9
1st, & 2nd degree	57	13.5	37	14.8	20	11.6

Early, at or before 12mo.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 a14.4% 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

Items	Total	%	OPD	%	CDC	%
1. Seizures						
GTCS	163	38.5	106	42.4	57	32.9
MC	141	33.3	56	22.4	85	
GT	109	15.8	49	19.6	60	
IS	80	18.9	24		32	
SPS/ CPS	54	12.8	33		21	
Multifocal sz	28	6.6	22		6	
GCL	24	5.7	7		17	
Absence (typical)	6	1.4	3	1.2	3	1.7
Atonic	4	0.9	1		3	
2. Epilepsy (clinical)						
P.generalised	255	65.4	144	64.3	111	66.9
S.generalised	56	14.4	40	17.9	16	9.6
Partial	40	10.3	25	11.2	15	9.0
Mixed partial&gen.	39	10.0	15	6.6	24	14.5
Total	390	100	224	100	166	100
Epilepsy (clinical&EEG)						
Generalised	205	52.6	117	52.2	88	53.0
Partial & S. gen.	165	42.3	99	44.2	66	39.8
Unclassified	20	5.2	8	3.6	12	7.2
Total	390	100	224	100	166	100
Etiological						
Idiopathic	135	34.6	105	46.9	30	18.1
Sympt.&crypt.	236	60.5	103	46.0	113	80.1
Remote sympt.	19	4.9	16	7.1	3	1.8
Total	390	100	224	100	166	100
Idiopathic	113	35.4	85	48.6	28	19.4
Symptomatic	206	64.6	90	51.4	116	80.6
Total	319	100	175	100	144	100

P. gen, primary generalised; S. gen, secondary generalised; sympt, symptomatic; crypt, cryptogenic.

Table 6.6: Diagnosis of 'malignant epilepsy syndrome' in 390 & 319 children

M.E.S	Total	%	OPD	%	CDC	%
1. M.E.S in 390 children						
None diagnosed	269	69.0	173	77.2	96	57.8
Diagnosed	121	31.0	51	22.8	70	42.2
Total	390	100	224	100	166	100
I.S	80	66	36	70.6	45	64.3
M.C.E	27	22.3	12	23.5	16	22.9
L.G.S.	11	9.0	3	5.9	8	11.4
L.K.S.	1	0.8	0		1	1.4
Total	121	100.0	51	100.0	70	100.0
2. M.E.S in 319 children						
None	223	69.9	136	77.7	87	60.4
Diagnosed	96	30.1	39	22.3	57	39.6
Total	319	100	175	100	144	100
EEG characteristic pattern in 319						
Hypsarrhythmia	34	58.6	14	60.9	20	57.1
LGS like pattern	10		2		8	
Burst suppression	7	12.1	3		4	
PLED	5	8.6	3		2	
CSWS	2	3.4	1		1	
Char.EEG pattern	58	18.2	23	13.1	35	21.7

MES, 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

Epileptiform discharges	Clinical diagnosis of epilepsy			
	Generalised	Partial	Unclassifiable	Total
Generalised discharges	40	2	6	48 (15.8%)
Focal or multifocal Discharges	75 (17.7%)	51	13	139 (43.8%)
No discharges	92	29	11	132 (41.4)
Total	207 64.9%	82 25.7%	30 9.4%	319

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)

Disorders	Total	%	OPD	%	CDC	%
1. Any disorder						
Present	242	57.2	113	45.2	129	74.6
Absent	181	42.8	137	54.8	44	25.4
Total	423	100	250	100	173	100
2. Motor disorder						
Mild	67	15.8	34	13.6	33	19.1
Moderate	15	5.2	5	2.0	10	5.8
Severe	137	32.4	58	23.2	79	45.7
3. Cogn.imp.(clinic.jud)						
Present	230	54.4	109	43.6	121	69.9
Absent	177	41.8	136	54.4	41	23.7
Uncertain	16	3.8	5	2.0	11	6.4
Cognitive imp.(IQ)						
<70	258	61.0	123	49.2	135	78.0
>70	165	39.0	127	50.8	38	22.0
Total	423	100	250	100	173	100
In 319 children						
None	108	33.9	82	46.9	26	18.0
Any disorder	211	66.1	93	53.1	118	82.0
Motor disorder						
Present	148	46.4	43	24.6	105	72.9
Absent	171	53.6	132	75.4	39	27.1
Cogn. imp.						
Present	192	60.2	86	49.1	106	73.6
Absent	127	39.8	89	50.9	38	26.4
Total	319	100	175	100	144	100

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

Based on clinical judgment	Based on IQ score		
	>70	<70	Total
Seems age appropriate	94	19	113
% Total	29.5%	6.0%	35.4%
Poor for the age	27	164	191
% Total	7.8%	52.0%	59.9%
Uncertain	6	9	15
% Total	1.9%	2.8%	4.7%
Total	127	192	319
% Total	39.8%	60.2%	100.0%

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-ratter agreement test (Section 6.6.10)

The inter-ratter 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

Tests	Total	%	OPD	%	CDC	%
1. EEG						
Normal	118	30.8	92	41.4	26	16.1
Abnormal	265	69.2	130	58.6	135	83.9
Not done	40	9.5	28	11.2	12	6.9
Total	423	100	250	100	173	100
Only epil.disch	88	23.0	55	24.7	33	20.5
Only back.abn.	58	15.1	22	9.9	36	22.4
Both	119	31.1	53	23.9	66	41.0
Total	383	100.0	222	100.0	161	100.0
Epil.disch.						
Absent	176	46.0	114	51.4	62	38.5
Present	207	54.0	108	48.6	99	61.5
Total	383	100	222	100	161	100
Type of discharges						
Focal	100	48.3	62	57.4	38	38.3
Generalised	52	25.1	25	23.1	27	27.3
Multifocal	46	22.2	20	18.5	26	26.3
Gen. & focal	9	4.3	1	0.9	8	8.1
Total	207	100	108	100	99	100
Background activity						
Normal	204	53.3	147	66.2	55	34.2
Abnormal	179	46.7	75	33.8	106	65.8
Total	383	100	222	100	161	100
2. Neuroimaging reports						
Abnormal	131	70.1	53	56.4	78	83.9
Normal	56	29.9	41	43.6	15	16.1
Tests done	187	100	94	100	93	100
Abnormalities						
Atrophy	76		28		48	
Hydrocephalus	12		7		5	
Nonspecific	15		5		10	
Ischemic damage	11		4		7	
Leukomalacia	7		3		4	
Lissencephaly	5		3		2	
Tuberous sclerosis	5		3		2	
Total	131		53		78	

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.

EEG features	Neurophysiologist (NP1)		Neurophysiologist(NP2)	
	n	%	*n*	%
Normal record	123	32.1	117	30.5
Only epil.disch.	92	24.0	88	23.0
Only backg.abn.	53	13.8	59	15.4
Both present	115	30.1	119	31.1
Total	383	100	383	100

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

diagnosed (OPD) and CDC group respectively. About one third (20- 35%) had less than 100% seizure reduction (poor seizure remission).

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

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

Seizure outcome	Number	%
Seizure remission	41	31.0
Poor sz. remission	90	69.0
Total	**132**	**100**
Sz. reduction		
80-99%	19	14.4
50-79%	14	11.2
30-49%	12	8.8
<30%	46	34.4
Total	132	100

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

Age at presentation	number	%
2 mo- 1 yr	60	39.7
>1 – 3 yrs	43	28.5
>2 – 5 yrs	18	11.9
>5 – 7 yrs	16	10.6
> 7 yrs	14	9.3
Sex		
Male	103	68.2
Female	48	31.8
Seizure type		
Single	80	53.0
Multiple	71	47.0
Seizure rate		
High	124	82.1
Low	27	17.9

Diagnosis & associated non-convulsive disorders		
Malignant syndrome	56	37.1
Motor disability	95	62.9
IQ < 70	118	78.1
EEG		
Abnormal	125	82.8
Normal	26	17.2
Background abn	26	17.2
Epileptiform disch	32	21.2
Both	67	44.4

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.

Non-convulsive disorders	At entry	%	last follow-up	%
Motor				
None	24		28	
Mild	7		3	
Moderate	4		4	
Severe	30		30	
Cognitive				
IQ< 70	46	68.7	51	76.1
Malignant syndrome	18	26.9		
No neurodisability	17	25.4		

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.

Predictors		Poor seizure remission		Total	Odds ratio	95% Confidence interval		*P* value
		No	Yes			Lower limit	Upper limit	
1.Malignant syndrome	No	133	90	223	2.575	1.571	4.222	.000
	Yes	35	61	96				
2. Motor disorder	No	115	56	171	3.682	2.315	5.852	.000
	Yes	53	95	148				
3. Low IQ	No	94	33	127	4.542	2.778	7.427	.000
	Yes	74	118	192				
4.Family history of epilepsy	No	158	137	295	1.615	.659	3.752	.265
	Yes	10	14	24				
5.Multiple seizures	No	136	80	216	3.772	2.287	6.221	.000
	Yes	32	71	108				
6.High rate of seizure	No	54	24	78	2.506	1.456	4.314	.001
	Yes	114	127	241				
7.Early onset of seizure	No	81	47	128	2.060	2.649	7.074	.002
	Yes	87	104	191				
8. Abnormal EEG	No	73	25	98		2.261	6.655	.000
	Yes	95	126	221	3.879			
Total		168	151	319				

Table 6.17: Multiple logistic regression analysis with 7 potential predictors

Analysis Done	Independent variables	Odds ratio	95% CI		*p*-value
Backward Stepwise Logistic Regression	Low IQ	3.126	1.746	5.59	.000
	Multiple seizure type	3.035	1.731	5.324	.000
	Motor disorder	1.813	1.047	3.140	.034

*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

Analysis Done	Variables entered	Odds ratio	95% CI		*p*-value
Backward Stepwise Logistic Regression	Low IQ	2.915	1.611	5.274	0.000
	Multiple seizure type	2.516	1.412	4.483	0.002
	Motor disorder	1.718	0.982	3.005	0.058
	Abnormal EEG	2.346	1.245	4.418	0.008

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.

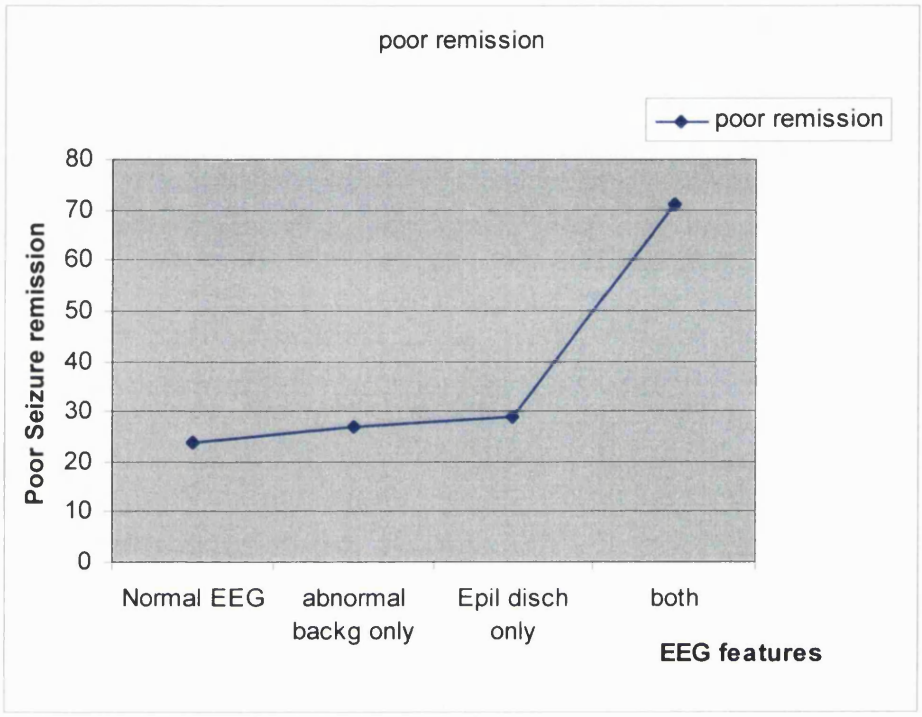
No significant change was noted when EEG entered into the model. However, small change was noted with the p value of motor disorder, but this is non-significant, i.e. point estimate and confidence intervals are very similar. EEG had independent association with p 0.008; odds ratio 2.346; and CI 1.245 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

Prevalence of poor seizure remission, positive &negative predictive value of the predictors

	In total population	OPD	CDC
Multiple seizure type:			
Sensitivity	0.47	0.32	0.58
Specificity	0.80	0.85	0.73
Motor disorder			
Sensitivity	0.63	0.43	0.79
Specificity	0.68	0.87	0.35
Low IQ			
Sensitivity	0.78	0.69	0.86
Specificity	0.56	0.63	0.43
Presence of any disability			
Sensitivity	0.83	0.75	0.64
Specificity	0.49	0.60	0.28

Chart 6.2: Correlation between poor seizure remission and 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

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

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)

At first day of assessment		At last follow-up
Motor disability		
None	171	161
Mild	17	11
Moderate	19	38
Severe	135	107
Total	319	317
Cognitive impairment		
None	127	124
Mild	26	18
Moderate	31	50
Severe	135	125
Total	319	317
		Expired 2
Total	319	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)

AEDs	Total	%	OPD	CDC
PB	103	32.3	62	29
CBZ	78	24.5	49	28
VPA	80	25.1	32	59
NTZ	72	22.6	43	58
CLZ	17	5.3	11	18
CLB	15	4.7		
PHT	10	3.1		5
LTZ	1			1
Topiramet	1			1
Poly therapy during the last follou-up in 83 (26.6%)				
Time gap to start regular treatment in months				
Mean, median, IQR	15 , 7, 15		16, 7, 15	13, 7, 15

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 and10% had increased seizures. Three children (2.2%) had severe side effects, as parents complaint 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)

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

Fu, fllow-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.

Effect of PD-therapy at 2wk	Seizure outcome at 1 year follow up >50% sz red.	<50% sz.red.	None	Total
Positive response to PD therapy	64	5	11	80
No response	9	7	41	57
Total	73	12	52	137

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

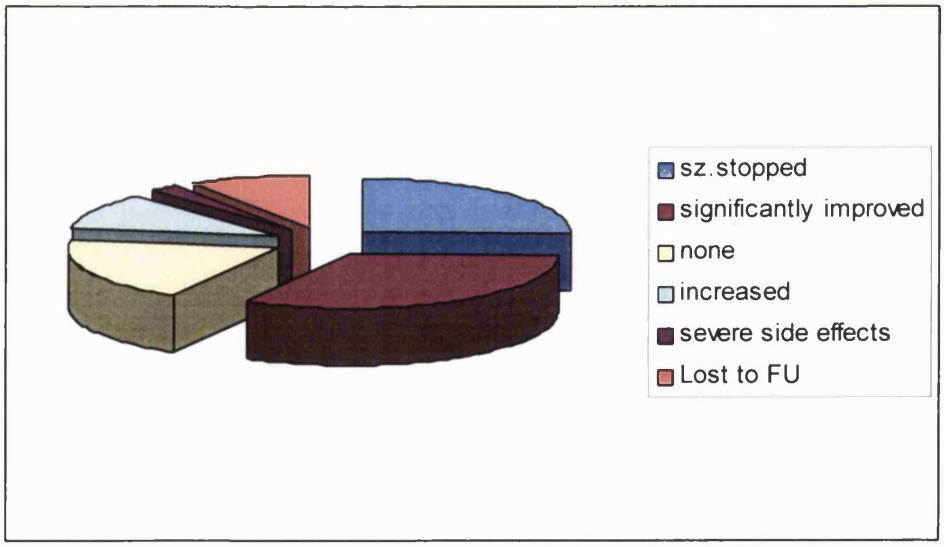


Chart 6.3 : initial response to prednisolone treatment among 137 children

z.stopped	significantly improved	none	increased	severe side effects	Lost to FU
35	45	26	15	3	13

Table 6.25: History of previous AED treatment and time gap

History of	Total	%	OPD	%	CDC	%
Prev. AED						
None	294	75.4	194	86.6	100	60.2
Yes	96	24.6	30	13.4	66	39.8
Total	390	100	224	100	166	100
Time gap to start regular treatment in months						
Mean	15.10		16.01		13.8	
Median	7		7		7	
Maximum gap	138		138		97	
Skeweness (st error)	2.680		2.607		2.624	

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

1985). 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 toxaemias 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 (Ellenbarg 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 cryptognic 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 and19.7% 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). Nicolletti 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 findings 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 in14.6% 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:

Neuroimagings including USG, CT scan and MRI of the brain was performed in 44.2% of the prospective population, and was abnormal in 51children (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 1090) 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, Ctaldo, 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 to15 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: $n > (Z_\alpha + Z_{2\beta})^2 \{\pi_1(1-\pi_1) + \pi_2(1-\pi_2)\}/\delta^2$

$n > 7.849 (40 . 60 + 15 . 85) / 25^2$

$7.849 \times 5.88 = 46$ 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 after12 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 & auther'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.

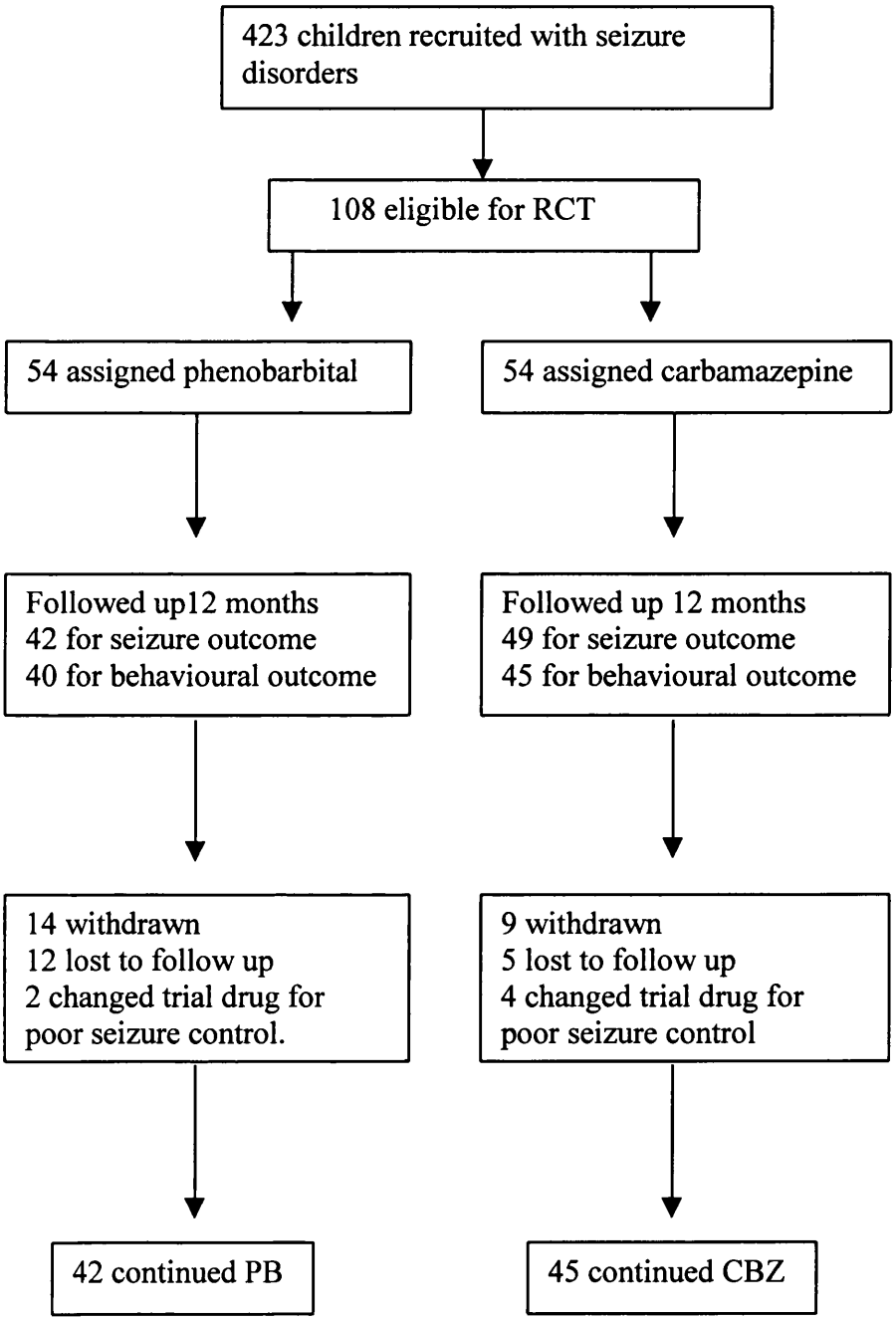
7.2.10: Outcome measures

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:



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)

Items	PB(%)	CBZ (%)	Total (%)
1.Family type			
Nuclear	33 (61.1)	35 (64.8)	68 (62.9)
Joint	21 (38.9)	19 (35.2)	40 (37.1)
2. Residence			
Rural	35 (64.8)	32 (59.3)	67 (62)
Urban	19 (35.2)	22 (40.7)	41 (38)
3. SES by monthly income			
Lower income	20 (37.0)	33 (61.1)	53 (49.0)
Middle income	32 (59.3)	13 (24.1)	45 (41.7)
Higher income	2 (3.7)	8 (14.8)	10 (9.3)
4. Age at present. (mo.)			
24	7 (13.0)	5 (9.3)	12(11.1)
25-60	23 (42.6)	21(38.9)	44(42.6)
61 &above	24 (44.4)	28(51.8)	52(46.3)
Total	54 (100)	54(100)	108(100)
Mean median (IQR) in years	5.3, 4.1, (5.7)	6, 5.5, (6.3)	5.7, 4.7, (6.30
5. Sex			
Male	37 (68.5)	24(44.4)	61 (56.5)
Female	17 (31.5)	30 (55.6)	47 (43.5)
6. Age at onset			
After 12 mo	41 (75.9)	46 (85.7)	87 (80.6)
Early	13 (24.1	8 (14.8)	21 (19.4)
Total	54 (100)	54 (100)	108(100)
Mean, med.,IQR in yr.	3.4, 2.4, (4.7)	4.1, 3, (4.8)	3.8, 2.7, (4.8)
7.Epilepsy classified			
Gen.	29 (53.7Z)	22(40.7)	51(47.2)
Partl.	25 (46.3)	32 (59.3)	57 (52.8)
8. Seizure type			
Single	49 (90.7)	49 (90.7)	98 (90.7)
Multi.	5 (9.3)	5 (9.3)	10 (9.3)
9. Seizure rate			
Low	32 (59.3)	34 (63.0)	66 (61.1)
High	22 (40.7)	20 (37.0)	42 (38.9)
10. Seizure frequency			
Daily sz.	14 (25.9)	15 (27.8)	29 (26.9)
Weekly,</1d	8 (14.8)	5 (9.3)	13 (12.0)
Mo.ly,<1/wk	21 (38.9)	23 (42.6)	44 (40.7)
Yearly, <1/mo	11 (20.4)	11 (20.4)	22 (20.4)
11. Etiological classification			

Idiopathic	40 (74.1)	31 (57.4)	71 (65.7)
Sympt.	14 (25.9)	23 (42.6)	37 (34.3)
12. Duration of epilepsy			
1 year	27 (50.0)	23 (42.6)	50 (46.3)
>1- 2	16 (29.9)	13 (24.1)	29 (26.9)
>2 – 3	5 (9.3)	8 (14.8)	13 (12.0)
>3 – 5	2 (3.7)	4 (7.4)	6 (5.6)
>5 years	4 (7.4)	6 (11.1)	10 (9.2)
Mean, med., (IQR) in mo.	19, 13, (18)	25, 16, (30)	22, 15, (24)
13. Number of sz.(prev. yr)			
< 10	18 (33.3)	21 (38.9)	39 (36.1)
10-20	15 (27.8)	15 (27.8)	30 (27.8)
>20	21 (38.9)	18 (33.3)	39 (36.1)
19. Previous H/O AED			
Absent	42 (77.8)	40 (74.1)	82 (75.9)
Present	12 (22.2)	14 (25.9)	26 (24.1)
20. Motor disability			
Absent	45 (83.3)	45 (83.3)	90 (83.3)
Present	9 (16.7)	9 (16.7)	18 (16.7)
21. Cognitive impairment			
Absent	37 (68.5)	37 (68.5)	74 (68.5)
Present	17 (31.5)	17 (31.5)	34 (31.5)
22. Pre-exist. bh. problem			
Absent	43 (79.6)	43 (79.6)	86 (79.6)
Present	11 (20.4)	11 (20.4)	22 (20.4)

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 (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 1year, 'seizure remission' (defined as 100% seizure reduction during the last 3 months of follow up period, see Section 4.3.I-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

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

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.

Tests applied	PB group	*p*	CBZ group	*p*
Conner's				
ADHD index	3.75 (-4.49, 11.99)	.348	2.64 (-64, 5.92)	.109
Richman	5.15 (1.25, 9.05)	.012	3.90 (.65, 7.15)	.021
BSID	-2.83 (-7.16, 1.49)	.153	1.25 (-6.26, 8.76)	.633

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

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

Tests applied	Difference (mean)	CI	*p*
Conner's			
ADHD index	-0.24	-10.16, 9.67	.96
Richman	.95	.783, 13.53	0.16
BSID	-12.08	-43.58, 19.41	0.501

Table 7.5: Main effect model showing correlation between outcome behavioural problem and individual variables

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

N, number; PB, phenobarbitone, CBZ, carbamazepine, bh, behaviour,

Table 7. 6: Multiple logistic regression model for outcome behavioural problems

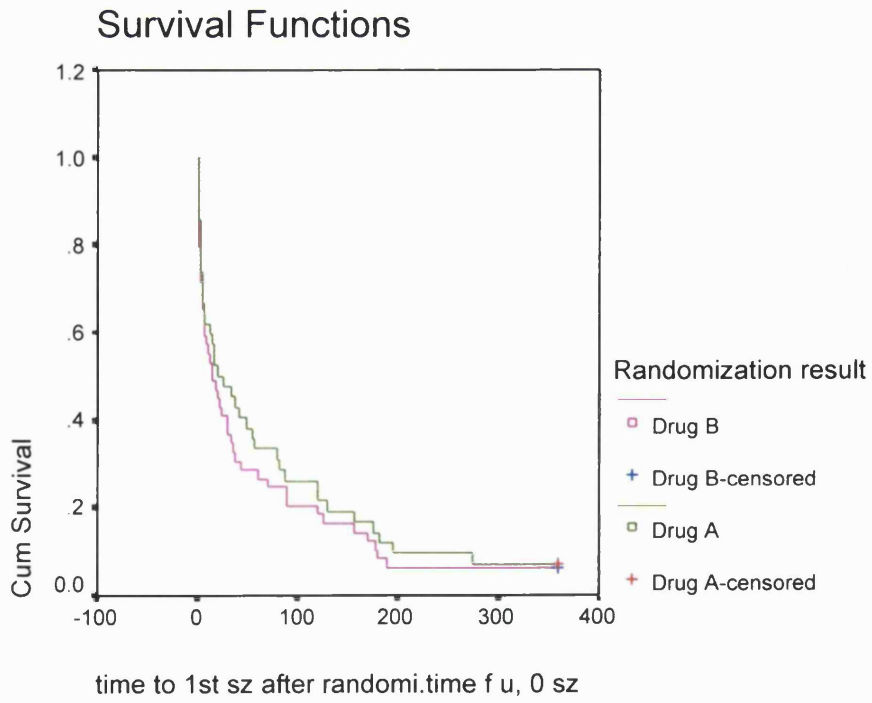
Variables	Odds ratio (95% CI) for behavioural problems		
1. PB *vs* CBZ	1.184	(0.283, 4.953)	0.817
2. Age at presentation	0.997	(0.979, 1.015)	0.757
3. Male *vs* Female	3.407	(7.87, 14.746)	0.101
4. IQ=>70 *vs*<70	.815	(.164, 4.055)	0.802
5. Motor disability Absent *vs* present	2.110	(.417, 10.685)	0.231
6. Bh problem Absent *vs* present	1.121	(.196, 6.395)	0.898

Bh, behavioural

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

Drug	Survival time	Standard error	95% CI
Unadjusted with other disability Phenobarbitone Mean survival time	102	18.03	66.68, 137.36
Carbamazepine Mean survival time	73.71	15.74	42.85, 104.57
Adjusted with other disability Phenobarbitone Mean survival time	122	31.61	60.26, 161.04
Carbamazepine Mean survival time	72.56	37.48	.00, 46.04

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



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 gastro-intestinal 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 Frpsuth'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, Ctaldo, 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 1year'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 <.001), low IQ (p <0.001), and motor disorder (p <.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 ratio10: 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 ---- Date of EEG done: ---/----/----
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
- ☐ Neonartal 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) /d /wk /m /yr

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 pleas write the major finding)

(Y/ N)

USG :

CT scan of brain:

MRI:
Other

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

Date of examination: -------/ ---------/ ---

(A.)Patient's name_____ sex _____ Date of birth: ----- / ----- / -----

Mother:_____ Present age: ---- yr ----- mo

Father:_____ Tel.ph.no ----------

Address: Village:_____ P/O: _____ Thana _____

District: _____ House no: _____ Road 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 [ ]

Insturctions:

Part I : Please administer semi-structured interview. Ask all the questions specified in this form . Use local terminologyif 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 porvided. 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,conider 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 factore ?
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
type1._____	_____	_____	_____
type2._____	_____	_____	_____
type3._____	_____	_____	_____

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 (mc.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, fidgidity, sudden restlessness,screaming,head drop,head jerk, reflex seizure, flushed face in children, all the episodic attacks should be writtenin 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 infludnced by seizure frequency and severity =1, no such relateion =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	No=1	somewhat limited=2	very limited=3
Emotional / behavioural difficulties?	☐	☐	☐
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 cousine-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 :

	Sibling	Mother	Father	Other relative(specify)	
Allergies ----------	☐	☐	☐	☐	----------
Asthma ----------	☐	☐	☐	☐	----------
Attention problems----------	☐	☐	☐	☐	----------
Behavioural or psychiatric problem	☐	☐	☐	☐	----------
Cerebral palsy ----------	☐	☐	☐	☐	----------
Developmental disability-----	☐	☐	☐	☐	----------
Epilepsy----------	☐	☐	☐	☐	----------
Febrile seizure----------	☐	☐	☐	☐	----------
Learning disability----------	☐	☐	☐	☐	----------
Speech delay----------	☐	☐	☐	☐	----------
Other disabilities or conditions	☐	☐	☐	☐	----------

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 miscarrages 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) Diabetis 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 pregnency period
j) Threatened abortion
k) Other (specify) ----------

Medical problem=1
Suspecte I.U.infetion=2
abortificiant =3
psychosocial =4
accident = 5
no problem =6
☐

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 delivary: *N.V.D.=1, assisted with forceps/vacume= 2, By LUCS = 3* ☐
Q. H/O Difficult labout? *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 delivary no P/A, 2= preterm ND with no P/A, 3=definite P/A with FT Vagingal delivary, 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. septicemia, 8=n. meningitis, 9=jaundice / kernicterus, not physiologicl
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 nurished 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	☐	hand regarded at ---------- mo	☐
rolled over at ---------- mo age	☐	sitting with support at ---------- mo	☐
head controlled at ---------- mo age	☐	independent sitting at ---------- mo	☐
crawling at ---------- mo	☐	bubbles at ---------- mo	☐
standing with support at ---------- mo	☐	single words meaningful, other than hello or bye bye	
Independent standing at---------- mo	☐	starts at ---------- mo	☐
walkint at ---------- mo	☐	simple sentence with 2-3 words at ---------- mo	☐
running at ---------- mo	☐	comprehension at ---------- years	☐

Comment : Mile stone of development

Achieved at appreprate 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 ----, 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 1wk time =3, 1wk to 1mo time=4, after 1 mo=5

Q.Has the child had tuberculosis? (No =1, yes =2, unknown =9)---------- ☐

Q. If yes, whether treatment was completed? *(No =1, yes =2, not applicable=8, unknown =9.* ☐

Q. Has history or recurrent infection such as diarrhoea, RTI, fever for which needed to take medication? ☐

No =1, Yes=2, Yes, but not taken to any doctor=3

number of infection or fever in last 6 months -_____ ☐

number of infection or fever in last 1 months_____

Q. Has the child been hospitalized for an over night 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	age or date
☐ 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

☐ Seizure or epilepsy ? Since ----------age

if yes for how long?

☐ Thyroid disorder ? Since ----------age

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	_____	_____
☐ Gen.clonic seizure	_____	_____
☐ gen.tonic seizure	_____	_____
☐ gen,tonic clonic sz.	_____	_____
☐ Atonic seizure	_____	_____
☐ Absence seizure	_____	_____
☐ Simple partial sz.	_____	_____
☐ complex partial sz.	_____	_____
☐ secondarily gen.sz	_____	_____
☐ not clear SPS/ CPS	_____	_____
☐ reflex sz. on sound	_____	_____
☐ reflex sz. On touch	_____	_____
☐ on photic stimulation	_____	_____
☐ Unclassifiable sz.	_____	_____

(uncl.sz.-includes those where classification is not possible because of inadequate information, or in hitherto described categories,i.e. rhthmic eye movement,chewing and swimming movement).

Minor attacks: *(discrete jerks, mild head drop, absences, group of muscle twitching, finger flickering*):

Frequency --------/---------- *duration* _____ *low rate of sz.=1 , high rate =2* ☐

Major attacks (big attacks which are sustained, GT, GTC, GCL):

Frequency. ------- */* ------ *duration*---------- *low rate of sz.=1, high rate=2* ☐

Total number of attacks since first seizure: _____

Total number of seizures in last year: _____

Total number of seizure 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, to 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 /alga batash= 3, don't know=5)

Other(specify) _____

Section III

Neurodevelopmental examination

A. Observation of function:

Please get friendly with the child and the attendent Give the child a toy for below 2yrs 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 responce=4

Gross motor - ☐

Fine motor ☐

Speech (motor) |

Speech(language) |

Hearing ☐ Comprehension ☐
Vision ☐

additional comment on observation of function of the child:_____

B. Physical examination (General)

Anthropometry: Child Mother
Hight _____ cm. weight:_____ kg. Hight: _____cm. Weight: _____kg
OFC : _____cm. MAC : _____ cm. OFC:_____cm. MAC:_____cm.
Neutritional status: *within normal limit=1, malnurished = 2, severely malnurished = 3, uncertain =4*

☐ ☐

Head size and shape: ☐
normocephalic=1, microcephalic=2, Macrocephalic=3, Dolicocephalic=4, other abnormal shape=5
Anterior Fontanellae:(Open,normal =1, open,abnormal=2, closed norm =3, closed abnor=4, buldged=5) ☐
Any overt dysmorphysm?: (absent =1, present =2, Uncertain = 3) ☐
Facial deformity (specify) _____
Other deformity (specify)_____
Compatible with any genetic Syndrome? (Specify): _____

General appearance:

☐ Alert
☐ Apprehensive
☐ Friendly and sociable
☐ Playful
☐ Nonresponsive
☐ Doped/ poor responce
☐ Irritable
☐ Hyperactive/restless
☐ Other (specify) _____

Hair:
☐ Brittle/ discolored
☐ Sparse
☐ Normal

Skin:
☐ hyperpigmented
☐ hyperpigmented
☐ caffe au lay spot
☐ rough, thick skin
☐ normal

Eyes
☐ Ptosis
☐ Nystagmus
☐ Squint
☐ cataract
☐ conjunctivitis
☐ conjunctival xerosis
☐ Xerophthalmia
☐ normal eye

Mouth
drooling ☐
gum bleeding ☐
dental caris ☐
hair lip ☐
cleft palet ☐
high arch palet ☐
normal mouth ☐

Social inter-activeness: ---------- ☐

1. Eye contact with examiner andinteracti either by language of 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 won but attends to other visual or auditory stimuli
5. Visually not fixate but responds to auditory stimuli
6. Does not attend to any visual or auditory stimuli
7. Other (specify)
8. Cannot assess (specify)

Commenton on general examination: 1= normal, 2= abnormal (specify) ☐

Attentiveness : 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? --------- ☐ shows odd repetitive movement ?
act very aggressively to other people? ☐ Head banging?-----
act extremely withdrawn and shy?-- ☐ 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(clinitian'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

	Rt.	Lt.
Arm posture ----------		
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
2 = Normal arm posture
3 = Normal hand function
4 = Abnormal body posture
5 = Abnormal arm posture
6 = Abnormal handfunction

G. Spontaneous motor activity

Four limbs during spontaneous movement----------

1-active symmetric, 2- asymmetric >on right ; 3- Asymmetric > on left,
4- no spontaneus 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 stares	☐

Abnormal movement:(Codes 1=none; 2=on right side only; 3=on left side only; 4=on both sides)

	ARMS	LEGS
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.

1-does task ; 2- does not do task, not yet reached=8) Rt Lt

Stands on one foot for at least 10 seconds ----------
Hops on one foot for at lest 6 times ----------
Walks on toes on command for 6 'or more----------
Walks on heels on command for 6'or more----------
Tandem walk on command 6' or more ----------

BALANCE (with eyes open, stand with feet together , where stands stable for 10seconds)

1-stable; 2- Unstable; 9-cannot stand. If 1- complete [Romberg test] if 2 or 9 skip

Romberg test

(1-does not sway or step off, 2-sways but does not step off, 3-steps off, 9-can't assess explain --------)

Finger to-nose test (test on six excursions)

Number of excursions off target ----------
Number of excursions with ataxia----------

Coordination: normal =1, poor =2, can not performe=3(explain)_____
not yet reached to test=8

COMMENT : On motor examination:

Mobility:

1= Normal gait/ functioning for the age
2= Not normal but ambulant, no aids, independent
3= Ambuland with aids, independent
4= Ambulant with aids, limited
5= Not ambulant, special chair/sitting
6= Not ambulant, bed riden

Hand function(observation and examination of function)

1= Normal functioning
2= Mild impairment but functioning independently
3= Moderate impairment performs daily living activity
4= Marked impairment no daily living activities
5= No useful function

C. SYSTEMIC EXAMINATION:

Is there any abnormality on examination of the following ?if yes specify

Heart ---------- Lungs ---------- genitalia----------
Liver ---------- spleen ----------

D. NEUROLOGICAL EXAMINATION

Examination of the cranial nerves:
Intact all the cranial nerves ? Yes =1, no =2, If 2 please specify _____

Muscle Tone and Strenght

1=normal, 2= reduced, 3= increased Rt.

Upper extremity (TONE)----------
Strength ----------

1=normal, 2= weak proximal only, 3= weak distal only, 4- weak proximal and distal
*8- other (specify)*_____
*9-cannot assess (explain)*_____

Rt. Lt.

Lower extremity: Tone: (1=normal, 2= reduced, 3= increased)
Strength ----------

1-normal, 2- weak proximal only, 3- weak distal only, 4- weak proximal and distal
*8- other (specify)*_____
9-cannot assess (explain) _____

REFLEXES:

Jaw jerk----------

1-no reflex elicited, 2-muscle contraction, 3- muscle contraction accompanied by clonus(exaggerated)

Rt. Lt

Biceps Jerk (upper limb) ---------- ☐ |

1-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)---------- ☐ |

Ankle jerk(same code)---------- ☐ |

Ankle clonous ---------- ☐ |

1 = absent, 2 = transient clonus , 3 =sustained cl, 4= spontaneus clonus

Planter response---------- ☐ |

flexor = 1, extensor =2, uninformative two trials (Equivocal) =3

Special senses: For <3 years and those who can not follow C or E chart do the functional assessment:

Functional assessment : **Visual function** ---------- rt eye

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 Landholt C chart, Otherwise use the E chart

code: 1 = 6/6 or better (20/20 or better) Rt. Eye

2 = 6/9 or better (20/30 or better)

3 = 6/18 or better (20/70 or better) ☐ |

4 = 6/60 or better(20/200 or better)

5 = 6/61 or light perception (20/201 thru light perception)

6 = No light perception

7 = Unstable 8=age <3 yrs.

9=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):

retinal abnormality:_____

cortical blindness:_____

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-other 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(solmnl)
- [ ] 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 before12 mo [ ] d after 12 months [ ]
1=none, 2= mild, 3=moderate, 4= svere

Motor developmental delay [ ] or developmental regression [ ]
1=none, 2= mild, 3=moderate, 4= svere

hearing problem since birth [ ] ression of normal hearing [ ]
1=none, 2= mild, 3=moderate, 4= svere

Visual problem since birth [ ] ession of normal vision [ ]
1=none, 2= mild, 3=moderate, 4= svere

Speech delay(expressive) [ ] ession of normal speech [ ]
1=none, 2= mild, 3=moderate, 4= svere

Cognition delayed development [ ] ression of normal cognition [ ]
1=none, 2= mild, 3=moderate, 4= svere

Behavoural problem since [ ] Behavioural problem recent onset [ ]
developing age
1=none, 2= mild, 3=moderate, 4= svere

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)

drug	starting dose/kg/day	maximum/kg/day
Phenobarbitone :	----------	----------
Phenytoin	----------	----------
Carbamazepine	----------	----------
Valproic acid	----------	----------
Clobazam	----------	----------
Nitrazepam	----------	----------
Clonazepam	----------	----------
Lamotrigine	----------	----------
Prednisolone/ACTH	----------	----------
Other	----------	----------

9. Previous history of antiepilepsic 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. Invesigation:
    - 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

1sr 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, intansity 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	continue only if tolerable
☐	temper tantrums,	continue only if tolerable
☐	aggression	continue only if tolerable
☐	Lethargy	continue only if tolerable
☐	Hirsutism	continue only if tolerable
☐	Uncertainty when walking	continue only if tolerable
☐	Diarrhoea	continue only if tolerable
☐	Shaking, trembling	continue only if tolerable
☐	Abdominal dyscomfort	continue only if tolerable
☐	increased of appetite	continue only if tolerable
☐	excessive drooling	continue only if tolerable
☐	skin rash	discontinue drug gradually
☐	gum bleeding, hyperplasia	discontinue drug gradually
☐	Lupus syndrome/ joint pains	discontinue drug gradually
☐	Stevens-Johnson Sndrome	discontinue drug gradually
☐	Osteoalacia/rickets	discontinue drug gradually
☐	Neuropathy	discontinue drug gradually
☐	Megaloblastic anaemia	discontinue drug gradually
☐	Ataxia or nystagmus	discontinue drug gradually
☐	Hepatitis	discontinue drug gradually
☐	Neuropathy	discontinue drug gradually
☐	Ataxia or nystagmus	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 Diabetis, 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 realson

Adjusted dose of AED: ------- mg/kg /day

-signed:----------

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

MAF

APPENDIX: V: Summary form

Pt's ID no _____

Section IV Name: _____ ma _____

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=secondaryly gen.	*3=LKS, 4=LGS,*	*3= Remote symptomatic*	*3= uncertain* ☐
4=mixed partial and gen.	*5=Myoclonic encephalopahty*	*4= Symptomatic*	
5=unclassifiable	*0=None*	*5= Uncertain*	*V.* Seizure rate
☐	☐	☐	1= low rate of sz.
			2=high rate of sz. ☐

VI. Age at onset of *epileptic seizure:*	VII. Event associated	VIII. Family h/o epilepsy	IX. F.H.of febrile seizure
in months _____	*1=none, 2=prental*	*1=None, 2=parents*	*1=None, 2=parents*
1=after 12 mo.age	*3=perinatal asphyxia*	*3=sibling, 4=grand parents*	*3=sibling, 4=grand parents*
2=before 12mo. age	*4=neonatal seizure*	*5=1st cousin,aunt,uncle*	*5=1st cousin,aunt,uncle*
☐	*5=CNS infection*	*6= Other blood relative*	*6= Other blood relative*
	6=head injury ☐	☐	☐
	7=recurrent febrile seizure		

X. Associated Imp.	Diagnosis	Severity grading (WHO,198	Treatment needs for
type of impairment	*1 = CP(type)*	*1=none*	*associated impariment*
on the first day of	*2=N.degenerative*	*2=mild*	*1=None, 2=stimulation*
examination:	*3=N.metabolic*	*3=moderate*	*3=dev.therapy*
circle yes or no	*4=hp.iscmic damage*	*4=severe*	*4=sp.schooling*
	5=other(specify)	*5=uncertain*	*5= other*
Motor impairment	_____	☐	☐
No Yes			
Gross motor	_____	☐	☐
No Yes			
Fine motor	_____	☐	☐
No Yes			
Visual impairment	_____	☐	☐
No Yes			
Hearing impairment	_____	☐	☐
No Yes			
Cognition(physician's judgement)	_____	☐	☐
No Yes			
Cognition(joint decision)	_____	☐	☐
No Yes			

Associated impairme	Diagnosis	Severity grading (WHO,198	Treatment needs for
Behavi. disorder	_____	☐	☐

MAF summary page no-1 Pt's ID no _____

phy's judgt: No Yes

Behavi. disorder _____ ☐ ☐

(Joint deci) No Yes

Seizure disorder _____ ☐ ☐

No Yes

Other disorder _____ ☐ ☐

No Yes

EEG finding: date of test: ------/ ------ / ------- E number _____

Background activity	Epileptiform discharges(B	Specific pattern ©	State of child dur-(D)
1= normal	1=gen.epil discharges	1=Hypsarrhythmic	ing recording
2=excess gen. slow w	2=focal epil.discharges	2=burst suppression	1= only awake
3=excess loc. slow w	3=multifocal epil.disch	3=PLED	2=only sleep
4=diffuse slow w	4=lateralized epil.disch.	4=CSWSS	3=sleep and awake
5=excess gen.beta w	5=no epil.discharges	5=none	4=cooperative
6=excess loc.beta w			5=irritable
7=mix beta,theta,delta w			6=other(describe)
8=asymetric amplitude			7=unaware/non-responsive
9=other(specify)			
☐	☐	☐	☐

Overal comment:

Compatible with any specific clinical diagnosis?_____

Normal study?_____

USG of brain:	CT scan of brain	MRI of brain	TORCH screen.
1= not done	1=not done		1=not done
2=normal study	2=normal study	Same	Antibody +ve for
3=abn.atropsy	3=abn.cortical atrophy		2=Toxopl. Pesitive
4=hydrocepahlus	4=T.sclerosis,gliosis		3=Rubella
5=nonspecific abno.	5=hydrocephalus		4=cytom.V
	6=ischemic damage		5=Herpis sympl
	7=agenesis		6=none ☐
☐	8=leukomalacia ☐	☐	
	9=leissencephaly/cong anomaly		

Blood test for drug level:

Other (specify):

APPENDIX: VI: Final assessment form

Final follow up form

Name of the child:

Age:_____ months

Sex: ☐

Pt's ID:_____

Psychological ID: _____

Date last FU: ____/____/____

Date of first visit:____/____/____

Date of EEG done:____/____/____

Weight:_____ kg

OFC I: _____ cm

OFC 2: _____ cm

OFC 3: _____ cm

EEG repeat test done? : ☐

(No=1, yes by us=2, yes by other=3)

Total visist: _____

Diagnosis:

COML: ☐

List of problems:

Date of last seizure: ____/____/_____

Entry sz frequency: _____ / _____ _____ /Year

Present sz frequency: _____ / _____ _____ /Year

Sz remission? _____ % of remission _____

(total/yr2 - total/yr1)

REMI : ☐

(1=total remission, 2= significant rem, 3= some remi, 4= minor remission, 5= none, 6= increased)

time taken for significant or toral remission after starting regular AED: _____

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 ?: ☐

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? _____

	at entry:	6mo	at last FU:	
Seizure type:	☐	☐	☐	single=1, multiple=2
Rate:	☐	☐	☐	1=low,2=high
Epilepsy type:	☐	☐	☐	1=Gen, 2=Prt, 3=scc.gen., 4=mix P&G, 5=uncl.
Syndrome type:	☐		☐	codes 1 through 6, summ sheet
F/H/O feb sz.	☐		☐	codes 1-6
F/H/O epilepsy:	☐		☐	codes summary sheet
H/O status ep:	☐	during follow up period	☐	

impairment grading: 1=none, 2=mild, 3=mod, 4=severe, 5=uncertain)

Final follow up form

Name of the child:

Date last FU: ____/____/____

Age:_____ months

Pt's ID:_____

Date of first visit:____/____/____

Sex: ☐

Date of EEG done:____/____/____

Psychological ID: _____

Weight:_____ kg

OFC I: _____ cm

EEG repeat test done? : ☐

OFC 2: _____ cm

(No=1, yes by us=2, yes by other=3)

OFC 3: _____ cm

Total visist: _____

Diagnosis:

COML: ☐

List of problems:

Date of last seizure: ____/____/_____

Entry sz frequency: _____ / _____ _____ /Year

Present sz frequency: _____ / _____ _____ /Year

Sz remission? _____ % of remission _____

(total/yr2 - total/yr1)

REMI : ☐

(1=total remission, 2= significant rem, 3= some remi, 4= minor remission, 5= none, 6= increased)

time taken for significant or toral remission after starting regular AED: _____

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?

_____

	at entry:	6mo	at last FU:	
Seizure type:	☐	☐	☐	single=1, multiple=2
Rate:	☐	☐	☐	1=low,2=high
Epilepsy type:	☐	☐	☐	1=Gen, 2=Prt, 3=scc.gen., 4=mix P&G, 5=uncl.
Syndrome type:	☐		☐	codes 1 through 6, summ sheet
F/H/O feb sz.	☐		☐	codes 1-6
F/H/O epilepsy:	☐		☐	codes summary sheet
H/O status ep:	☐	during follow up period	☐	

impairment grading: 1=none, 2=mild, 3=mod, 4=severe, 5=uncertain)

	at entry:	at last FU	
Motor functional development	☐	☐	
Vision at entry	☐	☐	IQ 1: _____
Hearing at entry	☐	☐	IQ 2: _____
Behaviour	☐	☐	
Cognition	☐	☐	

Antiepileptic drug history in last one year:

	starting date	age at starting
AED 1 _____ _____	____/____/____	____ yr. ____ mo
AED 2 _____	____/____/____	____ yr. ____ mo
AED 3 _____	____/____/____	____ yr. ____ mo
AED 4 _____	____/____/____	____ yr. ____ mo

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: date :

Any evidence of drug side effect? _____ ___ ___ __ Dose:

Present AED :

Compliance: Stopped medicatin 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:

EEG no ---------- RID no---------- Date -----/----- / ---- sex: (M=1 F=2)☐

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 ☐

Referral details:
Referred by: ---------- Hospital ----------
Hospital Reg.no ---------- Private clinic/chamber ----------
Question asked by the clinician: ----------

Parents' concern: 1. 2.
3. 4.

Seizure detail:

Seizure typ	Age of onset in months	Frequency at the beginning	Frequency at present	Date and type of last attack
GTC		--/d.---/w--/m----/y	--/d.---/w --/m---y	
GT				
GC				
MC				
IS				
Absence				
SPS				
CPS				
Secondarily gener.				
Mixed gen+partial				
Reflex				
Photosensetive				
Atypical febrile sz.				
Other (specify)				

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, Diabetis =2, ☐
PET =3 H/o taking abortificient = 4. None = 5
Perinatal history: Place of delivary: ☐ (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/obirth asphyxia? none =1 , if any of the 3 present = 2 ☐

Neonatal history: h/o seizure=1, jaundice(not physiological)=2, septicemia =3 ☐
Mile stone 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) ---------- previous AED ----------
How many times the child was hospitalized with seizure? -------- ☐

EEG - information

Any typical event during recording? Y/N ☐

If yes, explain the event:----------

Patients state during the test:
Awake ☐ alert ☐ cooperative ☐ non co-operative ☐ drowsy ☐ sleeping ☐ irritable
is unable to follow command ☐
Activating process used: photic stimulation ☐ hyperventilation ☐
sleep ☐ Touch ☐
Any seizure provoked by activating process? Y/N ☐

EEG report:

1 Background activity:
normal for the age and state of the child: ☐

	gen.	Local.	multifocal
2.Background activity:Abnormal (for the age and state) with presence of			
Excessive slow wave activity (delta w)	☐	☐	☐
Excessive fast (beta) wave activity	☐	☐	☐
Excessive Theta wave activity	☐	☐	☐
Mixed abnormal activity	☐	☐	☐
3.Abnormal with presence of			
bursts of epileptiform discharges	☐	☐	☐
spike wave complexes/spikes / sharp waves	☐	☐	☐

4. abnormal with recognisable abnormal EEG pattern).
Burst suppression pattern ☐
Hypsarrhythmic pattern ☐
PLED ☐
Other (specify)----------

5.Cerebral reactivity to activating process:

	normal	Epl. discharge.	Other aypi. resp.
Photic stimulation	☐	☐	
Hyperventilation	☐	☐	
Sleep	☐	☐	
Tactile stimulation	☐	☐	
Eye closure	☐	☐	

6. Overall Comment: suggestive electroclinical diagnosis

APPENDIX: VIII

Main antiepileptic drugs (AEDs)

Drugs	Indication	Starting dose mg/kg/day	Total daily dose mg/kg/day
Phenobarbitone(PB)	Generalised, partial seizures.	1.5	3-5
Carbamazepine(CBZ)	Partial, generalilsed.	4 to 5	10-20
Phenytoin(PHT)	Generalised, partial.	3 to 4	8-10
Sodium Valproate Valproic acid (VPA)	Primary gen. Epilepsies, MC, Generalised & partial sz.	10	20-50
Nitrazepam (NTZ)	Infantile spasms, Myoclonic epil.	<0.1	.150-.500
Clonazepam (CLZ)	all spc. MC.epil., LGS,	0.05	.05- 0.3
Clobazam	all forms, development of tolerance is frequent		0.25- 1.0
Diazepam	Mainly status epilepticus (SE)		0.25 -1.5 mg/kg 0.1 -0.3 mg/kg I.v. 0.25 -0.5 mg/kg p/r
Ethosuximide (ETH)	Absences epilepsy	10	20-40 mg/kg
Lamotrigine (LTZ)	Partial & secondary gen sz. primary gen.& myocl.sz. refractory absences, LGS.	1-2 mg	5- 20 mg/kg 0.1 -5 mg/kg for children receiving sodium valp.
ACTH	IS, LGS, sever myoclonic epil.		0.1 - 10 IU/kg
Prednisolone	Same as ACTH		1 - 2 mg/kg

SES Form

APPENDIX: IX: SES form

Patient's ID _____

SOCICONOMIC 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 _____ P/O: _____

Thana_____ District _____

Division _____ H no:_____ R no:_____

Phone no: _____

Informant (s): Mother-1, Father -2, child's grant 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	☐	Other source of income:
	☐ Business /trader	☐	1= Own house rent
	☐ Daily wedge earner/	☐	2=Own Land proparties
	☐ Service	☐	3=Other(specify)
	☐ Self employee	☐	☐
	☐ Unskilled worker	☐	
	☐ Professional	☐	
	☐ Mainly un-employed	☐	
	☐ Other	☐	

4. Do you/ your family have own land property ? if yes how mouch ☐

1= Has own land, 2= Has land inherited from parents, 3=No land but good Bank balance

4= Land less, depends on daily / monthly income

B. Health care:

5. Who pay for your child's health care ? ☐

1=Father/mother, 2=Grand father, 3=other family members(specify), 4=health care center. 5= other(speci

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 ? ☐

1=District Hospital, 2=Thana health complex, 3=nearest practicing doctor, 4=Village doctor,

5=Kabiraz/ozha/fakir, 6=religious people, 7= 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, hypertention,diabetis, 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 hous 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 ☐
Rikshow ☐ Shallow tube well ☐

D.Income

20. What is/ are the source of your family's income ? *Check all that apply* ☐

1= Employment, 2=1=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. _____

APPENDIX: X

Conners' Parent Rating Scale- Revised (S)

Child's Name: Gender: M F
Birth date: / / Age School grade
Parent's Name DOI: / /

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 your self, "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

Questions				
1.Inattentive, easily distracted ---------- অমনোযোগী, যেমন একটা কাজ করতে করতে অন্যদিকে মনোযোগ সরে যায়।	0	1	2	3
2 Angry and resentful ---------- রাগী, যে কোন ব্যাপারে ক্ষেপে ওঠে।	0	1	2	3
3. Difficulty doing or completing homework---------- প্রস্তুতিমূলক কাজ করা অথবা শেষ করায় অসুবিধা।	0	1	2	3
4 is always 'on the go' or acts as if driven by a motor.---------- সব সময় অতিদ্রিয় ও অস্বাভাবিকভাবে ছুটোছুটি করে বেড়ায়।	0	1	2	3
5 Short attention span---------- অল্প সময় মনোযোগ ধরে রাখতে পারে।	0	1	2	3
6 Argues with adults---------- বড়দের সাথে তর্ক করে।	0	1	2	3
7. Fidgets with hands or feet or squirms in seat---------- সুস্থিরভাবে বসে থাকতে পারে না, হাত-পা আইসাই করে, নোড়ায়।	0	1	2	3
8 Fails to complete assignments---------- কোন নির্দিষ্ট কাজ শেষ করতে পারে না।	0	1	2	3
9 Hard to control in malls or while grocery shopping ---------- দোকানে বা বাজারে সঙ্গে নিয়ে গেলে তাকে নিয়ন্ত্রনে রাখা কঠিন।	0	1	2	3
10 Messy or disorganized at home or school---------- বাড়িতে বা স্কুলে বিশৃঙ্খল ও আলোছালো।	0	1	2	3
11. Loses temper---------- নিজের মেজাজের ওপর নিয়ন্ত্রন নেই, খুব সহজেই রেগে যায়।	0	1	2	3
12. Needs close supervision to get through assignments---------- কোন নির্দিষ্ট কাজ করতে হলে তাকে সার্বক্ষন সাথে থেকে তাগিদ করতে হয়।	0	1	2	3
13. Only attends if it is something he/she is very interested in ---------- কেবল মাত্র নিজের পছন্দনীয় কাজটিই সে করে।	0	1	2	3

APPENDIX: X

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

Questions				
14. Runs about or climbs excessively in situations where it is inappropriate ------ যেখানে অতিরিক্ত ছুটোছুটি বা বেয়ে ওঠা উচিত নয়, সেখানে সে তাই করে।	0	1	2	3
15. Distractibility or attention span a problem ---------- যেকোন কাজে করার সময় সেদিকে মনোযোগ চলে যায়, সে বেশিক্ষন কোন বিষয়ে মনোযোগ ধরে রাখতে পারে না।	0	1	2	3
16. Irritable---------- সহজেই বিরক্ত হয়ে যায়।	0	1	2	3
17. Avoids, expresses reluctance about, or has difficulties engaging in tasks that require sustained mental effort (such as schoolwork or homework)---------- যে সব কাজে বিষয়ভিত্তিক ভাবে মনোযোগ ধরে রাখা এবং বুদ্ধি খাটানো দরকার, সে সব কাজ এড়িয়ে যায়, করতে চায়না, বা করানো কঠিন। (যেমন বাড়িতে স্কুলের কাজের প্রস্তুতি, নির্দিষ্ট কাজ বা স্কুলের কাজে).	0	1	2	3
18. Restless in the "squirmy" sense ---------- অস্থির, চঞ্চল, সারাক্ষন নড়াচড়া করতে থাকে।	0	1	2	3
19. Gets distracted when given instructions to do something---------- কোন কাজের নির্দেশ দিলে ও অন্যমনোযোগী /অন্যমনস্ক থাকে।	0	1	2	3
20 Actively defies or refuses to comply with adults' requests ---------- বড়দের কোন অনুরোধ বা আদেশ সাথে সাথে প্রতিবাদ করে বা করতে অস্বীকৃতি জানায়।	0	1	2	3
21. Has trouble concentrating in class---------- শ্রেণীকক্ষে মনোযোগ দিতে পারেনা।	0	1	2	3
22. Has difficulty waiting in lines or awaiting turn in games or group situations— লাইনে দাড়িয়ে অপেক্ষা অথবা খেলাধুলায় নিজের দান আসা পর্যন্ত অপেক্ষা করা তার জন্য কষ্টকর।	0	1	2	3
23. Leaves seat in classroom or in other situations in which remaining seated is expected---------- যে পরিস্থিতিতে নিজের জায়গায় বসে থাকার কথা, যেমন 'শ্রেণীকক্ষ' সেখানে সে নিজের আসন থেকে উঠে যায়।	0	1	2	3
24. Deliberately does things that annoy other people ---------- যে সব কাজে অন্যের বিরক্তি সৃষ্টি করে সে সব কাজগুলো ইচ্ছাকৃত ভাবে করে।	0	1	2	3
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)---------- কোন নির্দেশনা মেনে চলে না। কোন কাজ শুরু করলে শেষ করতে পারে না। যেমন স্কুলের কাজ, ঘরকন্নার কাজ অথবা কর্মক্ষেত্রে। (যেমন নয় যে সে আসলেই করতে চাচ্ছেনা বা নির্দেশনা বুঝেনি।	0	1	2	3
16. Has difficulty playing or engaging in leisure activities---------- অবসর সময়ে ও সাউন্ডভাবে কোন কাজ বা খেলাধুলি করতে পারে না।	0	1	2	3
27 Easily frustrated in efforts---------- যে কোন কাজে সহজেই হতাশান্বিত হয়ে পরে।	0	1	2	3

Score obtained:	T-score	percentile	Impression
A: ____	_____	_____	_____
B: ____	_____	_____	_____
C: ____	_____	_____	_____
D: ____	_____	_____	_____

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

শিশুর নাম : .....

সাক্ষাৎকার গ্রহণের তারিখ : ..... ☐☐/☐☐/☐☐ BS 1

BEHAVIOUR PROBLEMS RECORD SHEET

প্রত্যেকটি বক্তব্যের পাশের ঘরে যথাযথ চিহ্নের সাহায্যে উত্তর চিহ্নিত করুন।

খাওয়া

১। (ক) পছন্দ অপছন্দ সম্পন্ন খাওয়া..... ☐ BS 2

(খ) ক্ষুদা মন্দা..... ☐ BS 3

২। অখাদ্য জিনিস খাওয়া..... ☐ BS 4

রাতে বিছানায় প্রসাব করা

৩। কতবার ঘন ঘন রাতে বিছানায় প্রসাব করে..... ☐ BS 5.

কতবার ঘন ঘন দিনে বিছানায় প্রসাব করে..... ☐ BS 6

রাতে প্রথম কখন বিছানায় প্রসাব শুরু করেছে..... ☐ - Total Score এ আসবে না BS 7

দিনে প্রথম কখন বিছানায় প্রসাব শুরু করেছে ..... ☐ BS 8

বিছানায় পায়খানা করা

৪। কতবার ঘনঘন করে..... ☐ BS 9

প্রথম শুরু হয়েছে..... ☐ - Total Score এ আসবে না BS 10

Child's ID ☐☐☐☐

ঘুম

৫। (ক) ঘুমানোর ব্যবস্থা ..... ☐ - Total Score এ আসবে না BS 11

(খ) বিছানায় যাওয়া / ঘুমাতে যাওয়া ..... ☐ BS 12

রাতে ঘুম থেকে জেগে ওঠা..... ☐ BS 13

(গ) বাবা- মায়ের সঙ্গে ঘুমান..... ☐ BS 14

ভাই-বোনদের সঙ্গে ঘুমান/ পরিবারের অন্য সদস্যদের সঙ্গে ঘুমান ..... ☐ BS 15

অভ্যাস

নিজেকে নিজে কামড়ানো..... ☐ BS 16

৬। মাথা কোটা বা মাথা ঠোকা..... ☐ BS 17

শরীর দোলানো ..... ☐ BS 18

দাবড়ানোর মত প্রতিক্রিয়া উদাহরণ চোখ পিট পিট করা, মুখ টানা, দাঁত কিড়মিড়,

ঠোঁট চাটা বা জিহ্বা চোষা ..... ☐ BS 19.

চুল টেনে উঠানো, চুল টানা, চুল, ত্বক বা নখ খোঁটা ..... ☐ BS 20

বুরো আঙুল অন্য আঙুল চোষা ..... ☐ BS 21

নখ কামড়ানো ..... ☐ BS 22

বিরক্তিকর শব্দ করা, উদাহরণঃ গর্জন করা, ঠোঁটে ঠোঁট চাপিয়া গুণগুণ করা,

অবিরাম ফিকফিক করে চাপা হাসি হাসা বা বোকার মত হাসা ..... ☐ BS 23

খেয়াল খুশীমত জিনিস ব্যবহার করা ..... ☐ BS 24

নিজের যৌনাঙ্গ নিয়ে খেলা করা ..... ☐ BS 25

অন্যান্য ..... ☐ BS 26

Child's ID ☐☐☐☐

বিশৃংঙ্খল আচরণ

৭।	দৌড়ে চলে যায় বা দৌড়ে চলে যাওয়ার চেষ্টা করে	☐	BS 27
	থুথু ফেলা	☐	BS 28
	গায়খান ও প্রসাব করে ঘাটাঘাটি করা	☐	BS 29
	চিৎকার এবং / তীক্ষ্ণ আর্তনাদ করে	☐	BS 30
	লোকজনকে মারার ভয় দেখায় বা হুমকে দেয়	☐	BS 31
	ক্রোধ ণ.থ. লোকজনকে মারে , কামড়ায় বা ধাক্কা দেয়	☐	BS 32
	জমায় বা অন্য ব্যক্তির জিনিসপত্র নিয়ে নেয় (ছবি নয়)	☐	BS 33
	অসময়ে গায়ের জামা কাপড় খুলে ফেলে বা খালি গা হয়	☐	BS 34
	পরিবারের বাইরের লোকজনদের সাথে অনুপযুক্ত আচরণ / ব্যবহার করে ।		
	যেমন : অপরিচিত ব্যক্তিকে চুমু দেয় তার পোশাক চোষে	☐	BS 35
	অন্যের জিনিস পত্রে হস্ত ক্ষেপ করে বা কাজে বাধা দেয়	☐	BS 36
	দেয়াশলাই নিয়ে খেলে, জ্বালায় বা আগুন জ্বালাতে চেষ্টা করে	☐	BS 37
	ধ্বংসকারী জিনিস পত্রের ক্ষতি করে	☐	BS 38
	জিনিসপত্র ছড়ায় অথবা চারপাশে ছিটায়	☐	BS 39
৮।	কার্যকলাপ	☐	BS 40
৯।	ব্যস্ততা	☐	BS 41
	মনোযোগ	☐	BS 42
১০।	মনোযোগের আর্কষনের চেষ্টা	☐	BS 43
১১।	স্বনির্ভরতা	☐	BS 44
১২।	মেজাজ	☐	BS 45

Child's ID ☐☐☐☐

১৩। দুঃচিন্তা ..... ☐ BS 46

১৪। বাতিক গ্রস্ত আচরণ/ নিখুঁত ভাবে কাজ করার প্রবণতা ..... ☐ BS 47

১৫। ভয় / ভীতি

কুকুর ..... ☐ BS 48

বিড়াল ..... ☐ BS 49

অন্যান্য ..... ☐ BS 50

জন্তু/ কীট পতঙ্গ ..... ☐ BS 51

বাজ / জোরে শব্দ ..... ☐ BS 52

অন্ধকার ..... ☐ BS 53

অপরিচিত ব্যক্তি ..... ☐ BS 54
(গাড়ি, বাস, ট্রেন,এসব কি তার কাছে পরিচিত)?

পানি ..... ☐ BS 55

চুলকাটা ..... ☐ BS 56

ডাক্তার ..... ☐ BS 57

গল্প ..... ☐ BS 58

টেলিভেশন ..... ☐ BS 59

অন্যান্য অনুগ্রহ করে লিখুন ..... ☐ BS 60

১৬। ভাইবোনের সাথে সম্পর্ক ..... ☐ BS 61

১৭। সমবয়স্কদের সাথে সম্পর্ক ..... ☐ BS 62

১৮। অসামাজিক / সমবয়স্কদের সাথে সম্পর্কের ক্ষেত্রে সমস্যা

Child's ID ☐☐☐☐

চুরি ..... ☐ BS 63

মারামারি ..... ☐ BS 64

স্কুল বা ক্লাসে শান্তি বিঘ্নিত করে ..... ☐ BS 65

ক্লাস থেকে পালানো ..... ☐ BS 66

মিথ্যা কথা বলা ..... ☐ BS 67

কসম খাওয়া / খারাপ কর্কশ ব্যবহার করা ..... ☐ BS 68

অনেকক্ষণ বাইরে থাকা ..... ☐ BS 69

জীবজন্তু মারা/ কষ্ট দেওয়া ..... ☐ BS 70

নিজের মতামত প্রতিষ্ঠা করতে পারে না ..... ☐ BS 71

অন্যের গায়ে / বিদ্রুপ করে ..... ☐ BS 72

১৯। রাগে ফেটে পড়ে ..... ☐ BS 73

২০। সামলানো কঠিন ..... ☐ BS 74

মোট সাফল্যাঙ্ক ..... ☐☐☐ BS 75

সাক্ষাৎগ্রহণকারীর নাম্বর ..... ☐ B1 76

APPENDIX: XII: Children's behaviour questionnaire, Rutter. 1967

একটি শিশুর আচরণগত প্রশ্নমালা (Rutter, 1967)

শিশুর নাম _ _ _ _ _ _ _ _

জন্ম তারিখ _ _ _ _ _ রেকর্ডের তারিখ _ _ _ _ _

বিদ্যালয় _ _ _ _ _ _ _ _ _ _

প্রায়ই শিশুদের মধ্যে নিম্নোক্ত বিবৃতির বর্ণনামূলক আচরণগুলো দেখা যায়। প্রত্যেকটি উক্তির পর ৩টি করে সারি রয়েছে: "প্রযোজ্য নয়" "কিছু পরিমাণ প্রযোজ্য" এবং "নিশ্চিত প্রযোজ্য"। যদি শিশুটির আচরণ উক্তির বর্ণনার সাথে মিলে যায় তবে "নিশ্চিত প্রযোজ্য" এর নীচে টিক (✓) চিহ্ন দিন। যদি শিশুটির আচরণ উক্তির বর্ণনার সাথে মিলে কিন্তু সব সময় নয় প্রায়ই হয়, তখন "কিছু পরিমাণ প্রযোজ্য" নীচে টিক (✓) দিতে হবে। যদি, যতখানি পর্যন্ত না বুঝি সচেতন হয়েছে, যে শিশুটি উক্তির আচরণ করেনি, তখন "প্রযোজ্য নয়" এর নীচে টিক (✓) চিহ্ন দিতে হবে।

অনুগ্রহ করে প্রতিটি উক্তির প্রেক্ষিতে ১টি করে টিক (✓) চিহ্ন দিবেন। ধন্যবাদ।

উক্তি	0 প্রযোজ্য নয়	1 কিছু পরিমাণ প্রযোজ্য	2 নিশ্চিত প্রযোজ্য	শুধুমাত্র অফিসে ব্যবহারের জন্য
১। অত্যধিক অস্থির। প্রায়ই উঠে এবং নীচে লাফ দেয়। কদাচিৎ শান্ত থাকে।				
২। বিদ্যালয় থেকে পলায়ন করে				
৩। শিশু অস্থিরভাবে ছটফট করে				
৪। প্রায়ই নিজের অথবা অন্যের জিনিসপত্র নষ্ট করে থাকে				
৫। প্রায়শঃ অন্য শিশুদের সাথে মারামারি করে				
৬। অন্যান্য ছেলেমেয়েরা খুব একটা পছন্দ করে না				

	0	1	2	অজানা
৭। প্রায়ই চিন্তিত, অনেক জিনিস সম্পর্কে চিন্তা করে				
৮। নিজের মত করে করতে চিন্তা করে, অনেকটা নিঃসঙ্গ				
৯। খিটখিটে, সহজেই আয়ত্তের বাইরে চলে যায়				
N ১০। প্রায়ই দেখা যায় দুঃখী, অসুখী, অশ্রুসজল অথবা হতাশাগ্রস্ত				
১১।				
১২। ক্রমাগত বুড়ো আঙুল চোষে				
১৩। ক্রমাগত নখ এবং আঙুল কাটে				
১৪। খুচরা অজুহাতে বিদ্যালয়ে অনুপস্থিত বেশিক্ষণ থাকে				
১৫। প্রায়ই অবাধ্য হয়				
১৬। খুবই কম মনোনিবেশ করে, অথবা কম মনোযোগ দেয়।				
N ১৭। নতুন জিনিস অথবা নতুন পরিস্থিতিতে ভয়ের প্রবণতা আছে				
১৮। উত্তেজিত অথবা অতিরিক্ত উত্তেজিত শিশু অবস্থার কথা বলে।				
১৯। প্রায়ই মিথ্যা বলে				
২০। এক বা একাধিক অনুষ্ঠান থেকে জিনিস চুরি করে				
২১।				
২২। প্রায়ই ব্যথা ও অসুস্থতার অভিযোগ করে				
N ২৩। বিদ্যালয়ে পৌঁছার সময় চোখে পানি থাকে অথবা দালান/ভবনে যেতে অস্বীকৃতি জানায়				
২৪। তোতলামী আছে				
২৫। প্রায়ই কথায় অসুবিধা হয়				
২৬। অন্য শিশুদের খোঁচা/ভয় দেখায়				

A Children's Behaviour Questionnaire. Rutter, 1967.

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.

Statement	Doesn't Apply	Applies Somewhat	Certainly Applies	For Office use only.
1. Very restless. Often running about or jumping up and down. Hardly ever still	—	—	—	—
2. Truants from school	—	—	—	—
3. Squirmy, fidgety child	—	—	—	—
4. Often destroys own or others' belongings	—	—	—	—
5. Frequently fights with other children	—	—	—	—
6. Not much liked by other children	—	—	—	—
7. Often worried, worries about many things	—	—	—	—
8 Tends to do things on his own - rather solitary	—	—	—	—
9. Irritable. Is quick to "fly off the handle"	—	—	—	—
10. Often appears miserable, unhappy, tearful or distressed	—	—	—	—
11. Has twitches, mannerisms or ties of the face or body	—	—	—	—
12. Frequently sucks thumb or finger	—	—	—	—
13. Frequently bites nails or fingers	—	—	—	—
14. Tends to be absent from school for trivial reasons	—	—	—	—
15. Is often disobedient	—	—	—	—
16. Has poor concentration or short attention span	—	—	—	—
17. Tends to be fearful or afraid of new things or new situations	—	—	—	—
18. Fussy or over-particular child	—	—	—	—
19. Often tells lies	—	—	—	—
20. Has stolen things on one or more occasions	—	—	—	—
21. Has wet or soiled self at school this year	—	—	—	—
22. Often complains of pains or aches	—	—	—	—
23. Has had tears on arrival at school or has refused to come into the building this year	—	—	—	—
24. Has a stutter or stammer	—	—	—	—
25. Has other speech difficulty	—	—	—	—
26. Bullies other children	—	—	—	—

INDEPENDENT BEHAVIOUR ASSESSMENT SCALE (IBAS)

Name_____ Sex _____ Age _____ Psy. _____ Dated _____

	TOILETING	SCORE		DRESSING	SCORE		SELF-CARE	SCORE		DOMESTIC SKILL	SCORE
১.	প্যান্ট ভিজে গেলে অস্বস্থিবোধ করা।		১.	কাপড় পড়াতে এবং খুলতে সহযোগীতা করা।		১.	দাঁত মাজতে সহযোগীতা করা।		১.	কিছু চাইলে দেয়া। (পেপার)	
২.	মল মূত্র ত্যাগের কথা বলতে পারা।		২.	নিজের কাপড় বাছাই করা।		২.	চুল আচরানো, নখ কাটায় সহযোগিতা।		২.	নির্দিষ্ট স্থানে ময়লা ফেলা।	
৩.	নির্দিষ্ট জায়গায় বাথরুম করা।		৩.	সাধারণ কাপড় খুলতে পারা। (প্যান্ট/জামা)		৩.	পানির কল ছেড়ে নীচে হাত দেয়া।		৩.	বই/জামা/কুল ব্যাগ/খেলনা ব্যবহারের পর গুছিয়ে রাখা।	
৪.	বাথরুম শেষে উঠতে পারা।		৪.	সম্পূর্ণ দিগম্বর হয়ে যাওয়া।		৪.	তেজা মুখ টাওয়াল টিসু দিয়ে মোছা।		৪.	খেলনা/বাড়ী আসবাপত্র ময়লা হলে পরিষ্কার করা।	
৫.	দিনে মল নিয়ন্ত্রণ করতে পারা।		৫.	চেন, বোতাম খুলতে পারা।		৫.	আঙ্গুল/ব্রাশ/মাজন দিয়ে দাঁত মাজা।		৫.	ময়লা/পরিষ্কার কাপড় আলাদা স্থানে রাখা।	
৬.	একা বাথরুমে যেতে পারা।		৬.	সাধারণ কাপড় পড়তে পারা। (প্যান্ট/টিলাজামা)		৬.	গোসল করে শরীর মোছা।		৬.	খাবার এর সময় খাবারের পাত্র এগিয়ে নিয়ে যাওয়া।	
৭.	ঘুমের মধ্যে মল ত্যাগ না করা।		৭.	ঠিক ভাবে জুতা, সেন্ডেল পায়ে দেয়া।		৭.	সাবান দিয়ে হাত মুখ ধোয়া।		৭.	খাবার শেষে প্লেট সরানো।	
৮.	নিজের প্যান্ট খুলে বাথরুমে যাওয়া।		৮.	কাপড়ের চেন, বোতাম লাগাতে পারা।		৮.	নিজে ঠিকমত দাঁত মাজা।		৮.	সাধারণ জিনিস পরিষ্কার করা।	
৯.	বাথরুমে নিজে পরিষ্কার হওয়া। হাত ধোয়া		৯.	কাপড় পড়ে সঠিক ভাবে বোতাম ঘর লাগানো		৯.	নিজে নিজে গোসল করে জামা পরা।		৯.	অন্যকে আপ্যায়ন করা।	
১০.	মল ত্যাগ শেষে স্থানটি পরিষ্কার করা।		১০.	জুতার বকলেস ফিতা লাগাতে পারা।		১০.	খাওয়ার আগে পড়ে হাত ধোয়া।		১০.	ঘরের কাজে বাবা, মাকে সাহায্য করা।	
১১.	বাথরুমে বসে দরজা বন্ধ করা।		১১.	জামার পেছনের বোতাম/চেন খোলা		১১.	আগুন/পশু/পোকা মাকড় থেকে নিরাপদ থাকা।		১১.	কাপড় ধুতে পারা।	
১২.	পিকনিক বা বাজার যাত্রাকালে মলমূত্র নিয়ন্ত্রণ করা।		১২.	জামার পেছনের বোতাম/চেন বন্ধ করা।		১২.	ধারালো বস্তু সাবধানে ব্যবহার করা।		১২.	কুল/বাইরে যাওয়ার প্রয়োজনীয় কাজ করতে পারা টিফিন/পানি।	
১৩.	নতুন জায়গায় বাথরুম আছে কিনা বলতে পারা।		১৩.	শীত/গরমের কাপড় নির্বাচন করা।		১৩.	প্রতিদিন প্রয়োজন অনুযায়ী চুলের পরিচর্যা করা		১৩.	কুল/বাইরে থেকে আসারপর নিজের জিনিস গুছানো, ব্যাগ জামা।	
১৪.	দূরের যাত্রায় বাথরুম নিয়ন্ত্রণ করা। (বাস)		১৪.	রং ডিজাইন কাপড় মিলিয়ে পড়া।		১৪.	সাবান/শ্যাম্পু দিয়ে চুল পরিষ্কার করা।		১৪.	উঠান/ঘর/রুম পরিষ্কার করতে পারা।	
			১৫.	কুল/বাড়ী/বাইরে যাবার কাপড় নির্বাচন করা।		১৫.	আঙ্গুলের নখ কাটতে পারা।		১৫.	ভারী কাপড় নিঙরিয়ে মেলে দাওয়া, শুকিয়ে গেলে নিয়ে আসা।	
						১৬.	সামান্য কেটে/পুড়ে গেলে যত্ন নেয়া।		১৬.	ঘুমানোর আগে নিজের বিছানা করতে পারা।	
						১৭.	হেটে রাস্তা/পুল পার হওয়া।		১৭.	সাধারণ কাপড় ইস্ত্রী করা।	
						১৮.	নিজের কাপড়/বই/খেলনা গুছিয়ে রাখা।		১৮.	খাবার গরম করা, রাস্তাপার হয়ে দোকানে সঠিক জিনিস কেনা।	
						১৯.	খাবার ঢেকে রাখতে পারা।		১৯.	ঘরের টুকি টাকি জিনিস মেরামত করা।	
						২০.	সামান্য অসুস্থ হলে যত্ন নেয়া।				
		RS			RS			RS			RS

MOTOR SK	RS	
SOCEALIZ SK	RS	
COMM SK	RS	
DAILY. LSK	RS	

TOTAL SCORE	

APPENDIX: XIV

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.

Continuation of Appendix: XV

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.

Date	Morning	Afternoon	Night	Additional info.	Doctor's com.
	~~////~~ ////				
___/___/___			///	Sleeps les	
___/___/___					
___/___/___					
___/___/___					

APPENDIX: XVII

ঘন ঘন খিচুনী বা এপিলেপসি সম্পর্কে সাধারণ কিছু তথ্য:

শরীরে উচ্চতাপ বা জ্বরের সাথে খিচুনী (Febrile Convulsion)

শিশুর বয়স ৬ মাস থেকে ৭ বছর বয়স পর্যন্ত দ্রুত জ্বর ওঠার সময় খিচুনী হতে পারে। এটি মৃগীরোগ বা এপিলেপসি নয়। জ্বর হলে ঘন ঘন শরীর স্পঞ্জ করুন, মাথায় পানি ঢালুন এবং ডাক্তারের পরামর্শ অনুযায়ী ঔষধ খাওয়ান। তবে খিচুনীর স্থায়ীত্ব ১০-১৫ মিনিটের বেশী হলে দেরী না করে শিশুকে হাসপাতালে নিন।

জ্বর ছাড়া ঘন ঘন খিচুনী: (Epilepsy)

মৃগী রোগ বা এপিলেপসির উৎপত্তি স্থল মগজ বা ব্রেইন। এর প্রকাশ বিভিন্ন রকম হতে পারে , একসাথে সারা শরীর বা শরীরের কোন অংশ বিশেষ জুড়ে খিচুনী হতে পারে।

সারা শরীর শক্ত হয়ে উপর্যুপরি ঝাকুনি সহকারে মুখে ফেনা উঠে যাওয়া, ঘন ঘন পড়ে গিয়ে আঘাত পাওয়া, কয়েক মুহূর্তের জন্য সংগা হারানো, ঘন ঘন ঘাড় পড়ে যাওয়া বা মাথায় ঝাকুনি হওয়া, হাত পায়ে হঠাৎ ও ঘন ঘন কাঁপুনি অনুভূত হওয়া ইত্যাদি এপিলেপসির কিছু লক্ষণ।

আপনার শিশুর এধরনের লক্ষণ দেখা দিলে একজন অভিজ্ঞ চিকিৎসকের পরামর্শ নিন।

চিকিৎসক আপনার বাচ্চার এবং পরিবারের বিস্তারিত ইতিহাস জানার পর প্রয়োজনমত তার ব্রেইনের কিছু পরীক্ষা করতে উপদেশ দিবেন। ইইজি পরীক্ষাটি দ্বারা মগজের ক্রিয়াকলাপ দেখা হয় যা মৃগী রোগ ডায়াগনোসিসের সহায়ক।

যেকোন বয়সেই খিচুনী হতে পারে , তবে সাধারণ জরিপে দেখা যায় প্রায় শতকরা ৭৫ ভাগ খিচুনী রোগ শিশু অবস্থায় হয়। বাংলাদেশে জনসংখ্যার প্রায় শতকরা ৪৫ ভাগ শিশু (১৮ বছরের নিচে)। ঘন ঘন খিচুনী শিশুদের খুব সাধারণ সমস্যা। এদেশে ২-৯ বছর বয়স্ক শিশুদের নিয়ে করা একটি জরিপে দেখা গেছে যে প্রতি ১০০০ শিশুর মধ্যে ৮ থেকে ৯জনের এপিলেপসি রয়েছে।

আরো জানুন:

- এটি এসমা, উচ্চ রক্তচাপ বা ডায়াবেটিসের মতই শরীরের একটি ক্রনিক অবস্থা।
- এর সঠিক ডায়াগনসিস, কারণ নির্ণয় ও তার চিকিৎসার ফলে সম্পূর্ণ স্বভাবিক ও সুস্থ জীবন যাপন করা যায়।
- এপিলেপসি কোন অতি ইন্দ্রীয় উদ্ভূত কিছু নয়।
- এপিলেপসি ছোঁয়াচে রোগ নয়।

আপনার শিশুর এপিলেপসি হয়ে থাকলে তাকে নিয়মিত ঔষধ খাওয়ান এবং তার চিকিৎসকের সাথে নিয়মিত যোগাযোগ রাখুন।

APPENDIX: XVII EEG related information for parents

শিশুদের ইইজি (EEG) পরীক্ষার জন্য প্রয়োজনীয় তথ্য:

ইইজি এক ধরনের নন্- ইনভেসিভ পরীক্ষা পদ্ধতি , যাতে শরীরের অভ্যন্তরে কোন কিছু প্রবেশ করানোর প্রয়োজন নেই। এ পরীক্ষায় কোন বৈদ্যুতিক তরঙ্গ বা কোন ধরনের রশ্মি দেহের ভিতরে সঞ্চারিত হয়না । শুধুমাত্র মস্তিষ্কের ক্রিয়াকলাপ এ পরীক্ষার মাধ্যমে সংগৃহীত হয়।

অনুগ্রহপূর্বক ই.ই.জি. কেন্দ্রে আসার পূর্বে নিম্নলিখিত নির্দেশনা সমূহ অনুসরন করুন:

১. সাবান অথবা শ্যাম্পু দিয়ে মাথা এবং চুল ভাল করে ধুয়ে নিন। তেল অথবা কোন ধরনের তৈলাক্ত পদার্থ চুলে লাগাবেন না।

২. মনে রাখুন, সম্পূর্ণ শুষ্ক এবং পরিষ্কার চুলই সমাদৃত হবে।

৩. দীর্ঘক্ষণ অভুক্ত থাকলে শিশু বিরক্ত করতে পারে এবং তাতে পরীক্ষার ব্যাঘাত হতে পারে । তাই তাকে অভুক্ত রাখবেন না এবং সঙ্গে কিছু প্রয়োজনীয় খাবার রাখুন।

৪. আমরা এক ধরনের ক্রীমের সাহায্যে শিশুর মাথায় কিছু বোতাম জাতীয় লীড (Lead) লাগাবো। এতে আপনার শিশু কোনরকম ব্যাথা অনুভব করবে না। উল্লেখ্য, এই ক্রীম মোটেও ক্ষতিকারক নয় এবং অতি সহজেই তা উঠে যায়।

৫. পরীক্ষাটি করবার সময় আমরা তার জাগ্রত এবং ঘুম দুটি অবস্থাতেই রেকর্ড নেবার চেষ্টা করবো। অতএব, আপনার শিশুটি যদি জেগে থাকে এবং স্বতস্ফূর্ত, হাসিখুশী ও খেলাধুলায় রত থাকে, এতে আপনার উদ্বিগ্ন হবার কিছু নেই। পরীক্ষা চলাকালীন খিচুনির কোন লক্ষন দেখলে সঙ্গে সঙ্গে যিনি পরীক্ষা করছেন তাকে জানান।

৬. আপনার শিশুকে আগে থেকেই নির্ধারিত পরীক্ষাটি সম্পর্কে এভাবে অবহিত করতে থাকুন যে, তার মস্তিষ্কের ক্রিয়াকলাপ পরীক্ষাটিতে ধরা পড়বে। পরীক্ষা চলাকালীন সময়ে শিশুটি ইচ্ছে করলে কোন বই পড়তে পারবে, বই থেকে কোন গল্প শুনতে পারবে অথবা তার কোন প্রিয় এবং পরিচিত খেলনা নিয়ে খেলতে পারবে।

৭. আপনার জ্ঞাতার্থে আবারও জানাচ্ছি, এ পরীক্ষায় শিশুটির কোন ক্ষতির সম্ভাবনা নেই।

৮. পরীক্ষায় পর্যায়ক্রমিক ভাবে শিশুকে কয়েকবার চোখ বন্ধ করা/ খোলা, কোন ছবির দিকে তাকানো, ফুঁ দেওয়া অথবা জোরে শ্বাস-প্রশ্বাস নেওয়া, আলোর দিকে দৃষ্টি নিক্ষেপ, ক্ষেত্রবিশেষে ঘুমানো- এ জাতীয় কিছু করার অনুরোধ করা হবে।

৯. সম্পূর্ণ পরীক্ষাটি সম্পন্ন হতে ৪০-৬০ মিনিট সময় লাগতে পারে । তবে এই সময়সীমা নির্ভর করে আপনার শিশুটির সম্পূর্ন সহযোগিতা ও সার্বিক পরিস্থিতির উপর।

১০. আপনি যদি শিশুটির প্রিয় কিছু খেলনা আপনার সাথে রাখেন, যা নিয়ে সে কিছু সময় শান্ত এবং ব্যস্ত থাকবে তাহলে তা আমাদের জন্য বিশেষ সহায়ক হবে।

১১. অন্য বিশেষ কোন প্রস্তুতির (যেমন- Sleep deprivation test) প্রয়োজন হলে তা আপনার চিকিৎসকই আপনাকে অবহিত করবে।

আপনার সহযোগীতার জন্য আন্তরিক ধন্যবাদ। আমরা আপনার শিশুর সুচিকিৎসা ও দ্রুত নিরাময় কামনা করি।