

**Neonatal outcome of low birth weight infants
in Bangladesh**

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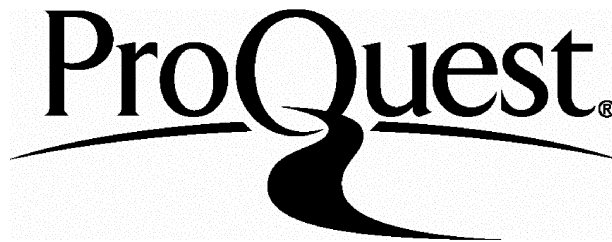
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Abstract

Perinatal and neonatal mortality is used as an important indicator of health status, a country's educational, social and public health system, and standards of obstetric and paediatric care. The formal services reflecting National Health policy for children in Bangladesh is called Maternal and Child Health Care integrated with Family Planning, which emphasizes mostly Family Planning with little attention to children and none for new-born infants. The Bangladesh commitment to 'Health for All by the year 2000' includes significant reductions in infant, child, and maternal mortality. To bring about further reductions in infant mortality we need to understand risk factors for neonatal mortality, especially for high risk, low birth weight (LBW) infants. Birth weight is the single most important determinant for neonatal survival in developing countries. Up to 50% of new-born infants in Bangladesh are born with a birth weight less than 2500g. This study was planned to help health planners with information on the nature and extent of perinatal mortality of LBW infants, important risk factors for LBW stillbirths and neonatal mortality and morbidity, and thereby ideas for programmes to reduce LBW deaths.

Aim: This study aims to study the pattern and risk factors for mortality and morbidity of low birth weight infants in Bangladesh.

Design: It was a prospective study, with a case control design, of 999 low birth weight live and stillborn infants selected from the labour ward of a large teaching hospital in Dhaka city. All the infants born with birth weight less than 2.5 kg were enrolled from the hospital for the period of May 1994 to September 1995, and followed up at home at 28 days of age. During this period those infants who died and those who were stillborn were taken as cases and those who survived as the controls.

Methods: Anthropometric details of infants at birth and follow up were collected. Obstetric and placental details after delivery, socio-economic and morbidity details of the mothers and infants at follow up, and verbal autopsy data for infants who died were used to identify the risk factors for stillbirth, neonatal mortality and morbidity.

Results: The overall neonatal mortality rate for LBW infants was 132 per 1000 livebirths, and the perinatal mortality rate 179 per 1000 total births. The overall percentage of low birth weight in this population was 26% and intrauterine growth retardation was 37%,

20% of low birth weight infants were proportionally retarded and 17% disproportionately retarded. The neonatal mortality was highest in the lowest birth weight group (less than 1.5 kgs) at 690 per 1000 live births, and 513 per 1000 live births for infants less than 32 weeks gestation.

Most infants died in the first week with early neonatal mortality (114 per 1000) representing 86% of neonatal deaths. After stepwise logistic regression analysis, abnormal placental colour (OR 5.78, CI 3.13 -10.70), maternal illiteracy (OR 1.45, CI 1.08-1.65), and lower social class (OR 11.72, CI 0.97-141.99) emerged as independent risk factors for stillbirth. For neonatal death independent risk factors were birth weight <1.99kg (OR 1.62, CI 0.75-3.47), low mid upper arm circumference (OR 0.29, CI 0.19-0.46), maternal anaemia <9gm (OR 3.05; CI 1.12 - 8.31), young age at marriage (OR 3.60, CI 1.49-8.72), maternal illiteracy (OR 2.52; CI 1.33 - 4.75), and no antenatal care (OR 2.31 CI 1.21-4.41). For poor neonatal growth (defined as those infants below the 25th centile for change in weight standard deviation score over the neonatal period) independent risk factors were resuscitation time (OR 1.44 CI 0.53-3.9), gestational age (OR 1.70, CI 0.79-3.66), diarrhoea (OR 0.28 CI 0.12-0.64), supplementary feeding (OR 5.46, CI 2.59-11.49) and length at birth (OR 0.81, CI 0.69-0.93).

Conclusion : The findings show that perinatal and neonatal mortality rates remain high among LBW infants even in this relatively privileged hospital population in Dhaka. Risk factor analysis suggests that some important factors associated with mortality and morbidity are potentially easily preventable and treatable. Special attention should be paid by health planners to care during the first three days. Provision of antenatal care, essential new-born care for infants less than 2.0 kg for the first three days, special attention (perhaps administration of antibiotic therapy) for infants born with abnormal placental colour, iron and folate supplementation to reduce maternal anaemia, and promotion of early breastfeeding are strategies which could significantly reduce low birth weight mortality and morbidity in Bangladesh.

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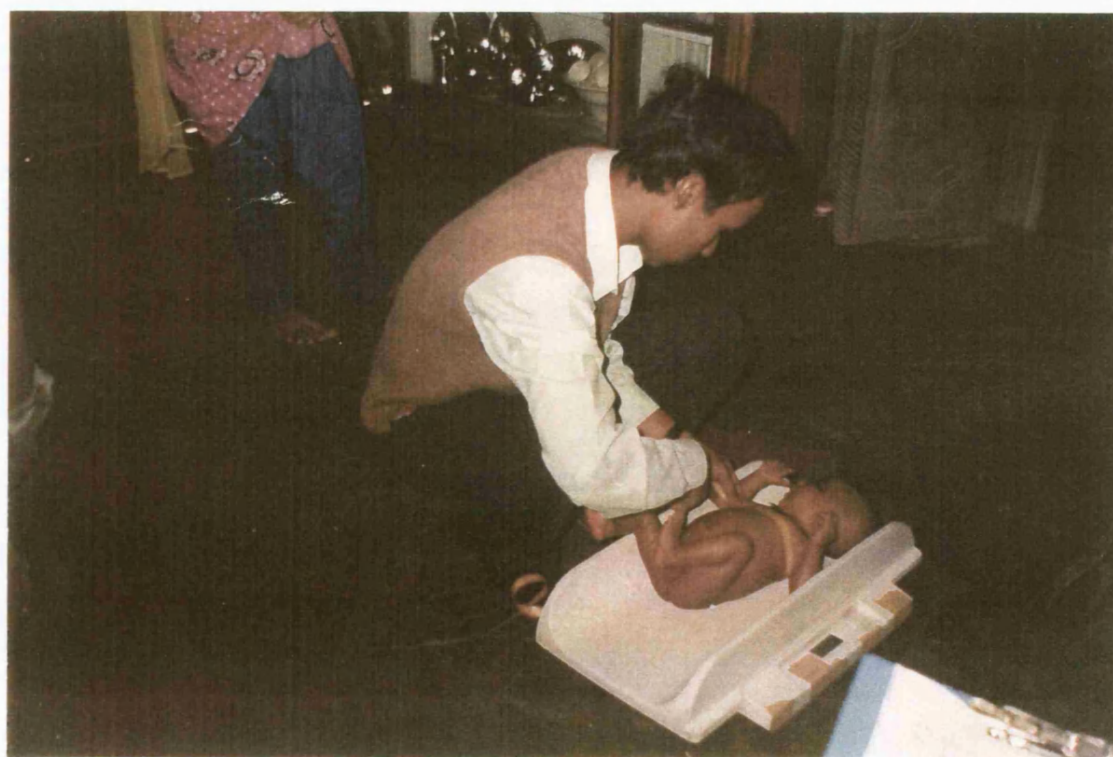
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4. Baby feeding only with sugar water since birth
5. Healthy baby with a good weight gain
6. Bamboo pool over the canal



1. Measurement of body weight by the research assistant at home.



2. Measurement of chest circumference by the research assistant at home.



3. Measurement of body length with the measure mat.



4. This baby lost weight because he was fed only by sugar water since birth.



5. This was a rather healthy baby with a good weight gain.



6. Bamboo pool over the canal.

List of abbreviations

1. APH	Antepartum haemorrhage
2. AGA	Appropriate for gestational age
3. BMI	Body Mass Index
4. ELBW	Extremely low birth weight
5. FWA	Family Welfare Assistant
6. FWV	Family Welfare Visitor
7. FWC	Family Welfare Clinic
8. HNP	Health Nutrition Population
9. IMR	Infant Mortality Rate
10. IUGR	Intrauterine growth retardation
11. ICDDR	International Centre for Diarrhoeal Disease Research Bangladesh
12. K-M	Kaplan Meier
13. LBW	Low birth weight
14. LFD	Large for date
15. LNMR	Late neonatal mortality rate
16. MCH	Mother and child health
17. MOMCH	Medical officer for Mother and child health
18. MUAC	Mid upper arm circumference
19. NMR	Neonatal mortality rate
20. PI	Ponderal Index
21. SD	Standard deviation
22. SSFD	Small for date
23. SGA	Small for gestational age
24. SAARC	South Asian Association for Regional Co-operation
25. VLBW	Very low birth weight
26. WHO	World Health Organisation

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CHAPTER 1

Introduction

1.1. General information about Bangladesh

Bangladesh is a small country of South East Asia with an area of 143,993 sq. km. and a population of 110 million with a population density of about 1000/sq. km. Each person has 0.25 acres of land in his possession and per capita income of 170 US dollar per annum. The country has got three main seasons. Winter (November - February), Summer (March-June), Monsoon (July-October). In the winter the average maximum temperature is 29°C and minimum temperature is 11°C and in the summer the average maximum temperature is 34°C and the minimum temperature is 21°C, in the monsoon the average rainfall is 1194 mm to 3454 mm. Administratively it is divided into four divisions, 64 districts, 460 sub-districts, 4500 Unions, and 68,000 villages. There are four deputy directors of health one for each division. The Civil Surgeon is the chief of health services in the district, who is responsible for overall management of health in the district, except medical colleges. In the Sub-district Thana Health and Family Planning officer is responsible for health care delivery. At the Union level there are Health and Family Welfare Centre/Subcentre.

Hospital facilities

The lowest level of static health facilities is located at the union. At present there are 3000 family welfare centres functioning against 4500. One Medical Officer/medical assistant is in charge of this union facility. At sub-district level there are 349 health complexes functioning with 31 beds in each 397 rural sub-districts. There are 59 district hospitals of different strength. There are 13 medical colleges, five postgraduate hospitals and 22 specialised hospitals. Moreover, outdoor facilities are also provided in the 44 TB clinics, 35 urban dispensaries, and 25 school health clinics. All together, there are 890 hospitals of which 490 are Thana Health Complexes and 400 rural health complexes.

Person per hospital bed is 3189. The number of registered physicians are 21004 and persons per physician is 5216 (Bangladesh Health Services Report 1990).

Maternal and child health services

The country is labelled as one of the least developed country in South Asia. The percentage of literacy is 24, with a wide gender gap, 31% males and 16% of females. The growth rate of the country is 2.17% (Bangladesh Bureau of Statistics, 95). The country has got one of the world's highest neonatal and infant mortality. The neonatal death rate and infant mortality rate are 80 and 80 per 1000 live births respectively (HNP Sector strategy, 1997). 90% of women in this country get married by the time they are 18 years old. Incidence of teenage pregnancy is about 80% and their outcome is not satisfactory. The gap between two pregnancies is also very small. Potentially all pregnancies are at risk. On an average, 15% of pregnancies in Bangladesh belong to high risk group and this accounts for six lac (600,000) pregnancies at any point of time. Nearly 23,500 Family Welfare Assistants (FWA) are engaged at the grass root level who are not technically competent to screen the high risk pregnancies. They usually refer women to 4000 Family Welfare Visitors (FWV) for service at Family Welfare Centres (FWC). FWVs are the only maternal and child health care providers at the grass root level and considered as the masters of all trades in the Ministry of Health and Family Welfare. They are the administrators, health educators, family planning promoters, and MCH service providers (Bhuiyan, 1993).

Family Welfare Centre (FWC) is the first static centre in the union level which is supposed to function as an initial service delivery centre. A physician is a drop of water in the midst of huge number of non-physician MCH workers. Only 872 Medical Officers are working under the MCH directorate and they are placed at the Thana level as MO MCH (Medical Officer of Maternity and Child Health) and in the district level as MO (Medical Officer) clinic. As a carer of clinical MCH services of the country, this number is too small. Moreover, they have never been exposed to any training to deal with high risk pregnancies and their outcome. The MCH directorate has no obstetrical and gynaecological and neonatal specialist to serve the estimated 600,000 high risk pregnancies and their outcome.

1.2 Background

In 1985 the following strategies were identified to improve maternal and child health

1. Functional integration of MCH services delivery at sub-district level and below.
2. Gradual development of comprehensive MCH services including :
 - a. immunisation against six major diseases
 - b. prevention and control of diarrhoeal diseases
 - c. effective management of pregnancy and delivery
 - d. nutritional surveillance and support
 - e. recognition and treatment of simple child health problems

Progress has been made since 1985 in the areas of immunisation, diarrhoeal diseases, and oral rehydration, but less progress in the maternal and child health portion.

Neonatal Health Services

Neonatal care starts from pregnancy to neonatal period. In Bangladesh there is no neonatal care service. The only service available related with neonatal and infant health is Family Planning, which is said to be MCH based. The idea was the care of mother from pregnancy to child up to five years of age. Although the idea was good, subsequent programmes did not go in that direction. Much of the inputs were given in family planning with little or no attention to MCH section. Effective family planning can reduce high risk pregnancies and thus reduce mortality and morbidity rates, but has its limitations and failure. As population explosion is the number one problem in Bangladesh, all the efforts of both government and non-government organisations are being given to family planning without any attention to MCH programme. The result is persistently high mortality and morbidity. Family planning programme did made progress but paradoxically the maternal and infant mortality and morbidity remained high. Provision of antenatal care has been labelled as a priority task which is offered by family planning without any attention to neonatal care. At the field level antenatal care is the responsibility of two cadres of workers; Family Welfare Assistants (FWA) and Family Welfare Visitors (FWV). FWAs are the front line service providers and do care for the pregnant women in their designated areas. They do oral screening for the high risk pregnancies and refer them to FWVs. They counsel women on nutrition, immunisation, and safe labour but no counselling on simple measure to neonatal care. The FWVs are

trained to provide proper antenatal care by both history taking and examination. They are also allowed to give simple treatment and health education. On the other hand, FWAs were reluctant to detect high risk pregnancy cases by taking history (Bhuiyan, 1993). It was regarded 'too long' for some of the FWAs. They don't understand the concept of 'high risk' pregnancy. None of the FWAs questioned about their past pregnancies, and in 60% of visits, FWAs did not questioned about the risk signs of pregnancy. Data on an average from 1990 to 1991 indicates that on average the FWAs made less than one visit per trimester per pregnant women. It is estimated that on an average a pregnant women is visited twice by the FWA during their whole pregnancy period whereas if they did it regularly that could minimise the chances of antenatal infection, placental insufficiency and hypertension and pre eclampsia. 83% of the women were advised and vaccinated for tetanus toxoid. Only 35% of the women went to see the FWV for antenatal check-up. Thus majority of the women did not receive antenatal check-up. The reason for not visiting FWV includes: lack of availability of FWV at Family Welfare Centre, lack of knowledge of satellite clinic near their locality and they did not perceive themselves to be sick.

General information about Dhaka city

Dhaka is the capital of Bangladesh where I have done this work. The area of Dhaka city is 1345 sq. km. with a population of 6,537,308. The number of households is 1,100,000 and size of households is 5.59 persons. It is situated by the bank of river Buriganga. In the municipality area of Dhaka city there are 75 wards, the population is 3,638,000 and the number of households is 644,000. The population density of landless per sq. km. is 2762 (1981 population census). 15.9% of the households do not own any land. The literacy rate of population at all ages is 43.35% (1991 census). My study population came not only from Dhaka municipal area but also from non-municipal area of 90 km around centring Dhaka city. This was a mixed population of urban, suburban, slum and poor and rich village people.

Chapter 2

Literature review

2.1 Perinatal and neonatal mortality in developing countries

2.1.1 Introduction

Perinatal and neonatal mortality is an issue of increasing public health importance in developing countries. Postneonatal mortality in many countries has decreased rapidly, largely due to interventions like immunisation, breast feeding campaigns and programmes to reduce acute respiratory infection and diarrhoea. World wide more than 8 million infants die each year before their first birthday. About two thirds of them (more than 5 million) die during the first month of their life, of which two thirds, approximately 3.4 million die within the first week of life. Ninety eight percent of these deaths occur in developing countries. For every infant who dies in the first week after birth, another is born dead (WHO, 1996).

Reducing neonatal death is the next step to further reduce infant mortality, with particular attention on the early neonatal period when most neonatal deaths occur.

Table 1: Global distribution of foetal and early neonatal mortality around 1995 (WHO/FRH/MSM/96.7; P-9)

	Foetal death rate	No. of foetal deaths (000s)	Early neonatal mortality rate	No. of early neonatal deaths (000s)
World	29	4270	24	3370
More developed regions	5	71	6	84
Less developed regions	32	4200	26	3280

Note : Foetal death rate was calculated by number of foetal deaths per thousand total births.

Number of foetal deaths calculated on the basis of estimated total births for 1995.

Number of early neonatal deaths calculated on the basis of the average projection of live births for 1995.

Perinatal and neonatal mortality rates are important indicators of the socio-economic development of a country. They reflect the nutritional status, obstetric practice, and the maternal health care services of a country with some reflection of the educational standards, social status of mothers, community health and condition of public health services.

Low birth weight is known to be one of the most important risk factors for neonatal and infant mortality but there have been few prospective longitudinal studies of outcome in low birth weight infants in a developing country setting, largely because the identification and weighing of new born infants in the community is difficult. In Bangladesh 23-60% (UNICEF, 1996 and 1997; Nahar, 1997; Roy, 1997) new born infants are born with a birth weight less than 2.5 kgs. If community based strategies to improve the outcome of this high risk group are to be effective we need to have detailed information about the pattern and risk factors for mortality especially in the crucial first four weeks of life, and about the risk factors for morbidity and poor growth during the neonatal period as this may predispose to postneonatal illness and death. This thesis reports a study of the neonatal outcome of 999 low birth weight infants in Bangladesh which attempts to provide some of this important information for health policy makers.

2.1.2 Definitions

Table 2: Definitions of mortality (WHO, 1996)

<i>Measure</i>	<i>Definition</i>
Foetal death ratio	$\frac{\text{Foetal deaths} \times 1000}{\text{Live births}}$
Foetal death rate	$\frac{\text{Foetal death} \times 1000}{\text{Total births}}$
Foetal death rate, weight specific	$\frac{\text{Foetal deaths weighing 1000g and over} \times 1000}{\text{Total births weighing 1000g and over}}$
Early neonatal mortality rate	$\frac{\text{Early neonatal deaths} \times 1000}{\text{Live births}}$
Early neonatal mortality rate, weight specific	$\frac{\text{Early neonatal deaths of infants weighing 1000g and over} \times 1000}{\text{Live births weighing 1000 g and over}}$
Perinatal mortality ratio	$\frac{\text{Foetal deaths and early neonatal deaths} \times 1000}{\text{Live births}}$
Perinatal mortality rate	$\frac{\text{Foetal deaths and early neonatal deaths} \times 1000}{\text{Total births}}$
Perinatal mortality rate, weight specific	$\frac{\text{Foetal deaths weighing 1000g and over} + \text{early neonatal infants deaths weighing 1000g and over at birth} \times 1000}{\text{Total births weighing 1000g and over}}$
Neonatal mortality rate	$\frac{\text{Neonatal deaths} \times 1000}{\text{Live births}}$
Neonatal mortality rate, weight specific	$\frac{\text{Neonatal deaths of infants weighing 1000g and over at birth} \times 1000}{\text{Live births weighing 1000g and over}}$
Infant mortality rate	$\frac{\text{Deaths under one year of age} \times 1000}{\text{Live births}}$
Infant mortality rate, weight specific	$\frac{\text{Infant deaths of live births weighing 1000g and over at birth} \times 1000}{\text{Live births weighing 1000 g and over}}$

Note : Early neonatal death : neonatal death within 0-7 days after birth

Birth weight : The first weight of the new-born infant obtained after birth.

The **perinatal period** commences at 22 completed weeks (154 days) of gestation, (the time when the birth weight is normally 500g), and ends seven completed days after birth.

Stillbirths : An infant born weighing at least 500 gm at delivery (or when birth weight is unavailable, of at least 22 week gestation) who did not breathe after birth or show any other sign of life.

Live birth : Live birth is the complete expulsion of or extraction from its mother of a product of conception, irrespective of the duration of the pregnancy, which, after such separation, breathes or shows any evidence of life, whether or not the umbilical cord has been cut or the placenta is attached.

Neonatal mortality : is the death of infants in the neonatal period, i.e. in the first four weeks of life. The **neonatal period** can be subdivided into early neonatal period, i.e. the first week of life (which is also a part of perinatal period), and late neonatal period, i.e. from the second to fourth weeks of life.

Table 3: Definitions of low birth weight (WHO, 1996)

Low birth weight	weight at birth of infants <2500 g irrespective of gestational age.
Low birth weight at term	infants below 2500 g after excluding pre-term infants.
Very low birth weight	infants with birth weight <1500 g.
Extremely low birth weight	infants of birth weight <1000 g.
Prematurity	gestational age <37 weeks i.e. up to and including 258 th days of gestational age.
Intrauterine growth retardation	birth weight below 10 th percentile of the reference distribution according to gestational age. (see later for discussion)
Small for gestational age	infants below 10 th percentile adjusted for gestational age.
Large for gestational age	infants above 90 th percentile adjusted for gestational age.
Appropriate for gestational age	those between 10 th and 90 th percentile adjusted for gestational age.

Classification and definition of infants at birth for any gestation

- Large for date (LFD): birth weight above +2SD;
- Appropriate for gestational age (AGA): birth weight between -1 SD and +2 SD;
- Intrauterine growth retarded (IUGR): birth weight between -1 SD and -2 SD
- Small for date (SFD): birth weight below -2 SD.

Note: These definitions have been taken from Sachdev (1998) . Sachdev has used this classification but the phase IUGR should really refer to a process, not a cut-off, although the -2SD cut off is a useful one.

Definition of small for gestational age

There is no general agreement as to what constitutes small for gestational age. Before coming to an agreement it is important to decide the aim for which gestational age has to

be assessed. For the obstetrician the purpose would be something related with the intrauterine environment or to fix the time to have a safe delivery; for the paediatrician it is important to decide the line of treatment and to prevent postnatal complications. A number of different cut off points have been introduced to define gestational age. Some studies have used 10th, 5th, 3rd, and 2.3rd centiles, where as others used 2 SD below the mean birth weight as the cut-off point (Assche, Foetal Growth Retardation, 1981).

Most commonly, small for gestational age or (small for dates) refers to those infants below the 10th percentile adjusted for gestational age, and large for gestational age or (large for dates) refers to infants above the 90th percentile, adjusted for gestational age. Those between 10th and 90th percentile are appropriate for gestational age (Polin and Fox, 1992). At present there is no universally accepted definition of intrauterine growth retardation. IUGR may be defined as the birth weight below the 10th percentile of reference weight distribution according to gestational age (Lin and Evans, 1984). Other definitions include birth weight below the 25th, fifth, and third percentiles and a birth weight two standard deviations below the mean (Martorell and Gonzalez, 1987).

The term intrauterine growth retardation, small for gestational age, or small for date has no generally accepted standard definition, but Kramer mentioned in his paper the definitions commonly used are as follows: a) birth weight less than 10th or 5th percentile for gestational age. b) birth weight less than 2500 gm and gestational age greater than or equal to 37 weeks. c) birth weight less than 2 standard deviation below the mean value for gestational age (Kramer, 1987). For classification I used minus two standard deviation below the mean value for gestational age to define IUGR. For analysis (see later) I used the British Growth Standards published by Cole and colleagues as my reference values (Cole, 1998) and took minus 2 SDs weight for gestational age as the cut off for IUGR .

2.1.3. Size of the problem

The high prevalence of perinatal and neonatal mortality remains a serious problem in the developing world. To obtain estimates of the levels and determinants of perinatal mortality in developing countries is very complex, because many births and deaths are not registered. Information on important risk factors such as birth weight, gestational age,

maternal characteristics or behaviours, and complications during pregnancy and delivery is difficult to find out. A perinatal or neonatal death is a relatively rare event (in epidemiological terms) and documenting death is a time consuming and costly effort. As the level of perinatal mortality is associated with the socio-economic development and availability of health care in the community (Ramachandran, 1986), it has become a more important public health challenge to policy-makers (Weekly Epidem Record, 1989; Gueri *et al*, 1977). Infant mortality is used as an important index of a nation's health and neonatal mortality is an important component of infant mortality. In Bangladesh, the rate of infant mortality per thousand live births has declined substantially, from 205 in 1911, 168 in 1951, to 118 in 1983 and subsequently 90 in 1993 and 80 in 1997 (Faroque, 1991; HNP Sector Strategy, 1997), but it is still very high when compared with developed countries. Two thirds of more than eight million infants death that occur each year are neonatal deaths (World Population Prospects, 1995).

The estimated level of perinatal mortality in Europe in 1983 and 1995 was 14 and 13 per 1000 live births respectively, but in Asia was 61 and 53 per thousand births. The global perinatal mortality rate has fallen by 10%, but total perinatal deaths remain almost unchanged as a result of an increasing number of births since 1983 (WHO, 1996).

Table 4: Comparison of infant, neonatal and perinatal death rates in different developing countries and UK from surveys (WHO, 1996)

perinatal	neonatal	Mortality rates per thousand live births/ total births				country
		infant	stillbirth	author	year	
75	70			Rahman	1989	Bangladesh
			37	Fauveau	1990	Bangladesh
	73			Nessa	1992	Bangladesh
85	65	96	96	WHO	1995	Bangladesh
75	57	86		WHO	1995	Nepal
95	59	102	79	WHO	1996	Pakistan
65	50	72		WHO	1995	India
121	97		26	Misra	1993	India
6	5	6		WHO	1995	UK

Table 5: Estimates of foetal deaths in different areas of Bangladesh ((WHO, 1992)

Bangladesh	Year	Foetal death	Total births
Dhaka	1977-1978	96	934
Narayangonj	1984	102	1072
Four Upazillas	1985-1986	36	6348
Matlab	1987-1988	29	1502

It is estimated that world wide there are more than 7.6 million perinatal deaths, 4.3 million of which are foetal deaths (WHO,1996). South-Central Asia has the highest neonatal mortality rate of all regions. It is possible that the global improvement has been less than it appears, because of margins of error.

2.1.4. Data collection is difficult

Data on perinatal mortality can be obtained from vital registration, hospital registration, and community studies. Vital registration is available for only one-third of the world's population (WHO, 1996). It is estimated that incomplete reporting and underreporting, or misreporting of vital statistics underestimates the perinatal mortality on average by 40% and neonatal mortality by 20% (Pawlik, 1994; Bobadilla, 1986). Locating neonatal death is difficult even among institutional deliveries as some occur on the paediatric and neonatal ward, and some in the obstetric ward. It is even harder to record the deaths occurring after discharge from hospital. Since a vital registration system is almost non-existent in Bangladesh, estimates of infant mortality are based on the retrospective reports by mothers on the survival status of their children (Faroque, 1991). As most deliveries in Bangladesh and many other developing countries occur at home (90%) and there is no birth and death registration system it is very difficult to get the data on mortality and thus to estimate the size of the problem.

2.2. Available data from South Asia

2.2.1. Bangladesh

In Bangladesh, despite the numerous publications on diarrhoea, feeding practices of infants, maternal health and family planning, only a few studies have attempted to document perinatal and neonatal mortality. There are only 17 references about neonates in the Bangladesh medical literature up to 1997; the highest sample size involves 984 infants (Rahman *et al*, 1989).

Only sixteen publications about perinatal and neonatal mortality were available from 1970 to 1996. Most of these studies were urban based and the sample sizes were small.

Six of these were retrospective studies of perinatal and neonatal mortality. Five were prospective and were on the pregnancy outcome and outcome of tetanus immunisation on pregnant women. Three were among the Bangladeshi immigrants in England. There were 74 publications available about infant mortality from 1970 to 1996. Of these seven were done in England among Bangladeshi residents, 26 were about infant mortality, nine were about children under-five with some information on infants, two about immunisation, three about diarrhoea, five about food, nutrition and breast feeding, and 11 about family planning, maternal health and traditional birth attendants. Nearly half of these studies were based in rural areas; though most of these studies were done in Matlab, Comilla a project area of ICDDRDB (The International Centre for Diarrhoeal Disease Research in Bangladesh). The remaining half were based on urban areas, mostly in hospitals. Preliminary analysis of Bangladesh maternity history data shows little change in infant mortality between 1979-1984. From 1980-84 it was 130/1000 live births. Following 1985 there was a sharp reported fall in infant mortality, which may be a genuine trend or may reflect data error. In 1989 IMR was 100/1000 live births (Kabir *et al*, 1995), and in 1993 it was 87/1000 live births (Bangladesh Demographic Survey, 1995). A gradual downward trend in infant mortality was observed from the mid-1980s (Salway and Nasim, 1994). Among the infant deaths, 21% of deaths are estimated to occur in the first three days of life (Salway and Nasim, 1994).

One community based survey conducted in Matlab of Bangladesh showed that the perinatal mortality rate was 75/1000 births (37 stillbirths and 38 first week births). This was a retrospective study done over an eight year period (1979-1986) in a rural Bangladeshi population of 196,000 (Fauveau *et al*, 1990). In another study the overall neonatal mortality was found to be 70/1000 live births; for premature new borne NMR was 222.2/1000 live births and 40.1/1000 live birth for term new borne. In this study, 984 mothers who delivered a live born infant were followed at home on the 28th day of birth (Rahman and Nessa, 1989). Another study showed a neonatal death rate of 80/1000 for the younger age group mothers (less than 20 years) and 43/1000 for the older age group mothers (more than 20 years), the perinatal death rate was 66.4/1000. This was a prospective study looking at the health and social situation of married women aged 13 to

23 years among a population of 175,000 who had been followed twice during pregnancy and twice postpartum (Rahman and Souza, 1980).

2.2.2. India

In 1995 the national levels of foetal, early neonatal, perinatal and neonatal mortality rates were reported as 11, 22, 46 and 49/1000 live births (WHO, 1996) respectively.

In a prospective community based study in rural area of Maharashtra, India, of 3173 births, the perinatal, stillbirth, neonatal, and early neonatal mortality rate was 66, 28, 38, and 22/1000 births and livebirths in the low birth weight group respectively (Shah *et al*, 1984). In Uttar Pradesh another prospective study showed a stillbirth rate of 26/1000 births, similar to the above study, but the perinatal mortality rate (121/1000 births) and early neonatal mortality rate (97/1000 live births) were almost double (Misra *et al*, 1993). Maharashtra state has better socio-cultural conditions than Uttar Pradesh. Low literacy, bad communication, poverty, deep rooted customs and beliefs related to antenatal and perinatal care might be a contributory factor for the higher rate of early neonatal and perinatal mortality in Uttar Pradesh.

The higher perinatal mortality and infant mortality rate in rural areas compared to urban areas of India are probably due to non-availability of health care services, poorer income and lower level of education. But in urban areas (slums) of some developing countries where there is poverty, overcrowding due to migration from the rural areas, the mortality is very high (Aksit, 1989; Bagenholm and Nashar, 1989; Johnston *et al*, 1989; Thaver, *et al*, 1990).

2.2.3. Other SAARC countries (Pakistan, Sri Lanka , Nepal)

In Pakistan estimates from different surveys in 1990-91 showed foetal, perinatal and neonatal mortality rates of 79, 95 and 59/1000 births and live births respectively. The early neonatal mortality rate was 24/1000 live births (WHO, 1996). A study in Karachi, showed a stillbirth rate of 81/1000 total births, and perinatal mortality rate of 101.8/1000 total births, of which 7.9% deaths occurred in booked and 92% occurred in the unbooked cases (Razia and Sadequa, 1991). The national rate of neonatal mortality in Nepal was

57/1000 live births (WHO, 1996). There is no national data reported for other mortality rates. But in Kathmandu the foetal, early neonatal and perinatal mortality rates were 29, 20, and 48/1000 births and live births respectively (WHO, 1996). There was some variation in mortality rate in the urban and rural areas in Nepal: a study showed perinatal mortality rate 96/1000 live births in rural areas and 48/1000 live births in urban areas (Geetha *et al*, 1995; Rana, 1995). There is no data available about Bhutan. The national rate in Sri Lanka for foetal death is 9/1000 (1987); early neonatal death 9/1000 (1987); perinatal death 20/1000 and neonatal death 16/1000 live births (WHO, 1996). The national rate masks wide variations across districts, from low 21/1000 to 100/1000 of infant mortality, and 9 to 62% of early neonatal deaths. Such regional variations have been shown to be related to a number of social, demographic and institutional characteristics (Sivagnanasundram, *et al*, 1985; Waxler *et al*, 1985; Fonseka *et al*, 1994). The Sri Lanka experience is important. Their perinatal health statistics are closer to European than South Asian levels. The most important contributing factors are very high female literacy and the universal presence of a skilled birth attendant at delivery.

Table 6: The national estimates of perinatal and neonatal mortality /1000 births in 1995 from Bangladesh, India, Pakistan and Sri Lanka (WHO, 1996)

Country	Year	Perinatal mortality	Neonatal mortality	Infant mortality
Bangladesh	1995	85	65	80
India	1995	65	50	69
Pakistan	1995	70	55	91
Sri Lanka	1995	20	16	23

2.2.4. Asian rates in UK

The immigrant mothers from India, Pakistan, and Bangladesh (Asian) in UK for the years 1982-85 showed significant differences in perinatal mortality: 10.1/1000 total births in UK born mothers from India, Bangladesh and Pakistan were 12.5, 14.3, and 18.8 respectively. The predisposing factor for this difference are illiteracy, ignorance about the benefit of medical care and its availability, short pregnancy interval and unplanned pregnancy, poor housing, genetic constitution, physique, poor and late antenatal care. These risks occur frequently together and are common in the immigrant mothers (Raleigh *et al*, 1990).

2.3 Risk factors for perinatal and neonatal mortality

The perinatal and neonatal mortality risk factors can be divided into the following groups

1. Socio economic and preconception risk factors.
2. Risk factors during pregnancy.
3. Risk factors during labour.
4. Risk factors in the early postnatal period.
5. Risk factors in the late neonatal period.

2.3.1. Socio-economic and preconception

Perinatal and neonatal mortality is the consequence of low social, economic, medical, and biological status of women. Perinatal deaths may reflect the quality of antenatal, natal and postnatal care. Poor maternal nutritional status is independently associated with perinatal death. But multivariate analyses indicates that socio-economic status operates through other proximate factors such as absence of antenatal care, and complications during labour and do not have an independent effect (Mavalankar, *et al*, 1991; Adlakha and Suchindram, 1985; Taha, *et al*, 1993). Bad obstetric history, higher parity, and maternal age under 20 and over 35 years, interval since the preceding birth, first birth, parity above five, were found to be significantly associated with adverse outcome (Zhang *et al*, 1991; Mavalankar *et al*, 1991; Rosetta and Quigley, 1990; Serrano and Puffer, 1974; Tiwari, 1989; Trussell and Pebley, 1984; Kofoed and Simonsen, 1988; Fung, 1990; Golding and Shenton, 1990; Hobcraft, *et al*, 1985; Kusin *et al*, 1989; Lumey and Reijneveld, 1996).

In Bangladesh neonatal mortality for singleton birth children was 38% higher for short preceding birth intervals (less than 15 months); those whose older sibling died in the neonatal period have a mortality risk 1.9 times that of children whose older siblings survived infancy. The risk of dying increased for infants of older mother more than 34yrs: 1.4 times higher than that of their counterparts aged 20 - 34 years (Alam, 1995). Perinatal mortality in Matlab (Bangladesh) was 22 percent higher for the infants of the youngest mothers (less than 20 years) than those of comparatively older mothers (Mostofa *et al*, 1995). In tribal India the risk factors associated with perinatal loss were: preference for traditional health care, a long distance from a health post, teenage pregnancy, illiteracy,

hard physical work, first or fifth and subsequent pregnancy (Daga and Daga, 1993), and neonatal mortality was 1.8 times greater in rural than in urban areas (Panikar, 1985).

Neonatal mortality exhibits a 'U' shaped distribution with parity; but for post neonatal mortality, the pattern is not as apparent (Stoeckel and Chowdhury, 1972; Ozumba and Igwegbe, 1992; Tjipta *et al*, 1989; Mostofa *et al*, 1995). Some authors believe neonatal deaths are mostly of biological origin whereas postneonatal deaths are sensitive to improvement in social conditions (Simmons *et al*, 1978). Different studies in Bangladesh found that neonatal mortality was related to endogenous causes such as the maternal environment during pregnancy, during delivery and to traditional unhygienic delivery practices, while exogenous causes (like infectious and parasitic diseases, maternal education and household status, source of water, place of defecation) are responsible for postneonatal mortality (Rahman *et al*, 1985; Paul, 1991; Khorshed *et al*, 1990). The findings that environmental factors have little effect on neonatal mortality is not surprising, because in Bangladesh almost all infants are breast fed especially in the first month. In Bangladesh there is poor sanitation system, with faeces near the house as a source of contamination. Insects, poultry, and pets help to transfer pollution from the environment to food, air and water. Overcrowding is another risk factor which helps to spread infectious disease. But this may not always apply, because larger house holds sometimes means more than one nuclear family, which means more wage earners and more women to take care of the children. Neonatal mortality is presumably related with the maternal environment during pregnancy, and during delivery, and as most of the neonates die within the first seven days of life there is little possibility of the infant being exposed to external environment. Moreover in Bangladesh there is a cultural tradition to keep the new-born and the mother inside a restricted room for 40 days.

2.3.2. Risk factors during pregnancy

Neonatal mortality is largely influenced by endogenous factors i.e. intrauterine conditions of the foetus or at birth. The direct causes of perinatal and neonatal deaths are poor weight gain and hard physical work during pregnancy (Ceesay *et al*, 1997), antepartum haemorrhage, hyper tension and bleeding, grand multiparity, and malnutrition, (Millat and Florey, 1992; Taha *et al*, 1993). But one study in Finland showed that bleeding during the

second trimester indicates a poor pregnancy outcome such as increased risk of low birth weight, pre-term labour, or congenital malformation which eventually results in a poor perinatal outcome, but no association existed between bleeding and perinatal mortality (Sipila *et al*, 1992). Poor perinatal outcome in the second trimester bleeding might reflect the fact that in Finland antenatal care has got a high frequency of check up visits, making an early intervention possible which could contribute low percentage of complications in the first trimester of pregnancy. So bleeding in the second trimester came as a significant factor. But the conclusion that there is no association between bleeding and poor perinatal outcome might suggest that good general health, environmental factors, free medical care, or all these factors together may contribute insignificant effect of bleeding and perinatal mortality.

In tribal India the risk factors associated with perinatal loss were: certain antenatal conditions (oedema, severe pallor, antepartum haemorrhage), intranatal events (prolonged labour, abnormal presentation) and postnatal factors (fever and excessive haemorrhage) with other socio-economic factors (Daga and Daga, 1993). An unfavourable perinatal outcome was found with eclampsia (Kuo *et al*, 1995). Certain pregnancy complications such as pre-eclampsia, gestational diabetes mellitus, placenta praevia, and chronic medical illness could have an effect on foetoplacental growth which indirectly influence adverse pregnancy outcome (Lao, 1996; Harrison, 1997). All these obstetrical conditions adversely affect uterine environment and causes adverse perinatal and neonatal outcome (Verma, 1992).

Table 7: Maternal and perinatal outcome in booked and unbooked women

Maternal and perinatal outcome in booked healthy women, in booked women with antenatal complications, and in unbooked emergencies in hospital births, Zaire, Nigeria 1976-1979			
	Booked healthy	Booked with antenatal complication	Unbooked emergencies
Maternal results			
Number of women	11,261	3,759	7,707
Disproportion (n)	274	299	1069
Destructive operations (n)	8	9	221
Blood transfusion (%)	2	10	25
Maternal deaths (n)	5	14	219
Foetal results			
Singleton births (n)	10,896	3296	5518
IUD on admission (n)	79	90	792
Perinatal deaths (n)	240	243	1375
Perinatal deaths /1000 deliveries	22	74	249

2.3.3. Risk factors during labour

Home delivery is an important risk factor for neonatal morbidity and mortality in poor communities (Beeram *et al*, 1995; Islam *et al*, 1982; McDermott *et al*, 1996). Beeram in Columbia showed that there was a two fold increase in neonatal morbidity and an 11 fold increase in mortality among home deliveries compared with infants delivered in hospital. Although the home born infants were less than 2% of the total deliveries, they accounted for 17% of total neonatal mortality. But there is some argument about home delivery. Some authors recommend that there is no risk either to the baby or the mother for healthy low risk women who wish to deliver at home, rather it makes birth proceed easier (Ackermann *et al*, 1996; Olsen, 1994). Other authors believe that home delivery should remain the exception since it is unable to guarantee a birth as undangerous as possible, and it is not possible to provide operative interventions (Berg and Suss, 1994; Olivier *et al*, 1994). Regarding home delivery there should be active participation in prenatal care, a realistic attitude regarding the risks, knowledge of benefits and potential complications of home delivery and preparedness for this, and the midwives attending birth must be highly trained (Arya *et al*, 1996; Vedam and Kolodji, 1995). One study in a remote rural area of Teknaf (Bangladesh) found the neonatal mortality rate with delivery complications was 153/1000 live births compared to 82/1000 live births for those without complications. The neonatal mortality was 400/1000 live births among the new-born with birth complications compared to 64/1000 live births among those with no complication (Islam *et al*, 1982). From this study we can imagine the mortality and morbidity conditions of Bangladesh where 90% of deliveries occur at home.

In developing countries birth trauma and asphyxia, infection, and tetanus are the result of inadequate/unskilled obstetric and neonatal care and inefficient referral systems. Asphyxia which is a major cause of perinatal mortality often results from obstructed labour. Moreover birth injury and intracranial haemorrhage may result from obstructed labour and unnecessary handling of the foetus by the untrained dai. Perinatal death of infants above 2500g birth weight is mostly influenced by obstetric causes, and neonatal

mortality of the low birth weight group is influenced by the quality of medical care (Wigglesworth, 1980).

2.3.4. Risk factors in the early postnatal period

Many low birth weight infants, especially if preterm, will die in the early postnatal period. The common observation from all countries is that neonatal mortality decreases with increasing birth weight (Ferraz and Gray, 1991; Hoffman, 1988). The three major causes of perinatal death in Shanghai were asphyxia, congenital malformation, and intracranial haemorrhage (Zhang *et al*, 1991). In a community based study in Bangladesh the causes of early neonatal deaths (within three days of birth), were largely the result of a very small size at birth (63%) or a birth trauma (31%) (Fauveau *et al*, 1990). But another prospective study in Tangail (Bangladesh) mentioned that the commonest cause of perinatal death was unknown. Most of these deaths occurred suddenly without any signs of respiratory distress or previous illness. It was assumed that death may have resulted from an apnoeic episode associated with aspiration. The second most common cause was sepsis and the third was respiratory distress (Hort, 1985). The most important factors responsible for perinatal and neonatal deaths in developing countries are birth weight, very pre-term infants, asphyxia, birth injury, congenital anomaly, neonatal infections, tetanus (Lin, 1993; Millat, 1992; Taha and Gray, 1993), and in the developed countries, endogenous factors such as congenital malformation (Klien, 1988; McCormick, 1985). Pre-term infants had a perinatal mortality rate 13 times higher than that of infants of appropriate birth weight and gestational age and twice that of IUGR infants (Barros *et al*, 1992).

2.3.5. Risk factors during late neonatal period

Neonatal mortality rate gradually decreases with the increment of birth weight and age. Half of neonatal deaths are related to low birth weight and associated complications, others result from neonatal infections and asphyxia at birth (Pratinidhi *et al*, 1986; Okoji and Oruamabo, 1992). Neonatal mortality is highest among infants with feeding problems and illness. Feeding problems were due to inability of the mother to maintain the nutrition

of the baby in a hygienic way when there is inadequate breast milk, sucking problem of the infant, or not maintaining proper nutrition due to ignorance (Pratinidhi *et al*, 1986).

Infections causing neonatal mortality include tetanus (Stanfield and Galazka, 1984), malaria (Looareesuwan *et al*, 1987), congenital syphilis (Schryver and Meheus, 1990) and HIV (Ryder *et al*, 1989). Pre-term and low birth weight neonates die primarily from problems of prematurity and or infection. Term and larger neonates died primarily from asphyxia. Proportionally small infants showed a consistently higher risk of death during the neonatal period (Boo and Lye, 1991).

Table 8: Summary table of perinatal and neonatal risk factors (prepared from the previous discussion).

Preconception	During pregnancy	During labour	Early postnatal	Late neonatal
Poor socio-economic status	Poor weight gain	Home delivery	Asphyxia	Feeding problem
Bad obstetric history	Hard physical work	Birth trauma	Congenital malformation	Illness
Higher parity	Antepartum hmg	Asphyxia	Intracranial hgm	Infection
Maternal age <20 and >35yrs	Hypertension and bleeding	Infection	Very small size at birth	Prematurity
Birth interval	Diabetes mellitus	Tetanus	Birth trauma	Respiratory problem
First birth	Placenta previa	Obstructed labour	Sepsis	Unsatisfactory housing condition
Parity >5	Chronic medical illness		Respiratory distress	
Preference for Traditional health care			Pre-term	
Distance from health post			Unknown	
Illiteracy				
Hard physical work				

Note: Factors tabulated from the following references: Zhang *et al*,1991; Mavalankar *et al*, 1991; Rosetta & Quigley,1990; Serrano,1990; Tiwari, 1989; Trussell & Pebley,1984; Kofoed and Simonsen, 1988; Fung,1990; Golding & Shenton,1990; Hobraft *et al*,1985; Kusin *et al*,1989; Lumey and Reijneveld, 1996; Ceesay,1997; Sipila,1992; Daga,1993; Kuo,1995; Lao,1996; Millat & Forley,1992; Taha *et al*,1993; Beeram *et al*,1995; Islam *et al*, 1982 McDermott *et al*, 1996; Berg & Suss, 1994; Oliver *et al*, 1994; Ackermann *et a*, 1996,; Olsen, 1994; Arya *et al*, 1996; Vedam Kolodji, 1995; Wigglesworth, 1988; ; Ferraz,1991; Hoffman, 1988; Zhang, 1991; Fauveau, 1990; Lin, 1993; Klien, 1988; Hort, 1985; McCormick, 1985; Barros, 1992; Pratinidhi, 1986; Looareesuwan, 1985; Schryver, 1990; Ryder, 1989; Boo, 1991; Sivagnanasundram, 1985; Rahman,1985. .

2.4. Low birth weight, intrauterine growth retardation and smallness for gestational age

2.4.1. Introduction

The birth weight of an infant is probably the most important factor that affects neonatal and infant survival and quality of life (Habicht *et al*, 1974; Habicht *et al*, 1973; Kaminski *et al*, 1973; Lechtig *et al*, 1977; Mata *et al*, 1975; Patros-Barvazian and Behar, 1978; Serrano and Puffer, 1974; WHO, 1978). Birth weight is dependent on two major factors:

duration of gestation and intrauterine growth rate. Low birth weight is thus caused either by a short gestation period or retarded intrauterine growth (or a combination of both) (Ghosh and Daga, 1967; WHO StatQ, 1980). In developing countries between 10% and 35% of new-borns typically suffer from IUGR. These represent most new borns with low birth weight (Belizan and Villar, 1988).

The World Health Organisation strategy to attain the objective 'Health For All by the Year 2000' unanimously acclaimed by all member states in Alma Ata in 1978 (WHO, 1981), identified 12 health indicators. The eighth health indicator states that the nutritional status of children is adequate if :

1. At least 90% of new born infants have a birth weight of at least 2500g.
2. At least 90% of children have a weight appropriate for his/her gestational age.

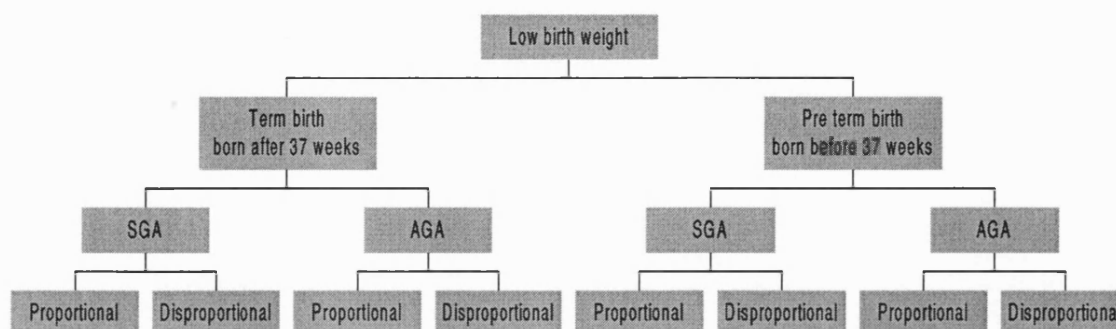
The most commonly used indicator of new born maturity is birth weight (Kramer, 1987) which is highly responsive in two important aspects (WHO Publications, 1978): firstly by the health and nutritional status of the mother, and secondly by the survivability and healthy growth and development. Targeted public health interventions have to be introduced to improve the birth weight.

The use of a WHO single cut-off point for birth weight has been criticised by numerous Indian authors who argued that the internationally agreed limit of low birth weight of 2500 gm should be replaced by definitions as appropriate for different populations. They defined low birth weight as those with birth weight less than or equal to 2250 g (Canosa, 1989).

Fig. 1

2.4.2 Classification of low birth weight

Classification of low birth weight



Infants of low birth weight may be classified into the following three groups. 1) pre-term or born before 37 weeks gestation and of appropriate weight for gestational age, 2) pre-term and growth retarded or born before 37 weeks gestation and weighing less than appropriate for gestational age, 3) term and growth retarded or born after 37 weeks gestation and weighing less than appropriate for gestational age.

2.5. Size of the problem of low birth weight in developing countries

Globally one in six live birth, or almost 25 million low birth weight new borns were born in 1990, accounting for 17% of total births (WHO, 1992). In 1979, there were 21 million low birth weight infants born in the world, representing 18% of all births, the vast majority of which were born in developing countries (WHO Stat Q, 1980; Bhargava *et al*, 1985; Weekly Epi. Rec., 1984). Regional data shows that the incidence of low birth weight is highest in Asia (21%), which accounts for almost a third of the world's births, followed by Oceania (20%), Africa (15%), Latin America (11%), North America (7%), and Europe (6%). No less than a third of all neonates in South Asian countries weigh less than 2500gm ((WHO, 1992).

Table 9: Global distribution of low birth weight prevalence (WHO 1992).

Region	low birth weight	
	1979 (%)	1990 (%)
World	18	17
Developing	20	19
Developed	7	7
Africa	15	15
Asia	22	21
Latin America	13	11
Northern America	7	7
Europe	7	6

The data gathered by WHO from different countries in the world have shown that South Asian countries have the lowest mean birth weight in the world, about 2.7 kg and has the highest prevalence of low birth weight (32%) compared to other regions in Asia (WHO, 1992). In Eastern Asia countries such as Thailand, Myanmar, and Indonesia, reduced low birth weight incidence probably reflects better maternal health care and better maternal nutrition.

Table 10: Distribution of low birth weight in different regions of Asia (WHO 1992)

<i>Prevalence of low birth weight in Asia</i>		
<i>Region</i>	<i>1979 (%)</i>	<i>1990 (%)</i>
Eastern	7	9
South Eastern	18	15
Southern	34	32
Western	12	11
Asia	22	21

The officially reported incidence of low birth weight in Bangladesh is 50%, in India 30%, and in Pakistan 25% (WHO,1992). Though there are some publications in India about low birth weight (175 from 1975 to 1996 in Medline search), in Bangladesh there are only 23 publications available, of which only eight were about low birth weight in a Medline search from 1975 to 1996, three in local journals. In Medline search there was no publication about IUGR in Bangladesh, although there were 30 publications in India from 1976 to 1996.

Table 11: Reported studies of the percentage of low birth weight among new-born infants in Bangladesh

<i>Author (Year)</i>	<i>Type of study</i>	<i>LBW %</i>	<i>n (sample)</i>	<i>Comment</i>
Goodburn (1994)	Prospective	51	204	weight was not taken at birth
WHO (1992)	WHO LBW data base	50	4796	national estimates
Khanam (1990)	Clinical study	47	206	n is small
Canosa (1989)	Population survey	70	624	information was not adequate
Tabib (1987)	Prospective	74 (<2 kg)	125	done only in referred cases
Rahman (1989)	Prospective	17	984	birth weight was not taken
Hort (1985)	Cross sectional	51	1772	hospital based
Khan (1978)	Cross sectional	50	1002	urban based

Data from global studies indicate that, over the last two decades, there has been some reduction in the proportion of low birth weight deliveries in most developed countries. However, in most of the developing countries there has not been any substantial reduction (WHO, 1996).

The incidence of low birth weight infants in Bangladesh like India is very high (Bhargava *et al*, 1984; Singh *et al*, 1982; Rawshan, 1978). In a cross sectional study in two major hospitals of Bangladesh from 1975-1976 (Khan *et al*, 1978) found the mean birth weight in males was 2547 grams and in females only 2281 grams and the percentage of low birth weight was 50%. This was an urban based study done on 1002 new born babies born during the year 1975 - 1976. Another prospective community based study showed low birth weight rate 51%, 9% of which were less than 2kg, and mean birth weight was 2.42kg (Goodburn *et al*, 1994). But as it was a community based study done in a rural area (Manikgonj), anthropometric measurements were taken between 1-6 days of birth, which might tend to underestimate accurate birth weight, as infants lose up to 15% of their initial birth weight through fluid loss in the first week after birth. In Khanam's study the sample was taken at hospital, so they had the birth weight, but as it was only urban based and the sample was small (206) it may not represent the whole population, although the percentage of low birth weight was close to the national level. The difference between the study of Goodburn and Khanam was that though in both of these studies the sample sizes were similar, in Goodburn's study the weight was not taken at birth. However, hospital studies are not appropriate for calculating mortality incidence unless all births are institutional. The study done by Rahman, 1989 found a low birth weight prevalence of only 17%, but it is questionable, because he followed these infants only at the age of 28 days, so it is not clear how he could comment on birth weight?

In the Bangladesh perinatal survey of 1983 the percentage of low birth weight was 70% and among these 81% suffered from IUGR i.e. birth weight less than 10th percentile of gestational age (Canosa, 1989).

2.6. Pathophysiology of intrauterine growth retardation

IUGR is a pathophysiologic process resulting in restriction of foetal growth, while SGA is a statistical grouping of infants below the 10th percentile for gestational age. But from a practical point of view there may be considerable overlap of these two groups. Statistically 10% of infants should fall below the 10th percentile regardless of medical

intervention. By contrast, a foetus who has stopped growing by clinical or ultrasound criteria, but who is delivered before the weight crosses the 10th percentile, should still be considered an infant subjected to a growth restricting process even if appropriate for gestational age (Polin and Fox, 1992). A classical picture of the growth retarded infant is with increased body length in relation to weight, relatively large head with wide skull sutures, muscle wasting, prominent ribs, an alert look and a dry, wrinkled skin.

Intrauterine foetal growth is a continuous change in the size of the foetus, and in the function of the various foetal organ system and is influenced by genetic and environmental factors. Rosso and Winick (1974) divided foetal cellular growth into three phases.

The first phase is cellular hyperplasia. This is the phase where the cells increase in number from fertilisation to 16 weeks of life, causing increase in the number of all cells in all foetal organs. A foetal insult in this phase results in the reduction of cell numbers, and impairs foetal cellular hyperplasia which causes a proportionate decrease in the size of all foetal organs and leads to the development of symmetric IUGR (Miller and Hassanein, 1971; Campbell, 1974). These infants are usually small in size with a reduction in all anthropometric measurements (height, length, and head circumference thus producing a normal Ponderal Index). These are called 'Proportional or Stunted IUGR or Symmetric or Type 1 IUGR' (See Fig 1). Type 1 IUGR refers to a growth pattern in which the growth of both foetal abdomen and head decrease proportionally (Lubchenco *et al*, 1963). It is defined as less than 10th percentile for both body weight and head circumference for the gestational age at birth. Pre-term IUGR was defined as less than 10th percentile for birth weight with a gestational age of less than 37 weeks (Lin *et al*, 1991). This type of growth retardation is often associated with congenital malformation. Proportional growth retardation is often the expression of a defective intrinsic growth potential rather than of an imposed constraint of that growth potential (Assche and Robertson, 1981).

The second phase (16 to 32 weeks) is the phase of cellular hyperplasia and hypertrophy. This phase is characterised by a progressive decrease in the rate of cellular hyperplasia with a progressive increase in cellular hypertrophy. Foetal insult in the early part of this phase results features of symmetric type of IUGR and in the later part results asymmetric type of IUGR.

The third phase is from 32 weeks to term. This is the phase of rapid increase in cell size with glycogen and fat deposition. An insult during this phase leads to the development of asymmetric IUGR with its brain sparing phenomenon; disproportionate decrease in foetal abdomen with respect to the foetal head. This pattern is also called 'head sparing'. Comparing the different phases of intrauterine development it can be hypothesised that the timing of the interaction between high risk factors and the stage of gestation is far more important than the nature of each high risk factor (Rosso and Winick, 1974; Winick, 1971).

From this hypothesis it can be concluded that 'proportioned' or 'symmetric' IUGR is the result of genetic influence or foetal insult in the early part of pregnancy with reduced body weight and length and a proportionally small head. The 'disproportioned' or 'asymmetric' new borne are associated with insults appearing in the later course of pregnancy with head and length of relatively normal size for their gestational age, but who are thin with low weight for length and skinfold measurements, which leads to a malnourished and wasted infant (Crane and Kopta, 1980; Warshaw, 1985; Mahran and Omran, 1988; Rosso and Winick, 1974; Campbell and Thoms, 1977; Miller and Hassanein, 1971). These are called 'disproportional' 'asymmetric or Type 2' IUGR (Fig 1).

Asymmetric IUGR was defined as birth weight less than 10th percentile with length more than 10th percentile and symmetric IUGR as both weight and length less than 10th percentile for gestational age (Salafia *et al*, 1995). The asymmetric group was defined as a birth weight of less than 10th percentile but head circumference of more than 10th percentile for gestational age. Asymmetric IUGR infants exhibit a low Ponderal Index,

with a considerable reduction in weight relative to their length and head circumference (Raphael and Michael, 1992).

2.7. International comparisons of intrauterine growth retardation and smallness for gestational age based on birth weight

In developing countries, between 10% and 35% of the new-borns suffer from IUGR i.e. birth weight less than 10th percentile of gestational age, of which between 49% and 87% of the new borne are born with symmetric proportionality (Raphael and Michael, 1992).

Since foetal growth in a community depends on many factors and it should be considered appropriate for that particular community depending on those factors, there is no general agreement to what constitutes smallness for gestational age.

Infants of Indian born mothers (mothers born in Bangladesh, India, Pakistan, Sri Lanka) tended to be lighter at birth than those of British born mothers (Moore *et al*,1995). The sample size in this study was small however many Indian mothers refused to enter the study.

Table 12: Mean (SD) values for head size, length, weight, and Ponderal Index at birth for boys and girls by mother's country of birth. (Moore, W.M.O; Early Human development; 111 - 121: 42: 1995).

Mothers country of birth	OFC (SD) (cm)	n	CHL (SD) (cm)	n	weight (SD) (kg)	n	Ponderal Index (kg/m3)	n
Boys								
British Isles	34.8 (1.2)	63	51.0 (2.2)	63	3376 (483)	65	25.2 (1.9)	63
Indian subcontinent	34.1 (1.1)	22	50.5 (2.0)	22	3244 (476)	22	25.1 (2.3)	22
Girls								
British Isles	34.2 (1.4)	61	50.0 (2.1)	61	3224 (492)	61	25.6 (2.5)	61
Indian subcontinent	33.9 (1.2)	12	49.1 (1.6)	12	3045 (367)	13	25.8 (1.2)	12

OFC = occipito frontal circumference; CHL = crown heel length; Birth OFC and CHL were measured at mean gestational age 282 (range 262 - 307) day; values () = SD. P=0.002

Birth weight was measured at mean gestational age 279 (range 259-297) days in boys of locally born mothers, at 278 (261-291) days in boys of Indian-born mothers, at 280 (261-299) days in girls of locally-born mothers, and at 277 (262-292) days in girls of Indian-born mothers.

Analysis by sex and mother's country of birth showed that 73% of boys and 77% of girls of Indian born mothers and 52% of boys and 52% of girls of locally (UK) born mothers had a birth weight below the 50th centile (Moore *et al*, 1995).

2.8. IUGR and birth weight

The term IUGR cannot be applied to infants on the basis of birth weight alone. Rather it is applied to those fetuses who have evidence of faltered growth (Altman and Hytten, 1989). For this reason using a lower limit of birth weight, such as 2500 gm or the 10th or 3rd centiles of birth weight for gestation, creates the problem of identifying IUGR infants who are normally grown but continuously small, while excluding larger infants who are really growth retarded (Daikoku *et al*, 1979; Patterson and Pouliot, 1987). Ponderal Index, skinfold thickness and detailed neonatal clinical examination have all been shown to be better methods of identifying the truly growth retarded infants than crude birth weight for gestation (Miller and Hassanein, 1971; Oakley and Parsons, 1977; Daikoku *et al*, 1979; Hill *et al*, 1984; Patterson and Pouliot, 1987). The most popular definition of proportionality is based on Rohrer's Ponderal Index (PI: body weight x 100 / length³).

The individualised birth weight ratio is a measure of the difference between the actual birth weight of an infant and a predicted birth weight which has been calculated for the relative contributions of gestation, maternal weight and height, parity, and ethnic origin to this weight. The use of individualised birth weight ratio identifies the group of infants at birth who are at risk of neonatal complications, and the mothers with small infants can be reassured that their babies are normally grown and not at risk though they are small in size. Applying the individualised birth weight ratio can be a valuable tool in the antenatal period to predict if the foetus is growth retarded.

The individualised birth weight ratio combines the simplicity of birth weight measurement with the accuracy of clinical measurement in the identification of growth retarded baby (David *et al*, 1994).

2.9. Gender and IUGR

The factor of sex relates to the genetic growth potential of the infant, whereas the factor of parity relates to a maternally imposed constraint of the foetal growth potential (Thomson *et al*, 1968, Kloosterman, 1970). Sex of the baby, season of the year have

highly significant effect on birth weight (Ceesay *et al*, 1997). The use of a common standard to define infants below the 10th centiles of weight for gestation selects 15.4 percent of first born female infants but only 6.4 percent of later born males at 40 weeks gestation (Thomson *et al*, 1968). In a subgroup of a given community the distribution of birth weight is dependent on many variables such as maternal height, maternal weight, social class and others. Correction up to 500g to standard centiles have been proposed for some of these variables (Thomson *et al*, 1968). The drawback of centile charts is that they cannot confidently be used in a mixed population, i.e. population from different ethnicity, different country and socio-economic background (Kloosterman, 1979).

Table 13: British Growth standard measurements for boys and girls at term gestation (40 weeks) on the 10th centile i.e. the cut-off for IUGR.

Measurements	boys	girls
weight	2.616 g	2.5344 g
height	47.06 cm	46.45 cm
head circumference	32.66 cm	32.08 cm
body mass index	11.04	10.93

2.10. Risk factors for low birth weight, IUGR and smallness for gestational age

The risk factors for low birth weight can be divided into those that affect gestational age without having much effect on foetal growth, and those that have an effect on foetal growth without having much effect on gestational age (Mittendorf *et al*, 1993). For example cigarette smoking has only a slight effect on the length of pregnancy (Buncher, 1969; Mittendorf *et al*, 1993), but it can cause substantial growth retardation. Infants of smoking mothers weigh about 150g less at birth than those of non-smoking mothers (Papoz *et al*, 1982).

The risk factors for IUGR are almost similar in both symmetric and asymmetric groups. Chronic hypertension, anaemia, symptomatic urinary tract infection, twin gestation, poor obstetric history, poor weight gain, antepartum haemorrhage, maternal age less than 17 years, smoking, use of alcohol, and drug abuse, are the common factors responsible for both type of IUGR (Lin *et al*, 1991; Robyn *et al*, 1989; Kramer, 1987). But pre-eclampsia produces a higher incidence of symmetric IUGR than asymmetric IUGR (Lin *et al*, 1991).

Pre-term delivery is higher in the symmetric group than asymmetric group of infants. Term symmetric IUGR infants have a lower mean birth weight and small placenta than asymmetric IUGR infants (Lin *et al*, 1991).

Many studies have established a significant relationship between low birth weight and a number of socio-demographic variables (Williams and Chen, 1982; McCormick, 1985; Villar and Belizan, 1982; Kramer, 1987; Pickering *et al*, 1986; Kleinman and Kassel, 1987; Stein *et al*, 1987; Brooke *et al*, 1989; Ferraz *et al*, 1990). Associations with socio-demographic factors is of public health interest, since it helps to identify the target group of people for the prevention of low birth weight (Carmen *et al*, 1995).

2.10.1. In developed and developing countries

The causes of low birth weight in developing countries are different from those of developed countries. In developing countries, low birth weight is due mainly to intrauterine growth retardation (McCormick, 1985), whereas in developed countries the low birth weight is mainly due to prematurity (Villar and Belizan, 1982; Belizan *et al*, 1978). Factors contributing to low birth weight for developed countries include in order of importance: cigarette smoking, low caloric intake, and low weight gain during pregnancy, low pre-pregnancy weight, prematurity, female sex of foetus, and short stature (WHO, 1992). The potentially preventable risk factors that cause either a shortened gestation or intrauterine growth retardation in the USA are cigarette smoking (14%), low pregnancy weight less than 45kg (6%), genital tract infection (5%), narcotic addiction (4%), alcohol consumption (2%) and urinary tract infection (1%) (Kramer, 1987). Generally North American and Western European women are taller, heavier, and have better weight gain during pregnancy, and have the benefits of excellent antenatal care. The fact that they have good nutrient intakes and adequate antenatal care largely account for the high birth weights of their offspring.

There has been speculation whether the higher birth weights in African neonates compared to their South Asian counterparts, in spite of poor health care, is due to the fact that the parents are taller and heavier.

In developing countries risk factors for low birth weight in order of importance are: low maternal caloric intake or inadequate weight gain during pregnancy, low pre-pregnancy weight, short stature, malaria, and female sex of the foetus (WHO, 1992). As maternal weight increases the incidence of giving birth with a birth weight of less than 2500g decreases (Fernando *et al*, 1989; Goodburn *et al*, 1994).

It has been recognised that in any community, birth weight follows a socio-economic gradient (Gopalan, 1962). In India, the magnitude of difference in birth weights between the high and low income groups has remained about 400-500gm in almost all the regions of the country (Ramachandran, 1989).

By the 28th week of pregnancy a normal foetus attains 30% of the weight and 71% of the stature that it will have at the end of gestation (Belizan and Villar, 1988). This hypothesis suggested that the period of gestation in which foetal malnutrition begins is a fundamental determinant of the type of IUGR from which the new born will suffer (Lin, 1984; Villar, 1982). Symmetric new-borns are the result of foetal malnutrition throughout pregnancy. Studies on animals have shown that when malnutrition is induced all over the entire gestation period, the offspring have symmetric proportionality at birth, and the cellular division in all foetal organs is reduced by 15 to 20% (Winick, 1973). This kind of IUGR (type 1) found most frequently in developing countries, is closely related to the conditions of poverty and chronic malnutrition of economically disadvantaged mothers (Lin, 1984; Villar, 1982). The pathogenic factors are high parity, short birth interval, breast feeding, a prior infant during pregnancy, and low maternal weight gain during pregnancy. These factors can gradually deplete the mother's nutritional reserves (Jelliffi and Maddock, 1964), and as a result, can prevent the foetus from receiving the necessary nutrients during pregnancy.

2.10.2. By timing - before conception, during conception and early pregnancy; in later pregnancy

The factors responsible for low birth weight can be grouped into those occurring before conception, during conception and early pregnancy, and those occurring in later pregnancy.

i. Before conception

Low birth weight, pre-term delivery, and smallness for gestational age have all been associated with a wide range of parental characteristics (Sanjose and Roman, 1991). The duration of gestation and intrauterine growth are all determined by the health and nutritional status of the mother. Maternal malnutrition, ill health, and physical and emotional stress are the most frequent causes of prematurity and IUGR (WHO, 1980). Consanguinity seems to be associated with a higher prevalence of congenital malformation and also begins to retard growth at the same time (Al-Eissa, 1991). Maternal cocaine use, prior infant death, and unplanned pregnancy are associated with infant survival among low birth weight infants (Summit *et al*, 1996).

Maternal height and short birth interval, pre-pregnancy weight, and smoking affect intrauterine growth, whereas maternal pre-pregnancy weight and maternal age were associated with pre-term births (Barros *et al*, 1992).

In Bangladesh all women who were less than 16 years of age at the time of the delivery had low birth weight infants, regardless of socio-economic status, and all women whose post delivery weight was less than 41 kg had low birth weight infants. Regardless of age, height, and social class, women with an arm circumference of less than 20cm always produced low birth weight infants. The highest birth weight was observed among mothers between 26 and 31 years (Canosa, 1989). Among the population sample (both urban and rural hospital) of low birth weight infants in Bangladesh, IUGR was present in 48% of the

high social class urban group and in 81.5% of the low social class rural group (Canosa, 1989). The mean birth weight increases with parity up to the third, fourth (Rehan and Tafida, 1979) and fifth (Kortman, 1972) pregnancy and with maternal age up until 34 to 36 years (Gebre-Medhin *et al*, 1976; Rehan and Tafida, 1976). In a study of Pakistani mothers in Birmingham, UK, an extra centimetre of maternal height was associated with an extra 12g of baby weight. A short birth interval of less than 12 months is associated with an increased risk of low birth weight (Wharton, 1989).

In Bangladesh, blood pressure has some influence on birth weight. The lower (less than 90 mm Hg) the systolic pressure the lower the birth weight (Canosa, 1989), although this may be confounded by parity; primigravida mothers have a greater risk of elevated blood pressure, and also of low birth weight.

In a study among Bangladeshi women in UK, although the mean abdominal circumference and estimates of foetal weight are smaller at 28, 32, and 36 weeks of gestation than the Anglo-Saxon fetuses, they grow at a similar rate during the third trimester (Spencer *et al*, 1995). Maternal height less than or equal to 155cm, mid upper arm circumference less than 24 cm, female sex of the infant, primipara, maternal weight less than 50kg, were associated with pre-term delivery and increased risk of IUGR (Meda *et al*, 1995).

ii. In early pregnancy

The growth rate of a foetus is influenced by the energy supply and energy consumption to the mother. Heavy physical labour during pregnancy affects the birth weight when mothers have energy intakes below the WHO/FAO recommended standard (Tafari *et al*, 1980; Lechtig, 1988). Anaemia is more frequent in mothers giving birth to low birth weight infants. More than 70% of women in Bangladesh are anaemic having less than 10g of haemoglobin and 90 percent are malnourished (Gordon *et al*, 1963). Abortion, premature births, low birth weight, and postpartum haemorrhage are associated with low haemoglobin levels during pregnancy (Royston, 1985). When maternal anaemia is sufficiently severe, the delivery of oxygen to the foetus becomes inadequate for the

demand of oxygen by the foetal tissue in experimental sheep; this response might explain in human pregnancies why pregnant anaemic women are more likely to be delivered of infant who are stillborn or hypoxic at birth (Paulone *et al*, 1987).

During pregnancy iron requirement is high because iron is necessary to cover basal losses, the increase in maternal cell mass and the constitution of the foetus to the placenta. The factors that affect the birth weight and intra-uterine growth also affect the placental ratio e.g. pre-eclampsia, and chronic medical illness (Lao and Wong, 1996). Large placental weight was associated with a low maternal haemoglobin and a fall in maternal mean cell volume during pregnancy. Each level of fall in mean cell volume is related with a rise of placental weight as haemoglobin fell. The highest ratio of placental weight to birth weight occurred in the most anaemic women with the largest fall in mean cell volume.

The important factors affecting birth weight and placental ratio are prematurity (Godfrey *et al*, 1991), maternal anaemia (Godfrey *et al*, 1991; Beischer *et al*, 1970), cigarette smoking (Wingerd *et al*, 1976), pre eclampsia (Readman, 1992) and a birth at high altitude (Kruger and Arias, 1970). Anaemia and iron deficiency during pregnancy were associated with large placental weight and a high ratio of placental weight to birth weight (Godfrey *et al*, 1991). Placental hypertrophy occurs at the cost of foetal growth and placental hypertrophy may be the adaptation for maternal malnutrition (Barker *et al*, 1993). Low birth weight rates were tripled, and of pre-term delivery were more than doubled, with iron deficiency, but not with other anaemia. But if anaemia is accompanied with vaginal bleeding then the odds ratios for low birth weight increased five fold for iron deficiency and two fold for other anaemias (Scholl *et al*, 1992). During the second trimester, anaemia approximately doubled the risk of pre-term delivery, but during the third trimester it was no longer a risk factor (Scholl and Hediger, 1994). Maternal illness during pregnancy, nulliparity and failure to attend three antenatal visits are risk factors for low birth weight (Meda *et al*, 1995).

iii. In later pregnancy

In later pregnancy gestational age is the most important factor affecting birth weight. An extra week of gestation was associated with an increase in birth weight of 150g (Wharton, 1989). Severe pre-eclampsia is significantly associated with low birth weight, higher incidence of intrauterine growth retardation, and respiratory distress syndrome. There is an increased risk of low birth weight, intrauterine growth retardation, preterm birth, and congenital malformation among the second and third trimester bleeders, but there was no association between bleeding and perinatal mortality (Sipila *et al*, 1992; Fourn *et al*, 1994) which is discussed in more details in 'risk factor during pregnancy'. The birth weight of infants born to mothers with infected placentas were lower than those of infants born from non-infected mothers: the difference of weight varied from 55g to 310g (Robyn *et al*, 1989).

iv. Seasonal variation

In Bangladesh, there is a seasonal variation of birth weight which may reflect poor maternal nutrition and variations in energy expenditure during the last trimester of pregnancy. Birth weight is lowest in the months of September to November. The reduction in birth weight was caused by a combination of increase in pre-term delivery and reduction in birth weight in term deliveries (Hort, 1987). There was a seasonal variation in birth weight in rural Gambia, which was 250gm higher in the harvest season (April to May) than in the hungry season (Ceesay *et al*, 1997).

Table 14: Factors responsible for low birth weight and IUGR (by timing); prepared from literature review

Before conception	In conception and early pregnancy	Later pregnancy
Maternal malnutrition	Heavy physical work during pregnancy	Gestational age
Ill health	and energy intake below WHO/FAO recommended standard	Pre-eclampsia
Physical and emotional stress	Anaemia	Bleeding
Consanguinity	Pre-eclampsia	Infection
Short birth interval	Chronic medical illness	Seasonal variation
Pre-pregnancy weight	Cigarette smoking	Placental abnormalities
Smoking	Birth at high altitude	Uterine malformation
<16 years old	Failure to attend 3 antenatal visit	
Post delivery weight <41kg		
Short birth interval <12 months		
Systolic blood pressure <90mm hg		

Note: Factors tabulated from the following references: Al-Eissa, 1991; Barros, 1992; Canosa, 1989; Wharton, 1989; WHO, 1980; Tafari, 1980; Gordon, 1963; Royston, 1985; Godfrey, 1991; Krueger, 1970; Scholl, 1992; Sipila, 1992; Robyn, 1989; Fourn, 1994; Ceesay, 1995; Hort, 1987.

2.10.3 By origin of the problem: foetal, placental and maternal causes

Factors associated with development of IUGR and low birth weight may also be classified as of foetal, placental or maternal origin.

Foetal causes

These include genetic abnormalities, congenital malformations and foetal transplacental infection (Robyn *et al*, 1989).

Placental causes

The placenta is the organ providing nutrition and respiratory support necessary to sustain foetal life. Therefore abnormalities of placental structure and function are related to development of IUGR. Placental abnormalities include abnormal cord insertion, multiple infarcts, placenta previa, abruptio placenta and circumvallate placenta (Raymond and Mills, 1993). Increased placental ratio, placental function and weight is associated with foetal growth retardation (Lao and Wong, 1996; Yu-KM, 1992). Placental insufficiency or chronic villitis is found in a large number of cases of IUGR than did appropriately grown pre-term infants. Cases with asymmetric IUGR tended to have more lesions than did cases with AGA infants (Salafia *et al*, 1995). Foetal growth retardation may not be due to placental lesion but to underperfusion of placenta. Most placental lesions associated with IUGR in pre-term infants are related to underperfusion. The extent of placental damage rather than uteroplacental vascular lesion determines foetal growth (Salafia *et al*, 1995).

Maternal causes

The growth and development of the foetus in utero reflects a balance between the foetus, placenta and the mother. The maternal causes of IUGR are nutritional, hypoxic, vascular, renal, haematological, and environmental (Raphael and Michael *et al*, 1992; Robyn, 1989). Maternal factors related to type 1 IUGR were nutritional and socio-demographic. Type 2 IUGR was found to be related to obstetrical characteristics such as the number of previous deliveries, and birth interval (Neela *et al*, 1991; Nieto *et al*, 1994). More symmetric than asymmetric pregnancies with IUGR result in pre-term delivery (Lin *et al*,

1991). Factors associated with pre-term labour were age more than 35 years, height less than 156 cm, anaemia or UTI in pregnancy, abruptio placenta, polyhydramnios, premature rupture of the membrane, IUGR, foetal distress and intrauterine death (Tabassum *et al*, 1994; Rahman,1984). Primiparity constitutes an independent risk factor for IUGR (Vardi *et al*, 1994). A previous low birth weight delivery increases the risk nearly two and a half times among non-smokers. If a mother both smoked and had a previous low birth weight, the relative risks rose to nearly five and a half. Low maternal pre-pregnancy weight less than 50kg, increased the risk of small for gestational age birth almost two fold among non-smokers, while low pre-pregnancy weight and smoking together increased the risk of small for gestational age birth fourfold. A low weight mother who smoked and also had previous low birth weight delivery, had a risk of small for gestational age birth that was nearly six times that of a mother without those characteristics, smoking throughout gestation could be associated with type 1 IUGR (Bukketeig *et al*, 1993; Belizan and Villar, 1988).

Prior delivery of a pre-term and or low birth weight SGA infant is the strongest determinant of a subsequent low birth weight infant delivery. Even adequate prenatal care during subsequent pregnancy did not provide the protection against the repeat delivery of low birth weight. The tendency of women having repeated low birth weight infants in spite of adequate prenatal care needs further research on the underlying pathophysiology of pre-term and SGA delivery (Raine *et al*, 1994).

Table 15: Summary of risk factors for low birth weight and IUGR (by origin of problem); prepared from literature review

Foetal	Placental	Maternal
Genetic abnormalities Congenital anomalies Foetal transplacental infection Foetal distress	Abnormal cord insertion Multiple infarct Placenta previa Abruptio placenta Circumvallate placenta Chronic villitis	Maternal malnutrition Hypoxic Vascular Renal Haematological Infection during Pregnancy Early rupture of membrane UTI in pregnancy No. of previous delivery Polyhydramnios Primiparity

Note: Factors are tabulated from the following references: Robyn,1989; Raymond,1993; Lao,1996; Yu-Km,1992; Salafia,1995; Raphael,1992; Neela,1991; Nieto,1994; Lin,1991; Tabassum,1994; Vardi,1994; Bukketeig,1993; Belizan,1988; Raine,1994

2.11. IUGR and subsequent growth and development

2.11.1. Effect of IUGR on neonatal and infant growth

In a UK study there was no difference in the postnatal growth between preterm infants whose size was appropriate for gestational age and those small for gestational age (Cooke *et al*, 1993). When postnatal weight /length ratio was examined, AGA and SGA infants grow similarly, no difference was noted in growth between the asymmetrically SGA and symmetrically SGA infants.

Within the low birth weight group there is a marked difference between the AGA and SGA children, with SGA children having significantly lower occipito frontal circumference than AGA children (Elliman *et al*, 1992).

The body weight, body length, and head circumference were significantly reduced in the full term SGA, pre-term AGA, and pre-term SGA infants in comparison to full term AGA infants. Minor neurological dysfunction was not related to body weight or length. Full term severely growth retarded infants showed a relationship between head circumference below the third centile and minor neurological dysfunction (Hadders *et al*, 1990).

2.11.2. IUGR and infant morbidity

The IUGR children have twice the risk of being hospitalised for diarrhoea compared with appropriate birth weight, term children. For pneumonia, pre-term and IUGR children were hospitalised significantly more than appropriate birth term children. Several studies have shown that pre-term and IUGR infants present a rather different pattern of evolution in terms of growth and morbidity. Pre-term infants with weight appropriate for their gestational age usually catch up in growth (Villar *et al*, 1984).

IUGR and low birth weight infants suffer from increased morbidity and mortality and different patterns of growth than infants of normal birth weight (McCormick, 1985; Casey *et al*, 1991). Although the growth velocity may be similar for the two groups, overall, low birth weight children are likely to be shorter and lighter than children of normal birth weight (Elliman *et al*, 1992; Vohr and Oh, 1983).

2.11.3. Effects of IUGR and growth trends

Some studies show that gestational age is a more accurate predictor of perinatal morbidity and mortality (Verloove *et al*, 1986; Writter, 1993). The outcome and quality of growth and development are better in those infants who had not suffered intrauterine growth retardation (Ramachandran, 1993).

Studies in Guatemala (Villar *et al*, 1984; Villar *et al*, 1990) showed that important differences exist in the growth and development of symmetric and asymmetric new borne. Asymmetric new borne do better than symmetric new borns in the long run.

Significantly more ELBW children were of short stature and low weight (less than 3rd centile). Intrauterine growth retarded infants remain smaller postnatally, however, especially if their Ponderal Index shows that they are chronically stunted rather than wasted, indicating long-term intrauterine suffering (Villar *et al*, 1984).

2.11.4. Effect of IUGR on cognitive development

Very low birth weight small for gestational age group of children scored significantly lower in visuospatial ability, non-verbal reasoning, strategy formation, and gross motor co-ordination (Smedler *et al*, 1992). Children born earlier (less than 33 weeks), had a high incidence of behavioural and educational problems. Very pre-term infants develop different neurobehavioural organisation than full term infants (Smedler *et al*, 1992). Small for gestational age infants develop a major handicap less often than appropriate for gestational age infants (Veelken *et al*, 1992; Calame *et al*, 1983; Commey and Fitzhardinge, 1979; Knobloch, 1982). Children born small for gestational age and children having very low birth weight, less than 1500gm, are at risk of developmental problems, even when obvious pathology and disability are absent (Smedler *et al*, 1992; WHO, 1988).

2.12. Outcome of low birth weight infants

Low birth weight is one of the most important determinants of subsequent mortality and morbidity of infants. The overall public health importance of low birth weight is determined not only by its relative risk of morbidity and mortality but also on its prevalence in a given population. If low birth weight is common, as it is in developing countries, even a small relative risk may be of public health significance.

2.12.1 Neonatal outcome of low birth weight infants

IUGR increases the risk of being born with asphyxia, hypoglycaemia, hypothermia, neonatal hyperviscosity, hyperbilirubinaemia (Belizan and Villar, 1988) and birth defects (Khoury, 1988). IUGR increased the risk of early neonatal mortality. The study done by Haas in Santa Cruz, Bolivia, found that infants who were born before 37 weeks of gestation had 23-100 times the mortality risk of infants born at full term and normal weight. The proportionately growth retarded infants had nearly twice the mortality of the full term, appropriate-weight infants, whereas disproportionately growth retarded infants had 2.9-5.7 times the mortality rate of the full term, appropriate weight infants (Haas *et al*, 1987).

In India neonatal mortality accounts for over 60% of all infant deaths (Bhave, 1989; Vajpayee and Govila, 1987). A high risk of neonatal mortality associated with low birth weight has been reported in both developed and developing countries (Martorell and Gonzalez, 1987).

Growth retarded neonates (full-term and premature) have various cellular and humoral immunological mechanisms, during their first days of life. Foetal growth retardation causes deficiencies to the immature neonatal host defence mechanisms. Impaired immuno competence in the growth retarded infants is probably the main cause of increased frequency and severity of infection. It has been reported that IUGR is associated with weaker cellular immunity during the first months of life (Xanthou, 1985).

When the infant is not breast fed in the first 2-3 days postpartum, neonatal death rates often rise (Pratinidhi, 1986). The sequel of prematurity and/or low birth weight are the problems of immediate survival from hypoxia and acidosis resulting from respiratory problems of small premature infants, hyperbilirubinaemia, hypoglycaemia, malnutrition, bacterial infection and jaundice (Bhave, 1989; Chen and Li, 1993; WHO, 1986; Komich *et al*, 1973; Epstein *et al*, 1988). The rates of bradycardia, respiratory distress syndrome, hypocalcaemia, ventilatory support, apneic crises, transient neurologic sign, and poor neonatal outcome (neonatal death or cerebral palsy) significantly correlated with the increasing severity of IUGR. In pregnancies complicated by idiopathic IUGR, most short-term neonatal complications are inversely related to the severity of growth failure (Spinillo *et al*, 1995). Morbidity defined by birth asphyxia, respiratory distress and neonatal infections was higher in proportionally small infants who were delivered at term (Cuttini *et al*, 1991).

In the case of very low birth weight infants (birth weight between 700 and 1500gm) no difference was found in the postnatal growth between infants whose size was appropriate for gestational age and those small for gestational age. This might be due to the small number (8) of symmetrically growth retarded infants in the study. Weight but not head or length gain was less in the smaller (<1000gm), than the larger (>1000g) VLBW infants (Cooke *et al*, 1993). This might reflect increased energy requirements or poorer fat assimilation in the smaller infants.

It has been reported from USA that black neonates with birth weight less than 2.5kg have higher survival rates than white neonates with similar low weight. This is because among blacks in the United States, as among Asians, a substantial proportion of infants born with birth weight less than 2.5 kg are mature but small for age and hence have a better survival rate, as compared to white neonates weighing less than 2500gm who are mostly pre-term. Among infants with low birth weights who survive, however, the ultimate outcome and quality of growth and development are better in those infants who had not suffered intrauterine growth retardation (Yerushalmy, 1967).

2.12.2. Outcome of symmetric and asymmetric IUGR

Different studies have shown different outcomes. Villar (Villar *et al*, 1990) indicates that neonatal morbidity among asymmetric new-borns tend to be higher than among symmetric new-borns. The reason for this is that asymmetric new-borns suffer from malnutrition during the last trimester of pregnancy and can therefore be at greater risk of morbidity and mortality in the neonatal period. On the other hand symmetric new-borns may have suffered foetal malnutrition during the entire gestation period; and so they may have experience reductions in both cell size and cell division. As a result, over the medium term symmetric new-borns face a higher risk of disorders affecting their physical and intellectual development. In some cases these risk differences disappear over time, as cultural, economic and environmental influences become more important determinants of childhood development than IUGR. In the vast majority (>86%) of healthy full term singleton SGA infants will achieve catch up in height during the first 6-12 months of life, and that this is almost independent of whether birth weight or birth length is used to define SGA. Of the remaining, non catch up SGA infants, about 50% remain short in final height, and thus constitute a high risk group for persistent short stature (Karlberg *et al*, 1995; Fitzhardinge and Stevens, 1972; Villar *et al*, 1984; Bhargava *et al*, 1982; Davies *et al*, 1983; Job and Rolland, 1986; Westwood *et al*, 1983; Fitzerdinge and Inwood, 1989). The asymmetric new-borns experienced accelerated early gains in weight, length, triceps skinfold, and head circumference relative to symmetric new-borns (Villar *et al*, 1984). The stature of children in the symmetric group was found similar to that of normal groups. The head circumference of children in the asymmetric group was comparable to that of the normal group up to 18 months; after that age, however, the speed of growth declined to the same level as that of the children in the symmetric group. In contrast, the growth of the symmetric new-borns was not accelerated, and their height and weight remain below those of the normal group (Villar *et al*, 1984).

Small for gestational age infants are heterogeneous: some are malnourished, some are preterm. There are differences between these two groups of infants in morbidity and mortality (Miller and Hassanein, 1971; Hill *et al*, 1984). The pre-term infants and neonates require greater per kg amounts of protein, calories, fluid, and micronutrients

than older children (Cochran *et al*, 1988). Pre-term children gradually caught up with their appropriate birth weight counterparts. The term small for gestational age infants were more likely to survive to one year of age than preterm, largely because of greater survival in the neonatal period, in all weight categories under 2500gm. Very small for gestational age and appropriate for gestational age infants who survived and who did not have severe, moderate, or mild impairment appeared to be approximately at equal risk of rehospitalisation and prolonged illnesses. There were no consistent difference between small for gestational age and appropriate for gestational age infants in the duration of hospitalisation, likelihood of rehospitalisation or total days of hospitalisation in the first year of life (Starfield *et al*, 1982). The main causes of illnesses were asphyxia neonatorum, infection, respiratory problems. Respiratory problems and infection constitute the main causes of death. Growth was much impaired by diarrhoea, lower respiratory infections, skin and eye infections (Woodruff *et al*, 1983).

Overall, wasted IUGR infants exhibit greater postnatal catch up growth and less severe cognitive deficits than those who are stunted. Thus the clinical importance of low birth weight may depend on its type, prematurity or IUGR, 'wasted' or 'stunted' IUGR.

Among IUGR infants the risk of death in the first month is significantly higher in the proportionately small than the disproportionately small infants especially when the infants are term birth. Symmetric IUGR has got a worse foetal outcome than asymmetric IUGR. Pre-term delivery, low Apgar scores at both 1 and 5 minutes, foetal acidosis, and neonatal mortality are common in symmetric IUGR (Lin *et al*, 1991). Cuttini shows neonatal morbidity is more common among proportionately small term infants, except in hyperbilirubinaemia which is higher for disproportionately small infants rather than proportionately small infants (Cuttini *et al*, 1992).

Morbidity rate for symmetric IUGR is higher than that for asymmetric pre-term IUGR neonates, and symmetric IUGR neonates have a lower body weight and a smaller placenta than do term asymmetric IUGR infants. Neonatal morbidity rate among pre-term symmetric IUGR infants is significantly higher than that of pre-term asymmetric IUGR

infants while symmetric new-borns confront a higher risk of impaired physical and mental development (Lin *et al*,1991; Perez *et al*,1992).

IUGR is significantly related to premature birth (Ott,1993). Because of the pathologic differences at birth, it is reasonable to suppose that symmetric and asymmetric new-borns respond differently to the environment. In this regard, differences have been found between symmetric and asymmetric new-borns with respect to the effects of maternal dietary supplementation, perinatal morbidity (Villar *et al*, 1990), postnatal growth, and behavioural development (Villar *et al*, 1984).

2.12.3. Longer term outcome of low birth weight infants

The importance of low birth weight for perinatal and infant mortality, particularly in developing countries is well recognised (Victoria *et al*, 1987), and recent studies have suggested links between birth weight and adult diseases, which may have important implications for developing countries as their populations age (Barker *et al*, 1993). Foetal growth retardation is found to be associated with the development of cardiovascular disease in adulthood, mortality from ischaemic heart disease specifically linked with head size at birth (Moore *et al* ,1995). It is possible to identify the infants who are at risk of developing hypertension and cardiovascular disease in the adulthood by means of the placental ratio (Lao and Wong, 1996).

There is sufficient evidence from follow up studies of high-risk infants that a high incidence of physical and mental defects is found in this group: spastic dislegia, delay in sitting, standing, and walking, with subsequent clumsiness and a tendency to walk in their toes (Lubchenco *et al*, 1963; Drilhen,1970; Paine,1969; Weiner,1967; Patricia *et al*,1973).

Studies have suggested a possible relation between low birth weight and infectious disease mortality (Jason, 1989; Victoria *et al*, 1992; Victoria *et al*, 1988; Gibson and Alexander, 1985). Infections occur more frequently and are more severe and longer lasting after IUGR. Moderate low birth weight renders individual vulnerable to infectious disease mortality during both infancy and childhood. This vulnerability appeared to be

attributable primarily to pre-term birth rather than to intrauterine growth retardation (Read *et al*, 1994). Compared with normal birth weight infants and children, moderately low birth weight infants and children were at increased risk for both infectious and non-infectious deaths (Read *et al*, 1994).

Most surviving children with birth weight <1500g remain free of significant functional impairments. Those infants who do not manifest severe disability do seem to be at risk for learning problems, although overall cognitive function is in the normal range. On an average, stature appears to remain lower, although there may be catch up growth later in childhood (Blackman, 1991).

2.13. Interventions to reduce neonatal mortality and morbidity of low birth weight infants in developing countries

The prevention of low birth weight is a public health priority in many developing countries (Kramer, 1987). The endogenous causes of death (prematurity, congenital malformation) occur most frequently in the neonatal period, so neonatal deaths are an indicator of the availability of health service resources, particularly in Bangladesh where little provision is made for prenatal and perinatal care (Paul, 1991). About two thirds of all first week deaths have been assessed preventable (Ghosh and Dagha, 1967; Mavalankar, 1991).

The problems for high perinatal mortality rate in developing countries are: shortage of medical staff; poor communications that affect the patients use of preventive services and the inability of mothers to get to the hospital in emergencies before the foetus has died; scaring of mothers about surgical manipulation in the hospital, shortage of drugs, equipment and consumable, low status and levels of education amongst women which often result in inadequate and late use of services which are offered (Larsen, 1992).

Maintenance of body warmth is an important aspect of neonatal care since even small changes of environmental temperature can significantly influence neonatal mortality

(Scope, 1970; Hey, 1975). Deaths in infants under 1500gm can be reduced by a quarter or more if their body temperature is maintained above 36⁰ C (Hey, 1971). Excessive warmth is equally harmful (Yashiro *et al*, 1973). Skin to skin contact is a valuable method of thermoregulation in developing countries where the rate of low birth weight is high, and incubators were not commonly used (Mondale *et al*, 1989).

Focusing on pregnant women rather than infants may result in fewer low birth weight infants (Marchione, 1990). Antenatal teaching might include subjects like feeding, recognition of infection, and growth and development, current health problems and managing within the health care system (Brooten *et al*, 1989) and antenatal clinic at the hospital to which mothers with high risk factors can be referred. It is important to develop a system of strategically placed health centres which can safely deliver low risk mothers and which have reliable means of transferring mothers who get into difficulties. There must be a constant movement of mothers from one part of the system to another. This means a patient based record keeping system is indispensable. The private medical practitioners should keep their records on the same hospital records, so that the patient and clinical staff can reap maximum benefit from their clinical observation. The hospital labour ward to which the high risk mothers come for delivery must have clear protocols of management for every common problems encountered in that population. A team approach is essential. A team of personnel should be trained who have the skills to provide a high standard of antenatal and intrapartum care so that the doctor can give full attention to those mothers who really need specialist skills, and to identifying those areas from which most of the obstetric disasters come. The most valuable method of raising the standard of antenatal, intrapartum and neonatal care is to select the most competent midwives in the unit, and train them for an extended role (Larsen, 1992).

In a study in India it was found that 77% of the perinatal deaths occurred in unbooked cases as compared to 23% in booked cases (three or more antenatal visits) (Parmar *et al*, 1994). Mothers who enjoyed intensive prenatal care had better chances of good neonatal outcome than those whose mother came to the hospital not before onset of preterm labour. So extensive prenatal care with very early assessment of risk factors for preterm

delivery is the prerequisite to reduce the rate of preterm delivery (Ohde *et al*, 1995). Survival of very low birth weight infants requires additional high technical, financial, and manpower resources, which most centres in developing countries cannot afford at present time. Therefore, efforts are probably better concentrated on decreasing the incidence of low birth weight (Dawodu and Effiong, 1985).

Neonatal and perinatal deaths can be caused by maternal factors. Maternal prepregnancy condition and delivery related factors are responsible for most of the neonatal loss. By definition health is not only related with medical factors, mental, social, economical and some other factors are closely related with the condition of health. As the extremes of age and birth spacing is related with low birth weight, and in Bangladesh 80% of the first pregnancy occur in teenage, an extensive female education programme might improve the condition. Education will increase the age of marriage, increase the utilisation of services, increase the opportunity of women's employment, which in turn will increase birth spacing. What kills mothers also kills infants. Therefore, early identification of pregnancy, antenatal care, identification and management of risk factors, and care during delivery can prevent maternal and neonatal deaths. The care activities to adverse outcome of pregnancy should include early registration of pregnancy to identify risk women, education about dangerous signs, treatment of medical problems, immunisation, nutrition education, deliveries with trained attendants and prepare referral system. The elimination of maternal modifiable factors would reduce neonatal mortality by 94% (Taha and Gray, 1993). To reduce the work load about maternal modifiable factors, 100% antenatal coverage of all primiparas and all first born infants is suggested. Home visitation by family welfare visitors is a promising strategy.

The home visitation should include:

1. Focus on mothers at greater need of services.
2. Continuing follow up from beginning of pregnancy to the whole first year of infant life.
3. Education and promotion of positive health behaviours, infant care, and personal hygiene (Olds, 1992). Training of TBAs with regard to antenatal, intranatal, and postnatal care of mothers and new-borns will improve their quality of care (Begum *et al*, 1990).

In Bangladesh, a study in Matlab showed that after a preventive, community based home delivery set of interventions overall neonatal mortality dropped by 17%, and infant mortality dropped by 39% (Fauveau *et al*, 1990). Here availability of resources is very limited, very few in relation to necessity, and most of the equipment are condemned. So alternative methods should be sorted out. Instead of incubators and ventilators, extra nursing staff, round the clock laboratory facilities, warm room (Daga *et al*, 1986), mother's participation in neonatal care (Daga *et al*, 1986), mother's milk (Daga and Daga, 1985), minimum handling and minimum interventions sound realistic (Daga and Daga, 1989).

2.14. Why this study is useful ?

The previous discussion clearly shows how serious the problem of low birth weight is in developing countries, and how deficient Bangladesh is in research and publications. There are very few publications concerning low birth weight infants and many are not statistically sound. It is very difficult to estimate the size of the problem accurately because there is no national registration system. As infant mortality remains high in Bangladesh, and most of the deaths occur in the perinatal and neonatal periods, reduction of neonatal mortality is the main priority to further reduce infant mortality.

Moreover we know that low birth weight is an important determinant of quality of life and neonatal mortality and that the low birth weight rate is the highest in Bangladesh than that of any country world-wide. Interventions to reduce infant mortality among this high risk low birth weight group are likely to have the most impact.

The risk factors for low birth weight start before pregnancy and continue after pregnancy. This study includes not only the low birth weight infants but their mothers as well, which helps our evaluation of risk factors. The infants were followed up for one month to identify risk factors for neonatal mortality and morbidity.

Morbidity is very difficult to define and measure. Morbidity surveys frequently obtain information on the presence of disease at the time of interview or over variable preceding interview. One disadvantage of this approach is that acute disease with a short duration or with a short survival time may be underestimated, whereas more chronic illnesses of longer duration may be over represented (Black *et al*,1984). The other disadvantage is that the research has to depend on mothers and relatives recall of disease during interview which may be misleading. In this study this problems have been overcome by ensuring that the recall period at the time of interview is no more than one month.

Bangladesh continues to have a high risk of mortality associated with pregnancy and its outcome. 80% of girls become mothers in their teenage years. Therefore efforts to reduce neonatal death in this population should focus on the prevention and care of low birth weight infants. But in developing countries the gap between need and availability of resources is wider than developed countries. However this gap cannot be narrowed in the near future by conventional high cost care.

As the latest infant mortality rate is 80/1000 live birth (HNP sector strategy,1997) and most of this mortality occurs among low birth weight neonates this study will help to determine the risk factors for neonatal mortality and morbidity, the potential for cost-effective interventions on neonatal care.

2.15 Aims and objectives

The overall aim of the study was to design more appropriate services and interventions which may be targeted to low birth weight infants in Bangladesh.

The objective of this study in relation to neonatal mortality and morbidity were :

1. A prospective cohort study of 1000 low birth weight infants to one month of age to measure mortality and morbidity outcome.
2. A case control study of low birth weight infants who die (cases) and matched survivors (controls) to evaluate risk factors :

- a) clinical
- b) haematological
- c) placental
- d) socio-economical

The result of this study will provide

- reliable information on the causes of neonatal death in a community
- knowledge of cause of death can also help to evaluate the impact of programmes
- directed towards reducing mortality
- successful design of health care delivery system
- selection of appropriate medical technology
- optimising the cost effectiveness of future health programme.

Chapter 3

Methods

3.1 Study population

The study population was selected from Mitford hospital, a large teaching hospital with 700 bed capacity. It has all major departments with all specialities and investigation facilities. The treatment is free including medicine subject to availability to the Government supply. The hospital is situated in the old part of Dhaka city by the side of the river Buriganga. It covers the urban, suburban, and rural areas. Rural people come from the other side of the river. Most of the people are from rural and urban slums. I enrolled 1000 low birth weight infants and their mothers who delivered in the hospital and fitted the inclusion criteria. Nearly 4000 deliveries occur in this hospital each year. 80% of these come directly to the hospital without any referral or antenatal check-up. 26% of the infants are born with low birth weight and 75% of the mothers come from poor socio-economic condition (data collected from hospital source).

3.2. Study design

This is a prospective, case control study based in hospital with community based follow up. The study population was all low birth weight infants born in the Mitford hospital during the period of May 1994 to August 1995. A cohort of low birth weight infants during the first month of life studied to find the risk factors for perinatal mortality, neonatal mortality and morbidity. Retrospective data on pregnancy of the mothers, labour, delivery, the infant condition, and treatment given at birth and during one month was recorded. Moreover prospective study on follow up after 28 days to find morbidity of infants, general condition of the mothers, detailed dietary history of mother and infant and socio-economic details was taken to find the risk factors for the morbidity and mortality of the infant. The cases are those who died during the first four weeks of life and those who survived were the controls. Verbal autopsy was done to find the cause of death. All the details of cases were compared with the controls (who survived).

3.3 Definition of cases and control

The study was analysed with the following comparisons made between subgroups:

1. comparison of the continuous and categorical variables between all deaths (stillborn and neonatal deaths) versus survival group.
2. comparison of continuous and categorical variables between stillborn and survival group.
3. comparison of all the continuous and categorical variables between the neonatal deaths and survival group.
4. comparison of variables between early death (0-7 days) group and late death (>7 days) group.
5. comparison of risk factors between poor growth and normal growth.

For ethical reasons this study included medications and treatment from health resources available to the community, local health systems, and from the investigator when illness detected.

3.4. Sample size calculation

In making the sample size calculations, we made a set of assumptions concerning the prevalence of low birth weight infants in the hospital population, the expected mortality rate for LBW infants, and for risk factor analysis an estimate of the differences we might reasonably detect. Our assumption were as follows:

(1) Prevalence of low birth weight:

We expected the prevalence to be 30-40 per 100 live births. If there were 4000 deliveries per year in the hospital we would expect 1200 -1600 low birth weight deliveries.

(2) Low birth weight mortality rate:

Based on previous studies (Rahman, 1985; Rahman, 1989) we estimated low birth weight mortality would be at least 80 per 1000.

(3) Expected and detectable risk differences:

We made projections based on 80% power, 95% probability that if the two samples differ this reflects a true difference in the two population (confidence interval), and two control infants enrolled for every case. The sample size was calculated with the help of Epi Info. [NB In fact we subsequently used all survivors as controls but we did not base our sample size calculations on this premise].

We hypothesised differences, or odds ratios for increased risk of neonatal deaths, for three variables

- a) maternal anaemia
- b) infant anaemia
- c) incidence of placental pathology

a) For maternal anaemia (Hb less than 11g/dl) we assumed that 75% of control would be anaemic and that this might increase to 90% or above in cases. This gave a sample calculation of 174 controls and 87 cases.

b) For infant anaemia (Hb less than 12 g/dl) we expected 20% of controls would be anaemic and hypothesised an increase to 40% among cases. This gave a sample size calculation of 132 controls and 66 cases.

c) For macroscopic placental pathology we expected 20% of controls would have some pathology which might increase to 40% in cases. This gave a sample size calculation of 132 controls and 66 cases.

On the basis of these calculations we assumed that we would need to enrol upto 90 low birth weight neonatal deaths. During the study it became clear that LBW mortality was greater than expected, so we enrolled 1000 (data on one infant was lost) and finished with 103 neonatal deaths.

Inclusion criteria

- mothers delivering a low birth weight (<2500gm) normal infant of >28 weeks gestation.
- mothers living around 80 km radius of the hospital.
- mothers delivering a fresh stillborn infant (within 48 hrs of death).
- mothers who are willing to join the programme.
- mothers who could give their detailed address.

Exclusion criteria

- mothers delivering a normal birth weight infant (>2500 gm).
- mothers living more than 80 km radius of the hospital or which takes more than 2 hrs. of journey.
- infants born with congenital anomaly.
- infants born before 28 weeks of gestation.
- mothers who are not willing to join the programme.

Study protocol

The test protocol was as follows:

For all low birth weight infants (n=1000), as soon as the infant born the birth weight was taken and if it was less than 2500 gm, detailed anthropometry was completed. The condition of the infant was assessed by taking Apgar score at one minute and five minutes, rectal temperature, and time taken to resuscitate were recorded. The other parameters included with the new born details were methods of resuscitation needed, drugs used and time and type of feeding given. If the condition of the infant was good the baby was given to the mother, but if poor then the infant was transferred to the neonatal unit as soon as possible.

In case of a stillborn infant I took all the anthropometric measurements.

Placental details

As soon as the infant was born the placenta was taken in a polythene bag and preserved. After initial management of the infant, placental details were taken. Placental length, breadth, weight and morphological details were taken.

Follow up details of infant

These were collected as close as possible to the 28th days after birth. Data includes anthropometry, history of illness, any treatment given, dietary history, information about carer. The illness history was based on the signs/symptoms present at the time of visit and mother's recall about illness. If the infant died all the details of illness was noted following the WHO criteria of verbal autopsy to find the cause of death.

Follow up details of the mother

Mother's general condition, illness during this period, dietary history and knowledge of the mothers about low birth weight was taken.

Stages of work

preparatory phase

data collection stage

data entry stage

3.6. Preparatory stage - (4 weeks)

Phase 1 - (1 week)

a) Selection of co-workers - 1 day

I selected the co-workers from Mitford Hospital. They were four medical graduates and one office assistant cum accountant. These doctors had completed their M.B.B.S course successfully and finished their internship. Two of them were female and two were male doctors. They all had six months training in paediatrics.

b) Discussion about background and rationale of the study - 1 day

After selection of the co-workers I told them about the importance of the study, the importance of accuracy of the data, time scheduled for the work, background, rationale, and problems we could have to do the work.

c) Introduction, discussion and opinion about the questionnaires - 2 days

Questionnaires were discussed with each variable. The questionnaires were made in English but asked in Bengali. It was a set of seven questionnaires. We discussed about the variables, importance of each variable, and made some changes if needed.

d) Training introducing mothers, collection and examination of placenta and blood sample - 2 days

We went to the obstetric ward and introduced with the mothers who are in labour. Training of the placental examination was given by the Professor of Obstetrics and Gynaecology. Training for collection of blood sample and estimation of haemoglobin level was given by the Professor of Pathology.

Phase 2 - (1 week)

a) Initially training was given in taking anthropometric measurements of all infants and their mothers whatever may be the birth weight. Training was given by a paediatrician. Weight was measured by two decimal points and other measurements were taken with one decimal points. Measurements were taken as accurately as possible.

b) Training to assess the Apgar score at one minute and five minutes and assessment of gestational age - 3 days

As soon as the infant was born the Apgar score at one minute and five minutes were measured and checked by the physician. The gestational age was assessed thereafter by Capurro (Capurro, 1978) method and checked by a paediatrician and obstetrician.

Phase 3 - (1 week)

Practising and checking anthropometric measurements, Apgar scores, gestational age, and mother's anthropometric measurements were taken by the co-workers and the principal investigator individually. Then the data was checked to see the interobserver variations and accuracy. Usually we did not have more than 0.1cm difference. The error was discussed and corrected. We practised it in 50 cases.

Phase 4 - (1 week)

Pretesting the questionnaire - 6 days.

Mode of offering the mothers to enrol in our study, asking questions to them, how to interpret the answers, coding of answers, labelling and grading the scores, each and every variables and questions was initially demonstrated by the principal investigator and then practised by the co-workers. They practised it for six days and attended all deliveries at

that time and practised with the questionnaire. They practised it in 40 cases. At the end of the week the principal investigator and co-workers met together in the office and discussed the problems and made some changes in the questionnaire before finalising it for printing.

3.7. Data collection phase

The labour ward in the Mitford hospital was open 24 hrs, so the research assistants worked in the hospital for 24 hrs with a shifting schedule. Three doctors worked in the hospital and one doctor worked with me in the field to see the infants at home.

Data collection started from 5th May 1994 and finished in September 1995. We worked six days in a week. We took off one day in a week, holidays for religious festivals (about 15 days), and sometimes for strike (about 10 days). The doctors did their work for full time in the hospital. I started my work in the morning at 8 o'clock. I went to the ward first, took information about the previous day's work and then went to field with one doctor. We sat together one day in a week, made the progress report, update the works, make schedule for the next week and discuss and solve the problems. I checked all the machines before going to work every day. The interobserver variations were checked once a week.

I maintained a registrar book where the entry and outcome of the infant was registered with the same serial number given as identification number of the infant.

3.8. Pilot survey

After preparing a sample study design I went to Bangladesh to see the feasibility of the study and to do some administrative work for logistic support. Before going I took ethical clearance from Bangladesh and British Medical Research Council. I took permission from the Director of Mitford Hospital and Head of the Department of Paediatrics and Obstetrics and Gynaecology, Dhaka.

3.9. Measurement Procedures

Head, arm and chest circumference was measured by plastic baby tape. The measurement range from 1/2 cm to 60 cm with accuracy of 1 mm. It is a non-stretch non-shrink thin plastic tape developed specifically to loop over a baby's head and or around its arms to make head/arm circumference measurement easier.

3.10. Length measurement

Length of the infant was measured with a length range of 0-92 cm with accuracy of 1/2 cm. It is a light weight, portable, non-stretched, non-shrink and hygienic toughened plastic roll-up mat designed for measuring from birth to 2 years. The baby was laid supine on the mat in a flat surface either on the floor or in the hard flat bed. The head was positioned firmly against the fixed head-board, with the head in a vertical Frankfurt plane (imaginary line from the centre of the ear hole to the lower border of the eye socket in horizontal line). The co-worker hold the child's head in firm contact with the head board. At the same time the knees were extended by gentle and firm pressure, and the feet were flexed at right angle to the lower legs. The foot piece were moved to obtain firm contact with the heels and the length read to the nearest 0.1 cm.

Head circumference

Head circumference was measured by plastic baby tape. The head steadied firmly and the tape was winded firmly round the head, in front midway between the eye brows and the hairline or round the frontal bones just above the supraorbital ridges, and behind over the occipital prominences. Measurements were made to the nearest of 0.1 cm.

Chest circumference

Measurements were taken by plastic baby tape around the nipple line, preferably in the mid inspiration. The measurement was made to the nearest 0.1 cm.

Mid upper arm circumference

It was measured midway between the acromion and olecranon process. The plastic baby tape was hold firmly around the arm midway between the acromion and olecranon process and the measurement was taken to the nearest 0.1 cm.

Weight of the infant

Weight of the infant was measured by SOEHNLE 831000 with a range of 0-20 kg/40 lbs accuracy to within 10g. It is light weight and easy to operate. It has a slide-off flat bed bowl. It has a simple self-calibration facility, is robust, splash proof and hygienic design. It powers down automatically after being idle for two minutes and has low battery consumption. It is portable because it has a light weight shoulder strap. As soon as the infant born after separation of the placenta the APGAR score and weight was measured. The machine was calibrated before each measurement. We had a pre-weighed fixed piece of cloth to wrap the baby. The baby was weighed wrapped up with that cloth to avoid hypothermia and then from the total weight the weight of the cloth was subtracted. I used two scales, one in the field and one in the ward. The two scales were checked weekly against each other.

Mother's anthropometry

Mother's weight was measured by using SOEHNLE 7209 machine with a weight range of 0-130 kg and accuracy within 200 gm. It is light weight and easy to operate. It displays weight either in kg or in lbs. It has a self calibrated facility. Mothers were weighed bare footed wearing light clothes.

Mother's height was taken with the Minimeter 183 with length range of 0-183 cm accuracy of one mm. It is a light weight plastic injection moulded portable device which was permanently hung in the ward. Mothers were measured without shoes, standing up straight on a flat floor, with the feet together and with heels, buttocks, shoulders and back of the head touching the upright. the legs were straight and the shoulders relaxed. the head was positioned in the 'Frankfurt plane' and the arms hanging by the sides. Height was measured by the head piece compressing the hair and gently making contact with the top of the head.

Placental examination

As soon as the baby was born all placentas were examined macroscopically, by the attending doctor. The tools for the examination was a ruler, a toothed forceps, a pair of

scissors, a scale and a board. The ruler was permanently mounted over the cutting board, thus enabling rapid measurement of placental diameter. The shape of placenta was ascertained by stretching the placenta flat on the cutting board. Then the placenta was inverted by the examiner so that it assume the in utero position to ascertain the completeness of the membrane. Then the colour and appearance of the foetal surface of the placenta was determined. The colour of the membrane was examined. Thus both the maternal and foetal surface was examined. Then the cord was examined. The insertion, condition, no of vessels in the cord was examined. The net weight of the placental disc (excluding the cord) was measured. Measurement was taken by putting it in a polythene bag and weighed in the same weight machine for the infant. The colour of the placenta, presence of clot, fibrous tissue, insertion of the cord, integrity of the membrane was examined by the naked eye.

Haemoglobin estimation

Haemoglobin level was measured by Hemo-Cue B haemoglobinometer. It consists of disposable micro cuvettes with reagent in dry form and a single purpose photometer. The microcuvette is used for measuring the sample, as reaction vessel and as measuring cuvette. No dilution is required. Reading of haemoglobin takes place in the photometer, which follows the reaction and presents the results only when the reaction has stopped. The photometer is calibrated at the factory against the hemoglobinocyanide (HiCN) method, which is the international reference method for the determination of the total haemoglobin concentration in blood. The materials needed for the test are photometer, a microcuvette and a drop of blood. The microcuvette fills itself from capillary or venous blood by capillary action and is placed in the photometer which will automatically display the reading in less than 60 seconds (45-60 seconds). There is no dispensing, pipetting of mixing of blood and reagents as with traditional haemoglobin methods. there is no risk of broken glass ware because all processing take place in disposable plastic microcuvette. As a result direct contact with blood was minimised. The photometer automatically zeroes itself after each sample measurement and also check the intensity of the light source and the operation of the photocell. The haemoglobin level of all mothers and infants was measured.

All the blood samples were collected with strict aseptic precaution. After the initial resuscitation of the infant, the baby was given to the mother. Then the investigator went to mother and took the blood sample from both the mother and the infant.

3.11. Questionnaires: seven sets of questionnaires were filled up to collect details.

Questionnaire -1 New born details at birth and during hospital staying.

Questionnaire -2 Morphological details of the placenta.

Questionnaire -3 Present and past history of maternal pregnancy.

Questionnaire -4 Follow up details of the infant.

Questionnaire -5 Follow up details of the mother.

Questionnaire -6 Socio-economic details of the parents.

Questionnaire -7 Verbal autopsy

Questionnaire 1 : Clinical and anthropometric details of new born infant

This included all details about the new born infant. As soon as the infant was born as much detail as possible was taken. An identification number named as sl. no. was given. The same serial number included the follow up details, maternal details, placental details, and verbal autopsy. After the selection of the infant as our sample the APGAR score at 1 minute and five minutes, assessment of gestational age, rectal temperature, all anthropometric measurements, time taken to resuscitate, the drugs used to resuscitate the infant, feeding details were taken and filled up in the questionnaire. The name of the doctor who took the details was written in the top. The idea was that if he/she made some mistake I could correct it in the meeting. In each sample the address was written in details, how to go there, time required for the journey, cost of the journey, exactly where the home is situated, who is the owner of the house all these were taken in details.

Questionnaire -2 : Details of placental examination

These had the same serial number as the new born infant. The detailed weight, length, breadth of the placental disc, colour of maternal and foetal surface, integrity of the membrane and surface, point of rupture from the margin and signs of calcification was noted.

Questionnaire - 3 : Details of mother's present and past pregnancy

The questionnaire included age and religion of the mother, number of living children, number of still births, abortion, dead children, cause of death of previous child, place of previous delivery, number of antenatal visits, any medical problems during pregnancy, antenatal complication, mode of delivery, any complications at labour, maternal anthropometry, haemoglobin level, and blood pressure.

We had some missing data, the reason for this is that sometimes mothers refused to give any history or did not allow us to do any examination on them. Specially when they gave birth to a stillborn or extremely low birth weight infants, they sometimes become upset and annoyed as if the hospital was responsible for this undesirable event, so they didn't want any hospital staff to talk with them. Sometimes the mothers were under deep sedation so they could not talk. Moreover sometimes mothers leave the hospital after delivery of the baby without the duty doctor being informed. So we lost some of the details.

Questionnaire - 4 : Follow up details of the live infant at the age of 28 days.

This questionnaire includes detailed anthropometry of the infant, age in days, sex, diet and history of illness. The illness history was taken by mother's recalls about illness during the 28 days period. The illness present in the day of follow up was examined by the principal investigator. Illnesses include diarrhoea, respiratory illness, fever, skin disease, jaundice, umbilical sepsis, rash and others. When an illness was found the detailed history of that illness was taken and if necessary treatment was given. The treatment history included who treated, what medicine was given, how many days the infant was ill.

Questionnaire -5 Follow up details of the mother

The mother's general condition and dietary history was taken at 28 days postpartum. Mother's blood pressure, history of illness, knowledge about low birth weight, and other information if relevant was taken.

Questionnaire - 6 : Socio-economic details

The socio-economic condition of the parents was measured by some parameters. These include parents education, occupation and income, number of family member, structure of house, source of drinking water, type of latrine, household possession, method of cooking, no of children and age of marriage. As in developing countries collection of accurate data in socio economic status is difficult, we used some of the determinants of socio economic status to assess the overall status of the families. Co-workers and I developed a scoring system by taking some of the parameters and scoring them subjective to personal assessment, and comparison with other studies in some of the villages of Bangladesh (Bhuiyan, 1983; Islam and Becker, 1979). These parameters were scored according to grade and then the socio-economic condition was graded with scoring as high, medium and low. The scoring details was given in the questionnaire. We missed some of the socio-economic details, because we could not follow all the infants at home. We lost some of the families, because they moved to other places, or some of them had the wrong address. We found some values were missing either by mistake, or by wrong information as well.

Questionnaire - 7 : Verbal autopsy

This questionnaire was designed to diagnose the cause of death of infants who died during the 28 days period. This method was first used in John Hopkins University Narangwal Research Project (Bang and Bang, 1992). Since it is based on interview after death, it does not require observation by health workers on the live patient. If the infant died in the hospital then the research assistant did the verbal autopsy in the hospital and confirmed the diagnosis with attending doctors. But if the infant died at home then the principal investigator and the co-worker together did the interview and made the diagnosis. This is a set of questionnaire made by widely experienced consultant paediatricians (five from India, five from USA) with a list of proposed criteria for each cause of death. It has got a minimum list of causes of death in infants in developing countries. We followed these criteria and, in addition to this for our study purpose, we added place of death and age of death. The principal investigator and the attending co-workers in the field and in the ward conducted it very carefully. Sometimes we conducted the interview twice (once in the ward and once at home) on infants who died in the

hospital to double check the diagnosis. 90% of our diagnoses correlated with hospital diagnoses. This verbal autopsy included 14 causes of deaths of infants with an additional column unknown/others. Finally at the end of the study, I double checked the diagnosis of all my diagnosis of cause of death with hospital records, 90% of which was similar.

3.12. Analysis of data

Data was analysed in the statistical package STATA. All the data was cleaned. I had 1000 samples, (but during entry I lost one sample) and I followed them up at the age of four weeks. I could manage to follow up 78% cases. It was descriptive and analytical analysis.

The qualitative and quantitative data were summarised by frequency distribution. The joint influences of the variables, taking account of possible correlation among the variables was analysed by logistic regression. Contingency tables were used for discrete quantitative variables and for continuous quantitative variables whose values have been grouped. Chi-squared test was used to find out the association between the row variables and the column variables. The matched sets of each case and its associated controls and their confidence intervals were analysed by Mantel Haenszel procedures.

Risk factors for morbidity and mortality were analysed by logistic regression. The growth of the infants were measured by their anthropometric measurements at age of around 28 days. The weight at birth and follow-up were converted to standard deviation scores using the British Standards (Cole, 1998), then the change in standard deviation score over the neonatal period was calculated by simple subtraction. The values for 'proportional weight gain' for all the LBW infants studied were converted in to centiles, and all infants with proportional weight gain below the 25th centile were considered to have 'poor growth' considered as cases and were compared with the infants above the 25th centile as 'good growth' and controls.

Calculation of percentage of low birth weight infants delivering in the hospital during the study period

The percentage of low birth weight infant was calculated from total number of deliveries during the period of November '94 to August '95, total number of working days and total number of lowbirth weight infants born during that period.

Total number of deliveries (all live born) from Nov'94 to Aug'95 = 3503

Number of days in study from Nov'94 to Aug'95 = 219

Number of days in all from Nov'94 to Aug'95 = 295

Formula for proportion of LBW : a / b

Number of days in all (295) = a

no.of working days in study (219)

Number of LBW babies in study (664) =b

Number of deliveries in study period(3505)

$$\text{Percentage of low birth weight infants} = \frac{295}{219} \times \frac{664}{3505} = 26\%$$

Chapter 4

Results

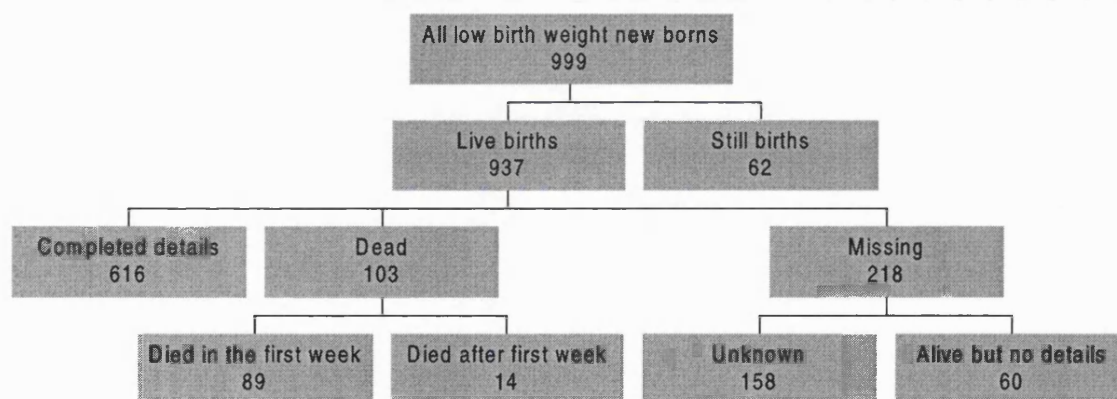
4.1. Baseline details of the low birth weight sample

4.1.1. Sample structure

Figure: 2

The flow sheet summarises the structure of the study sample and the outcomes in terms of births, deaths and losses to follow up.

Flow sheet of birth status

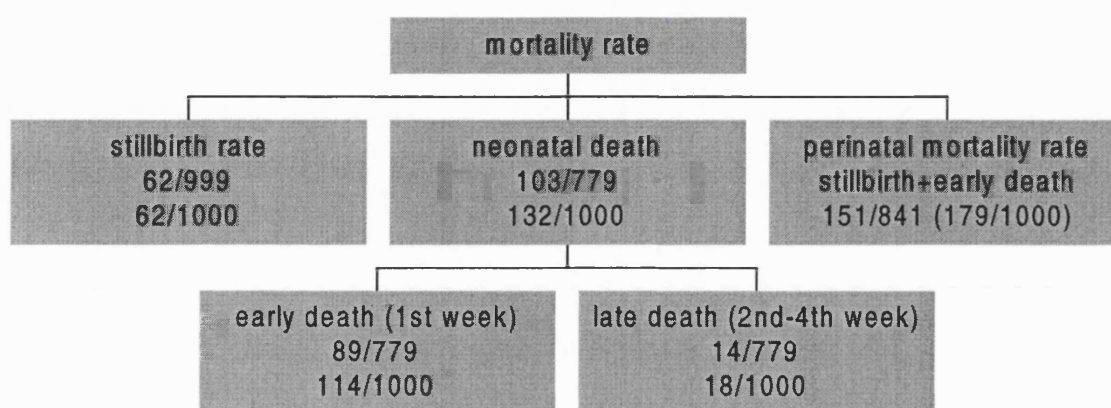


All the live born infants were followed up at home at approximately 28 days of age. During follow-up 218 infants were dropped from the study because we could not find their address. 60 infants were known to be alive when they moved from their place of birth, but we were unable to collect further follow up details. 158 were completely lost and we had no further details about them. For calculations of neonatal mortality rate we have therefore used the denominator as 999 minus 62 stillbirths minus 158 unknown to follow up.

Figure: 3

Figure 3 summarises the perinatal, post perinatal and neonatal mortality rates of low birth weight infants.

Mortality rates in low birth weight infants



The net mortality rate was 132 per 1000 live births estimated from 103/779 number of infants. The number of deaths in the first seven days was six times more than that of eight to twenty eight days of age. The perinatal mortality was 179/1000, which included the stillbirths and the infants who died during the first week.

4.1.2 Clinical and neonatal anthropometric details

Table 16 describes the anthropometric measurements and haemoglobin level of the low birth weight infants at birth, giving standard deviation, minimum and maximum values and median values. From the table it is evident that though mean birth weight was 2.1, Sd 0.4, a few infants were extremely low birth weight (0.5kg), and had a very low haemoglobin level at birth (8.3 g/dl).

Table 16: Clinical and neonatal anthropometric details of the study of new born infants $n = 999$

Variable	mean	std dev	min - max	median	interquartile range
weight (kg)	2.1	0.4	0.5 - 2.5	2.2	1.9 - 2.4
length (cm)	44.3	3.4	25.0-54.5	45.0	42.8 - 46.5
mid upper arm circumference (cm)	8.7	1.0	4.3 - 13.0	9.0	8 - 9.5
head circumference (cm)	32	2.0	18 - 39.5	32	31 - 33.1
chest circumference (cm)	28.9	2.4	16 - 36.6	29	28 - 30.5
haemoglobin (g/dl)	16.0	1.9	8.3 - 21.3	16.2	15.1 - 17.2

4.1.3 Socio-economic details

Table 17 describes the baseline details of the socio-economic conditions of the families of the low birth weight infants. The socio-economic conditions were described with different parameters, and assessed by scoring these parameters. For example, if mothers had no education she was scored as '0', primary education was scored as '1' and secondary education was scored as '2'. Details of scoring is described in the questionnaire of 'socio economic details of parents' and in methodology. Adding all these scores, a total social score was measured, and social status was defined as high with score (25-34), medium (14 - 24) and low (<14). The lowest cut-off value of income was taken as <3000 taka/month. We assumed from our previous knowledge that if a day labour earns 50.00 taka per day he will earn 1500.00 taka/month. Usually the daily earner group cannot earn more than 3000 taka/month, so we took 3000.00 taka/month as the cut-off value. Age at marriage is divided as less than 20 and 20yrs and above. In Bangladesh 90% of marriages occur in the teenage period and 80% of the girls become mothers as teenagers (Bhuiyan,

1993). Teenage marriage is a risk factor for adverse pregnancy outcome (Zhang, 1991; Mavalankar, 1991; Lumey, 1996). So 20 yrs was taken as a cut-off value.

Table 17: Socio-economic details of the study samples

Variable	Frequency (percent) n = 773
Maternal education	
none	283 (37)
primary	389 (50)
secondary	101 (13)
Fathers education	
none	156 (20)
primary	409 (53)
secondary	207 (27)
Income	
<3000 taka / month	421 (55)
3001 - 5000 taka /month	196 (25)
5001 - 10000 taka /month	115 (15)
>10000 taka /month	40 (5)
Fathers occupation	
day labour	115 (15)
unskilled worker	245 (32)
skilled worker	412 (53)
Age at marriage	
teenage (<20 yrs)	560 (73)
above teenage (>20 yrs)	211 (27)
Latrine	
open	167 (22)
pit	140 (18)
sanitary	465 (60)
Social score	
high	131 (17)
medium	442 (57)
low	197 (26)
Structure of house	
jute stick	81 (10)
jute + tin	183 (24)
tin	229 (30)
brick	278 (36)

Note : One thousand taka is equal to £ 14 .00

In our study 73% of the women were married as teenagers. Half of the mothers were from ‘middle class’ families, and had received primary education. It should be noted that even ‘middle class’ mothers in Bangladesh would be considered poor and deprived elsewhere.

Of the remaining, most (37%) had no education and very low income. Only 13% of the mothers had secondary education or above and 17% achieved a high social score. The educational condition among the fathers were also similar, with only 27% having secondary education and above. Half of the fathers were skilled workers, and the rest were unskilled or labourers with low income. 60% shared or had their own sanitary latrine, although some used open or pit latrines.

Table 18: Distribution of infants of different birth weight categories in different social classes

$\chi^2 = 31.35$

$P=0.000$

Variable	0.5 - 1.49 kg (%)	1.5 - 1.99 kg (%)	2.0 - 2.5 kg (%)	Total
<i>Social class</i>				
High	5 (4)	24 (18)	102 (78)	131 (100)
Medium	24 (5)	100 (23)	319 (72)	443 (100)
Low	30 (15)	57 (29)	110 (56)	197 (100)
Total	59 (8)	181 (23)	531 (69)	771 (100)

The percentage of extremely low birth weight infants was highest (15%) in the lower socio-economic group, and lowest (4%) in the upper socio-economic group. Even if we add the upper and middle class together the percentage of extremely low birth weight group was still highest in the lower social class group. Conversely the percentage of moderate low birth weight (2.0-2.5kg) is lowest (56%) in the lower social class group whereas it is highest (78%) in the upper social class group. Birth weight is inversely related with social class.

4.1.4 Maternal anthropometric and obstetric details

Table 19 shows the base line details of the mother's nutritional status with some clinical condition and obstetric history.

The mothers were generally short stature, the mean weight and height both within the risk group of mothers. 34% of the mothers were <45kg. The mean haemoglobin level was below the WHO standard, and 78% of the mothers were anaemic (<11g/dl) (WHO definition). Some were extremely anaemic (4.4g/dl). Most mothers had normal blood pressure though there were some (29) with systolic blood pressure as high as 200 mm. Hg (SD 16) and diastolic blood pressure of 140 mm. Hg. Most of the mothers had at least one

antenatal visit, 23% had no visit. Half of the mothers were primi-gravidae which is itself a predisposing factor to smaller birth weight. 90% of the mothers had no bad obstetric history.

Table 19: Maternal anthropometric and obstetric details

Variable	mean	sd	min - max	n
<i>Maternal anthropometry</i>				
weight (kgs)	47	6	31 - 77	943
height (cms)	150	5	128 - 168	955
haemoglobin (g/dl)	9.9	1.5	4.4 - 17.1	976
systolic blood pressure (mm Hg)	116	16	60 - 200	971
diastolic blood pressure (mm Hg)	76	14	40 - 140	971
no. of antenatal visit	4	3	0 - 16	971
<i>Obstetrical details</i>				
<i>frequency percent</i>				
<i>no. of previous pregnancies</i>				
0	493	49		996
1	205	21		
2	153	15		
>2	145	15		
<i>no. of live children</i>				
0	581	58		
1	220	22		996
2	123	12		
>2	72	7		
<i>no. of stillbirths</i>				
0	939	94		996
1	46	5		
>1	11	1		
<i>no. of previous child deaths</i>				
0	884	89		996
1	23	2		
2	16	2		
>2	73	7		
<i>no. of previous abortions</i>				
0	896	90		996
1	76	8		
>1	24	2		

Note: the percentages of mothers weight, Hb, blood pressure, and antenatal visits was not shown in the table.

Table 20 shows mother's BMI estimated from height and weight of the mothers of study samples

Table 20: BMI of the mothers of low birth weight infants

BMI group	Frequency	Percentage	Cumulative percentage
25/max	56	6.0	6.0
18.5/24.9	756	80.8	86.8
17.0/18.49	103	11.0	97.8
16.0/16.9	18	1.9	99.7
15.9/min	3	0.3	100.00

The mothers with BMI 25 and above are in the 'over-nutrition' group. Mothers of BMI 25 to 18.5 are considered normal (Nutrition News, 1991). In my study 81% of the mothers had a normal BMI. There might have been some over estimation because all mothers were weighed on the first postpartum day except those having caesarean section. In the first postpartum day some mothers had oedema, and some were having intravenous fluid infusion which might overestimate the weight.

Percentage distribution of intrauterine growth retardation

Table 21. Percentage distribution of intrauterine growth retardation

<i>Birth weight by gestational age</i>	<i>Frequency</i>	<i>Percentage</i>	<i>Cumulative percentage</i>
birth weight by gestation > minus 2SD	396	64.3	64.3
birth weight by gestation < minus 2SD	220	35.7	100.0
Total	616	100	

Note: We could not classify all live born infants because we had determined sex at follow up, and British Growth Standard cannot provide SD score without sex.

Table 21 shows the percentage of infants born with intrauterine growth retardation. The classification was taken from Sachdev (1998), and classified on the basis of less than minus 2SD weight for gestational age at birth. 36% of the infants were defined as below - 2SD weight for gestational age.

Percentage distribution of proportionally growth retarded infants in terms of weight for height

This is the table showing percentage of infants who are disproportionally and proportionally growth retarded. The proportionality was determined in terms of being less than minus 2 Sds for both weight and height. 37% of the infants were growth retarded. Of these 222 infants 120/219 (55%), or overall 20% were short (less than minus 2 SDs for height), proportionally growth retarded, and 99/219 (45% or overall 17%) were not short so they were disproportionally growth retarded.

Table 22. Percentage distribution of proportionally intrauterine growth retarded infants

<i>% with SDs weight at birth</i>	<i>% > minus 2 SDs height at birth</i>	<i>% < minus 2 SDs height at birth</i>	<i>Total</i>
≥ 2SDs weight at birth	265 (72%) (normal) (73%)	102 (28%) (46%)	367 (100%) (63%)
≤ 2Sd weight at birth	99 (45%) (disproportional) (27%)	120 (55%) (proportional) (54%)	219 (100%) (37%)
Total	364 (63%) (100%)	222 (37%) (100%)	586 (100%) (100%)

Note : Top = row %s Bottom = Column %s .

British growth standards do not provide height SD scores below 32 weeks gestation. This accounts for the thirty missing infants in Table 22 compared with Table 21.

Table 23 showing the percentage of different birth weight groups in different gestational age groups and in mothers with antenatal visits or without antenatal visit.

The number of extremely low birth weight infants (<1.5kg) was 50 times more in the less than 32 weeks gestational age group (49%), than in the term gestational age group (0.7%). The number of larger infants (2.0 - 2.5 kg) was seven times more in the term gestational age group (85%) than in the <32 weeks gestational age group (12%). The percentage of extremely low birth weight infants were almost same in the mothers who had not and who had attended antenatal visits, while the percentage of larger infants (>2.0 kgs) was higher (72%) in the group of mothers who received antenatal care than those who have not received (58%).

Table 23: Distribution of birth weight categories in different gestational age group and antenatal visits

χ^2 for gest.age 356.9 $P=0.000$

χ^2 for ant.visit 27.8 $P= 0.000$

Variable	Birth weight group (percent)			Total
	0.5 - 1.49 kg	1.5 - 1.99 kg	2.0 - 2.5 kg	
<i>Gestational age</i>				
<32 weeks	43 (49)	33 (38)	12 (13)	88 (100)
32-36 weeks	24 (9)	105 (38)	145 (53)	274 (100)
37-42 weeks	4 (1)	81 (14)	484 (85)	569 (100)
Total	71 (8)	219 (24)	641 (68)	931 (100)
<i>Antenatal visit</i>				
attended	42 (16)	163 (22)	520 (72)	725 (100)
not attended	41 (15)	73 (27)	157 (58)	271 (100)
Total	83 (8)	236 (24)	677 (68)	996 (100)

4.1.5 Placental details

The number of placentas described was fewer than for infants born: there were some missing data. Sometimes the attending doctor was busy with the resuscitation of the baby and the cleaner threw the placenta away without doctor's knowledge. Mean placental weight was 0.4 kg (sd 0.1), with a wide range of 0.2 to 1.9 kg. There were some (8) heavier placentas (>1.0 kg) which were of the twin pregnancy. 17% of the placental colour was abnormal i.e. black or green.

Table 24: Morphological details of the placenta of low birth weight infants after birth

Variable	mean	sd	range	n
placental weight (kg)	0.4,	0.1,	0.2 - 1.9	995
placental length (cm)	17,	3,	8 - 25	993
placental breadth (cm)	16,	2,	9 - 25	993
<i>Placental surface</i>				
normal	972	(98%)		
abnormal	23	(2%)		
<i>Placental colour</i>				
normal	820	(83%)		
abnormal (black and greenish)	170	(17%)		

Table 25 describes the distribution of normal and abnormal placental colour with different birth weight categories.

The distribution of abnormal placental colour was nearly equal in all birth weight categories.

Table 25 : Distribution of different birth weight categories with abnormal and normal placental colour group
 $\chi^2=1.4$ $P=0.5$

Variable	Birth weight group (percent)			Total
	0.5 - 1.49 kg	1.5 - 1.99 kg	2.0 - 2.5 kg	
<i>placental colour</i>				
normal	65 (78)	197 (84)	558 (83)	820 (83)
abnormal	18 (22)	38 (16)	114 (17)	170 (17)
Total	83 (100)	235 (100)	672 (100)	990 (100)

Note: Normal placental colour was defined by dull red, with a thin, greyish, shaggy layer on the surface.

4.1.6. Key findings of base line details

1. This was a mixed population of social class groups, most mothers coming from the middle social class group (57%). The social groups were scored using education, occupation, income and other socio-economic parameters. The hospital population we sampled is probably of slightly better socio-economic status than the community as a whole.

2. The mothers were generally short stature and had a high anaemia prevalence rate (78%) according to WHO criteria (Hb <11.0 g/dl).

3. The incidence of extremely low birth weights infants (0.5 - 1.5 kg) and premature infants (<37 wk.) was highest in the lower social class group and lowest in the upper social class group.
4. An abnormal placental colour was found in 17% of deliveries.
5. Nearly a quarter had not attended for antenatal care.
6. Eighty one percent of the mothers had a normal BMI, measured postnatally.
7. Thirty seven percent of the infants had intrauterine growth retardation, just over half proportionally growth retarded.
8. The percentage of low birth weight in the study population was 26%, 22/1000 was the twin pregnancy rate and 2/1000 the triplet pregnancy rate.

4.2. Mortality rates and survival analysis

4.2.1 Neonatal mortality

Table 26 describes the neonatal mortality rate of low birth weight infants with birth weight and gestational age categories. The overall neonatal mortality rate for LBW infants was 132 per 1000 livebirths, and the perinatal mortality rate 179 per 1000 total births. The mortality rate varied widely with different birth weight groups. It was highest in the lowest birth weight (690/1000 live births) and <32 weeks gestational age group (513/1000 live births). As birth weight and gestational age increases mortality rate decreases. In the lowest birth weight group mortality was thirteen times more than in the highest birth weight group. In all birth weight groups early neonatal death was s times more than the late neonatal death. The mortality rate was ten times higher in the lowest gestational age group (26-33wks) than highest gestational age group. Early neonatal death rate was also ten times higher (462/1000 live birth) in the lowest gestational age group than highest gestational age group.

Table 26: Perinatal and neonatal mortality rate of low birth weight infants by birth weight and gestational age categories.

	<i>Number enrolled: number in whom mortality outcome is known at 28 days</i>	<i>Number of stillbirths n=62</i>	<i>Number of deaths n = 103</i>	<i>Percentage of all neonatal deaths</i>	<i>Total PMR (per1000 births) stillbirth+ early deaths</i>	<i>Total NMR (per1000 livebirths)</i>	<i>Early NMR (0 - 6 days) (per 1000 live births)</i>	<i>Late NMR (7 - 28 days) per 000 livebirths)</i>
<i>Birth weight group</i>								
<1.5 kg	73:58	11	40	39 (40/103)	695 (48/69)	690 (40/58)	638 (37/58)	52 (3/58)
1.5 - 1.99 kg	221:184	16	35	34 (35/103)	220 (44/200)	190 (35/184)	152 (28/184)	38 (7/184)
2.0 - 2.49 kg	643:537	35	28	27 (28/103)	103 (59/572)	52 (28/537)	44 (24/537)	7 (4/537)
<i>Gestational age group</i>								
26 - 32 weeks	88:78		40	39 (40/103)		513 (40/78)	462 (36/78)	51 (4/78)
33 - 36 weeks	274:221		37	36 (37/103)		167 (37/221)	140 (31/221)	27 (6/221)
37 - 42 weeks	569:480		26	25 (26/103)		54 (26/480)	50 (24/480)	8 (4/480)
All LBW infants	937:779		103	100 (103/103)	179 (151/841)	132 (103/779)	114 (89/779)	18(14/779)

Table 27: Neonatal mortality rates by maternal age, education and social score groups

Variable	Number enrolled	Number followed up	Number of deaths	Total NMR (per 1000 live births)	Early NMR (0-6 days) per 1000 live births)	OR (95% CI)	P
Education							
secondary	99	99	7	71 (7/99)	71	1.00	
primary	371	367	23	63 (23/367)	54	1.14 (0.40-2.9)	0.77
nil	240	237	58	245 (58/237)	211	4.85 (2.81 - 8.39)	0.000
Social score							
high	130	130	8	62 (8/130)	62	1.00	
medium	417	413	30	73 (30/413)	61	1.19 (0.51 - 2.91)	0.81
low	161	158	50	316 (50/158)	278	7.06 (3.05 - 16.92)	0.000
Maternal age							
20-35 yr.	726	609	73	120 (73/609)	103	1.00	
<20 yr.	170	134	20	149 (20/134)	127	1.29 (0.73 to 2.26)	0.15
>35 yr.	36	32	10	313 (10/32)	281	3.34 (1.41 to 7.76)	0.000

Note: Maternal age was compared with 20-35 yrs age group to <20 and >35 yrs age group

Maternal education was compared with nil educated group to primary and secondary educated group together

Social class was compared with low social class to high and medium social class together

Table 27 describes the distribution of neonatal mortality by maternal age, education and social score. Neonatal mortality has got a 'U'-shaped distribution with maternal age. Compared with the 20-35 yrs age group mortality rate was higher (149/1000) in the teen age group (but this did not reach statistical significance) and highest in the more than 35 years old age group (313/1000) of mothers. Maternal education has got a relationship with neonatal mortality. The odds for mortality risk is five times more (OR 4.85, CI 2.81 to 8.39) among the nil educated group of mothers than the higher educated group, and seven times more in lower socio-economic group (OR 7.06, CI 3.05 to 16.92) than higher socio-economic group.

Table 28: Neonatal mortality rates by Apgar score at 5 minutes and resuscitation time

variable	number enrolled	number followed up	number of deaths	% of neonatal deaths	Total NMR	Early NMR	OR (95% CI)	P
Apgar score at 5 minute								
7 or above	805	670	39	39/670	58	45	1.00	
<7	131	105	64	64/105	610	562	24.6 (13.4 to 45.2)	0.00
Resuscitation time to first cry								
1 minute	754	625	30	30/625	48	37	1.00	
>1 minute	177	146	69	69/146	473	425	15.4 (9.6 to 24.7)	0.00

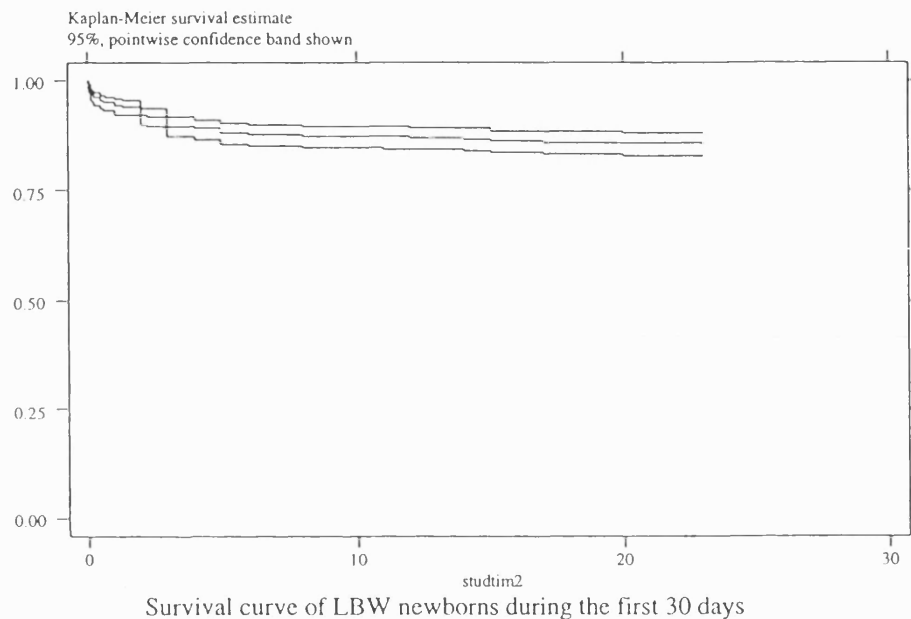
Note: The odds ratio of Apgar score and resuscitation time was compared with total neonatal deaths.

The neonatal mortality rate was highest in the infants born with an Apgar score of less than 7 at five minutes (OR 24.62; CI 13.4-45.2), and resuscitation time taking more than one minute

than one minute (OR 15.4; CI 9.6-24.7). Neonatal mortality risk was ten times more in the >1min group. The early neonatal mortality rate was twelve times more for infants of Apgar score <7 at five minutes than >7 and eleven times more at resuscitation time >1 minutes than <1 minute group.

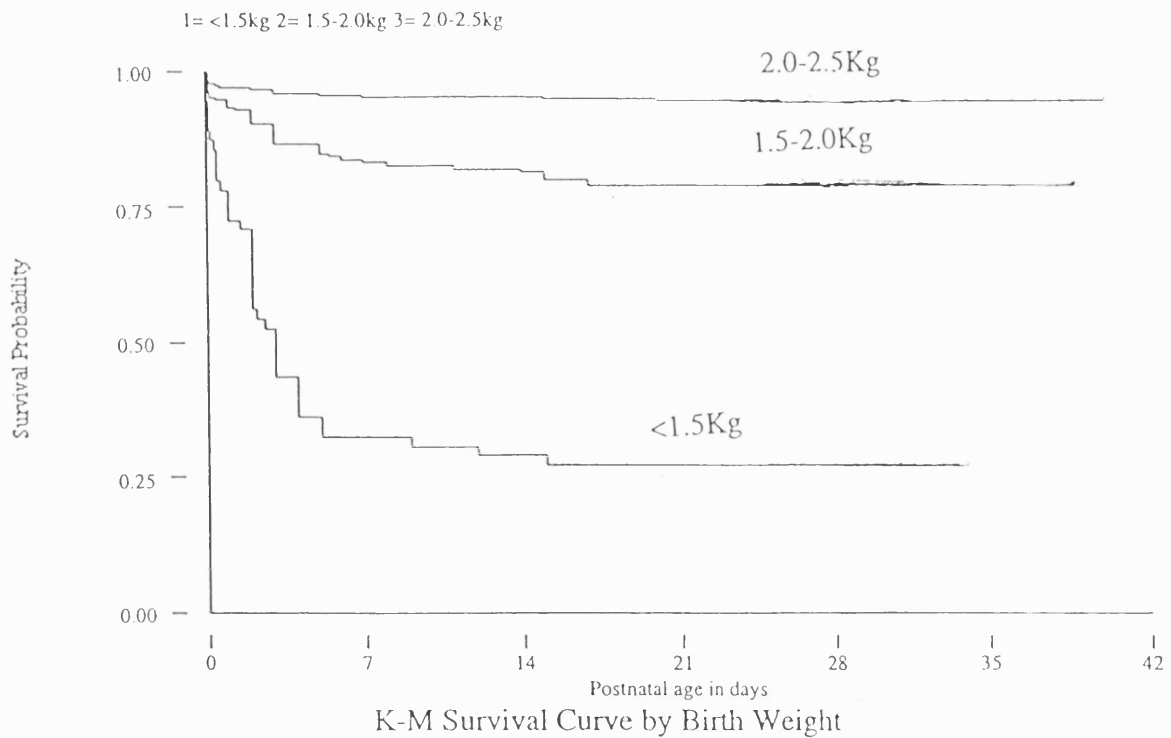
4.2.2. Survival patterns

Fig 4: Overall Kaplan-Meier (K-M) neonatal survival curve for low birth weight infants with Greenwood confidence limits



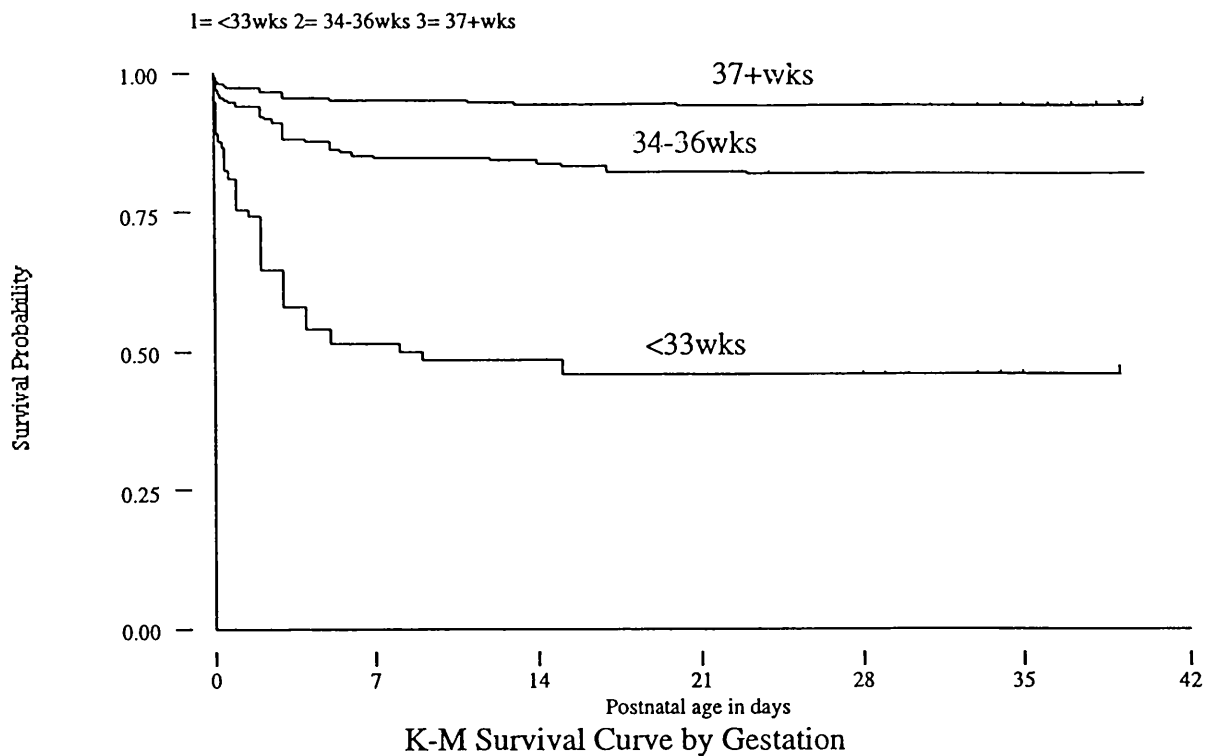
Survivability was poor in the first seven days in all birth weight group. After seven days survivability was almost same in all birth weight groups.

Fig 5: K-M neonatal survival curve for low birth weight infants by birth weight group
 $\chi^2(2)=256.66$ $Pr>\chi^2=0.000$



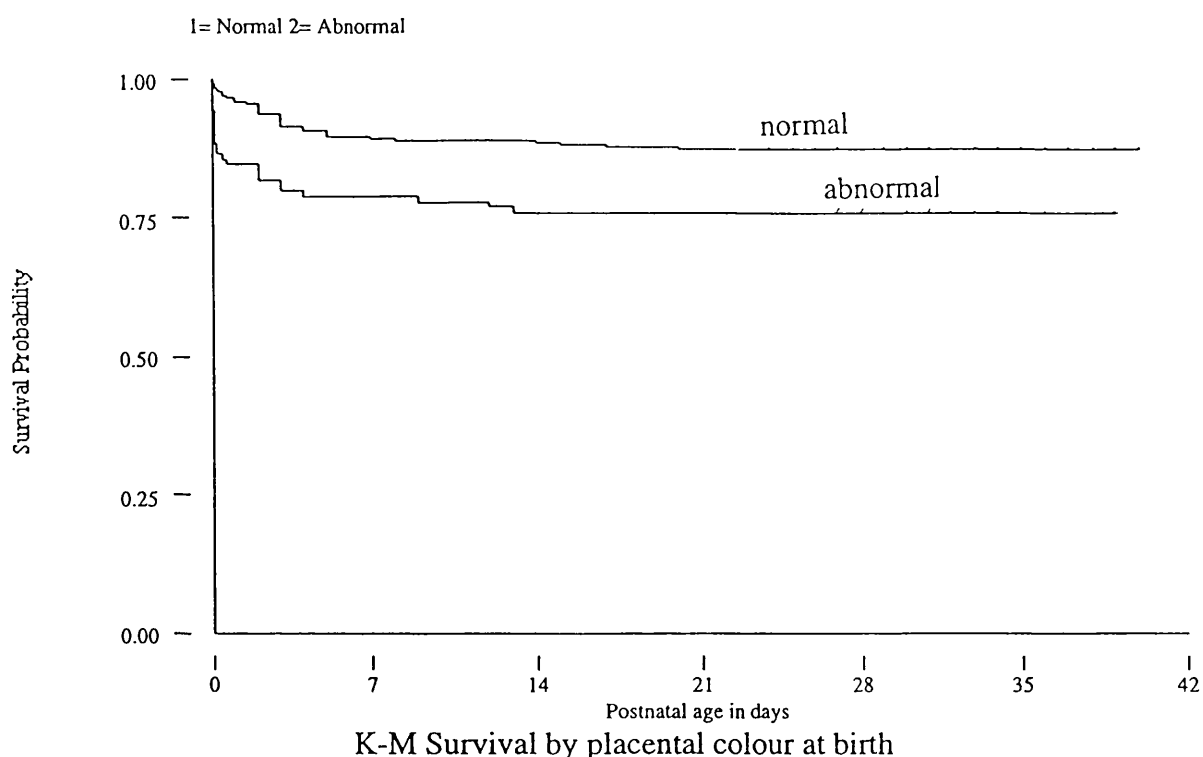
The infants were divided into three groups according to their birth weight. Group 1=<1.5kg, group 2=1.5-2.00kg, and group 3=2.00-2.5kg. Although we intended to follow up infants at 28 days but due to inconvenience (like unavailability of the infant, flood) some of the infants were only followed up to 42 days. Birth weight has got a significant relationship with survivability. As birth weight increases survivability increases. Mortality is highest in the <1.5 kg group. The rate of mortality is highest in the first seven days in all birth weight groups, but it falls very sharply in the group of infants below 1.5 kgs. There is a very good possibility of survivability in the comparatively bigger infants. After 14 days in all three groups survival probability was same and it could be possible that at some stage these three groups might unite together. Emphasis on care during the first seven days would have the maximum improvement in survival.

Fig 6: K-M neonatal survival curve for low birth weight infants by gestation group
 $\chi^2 (2)=147.44$ $Pr>\chi^2=0.000$



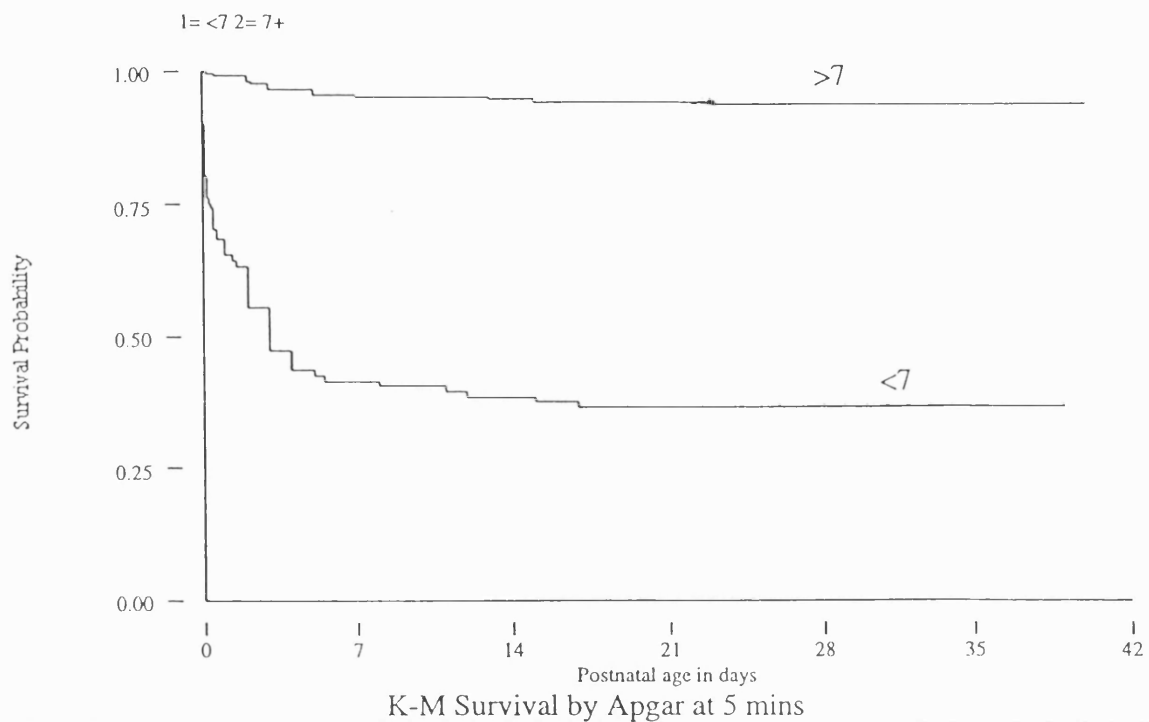
Mortality was highest within the first seven days in all age groups, but in the < 33wks gestational age groups the survival curve falls very steeply in the first seven days. In all age group there was a good probability of survival after 14 days. Survivability is directly related with gestational age. Survival probability was highest in the longest gestational age group.

Fig 7: K-M neonatal survival curve for low birth weight infants by placental appearance
 $\chi^2 (1)=10.80$ $Pr>\chi^2=0.001$



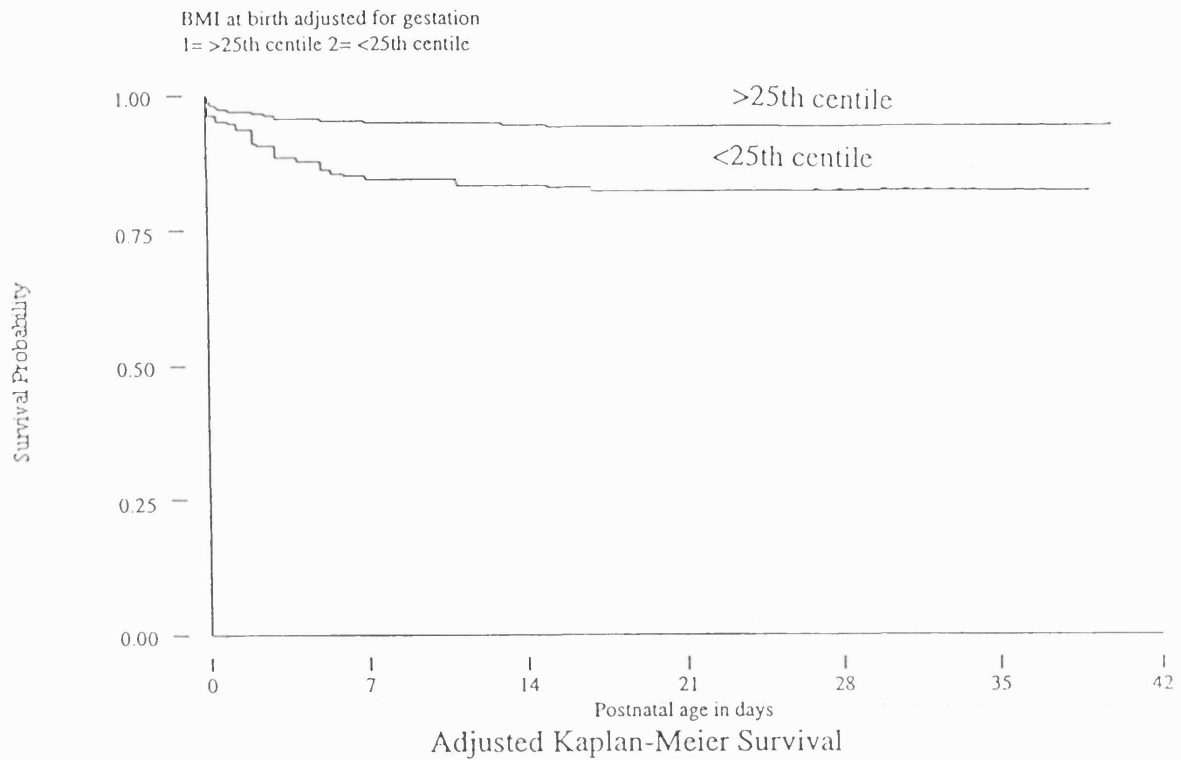
All placentas were divided into two groups according to colour. Group one was placenta with normal colour and group two with abnormal colour i.e. blackish or greenish or pale. Infants born with normal placental colour had a very good chance of survivability compared with those with abnormal colour. A significant relationship was found between abnormal placental colour group and neonatal mortality. In both colour group mortality was highest in the first seven days, there after the survival probability curves run parallel in both colour groups.

Fig 8: K-M neonatal survival curve for low birth weight infants by Apgar score at 5 minutes (<7 vs 7+)



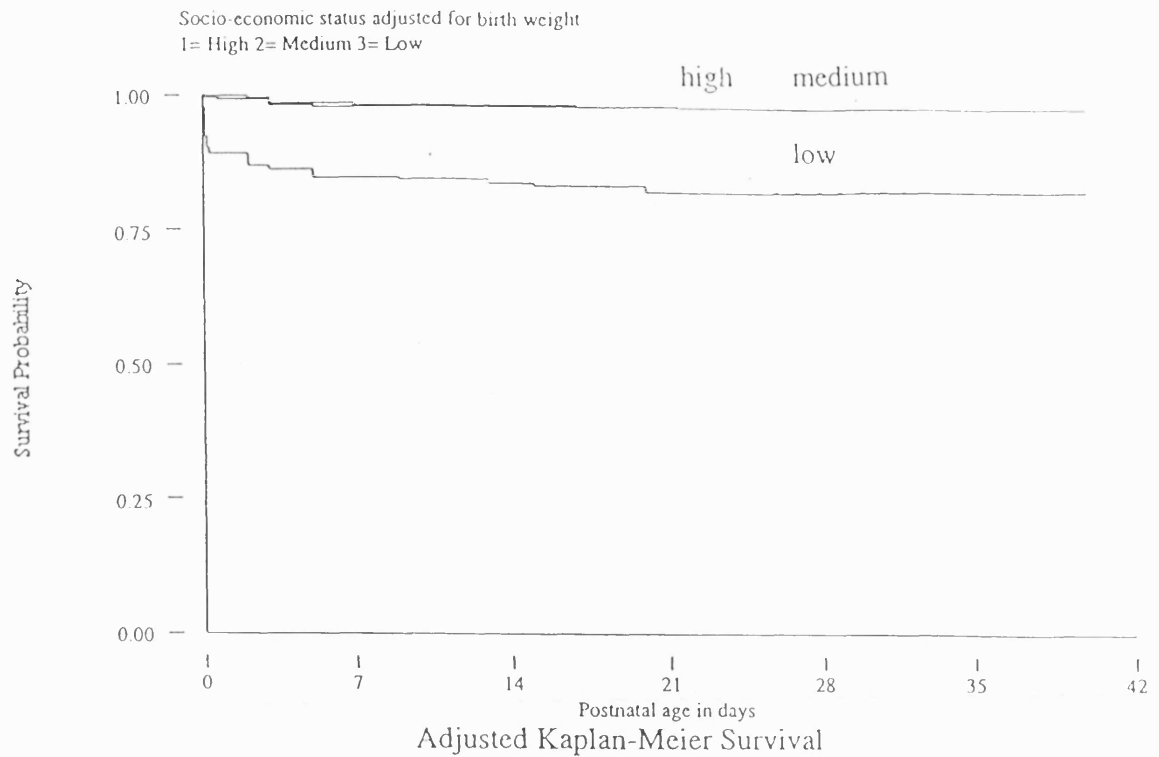
All the infants were divided into two groups with their Apgar score at five minutes. The cut-off value was seven. Group one was the infants having Apgar score <7 at five minutes and group two >7. There was a huge difference in the survival probability between the two groups. Incidence of mortality was higher in the first seven days. Apgar score is an important indicator of infants survivability.

Fig 9: K-M neonatal survival curve for low birth weight infants by body mass index group (<25th vs >25th centile)



The infants body mass index adjusted by their gestational age and then divided into two groups, group 1= >25th centile and group 2 = <25th centile. Percentage of mortality was higher in the group two than group one. Percentage of mortality was higher in the first seven days in both groups. In both groups survival probability is equal after seven days.

Fig 10: K-M neonatal survival curve for low birth weight infants by socio-economic score



The socio-economic classes of the sample was divided into three classes according to their socio-economic score. The sample infants were divided into 1=high, 2=medium, and 3=low socio-economic classes. Survival probability was same in the high and medium class group, but it was significantly lowest in the lower class group. Postnatal age had little effect on survivability. In all groups survival probability curves run almost parallel after seven days.

4.2.3. Key findings of neonatal mortality and survival patterns

1. Overall the perinatal mortality rate for our sample of LBW infants was 179/1000 total births and the neonatal mortality rate was 132/1000 livebirths, with an early (0-6 days) neonatal mortality rate of 114/1000 and a late neonatal mortality rate of 17/1000 live births.
2. As birth weight and gestational age increases mortality rate decreases. In the lowest birth weight group, mortality was thirteen times more than in the highest birth weight group. In all birth weight groups, early neonatal death was six times more than the late neonatal death.
3. Mortality was highest among uneducated and eldest mothers (more than 35 yrs).
4. Seventy two percent of the infants died in the first three days.

4.3. Risk factors for stillbirths and neonatal deaths

4.3.1 Risk factors for stillbirth

Univariate analysis

Table 29 compares individual variables between stillborn and live born infants. All the anthropometric measurements had a significant and inverse relationship with risk of still births ($P < 0.001$), except the head circumference which was similar for both stillborn and liveborns (mean 31.9 cm, $P < 0.887$).

Among the placental and obstetrical details only placental length, breadth, color and number of antenatal visits had significant relationship with risk of still births ($P < 0.001$).

Maternal height, weight and blood pressure did not show a relation with stillbirth births. The only factor related with stillbirth was maternal haemoglobin ($P < 0.001$).

The most important univariate risk factors for stillbirths were socio-economic condition of the family. All the socio-economic parameters, maternal education, family income, and social status were highly significantly associated ($P < 0.001$) with risk of stillbirths.

Table 29 : Univariate (Unadjusted) odds ratios for important variables of stillbirths (n=62) vs low birth weight live born infants (n= 937)

Variable	stillborn infants			liveborn infants			odds ratios	P value
<i>New born details</i>	<i>mean</i>	<i>sd</i>	<i>n</i>	<i>mean</i>	<i>sd</i>	<i>n</i>		
birth weight (kg)	1.92	0.44	62	2.08	0.38	937	0.35 (0.18 - 0.68)	0.002
length at birth (cm)	42.9	4.5	62	44.3	3.3	937	0.88 (0.82 - 0.95)	0.001
head circumfer (cm)	31.9	3.09	62	31.9	1.9	937	0.99 (0.87 - 1.12)	0.887
chest circumfer (cm)	27.9	3.4	62	29	2.3	937	0.82 (0.73 - 0.91)	0.001
arm circumfer (cm)	8.2	1.25	62	8.7	0.98	937	0.59 (0.46 - 0.74)	0.001
<i>Placental and Obstetric details</i>								
placental length (cm)	15.7	2.5	62	16.8	2.4	931	0.84 (0.76 - 0.93)	0.001
placental bdth. (cm)	5.6	2.5	62	16.5	2.5	931	0.85 (0.77 - 0.95)	0.003
placental weight (kg)	0.38	0.13	62	0.40	0.14	933	0.34 (0.06 - 2.05)	0.239
placental color							0.20 (0.11 - 0.39)	0.000
no. of prev. preg	1.4	1.5	62	1.05	1.4	934	1.17 (0.98 - 1.40)	0.090
no. of live child	0.99	1.2	62	0.72	1.09	934	1.25 (0.99 - 1.60)	0.063
no. of still born	0.11	0.37	62	0.07	0.32	934	1.54 (0.7 - 3.4)	0.290
no. of dead child	0.15	0.4	62	0.14	0.43	934	1.04 (0.57 - 1.9)	0.900
no. of abortion	0.11	0.32	62	0.13	0.42	934	0.9 (0.5 - 1.7)	0.775
no. of antenatal visits	1.38	2.12	62	3.7	3.2	934	0.80 (0.73 - 0.86)	0.001
<i>Maternal details</i>								
weight (kg)	47.7	5.7	58	47.6	6.13	885	1.01 (0.97 - 1.06)	0.635
height (cm)	150.8	4.8	60	150	4.7	895	1.03 (0.9 - 1.08)	0.302
haemoglobin (g/dl)	9.27	1.36	60	9.9	1.5	916	0.74 (0.62 - 0.88)	0.001
systolic BP (mm.hg)	17.4	19.7	61	116	15.8	910	1.0 (0.99 - 1.02)	0.579
diastolic BP(mm.hg)	78.3	17.7	61	76.3	13.8	910	1.01 (0.99 - 1.03)	0.280
<i>Socio-economic details</i>								
<i>Mothers education</i>								
none	43,	69%		240,	34%		1.00	
{primary	17,	28%		372,	52%		0.35 (0.24 - 0.51)	0.001
secondary}	2,	3%		99,	13%			
<i>Income</i>								
<3000 taka	53,	85%		368,	52%		1.00	0.001
{3000 - 5000 Tk	7,	12%		189,	27%		0.5 (0.37 - 0.66)	
5001 - 10000	2,	3%		113,	16%			
>10000 taka}	0			40,	6%			
<i>Social score</i>								
{high	1,	1%		130,	18.3%		1.00	0.001
medium}	25,	40%		418,	59%		3.44 (2.3 - 5.1)	
low	36,	58%		161,	23%			

Note: Primary and secondary education together compared with no education.
<3000 taka compared with the rest.

Multivariate analysis

Table 30: Stepwise backward multivariate logistic regression analysis of risk factors for low birth weight stillbirths (n=62) compared with low birth weight livebirths (n=937)

Number of observation = 738

chi2 (10) = 97.99

<i>stillbirths</i>	<i>odds ratios</i>	<i>P>z</i>	<i>95% CI</i>
stillbirths	odds ratios	P>z	95% CI
birth weight			
2.00 - 2.5 kg	1.0		
1.5 - 1.99kg	0.98	0.96	0.47 - 2.01
<1.5kg	1.99	0.12	0.83 - 4.83
maternal details			
>147 cm	1.0		
<147 cm	1.02	0.96	0.50 - 2.05
>11g/dl hemoglobin	1.0		
<11 gm hemoglobin	1.04	0.91	0.43 - 2.55
Secon education	1		
prim education	0.89	0.44	0.80 - 3.02
no education	1.06	0.94	0.17 - 9.69
with visit	1.0		
no antenatal visit	1.49	0.23	0.76 - 2.94
placenta			
normal color	1.0		
abnormal color	6.47	0.00	3.51 - 11.9
socio economic class			
high	1.0		
medium	6.88	0.12	0.61-77.5
low	13.44	0.03	1.09 -165.8

The variables showing a P value <0.2 in univariate analysis were entered for multivariate analysis. Where group of variables were related (e.g. anthropometric variables like birth weight, length etc.), they were first entered into a regression model as a group and the one which remained significantly correlated with the dependent variable (e.g. neonatal death, stillbirth etc.) was the one selected for the final regression model.

Though in univariate analysis neonatal anthropometric measurements, maternal haemoglobin, antenatal visits, and socio economic parameters relate significantly, but in multivariate analysis all these factors were confounded. The most significant variables remain after

multivariate analysis were abnormal placental colour ($P<0.001$), and low social score ($P<0.03$). As we compared levels of maternal education separately it was not significant, but when we compared secondary education with primary and nil education then it became significant.

In summary the important independent risk factors for stillbirths, which remained after multivariate analysis were low socio-economic status, and the abnormal colour of the placenta, presumably indicating some infection or degenerative pathology.

4.3.2. Risk factors for neonatal deaths

Univariate analysis

Table 31 shows the univariate analysis of risk factors for low birth weight neonatal deaths ($n=103$) compared with low birth weight survivors ($n=692$).

All the anthropometric measurements, neonatal hemoglobin and gestational age were significantly less in the neonatal death group ($P<0.001$). Which is not surprising given that gestational age is a powerful predictor of survival.

The placental weight, number of previous stillborn, and number of previous abortions did not show a relationship with neonatal death. The important factors related with neonatal deaths were placental length and breadth, and colour, number of previous dead child and number of antenatal visits ($P<0.001$).

Maternal height, weight did not show any relationship with neonatal deaths, but maternal haemoglobin ($P<0.006$), and systolic blood pressure did ($P<0.004$).

All the socio-economic factors were significantly related with neonatal mortality but not presented in the table. Maternal education ($P<0.001$) which came as a significant factor after multivariate analysis was presented in the table.

Table 31: Univariate (unadjusted) analysis of risk factors for low birth weight neonatal deaths (n=103) compared with low birth weight survivors (n= 896)

a. anthropometric variables

b. maternal variables

c. social variables

Variable	neonatal dead			neonatal survivors			odds ratios 95% CI	P value
	mean	sd	n	mean	sd	n		
New born details								
birth weight (kg)	1.5	0.50	103	2.1	0.33	896	0.30 (0.18 - 0.51)	0.001
birth length (cm)	40.5	4.75	103	44.7	2.9	896	0.69 (0.65 - 0.74)	0.001
head circumf. (cm)	29.8	2.8	103	32.2	1.7	896	0.59 (0.50 - 0.62)	0.001
chest circumf. (cm)	26.5	3.1	103	29.2	2.11	896	0.62 (0.57 - 0.68)	0.001
arm circumf. (cm)	7.5	1.15	103	8.8	0.90	896	0.28 (0.23 - 0.34)	0.001
haemoglobin (g/dl)	14.8	2.4	103	16.2	1.7	827	0.67 (0.6 - 0.75)	0.001
resuscitation (mins)	18.9	17.5	99	3.3	5.5	833	1.2 (1.18 - 1.2)	0.001
gestational age (wks)	34.2	3.2	103	37	1.8	828	0.56 (0.51 - 0.61)	0.001
Placental +Obstetrical details								
placental length (cm)	15.9	3.3	102	16.5	2.4	891	0.85 (0.77 -0.92)	0.001
placental breadth (cm)	15.5	3.3	102	16.6	2.3	891	0.84 (0.76 - 0.90)	0.001
placental weight (kg)	0.38	0.17	102	0.40	0.13	893	0.26 (0.06 - 1.04)	0.056
placental color							0.51 (0.21 - 0.88)	0.017
no. of prev preg.	1.5	1.6	103	.02	1.4	893	1.3 (1.09-1.5)	0.001
no. of live child	1.01	1.15	103	0.7	1.1	893	1.3 (1.07-1.7)	0.006
no. of still born	0.08	0.37	103	0.06	0.31	893	1.2 (0.63-2.5)	0.590
no. of dead child	0.32	0.64	103	0.11	0.4	893	3.01 (1.8 - 4.8)	0.001
no. of abortion	0.10	0.4	103	0.13	0.4	893	0.87 (0.53-1.4)	0.592
antenatal visits	1.9	2.7	103	3.7	3.2	893	4.14 (2.68 -6.67)	0.000
Social variables								
maternal education								
no education	182 (29%)			58 (65%)			1.00	0.001
primary education	348 (565)			24 (27%)			0.37 (0.26 - 0.52)	
secondary education	92 (15%)			7 (7%)				
Maternal details								
maternal weight (kg)	47.05	2.7	93	47.4	6.05	850	0.99 (0.95 - 1.02)	0.557
maternal height (cm)	149.2	5.7	91	150	4.67	864	0.91 (0.91 - 1.00)	0.052
haemoglobin (g/dl)	9.5	1.4	99	9.9	1.5	877	0.82 (0.71 - 0.94)	0.006
systolic BP (mm hg)	120.8	21.3	95	115	15.3	876	1.02 (1.0 - 1.03)	0.004
diastolic BP (mm hg)	80	19.01	95	76.09	13.4	876	1.02 (1.0 - 1.03)	0.010
after teen age	10 (11%)			188 (30.4%)			1.0	0.03
teen at marriage	78 (88%)			432 (69.6%)			1.04 (1.00 - 1.09)	

Multivariate analysis

Multivariate analysis was done by stepwise backward logistic regression analysis of risk factors for neonatal deaths compared with neonatal survivor group.

Criteria for entry of variables into the model were a P value <0.2 on univariate analysis.

Where group of variables were related (e.g. anthropometric variables like birth weight, length,. etc.), they were first entered into a regression model as a group and the one which remained significantly correlated with the dependent variable (e.g. neonatal death, stillbirth etc.) was the one selected for the final regression model.

Being confounded by other factors most of the variables were dropped off from the stepwise backward logistic regression analysis. The most important factors which remained significant were:

- birth weight between 500 to 1500 gms.
- mid upper arm circumference of the infant at birth (which probably reflects gestation as well as nutritional status)
- abnormal placental colour (green and black)
- lack of antenatal care
- maternal haemoglobin <9 gm/dl
- teenage at marriage
- fathers occupation
- no maternal education

Table 32 : Stepwise multiple logistic regression analysis for the risk factors for neonatal deaths compared with neonatal survivor group

Backward stepwise logistic regression:

Significance level for removing = 0.4

Significance level for entering = 0.2

Number of obs = 687

chi2(11) = 221.54

<i>Neonatal death</i>	<i>Odds ratio</i>	<i>p>z</i>	<i>95% con. interval</i>
birth weight >2.00	1.00		
birth weight (1.5-1.99)	1.62	0.21	0.75 - 3.47
birth weight (0.5-1.49)	6.28	0.002	1.98 - 19.91
MUAC at birth	0.29	0.00	0.19 - 0.46
normal placenta colour	1.00		
abnormal placenta colour	2.36	0.02	1.09 - 5.06
antenatal care	1.00		
no antenatal care	2.31	0.01	1.21 - 4.41
maternal hb (>11 gm)	1.00		
maternal hb (11-9.99g)	2.50	0.05	0.96 - 6.49
maternal hb (<9 g)	3.05	0.02	1.12 - 8.31
<i>Age at marriage</i>			
after teenage	1.00		
at teenage	3.60	0.004	1.49 - 8.72
<i>Fathers occupation</i>			
skilled labour	1.00		
day labour	2.67	0.002	1.44 - 4.95
<i>Mothers education</i>			
secondary and above	1.00		
nil	2.52	0.004	1.33 - 4.75

Note : MUAC was entered as a continuous variable because there are no agreed cut-off values for new born infants. The odds ratio reflects the risk of neonatal death for a unit increase (one cm) in MUAC.

Table 33 shows that resuscitation time has got a significant relationship with neonatal mortality with a high odds ratio, but I did not consider it in multivariate logistic regression analysis as a risk factor because it may be argued as not a true risk factor as it is on the causal pathway of neonatal death. Odds ratios reflect the change in risk for a unit change in a continuous variable or for the presence of the categorical variable.

Table 33 :neonatal mortality in relation to resuscitation time at birth

	resuscitation time > 1 minute	resuscitation time < 1 minute	odds ratio 95% CI	P value	total
neonatal deaths	69	30	15.4 (9.6 - 24.7)	0.000	99
survivors	108	724	1		832
total	177	754			931

4.3.3. Risk factors for early versus late neonatal deaths

Table 34 shows the distribution of early (within 7 days) and late (after 7 days) neonatal deaths by birth weight and gestational age. Overall the rate of early neonatal death (86%) was six times more than late death (14%). There was no difference in the pattern of death rates between the birth weight and gestational age groups.

Table 34 : Distribution of early (within 7 days) and late (after 7 days) neonatal deaths by birthweight and gestational age group

Variable	early death within 7 days	late death after 7 days	Total
Birth weight group			
0.5 - 1.49 kg	37 (42%)	3 (21%)	40 (39%)
1.5 - 1.99 kg	28 (31%)	7 (51%)	35 (34%)
2.0 - 2.5 kg	24 (27%)	4 (28%)	28 (27%)
Total	89 (86%)	14 (14%)	103(100%)
Gestational age group			
26.6 - 33.9 weeks	36 (40%)	4 (29%)	40 (39%)
34.0 - 36.9 weeks	31 (35%)	6 (42%)	37 (36%)
37.0 - 42.0 weeks	22 (25%)	4 (29%)	26 (25%)
Total	89 (86%)	14 (14%)	103 (100%)

Note: the total percentage of birth weight and gestational age group was shown in row percentage, but the birth weight groups and gestational age groups were shown in column percentage

Univariate analysis

The variables analysed here were new-born anthropometry, maternal variables, and social variables. The only variable found significant was Apgar score at five minutes. This is quite natural because if the Apgar score was low at five minutes then obviously the infant was at risk and there was every possibility that the infant might die in a short time. If the Apgar score was good at five minutes then there was every possibility that the infant might survive. As we could not find out any significant factor in univariate analysis we excluded multivariate logistic regression.

Table 35 : Univariate (unadjusted) analysis of risk factors for early (<7 days) neonatal deaths (n=89) compared with late neonatal deaths (>7 days) (n=14)

a. anthropometric variables

b. maternal variables

c. social variables

Variable	dead <7 days			dead >7 days			odds ratios 95% CI	P value
	mean	sd	n	mean	sd	n		
<i>New born details</i>								
birth weight (kg)	1.6	0.5	89	1.7	0.4	14	1.93 (.62 - 5.91)	0.250
birth length (cm)	40.5	4.9	89	40.9	3.6	14	1.02 (0.9 - 1.15)	0.717
head circumference (cm)	29.7	3.0	89	30.9	2.0	14	1.15 (0.9 - 1.41)	0.147
chest circumference (cm)	26.3	3.2	89	28.0	2.0	14	1.19 (0.99 - 1.42)	0.056
arm circumference (cm)	7.6	1.2	89	7.5	0.9	14	0.97 (0.6 - 1.6)	0.922
haemoglobin (g/dl)	14.6	2.5	89	15.8	1.4	14	1.2 (0.96 - 1.55)	0.096
resuscitation (min)	21	18	85	9	7	14	0.96 (0.93 - 0.99)	0.024
Apgar score 1 min	4	2	89	5	2	14	1.35 (1.02 - 1.7)	0.031
Apgar score 5 min	6	2	89	7	1.0	14	1.56 (1.12 - 2.2)	0.008
Gestational age (wks)	34.08	3.34	89	35.3	2.11	14	1.13 (0.94 - 1.34)	0.174
<i>Placental details</i>								
placental weight (kg)	0.4	0.2	88	0.4	0.2	14	1.49 (0.06 - 37.3)	0.806
<i>placental colour</i>								
normal	67 (75%)			11 (79%)			0.85 (0.25 - 2.9)	0.794
abnormal	22 (25%)			3 (21%)				
<i>Maternal details</i>								
weight (kg)	47	7	81	46	5	12	0.98 (0.89 - 1.06)	0.553
height (cm)	149	6	79	148	5	12	0.95 (0.85 - 1.05)	0.327
<i>Socio-economic status</i>								
<i>Mothers education</i>								
none	50 (65%)			8 (73%)			0.66 (0.24 - 1.7)	0.412
primary	20 (26%)			3 (27%)				
secondary	7 (9%)			0				
<i>Social score</i>								
high	8 (10%)			0			1.2 (0.45- 3.11)	0.714
medium	25 (32%)			5 (45%)				
low	44 (57%)			6 (55%)				

4.3.4. Summary of risk factors for stillbirths and neonatal deaths

Table 36 is a summary table showing the risk factors for stillbirth and neonatal deaths.

The important independent risk factors for stillbirths were abnormal placental colour and low social class, no maternal education. The important risk factors for neonatal deaths were low birth weight, small MUAC, lack of antenatal care, maternal anaemia, teenage at marriage and no maternal education.

Table 36 : Summary of risk factors for stillbirth and neonatal deaths

	Odds ratios	P>z	95% CI
Stillbirths			
<i>Education</i>			
secondary	1.00	0.032	1.08 - 1.65
primary and nil	1.45		
<i>Placental colour</i>			
normal	1.00	0.000	3.13 - 10.70
abnormal	5.78		
<i>Social class</i>			
high social class	1.00	0.053	0.97 - 141.99
low social class	11.72		
Neonatal death			
birth weight >2.00	1.00		
birth weight (1.5-1.99)	1.62	0.21	0.75 - 3.47
birth weight (0.5-1.49)	6.28	0.002	1.98 - 19.91
MUAC at birth	0.29	0.00	0.19 - 0.46
normal placental colour	1.00		
abnormal placental colour	2.36	0.02	1.09 - 5.06
antenatal care	1.00		
no antenatal care	2.31	0.01	1.21 - 4.41
maternal hb (>11 gm)	1.00		
maternal hb (11-9.99g)	2.50	0.05	0.96 - 6.49
maternal hb (<9 g)	3.05	0.02	1.12 - 8.31
<i>Age at marriage</i>			
after teenage	1.00		
at teenage	3.60	0.004	1.49 - 8.72
<i>Maternal education</i>			
secondary and above	1.00		
nil	2.52	0.004	1.33 - 4.75

4.3.5 Key findings for risk factors for stillbirths and neonatal deaths

1. Key variables for stillbirths identified by univariate analysis were all anthropometric variables ($P < 0.002$) except head circumference ($P < 0.887$), placental length (OR 0.84, CI 0.76-0.93) and breadth (OR 0.85, CI 0.77-0.95), abnormal placental color (OR 0.20, CI 0.11-0.38), antenatal visits (OR 0.80, CI 0.73-0.86), maternal anaemia (OR 0.74, CI 0.62-0.88), mothers education (OR 0.35, CI 0.24-0.51), and low social score (OR 3.44, CI 2.3-5.1).

2. Variables which remained after multivariate logistic regression analysis for the risk of stillbirths were, mothers education (OR 1.45, CI 1.08 to 1.65); abnormal placental colour (OR 5.78; CI 3.13 to 10.70), and social class (OR 11.72, CI 0.97 to 141.90).

3. Key variables for neonatal deaths identified by univariate analysis were all anthropometric variables ($P < 0.001$), infant haemoglobin (OR 0.67, CI 0.6-0.75), and gestational age (OR 0.56, CI 0.51-0.61), placental length (OR 0.85, CI 0.77-0.92), breadth (OR 0.84, CI 0.76-0.90), and color (OR 0.50, CI 0.21 - 0.88), number of previous pregnancy (OR 1.3, CI 1.09-1.5) no. of dead child (OR 3.01, CI 1.8-4.8), antenatal visits (OR 4.14, CI 2.68 -6.67), mothers education (OR 0.37, CI 0.26-0.52), maternal haemoglobin (OR 0.82, CI 0.71-0.94) and blood pressure (OR 1.02, CI 1.0-1.03).

4. Variables remaining after multivariate logistic regression analysis for neonatal deaths were extremely low birth weight infants (OR 6.28, CI 1.98-19.91), MUAC (OR 0.29, CI 0.19-0.46), abnormal placental colour (OR 2.36, CI 1.09-5.06), antenatal care (OR 2.31; CI 1.21-4.41); Maternal anaemia, Hb $< 9\text{g/dl}$ (OR 3.05, CI 1.12-8.31), teenage marriage (OR 3.60, CI 1.49-8.72), fathers occupation (OR 2.67 CI 1.44-4.95) and mother's education, nil compared with secondary education (OR 2.52, CI 1.33-4.75).

5. No difference was found when we compared infants dying in the first week with those dying after the first week, except for low Apgar score in the early deaths.

4.4. Verbal autopsy data for causes of neonatal deaths and stillbirths

4.4.1. Causes of neonatal deaths

Table 37 : Overall causes of neonatal death

Overall causes of death	frequency	percent
birth asphyxia	66	34
prematurity	47	24
low birth weight	41	21
respiratory distress syndrome	16	8
sepsis	9	5
neonatal pneumonia	7	4
sudden death	5	2.5
others	6	3

Table 37 is the percentage distribution of causes of neonatal death, as assessed at verbal autopsy. Some infants were considered to die from more than one cause.

The major causes of neonatal death were assessed to be due to birth asphyxia, prematurity and low birth weight. Other causes were respiratory distress syndrome, sepsis, neonatal pneumonia, sudden death, diarrhoea, postnatal aspiration, hypothermia, and unknown. Of these 103 deaths, 81 infants died in the hospital and 22 at home.

4.4.2. Causes of still births

Table 38: Causes of stillbirth

cause by doctor	frequency	percent	cause by mother	frequency	percent
asphyxia	8	16	devils eye	5	19
prolonged labour	7	14	excessive handling	5	19
eclampsia	6	12	prolonged labour	4	15
hand prolapse	5	10	eclampsia	4	15
excessive handling	4	8	communication	4	15
hypertension	3	6	hand prolapse	2	7
cord prolapse	3	6	cord prolapse	2	7
transverse lie	3	6	trauma	1	4
obstructed labour	2	4			
sepsis	2	4			
placental insufficiency	2	4			
premature separation of placenta	2	4			
ruptured uterus	2	4			
PET	1	2			
cord around neck	1	2			

Table 38 presents causes of stillbirths assessed by doctors and from maternal interview.

Causes of stillbirth were malpresentation (cord prolapse, hand prolapse, and transverse lie), asphyxia, eclampsia, excessive handling, hypertension. Other causes included obstructed labour, sepsis, placental insufficiency, premature separation of placenta, ruptured uterus. All of these causes were the result of inefficient management and or complications during labour. We found some difference of opinion between the mothers and doctors about the cause of foetal death. In the villages any unexplained and unwanted event are expressed as 'devils eye'. Sometimes they cannot notice that the foetus is dead, so when they deliver a dead baby they mention it as 'devils-eye'. Even the eclamptic fit was also designated by villagers as the 'devils eye'. Other causes explained by mothers was the transport problem, which is a real problem in the villages. Usually they put all effort to have a delivery at home, but when they fail they take the decision to come to the hospital. Then they find difficulty in coming there because of transport problems; after a long effort to reach the hospital it is often too late.

4.4.3. Key findings of verbal autopsy and still births

1. The most important causes of death were birth asphyxia, prematurity, and low birth weight. The other major causes were respiratory distress syndrome, sepsis, neonatal pneumonia, and sudden death.

Caution is needed when assigning a neonatal cause of death by verbal autopsy because the method has not been validated against a gold standard of actual autopsy.

2. The major causes of stillbirth were malpresentation, asphyxia, eclampsia, excessive handling, and maternal hypertension

4.5. Neonatal details at follow up

4.5.1. Neonatal growth and morbidity in low birth weight infants

Table 39: Anthropometric details of study infants at birth and at follow up at 28 days

Variable	mean	sd	min - max	n
<i>New born details</i>				
weight (kg)	2.1	0.4	0.5 - 2.5	999
length (cm)	44.3	3.4	25 - 54.5	999
mid upper arm circumference(cm)	8.7	1.0	4.3 - 13.0	999
head circumference (cm)	32	2.0	18 - 39.5	999
chest circumference (cm)	28.9	2.4	16 - 36.6	999
haemoglobin (g/dl)	16.0	1.9	8.3 - 21.3	918
<i>Follow up details</i>				
weight (kg)	3.0	0.6	1.0 - 4.6	616
length (cm)	50.2	2.8	35 - 58	616
mid arm circumference (cm)	10.1	1.3	6 - 13.5	616
head circumference(cm)	34.8	1.7	27.4 - 39	616
chest circumference (cm)	32.4	2.6	22.5 - 39.7	616

Table 39 shows the anthropometric details of study infants at the age of 28 days.

Though we enrolled 999 infants, we had only 616 complete follow up measurements. The rest were dropped either because they died or we could not find their address. From the minimum value of follow up weight it was evident that there were some (1.3%) infants who were in the extremely low weight group (<1.5kg) even at one month of age.

Table 40 shows the distribution of neonatal morbidity collected by interviewing the mother at the follow up visit.

During the follow up study the infants were seen by the principal investigator, and all the clinical details and morbidity during the month and at the time of visit were taken into account. 35% of infants were reported to have suffered an illness. The major illnesses found were fever (22%), respiratory illness (21%), cold (19%), diarrhoea (18%), rash (14%), jaundice (12%), umbilical sepsis (5%), and skin disease (3%). Overall 35% of the infants were found suffering from one of these problems indicating that neonatal morbidity among LBW infants is extremely common.

Table 40: Distribution of neonatal morbidity

Distribution of illness	frequency (percent)	
fever	46	22
respiratory illness	45	21
cold	40	19
diarrhoea	39	18
rash	29	14
jaundice	26	12
umbilical sepsis	10	5
skin disease	7	3
total	214	35

Table 41 is the distribution of neonatal growth according to socio-economic level, sex of the infant, feeding practices, and morbidity.

Table 41: Distribution of neonatal growth according to socio-economic condition, sex of the infant, breast feeding and morbidity

Variable	proportional weight at 28 days		P	Total
	below 25th percentile (%)	above 25th percentile		
<i>Social score</i>				
high	27 (22)	95 (78)	0.022	122 (100)
medium	87 (23)	297 (77)		384 (100)
low	38 (35)	70 (65)		108 (100)
Total	152 (25)	462 (75)		614 (100)
<i>Sex</i>				
male	71 (23)	233 (77)	0.388	304 (100)
female	82 (26)	230 (74)		312 (100)
Total	153 (100)	463 (100)		616 (100)
<i>Feeding practice</i>				
breast + water	68 (18)	314 (82)	0.000	382 (100)
others	80 (38)	133 (62)		213 (100)
Total	148 (25)	447 (75)		595 (100)
<i>Morbidity</i>				
illness present	87 (41)	125 (59)	0.958	212 (100)
no illness	126 (33)	257 (67)		383 (100)
Total	213 (35)	382 (65)		595 (100)

The growth of the infants were measured by their anthropometric measurements at age of around 28 days. The weights at birth and follow-up were converted to standard deviation scores using the British Growth Standards (Cole *et al*,1998), then the change in standard deviation score over the neonatal period was calculated by simple subtraction. The values for

‘proportional weight gain’ for all the LBW infants studied were converted in to centiles, and all infants with proportional weight gain below the 25th centile were considered to have ‘poor growth’ (cases), and were compared with the infants above the 25th centile who acted as ‘good growth’ (controls). All the infants divided into these two groups were compared by social status, sex, feeding practices, and morbidity variables.

35% of the infants had an illness during the neonatal period. The percentage of infants of the >25th centile group was highest (78%) in the high social class, and lowest (65%) in the lower social class. The feeding practices was divided into two groups, breast + water and others. Other foods include formula food, sugar water, rice water, and barley. Usually the rural mothers never use the recommended formula to prepare the food, rather they use a diluted form of food, because they do believe that recommended formula is highly concentrated and high concentration might cause some tummy problem for their baby. Infants having the growth of >25th centiles were mostly (82%) breast fed, infants of <25th centile groups were mostly non-exclusively breast fed (38%).

Univariate analysis

Table 42 shows the risk factors for poor neonatal growth by univariate analysis.

Univariate (unadjusted) analysis of risk factors for poor neonatal growth (n=153) compared with normal neonatal growth (n=463) failed to show any significant factor except the anthropometric measurements. Having neonatal illness did not have any significant relation with growth but diarrhoea ($P<0.001$) and feeding practices ($P<0.000$) were significantly related ($P<0.001$) with poor growth. Maternal education and fathers education were also identified as a risk factor for poor growth. The important variables showing no relation were illness during the 28 days period, included maternal height and weight, and social class.

Table 42: Univariate (unadjusted) analysis of risk factors for poor neonatal growth (n=153) compared with normal neonatal growth (n=463)

a. morbidity variables

b. maternal variables

c. social variables

Variable	odds ratio	confidence interval	P value
<i>Morbidity variables with follow up anthropometry</i>			
weight	0.08	0.02 - 0.08	0.000
length	0.67	0.62 - 0.72	0.000
head circumference	0.55	0.49 - 0.61	0.000
chest circumference	0.62	0.58 - 0.66	0.000
arm circumference	0.37	0.32 - 0.43	0.000
follow up illness	0.99	0.68 - 1.46	0.983
follow up food	1.29	1.20 - 1.38	0.000
gestational age	0.77	0.70 - 0.85	0.000
discharge time	1.00	1.00 - 1.00	0.000
resuscitation time	1.08	1.05 - 1.12	0.000
diarrhoea	0.29	0.14 - 0.62	0.001
<i>Maternal variables</i>			
maternal weight	1.01	0.95 - 1.03	0.463
maternal height	0.99	0.50 - 0.99	0.680
<i>Social variables</i>			
maternal education	0.66	0.50 - 0.88	0.004
fathers education	0.67	0.58 - 0.88	0.005
fathers occupation	0.69	0.53 - 0.97	0.010
social score	1.40	1.04 - 1.89	0.027

Note: follow up food was defined as breast milk + water and any food other than breast milk.

diarrhoea was defined by asking about smell (foul), and frequency(>5 per 24 hrs), time of defecation(not related with food).

Multivariate analysis

Table 43: Stepwise backward multivariate logistic regression analysis of risk factors for poor neonatal growth (n=152) compared with normal neonatal growth (n=463)

Significance level for removing = .4

Significance level for entering = .2

Number of obs = 595

$\chi^2(4) = 51.16$

Prob >chi2 = 0.0000 Pseudo R2 = 2.166

Proportion of weight gain	Odds ratio	P> t	[95% Conf. Interval]
<i>Resuscitation time</i>			
>1 min	1.0		
<1 min	1.44	0.47	0.53 - 3.9
<i>Gestational age</i>			
>37 weeks	1.0		
<37 weeks	1.70	0.17	0.79 - 3.66
<i>diarrhoea</i>	0.28	.003	0.12 - 0.64
<i>Follow up feeding</i>			
breast + water	1.0		
others	5.46	0.000	2.59 - 11.49
Length at birth	0.81	0.004	0.69 - 0.93

This table shows the backward stepwise logistic regression analysis of factors for infants growth. After doing the univariate analysis the important factors came into consideration for logistic regression analysis was resuscitation time, gestational age, diarrhoea, bad feeding practices, and short length of the infant at birth.

4.5.2 Key findings of risk factors for poor neonatal growth among low birth weight infants.

1. Key variables identified by univariate analysis were all the anthropometric measurements, low gestational age, prolonged resuscitation time, time of discharge from the hospital, feeding practices, diarrhoea, and socio- economic parameters.
2. After multivariate analysis by logistic regression, the key variables identified as risk factors for poor neonatal growth were resuscitation time (OR 1.44; CI 0.53-3.9); gestational age (OR 1.70; CI 0.79-3.66); diarrhoea (OR 0.28, CI 0.12 to 0.64), feeding with breast milk substitutes (OR 5.46 CI 2.59 to 11.49), and short length of infant at birth (OR 0.81, CI 0.69 to 0.93).

Chapter 5

Discussion

Study Design Issues

The study was aimed to measure prospectively the mortality and morbidity outcome, and risk factors, for low birth weight infants in Dhaka. It was a prospective study in which new born infants were followed up only for one month, which is a very short time to predict growth, but is the peak risk period for mortality in infancy.

a) Target population

I selected only low birth weight infants. It might be questioned why normal birth weight infants were not included. As 50% of infants in Bangladesh are low birth weight, and low birth weight itself is an important factor for neonatal mortality, a focus on low birth weight infants will be more cost effective. There was limited time and budget, so we decided to look at a large sample of the highest risk group in order to study the risk factors in more detail, and to increase the power of the study.

b) Follow up

It is very difficult to do a follow up study in Bangladesh, where many people are homeless, there is no housing plan and rarely specific addresses. Moreover many people are illiterate so they cannot report their address properly. However in spite of these problems 80% of the study population were followed up. The outcome measures from the follow up study were to find out neonatal mortality and, morbidity rates shown in the flow sheet: 132 per thousand was the neonatal mortality rate, of which 114 per thousand died in the first week and 18 per thousand in the second to fourth weeks of life, still birth rate 62 per thousand, perinatal mortality rate was 179 per thousand, 22% were missing, 16% of them were totally lost and 6% were alive at the time when they were lost, so we don't know exactly about their fate. The rest of the infants were followed up completely and all the details about them were taken into consideration.

c) How representative of Bangladesh as a whole?

- Most of the population (55%) I studied were poor (income average of <3000.00 taka per month). They were drawn from Mitford Hospital. This probably biases towards the better off

because -of higher income level (<3000.00 taka per month) than national average (700.00 taka per month) (Bangladesh Bureau of Statistics,1995) and accessibility to the hospital.

- Low birth weight in the hospital (26%) was below the national average (50%) (WHO, 1992).Therefore my low birth weight population might be slightly socio-economically advantaged. Moreover as they were in and around Dhaka city they had at least some accessibility to the antenatal care services. But because it is a hospital population we might have selected higher risk mothers and infants.

5.1. Summary of base line details

From the base line details we can summarise that :

- This was a mixed population from different social class group, coming from different areas of Dhaka city and around.
- Most of the population were coming from middle social class group (57%).
- Total population was a group of mixed birth weight categories from extremely low birth weight to moderately low birth weight groups.
- The mothers have different nutritional status from well nourished to poor nourished.
- The extremely low birth weight and premature infants were highest in lower social class and lowest in the upper social class group.

The base line details of the mother's nutritional status and socio-economic distribution of low birth weight infants were comparable with the other studies done in Bangladesh (Rawshan, 1978;Canosa,1989).Obviously in my study all anthropometric measurements of the mothers were taken postpartum, when there is a possibility of over-reading and/ or under-reading because of oedema and excessive postpartum bleeding. Maternal growth during pregnancy is significantly associated with decreased birth weight, when maternal growth continues during subsequent adolescent pregnancy (Scholl *et al*, 1992).

The number of extremely low birth weight infants was high in the lower social class group. Adverse pregnancy outcome in the lower social class group is a common feature in the developed and developing countries (Sanjose and Roman, 1991; Fikree *et al*, 1994; Summit *et al*, 1996; Hoa *et al*, 1996). But in a Nigerian study they found that there was no relationship of birth weight with maternal education and socio-economic status (Lawoyin and Oyediran,

1992), though they found a significant relationship with maternal age, parity, height, weight, body mass index, seasonal variation, which are the indirect socio-economic parameters. It might be explained by the fact that all these Nigerian mothers were recruited from the antenatal clinic and we can assume that because they have visited antenatal clinics they were from better social status so they could not find any relationship with maternal education and socio economic status, or it could be that they were confounded by other socio-economic parameters.

Limitation of base line information

As this base line information was taken from a hospital in an urban setting, this study does not claim to represent all women in Bangladesh. We have taken only mother's postnatal anthropometry when many of them were oedematous, had profuse blood loss, and we didn't have any antenatal data by which we can compare. Many of them did not make antenatal visits, or the visits were unrecorded. We also had a limited time and budget. But when we compare our results with some other studies (Sanjose and Roman, 1990; Fikree *et al*, 1994) it concurs with their results, which suggests our population is reasonably representative of urban and periurban women in Bangladesh. From our base line information we can say that women's education level is still very poor in our country. If we are to improve the social level at the community much effort is needed to improve women's education.

5.2. The summary of risk factors for stillbirth to neonatal survivors are

- Maternal illiteracy increases the risk of stillbirth (OR 1.45; CI 1.08 - 1.65), primary and nil education compared with secondary and above.
- Abnormal placental colour is strongly associated with stillbirth (OR 5.78; CI 3.13 - 10.70).
- Mothers from lower social class has high risk of stillbirth (OR 11.72; CI 0.97 - 141.9).

In univariate analysis small fetuses were found to be significantly ($P < 0.00$) associated with stillbirths, though it was found that foetal head circumference was not significant ($P < 0.887$); it increases with the same rate in the stillbirth and survivors group. Very small birth weight and larger birth weight, and primiparity and grandmultiparity (4+) had a significant increase in stillbirth rate (Petridou *et al*, 1996; Raymond *et al*, 1994). In our study we had only the

small birth weight group, so we can't comment on the larger group, and we could not find any relation with parity but we found a significant relationship with a history of previous abortion.

Socio-economic conditions when independently considered were significantly associated with stillbirth, which was supported by others (Arntzen *et al*,1996; Fikree *et al*,1996; Petridou *et al*, 1996; Meis *et al*,1995; Gadow *et al*,1991). Although univariate analysis identified foetal anthropometric measurements, maternal factors and socio-economic factors related with stillbirth, in multivariate logistic regression all these factors confounded by each other and dropped from the analysis.

The most predictive risk factors for low birth weight stillbirths after multivariate logistic regression were

- abnormal placental colour (OR 5.78, CI 3.31-10.70).
- mothers who have no education (OR 1.45, CI 1.08 - 1.65).
- mothers from lower socio-economic class (OR 11.72, CI 0.97-141.99).

Mother's education and lower socio-economic class are more prone to unhygienic conditions, leading to clinical and subclinical infections. We haven't got any evidence about the antenatal infection of the mothers, because we do not have any antenatal data, nor was there any study about maternal antenatal infection or STD. There is evidence from different parts of India that one fourth of women had clinical evidence of pelvic inflammatory disease and cervical ectopy and 10 percent with sexually transmitted disease. In cervical cytology 85% had got inflammatory epithelial changes (Imseis *et al*, 1997; Singh *et al*,1995; Bhatia *et al*,1997).

Mothers might have sexually transmitted diseases which we do not know about, because there are no data about STDs in Bangladesh. We know from our experience, women might have got infected with STDs from their husbands or clients. It is reasonable to believe the relative effect of various maternal sexually transmitted disease on adverse pregnancy outcome, pre-term labour, premature membrane rupture (Goldenberg *et al*,1997; Calleri *et al*, 1997). There is also evidence that bacterial vaginosis is a predictor of intraamniotic infection (Newton *et al*,1997).

Maternal infection leads to placental infections. In our study we found placental infection as a strong predictor of stillbirth and neonatal death. Moreover these mothers might have some micronutrient deficiency and lower immune response. There is also evidence of a slow trend of maternal anaemia among the stillbirth group. Finally this data supports the argument to test targeted antibiotic intervention in the antenatal period for high risk mothers, which is supported by some studies (Steele,1996; Begum *et al*, 1997). This was argued by Colli who found the results of controlled clinical trial for bacterial vaginosis during pregnancy were not entirely consistent, but he mentioned that there is a strong association between the presence of bacterial vaginosis during pregnancy and the risk of pre-term birth (Colli *et al*,1996). There is evidence that subclinical intraamniotic infections are present in 30% of asymptomatic patients with premature rupture of membranes (Alessandro *et al*, 1997). 15% of mothers in our study had premature rupture of membranes.

In our study we found maternal eclampsia and hypertension (18%), asphyxia (16%), and malpresentation (hand prolapse) (10%) were the major causes of stillbirths. It is evident from different studies (Brown,1995) that pre-eclampsia and hypertension are the major causes of placental disorders. Most cases of placental insufficiency resulting from inadequate placentation are the result of maternal vascular insufficiency during the early stages of pregnancy. In pre-eclampsia placenta releases a cytotoxic factor causing widespread maternal endothelial cell damage. Its manifestations are organ hypoperfusion arising from vaso constriction, intravascular coagulation, and reduced maternal blood volume. As a result the foetus is affected by the placental insufficiency, causing intrauterine growth retardation, small for date, and intrauterine foetal death (Brown, 1995; Salafia *et al*, 1995; Kumar and Singhi, 1992; Kalder *et al*, 1995; McMahon *et al*, 1993; Redman, 1992; Ahlenius *et al*, 1995; Raymond *et al*, 1994; Axemo *et al*, 1993; Alessandri *et al*, 1992; Assche and De Prine, 1981). In our study we found a strong association between stillbirth and abnormal placental colour, but we could not find any association with blood pressure . We did not have attended details of blood pressure so we cannot rule out this association.

Asphyxia was another cause of stillbirth which might result from placental insufficiency, pregnancy induced hypertension, anaemia, infection, and prolonged labour. As any of the

above conditions might cause asphyxia, and any new-born who died passes through the stage of asphyxia, it is very difficult to diagnose the actual cause of death and rather preferable to express as a common term asphyxia. Moreover there is limited facilities for diagnosis of foetal pathology, and as most of these patients come at labour, antenatal foetal diagnosis was impossible. There is evidence of intrauterine foetal death on the basis of these maternal complications (Gai,1990).

Prolonged labour, malpresentation (hand prolapse and cord around the neck), and excessive handling were the other important causes of foetal death in my study. These are strong evidence of poor obstetric and antenatal care services. In our univariate analysis we found the number of antenatal visits was independently associated ($P<0.00$) with stillbirths. All these studies confirm the same that inadequate obstetric care and insufficient antenatal visits are the important determinant of foetal loss (Fernando *et al*, 1989; Kapoor *et al*, 1985; Kramer, 1987; Rahman *et al*, 1984; Korejo and Jafarey, 1991; Goffinet *et al*, 1996).

The causes we found in our study are the common causes of stillbirth found in other studies as well (Fauveau *et al*, 1990; Coard *et al*, 1991; Pratinidhi, 1986; Mavalankar *et al*, 1991; Were, 1994). In our study these dead fetuses were all low birth weight and without any congenital malformation. We know congenital anomaly is an important risk factor for stillbirth (Seku *et al*,1991) but from our study we have excluded congenital malformation. Because the incidence of stillbirth from other preventable causes was so high, we should emphasise preventable causes first if we are to reduce the rate. It is the antenatal visits and safe delivery which can minimise these complications and reduce foetal loss.

Raymond found that maternal age, nulliparity, and smoking is associated with stillbirths, as age advances the medical diseases like diabetes, hypertension, and placental complication increases, so risks of stillbirths increases. In my study I found foetal death is highest in the less than 20yrs and more than 35yrs age group. In Bangladesh it is very difficult to measure the age of the mothers because we don't have any birth registration system and mother often don't know their age. Maternal smoking is not a problem in Bangladesh, because women are mostly non-smokers.

We did not measure gestational age for stillbirth group, because mothers do not reliably give the date of their last menstrual period, and clinical gestational assessment is difficult for a stillbirth.

Limitations of the study

As the appearance of the placenta was found to be an important determinant of stillbirth we should study placenta in detail. We have done only the gross morphological study of the placenta. The laboratory facility was limited with limited resources, budget and time so it was not possible to perform the microscopical examination of the placenta or biochemical studies. This was a fifteen months study and in one hospital only, a teaching referral hospital. So a question may arise about bias, that only complicated cases are coming here for treatment. But though it was a referral hospital, it is also a Government hospital which gives free treatment, and many poor patients come here for free treatment without referral.

5.3. Pattern of neonatal deaths,

- Death rate in the early neonatal period (0-6 days) was 12 times higher than the late neonatal period (7-28 days) in very and extremely low birth weight group of infants (500gm - 1.5kg).
- The extremely low birth weight (0.5-1.49kg) group of infants are the highest risk group for perinatal and neonatal death.
- Death rate was three times higher in the premature group (<37 weeks) than the mature groups (>37 weeks).
- Survivability is proportionally related with birth weight and gestational age.
- The major causes of death were birth asphyxia, prematurity, and low birth weight. The other causes are respiratory distress syndrome, sepsis, neonatal pneumonia, sudden death, and others.

In our study no infants of <1.00 kg survived. The highest survivability of the infant of <1kg was 120 hrs. It is a good sign that the infant of <1kg has survived 120 hrs: if we could take extra care for this group of infants their survivability might increase. The smallest infant survived in our study was 1.1kg. The neonatal mortality rate in this population of low birth weight infants was 133/1000 live birth. Other studies found neonatal mortality rate in rural Bangladesh around 70-100/1000 live births (Rahman and Nessa, 1989; Nessa *et al*, 1992,

Bangladesh Demographic and Health survey, 1995; Rahman *et al*, 1985). Our rate is higher because we have studied only the low birth weight group, which itself is a risk group for neonatal mortality. In univariate analysis smaller infants and lower gestational age were found to be significant ($P<0.00$) for neonatal death.

Prematurity is another risk factor for neonatal mortality (Rahman and Nessa, 1989). We found mortality in premature infants was three times higher than the mature group. Rahman found five times the risk in the premature group, but his study included all birth weight infants so the risk differential should be higher (Rahman and Nessa, 1989). Moreover it may be that they did their study among infants born at home and followed up at home where there were no facilities for the management of high risk groups. Our study was done in the hospital where there were facilities for the management of risk group. This might be the cause of comparatively lower mortality in the premature group. As birth weight increases, the risk of mortality decreases, which has been supported by other studies (Parazzini *et al*, 1992).

5.4 Risk factors for neonatal deaths among low birth weight infants

Univariate analysis

In univariate analysis haemoglobin level of infants at birth was significantly associated (OR 0.67; CI 0.6 to 0.75) with neonatal death. Neonatal anaemia is associated with antepartum maternal haemorrhage, maternal anaemia, and intrapartum maternal blood loss and there is evidence that neonatal anaemia is a risk factor for neonatal mortality and morbidity (Fay, 1983; Agarwal, 1982; Fourn, 1994). As we don't have good antenatal records we can't say about the maternal antenatal conditions. But we found 78% of the mothers had a haemoglobin level below WHO standard (11g/dl).

Maternal anaemia is a contributory factor for neonatal anaemia which was found as a risk factor for neonatal death. There might be some intrapartum subclinical infection which could be a cause of a lower haemoglobin level in the neonatal death group.

We also found that antenatal visits and the number of previous dead children were significant ($P<0.00$) risk factors for neonatal death, but previous stillbirths, abortion and maternal weight had no relation with neonatal mortality, which was supported by other authors (Shah, 1984;

Millat, 1992; Mavalankar, 1991). However, some authors found that a bad obstetric history, and maternal height and weight has a significant relationship with low birth weight, (Vega, 1993; Ahmed, 1994; Taha, 1993) but not with neonatal mortality, though low birth weight itself is a risk factor for neonatal mortality. We found 22% of the mothers were <147 cm height and 73% were <50 kg weight. It is assumed from this data that most of our mothers were underweight, which according to some author is a predisposing factor for low birth weight (Vega, 1993; Ahmed, 1994; Taha, 1993). Prentice said that maternal size is a good predictor of birth weight, as a natural biologic phenomenon small mothers can produce a normally proportioned but small babies without any health risk (Prentice, 1994). From these arguments the international definition of low birth weight could be modified for different regions of the world. But we did not find any association of maternal height and weight with neonatal mortality. As we have considered only low birth weight we cannot compare relationship of normal birth weight infants with maternal height and weight.

Multivariate analysis

Many of the factors identified by univariate analysis were dropped in stepwise multivariate analysis. After exclusion, the important variables came into consideration were:

- extremely low birth weight infants (0.5 - 1.49 kg), OR 6.28; CI 1.98 to 19.91
- mid arm circumference, OR 0.29; CI 0.19 to 0.46
- abnormal placental colour, OR 2.36; CI 1.09 to 5.06
- no antenatal care, OR 2.31; CI 1.21 to 4.41
- maternal anaemia (haemoglobin level <9g/dl), OR 3.05; CI 1.12 to 8.31
- young age at marriage OR 3.60; CI 1.49 to 8.72
- no maternal education OR 2.52; CI 1.33 to 4.75

These were the important variables found as significant risk factors for neonatal mortality. Low birth infants were prone to early death (Chen *et al*, 1980) and later to cardiovascular disease and hypertension at an early age (<65yrs). Later gestational insults impair longitudinal bone growth and poor liver development which causes disturbance in cholesterol mechanism, blood clotting mechanism and hypertension (James *et al*, 1997).

Age at marriage and maternal illiteracy is the index of poor social class. In Bangladesh 90% of the girls get married at teenage. Some of them before menarche. They don't have any opportunity for education. At the age of their growth and development the girls become pregnant, and the foetus develops at the expense of the mother. Because of illiteracy and poverty they suffer from anaemia and malnutrition and don't have any antenatal care. All these factors together lead the mothers with adverse pregnancy outcome.

Abnormal placental colour that is black and green indicates clinical or subclinical infection during pregnancy which predisposes placental insufficiency, and causes vulnerability to neonatal death. There is evidence that exposure to maternal or placental infection is related to pre-term birth, and in premature infants, brain lesions are predictive of cerebral palsy (Grether and Nelson, 1997) which has got serious public health importance. Maternal anaemia to some extent is a cause of placental insufficiency and neonatal anaemia, which increases the risk of giving birth to a low birth weight infant and risk of dying in the neonatal period. The inadequate iron availability may be related to a high placental/birth weight ratio and predictive of long term cardiovascular disease and hypertension. It is suggested that hypertrophied placenta may result alteration in foetal metabolism and any alteration in placental cortisol metabolising system might result low birth weight infants being susceptible to hypertension (James *et al*, 1997). But Heilmann observed perinatal morbidity and maternal hyperviscosity in women with a high haemoglobin level (Heilmann *et al*, 1993).

5.5 Risk factors for early versus late deaths

Univariate analysis of risk factors for early and late neonatal deaths reveals that new-born birth anthropometry and gestational age do not have any significant relationship with early (<7 days) compared with late (>7 days) neonatal death. The significant factors that affect the time of death are resuscitation time ($P<0.024$), Apgar score at 1 minute ($P<0.031$) and 5 minutes ($P<0.008$). It was evident from different studies that Apgar score at 1 minute <3 was regarded as severe asphyxia and = or >6 as no asphyxia, and the best predictor of foetal outcome (Gonzalez *et al*, 1996; Lenox *et al*, 1990; Williamson *et al*, 1989; Yudkin *et al*, 1994; Hsieh *et al*, 1994; Spinillo *et al*, 1993; Williamson and LeFever, 1992; Lam and Yeung, 1992; Ong *et al*, 1989; Stevenson *et al*, 1988; Takahashi *et al*, 1984; Batzofin *et al*, 1984;

Bhatia *et al*, 1984). Obviously these are the important signs of complicated labour. Lower Apgar score is the result of IUGR and pre-term labour and longer resuscitation time.

There are many socio-cultural factors associated with IUGR and pre-term labour (Gray *et al*, 1991). It could be argued that interventions for these factors could help to reduce adverse pregnancy outcome, but these are long-term interventions. For short term intervention we can suggest simplified methods of neonatal care (Hey, 1975). Other factors like placental factors, obstetrical factors, socio-economic factors do not show any significant relationship with early compared with late neonatal death. As univariate analysis does not show any important significant factor for early neonatal death, we didn't do multivariate logistic regression analysis. We can't conclude from this analysis any significant factor which predicts early versus late neonatal death, though 89% of deaths occur within seven days of birth.

5.6. Causes of stillbirths and neonatal deaths

Limitation of verbal autopsy

Information on causes of death is important for policy making, planning, evaluation of health programme and research. In developing countries this information is incomplete and poor quality especially in case of childhood death. The major difficulty in verbal autopsy was the lack of standardised diagnostic criteria and instruments of inquiry. Every study has got its own set of diagnostic criteria for various causes of death, that introduces considerable variation, which makes cross comparison meaningless. There is a need to develop a standardised diagnostic criteria and a questionnaire. In our study we followed a WHO proposed set of criteria to diagnose the cases (Bang and Bang, 1992). All of our verbal autopsies were done by doctors. We have few doubts about the accuracy of the history. Most of the time the history was given by the mothers, and it was taken within 28 days of death. The limitation of our data was that mothers cannot give an accurate history, and as it was a recent event they were upset and did not want to talk about it, so it was difficult to find out the cause of death. Sometimes we double check the cause of death, by taking the history and by looking at the attending doctors diagnosis, if the infant died in the hospital. However case notes are rarely complete, data on events in labour may not have been recorded, and often there are several causes of death rather than a single cause.

The major causes of death were birth asphyxia (34%), prematurity (24%), low birth weight (21%). The other causes were respiratory distress syndrome, sudden death, sepsis, neonatal pneumonia, and others. These causes were similar to studies done in Bangladesh and other developing countries (Islam *et al*, 1982; Tabib *et al*, 1987; Rahman and Nessa, 1989; Fauveau *et al*, 1990; Shah *et al*, 1984; Millat and Florey, 1992; Coard *et al*, 1991; Zhang *et al*, 1991; Barros *et al*, 1992; Daga and Daga, 1993; Bai *et al*, 1991). Tetanus (21%) and congenital anomaly (12%) is an important cause of death in Bangladesh (Rahman, 1982; Chen *et al*, 1980). Tetanus occurs mostly in case of home deliveries where there is no sterile aseptic delivery practices. As this study was done in the hospital all the deliveries were conducted in aseptic way, so we can presume there was little chance of tetanus. Birth injury was another cause of neonatal death which occurs mostly in home delivery where there is excessive manipulation to deliver the baby by the untrained birth attendants (Fauveau *et al*, 1990).

Congenital anomaly is another cause of neonatal death for both developing and developed countries. Only one study in Bangladesh (Islam *et al*, 1982) mentioned congenital anomaly as a cause of death (12%) while in other studies they did not mention congenital anomaly as a cause of death (Fauveau *et al*, 1990). I excluded congenital anomaly from my samples, because I wanted to see the mortality and morbidity pattern only in low birth weight infants (normally born) without any congenital anomaly and the prevention of which will be cost effective.

The common causes of stillbirths were asphyxia, prolonged labour, eclampsia, hand prolapse, excessive handling, delay in hospital attendance, hypertension, and others. These are the common causes found in other studies (Coard *et al*, 1991; Mavalankar *et al*, 1991; Fauveau *et al*, 1990; Were, 1994). One study found maternal age, nulliparity, and smoking has been associated with stillbirths (Raymond *et al*, 1994). As maternal age advances medical diseases like diabetes, hypertension, and placental complications increase so the risks of stillbirths rise. Moreover smoking causes placental insufficiency (Cnattingius *et al*, 1988). But maternal smoking is not a problem in Bangladesh.

5.7. Neonatal growth and morbidity

It is difficult to assess overall infant growth by following only for one month. We had only one follow up visit at the age of 28 days. During this visit we took all anthropometric details of the infant, a history of illness, and feeding practices; and then we divided the infants into a group of poor growth rate (<25th centiles) and normal growth rate (>25th centiles). These two groups were compared with morbidity variables, maternal variables and social variables by univariate analysis and backward stepwise logistic regression analysis.

Summary of risk factors for neonatal growth

- At the age of 28 days 22% of the infants were still <2.5kg.
- The common causes of illness were fever, respiratory illness, rash, jaundice, common cold, diarrhoea and skin infection.
- The infants who were breast fed (80%) had better growth than those who were non-breast fed (OR 5.46, CI 2.59 to 11.49).
- There were no differences in growth between sex.
- Infants of better growth were from higher social class than from lower social class (OR 1.4, CI 1.04 to 1.89).

The risk factors for poor neonatal growth were long resuscitation time (OR 1.44, CI 0.53-3.9), gestational age (OR 1.70 CI 0.79-3.66), small length at birth (OR 0.81, CI 0.69-0.93), feeding practices after birth (OR 5.46, CI 2.59 - 11.49) and diarrhoea (OR 0.28, CI 0.12 - 0.64).

The average weight of our study infants at birth was 2.1 kg and after one month 3 kg. At the age of 28 days 23% of infants were still below 2.5 kg, i.e. below the standard of WHO birth weight. The average chest circumference below 31 cm was diagnosed as a infant with low birth weight, <29 cm being diagnosed as 'highly at risk' and between 29 and 30 cm as 'at risk' with head circumference of 31 cm or less (WHO, 1993; Raymond *et al*, 1994; Huque and Hussain, 1991; WHO, 1987). These studies were done on both normal and low birth weight infants. My study was on the low birth weight infants only, so I found all the

anthropometric measurements below their levels. In my study the average chest circumference at birth was 28.9 cm, 70% had chest circumference below <30cm and head circumference was 32 cm, 28% had head circumference below <31 cm at birth.

The study in West Africa showed that MAC <9.5 cm had a best predictive value for low birth weight infants (Gozal *et al*, 1991). This value was also the best of all variables for the prediction of early postnatal morbidity (Gozal *et al*, 1991; Neela and Alvarez, 1991). I found 82% of infants had arm circumference of <9.5 cm at birth. The proportion of weight gain was less in smaller infants (.5 -1.5 kg) than the comparatively larger infants (1.5 - 2.5 kg). Richard J Cooke found the same for the smaller infants (Cooke, 1993) but he also mentioned that poorer weight gain couldn't be related to more illness or less nutrient intake in smaller infants.

Risk factors for neonatal growth

Overall 35% of the infants were found to have illnesses during the neonatal period. The major illnesses were fever (22%), respiratory illness (21%), common cold (19%), diarrhoea (18%), rash (14%), neonatal jaundice (12%), umbilical sepsis and skin disease. These are the common illnesses found all through the year in Bangladesh and in other developing countries (Chen *et al*, 1980; Rahman *et al*, 1993; Cuttini *et al*, 1991; Barros *et al*, 1992; Tabib *et al*, 1987,). It might be argued why diarrhoea is so common if they are breast fed. The percentage of exclusively breast fed infants is small (36%): most of them have breast with water together or other milk. So there is a possibility of bacterial contamination.

Sex

The growth was related with social class group: the lower the social class the poorer the growth. This is found in other studies (Rahman *et al*, 1985; Novotny *et al*, 1992; Brush *et al*, 1993). As birth weight advances growth advances, although one study found that weight gain was similar for all birth weight groups (Shaffer *et al*, 1987). There was a difference of weight gain in birth weight group, but no difference was found in the growth rate of boys and girls. Our study varies with most of the studies who found a growth difference between boys and girls (Moore *et al*, 1995). I didn't find any difference of growth between boys and girls

because I followed them only for one month which is a very short period to predict and comment on the growth of a child.

Morbidity

In univariate analysis the risk factors that could not come into consideration were illness of the infants during one month of follow up, maternal weight and height, and social score. It is very difficult to explain why infant's illness could not come into consideration, may be those who were ill some of them had good feeding, and or of high social class, which confounded the variable for significance.

Social class

Social score could not come into consideration independently as significant variable but mother's education and income came as a significant factor. As parent's education and income are important parameter of socio economic status social score may be confounded by these two factor. When backward multivariate logistic regression analysis was done many of the variables dropped confounded by other factors. The important variables strongly associated with growth of the infant was length at birth, gestational age, feeding practices after birth, and resuscitation time. Birth weight dropped from multivariate analysis, but length at birth came as a strong predictor may be due to surface area. The other factors, resuscitation time, and gestational age are inter related, usually shorter gestational age new-borns need longer resuscitation time. Asphyxiated foetus also need longer resuscitation time. This was supported by other studies in India (Sinha and Kumar, 1991). Studies in Bolivia and in India highlighted the importance of breast feeding for premature and low birth weight infants (Contreras *et al*, 1992; Ramashethu *et al*, 1993). Another study showed that VLBW infants have a long term deficit in growth (Sung *et al*, 1993), but we couldn't show this effect because our follow up period was short.

Chapter 6

Conclusion and Recommendation

This was a prospective study with a case control analysis to identify the risk factors for the mortality and morbidity of low birth weight infants in Bangladesh. The overall aim of the study was to target the interventions and recommendations to reduce the mortality and morbidity of low birth weight infants. The study was conducted in the labour ward of Mitford Hospital, Dhaka, Bangladesh which is a large teaching hospital. All low birth weight infants born during study period were included in the study and after one month they were followed up to find out their growth, mortality and morbidity status.

Main conclusion

Low birth weight percentage in our hospital population

In this hospital the percentage of low birth weight infants was 26%, which is below the national average (40- 50%). They were normal infants as we excluded any congenital anomaly. The percentage was lower than the national level because this study was done in an urban area and among a hospital population which could be a better off situation. So our population does not represent country generally, although useful conclusion may still be drawn.

Mortality patterns

The neonatal mortality rate was 132 per thousand live birth and perinatal mortality rate was 179 per thousand total birth. The major causes of death were asphyxia, low birth weight, prematurity, respiratory distress syndrome, sepsis, neonatal pneumonia, sudden death and others. Neonatal deaths were highest in the first three days. Birth weight and gestational age is strongly related with neonatal death. These two factors can be regarded as an indicator for neonatal death. Birth weight could be taken as a screening measure for special care to prevent the risk of death.

Still births

Multivariate logistic regression reveals abnormal placental colour as an important predictor for stillbirth, so abnormal placental colour could be regarded as a screening tool to target care to high risk infants.

Risk factors for neonatal mortality

The important identified risk factors for neonatal mortality were birth weight, mid arm circumference, abnormal placental colour, maternal anaemia, mothers education, and age at marriage. As placental colour is an indication of maternal infection, so measures to prevent antenatal infection could be argued. The other important factor, age at marriage needs social motivation.

Social characteristics

All the socio-economic parameters came as a risk factor for stillbirths and neonatal death. Of these, mother's education and parent's income could be regarded as measure for socio-economic condition. So emphasis on these factors especially women's education could improve the overall socio-economic conditions. Though 50% of the mothers have got primary education in my study, in practice most of them only had got their names in the school. It is questionable how much they have learned, as most of them even don't know how to read. So literally they are illiterate, that's why mother's education came as a strong factor for neonatal mortality.

Early and late neonatal deaths

89% of the infants died in the first 7 days of birth. Unfortunately we could not identify any factor significant for early death. In univariate analysis, Apgar score at five minute ($P < 0.00$) came as the only significant factor, but in multivariate logistic regression analysis all the factors were confounded and nothing came as significant. As we could not compare any variable related with neonatal care we cannot comment why early death is so high and how we can reduce this rate. There might have some relation with intensive neonatal care.

Growth of the infants

Feeding practices is the identified risk factor for poor growth, so initiation of breast feeding as soon as the infant born and continuation of it should be targeted. Other factors resuscitation time and gestational age are interrelated, the smaller the gestational age longer the resuscitation time. Smaller infants should have a special care for their growth and development.

Morbidity pattern

35% of infants were suffered from illness in the neonatal period. The common illnesses found were fever, respiratory illness, common cold, diarrhoea, rash, jaundice, umbilical sepsis, and skin infection. These were the very common causes of illness found all over the country. The contributing factors for these illnesses were poor socio-economic conditions leading to unhygienic conditions, overcrowding, hot and humid temperature, and air pollution.

Recommendations

Recommendation suggested on the basis of identified risk factors could be divided into two groups

- A. Recommendations for policy
- B. Recommendations for future research

Recommendations for policy

1. Low birth weight was identified as an important risk factor for mortality. This can be improved by effective care of the mothers during pregnancy. Proper antenatal care, treatment of infections, correction of anaemia, increasing the age of marriage are important intervention to increase the birth weight of the infants. Education about the consequences of low birth weight at the first antenatal visit should be instituted.

2. Prematurity was another cause of neonatal death. Hypertensive disorder, infection, and placental disorder cause pre-term birth. Monthly domiciliary check up of blood pressure, treatment of infection, will help to reduce premature birth and neonatal and foetal death.

3. Age at marriage : 90% of the women in Bangladesh get married in their teenage years, many of them married before menarche and have their menstrual cycle after becoming mother. Teenage marriage was identified one of the risk factor for neonatal death. Legislative action should be taken to raise the marriageable age, and this should be executed strictly.

4. Maternal education was strongly related with neonatal death. Female literacy rate should be improved. Female literacy will raise female employment opportunity. These facilities, female

education, and employment will inhibit early marriage and conception. Compulsory schooling of the girls up to secondary level should be put into action.

5. Poor social class was a factor for neonatal death. Social class is measured by maternal education, father's income, and all other socio-economic variables. As we said before women's literacy, will help to improve the family income which in turn help to improve socio-economic level.

6. Placental colour came as an important factor for both stillbirth and neonatal death. Abnormal placental colour e.g. green and black is an indication of placental insufficiency and infection. Placental insufficiency might result from hypertension or some other medical causes during pregnancy. Introduction of antibiotic therapy for the high risk mothers might be recommended, but further studies are needed.

7. Maternal anaemia causes low birth weight which in turn causes neonatal death. Introduction of folic acid to the pregnant mothers whose haemoglobin level is $<11\text{ gm/dl}$ can be recommended. Maternal anaemia was an important and independent risk factor for neonatal death.

8. Neonatal growth is strongly influenced by feeding practices. All mothers should start breast feeding their baby as soon as the baby born. Training should be given how to exclusively breast fed and when to start before the mother leave the hospital.

9. Resuscitation time is important for the growth of the baby. Training for essential new-born care including resuscitation for the infant of $<2\text{ kg}$ during first two or three days is recommended.

10. Overall health education of the mothers and head of the family could help to improve the risk of low birth weight infants and reduce the mortality of the neonates

Recommendations for future research

1. As antenatal care identified as a risk factor for stillbirth and neonatal death, further research should be recommended on the planning and effective implementation and evaluation of antenatal care.
2. Follow up research for evaluating the impact of low birth weight on subsequent growth and development.
3. Further research on introduction of antibiotics to the risk group of infants after screening placental colour. Naked eye examination of placental colour, which usually all the obstetricians do after every delivery routinely could be a screening tool to identify high risk infants.
4. Further research on introduction of simplified neonatal special care units, for the risk group of infants are recommended. During training period if each and every doctor and nurse have a training on neonatal special care for at least one month in addition to the paediatric training that might solve the problem to some extent. This training should be included in the course curriculum and compulsory.
5. As most deliveries in Bangladesh occur at home we need health promotion activities in the community. Ideally these should be evaluated using randomised and controlled design, with neonatal and perinatal mortality as outcome measure.

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For new born and during hospital staying

1. SI No.
2. Date:
3. Address
4. Date of birth
5. Apgar score

1 minute	5 minutes
----------	-----------
6. Gestational age
7. Weight at birth
8. Length at birth
9. mid arm circumference
10. Head circumference
11. Chest circumference
12. Temperature
13. Resuscitation time
14. Resuscitation given

none	oxygen
mouth to mouth	intubation
aminophylline	others
15. Medicines given to the baby

oradexon	glucose
vit K	sodi bi carb
antibiotic	others
16. When feeding started
17. Type of feeding

breast feeding	bottle feeding
spoon feeding	nasogastric feeding
18. Type of milk

breast milk	formula milk
cows milk	honey
sugar water	
19. When breast started
20. Level of hemoglobin
21. Final outcome

discharge	transferred
died	
22. Date

Report of placental examination

1. Sl No.
2. Type of removal
 - normal cesarean section
 - manual removal incomplete
3. Weight of the placenta
4. Length
5. Breadth
6. Insertion of cord
 - central marginal
 - eccentric velamentous
7. No. of vessels
8. Thrombosis
- Membrane**
9. marginal circumvallate
10. color
 - green opaque
 - normal
11. Point of rupture from margin
- Maternal surface**
12. intact not intact
13. Calcification
 - marked normal
14. Color
 - normal pale
 - greenish blackish
15. Abruptio
 - yes no

Obstetric history

- | | | |
|-------------------------------------|------------------|-----------------------|
| 1. SI No. | | |
| 2. Date | | |
| 3. name | | |
| 4. Age | | |
| 5. Religion | | |
| 6. No. of living child | boy | girl |
| 7. No. of stillborn | boy | girl |
| 8. No. of abortion | | |
| 9. No. of previous pregnancy | | |
| 10. Cause of death previous child | diarrhoea | respiratory disease |
| | tetanus | fever |
| | prematurity | congenital anomaly |
| | small for death | others |
| 11. Type of previous delivery | home | institute |
| History of present pregnancy | | |
| 1. Attended antenatal clinic | yes | no |
| 2. No. of antenatal visits | | |
| 3. Medical problems | none | anemia |
| | fever | diabetes |
| | UTI | heart disease |
| | hypertension | others |
| 4. Antenatal complication | none | pre-eclampsia |
| | bleeding | toxaemia of pregnancy |
| | early rupture | others |
| 5. Mode of delivery | vaginal | cesarean section |
| | forceps | others |
| 6. Presentation | vertex | breech |
| | others | |
| 7. Complication at labour | none | cord prolapse |
| | malpresentation | maternal death |
| | prolonged labour | ruptured uterus |
| | others | |
| 8. Height | | |
| 9. Weight | | |
| 10. Level of hemoglobin | | |
| 11. Blood pressure | | |

Follow up

1. Sl No.
2. Date
3. Age
4. Sex
5. Anthropometry

height	weight
mid arm circumference	chest circumference
head circumference	temperature
6. Has he got any illness

yes	no
-----	----
7. How many days he had suffered
8. Type of illness

respiratory illness	fever
diarrhoea	skin disease
jaundice	umbilical sepsis
rash	others
- Diarrhoea**
9. How many days he had suffered
10. How many times in a day
11. What was the type of stool

watery	mixed with blood and mucus
watery mixed with mucus	persistent
12. Color of stool

yellow	red
green	black
13. Bad smell

yes	no
-----	----
14. Is there any sign of dehydration

cond. of patient	no symptoms	some dehydration	severe dehydration	
sign	absent	irritable	drowsy/unconc	eye
	not sunken	sunken	very sunken	
tear	present	absent	absent	
mouth/tounge	wet	dry	very dry	
skin pinch	goes back immediate	slowly	very slowly	
thirst	not thirsty	thirsty	drinks poorly	
drinks	drinks normally	drinks eagerly	unable to drink	
15. Treatment given

no treatment	medicine
ORS	medicine + ORS
16. Who treated

parents	doctor
medicine seller	health worker
homeopathy	
17. Is there any vomiting

yes	no
-----	----
18. How many times in a day

Respiratory illness

19. Is there any cough
yes no
20. How many he suffered
21. What was the other symptom
fever cough + fever
cough + fever + running nose cough + running nose
cough + wheezing sound
22. Was there any exudate
yes no
23. Was the breathing rapid
yes no
24. Did the chest goes in and out with breathing
yes no
25. Who treated the baby
no treatment local village doctor
health worker medicine salesman
qualified doctor homeopath
admitted to hospital

Fever

26. Does he have any fever
yes no
27. Any convulsion
yes no
28. Other accompanying illness
fever + cough fever + diarrhoea
fever + convulsion fever + unconcious
fever + vomiting fever only
skin disease jaundice
common cold rash
umbilical sepsis others
29. How many days was ill
30. Who treated
no treatment medicine salesman
local practitioner qualified doctor
admitted to hospital health worker
homeopathy
31. Did you stopped breast durign illness
yes no
32. Did you stopped usual diet during illness
yes no
33. What was the usual food
exclusive breast breast + water
breast + cowsmilk (1-2; half half; large suppl)
breast + tin (1-2; half half; large suppl)
only tiin milk only cows milk

For the mother

1. General condition
healthy ill looking
2. Blood pressure
3. Pulse
4. Are you ill
yes no
5. Type of illness
lethargy fever
abdominal pain birth canal pain
skin problem stitch problem
diarrhoea others
6. Did you take any medicine
yes no
7. Name of medicine
antibiotic paracetamol
pain killer vitamin
8. Who prescribed
self doctor
medicine seller health worker
9. How many times do you take meal in a day
3 meals 2 meals 1 meal
fish days in a week
meat days in a week
vegetable days in a week
10. Do you need to do lot of work
resting mainly domestic work
heavy work outside
11. Who is nursing the baby
mother relative both
12. Your baby is small, is this good
yes no dont know
13. Did this worry you
yes no
14. If yes, why
maintanance survival
development

Socio economic score

1. Mothers occupation	house wife	0
	earning	1
2. Mothers education	none	0
	primary	1
	secondary	2
3. Fathers occupation	landless, share cropper	0
	farmer, salaried worker	1
	salaried worker	1
	skilled worker	2
	businessman	2
4. Fathers education	none	0
	primary	1
	secondary	2
5. Income of the family	<3000 taka/month	0
	3001 - 5000 taka/month	1
	5001 - 10,000 taka/month	2
	>10,000 taka/month	3
6. Member of the family	8 - 10	0
	4 - 7	1
7. Structure of the house	wall jute stick+roof thatched	1
	wall bamboo + roof tin	2
	wall jute stick + roof tin	2
	wall tin + roof tin	3
	wall brick + roof brick	4
8. Source of drinking water	river	0
	tap/tubewell other compound	1
	tap/tubewell own compound	2
9. Toilet	open	0
	pit	1
	sanitary	2
10. Household possessions	wooden bedstead	1
	fan	2
	TV	2
	cassette player	8
	freeze	16
House hold possessions further categorised and scored as follows		
	possession score (1 - 14)	1
	possession score (15 - 23)	2
	possession score (>23)	3
11. Presence of electricity		2
12. Method of cooking	wood	1
	gas (common)	2
	kerosene	3
	gas (individual)	4

13. Age of mother at marriage	teen age	1
	after teen age	2
14. No. of children	>3	1
	<3	2
After adding all the scores if it scores	25 - 34	high
	score 14 - 24	medium
	score <14	low

Verbal autopsy

Suggested criteria for diagnosis of causes of death by verbal autopsy

Categories of criteria

E = essential : this criteria must be fulfilled to make a diagnosis, but is not sufficient evidence for diagnosis.

C = confirmatory: clinches the diagnosis if E is also fulfilled.

S = supportive: helps in making a differential diagnosis from other possible causes of death and provides circumstantial evidence.

The diagnostic criteria suggested for each causes are the minimum necessary; the presence of more criteria provides stringer evidence.

1. Prematurity

C: history of <37 weeks gestation (physical signs of prematurity were not noticed by women/ traditional birth attendants in the study area).

Most probable diagnosis = 1C

2. Low birth weight

C: too small at birth (since the usual birth weight in developing countries tends to be low, parents judgment of 'small size' usually means gross low birth weight).

C: twins (twins born in rural areas area almost invariably low birth weight).

Most probable diagnosis = 1C

3. Congenital malformation

C: grossly malformed baby

4. Birth injury/asphyxia

C: did not cry immediately after birth (late cry = >3 minutes) or didn't breathe or had very slow gasping respiration at birth.

C: drowsy or unconscious or convulsions at birth or within first 72 hours.

C: generalized flaccidity at birth or within 72 hours in a full term baby.

S: sucking and swallowing absent at birth or within 42 hours in a full term baby.

S: history of prolonged labor (>24 hours in primipara : > 12 hours in others).

S: fracture or paralysis of a limb.

S: excessive moulding of skull, or caput or bruises at birth.

S: cyanosis or pallor at birth.

S: presentation other than vertex.

S: history of instrumentation in hospital or manual manipulation in home delivery.
S: second born of a twin birth.
S: small sized baby (babies with intrauterine growth retardation are very prone to birth asphyxia).
S: very large baby.
S: meconium stained liquor.

Possible diagnosis = 1 C or 2 S
Most probable diagnosis = 2 C or 1C + 1S

5. Neonatal tetanus

E: age at death > 4 days (although the minimum possible incubation period is 48 hours, 90% of the deaths due to neonatal tetanus occur between the 5th and 14th postpartum).
E: baby stopped sucking from the 4th day or later.
C: stiffness of body and arching of back with spasm on 4th day or later.
C: inability to open mouth to feed (trismus).
S: mother did not have the minimum one dose of tetanus toxoid during this pregnancy
S: family called the tetanus in local term.
S: umbilical cord cut using a dirty instrument.
S: birth attendant did not wash her hands before delivery.
S: omphalitis.

Possible diagnosis = 2 E + 1C + 1S
Most probable diagnosis = 2 E + 2 C

6. Neonatal pneumonia

E: onset of respiratory symptoms >6 hours after birth.
C: tachypnoea for more than 2 hours before death (to differentiate from terminal gasping).
C: respiratory distress (severe indrawing of suprasternal, intercostal, or subcostal region).
c: expiratory grunt or groaning.
S: cough (neonates often do not cough despite having pneumonia; hence it is not supportive).
S: fever.
S: refusal of food.
S: cyanosis.

Possible diagnosis = 1 E + 1 C
Most probable diagnosis = 1E + 2 C or 1 E + 1 S

7. Post-natal aspiration

The same criteria were used as for pneumonia + onset preceded by choking or a severe bout of coughing after feeding or vomiting.

8. Respiratory distress syndrome

This include hyaline membrane disease, congenital pneumonia or meconium aspiration.

E: onset of respiratory symptoms within 6 hours of birth.

C: tachypnoea.

C: respiratory distress - severe indrawing of suprasternal, intercostal, or subcostal regions.

C: expiratory grunt or groaning.

S: cyanosis.

S: feeble cry at birth (indicate probable intrauterine infection).

S: presence of one of the following predisposing factors.

prematurity; or

prolonged labor (>24 hours on primiparous mothers; others >12 hours).

Possible diagnosis = 1 E + 1 C

Most probable diagnosis = 1 E + 2 C or 1 E + 1 C + 2 s

9. Diarrhea

E: >3 loose, watery stools per day.

S : vomiting.

S: restriction of breast feeding or fluids by parents.

C: dehydration (depressed eyeballs or fontanelles, oliguria, or dark urine - any one of these).

Possible diagnosis = 1 E

Most probable diagnosis = 1 E + 2 S or 1 E + 1 C

10 . Dysentery

E: >3 loose stools per day.

C: blood, pus or mucus in stools.

Most probable diagnosis = 1 E + 1 C

11. Hypothermia

C: head, chest, and abdomen of baby cold for 2 hours or more before death.

Most probable diagnosis = 1 C

12. Neonatal sepsis (includes septicemia, meningitis)

C: became drowsy, or lethargic, or unconscious 72 hours after birth (compare with birth injury).

C: refused feeds (having accepted feeds earlier), but mouth could be opened (compare with tetanus).

S: feeble cry in full-term baby.

S: sepsis in skin or umbilicus.

S: fever.

S: hypothermia in a baby unexposed to cold (covered parts of body were cold).

S: vomiting, diarrhea, or abdominal distention (any one or more).

S: convulsion or spasms after first 72 hours.

S: jaundice.

S: cyanosis of extremities.

S: apnoeic spells - stop breathing for period greater than 20 seconds, after good breathing at birth.

S: presence of one or more of the following maternal factors

prolonged rupture of membranes (>24 hours).

prolonged or obstructed labor (>24 hours in primipara, > 12 hours in others).

foul-smelling liquor and

maternal fever lasting >24 hours during or within 1 week of delivery.

Possible diagnosis = 1 C + 1 s or 2 S

Most probable diagnosis = 1 c + 2 S or 2 C + 3 S

13. Sudden death

C: sudden death of an otherwise normal baby.

Most probable diagnosis = 1 C

14. Feeding problem (refusal to feed/failure to feed/bottle feed)

C: baby did not suck or was not fed milk for two continuous days or more before death.

C: baby was bottle-fed (which invariably results in under feeding due to dilute formula milk and infection in rural areas).

Most probable diagnosis = 1 C

15. Others

16. cause not known