Original Article

MORTALITY AND MORBIDITY IN HOSPITALIZED PRETERM NEONATES

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Objective: To determine pattern of morbidity and mortality in hospitalized preterm neonates.

Material and Methods: All preterm babies presenting to the Neonatology Ward of Services Hospital except those with major congenital malformations were selected for the study. A predesigned proforma was used to record clinical data on presentation. This included physical characteristics like gestational age, weight, gender, presenting complaints. The profroma was updated on daily basis to make note of any clinical problems or complications arising during the course of hospital stay till outcome (discharge, leave against medical advice or death). Note was made of respiratory complications, infections, metabolic, neurological and hematological problems and complications related to feeding and weight gain. The data was subsequently computed and analyzed using SPSS (Statistical Package for the Social Sciences) version 14 by the authors.

Results: Three hundred and one preterm babies ranging in gestational age from 22 to 36 weeks (mean 31.2 SD +/- 2.9) were included in the study. The overall mortality was 53.8%. Survival was significantly better in more mature, larger babies and those who could be started successfully on enteral feed. Most deaths were encountered within the first 7 days of admission. The chances of survival increased significantly with longer duration of admission. There was no significant difference in mortality between males and females. Respiratory distress was the commonest admitting complaint seen in 46.5% cases. During hospital stay respiratory problems (requiring varying degree of ventilatory support) were seen most frequently, followed by metabolic complications and infection related morbidity.

Conclusion: Prematurity is associated with significant mortality and morbidity seen in hospitalized neonates.

Key words: Preterm, Hospitalized, Mortality and Morbidity.

Introduction

While the infant mortality rate in Pakistan has declined from 124/1000 live births in 1990 to 87 in 2010, the neonatal mortality rate has remained almost unchanged (51 vs 41) during this period. Neonatal mortality in Pakistan accounts for 57% percent of under 5 mortality.[1] It is evident that achieving Millennium Development Goal 4 would not be possible unless neonatal mortality is addressed.[2] Prematurity, neonatal infections and perinatal asphyxia is one of the three main causes of neonatal mortality.[3,4] The burden imposed by preterm babies in terms of contribution to neonatal morbidity and mortality in Pakistan remains largely undetermined. The magnitude of this problem needs to be evaluated before appropriate steps may be taken to improve survival of this high risk group of newborn babies.

Methodology

This observational study was carried out in the Neonatal Unit of Services Hospital, Lahore over a 8 month period from 1st March 2010 to 31st October 2010. All neonates born at or before 36 weeks of completed gestational age were included in the study. Babies with major congenital malformations and those in whom gestational age could not be ascertained for any reason were excluded from the study. Gestational age was calculated using either last LMP (last menstrual period), dating scan record or Ballards Score. The latter was used where information by first two methods was either unavailable or of doubtful accuracy. Ballards Score was done within the first 48 hours of admission.

Information regarding weight, sex, age on admission, clinical course and problems arising during stay were recorded on a predesigned proforma that was updated on daily basis until outcome (discharge, death of left against medical advice). Statistical analysis was carried out using the SPSS 14 programme. P value using Chi-square test was calculated where applicable and was considered as significant if <0.05.

Results

A total of 301 babies were included in the study. This included 174 (57.8%) males and 125 (41.5%) females. There were two (0.66%) babies who had ambiguous genitalia and died before sex could be ascertained. Overall 124 (41.2%) babies survived and 15 (5%) left against medical advice (Figure-1Outcome). Cases ranged in gestational age from 22 to 36 weeks (mean 31.23; SD ±2.896). The mean weight of the cases was 1457 grams (range 600-3300 grams; SD ± 474 grams). The age at admission ranged from 1-27 days with mean age of admission of 2.36 days. The mean duration of stay on the unit was 7.95 days (range 1-52 days).

The commonest presenting complaint was respiratory distress which was seen in 46.5% of admissions. Fifty nine (19.6%) babies were brought to the hospital for care without a specific complaint. This was either on advice of the birth attendant or because the parents themselves felt that it was unsafe to keep the baby at home. Other presenting complaints in order of frequency were: cyanosis (10.3%), delayed/ weak/ absent cry at birth (8%), poor feeding (6%), lethargy (4.3%), seizures (2.7%), bleeding (0.3%) and other causes (2.3%) (Figure 2 Presenting Complaint). During the course of stay 266 (88.4%) required supplemental oxygen (Table 1 Morbidity). One hundred and fourteen (37.9%) required nasal CPAP (continuous positive airway pressure) at some point during their stay while 62.1% needed mechanical ventilation (either manual ambubagging or ventilator). Because of limited number of available ventilators many babies requiring mechanical ventilator had to be intubated and hand bagged. Other respiratory complications encountered during hospital stay included pneumonia (3.3%), pulmonary hemorrhage (6%), pneumothorax (0.7%). Apnoea of prematurity defined as apnoea with bradycardia responding to tactile stimulation or bagging, was seen in 37.5% cases. One hundred and sixty three (54.2%) were diagnosed with sepsis on combination of clinical grounds and raised CRP (C-reactive protein value greater than 6 microgram/ml) or band neutrophil ratio (value greater than 0.2). Six babies had spinal fluid findings compatible with meningitis. Positive blood culture was seen in 8 cases. Organisms isolated included Klebsiella, Pseudomaonas, E.coli, Coagulase negative staphylococci and Candida. During the course of their stay 25.9% needed packed cell transfusions because either the baby's hemoglobin levels fell below 8 mg/dl or with higher hemoglobin levels if anemia was considered clinically significant. Thirty five (11.6 %) cases had thrombocytopenia warranting platelet transfusion (platelet counts less than 30,000/ml in asymptomatic babies or at any level less than 100,000/ml in babies with clinically overt bleeding). Ninety nine (32.9%) babies could not be started on enteral feed because of poor clinical status. Every attempt was made to start enteral feed with breast milk as early as possible. Formula milk was used if breast milk was unavailable or insufficient. Of the 202 cases that were started on enteral feed, exclusive breast milk was available in 79 (39.1%) cases only. This was because in many cases mothers were not present on site. Sixty nine cases out of 202 developed feeding intolerance at some point of their stay necessitating reduction or stopping of feed. Although not statistically significant, exclusive breast milk seemed to confer a better chance of survival (50/79; 63.3%) than mixed or exclusive formula feeding (69/123; 56.09%); lowest survival occurring in those who could not be started on enteral feeding (8/99; 8.1%) (p<0.000)

Other problems that were encountered in the study group include metabolic acidosis at some point during hospital stay (41.9%), hyperbilirubenemia warranting treatment predominantly indirect-27.6%, predominantly direct-5.65%), disseminated intravascular coagulation (DIC ; 19.6%), symptomatic hypoglycemia (15.9%), symptomatic hypocalcemia (5.6%), necrotizing enterocoloitis (12%), patent ductus arteriosus (3%) and spontaneous intestinal perforation (1%). Metabolic acidosis was reflective of severity other morbid conditions like infections. All babies had axillary temperature measured at admission using a mercury thermometer. Hypothermia (defined as axillary temperature < 97°F) at admission was seen in more that 41% of babies. Intraventricular hemorrhage was diagnosed by bed side ultrasonography in 40 (13.3%) cases. Fourteen (4.7%) cases had clinical evidence of hypoxic insult at birth. Majority (82.7%) of our patients presented to the hospital at day 1 of age. Forty two babies (42/162; 25.9%) succumbed on day 1 of admission. Majority of deaths occurred within 7 days of admission (121/162; 74.7%). If a baby survived the first 7 days of admission the chance of dying became significantly less (p<0.005). Mortality was significantly less with increasing weight (p<0.00) and gestational age (p <0.001).

Discussion

The neonatal mortality rate for Asia is 24/1000 live

Table-1: Morbidity.

Morbidity	No of Pt's	Percentage
Respiratory		
Pneumonia	10	3.3
Pneumothorax	02	0.66
Pulmonary hemorrhage	18	5.98
Needed oxygen	266	88.4
Required CPAP	114	37.9
Required mechanical ventilation	187	62,.1
Apnoea with bradycardia	113	37.5
Infections		
Sepsis	163	54.1
Meningitis	06	1.99
DIC	59	19.6
NEC	36	11.96
Spontaneous perforation	03	0.99
Metabolic		
Direct hyperbilirubinemia	17	5.7
Hypoglycemia	48	15.9
Hypocalcemia	17	5.7
Hypothemia	125	41.5
Metabolic acidosis	126	40.9
Indirect hyperbilirubinemia requiring therapy	83	27.6
Neurological		
Kernicterus	02	0.66
IVH	40	13.3
HIE	14	4.7
Feeding		
Poor weight gain	52	17.3
Feeding intolerance	69	22.9
Miscellaneous		
PDA	09	2.99
Anemia requiring transfusion	78	25.9
Thrombocytopenia	35	11.6

births. The figure for Pakistan stands at 41/1000 live births. In comparison, the neonatal mortality rate for
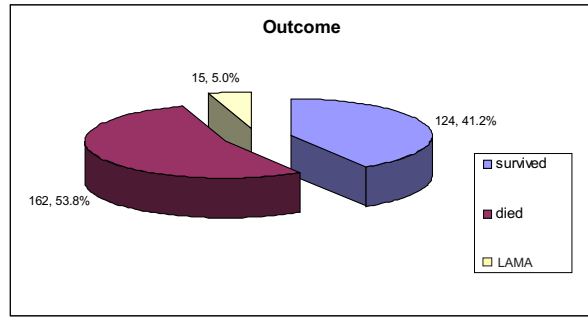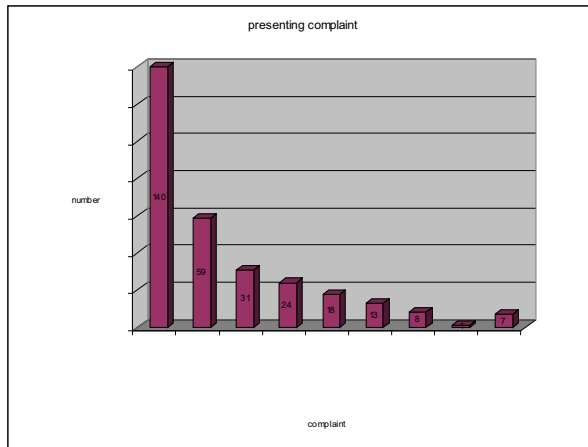

Fig-1: Outcome.

Fig-2: Presenting Complaint.

India is 32 while that for Bangladesh 27/1000 live births. It is therefore clear that Pakistan has failed to keep pace with other countries in the region.[5]
There are many studies looking at the causes of neonatal mortality both locally and globally. Prematurity is consistently quoted as one of the leading contributors to death in newborn babies.[6,7,8,9] Preterm labour was the primary cause of neonatal death in a population based study.[10] Data on cause of death in hospitalized newborns is no different. Prematurity and its complications is a leading contributor to mortality in neonatal units in different regions of the world.[11,12] In our study group 162 (53.8%) babies succumbed. This is in keeping with the high mortality observed in preterm babies in general. Even in centers with advanced care facilities the mortality of 49.5% has been reported.[13]
The higher mortality and adverse outcomes noted in preterm babies is a result of both immaturity per se (low gestational age) and of maternal complications leading to preterm birth in the first place.[14]
Respiratory distress was the commonest presenting complaint in our group. This is in keeping with the high rates of respiratory morbidity noted in other studies. As many as 95% preterm babies were noted

to require endotracheal intubation at birth in a large cohort studied across UK. Upto 61% of survivors had severe bronchopulmonary dysplasia at 36 weeks of post menstrual age.[15] In the same study all but one survivor needed total parenteral nutrition and 8% underwent laprotomy for necrotizing enterocoloitis. We did not have the facility for TPN (total parenteral nutrition) and relied on proactive introduction of enteral feed using preferably breast milk. Formula milk was used under circumstances where breast milk was either unavailable or insufficient. Two hundred and two (67.1%) infants could be started on enteral feed at some point during their stay. The rest were not considered for enteral feed due to poor clinical status. Feeding intolerance was encountered in 69 cases. Thirty six babies (12%) developed necrotizing enterocolitis (NEC) during their stay. This figure is somewhat higher than the 5.1% incidence reported by Yee et al.[16] Reason may be that only 39.1% cases could be given exclusive breast milk as many mothers were not available on site. High rate of infections encountered in our group could be another contributor. Infections in hospitalized preterm along with length of mechanical ventilation were found to be the primary predictors of NEC in preterm infants.[17]

More than half (54.15%) cases were diagnosed with sepsis on a combination of clinical features and raised CRP and/or band neutrophil ratio of more than 0.2. Neonatal infection is the leading cause of admission in many neonatal units across Pakistan[18] and in other countries of the region.[19] Neonates in general and premature babies in particular are at high risk of infections due to functional deficiency of innate immunity. Prematurity is a known risk factor for development of late onset sepsis.[20] Neutrophils display functional immaturity in preterm babies.[21] It is therefore not unexpected that more than 50% of our cases were diagnosed with sepsis. The commonest organisms isolated were gram negative (Klebsiella, E. Coli and Pseudomonas). This is in keeping with data from other centers in Pakistan and other developing countries where a predominance of gram negative organisms have been reported to cause neonatal sepsis[22,23] Culture positivity rate was low in our group. This may be due to intrapartum antibiotics received by the mother, prior to admission use of antibiotics on prescription of general practitioners, or the small volume blood samples used. Similar problems in reporting blood cultures in neonates have been noted by other researchers als.[24] Disseminated intravascular coagulation noted was seen as a mostly as a complication of underlying infection.

Metabolic problems including symptomatic hypoglycemia, hypocalcemia and hyperbilirubinemia (indirect requiring therapy and direct) was noted in 15.9%, 5.7% and 33.2% respectively of our cases. These have been noted in other studies as well and attributed to organ immaturity.[25]

Although not statistically significant, higher percentage of babies fed exclusively on breast milk survived till discharge. Breast feeding is known to confer protection against necrotizing eneterocolitis.[26] The reason why we could not demonstrate a statistical significance may be explained by considering several factors contributing towards mortality were operative in our study group that may have masked the beneficial effect of breast milk.

The highest mortality was noted in the smallest and the most premature babies. This is not surprising as survival increases proportionately with increasing weight and gestation.[15] If a baby survived the first seven days of admission the chances of survival increased significantly. These babies succumbed early may have had greater severity of underlying pathology to begin. Patients who survived beyond 7 days of admission perhaps represented those with pathology of lesser severity at admission. Generally speaking, early neonatal period is associated with greater mortality than late neonatal period. In a population based cohort study researchers found that neonatal mortality with the first 48 hours of life was 45.3%, 28.3% between three and seven and 26.4% between eight and 28 days of life.[14] Our data may be reflective of the same trend in neonatal mortality. Likewise, greater survival in those who could be started on early enetral feed perhaps represents cases that had lesser severity and magnitude of problems to begin with and therefore were capable of tolerating enteral feed. As many as 41.5% babies had hypothermia (axillary temperature <97°F) at admission. The global burden of hypothermia as a contributor to mortaltilty and morbidity in newborns (particularly preterms) as a co morbid condition, even in tropical countries, is often under appreciated. A recent systematic review showed that the prevalence of hypothermia ranged from 32% to 85% in hospital delivered newborns.[27]

Anemia requiring blood transfusion is very common in neonatal intensive care units. Reasons in the critically sick newborn are manifold: suppression of bone marrow, increased destruction of red cells and repeated phlebotomies.[28] Seventy eight (25.9%) of

during their stay. Thirty five (11.63%) babies needed platelet transfusion for thrombocytopenia (without DIC). Thrombocytopenia is also a fairly common hematological problem in NICUs. The over all prevalence of thrombocytopenia in neonatal intensive care patients ranges from 22-35%.[29] Our figure is lower in comparison, perhaps because we have considered only those babies with thrombocytopenia (without DIC) in whom it was significant enough to merit platelet transfusion.

Intraventriclar hemorrhage was noted in 40 (13.29%) of cases. Preterm babies are known to be risk from this complication. This is probably because the premature germinal matrix is vulnerable to hemorrhage. Coagulation deficiency in preterm babies has also been also been postulated to contribute to this problem .[30]

Conclsion

Premature babies represent the most vulnerable group amongst neonatal population. They are at a high risk of mortality and morbidity. Respiratory problems, metabolic immaturity and infections (mainly due to gram negative organisms) including necrotizing enterocolitis are the main causes of morbidity. Chances of survival at discharge increase if the babies survive the first few days of admission and in those who can be started successfully on early enteral feeding.

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