Predictors of mortality in very low birth weight neonates in India

Basu S, Rathore P, Bhatia B D

ABSTRACT

Introduction: Very low birth weight (VLBW) neonates constitute approximately 4–7 percent of all live births and their mortality is very high. The objective of the present study was to determine the predictors of mortality in VLBW neonates.

Methods: A retrospective cohort of VLBW neonates admitted over three years was studied. Exclusion criteria were: (1) neonates weighing less than 500 g and with gestational age less than 26 weeks; (2) presence of lethal congenital malformations; and (3) death in the delivery room or within 12 hours of life. The outcome measure was in-hospital death. Medical records were reviewed and data was analysed. Univariate analysis and logistic regression analysis were done to determine the predictors of mortality.

Results: A total of 260 cases were enrolled, of which a total of 96 (36.9 percent) babies died. The survival rate was found to increase with the increase in birth weight and gestational age. Univariate analysis showed maternal per vaginal bleeding, failure to administer steroid antenatally, Apgar score less than or equal to 5 at one minute, apnoea, gestational age, neonatal septicaemia and shock are the factors directly responsible for neonatal mortality. Logistic regression equation showed maternal bleed (1.326), apnoea (3.159), birth weight (0.037), gestational age (0.063), hypothermia (1.132) and shock (3.49) predicted 65 percent of mortality in VLBW babies.

Conclusion: Common antenatal and perinatal predictors of mortality in VLBW infants in India include maternal bleed, failure to administer antenatal steroids, low Apgar score, apnoea, extreme prematurity, neonatal septicaemia and shock.

Keywords: infant mortality, newborn, very low birth weight neonates

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Division of Neonatology, Department of Paediatrics, Institute of Medical Sciences, Banaras Hindu University, Varanasi 221005, India

Basu S, MD
Lecturer

Rathore P, MD
Resident

Bhatia BD, MD
Professor

Correspondence to:
Dr Sriparna Basu
Tel: (91) 3 529 935 340 260
Fax: (91) 5 422 367 568
Email: drsriparnabasu@rediffmail.com

INTRODUCTION

Very low birth weight (VLBW) babies constitute approximately 4%–7% of all live births but need a major share of effort, time and resources for their care. Despite this attention, the mortality in this subgroup is high, contributing to as much as 30% of early neonatal deaths.[1] Survival is directly associated with their birth weights and inversely associated with illness severity and gestation.[2] But these factors alone are insufficient to explain the large variations in neonatal mortality among various neonatal intensive care units (NICUs). The interaction of illness severity and physiological alterations complicate the management policies, the appropriateness of which determines the neonatal outcome. Hence, there has been an effort in recent times to define physiological and laboratory parameters, which would be predictive of neonatal mortality in the VLBW group. The present study aimed to analyse the effects of various maternal, foetal and laboratory parameters on the mortality of VLBW infants.

METHODS

A retrospective study was conducted at the University Hospital of the Institute of Medical Sciences, Banaras Hindu University, India, over a period of three years. The medical records of VLBW infants admitted to the NICU were reviewed with the help of Medical Records Section. The objective of the study was to determine the predictors of unfavourable outcome of VLBW infants. The outcome measure was in-hospital death. Survival was defined as the discharge of a live infant from the hospital. All newborns weighing less than 1,500 g admitted to NICU was included in the study. Exclusion criteria were: (1) neonates weighing less than 500 g and with gestational age less than 26 weeks; (2) presence of lethal congenital anomalies; and (3) death in the delivery room or within 12 hours of life.

Data collected included detailed antenatal and natal histories, anthropometric measurements, gestational age as per New Ballard Score,[3] Apgar scores (one minute, five minutes, and extended scores if available), details of clinical examination including vitals, and progress during the hospital stay and outcome. Details of morbidities and mortalities developed during the hospital stay, if any, were noted. Laboratory parameters recorded were haemoglobin level, total and differential leucocyte counts, blood sugar, serum bilirubin and serum IgG levels. Of the babies in

Table I. Distribution of very low birth weight babies in relation to gestational age and birth weight.

Age (weeks):	25–26		27–28		29–30		31–32		33–34		35–36		> 37		Total	Survival, no. (%)
Birth weight (g)	T	S	T	S	T	S	T	S	T	S	T	S	T	S		
500–600	-	-	3	0	-	-	-	-	-	-	-	-	-	-	3	0 (0.0)
601–700	-	-	2	0	-	-	-	-	-	-	-	-	-	-	2	0 (0.0)
701–800	2	0	2	0	3	2	-	-	2	0	-	-	-	-	9	2 (22.22)
801–900	3	0	6	3	1	1	2	1	-	-	1	0	-	-	13	5 (38.46)
901–1,000	1	0	8	4	6	2	1	1	-	-	1	1	1	1	18	9 (50.00)
1,001–1,100	2	0	7	1	3	3	6	6	6	3	2	2	1	1	27	13 (48.15)
1,101–1,200	-	-	7	2	12	7	7	6	2	2	5	3	-	-	33	20 (60.61)
1,201–1,300	-	-	1	1	2	1	8	7	13	7	5	3	2	2	31	21 (67.74)
1,301–1,400	-	-	1	0	6	3	16	12	12	10	8	5	2	2	45	32 (71.11)
1,400–1,500	-	-	1	0	8	6	22	14	24	20	17	16	7	6	79	62 (78.48)
Total	8	0	38	11	41	25	62	47	59	42	39	28	13	11	260	164 (63.08)

T: total; S: survived

Table II. Distribution of expired babies in relation to birth weight and primary cause of death.

Birth weight (g):	< 750	750–1,000	> 1,000	Total
Cause of death, no. (%)	(n = 9)	(n = 21)	(n = 66)	(n = 96)
Birth asphyxia	1 (11.11)	6 (28.57)	24 (36.36)	31 (32.29)
RDS	4 (44.44)	7 (33.33)	12 (18.18)	23 (23.96)
Apnoeic spells	2 (2.22)	2 (9.52)	0 (0.0)	4 (4.17)
Hypothermia	2 (2.22)	3 (14.29)	5 (7.58)	10 (10.42)
Hypoglycaemia	0 (0.0)	0 (0.0)	2 (3.03)	2 (2.08)
Shock	0 (0.0)	1 (4.76)	4 (6.06)	5 (5.21)
Sepsis	0 (0.0)	1 (4. 76)	6 (9.09)	7 (7.29)
IVH	0 (0.0)	1 (4. 76)	13 (19.70)	14 (14.58)
Mean ± SD of age of death [range] (hours)	11.11 ± 10.56 [1–40]	41.67 ± 34.05 [2–120]	72.35 ± 66.94 [2–366]	60.31 ± 59.01 [1–336]

RDS: respiratory distress syndrome; IVH: intraventricular haemorrhage; SD: standard deviation.

whom multiple observations of the same parameter were done, the mean value was taken for analysis. Serum bilirubin was sent in for those babies who showed clinical evidences of jaundice, and the mean value was taken for statistical calculation. Statistical analysis was performed using the commercial statistical software, Statistical Package for Social Sciences version 10.0 (SPSS Inc, Chiacgo, IL, USA). Relative risks were calculated. Univariate analysis was done to identify the risk factors of mortality. To find out the overall effects of significant variables, logistic regression analysis was done.

RESULTS

A total of 260 VLBW newborns fulfilled the inclusion criteria of the study; of which a total of 96 (36.92%) babies died during the hospital stay. The survival rate increased with the increase in birth weight as well as gestational age. None of the babies below 27 weeks or < 700 g survived (Table I). Primary causes of mortality are summarised in Table II. Common causes of mortality in babies less than 750 g were respiratory distress, hypothermia and apnoea, while birth asphyxia (BA) and intraventricular haemorrhage (IVH) topped the list in those weighing more than 1,000 g. Maternal and foetal variables were compared between the two groups: group I (the deceased group) and group II (the survivor group) (Table III). Among the maternal variables, a significantly higher incidence of per vaginal (PV) bleeding was noted in group I. The various causes of PV bleeding recorded were placenta previa, vasa previa and abruptio placenti, but the exact distribution of causes were unknown, because in many of the cases the cause could not be determined due to late referral.

Group II had significantly higher gestational age, birth weight, crown-heel length and head circumference. The number of intrauterine growth retardation (IUGR) cases was significantly higher in group II. Out of 260, only 46 mothers had received antenatal steroids, nine in group I and 37 in group II, which was statistically significant ($p < 0.01$). Laboratory parameters are summarised in Table IV. Apart from serum IgG, no other parameter showed a significant difference between the two groups. Relative risks of various morbidities in the two groups are shown in Table V. Relative risks of septicaemia, hypothermia, shock, IVH, apnoea and BA were significantly higher in the deceased group. Univariate analysis showed maternal PV bleeding, failure to administer steroids antenatally,

Table III. Comparison of maternal and foetal variables between survived and expired groups.

Maternal and foetal variable	Group I (expired) (n = 96)	Group II (survived) (n = 164)	p-value
Maternal age (years)	24.1 ± 4.18 [17–35]	23 ± 3.78 [18–34]	NS
Gravida	2.7 ± 2.03 [1–11]	2.5 ± 1.82 [1–10]	NS
Leaking per vagina	42 (43.75)	68 (41.46)	NS
Bleeding per vagina	38 (39.58)	24(14.63)	< 0.01*
Hypertensive diseases of pregnancy	40 (41.67)	63 (38.41)	NS
Anaemia	11 (11.46)	15 (9.15)	NS
Heart disease	6 (6.25)	8 (4.88)	NS
Foetal distress	11 (11.46)	11 (6.70)	< 0.01*
Meconium-stained amniotic fluid	10 (10.42)	11 (6.70)	< 0.01*
Mean Apgar score at one minute	4.68 ± 2.79	6.34 ± 2.11	< 0.01*
Mean Apgar score at five minutes	7.07 ± 2.07	8.07 ± 1.12	< 0.01*
Mean gestational age (weeks)	30.3 ± 4.37 [20–40]	32.2 ± 2.78 [22–40]	< 0.01*
Mean birth weight (g)	1,120 ± 258 [550–1,500]	1,279 ± 201 [720–1,500]	< 0.01*
Mean crown-heel length (cm)	37.6 ± 3.75 [28–47]	39.8 ± 2.99 [30–49.3]	< 0.01*
Mean head circumference (cm)	26.5 ± 3.65 [23.5–32.7]	27.9 ± 3.35 [26–34]	< 0.01*
Intrauterine growth retardation	39 (40.63)	101 (61.59)	< 0.01*

Data is expressed either in mean ± SD [range], or number (percentage).
*statistically significant; NS: not significant

Apgar score ≤ 5 at one minute, apnoea, gestational age, neonatal septicaemia and shock are the factors directly responsible for neonatal mortality. Logistic regression analysis showed maternal PV bleeding (1.3261), apnoea (+ 3.159), birth weight (0.0372), gestational age (0.0627), hypothermia (1.1323) and shock (+ 3.49) predicted 65% of mortality in VLBW babies.

DISCUSSION

Neonatal death is a serious concern, both in the developing and the developed worlds. While infant mortality rates have been decreasing steadily all over the world, changes in neonatal mortality rate have been much slower. One of the commonest causes of neonatal mortality in India is prematurity and low birth weight. The chance of survival of VLBW babies is still poorer. In India, all neonatal set-ups do not have level III newborn care facilities. Most of the centres, especially in the rural districts, have only level II care facilities, and the burden of sick newborns is too high to be referred and managed at the level III centres. This further brings down the chance of neonatal survival, especially in the VLBW neonates who are already compromised since birth.

Prognosis depends not only on birth weight and gestational age, but also on other perinatal factors and physiological conditions of the individual infants, in particular, disease severity in the first hours of life.[4] Various illness severity scores have been developed and subsequently modified to predict the mortality in this weight group. CRIB (clinical risk index for babies)[5] and SNAPPE (score for neonatal acute physiology—perinatal extension)[6] are the most commonly-used scores, and their performance have been extensively validated.[7-9] Calculation of the scores needs estimation of fractional inspired oxygen (FiO_2), arterial blood gas analysis and monitoring of vitals including blood pressure. But monitoring and ventilatory facilities are not available in the level II care set-up. The present study was undertaken to assess the predictors of mortality of VLBW infants and identify those neonates who require early referral and higher level care.

Neonates who died in the delivery room or within 12 hours of life were excluded from the study as intrauterine causes are more likely to be the factors of death in these cases. In our set-up, we documented a mortality rate of 37%. Other studies have documented a mortality rate varying from 23% to 29%.[10-12] A number of antenatal and intrapartum factors have been reported in the literature to be significantly associated with perinatal and neonatal deaths. In the present study, only maternal factors found to be significantly associated with mortality of VLBW babies were PV bleeding and failure to give steroids antenatally at least 24 hours prior to childbirth. The risk of mortality was found to decrease with increase in birth weight and gestational age. Though their relative contribution in reducing mortality is not clear, probably increased maturity helped in the maturation of lungs and reduced the chance of IVH. It is known that the foetus responds to a stressful environment by increasing adrenal glucocorticoid production, which leads to

Table IV: Comparison of laboratory parameters between survived and expired groups.

Laboratory parameters	Group I (expired) (n = 96)	Group II (survived) (n = 164)	p-value
Haemoglobin (g/dL)	18.1 ± 1.44	18.8 ± 1.52	NS
Total leucocyte count	11,605.49 ± 2,898.49	12,940.62 ± 2,674.41	NS
Polymorphs (%)	57.37 ± 8.37	60.29 ± 39.38	NS
Lymphocytes (%)	42.11 ± 8.03	42.15 ± 8.19	NS
Eosinophils (%)	1.55 ± 0.51	1.73 ± 0.73	NS
Monocytes (%)	1.65 ± 0.70	1.68 ± 0.65	NS
Blood sugar (mg/dL)	46.54 ± 17.67	51.03 ± 18.98	NS
Total serum bilirubin (mg/dL)	11.35 ± 2.42	11.73 ± 3.47	NS
Direct bilirubin (mg/dL)	1.25 ± 0.46	1.68 ± 0.69	NS
Serum IgG (mg/dL)	746.9 ± 99.8	840.9 ± 80.18	< 0.01*

*statistically significant; NS: not significant

Table V. Relative risk of various morbidities in two groups of infants.

Morbidities	No. patients (n = 260)	No. expired (%) (n = 96)	No. survived (%) (n = 164)	Relative risk
Birth asphyxia	86	44 (51.16)	42 (48.84)	1.71*
Hypoxic ischaemic encephalopathy	20	14 (70.0)	6 (30.0)	2.10*
Apnoea	86	69 (80.23)	17 (19.77)	5.17*
Hypoglycaemia	44	16 (36.36)	28 (63.64)	0.98
Hyperbilirubinaemia	65	10 (15.38)	55 (84.62)	0.35
Septicaemia	40	23 (57.50)	17 (42.50)	1.73*
Respiratory distress	79	29 (36.71)	50 (63.29)	0.99
Hypothermia	40	29 (72.50)	11 (27.50)	2.38*
Shock	28	27 (96.43)	1 (3.57)	3.24*
Intraventricular haemorrhage	17	17 (100.0)	0	3.08**

statistically significant

accelerated foetal lung maturation.[13] The proportion of IUGR among VLBW survivors was significantly higher compared to the proportion in non-survivors. It showed that appropriate for gestational age (AGA) VLBW babies were more prone to death due to their shorter gestation. Anthropometry was also found to be a determining factor as all the anthropometric parameters were higher in group II.

Apgar score was found to be a significant variable in the study. The mean Apgar scores at one and five minutes were significantly lower in the deceased group. Hypoxic ischaemic encephalopathy was more common in group I. Shock appeared to be a strong predictor of mortality. It was almost exclusively limited to the deceased group of babies as out of 28 VLBW babies with shock, 27 were in the deceased group. Even after adjustment for birth weights, shock was found to be an independent variable. Documented IVH was seen only in expired group of VLBW babies. Mild bleeds might have been missed as cranial ultrasonography was done only in cases of strong clinical suspicions because of financial constrains. Apnoea was also four times commoner in the deceased group. Sepsis and hypothermia were other risk factors. Hyperbilirubinaemia was found to be less common in the deceased group, the reason may be that they did not survive long.

Locatelli et al showed that smaller gestational age and birth weight, female gender, low five-minute Apgar score and failure of steroid administration were independent predictors of survival.[14] Cumulatively, these five predictors explained 69% of neonatal survival. Gagliardi et al compared CRIB, CRIB-II and SNAPPE-II, and found that antenatal steroid prophylaxis, singleton birth, absence of congenital anomalies, and gestational age were independent predictors of survival for CRIB, CRIB-II and SNAPPE-II, in addition to caesarean section, not being small for gestation and a five-minute Apgar score of ≥ 7 (for SNAPPE-II alone).[15] Chen et al found that, with multiple logistic regression analysis, only low birth weight and higher IVH grades were the significant predictors of unfavourable outcomes.[16] Brito et al showed that VLBW infants with birth weight of less than 750 g, less than 29 weeks gestational age and CRIB scores above ten had higher mortality rates.[10] An Indian study showed that VLBW neonates with disturbed cardiopulmonary physiology during the first 24 hours of life, especially those in need of mechanical ventilation, were at an increased risk of early neonatal mortality.[17] Laboratory parameters were found not to be of much importance in predicting neonatal mortality. Only IgG was significantly reduced in the expired group. This may be explained by the fact that maternal to foetal transport of

IgG occurs in the third trimester of pregnancy,[18] and the number of IUGR babies was more in the survived group.

The results of the present study suggest that presence of maternal bleeding and failure to administer steroids to the mother when premature delivery is anticipated are the antenatal predictors of mortality. Steroids can easily be administered at any set-up, and mothers with profuse blood loss can be transfused and referred early to a better facility, provided the pregnant mothers present to the health facility in time, i.e. at least 24 hours prior to the onset of labour. Moreover, maternal PV bleeding should not be a predictor of neonatal death in a hospital set-up. Most probably, the delay in management, and not the cause itself, was the factor responsible for higher mortality. Among the perinatal factors, poor resuscitation, sepsis and hypothermia can be easily prevented at any set-up. Other critically-ill cases need early referral. In India, the majority of the deliveries are conducted in villages by basic level health workers (medical and paramedical personnel) and transport facilities are poor. Policies should be made to train these people regarding simple essential measures of maternal and neonatal care, and anticipation of premature and high-risk deliveries where expectant mothers can be referred to higher centres directly as the uterus is the best incubator for a premature baby. Another important aspect for the betterment of neonatal mortality is a generation of awareness among people so that they can seek early medical help. Both measures can help salvage many of these neonates and improve our neonatal mortality.

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