



Original Article

Predictors of mortality in very low birth weight neonates

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Abstract

The objective of the study is to identify the predictors of mortality in very low birth weight neonates. It is a nested case control study in a prospectively assembled cohort. Total 260 inborn VLBW newborn admitted to NICU were enrolled. Mean gestational age was 33.58 ± 4.8 week and mean birth weight was 1256.56 ± 182.8 g. Overall case fatality rate was 50.38%. Preterm delivery, low birth weight, APGAR score at 1 and 5 minute were found to be significant predictors of mortality. VLBW who are critically ill due to disturbance in pulmonary and circulatory physiology have a very high risk of mortality.

Keywords: Prematurity, very low birth weight, mortality, APGAR score, maternal BMI.

Introduction

The major causes of newborn deaths in India are Prematurity (35%), neonatal infections (33%), perinatal asphyxia (20%) and congenital malformations (9%)¹. Every year 70% of neonatal deaths occur because effective yet simple interventions are not available readily². VLBW preterm infants are increasing over the past two decades due to advances in obstetrical practice, bringing more burden to public health³. Very low birth weight babies constitute approximately 4-7% of all live births but constitute a major share of effort, time and resources for their care. The survival rate of VLBW infant in India is only about 63%⁴.

Doubts are still there about the risk factors which accompany VLBW deliveries and that may be critical in determining proportion of survivors⁵.

The prognosis depends not only on birth weight and gestational age but also on perinatal factors and physiological condition of infants⁶. Thus the purpose of this study was to determine the factors predictive of mortality in VLBW neonates within the Indian settings.

Methods

A nested case control study was conducted in prospectively assembled cohort at Department of Paediatrics Government Medical College and Hospital, Nagpur, India, over a period of 2 year. Intramural neonates admitted in NICU with birth weight of 500-1500g were included in the study. Newborns with major congenital malformation and those who died in delivery room or within 12 hr of birth were excluded from the study. The objective was to evaluate predictors of mortality

in Very Low Birth Weight neonates. The outcome measure was in-hospital death. Survival was defined as the discharge of a live infant from the hospital. After ethical clearance from institutional ethical committee, all inborn VLBW neonates who fulfilled inclusion criteria were enrolled. All deliveries were attended by a paediatrician, trained in resuscitation. Surfactant was not used in any of the babies. Careful attention was given to fluids, nutrition, metabolic, hematologic and environmental parameters. Standard indications for mechanical ventilation were used. Proper antenatal and natal history was taken. Data was collected using structured data collection sheet. It included:

Birth Data: Birth weight, Gender, Gestational age (as per New Ballard Score), Intrauterine Growth Status, APGAR at 1, 5 minutes, need for Resuscitation at birth.

Maternal antenatal and perinatal data: Age, parity, maternal BMI, presence of severe anaemia, any addiction, other maternal health related problems, no. of antenatal visits, mode of delivery, multifetal gestation, pregnancy related complications like pregnancy induced hypertension, ante partum haemorrhage, leaking per vagina, presence of fetal distress, meconium stained liquor.

Physiologic data: Heart rate, respiratory rate, presence of Shock, temperature, urine output, blood glucose, serum electrolyte, seizures and apnoea.

Laboratory data: Haematocrit, total white cell count, immature/total polymorphonuclear cell ratio, platelet count, serum electrolytes, blood glucose levels. Interventional data: Need for and

amount of oxygenation required, and need for ventilatory support was recorded. All patient were followed up till discharge or death.

Statistical analysis: Considering the expected proportion of mortality in very low birth weight neonates in a tertiary care hospital be 40.8%, with relative precision of 15% , considering desired confidence level (1- α) being 95%,the minimum sample size was found to be 256.

The statistical software STATA Version 14.0 was used for data analysis. Categorical variables were compared by chi-square test and calculating Odds ratio and 95% confidence interval. Continuous variables were compared by independent t- test. $p < 0.05$ was considered as statistically significant. Logistic regression analysis was performed to determine predictors for mortality.

Results

Out of total 260 VLBW neonates enrolled in the study 129 survived, 131 died. Overall case fatality rate was 50.38%. The mean gestational age of all cases was 33.58 ± 4.8 week, which ranged from 28 week to 39 week. Mean birth weight of cases enrolled was 1256.56 ± 182.8 gram. Among the 15 neonates with gestational age less than or equal to 30 week gestation, only 13.3% survived. The overall case fatality rate among VLBW neonates was documented to be as high as 50.38 %. The primary causes of neonatal deaths were documented as septicaemia (28.4%), respiratory distress syndrome (38.46%), birth asphyxia (23.07% C), necrotising enterocolitis (6.1%), intraventricular haemorrhage (3.07%), meconium aspiration syndrome(0.70%).

Table No. 1 Distribution of very low birth weight Neonates in relation to Gestational Age and Birth Weight

Gestational age/Birth weight	≤30 week		31-32 week		33-34 week		35-36 week		≥37 week		Total	Survived
	Total	Survived	Total	Survived	Total	Survived	Total	Survived	Total	Survived		
500-700	3	0	0	0	0	0	0	0	0	0	3	0
701-900	7	0	4	0	0	0	0	0	0	0	11	0
901-1100	5	2	21	5	3	3	5	3	0	0	34	13(38.20%)
1101-1300	0	0	16	12	49	30	17	12	0	0	92	54(58.2%)
1301-1500	0	0	18	8	34	24	51	18	17	12	120	62(51.66%)
Total	15	2(13.33%)	59	25(42.37%)	86	57(66.27%)	73	33(45.20%)	17	12(70.58%)	260	129(49.61%)

Risk factors for neonatal mortality

Neonatal factors such as sex and intrauterine growth status were comparable between the two groups. On analysing mortality pattern according to birth weight it was observed that with increase in birth weight the mortality decreased. In similar way, the case fatality increased with decrease in gestational age.

The neonates who died had significantly lower 1 minute and 5 minute APGAR score than the survivors. (**Table no. 2**). The odds for mortality among VLBW neonates requiring resuscitation at

the time of birth was 2.54 {(95% C.I.=1.22-4.51) p value = 0.001 HS}. Need for supplemental oxygen predicted a 6.7 times higher risk of mortality in VLBW neonates.Hence need of supplemental O₂ was found to be a significant variable to predict mortality in VLBW (OR =6.7, P<0.001). It was also observed that a significantly larger number of neonates who died required mechanical ventilation as compared to those who survived. Need for mechanical ventilation predicted a 3.61 times higher risk of mortality in VLBW neonates.

Table No 2 Univariate Analyses of Fetal Variables in Expired and Survived Group

Fetal variables	Died (n=131)	Survived(n=129)	OR	95% C.I.	p-value
Intrauterine Growth status (small for gestational age)	98(74.80%)	97(75.19%)	0.98	0.53-1.78	0.943,NS
Mean birth weight(g)	1190.51 ±197.70	1323.63± 136.81	-	-	<0.0001,HS
Mean gestational age (week)	33.03 ±2.32	34.13 ±1.91	-	-	<0.0001,HS
Mean Apgar at 1 min	4.87± 1.14	6.24 ±1.31	-	-	<0.0001,HS
Mean Apgar at 5 min	6.92 ±1.02	8.13± 0.87	-	-	<0.0001,HS
Resuscitation(%)	57(43.51%)	30(23.25%)	2.54	1.44-4.51	0.001,HS
Supplemental O2 need(%)	104(79.38%)	47(36.43%)	6.72	3.72-12.19	<0.001,HS
Need of mechanical ventilaton(%)	55(41.98%)	24(18.60%)	3.16	1.74-5.81	0.001,HS

Univariate analysis of various co-morbidities showed that hypothermia, present of apnoea, shock, seizure, respiratory distress and sepsis were

significant risk factor for mortality (p < 0.001). (**Table no. 3**)

Table no. 3 Univariate Analysis of Various Comorbidities in Expired and Survived Group

Comorbidity	No. of cases N=260	Expired n=131	Survived n=129	OR	95% C.I.	p-value
Hypothermia	135(51.92%)	80(60.06%)	55(42.63%)	2.11	1.14-3.57	0.003, HS
Hypoglycaemia	66(25.38%)	34(25.95%)	32(24.80%)	1.06	0.58-1.93	0.832,NS
Apnoea	44(16.92%)	39(29.77%)	5(1.52%)	10.51	3.89-35.22	<0.001, HS
Shock	105(40.38%)	69(52.67%)	36(29.90%)	2.87	1.66-4.98	<0.001,HS
Seizure	79(30.38%)	52(39.69%)	27(20.93%)	2.48	1.38-4.49	0.001, HS
Respiratory distress	132(50.76%)	78(59.54%)	54(41.86%)	2.04	1.21-3.45	0.004,HS
Sepsis	112(43.07%)	77(58.77%)	35(27.13%)	3.82	2.20-6.68	<0.001,HS

Multivariate analysis was used for birthweight, gestational age, Apgar score at 1 minutes and 5 minutes, resuscitation at birth, need for mechanical ventilation, need for supplemental oxygen, apnoea, shock, hypothermia, apnoea, seizure sepsis. Independent predictors of mortality were found to be Apgar score at 5 minutes, need for supplemental oxygen, resuscitation at birth, hypothermia, shock, sepsis, apnoea. (**Table no. 4**)

Table No. 4 Multiple Logistic Regression Analysis For Risk Factors For Early Neonatal Mortality

Variables	Adjusted OR	95 % C.I.	p-value
Gestational Age	0.8474	0.66 -1.08	0.1880,NS
Birth Weight	0.9983	1.00-1.00	0.2270,NS
Apgar 1min	0.6188	0.38-1.02	0.0590,NS
Apgar 5min	0.3529	0.21-0.60	<0.0001,HS
Need oxygen	3.2307	1.37-7.61	0.0070,HS
Resuscitation	0.1875	0.05-0.67	0.0100,S
Hypothermia	0.3278	0.14-0.79	0.0130,S
Apnoea	6.7862	1.71-26.86	0.0060HS
Shock	4.0657	1.71-9.66	0.0010,HS
Seizure	0.9426	0.34-2.62	0.9100,NS
Mechanical ventilation	0.6805	0.21-2.17	0.5160,NS
Sepsis	4.3018	1.86-9.93	0.0010,HS

Maternal factors such as age, parity, presence of severe anaemia were comparable between survived and expired group. Similarly maternal medical and obstetric complications like leaking pervagina, pregnancy induced hypertension, multifetal gestation were not significantly associated with neonatal mortality. Maternal BMI less than 18.5 g/m², (p value of 0.0019 [(OR= 3.23) (95% C.I. 1.43-7.80)]) and ante partum haemorrhage (p value of 0.0001[(OR= 3.57) (95% C.I. 1.82-7.22)]), were two maternal factors which significantly increased the risk of death.

Discussion

The Mortality rates of VLBW babies admitted to NICUs in India is quite higher than the developed world, with wide variation in the performance in different NICUs within country. This situation is mainly due to the poor infrastructure and limited resources. There is an absence of data to explain, the way in which birth weight, gestational age and preterm risks interact and lead into neonatal mortality in high mortality burden setting. The predictors indicating risk of mortality in very low birth weight neonate have very important role in health service research, planning and clinical audit.

Present study reported case fatality rate of 50.38%, which is higher than similar studies by **Basu S et al**⁷ and **Tarun Gera et al**⁸. Lower availability and less experience with prophylactic and rescue surfactant therapy for premature neonates, high sepsis rate, high admission rate and lower doctor to patient ratio in our setup may be the cause of high mortality in our study.

Similar to the study conducted by **Tarun G et al**, the present study also suggests that small for gestation is not a significant risk factor of mortality after both univariate and multivariate analysis.

K.K. Roy et al⁹ found in their study that mortality rate was highest in 26 to 30 weeks gestation babies. Study conducted by **Basu S. et al**⁷ has concluded that prematurity and low birth weight are significant contributors to neonatal mortality.

Similar results were shown by **Terzic et al**¹⁰ and **Manuel Moro et al**¹¹. The present study does show that with increase in gestational age the mortality decreases. Similarly it was found that the mortality rate is inversely proportional to mean birth weight. On univariate analysis we found gestational age and birth weight as significant predictor of death.

In the present study low APGAR scores both at 1 minute and at 5 minute were found to be associated with increased risk of mortality. This finding is similar to the observations made by **Terzic et al**¹⁰ and **Basu S et al**⁷.

After multivariate analysis APGAR score at 5 minute was found to be much more significant variable to predict risk of neonatal mortality. This finding may be due to the poor correlation of 1min Apgar for assessing clinical status of a preterm due to infant's physiologic immaturity. The healthy preterm with no evidence of asphyxia may have low Apgar score only because of immaturity. Regardless of the subjective way of evaluation and dependency on infant physiologic condition, the score still holds its place in the prediction of mortality in VLBW infants.

Resuscitation at birth and need of supplemental O₂ were found to be significantly associated with mortality in VLBW in both. However the Odds for supplemental O₂ requirement is much higher than for resuscitation, indicating pulmonary immaturity as the major cause of neonatal mortality in preterm neonates. The present study revealed that the presence of respiratory distress predicts mortality. In our study the percentage of death due to RDS was as high as 38.46%. This confirms the fact that RDS persists as a problem, regardless of treatment given by CPAP. This result can be improved by regular availability and routine use of surfactant as well as CPAP in NICU.

After multivariate analysis the odds for mortality among VLBW neonate who has apnoea was 6.78 indicating the risk of death in neonates having apnoea was very high. Basu S et al also concluded that apnoea was a significant risk factor for

neonatal mortality. Sepsis and shock ie circulatory failure were leading cause of neonatal death in present study with high odds. In the present study 39.69% of VLBW neonates having sepsis died.

Sepsis is a preventable cause of neonatal mortality can be reduced by simple hand hygiene practices, promotion of early entral feeding with human milk, a good antibiotic protocol in NICU and identifying high risk neonates. These easy practices can result in significant decrease in neonatal mortality.

In our study shock was found to be a significant risk factor predicting mortality in very low birth weight neonates (p value <0.001) with an odds ratio of 2.87. This finding was same as the results reported by **Jae Woo Lim et al**¹² in which there was significant difference in no of neonates having shock in survived and expired groups.

Statistically there was no significant difference noted in blood glucose level between expired and survived groups. This was similar to study by **Basu S et al** in which hypoglycemia was not found a significant risk factor.

The study of the risk factors of neonatal death enable us to understand the links in the chain of determinant events that lead to death and to indentify groups exposed to different risk. In the case of very low birth weight newborns, the study of factors associated with death will lead to the critical analysis of health care services and actions aimed at improving care for this group.

The strength of our study is that it is a prospective cohort study with case control design, which allowed us to assess the association between various neonatal risk factors and neonatal outcome in very low birth weight neonates of birth weight (500 g to 1500 g).

- The interpretation of the results of our study should take into consideration some study factors and limitations:

- 1) Firstly, we lacked sufficient antenatal data. We did not include data about the antenatal corticosteroids status of mothers of enrolled cases, because of unavailability and unreliability of antenatal data provided with

mothers who were referred to our institute. Since Antenatal corticosteroids may have significant impact on neonatal mortality in preterm, ignoring this data may have had significant impact on our results.

- 2) We did not include severity scoring in our study because calculation of the scores needs estimation of fractional inspired oxygen (FiO₂), arterial blood gas analysis and monitoring of vitals including blood pressure but ABG analysis was not possible for all subjects at our facility.
- 3) We analysed only inborn neonates in our study and all of them were admitted just after delivery. All those who were born outside were excluded from the study group. Thus results of study may not have full applicability over very low birth weight neonates born in actual population.

The continental dimensions of India and the diversity of social and cultural characteristics in different states of country, justify the need to conduct some larger multicentre studies, so that more accurate knowledge of the Indian reality may come up.

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