Original Article

Effects of Maternal, Fetal and Neonatal Parameters on the Mortality of VLBW Infants admitted in NICU of a Tertiary Care Hospital

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ABSTRACT

Introduction: There has been an effort in recent times to define physiological and laboratory parameters, which would be predictive of neonatal mortality in VLBW group. The present study was aimed to analyze the effects of various maternal, fetal and neonatal parameters on the mortality of VLBW infants admitted in NICU and to find out the causes of mortality in intramural very low birth weight babies.

Methods: This is a hospital based prospective observational study from 1st July 2019 to 30th September 2020 at a tertiary care hospital in Surat. All intramural newborn babies who get admitted in NICU with birth weight <1500 grams were included in the study. The data was entered in MS-Excel database. All the analysis was done using the SPSS-20 software.

Results: In this study out of total 108 patients, 45(41.6%) patients were discharged, 63 (58.3%) expired. In less than 1000 grams babies, 88.8% mortality was observed. In 1401-1500g, total 13 patients in which 5 patient (38.5%) expired and 8 (61.5%) patients survived. So higher rate of survival was observed with increase in birth weight. RDS (p value 0.00), Shock (p value 0.00), sepsis (p value 0.001) and birth asphyxia (p value 0.00) are statistically significant factors contributing to neonatal mortality.

Conclusion: Common maternal risk factors predicting mortality in VLBW infants that were statistically significant observed were PIH, Meconium stained amniotic fluid, fetal distress, PROM and non-administration of 2 doses of antenatal steroids. Common fetal variables predicting mortality in VLBW that were statistically significant observed were smaller gestation age, crown heel length, head circumference and birth weight.

Key words: Maternal, Fetal, Neonatal, Mortality, VLBW, Infants, NICU

INTRODUCTION

Birth weight is the first weight of the fetus or newborn obtained after birth. Low birth weight has been defined by the WHO as birth weight of less than 2500 grams.[1] Babies with birth weight of < 1.5 kg are defined as very low birthweight.[2]

In 2015, 20.5 million newborns, an estimated 14.6 percent of all babies born globally that year, suffered from low birthweight. These babies are 20 times more likely to die then heavier babies. In 2012, World Health Assembly (WHA) nutrition target to reduce low birth weight by 30 percent before 2025. The prevalence of LBW babies is also more in developing countries as compared to developed countries.[2]

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.[3] Survival is directly associated with their birth weight and inversely associated with illness severity and gestation.[3] The government of India initiative to start sick newborn care unit and free of cost treatment in less than one year that results in improvement in reducing the morbidity and mortality. According to INAP (Indian Newborn Action Plan), the target proposed in the INAP is "Single Digit NMR by 2030." Current NMR of India is 24 per 1000 live birth.[1]

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 VLBW group. Thus, the present study was aimed to analyze the effects of various maternal, fetal and neonatal parameters on the mortality of VLBW infants admitted in NICU and to find out the causes of mortality in intramural very low birth weight babies.

MATERIAL AND METHODOLOGY

This is a hospital based prospective observational study from 1st July 2019 to 30th September 2020 at SMIMER medical college, Surat. Sample size was calculated by using OPENEPI software by considering data of a previous reference study conducted by Basu et al[3], on predictors of mortality in very low birth weight neonates in India. The level of significance was set at 95%. The calculated sample size was 108 very low birth weight neonates.

All intramural newborn babies who get admitted in NICU with birth weight <1500 grams were included in the study.

Newborn with birth weight ≥1500 grams, newborn with lethal congenital malformation, newborn who are either referred to other places or those who have taken DAMA, newborn weighing less than 500 grams and with gestational age less than 26 weeks and newborn who are out-born were excluded from the study.

All required details of the baby of <1500 grams weight were collected including- Full name, gender, SNCU number, address, date of birth, date of admission, age on admission in hour/days of life. Weight on admission and birth weight-in grams with digital weight scale with accuracy of 0.001 gm was recorded. Gestational age according to LMP and/or 1st trimester USG and lastly if none of them were available then through new Ballard score was noted. They were treated according to standard protocol. Data collected included detailed antenatal and natal histories, anthropometric measurements, Apgar score (one minute and five minute), details of clinical examination including vitals and progress during the hospital stay and outcome.

Statistical analysis: The data was entered in MS-Excel database. All the analysis was done using the SPSS-20 software. Descriptive statistics for inter-group comparison was used where qualitative data was depicted in percentage and quantitative data was depicted in mean and standard deviation. Independent t-test was applied to observe significant difference between 2 independent groups of quantitative data. A P value of <0.05 was considered significant. Confidence intervals was at 95% confidence limit.

RESULTS

This study was conducted in a tertiary care hospital to determine the predictors of mortality in very low birth weight neonates. The study population was 108 patients having birth weight < 1500 grams. This study was conducted from July 2019 to September 2020. This was a prospective observational study. In this study out of total 108 patients, 45(41.6%) patients were discharged, 63 (58.3%) expired.

In less than 28 weeks of gestational age, 100% mortality was observed. In more than 34 weeks of gestational age, mortality was less (14.3%). so with increasing gestational age, mortality reduced.

There is statistically significant difference between the two group (p value 0.00). Hence, neonatal mortality was higher in neonates with gestational age of ≤32 weeks. There is statistically significant difference between the two group (p value 0.00).

Table 1: Outcome of VLBW babies in relation to gestational age

Gestational age	Total (n=108)	Discharged (n=45)	Expired (n=63)
<28 wks	9	0	9 (100)
28-30 wks	26	5 (19.23)	21 (80.76)
31-32 wks	32	11 (34.38)	21 (65.62)
33-34 wks	34	23 (67.64)	11 (32.35)
>34 wks	7	6 (85.7)	1 (14.3)

Figure in parenthesis indicate percentage

Table 2: Comparison of mortality in ≤ 32 weeks and >32 weeks of gestational age

	Total (n=108)	Discharged (n=45)	Expired (n=63)	P value
Gestational age (weeks)				
≤32 wks	67 (62.1)	16 (23.8)	51 (76.1)	0.00
>32 wks	41 (37.9)	29 (70.7)	12 (29.2)	
Birth weight				
≤1.2 kg	47 (43.5)	10 (21.2)	37 (78.7)	0.00
>1.2 kg	61 (56.4)	35 (57.3)	26 (42.6)	
Gender				
Male	57 (52.7)	27 (48)	30 (52)	0.102
Female	51 (47.2)	18 (35.3)	33 (64.7)	

Figure in parenthesis indicate percentage

Table 3: Outcome of VLBW babies based on birth weight

Birth weight	Total patients n=108 (%)	Discharged n=45 (%)	Expired n=63 (%)
<1000 g	9	1 (11.1)	8 (88.8)
1001-1100 g	15	2 (13.4)	13 (86.6)
1101-1200 g	23	7 (30.4)	16 (69.5)
1201-1300 g	30	17 (56.6)	13 (43.3)
1301-1400 g	18	10 (55.5)	8 (44.4)
1401-1500 g	13	8 (61.5)	5 (38.5)

Table 4: Outcome of VLBW babies with regard to neonatal factor contributing to mortality

Neonatal factor	Total patients n=108 (%)	Discharged n=45 (%)	Expired n=63 (%)	P value
RDS	71 (65.7)	21 (53.8)	50 (78.1)	0.00
Apnea	56 (51.8)	23 (41)	33 (58.92)	0.44
Shock	51 (47.2)	7 (13.7)	44 (86.27)	0.00
Hypothermia	36 (33.3)	11 (30.5)	25 (69.4)	0.09
Sepsis	39 (36.11)	9 (23)	30 (76.9)	0.001
Neonatal jaundice	32 (29.6)	25 (78.1)	7 (21.8)	0.05
Hypoglycemia	32 (29.6)	10 (31.2)	22 (68.7)	0.07
Birth asphyxia	21 (19.4)	2 (9.5)	19 (90.4)	0.00
Extreme preamaturity	9 (8.33)	0	9 (100)	-
Intra cranial haemorrhage	2 (1.8)	0	2 (100)	-
Pneumothorax	1 (0.9)	0	1 (100)	-

Table 5: Distribution of expired VLBW babies in relation to primary cause of death

Primary cause of death	Patient (n=108) (%)	Death (n=63) (%)	P value
RDS	71 (65.7)	20 (31.7)	0.00
Apnea	56 (51.8)	2 (3.17)	0.44
Shock	51 (47.2)	13 (20.63)	0.00
Hypothermia	36 (33.3)	3 (4.76)	0.09
Sepsis	39 (36.11)	14 (22.22)	0.001
Birth asphyxia	21 (19.4)	10 (15.87)	0.00
ICH	2 (1.8)	1 (1.58)	0.41

ICH=Intra cranial haemorrhage

Table 6. Mortality observed in VLBW babies treated with ventilator and CPAP

	Total (n=85)	Discharged (n=21)	Expired (n=63)	P value
Ventilator	66 (61.1)	7 (10.6)	59 (89.3)	0.00
CPAP	19 (17.5)	15 (78.9)	4 (21.05)	0.00

Figure in parenthesis indicate percentage

Hence, neonatal mortality is higher in neonates with birth weight of ≤1.2 kg. This table shows 52% and 64.7% mortality in Male and Female babies respectively which is not statistically significant. (p value 0.102)

In less than 1000 grams babies, 88.8% mortality was observed. In 1401-1500g, total 13 patients in which 5 patient (38.5%) expired and 8 (61.5%) patients survived. So higher rate of survival was observed with increase in birth weight.

RDS (p value 0.00), Shock (p value 0.00), sepsis (p value 0.001) and birth asphyxia (p value 0.00) are statistically significant factors contributing to neonatal mortality. Statistically significant Primary causes of death in VLBW observed were RDS (P value 0.00), shock (P value 0.00), sepsis (P value 0.001) and birth asphyxia (P value 0.00).

Mortality in patient who required ventilation and CPAP is 89% and 21% respectively. There is statistically significant difference between discharged and expired group in patient who require Ventilation or not and who require CPAP support or not. (p value 0.00).

Table 7. Comparison of neonatal laboratory parameters between discharged and expired VLBW babies

Laboratory parameter	Expired group (n=63) (mean ± SD)	Discharged group (n=45) (mean ± SD)	P value
Hemoglobin (g/dl)	14.9±2.7	16.6±3.5	0.19
Total leucocyte count	12265±3124	13250±2536	0.85
Polymorphs (%)	45.2±10.6	43.5±13.2	0.38
Lymphocytes (%)	47.2± 6.3	45.3± 7	0.21
Eosinophils (%)	1.9± 0.5	2.1± 0.6	0.94
Monocytes (%)	1.7± 0.6	1.8± 0.7	0.45
Platelets	165648± 82434	181463± 74582	1.01
Serum calcium (mg/dl)	8.1± 0.6	9.2± 0.7	0.73
Total serum bilirubin (mg/dl)	11.5± 3.8	12.4± 3.5	0.14
Blood sugar (mg/dl)	56.5± 8.5	60.2± 6.2	0.22

Table 8: Comparison of fetal variable between discharged and expired group

Fetal variable	Discharged group (n=45) Mean±SD	Expired group (n=63) Mean±SD	P value
Mean APGAR score at 1 min	8.23±2.52	7.58±2.63	0.00
Mean APGAR score at 5 min	9.10±1.52	8.66±1.32	0.01
Mean birth Weight (kilograms)	1.37±0.11	1.24±0.15	0.00
Mean gestational Age (weeks)	34.55±2.44	32.82±2.81	0.04
Mean crown heel lengh (cm)	40.71±2.02	39.58±2.48	0.02
Mean head circumference (cm)	31.59±2.42	28.44±2.52	0.01

Table 9. Observation of maternal risk factors in relation to mortality of VLBW babies

Maternal Risk factor	Total patients n=108 (%)	Discharged n=45 (%)	Expired n=63 (%)	P value
Maternal age < 18 or >40 years	5	1 (20)	4 (80)	0.15
PIH	13	2 (15.4)	11 (84.6)	0.02
Anaemia	21	9 (42.8)	12 (57.1)	0.45
Eclampsia	1	0	1 (100)	-
H/o fever	6	2 (33.3)	4 (66.6)	0.33
H/o hypothyroidism	5	2 (40)	3 (60)	0.46
GDM	5	2 (40)	3 (60)	0.46
Oligohydramnios	18	6 (33.3)	12 (66.6)	0.21
Premature rupture of membrane (PROM)	16	12 (25)	4 (25)	0.01
Meconium stained amniotic fluid (MSAF)	12	10 (83.34)	2 (16.66)	0.00
Fetal distress	11	9 (81.9)	2 (18.1)	0.00
No history of antenatal steroids (2 doses)	74	24 (32.43)	50 (76.56)	0.00

Table 10: Outcome of VLBW babies in relation to parity of mother

Gravida	Total (n=108)	Discharged (n=45)	Expired (n=63)	P value
Primi gravida	57 (52.7)	22 (38.59)	35 (61.4)	0.24
Multi gravida	51 (47.2)	23 (45.09)	28 (54.9)	

This table shows mean value, standard deviation and p value of various laboratory parameters of discharged and expired groups. There is no statistically significant difference in mean value of any laboratory parameter between discharged and survived group.

There is statistically significant difference in APGAR score at 1 min & 5 min and fetal anthropometry between discharged and expired VLBW babies. (P value <0.05)

Maternal eclampsia, Premature rupture of membrane (PROM), Meconium-stained amniotic fluid (MSAF) and Fetal distress were found associated with higher mortality.

Primigravida and multigravida are associated with mortality 61.4% and 54.9% respectively. However, there is no statistically significant difference between discharged and expired babies in terms of gravida. (p value 0.24).

DISCUSSION

Neonatal death is a serious concern, both in the developing and the developed world. 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 cause of neonatal mortality in India is prematurity and low birth weight.[4] The chances of survival of VLBW babies is still poor. In India, all neonatal set ups do not have level 3 newborn care facilities. Most of the centers, especially in the rural districts, have only level 2 care facilities and the burden of sick newborns is too high to be referred and managed at the level 3 centers. This further brings down the chance of neonatal survival, especially in the VLBW neonates who are already compromised since birth.[4]

Prognosis depends not only on birth weight and gestational age but also on the Perinatal factors and physiological conditions of the individual infants, in particular, disease severity in the first hours of life.[5]

In our study we documented a mortality rate of 58.3%. Basu et al[3] study (done in 2008), Anuradha Bansal et al[6] study (done in 2016) and Mukharajee et al[7] study (done in 2017) have documented a mortality rate varying from 12.9 to 36.9%. So mortality is bit higher in our study.

Higher gestational age and birth weight was associated with higher chances of survival. The risk of mortality was found to be lower with increase in birth weight and gestational age. Though their relative contribution in reducing mortality is not clear, probably increased maturity helps in maturation of lungs and reduces the chances of IVH. It is known that the fetus responds to a stressful environment by increasing adrenal glucocorticoid production, which leads to accelerated fetal lung maturation.[3] As we compare all these studies, Mortality is higher in female patient as compare to male patient. However, this difference is not statistically significant.

According to our study in VLBW babies respiratory distress syndrome (RDS) (p value 0.00), shock (p value 0.00), sepsis (p value 0.001) and birth asphyxia (p value 0.00) are the statistically significant factor leading to mortality.

According to Basu et al[3] study done in 2008 Apnea, shock, hypothermia, Sepsis, Intracranial haemorrhage (ICH) and birth asphyxia were statistically significant factors with relative risk of mortality were 5.17, 3.24, 2.38, 1.73, 3.08 and 1.71 respectively. According to Mukharajee et al[7] study done in 2017 RDS (p value <0.001), apnea (p value <0.001), sepsis (p value <0.001) and ICH (p value <0.001) were the statistically significant factors for mortality. So, on comparing all 3 studies, leading neonatal factor predicting mortality are respiratory distress syndrome (RDS), sepsis, shock, apnea, birth asphyxia and Intracranial haemorrhage (ICH).

According to Basu et al[3] study done in 2008 primary cause of death are Birth asphyxia (32.29%), RDS (23.96%), Intracranial haemorrhage (14.58%) and hypothermia (10.42%). Where as in our study primary causes of death were RDS (31.7%), Shock (20.63%), Sepsis (22.22%) and birth asphyxia (15.87%). Antenatal steroids in pregnant women at 24 to 34 weeks of gestation with preterm labour help in preventing RDS in preterm babies. Surfactant also helps in patients who already developed RDS when surfactant is given by maximum of 24 hrs. Sepsis can be prevented by following standard NICU protocol and by maintaining aseptic precautions and by using proper hand washing technique.

In Present study, Out of 66 (61.1%) of patients required ventilatory support of which 59 (89.3%) patients died. From 19 patients required CPAP, 4 (21.05%) patients died. According to Ballot et al[5] study done in 2015, in VLBW babies 63.33% died who required ventilation and 27 % died who required CPAP. According to Seyyed et al[9] study done in 2013, in VLBW babies 50% who died required ventilation and 30.72 % died who required CPAP. On comparison of these 3 studies, mortality were more in patient treated with ventilator contributed to by severe illness. CPAP were associated with more survival. (p value <0.05)

As we compare laboratory parameter between expired and discharged group, none of the laboratory parameter shows statistically significant difference between two group in both the study. Hence, laboratory parameter were found to have less importance in predicting neonatal mortality.

As we compare both the study, in both of them APGAR score at 1 min and 5 min and all anthropometry including mean birth weight, mean crown heel length, mean head circumference and mean gestational age was higher in discharged group in comparison to expired group. And this difference of all fetal variable of this table is statistically significant in both the study. (p value<0.05). So, anthropometry and APGAR score was also found to be a determining factor as all this fetal variable was higher in discharged group.

In our study statistically significant maternal factors found were PIH (P value 0.02), Premature rupture of membrane (PROM) (P value 0.01), Meconium-stained amniotic fluid (P value 0.00), fetal distress (P value 0.00), no history of receiving 2 doses of antenatal steroids (p value 0.00) affecting neonatal mortality as 11 (84.6%), 4 (25%), 2 (16%), 2 (18%), 50 (67.5%) respectively. Though, even multiple maternal factors affect fetal growth and health which leads to neonatal morbidity and mortality.

In Basu et al study[3] done in 2008, statistically significant maternal risk factors found were meconium-stained amniotic fluid (P value <0.01), fetal distress (P value <0.01) and no history of antenatal steroids (p value <0.01) affecting mortality as 11 (50%), 11 (42%), 87 (41%) respectively.

In Das et al[10] study done in 2018, statistically significant maternal risk factors found were meconium stained amniotic fluid (P value 0.001) , fetal distress (P value 0.001) and Premature rupture of membrane (PROM) (P value 0.015) affecting mortality as 29 (31.8%), 23 (26.7%) and 36 (36.7%) respectively. Failure to administer antenatal steroids was also statistically significant (p value 0.0001) maternal risk factor in this study. So if we compare all the 3 studies, Meconium stained amniotic fluid, fetal distress and Premature rupture of membrane (PROM) and absence of administration of antenatal steroids are the leading maternal risk factors affecting the neonatal mortality.

In our study, in patients where maternal antenatal steroids given neonatal mortality was 32% while in patients where mother didn't receive antenatal steroids neonatal mortality was 67%. According to Mukherjee et al[7] study done in 2017, in patients where maternal antenatal steroids given neonatal mortality was 4% while in patients where mother didn't receive antenatal steroids neonatal mortality was 60%. According to Cochrane systemic review[11] treatment with maternal antenatal corticosteroids reduces perinatal death by 28%, neonatal death by 31%, RDS by 34%, and IVH by 45% in preterm infants.

In present study mortality in primi gravida and multi gravida are 61.4% and 54.9% respectively. In Seyyed et al[9] study done in 2013, mortality in primigravida and multigravida were 28.8% and 29.5% respectively. However, there is no statistical difference between expired and discharged group in both the study in terms of gravida, so maternal gravida was found to be less important in predicting neonatal mortality.

CONCLUSION

Common maternal risk factors predicting mortality in VLBW infants that were statistically significant observed were PIH, Meconium-stained amniotic fluid, fetal distress, PROM and non-administration of 2 doses of antenatal steroids. Common fetal variables predicting mortality in VLBW that were statistically significant observed were smaller gestation age, crown heel length, head circumference and birth weight. Common neonatal factors predicting mortality in VLBW infants that were statistically significant observed were low APGAR score at 1 min and 5 min, RDS, shock, sepsis and birth asphyxia. Interventions such as the need for mechanical ventilation may increase the burden of mortality contributed to by severe illness. Primary causes of death in VLBW were observed to be RDS, shock, sepsis and birth asphyxia.

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