Original Article

Risk Factors, Complications and Immediate Outcome of Very Low Birth Weight Neonates in a level-III NICU

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Abstract:

Background: Last two decades have witnessed a steady improvement in the quality of perinatal care in Bangladesh. Around 4-8% of all live births are very low birth weight (VLBW) & low birth weight (LBW) is 10.6%. The present study was done to determine risk factors, complications and immediate outcome in VLBW babies.

Methods: It was a prospective cohort study conducted in a level-III NICU of Ad-din Hospital over two years period (April 2019-March 2021). 356VLBW babies (birth weight <1500 g) were assessed for demographic characteristics, risk factors (both maternal & fetal) and neonatal complications. The American Academy of Pediatrics protocol for neonatal resuscitation was followed for the management of VLBW. Screening for retinopathy of prematurity was done. Data were entered in predetermined proforma and statistical analysis was done.

Results: Out of 356 VLBW babies, 268 (75.2%) survived. Maternal risk factors associated with birth of VLBW babies were primiparity (46.8%), poor socio-economic status (40.86%), multiple gestations (36.83%), Premature rupture of membrane (PROM) (21.6%), hypertension (20%) and under nutrition (17%). Significant morbidities were found Jaundice (43.31%), Respiratoy Distress Syndrome (RDS) (28.08%), apnoea (26.34%), birth asphyxia (20.43%), and sepsis (22.5%). Mortality was higher among males (20.43%) than females (12.9%). None below 26 weeks of gestation and birth weight of 750g survived. RDS was the main cause of death (46.15%) followed by birth asphyxia (23%), sepsis (19.2%) and Intraventricular Haemorrhage (IVH) (11.5%). Antenatal steroid improved the survival (77.4%) and reduced the incidence of RDS, Necrotizing Enterocolitis (NEC) and IVH. Retinopathy of Prematurity (ROP) was detected in 30.9% VLBW babies.

Conclusions: Higher birth weight, gestational age, female sex and antenatal steroids improved survival amongst babies. Antenatal steroids reduced incidence of RDS, NEC and IVH when preterm delivery was inevitable. Judicial use of supplemental oxygen and blood products prevent development of ROP.

Keywords: Neonate, Low birth weight, NICU, Neonatal mortality, Risk factors, Very low birth weigh.

Introduction

Very low birth weight is the condition where the weight of the new born is less than 1500g as against the normal weight at term between 2500g and 4000g. Around 4-8% of all live births are very low birth weight (VLBW) infants. Around one-third of the neonatal deaths are witnessed in this group.

WHO estimates that globally about 25 million LBW babies

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were born at each year, consisting 17 % of all live births, nearly 95% of them in developing countries.³In Bangladesh, VLBW infants made up 7%, low birth weight 10.6%, respectively, of the births were preterm. Europe, where 6.2% of the births were preterm, had the lowest rate.⁴ In Bangladesh, VLBW infants made up 7% of low-birth-weight total, but accounted for a third of infant's death.⁵

The outcome of VLBW babies is affected by prematurity as well as the presence of short-term morbidities such as RDS, patent ductus arteriosus (PDA), sepsis, NEC, IVH, periventricular leukomalacia (PVL), ROP, and chronic lung disease (CLD). Identification and thence, efforts to modify the factors associated with these morbidities will influence the intact survival of VLBW babies.

In the past two decades, the field of neonatology has experienced significant progress in medical care and improvement in overall patient survival. Advancement in technology, greater use of antenatal steroids and neonatal surfactant replacement therapy, better regionalization of prenatal and high-risk neonatal care, and a more comprehensive understanding of the physiology of the immature infants have all contributed to dramatic increase in survival of very preterm infants.⁷

Although they represent a small percentage of overall births and Neonatal Intensive Care Unit (NICU) admissions, VLBW

infants are often the most critically ill and at the highest risk for mortality and long term morbidity of any NICU patient contributing disproportionately to overall hospital days and consuming a large percentage of NICU personnel time, effort and cost of care.⁸

Prematurity and low birth weight are major factors for neonatal mortality especially VLBW, hence this study has been undertaken with an aim and objectives to determine maternal risk factors, morbidity patterns and outcome of VLBW babies during their period of hospital stay inVLBW (<1.5Kg), so that necessary steps can be taken to reduce NMR in thisVLBW group and ultimately reach target NMR.

Materials and Methods

The present study was done to determine maternal risk factors, frequency of disease, complications, survival rate and risk factors for morbidity and mortality in VLBW during their period of hospital stay admitted to NICU of Addin Medical College & Hospital.

This was a prospective cohort study conducted in a tertiary care centre, NICU of Ad-din Medical College & hospital in Dhaka. After taking approval from IRB of AMCH, Study was done over two years period from April 2019 to March, 2021, total 2590 neonates were admitted, of those 389 neonates were enrolled for study, 33 neonates took discharge against medical advice. AllVLBW (<1500g) neonates admitted within 72 hours of birth in the NICU duringstudy period were enrolled in the study. Babies with birth weight < 600 grams, with major congenital anomalies incompatible with life were excluded. Cases were studied after taking informed consent from the parents. Gestational Age (GA) was obtained from maternal last menstrual period and confirmed with a 1st trimester ultrasound. Then they were classified into preterm (< 37 weeks of GA), term(37-42 weeks of GA), posterm (>42 weeks of GA).9-11 Gestational maturity was assessed by New Ballard Score.¹² The birth weight was plotted on fetal infant growth chart by Fenton TR (2003) to classify the babies into small for gestational age (SGA) (birth weight < 10th percentile for GA) and Appropriate for Gestational Age (AGA) (birth weight between 10th - 90th percentile for GA).¹³ Delivery details, birth weight, sex, ANC check up, doses of antenatal steroids were obtained from the delivery records. Maternal risk factors were assessed with proper history, physical examination and evaluating previous medical records. Maternal BP 140/90 mm mercury was taken as hypertension. (Division of nutrition, National Centre for Chronic Disease Prevention and Health). Neonates with Respiratory Distress Syndrome (RDS) received early and Continuous Positive Airway Pressure (CPAP) or Mechanical Ventilation as and when needed. Enteral feeding was initiated at the earliest and transitioned to full feeds depending on tolerance. Morbidities like Respiratory Distress Syndrome (RDS), birth asphyxia (HIE), sepsis, jaundice intraventricular hemorrhages (IVH), necrotizing enterocolitis (NEC), apnoea, pulmonary haemorrhage, PDA, Bronchopulmonary dysplasia (BPD) were predefined. IVH was graded using Volpe's classification.14 NEC was defined as per modified Bell's staging.¹⁵ Packed red blood cell transfusion was given when

Hct was <35% in neonates with ventilator support, <30% in neonates with heart failure & required resp. support and <21% in asymptomatic neonates. VLBW babies who were Appropriate for Gestational Age (AGA) were compared with those born Small for Gestational Age (SGA) in terms of associated maternal risk factors and morbidities. Appropriate investigations like hemoglobin, blood counts, serum electrolytes, blood glucose, serum bilirubin (total and direct), full septic work up, CSF study, urine examination, stool for occult blood test, chest X ray, Transcranial Ultrasound and Echocardiography were done to confirm diagnosis. ROP (retinopathy of Prematurity) screening was done. Data obtained were tabulated and necessary statistical analysis was done using SPSS 22 software. Descriptive statistics of the study population was generated by calculating percentages, mean and standard deviation.

Table 1: Characteristic features of the study.

Characteristic	No	(%)				
Gender	Male	195 (54.6)				
	Female	161 (45.4)				
Mean birth weight (mean ±SD)						
Birth weight	<750	6 (1.6)				
	750-<1000	29 (8.2)				
	1000-1250	88 (25)				
	1251-1499	233 (65.5)				
Gestational age (GA-weeks) me	ean ±SD)					
	<28	29 (8.2)				
	28-32	182 (51)				
	>32-36	119 (33.4)				
	>36	26 (7.3)				
Birth Weight						
according to GA	AGA	267 (75)				
	SGA	89 (25)				
Plurality	Single	255 (72)				
	Twin	37 (10.4)				
	Triplet	3 (0.8)				
Place of birth	Inborn	340 (95.5)				
	Outborn	169 (4.5)				

Results:

This cross-sectional prospective study was done at AMCH in Dhaka in a level-III NICU over 2 years period , with >95% inborn admissions. There were 195 males (54.6%) and 161fe males (45.4%). The mean birth weight was 1.198 with S.D of 0.211. The mean gestational age in weeks was 31.9 with S.D of 3.095. Majority of them were in the gestational age 28-32 weeks (n=182, 51%), small for gestational age (n=89, 25%), singletons (n=255, 72. %), inborn (n=340, 95.5%) Table 1 depicts the findings from the study.

Table 2 shows maternal major risk factors associated with incidence of VLBW babies were primiparity (46.8 %), poor socio-economic status (40.86%), multiple gestations (38.8%), PRO the (21.6%), hypertension (20%) and maternal under-nutrition (17%) with AGA and SGA babies.

Table 3 Shows the relative risk of complications in AGA and SGA babies. Jaundice (43.31%), apnoea (26.34%), Hypoxic ischemic encephalopathy (HIE) (20.43%), RDS (19.89%),

Sepsis (18.82%) were documented. Need for NICU admission and Mechanical ventilation was more among AGA babies compared to the SGA babies (p <0.0001). The major indication of Mechanical Ventilation in VLBW babies was and RDS in 56 (51.16%) cases) apnoea in 42 (48.84%)

Only 152 out of 356(42.7%) VLBW babies received antenatal steroids. Table 4 shows that antenatal steroids improved survival in these babies (p value 0.033).

Table 2: Association of Maternal Risk Factors with AGA and SGA babies

	AGA	SGA	Odds ratio	95% confidence interval (CI)	P -value
Poor socioeconomic conditio	n				
Present	90	30	1.00	0.58-1.72	0.001
Absent	177	59			
Maternal nutrition					
BMI <18.5 kg/m2	17	10	0.54	0.22-1.32	0.133
BMI >18.5 kg/m2	250	79			
Short stature					
< 145 cm	26	11	0.76	0.34-1.73	0.483
>145 cm	241	78			
Maternal Anemia					
Hb <11 g/dl	22	13	0.52	0.24-1.16	0.080
Hb > 11 g/dl	245	76			
Bad obstretric history					
Present	28	21	0.38	0.19-0.74	0.002
Absent	239	68			
Maternal Hypertension					
Present	41	30	0.36	0.20-0.64	0.001
Absent	226	59			
Chronic illness					
Present	21	12	0.55	0.24-1.24	0.113
Absent	246	77			
Antenatal care					
>3 visit	152	54	0.86	0.51-1.44	0.535
<3 visit	115	35			
Premature rupture of memb	rane				
Present	52	25	0.62	0.34-1.12	0.087
Absent	215	64			
Cervical incompetence					
Present	5	2	0.83	0.14-6.30	0.557
Absent	262	87			
Antepartum Hge					
Present	21	10	0.67	0.29-1.61	0.329
Absent	246	79			
Intrauterine infections					
Present	12	5	0.79	0.25-2.66	0.426
Absent	255	84			

Table 3: Relative risk of complications in AGA and SGA babies.

		AGA	SGA	Relative risk (RR)	95% confidence interval (CI)	P value
Respiratory distress syndrome(RDS)	Yes	82	18	1.13	1.01-1.28	0.057
	No	185	71			
Apnoea	Yes	74	16	1.13	1.00-1.28	0.067
	No	193	73			
Hypoxic Ischemic Encephalopathy	Yes	21	8	0.96	0.76-1.22	0.737
	No	246	81			
Pul. Hemorrhage	Yes	10	2	1.12	0.86-1.45	0.387
	No	257	87			
Polycythemia	Yes	42	12	1.04	0.89-1.22	0.609
	No	225	77			
Jaundice	Yes	78	27	0.99	0.86-1.13	0.840
	No	189	62			
Anemia	Yes	21	10	0.89	0.70-1.15	0.329
	No	246	79			
(DIC)	Yes	26	16	0.81	0.63-1.03	0.037
	No	241	73			
Sepsis	Yes	64	16	1.09	0.95-1.24	0.241
	No	203	73			
Pneumonia	Yes	18	7	0.96	0.74-1.23	0.719
	No	249	82			
Meningitis	Yes	5	2	0.95	0.59-1.53	0.557
	No	262	87			
Hypoglycemia	Yes	18	15	0.71	0.52-0.97	0.004
	No	249	74			
Hyperglycemia	Yes	23	10	0.92	0.73-1.17	0.460
	No	244	79			
Acute kidney Injury (AKI)	Yes	3	0	1.34	1.26-1.42	0.421
	No	264	89			
Necrotizing enterocolitis (NEC)	Yes	18	5	1.05	0.84-1.31	0.709
	No	249	84			
Patent ductus arteriosus (PDA)	Yes	48	13	1.06	0.92-1.23	0.465
	No	219	76			
Intraventricular hemorrhage (IVH)	Yes	7	4	0.84	0.54-1.33	0.285
	No	260	85			
Bronchopulmonary						
Dysplasia	Yes	4	1	1.07	0.69-1.66	0.633
• •	No	263	88			

Table 4: Relation of outcome with antenatal steroids

	Incidence	Anten	atal steroid	Total	P value
		Given n(%)	Not given n(%)		
RDS	Yes	40(26.32)	60(29.41)	100	0.520
	No	112(73.68)	144(70.59)	256	
NEC Yes	Yes	12(7.89)	9(4.41)	21	0.168
	No	140(92.11)	195(95.59)	335	
IVH	Yes	5(3.29)	6(2.94)	11	0.542
	No	147(96.71)	198(97.06)	345	

Table 5: Relative risk of complications in AGA and SGA babies.

		Out	come	Total	P value
		Survived n(%)	Expired n(%)		
Antenatal	Given	126(45.3)	26(33.3)	152	0.059
steroid	Not given	152(54.7)	52(66.7)	204	
	Total	278(100)	78	356	

Discussion:

Due to advance of prenatal and neonatal care now a day's more preterm and very low birth weight babies are survived. However, published data on outcomes of very low birth weight infants from Bangladesh are limited. Morbidities and mortality of VLBW babies vary between countries and in different hospitals as a result of specific treatment pattern employed in individual intensive care units. Incidence of VLBW neonates (1.7%) in this report was lesser than from other countries; world-wide prevalence of VLBW babies has been reported between 5-7% and that of ELBW as 1%; however, studies from the United States reported as 1.1% and 0.7% respectively. This study was conducted in a level three NICU in a tertiary hospital; therefore, our figures may not represent nationwide prevalence of very low birth weight infants.

Majority (54.6%) of VLBW babies admitted, were males which was much higher than the normal sex distribution of the general population of the country, probably indicating preference of the parents to seek health care for the male babies. Mannan et al.17 in Bangladesh showed that 62.86% of VLBW babies in their study were male, values being quite similar to this study, showing male sex as a risk factor for VLBW delivery. Maternal risk factors associated with incidence of VLBW babies in this study were primiparity, PROM, hypertension and under-nutrition. Undernutrition, hypertension, PROM and APH were found to be associated more with the incidence of SGA babies in comparison to AGA babies. Mannan et al.¹⁷, Manganaro et al. ^{4,18}, and Roy et al.¹⁹ found the similar risk factors as common associations contributing to the increased incidence of VLBW babies in varying percentages. Majority (76.4%) of VLBW babies in this study were preterm with significant proportion (39.62%) being both preterm and SGA, the results being quite similar to previous studies^{16,18} suggesting that multiple factors were acting together. Neonatal Jaundice,RDS, sepsis, apnoea, HIE, pulmonary hemorrhage, PDA and NEC were found to be significant morbidities. Compared to the study of Mannan et al., the incidence of jaundice and RDS were much higher in this study but the incidence¹⁷.

The incidence of IVH was quite similar in both studies. Ahmed et al.²⁰ showed the incidence of Jaundice needing phototherapy to be 26.7% whereas in this study the incidence was much higher (43.31%). Incidence of birth asphyxia was found to be much lower (20.43%) compared to their study reflecting improved perinatal care. Anemia was detected in 31 cases (9.68%) out of which10 (5.38%) needed blood transfusion in the present study, the incidence being comparable with the study of Ahmed et al.

Neubauer et al.²¹ showed that 72% of mothers having been given antenatal corticosteroids for neonatal RDS prophylaxis, 46% of ELBW developed RDS and 41% received surfactant treatment. Raju et al.²² showed the incidence of RDS as 12% at 33-34 week, 2% at 35-36 week and 0.11% at term in their study of outcome of late preterm infants. Overall incidence of RDS was found to be much higher (28.08%) in this study probably due to poor coverage of antenatal steroids. However, exposure to antenatal steroids was found to be associated with improved survival and significant reduction of incidence of RDS, NEC and IVH. Higher birth weight & gestational age and female sex were each found to be associated with improved survival which has been well established in previous studies.²⁰

The American Academy of Pediatrics²³ reported the BPD rate among infants <1500 g to be 23%. Lemons et al ²⁴ also showed BPD affected 23% of all infants. Zhang et al.²⁵ reported the incidence of BPD to be 48.3% in infants with BW of \leq 1500 g.

In our study, the incidence of BPD was 1.4%. Appropriate respiratory support with a policy for safe administration of oxygen, optimal fluid and nutrition management and infection controls at proper time, might be associated with the low incidence of BPD.

The incidence of ROP among ELBW babies in our study (78.6%) was slightly lower than the study of Nelumdeniya et al.²⁶ (83.3%), but much higher than that of Neubauer et al.²¹, (10%).

Ninety-two babies (78%) survived during the study period. Rate of overall survival for VLBW newborns has been widely different in studies from different parts of the world, 63% from India, 35.6% from a study in Iran, 70% and 71% and from South Africa, 74.5% from Turkey.²⁷⁻²⁹ These differences mainly related to gestational age, birth weight and associated diseases of the newborns and standard care of NICU in different studies. Neonates' weighing ≤700grams at birth had the highest mortality rate. None of them survived, similar to other studies.^{29,30} Main cause of mortality in our patients was RDS leading to respiratory failure; perinatal asphyxia, sepsis and major congenital anomalies were also common causes of death, which need improving quality of care in the antenatal, perinatal and postnatal periods of the newborn.

Limitations: This was a hospital-based study and does not give a complete idea of the community at large. Further follow up studies are necessary to have a better understanding of the long-term outcome among the survivors.

Conclusions: Proper antenatal and perinatal care is necessary to prevent the incidence of VLBW babies and the associated complications. Higher birth weight and gestational age, female sex and exposure to antenatal steroids were associated with improved survival and reduction of morbidities. Prematurity and need for neonatal intensive care were associated with poor audiological outcome.

Recommendations: Widespread coverage with antenatal steroids should be done when preterm delivery is inevitable. Judicial use of supplemental oxygen and blood products should be done to prevent development of ROP. Regular follow up of the survivors for growth monitoring, neurodevelopmental assessment and early detection of complications with prompt intervention, to have a neurologically intact outcome with minimum disability will be highly appreciated and remain as crucial.

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Bangladesh Crit Care J September 2021; 9 (2): 94-100

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