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Maternal Risk Factors, Complications and Outcome of Very Low Birth Weight Babies: Prospective Cohort Study from a Tertiary Care Centre in Odisha

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Abstract

Background: Last two decades have witnessed a steady improvement in the quality of perinatal care in India. Better understanding of the pathophysiology and newer treatment strategies like antenatal steroid, surfactant use, newer modes of ventilation and stringent aseptic measures have contributed to the improved survival of very low birth weight babies.

Methods: In a prospective cohort study conducted in a tertiary care center over two years period (October 2011-September 2013), 744 VLBW babies (birth weight <1500 g) were assessed for gestational age, maturity, maternal risk factors and administration of antenatal steroids. Morbidities like birth asphyxia, sepsis, jaundice, respiratory distress syndrome, intraventricular haemorrhage, necrotisingenterocolitis, apnoea, pulmonary haemorrhage and patent ductusarteriosus were noted. Screening for retinopathy of prematurity and hearing impairment was done. Outcome in terms of survival till discharge was recorded.

Results: Out of 744 VLBW babies, 496 (66.67%) survived till discharge. Maternal risk factors associated with birth of VLBW babies were primiparity (58.06%), poor socio economic status (40.86%), multiple gestations (36.83%), PROM (26.34%), hypertension (13.44%) and under nutrition (12.36%). Jaundice (43.31%), apnoea (26.34%), birth asphyxia (20.43%), RDS (19.89%) and sepsis (18.82%) were found to be significant morbidities. Mortality was higher among males (20.43%) than females (12.9%). None below 27 weeks of gestation and birth weight of 800 g survived. RDS was the main cause of death (46.15%) followed by birth asphyxia (23%), sepsis (19.2%) and IVH (11.5%). Antenatal steroid improved the survival (72.9%) and reduced the incidence of RDS, NEC and IVH. ROP was detected in 30.49% VLBW babies. 33.3 % of the survivors failed in the initial hearing screening.

Conclusions: Higher birth weight, gestational age, female sex and antenatal steroids improved survival amongst VLBW 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: Maternal risk factors; Morbidity; Mortality; Outcome; Very low birth weight

Abbreviations

ABR: Auditory Brainstem Response; AGA: Appropriate for Gestational Age; APH: Antepartum Hemorrhage; BOA:Behavioral Observation Audiometry; CPAP: Continuous Positive Airway Pressure; DIC: Disseminated Intravascular Coagulation; ELBW: Extremely Low Birth Weight; GA: – Gestational Age; HIE: Hypoxic Ischemic Encephalopathy; IVH: Intraventricular Hemorrhage; NEC: Necrotising Enterocolitis; NICU: Neonatal Intensive Care Unit; OAE: Oto Acoustic Emission; PDA : Patent Ductus Arteriosus; PROM: Premature Rupture of Membrane; RDS: Respiratory Distress Syndrome; ROP: Retinopathy of Prematurity; SGA: Small for Gestational Age; VLBW : Very Low Birth Weight

Background

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 prenatal glucocorticoids and neonatal surfactant replacement therapy, better regionalization of perinatal 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 [1-3]. Decreasing morbidity is highly essential for further improvement in the outcomes in VLBW infants.

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 [4].

Figure 1: Preterm baby born Appropriate for Gestational Age (AGA)

Figure 2: Term baby born Small for Gestational Age (SGA)

Those born preterm (Figure 1) are anatomically and functionally immature developing apnoea, Respiratory Distress Syndrome (RDS), Intraventricular Haemorrhage(IVH), anaemia, hyperbilirubinemia, sepsis, hypoglycaemia, Necrotising Enterocolitis (NEC), cognitive, motor and sensory impairment like Retinopathy of Prematurity (ROP) and hearing impairment while those born Small for Gestational Age (SGA) (Figure 2) have more risk of congenital anomalies, perinatal depression, meconium aspiration syndrome, pulmonary haemorrhage and polycythemia [4-6].

For many reasons, survival statistics vary by institution as well as geographic region and country. Odisha, a poverty stricken state of Eastern India with illiteracy and malnutrition being widely prevalent, VLBW appears to be a very common occurrence. However, there is dearth of data regarding the morbidity spectrum and survival statistics of these babies from this part of the country. The present study has been undertaken with an aim and objectives to study the maternal risk factors, morbidity patterns and outcome of VLBW babies during their period of hospital stay.

Materials and Methods

This was a prospective cohort study conducted in a tertiary care center in Odisha over two year period from October 2011 to September 2013, comprised of 744 VLBW babies (birth weight < 1500 g) admitted to this hospital within 72 hours of birth. Cases were studied after taking informed consent from the parents. Babies with major congenital anomalies incompatible with life were excluded. 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 weeks–42 weeks of GA) and post terms (>42 weeks of GA) [7-9]. Gestational maturity was assessed by New Ballard Score [10,11]. 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) [12]. Delivery details, birth weight, timing and 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. Socioeconomic status was assessed using Modified Kuppuswamy Scale. Maternal body mass index <18.5 kg/m^2 was taken to be under nutrition. Maternal arterial blood pressure >140/90 mm of mercury was taken to be hypertension. (Division of nutrition, National Centre for Chronic Disease Prevention and Health).

Neonates with Respiratory Distress Syndrome (RDS) received early rescue surfactant 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 birth asphyxia (HIE), sepsis, jaundice, Respiratory Distress Syndrome (RDS), intraventricular haemorrhage (IVH), necrotisingenterocolitis (NEC), apnoea, pulmonary haemorrhage and PDA were predefined. IVH was graded using Volpe's classification [13]. NEC was defined as per modified Bell's staging [14]. Packed red blood cell transfusion was given when PCV was <35% in sick neonates 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), sepsis screen, blood culture by BACTEC method, CSF study, urine examination, stool for occult blood test, chest X ray or infantogram, Transcranial Ultrasound and Echocardiography were done to confirm the diagnosis.

ROP Screening was done with Binocular Indirect Ophthalmoscopy at the scheduled date as shown in Table 1.

Hearing screening: All babies surviving beyond 24 hours were initially screened using Behavioral Observation Audiometry (BOA)

and Oto Acoustic Emission (OAE). Those who failed the initial screening were screened at 1 month of age and those failing again were subjected to ABR (Auditory Brainstem Response). These neonates were followed till death or discharge. For the purpose of analysis, those neonates who discontinued care (n=10) were grouped under those who died.

This study was approved by the Institute Ethics Committee.

Age at screening (Post natal age)	Gestational age
6 weeks	< 26 weeks
5 weeks	27 – 28 weeks
4 weeks	29 – 30 weeks
3 weeks	>30 weeks

Table 1: Timing for initial Ophthalmological examination

Analysis of Data

Data thus obtained was tabulated and necessary statistical analysis was done using SPSS 20 software. Descriptive statistics of the study population was generated by calculating percentages, mean and standard deviation. Adjusted odds ratio with a 95% confidence interval was calculated for the maternal risk factors associated with incidence of VLBW babies and correlation between the two comparison groups of AGA and SGA babies was determined. Relative risk with 95% confidence interval was calculated for the various complications developed and correlated between the AGA and SGA groups. To compare the complications between the AGA and SGA groups, chi square test was used for categorical variables, independent t test for normally distributed continuous data and Mann–Whitney U test for skewed data. Those risk factors that were significant on univariate analysis ($p < 0.05$) were entered into a forward stepwise multivariate logistic regression model and independent risk factors were determined. P value <0.05 was considered significant.

Results

Population characteristics: Incidence of VLBW babies in this hospital was 4.91%. Out of 744 VLBW babies studied, 496 (66.67%) survived till discharge. Mean birth weight was 1256.20 +/- 240.84g (range 630-1495 g). Mean gestational age was 32.18 +/- 3.45 weeks (range 43 -24 weeks). Males constituted 57.53%. 36.02% were twins, 86.02% were born preterm (<37 completed weeks) and 58.6 % born Small for Gestational Age (SGA).

Maternal risk factors: Maternal risk factors associated with incidence of VLBW babies were primiparity (58.06%), poor socio economic status (40.86%), multiple gestations (36.83%), PROM (26.34%), hypertension (13.44%) and maternal under-nutrition (12.36%).

	SGA	AGA	Odds Ratio (OR)	95% Confidence Interval(CI)	p value
Poor Socioeconomic status					
Kuppuswamy<5	184	120	1.1439	0.8495 - 1.5404	0.3759
Kuppuswamy 5-29	252	188			
Maternal under nutrition					
BMI < 18.5 Kg/m^2	64	28	1.7204	1.0748 – 2.7538	0.0238
BMI > 18.5 Kg/m^2	372	280			
Maternal short stature					
< 145cm	16	20	0.5486	0.2795 – 1.0766	0.0809
> 145 cm	420	288			
Maternal Anemia					
Hemoglobin<11g/dl	32	12	1.9538	0.9896 – 3.8573	0.0536
Hemoglobin>11g/dl	404	296			
Bad Obstetric history					
Present	32	32	0.6832	0.4089 – 1.1415	0.1457
Absent	404	276			
Maternal hypertension					
Present	48	52	0.609	0.3990 – 0.9296	0.0215
Absent	388	256			
Chronic illness					

Present	8	9	0.621	0.2369 – 1.6279	0.3326
Absent	428	299			
Antenatal care					
< 3 visits	24	12	1.4369	0.7072 – 2.9193	0.3162
>3 visits	412	296			
Premature Rupture Of Membrane (PROM)					
Present	132	64	1.6554	1.1750 – 2.3323	0.004
Absent	304	244			
Cervical Incompetence					
Present	4	4	0.7037	0.1746 – 2.8357	0.6212
Absent	432	304			
Antepartum Hemorrhage (APH)					
Present	40	16	1.8434	1.0125 – 3.3561	0.0454
Absent	396	292			
Intrauterine Infections					
Present	21	12	1.2482	0.6047 – 2.5766	0.5488
Absent	415	296			

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

Table 2 shows that maternal under nutrition, hypertension, PROM and antepartum hemorrhage were associated more with the incidence of SGA babies in comparison to AGA babies.

Neonatal complications: Jaundice (43.31%), apnoea (26.34%), HIE (20.43%), RDS (19.89%), Sepsis (18.82%), pulmonary haemorrhage (11.5%), PDA (7.6%) and NEC (3.23%) were found to be significant morbidities among the studied VLBW babies.

	Incidence	No. of SGA	No. of AGA	Relative Risk(RR)	95% Confidence Interval(CI)	p value
Hypoxic Ischemic Encephalopathy(HIE)	Yes	88	64	0.9713	0.7290-1.2943	0.8426
	No	348	244			
Apnoea	Yes	92	104	0.6249	0.4918-0.7941	0.0001
	No	344	204			
Respiratory Distress Syndrome(RDS)	Yes	48	100	0.3391	0.2483-0.4631	<0.0001
	No	388	208			
Jaundice	Yes	188	164	0.8098	0.6968-0.9411	0.0059
	No	248	144			
Anemia	Yes	44	28	1.1101	0.7073-1.7424	0.6498
	No	392	280			
Polycythemia	Yes	44	20	1.5541	0.9351-2.5830	0.0889
	No	392	288			

Sepsis	Yes	156	96	1.1479	0.9321-1.4137	0.1941
	No	280	212			
Pneumonia	Yes	16	8	1.4128	0.6123-3.2598	0.4178
	No	420	300			
Meningitis	Yes	8	4	1.4128	0.4292-4.6504	0.5696
	No	428	304			
DIC	Yes	28	8	2.4725	1.1424-5.3511	0.0216
	No	408	300			
Hypoglycemia	Yes	84	24	2.4725	1.6091-3.7991	<0.0001
	No	352	284			
Hyperglycemia	Yes	32	40	0.5651	0.3635-0.8787	0.0113
	No	404	268			
Necrotising Enterocolitis(NEC)	Yes	4	20	0.1413	0.0488-0.4093	0.0003
	No	432	288			
Intraventricular Hemorrhage (IVH)	Yes	16	22	0.5138	0.2744-0.9620	0.0374
	No	420	286			
Patent Ductus Arteriosus(PDA)	Yes	12	12	0.7064	0.3216-1.5515	0.3866
	No	424	296			

Table 3: Relative Risk of complications in AGA and SGA babies

Table 3 shows that apnoea, RDS, NEC, IVH, jaundice needing phototherapy and hyperglycemia were found to be occurring more among the AGA babies in comparison to SGA babies whereas hypoglycemia and DIC were found more in the SGA babies in comparison to AGA babies.

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 apnoea in 84 (48.84%) and RDS in 88 (51.16%) cases. AGA babies had shorter duration of NICU stay (maximum 21 days) than SGA babies (maximum 28 days) and also shorter duration of Mechanical ventilation (maximum 14 days) as compared to the SGA babies (maximum 21 days).

		Outcome		Total (%)	p value
		Died during Hospital stay (%)	Survived till Discharge (%)	0.033	
Antenatal Steroid	Given	52 (6.99)	140 (18.82)	192 (25.81)	
	Not given	196 (26.34)	356 (47.85)	552 (74.19)	
Total		248 (33.33)	496 (66.67)	744(100.00)	

Table 4: Relation of outcome with administration of antenatal steroids

Only 192 out of 744 (25.81%) VLBW babies received antenatal steroids. Table 4 shows that antenatal steroids improved survival in these babies (p value 0.033).

Table 5 shows administration of antenatal steroids significantly reduced the incidence of RDS (p value 0.046), NEC (p value 0.015) and IVH (p value 0.034).

	Incidence	Antenatal Steroids		Total	p value
		Given	Not given		
RDS	Yes	48	100	148	0.046
	No	144	452	596	
NEC	Yes	12	12	24	0.015
	No	180	540	720	
IVH	Yes	4	34	38	0.034
	No	188	518	706	

Table 5: Relation of antenatal steroids with neonatal complications

ROP Screening: 30.49% of VLBW babies and 78.6% of ELBW babies developed ROP, the association with birth weight being statistically significant (p value 0.0001). The incidence of ROP in infants <28wks was 66.7%, infants between 28wks – 32wks was 20% & infants >32wks was 9%. Oxygen therapy (p value <0.0001) and blood

transfusion (p value < 0.001) was associated with increased incidence of ROP. RDS (p value 0.0009), sepsis (p value 0.0035), apnoea (p value <0.0001) and shock (p value 0.036) were each associated the development of ROP.

Hearing screening: 33.33% of VLBW babies failed in the initial hearing screening test. More of SG babies (42.47%) passed the test than AGA babies (24.2%), (p value 0.0001). Babies needing NICU care had higher (p value < 0.0001) failure rates (72%) in the initial hearing screening test compared to those not admitted to NICU (19.12%). Out of 25 VLBW babies who were discharged from NICU, 4(16%) needed second hearing screening test and 1 out of those 4 was detected to have Sensorineural deafness after Auditory Brainstem Response (ABR) test.

Outcome: Out of 744 VLBW babies, 496 (66.67%) survived till discharge. Mortality was higher among males (20.43%) than females (12.9%). None below 27 weeks of gestation and birth weight of 800 g survived. RDS was the main cause of death (46.15%) followed by birth asphyxia (23%), sepsis (19.2%) and IVH (11.5%).

Discussion

Incidence of VLBW babies in this hospital was quite higher (4.91% of live births) as compared to the study of Manganaro et al. [4] (1.1% of live births) done in 1991. Majority (57.53%) 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 MA et al. [5] in Bangladesh (2012) 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, poor socio economic status, multiple gestations, PROM, hypertension and under-nutrition. Under-nutrition, hypertension, PROM and APH were found to be associated more with the incidence of SGA babies in comparison to AGA babies. Manganaro et al. [4] (1991), Mannan MA et al. [5] (2012) and Roy et al. [6] (2006) found the similar risk factors as common associations contributing to the increased incidence of VLBW babies in varying percentages.

Majority (86.02%) of VLBW babies in this study were preterm with a significant proportion (44.62%) being both preterm and SGA, the results being quite similar to previous studies [4-6] suggesting that multiple factors were acting together making them small. Neonatal jaundice, apnoea, HIE, RDS, sepsis, pulmonary haemorrhage, PDA and NEC were found to be significant morbidities. Compared to the study of Mannan et al. [5] (2012), the incidence of jaundice and RDS were much higher in this study but the incidence of apnoea, sepsis and NEC were much lower. The incidence of IVH was quite similar in both studies.

Ahmed A et al. [15] (2008) 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 72 cases (9.68%) out of which 40 (5.38%) needed blood transfusion in the present study, the incidence being comparable with the study of Ahmed A et al.

Roy et al. [6] in their study showed the common neonatal complications in both VLBW and ELBW babies to be RDS, neonatal jaundice and sepsis.

Neubauer et al. [16] showed that 72% of mothers having been given antenatal corticosteroids for neonatal RDS prophylaxis, 46% of ELBW developed Respiratory Distress Syndrome (RDS) and 41% received surfactant treatment. Reempts et al. [17] showed that overall 62.5% of very low birth weight babies studied in Belgium developed RDS. Raju et al. [18] (2005) 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 (19.89%) 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 [2,15].

The incidence of ROP among ELBW babies in our study (78.6%) was slightly lower than the study of Nelumdeniya et al. [19] (83.3%) done in 2012, but much higher than that of Neubauer et al. [16], 2007 (10%). This wide variation in the outcome may be because of the differences in the level of neonatal care, subjective variation in diagnostic procedures and presence of treatable co-morbidities.

Prematurity (p value 0.0001) and the need for neonatal intensive care (p value < 0.0001) were each found to be associated with poor audiological outcome. This study results were similar to that of Korres et al. [20] (2005) and Roth D et al. [21] (2006).

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, neuro-developmental 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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