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Morbidities of ELBW babies affecting their outcome: An observational study

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Abstract

Introduction: There are significant risk factors like birth asphyxia, HMD, sepsis, pulmonary hemorrhage, IVH etc. predicting survival of the ELBW neonates and is associated with increased mortality. Expectant parents of ELBW neonates, physicians and policymakers need estimates for chances of survival.

Objective: To evaluate the different antenatal factors related to ELBW babies and their associations with outcome. To determine the different complications associated with the outcome of ELBW babies.

Methods: A Hospital based observational analytical study of all ELBW neonates admitted to SNCU/NICU of PG department of pediatrics, VIMSAR, Burla after fulfilling the predefined criteria, ethical committee approval & consent from the legal heir, all the relevant data were recorded in to a predesigned proforma, entered in to Microsoft excel v 16 software and analyzed by binary logistic regression model using SPSS v 24 software.

Results: There is significant association between outcome and babies encountered with morbidities like RDS, Pulmonary hemorrhage, Sepsis, Hypoglycemia, Hypothermia, Neonatal Jaundice, NEC, Blood Transfusion, Generalized edema with p values of each association <0.05. By logistic regression, prediction of outcome from antenatal factors is 68% & morbidities are 84.2%.

Conclusion: Morbidities like sepsis, neonatal jaundice, IVH, Sclerema, anemia & antenatal factors like previous preterm delivery and multiple pregnancies predicts the outcome of ELBW.

Keywords: ELBW neonates, Logistic Regression, IVH, NEC, HMD, Antenatal Factors.

Introduction

There is no indicator in human biology which tells us so much about the past events and future trajectory of life, as the weight of the new born at birth.(1)

A neonate born before 37 completed weeks (<259 days) of gestation irrespective of the birth weight are preterm neonate.(2)

Prematurity is a particularly significant risk factor for survival of the neonate and is associated with increased perinatal mortality.(3) These newborns are physiologically so immature that they are prone to develop various complications and long term sequel with high mortality rate as compared to term appropriate for gestational age(AGA) babies. The prognosis depends not only on birth weight and gestational age but also on perinatal factors and physiological condition of infants.(4) The outcome and survival of preterm babies has improved by use antenatal corticosteroid, administration of exogenous surfactant, and respiratory support (CPAP, assisted ventilation).(5) The consequences of prematurity are not only medical, but also social and economic, having a negative impact on the families involved.

Neonatal mortality rate in India is 39 per 1000 live births that accounts for 2/3rd of all infant death & 40% of under 5 child death.(5) Millennium development goal 4 (reducing under 5 mortality by two-thirds) cannot be achieved without substantial reduction in neonatal mortality.(5) According to WHO 2000 preterm birth contribute 27% to all main direct causes of neonatal death.(5)

About 28% of babies in India are LBW as opposed to about 5 to 7% of newborns in the west.(1) In India 6 to 8 billion LBW infants are born annually.(1) Over 80% of all neonatal deaths, in both the developed and developing countries, occur among the LBW babies.(1)

Low birth weight is also a major determinant of malnutrition during infancy because over 40% of LBW babies are malnourished at one year of age.(1) LBW infants have 2.3 times increased risk of mortality due to infections compared to normal birth weight babies after controlling for all the confounding variables.(1) Small for date babies may remain stunted throughout life leading to impaired physical work capacity. They are more vulnerable to develop atherosclerotic coronary artery disease, hypertension and diabetes mellitus during adult life.(1)

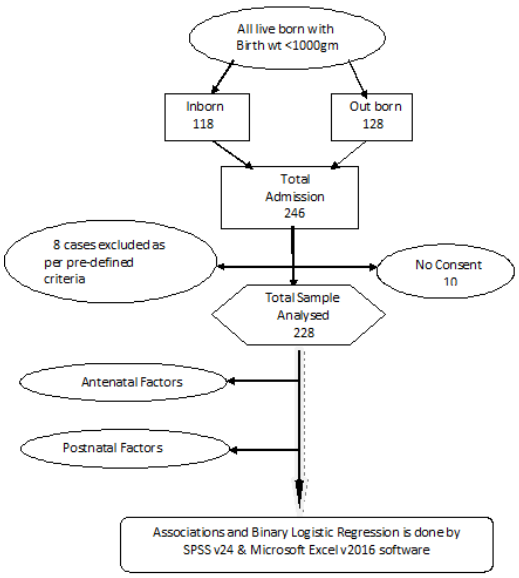
About 10 to 12% of Indian babies are born preterm (less than 37 completed weeks) as compared to 5 to 7% incidence in the west.(1) These infants are anatomically and functionally immature, and therefore, their neonatal mortality is high.

In the last 2 decades, the neonatal care has improved and more VLBW and ELBW babies are surviving in our country. Close Neonatal-Obstetric collaboration, successful implementation of NALS programs, better understanding of pathophysiology and management of neonatal problems, technological advances in neonatal care and above all the concern of pediatricians to enhance the intact survival of newborn babies have contributed to this increased survival of high risk newborns but the incidence of chronic morbidities and adverse outcome in survivors continues to be high.

Methods

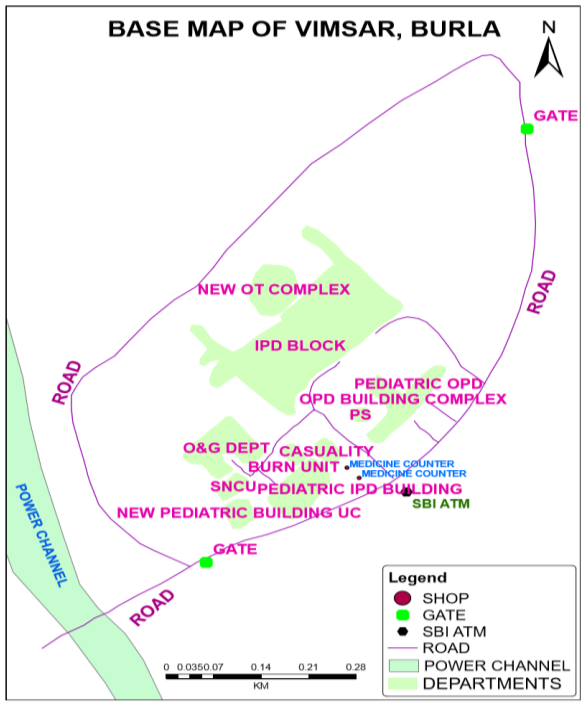
Study Design

This is an observational analytical study done in the PG department of Pediatrics, VIMSAR, Odisha (Fig. 1).



Study Setting

SNCU/NICU, P.G. Dept. of Paediatrics, V.S.S Medical College & Hospital, Burla as evidenced by the large scale map done by QGIS Software (Fig. 2).



Study Period: November 2014 to October 2016

Sample Size

All ELBW babies admitted to SNCU/NICU, V.S.S MCH satisfying inclusion and exclusion criteria from Nov 2014 to Oct 2015.

Sampling Technique: By simple convenient sampling method.

Study Subjects

Inclusion criteria:

All live born infants with birth weight less than 1000gm irrespective of gestational age & sex admitted in SNCU/NICU, V.S.S Medical College Hospital.

Exclusion criteria:

- All newborns with birth weight less than 400gm[6]
- All newborns with congenital lethal anomalies.

Methodology

All ELBW neonates admitted to SNCU/NICU, V.S.S. Medical College and Hospital, satisfying exclusion and inclusion criteria and after taking consent, Prenatal events from previous medical reports, birth ticket and referral tickets with details of the diagnosis (by clinical features and investigations), onset, duration, and clinical management of any relevant condition were noted in a predesigned proforma.

The data collected were analysed by binary logistic regression model using SPSS v24 & Microsoft Excel v2016 software.

Perinatal Asphyxia defined According to American Academy of Pediatrics Committee on fetus and Newborn –

- Persistence of Apgar score of 0-3 for >5min
- Neurological manifestations e.g. Seizures, coma, hypotonia in the immediate neonatal period
- Evidence of multiorgan dysfunction in immediate neonatal period
- pH =<7 or base deficit >=16mmol/L on the cord or first blood gas.(2)

Respiratory distress syndrome diagnosed by clinical features like shortly after Birth having tachypnea, retraction, nasal flaring, grunting, cyanosis with Radiographic appearance of diffuse reticulogranular pattern and air bronchogram.(7)

Pulmonary hemorrhage defined by Pink or red frothy discharge per mouth with presence of Hemorrhagic fluid in the trachea accompanied by respiratory decompensation requiring increased respiratory support or intubation within 60 min of the appearance of fluid.(8)

A newborn was diagnosed as sepsis by clinical signs and symptoms like respiratory distress, irritability, lethargy, temperature instability, refusal to feed, poor perfusion, petechiae and purpura (DIC in septic shock), vomiting, seizure, apnea, etc. with presence of risk factors like intrapartum fever (>38°c), prolonged rupture of membrane(>18hr), foul smelling liquor, difficult or prolonged labour in mother and Confirmed by Blood culture (BACTEC Method).(9)

Hypoglycemia was taken as blood glucose less than 40 mg/dl, using reagent strip[10] and confirmed by laboratory method.

Axillary temperature was measured by a digital thermometer (model-YB-009) reading as low as 32ºC an accuracy of ± 0.10C and observed temperature was graded as per standard guidelines WHO [11] to recognize hypothermia.

Babies with serum bilirubin level requiring phototherapy or exchange blood transfusion were taken as neonatal jaundice.[12]

PDA was diagnosed by clinical features and confirmed by ECHO

Intraventricular hemorrhage defined by decreased level of consciousness and spontaneous movement, hypotonia, abnormal eye movements, generalised tonic posturing(seizure) confirmed by cranial ultrasound.

Necrotizing Enterocolitis diagnosed by systemic and abdominal signs-

- Systemic signs-Respiratory distress, apnea and or bradycardia, lethargy, temperature instability, irritability, poor feeding, decreased peripheral perfusion, acidosis or bleeding diathesis.
- Abdominal signs-Abdominal distension or tenderness, gastric aspirates (feeding residuals), vomiting (bile, blood or both), ileus (decreased or absent bowel sounds), bloody stools, abdominal wall erythema or induration, persistence localised abdominal mass or ascites.
- Confirmed by diagnostic radiography with other laboratory features
- Abdominal X ray both AP and lateral-Bowel wall edema, pneumatosis intestinalis, portal and hepatic venous air, pneumobilia or pneumoperitoneum [13]

Baby Requiring Blood Transfusion [14]

- Asymptomatic infants with Hct <21% and reticulocytes <100,000/ul (2%)
- Infants with Hct <31% and hood <36% or >9 apneic and bradycardic episodes per 12hr requiring bag and mask ventilation while on adequate methyl xanthine therapy or HR >180/min or RR>80/min sustained for 24hr or weight gain of <10g/d for 4 day on 100 Kcal/kg/day or having surgery.
- Infants with Hct <36% and requiring >35% O_2

Results

Table 1: Frequency of different obstetrical variables

Variable		Frequency
Premature rupture of membrane	Yes	14.5%(33)
	No	85.5%(195)
Relevant drug intake	Yes	0%(0)
	No	100%(228)
Previous preterm delivery	Yes	13.2%(33)
	No	85.5%(195)
Infections	Yes	17.1%(39)
	No	82.9%(189)
Multiple pregnancy	Yes	23.7%(54)
	No	76.3%(174)
Renal diseases	Yes	0.4%(1)
	No	99.6%(227)
Cardiovascular disease	Yes	2.2%(5)
	No	97.8%(223)
Pregnancy induced hypertension	Yes	17.1%(39)
	No	82.9%(189)
Antepartum hemorrhage	Yes	15.4%(35)
	No	84.6%(193)
Diabetes mellitus	Yes	1.8%(4)
	No	98.2%(224)
Gestational diabetes mellitus	Yes	1.8%(4)
	No	98.2(224)

From the above table, multiple pregnancy is the highest frequency associated with the ELBW neonates

Table 2: Association of Antenatal factors with Outcome

Antenatal factors		Survival	Death	Statistical association
Previous preterm delivery	Yes	5.5%	16.8%	$\chi 2(1)=5.541$, p=0.020, Φ=-0.118
	No	94.5%	83.2%	
Premature rupture of membrane	Yes	20.5%	11.6%	$\chi 2(1)= 3.201$, p=0.105, Φ =-0.118
	No	79.5%	88.4%	
Maternal infections	Yes	20.5%	15.5%	$\chi 2(1)= 0.898$, p=0.351, Φ=-0.063
	No	79.5%	84.5%	
Multiple pregnancy	Yes	13.7%	28.4%	$\chi 2(1)=5.924$, p=0.019, Φ=0.161
	No	86.3%	71.6%	
Renal diseases	Yes	0%	0.6%	$\chi 2(1)=0.473$, p=1.000, Φ=0.046
	No	100%	99.4%	
	Yes	1.4%	2.6%	

Cardiovascular diseases	No	98.6%	97.4%	$\chi 2(1)=0.339$, p=1.000, Φ=0.039
Pregnancy induced hypertension	Yes	17.8%	16.8%	$\chi 2(1)=0.037$, p=0.852, Φ=-0.013
	No	82.2%	83.2%	
Antepartum hemorrhage	Yes	9.6%	18.1%	$\chi 2(1)=2.743$, p=0.117, Φ=0.110
	No	90.4%	81.9%	
Diabetes mellitus	Yes	4.1%	0.6%	$\chi 2(1)= =3.456$, p=0.098, Φ=-0.123
	No	95.9%	99.4%	
Gestational diabetes mellitus	Yes	0%	2.6%	$\chi 2(1)=1.918$, p=0.309, Φ=0.092
	No	100%	97.4%	

From the above table outcome of ELBW neonates are significantly associated with Previous preterm delivery and Multiple pregnancy.

Table 3: Logistic regression model for prediction of mortality

Antenatal factors	Adjusted odds ratio 95% CI	p value
Previous preterm delivery	0.242(0.077-0.761)	0.015
Premature rupture of membrane	1.747(0.763-4.003)	0.187
Maternal infection	1.104(0.496-2.458)	0.808
Multiple pregnancy	0.319(0.144-0.706)	0.005
Renal disease	0.000(0.000-0.000)	1.000
Cardiovascular disease	0.341(0.036-3.257)	0.380
Pregnancy induced hypertension	0.765(0.336-1.744)	0.524
Antepartum hemorrhage	0.494(0.190-1.285)	0.148
Diabetes mellitus	5.814(0.554-61.074)	0.142
Gestational diabetes mellitus	0.000(0.000-0.000)	1.000

From the above table as only previous preterm delivery and multiple pregnancy predicts the mortality of ELBW so regression model of these antenatal factors are again evaluated.

Regression model for ELBW Outcome

p values for STEP, BLOCK, MODEL is 0.000 which is significant (i.e., <0.05). This means there has been significant improvement in predictor power as compared to previous step model with predictors (independent variable) is significantly better than the model with constant only. Model is good to fit as evidenced by Cox and Snell R square=0.063 & Nagelkerke R square=0.088. This model fits the data as Hosmer and Lemeshow Chi-square test (1): 0.002, p=0.967. We can predict 68% of the time correctly with this model.

Outcome = (-1.438×PPD) + (-1.063×MP) + 2.886

$p=1/1+e^{-[(-1.438\times PPD)+(-1.063\times MP)+2.886]}$

(where p is the probability that variable outcome has a value of 1).

Table 4

Antenatal factors	Adjusted odds ratio 95% CI	p value
Previous preterm delivery (PPD)	0.238(0.079-0.715)	0.011
Multiple pregnancy (MP)	0.345(0.162-0.740)	0.006

Table 5: Logistic regression model for prediction of mortality

Risk factor	Adjusted odds ratio (95% CI)	p value
Birth asphyxia	1.305(0.408 - 4.178)	0.653
HMD	1.208(0.487 – 3.406)	0.671
Pulmonary hemorrhage	0.455(0.109 – 1.893)	0.279
Sepsis	5.406(1.746 – 16.737)	0.003
Hypoglycemia	0.159(0.307 – 2.993)	0.942
Hypothermia	1.786(0.556 – 5.737)	0.330
Neonatal jaundice	5.062(1.674 – 15.304)	0.004
PDA	0.291(0.063 – 1.341)	0.113
IVH	0.157(0.033 – 0.737)	0.019
Sclerema	0.024(0.004 – 0.156)	0.000
NEC	1.092(0.336 – 3.554)	0.883
Blood transfusion	0.876(2.140 – 45.576)	0.003
Generalized edema	2.715(0.446 – 16.513)	0.278

As only sepsis, neonatal jaundice, IVH, Sclerema, NEC and Blood transfusion only predicts the mortality of ELBW according to the above table so regression model of these complications are again evaluated.

Regression model for ELBW Outcome

p values for STEP, BLOCK, MODEL is 0.000 which is significant (i.e. <0.05).This means there has been significant improvement in predictor power as compared to previous step model with predictors (independent variable) is significantly better than the model with constant only. Model is good to fit as evidenced by Cox and Snell R square=0.398 & Nagelkerke R square=0.557. This model fits the data as Hosmer and Lemeshow Chi-square test: 2.257(5), p=0.813. We can predict 84.2% of the time correctly with this model.

Outcome = (1.617×sepsis) + (1.768×neonatal jaundice) + (-1.978×IVH) + (-3.061×sclerema) + (2.386×blood transfusion) + 1.535.

$p=1/1+e^{-[(1.617\times sepsis)+(1.768\times neonatal\ jaundice)+(-1.978\times IVH)+(-3.061\times sclerema)+(2.386\times blood\ transfusion)+1.535}$

(where p is the probability that variable outcome has a value of 1 i.e., death).

Table 6

Risk factors	Adjusted odds ratio (95%CI)	p value
Sepsis	5.039(2.013 – 12.613)	0.001
Neonatal jaundice	5.860(2.179 – 15.756)	0.000
IVH	0.138(0.030 – 0.628)	0.010
Sclerema	0.047(0.011 – 0.194)	0.000
Blood transfusion	10.870(3.005 – 39.323)	0.000

Discussion

A total of 246 live born ELBW babies admitted with weight ranging from 500 to 990gm born between 21 to 35 week in SNCU/NICU, Burla. Out of 246, 118 was inborn and 128 was out born but 10 didn't give consent for the study and 8 were excluded as per predefined criteria. So, a total of 228 sample was analyzed.

Of all the obstetrical variables related to ELBW babies multiple pregnancy has the highest frequency (23.7%) followed by maternal infections (17.1%) and pregnancy induced hypertension (17.1%), PROM (14.5%), Previous preterm delivery (13.2%).

A study at West Indies, Jamaica[15] shows pre-eclampsia 40%, previous pregnancy losses 36%, previous preterm delivery 17%, antepartum haemorrhage 13% & multiple gestation 4%.

A study at Israel[16] shows multiple birth 35.8%, toxemia 24.5%, abruptio placentae 22%, PROM 18.9%.

In the present study, multiple pregnancies has the highest frequency followed by maternal infections which may be due to higher prevalence of infections still persisting in developing countries and Table 2 shows there is significant association between outcome and multiple pregnancy while maternal infection is not significantly associated with the outcome of ELBW babies.

There were 5 cases of maternal cardiovascular disease, out of which 1 was a case of hypertension with irregularly treated antihypertensive drug and 4 cases of Rheumatic heart disease. There was 1 case of maternal chronic renal disease diagnosed as SLE class III lupus nephritis. But as per Table 2 association between outcome of ELBW babies and maternal cardiovascular or renal disease are not significant.

Maternal co-morbidities are linked with neonatal morbidity and mortality.[17,18] In the present study there is no significant association between outcome of ELBW babies and obstetrical variables like PROM, PIH, APH, Diabetes mellitus, Gestational diabetes mellitus except previous preterm delivery and multiple pregnancy.

In the present study, the logistic regression models showed good internal prediction accuracies. Sepsis, Neonatal jaundice, IVH, Sclerema and Blood transfusion are the complications in ELBW found to independently predicts the outcome of ELBW.

Conclusion

Sepsis, Neonatal Jaundice, IVH, Sclerema and Blood transfusion were independent predictors of mortality among them. Sepsis is an important preventable cause of mortality in ELBW neonates that can be prevented by strict aseptic measures. Even if the study is in a tertiary health care hospital, it is a limited resource setup. No study on long term morbidities like ROP, Neurodevelopmental, Bronchopulmonary dysplasia etc. Hospital based study, results not extrapolated to the general population. This study did not

use a clinical score at baseline for assessing the severity of illness in these neonates.

Author's Contribution

NRM & KHSP done the study design, data analysis and proof reading.

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Self

Competing Interests

None stated

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