

## Original Research Article

# Morbidity and mortality pattern of very low birth weight and extremely low birth weight neonates in a tertiary care hospital

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## ABSTRACT

**Background:** Although the mortality and morbidity rates for Very Low Birth Weight (VLBW) and Extremely Low Birth Weight (ELBW) neonates have improved over last few decades, they still remain highly vulnerable groups. This study determines the neonatal morbidity and mortality within first four weeks of life in VLBW and ELBW neonates.

**Methods:** It was a hospital based prospective study conducted in the department of paediatrics at GB Pant hospital, an associated hospital of Government Medical College Srinagar. All included neonates were evaluated in neonatology section and were followed up to 4 weeks of life. Standard protocols were used for management of these neonates.

**Results:** A total of 116 neonates were included in the study. Among the 116 neonates 82 (70.69%) were VLBW and 34 (29.31%) were ELBW. 28 (34.14%) VLBW and 18 (52.94%) ELBW neonates died. Among the morbidities Respiratory Distress Syndrome was found in 35.37% of VLBW and 70.59% of ELBW neonates, out of which 12.20% VLBW and 20.58% ELBW neonates developed Bronchopulmonary dysplasia. Perinatal asphyxia was found in 20.73% of VLBW and 29.41% of ELBW neonates and Pathological apnea occurred in 28.04% VLBW and 85.29% ELBW neonates. 40.24% VLBW and 73.53% ELBW neonates developed clinically significant jaundice requiring treatment. Clinical sepsis was found in 43.90% VLBW and 67.65% ELBW neonates while as culture proven sepsis was found in 26.83% VLBW and 41.18% ELBW neonates. Intra ventricular haemorrhage was found in 15.85% VLBW and 52.94% ELBW neonates. Necrotizing enterocolitis developed in 18.29% VLBW and 35.29% ELBW neonates. Retinopathy of prematurity was found in 21.95% VLBW and 26.47% ELBW neonates. Patent ductus arteriosus was found in 14.63% VLBW and 32.35% ELBW neonates.

**Conclusions:** Present study has shown Respiratory distress syndrome, perinatal asphyxia and sepsis as the predominant causes of neonatal morbidity and mortality and these are preventable with a proper health care system and policy directed to the primary prevention.

**Keywords:** Extremely low birth weight, Perinatal asphyxia, Respiratory distress syndrome, Very low birth weight

## INTRODUCTION

All very low birth weight (VLBW) and extremely low birth weight (ELBW) neonates form a very special and high risk cohort among the newborns. VLBW neonates are defined by weight between 1000g and 1500 g at birth

and ELBW neonates have weight less than 1000 g at birth.<sup>1</sup> The VLBW or ELBW birth is caused either by a preterm delivery or an Intrauterine growth restriction (IUGR) but mostly it is a premature delivery that leads to it. The birth weight in itself is the single most determinant of survival and subsequent morbidity in newborn humans but it is the prematurity that makes

these groups to have high mortality rates and also suffer a lot of morbidities.<sup>2</sup> An early complication of prematurity is respiratory distress syndrome (RDS) caused by surfactant deficiency. Clinical signs include tachypnea (>60 breaths/min), cyanosis, chest retractions, nasal flaring and grunting. It may lead to air leak syndromes, chronic lung disease or bronchopulmonary dysplasia (BPD) and retinopathy of prematurity (ROP). Surfactant agents are administered as prophylaxis or as rescue intervention for RDS. Prophylactic use in infants younger than 28 weeks gestation has been shown to decrease short term ventilatory needs but no decrease in incidence of chronic lung disease (BPD) has been proven.<sup>3</sup>

The incidence of RDS in preterm infants has been significantly reduced with the use of antenatal steroids that promote lung maturity. The use of antenatal steroids has also been linked to a reduction in the incidence of clinically significant patent ductus arteriosus (PDA) and severe intra ventricular haemorrhage (IVH). In the last decade, surfactant has been widely used to treat RDS and mortality from RDS has been reduced. It is recommended to be administered as prophylaxis in infants younger than 28 weeks gestation as early as possible.<sup>4,5</sup> However, recent meta-analysis have shown that this practice of prophylactic use of surfactant is no more superior to early selective treatment with surfactant as soon as the clinical signs of RDS appear.<sup>6-9</sup>

A major long term morbidity of premature birth is Bronchopulmonary dysplasia which is defined as a need for supplemental oxygen or ventilatory support at 36 weeks post last menstrual period (LMP). This is a clinical sequela of prolonged ventilation as a result of abnormal reparative processes in response to injury and inflammation. Another morbidity is apnea of prematurity (AOP) which is cessation of respiratory activity for more than 20 seconds or a shorter respiratory pause associated with bradycardia or cyanosis in neonates younger than 37 weeks gestation.<sup>10</sup> AOP is secondary to immature respiratory drive in the brain. Treatment of AOP includes nasal continuous positive airway pressure (CPAP) and use of pharmacologic agents, such as theophylline and caffeine.

Perinatal asphyxia is a condition of impaired gas exchange during the perinatal period that may lead to foetal hypoxic ischemic brain injury (HIE). It increases the mortality and also leads to an adverse neurodevelopmental outcome of VLBW and ELBW neonates.

Neonatal sepsis remains an important cause of morbidity and mortality especially in VLBW and ELBW who are less capable of mounting a response to the infection because of inadequate immunity and existing comorbidities. Early onset sepsis that occurs in the first 72 hours of age is usually due to vertical transmission by contaminated amniotic fluid or infected mothers' lower genital tract while as late-onset sepsis that occurs after 72

hours of age is from horizontal transmission from direct contact with care providers or environmental sources.

Necrotizing enterocolitis (NEC) is one of the most common gastrointestinal emergencies in a neonate characterized by ischemic necrosis of the intestinal mucosa which is associated with severe inflammation, invasion of enteric gas forming organisms and dissection of gas into the bowel wall and portal venous system.<sup>11</sup> Incidence of NEC is directly related with decreasing gestational age and it accounts for substantial long term morbidity in survivors of neonatal intensive care particularly in preterm VLBW infants. Breast milk is considered to be the best choice for enteral feeding and has protective effects against NEC.

Most ELBW and VLBW infants develop clinically significant jaundice that requires treatment. Hyperbilirubinemia develops as a result of increased red blood cell (RBC) turnover and destruction in the context of an immature liver that has physiologically impaired conjugation and elimination of bilirubin. In addition most preterm infants have reduced bowel motility which delays elimination of bilirubin-containing meconium.

These infants due to a high body surface area to body weight ratio, less brown fat stores, and nonkeratinized are prone to develop hypothermia. In full-term new born the ductus arteriosus typically closes within 48 hours of birth because of oxygen-induced constriction. However, the PDA in preterm neonates is less responsive to this effect of oxygen and most of infants who are ELBW may have a clinically significant PDA. Another vascular complication is in the brain that begins in the periventricular subependymal germinal matrix bleed that can progress into the ventricular system causing intra ventricular hemorrhage (IVH).

The incidence and severity of IVH are inversely related to gestational age. ELBW infants are at higher risk for IVH because of vulnerability of the germinal matrix and absence of the protective cerebral autoregulation present in older babies. Any event that results in disruption of vascular autoregulation can cause IVH which can include hypoxia, ischemia, rapid fluid changes or pneumothorax. Prognosis is correlated with the grade of IVH.<sup>12</sup>

## METHODS

The study was conducted in the Department of Pediatrics and Neonatology at G.B. Pant hospital, a tertiary care hospital and associated hospital of Government Medical College Srinagar, Kashmir. It was a hospital based prospective study over a period of one year and included all ELBW and VLBW infants admitted to neonatology section of hospital within first 7 days of life. All neonates enrolled were followed for first four weeks of life. For assessment of retinopathy of prematurity and bronchopulmonary dysplasia suspected neonates were followed till 36 weeks of completed gestation. Infants

with gross congenital anomalies or those with clinically defined chromosomal syndromes or those admitted after seven days of life were excluded from the study. Relevant history was noted and examination done.

Examination included weighing the newborns and determination of gestational age which was estimated by obstetric means (LMP and Antenatal USG) and physical assessment by using the new ballard score and there by newborns were labeled as small for gestational age (SGA), appropriate for gestational age (AGA) and large for gestational age (LGA) using the Lubchenco growth charts. All the baseline investigations were done and repeated as and when indicated. After initial stabilization of neonates, those with respiratory distress syndrome were managed with early CPAP and surfactant administration when signs and symptoms of RDS appeared. Those who failed CPAP and those needing surfactant were mechanically ventilated. Blood cultures for growth and sensitivity of bacteria and fungus were sent in suspected cases of septicemia.

Echocardiography was used for identification of hemodynamically significant PDA in symptomatic babies and USG cranium was done to screen for IVH. ROP screening was done at 28 days postnatal age by an ophthalmologist and laser therapy provided when indicated. RDS was diagnosed by clinical findings of tachypnea (RR >60) with grunting, intercostals/subcostal retractions, nasal flaring and cyanosis plus radiological findings consistent with RDS.

Diagnosis of apnea was made when there was cessation of breathing for more than 20seconds or a shorter respiratory pause associated with bradycardia or cyanosis.<sup>10</sup>

Hypoglycemia was taken as blood glucose <45 mg/dl and hypothermia was defined as per WHO as body temperature below the normal range of 36.5°C -37.5°C. Infants diagnosed with symptomatic PDA were confirmed to have at least 3 of these clinical signs of harsh systolic murmur, hyperdynamic precordial impulse, bounding pulse, widening pulse pressure and or worsening respiratory status.<sup>13</sup>

NEC was defined according to the criteria of Bell et al.<sup>14</sup> ROP was classified according to the international classification of retinopathy of prematurity.<sup>15</sup> IVH was graded by Papile's classification.<sup>16</sup> Bronchopulmonary dysplasia was defined as a need for supplementary oxygen or ventilator support at 36 weeks postmenstrual age.<sup>17</sup>

Neonatal hyperbilirubenemia (NNH)/Jaundice was defined and managed as per guidelines of American academy of paediatrics guidelines. Authors considered jaundice significant when it needed phototherapy as per American Academy of Pediatric guidelines or needed blood exchange. Sepsis was diagnosed on basis of

clinical evaluation, total leucocyte counts (TLC), blood culture and CRP. Probable sepsis as positive septic screen i.e. two out of five parameters (TLC <5000/mm<sup>3</sup> or >15000/mm<sup>3</sup>, I/T immature to total polymorph ratio of >0.2, absolute neutrophil count <1500/mm<sup>3</sup>, positive CRP and platelet count <1 lakh/mm). Proven sepsis was defined as isolation of pathogen from blood, CSF or urine. CSF examination was also done in cases of suspected sepsis/proven sepsis. Perinatal asphyxia was defined as per American Academy of Pediatrics (AAP) and American College of Obstetrics and Gynecology (ACOG).

The initiation of mechanical ventilation was based on clinical condition of the infant and evaluation of blood gases and all other neonatal complications if identified were managed as per standard protocols.

### Statistical analysis

Statistical analysis was performed by using SPSS 20 (IBM) and results drawn as under.

## RESULTS

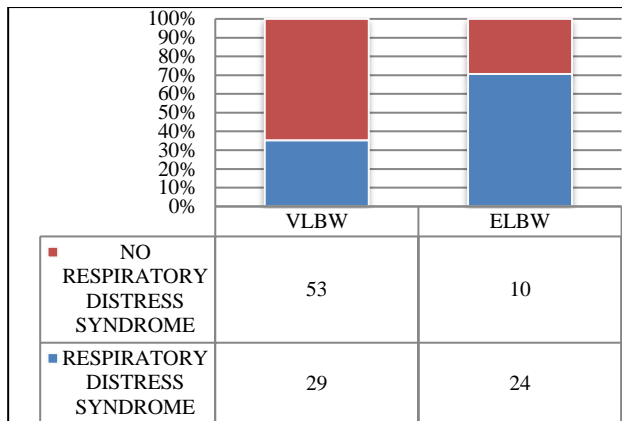
A total of 116 neonates were included out of which 82 were VLBW and 34 ELBW neonate. Respiratory distress was present in 45.69% of 116 total cases. In the VLBW neonates it occurred in 35.36% while in ELBW group it was present in 70.58% cases (Figure 1).

Broncho Pulmonary Dysplasia developed in 14.63% VLBW neonates and 20.58% of ELBW's (Figure 2).

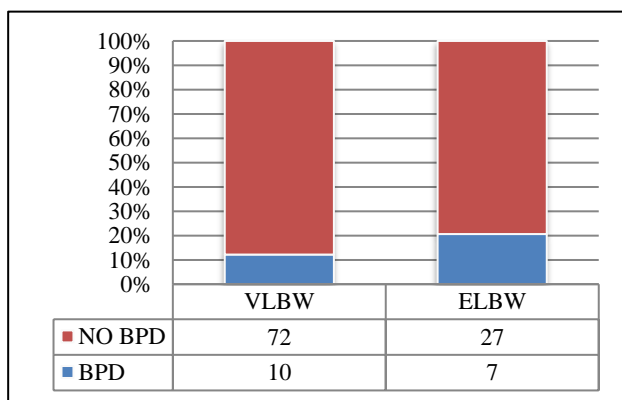
**Table 1: Base line variables.**

Variable	VLBW (n=82)	ELBW (n=34)
Birth weight (Kg)	1.270	0.780
Mean (SD)	±0.220	±0.210
Gestational age weeks mean (SD)	30.2±3.4	27.7±2.9
Males N (%)	36 (43.90)	16 (47.06)
Weight for gestation n (%)	AGA	61 (74.39)
	SGA	17 (20.73)
	LGA	4 (4.88)
Mode of delivery	Vaginal n (%)	24 (70.59)
	Caesarean n (%)	9 (26.47)
Maternal infections n (%)	18 (21.95)	1 (2.94)
Antenatal steroids received n (%)	64 (78.05)	29 (85.29)
	18 (21.95)	5 (14.71)
	42 (51.22)	15 (44.12)

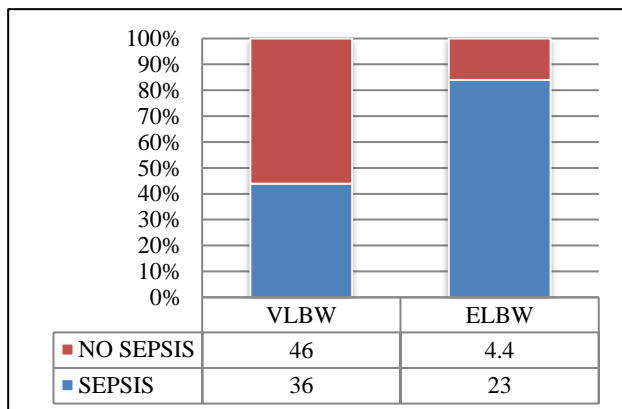
n-number of cases, %-percentage



**Figure 1: Percentage of neonates having respiratory distress syndrome.**



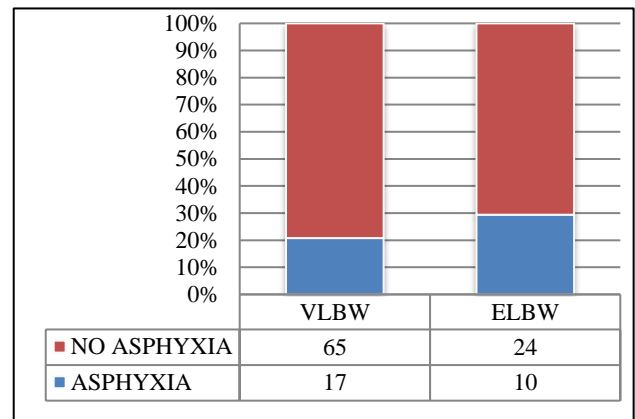
**Figure 2: Percentage of neonates having Broncho pulmonary dysplasia.**



**Figure 3: Percentage of neonates having neonatal sepsis.**

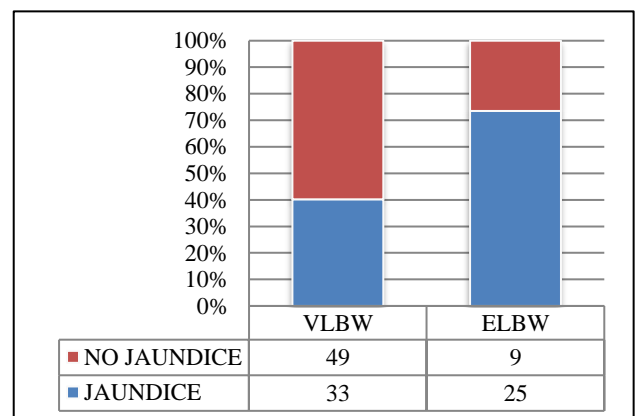
About half of present study group had neonatal sepsis (mostly late onset), 43.9% of VLBW neonates and 67.7% of ELBW neonates got sepsis (Figure 3). Culture proven sepsis was found in only 26.83% VLBW and 41.2% ELBW neonates. The most common organisms isolated were *Klebsiella* (sensitive to amikacin and meropenem), *Staphylococcus aureus* (sensitive to ampicillin and

vancomycin) and *Escherichia coli* (sensitive to amikacin and imipenem).

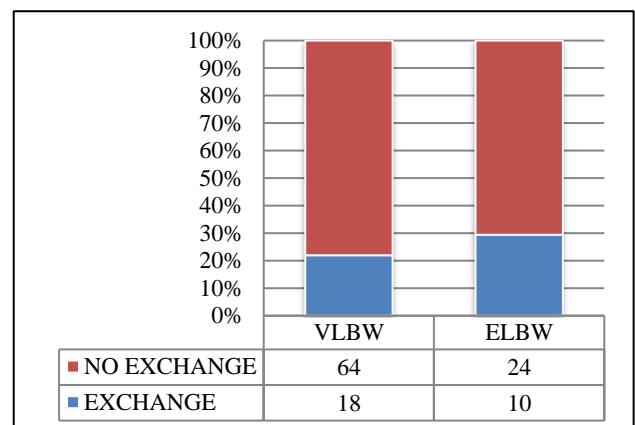


**Figure 4: Percentage of neonates having perinatal asphyxia.**

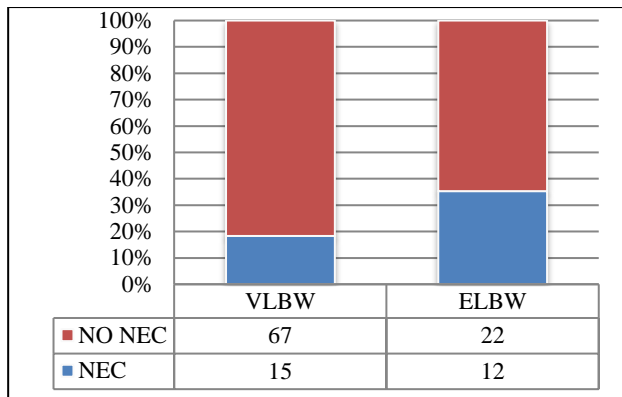
Clinically significant Jaundice requiring phototherapy or blood exchange was found in 40.2% VLBW neonates and 73.53% ELBW neonates out of which 21.9% VLBW and 29.4% ELBW neonates required exchange transfusion (Figure 5 and 6).



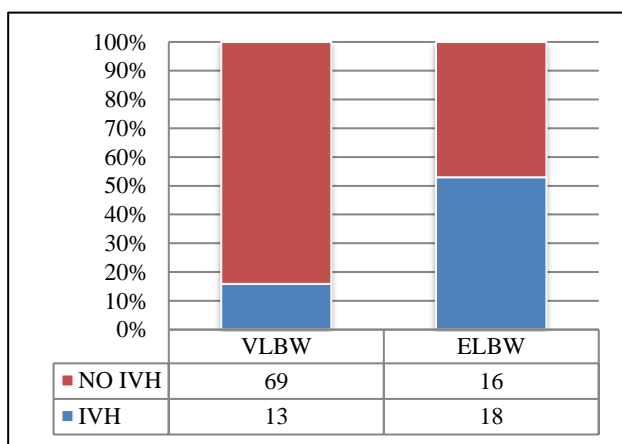
**Figure 5: Percentage of neonates having jaundice.**



**Figure 6: Percentage of neonates requiring DVET for jaundice.**

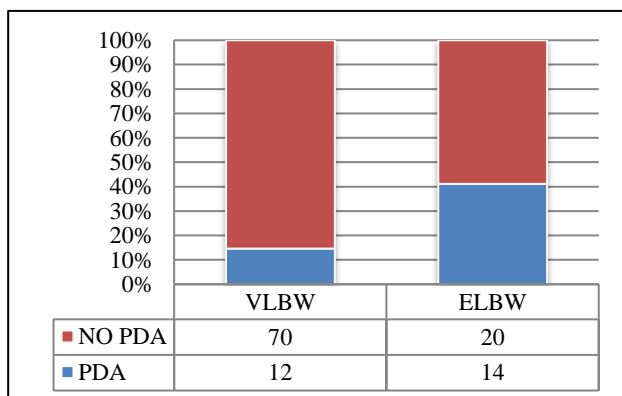


**Figure 7: Percentage of neonates having necrotizing enterocolitis.**

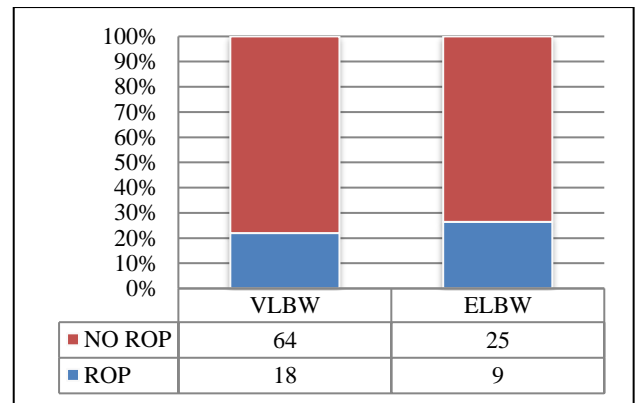


**Figure 8: Percentage of neonates having Intraventricular hemorrhage.**

NEC was found in 18.29% VLBW neonates and 35.3% ELBW neonates while as NEC stage II or higher was found in 7.32% VLBW and 17.64% ELBW neonates (Figure 7). Intra ventricular hemmorrhage was seen in 15.85% VLBW and 52.94% ELBW neonates but an IVH of grade II or higher was found only in 6.1% VLBW and 29.4% ELBWL neonates (Figure 8).



**Figure 9: Percentage of patent ductus arteriosus in neonates.**

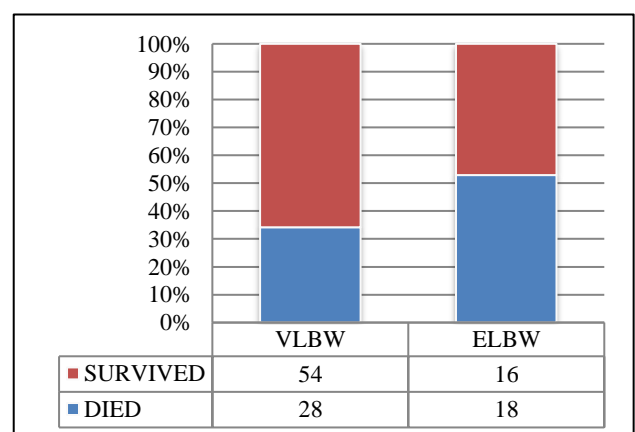


**Figure 10: Percentage of retinopathy of prematurity in neonates.**

Present study found PDA present in 14.63% VLBW and 41.17% ELBW neonates and ROP in 21.95% of VLBW and 26.47% of the ELBW neonates (Figure 9 and 10).

Significant apneas occurred in 28.04% of VLBW neonates and 85.29% ELBW neonates. Hypoglycemia episodes occurred in 19.5% VLBW and 41.2% ELBW neonates and overall hypoglycemia occurred in 25.9% of all the cases. Overall, 48.3% Of our study population was found to be in hypothermia at admission as per WHO criterion, composing of 36.6% VLBW and 76.5% ELBW neonates. In current study 28 VLBW neonates died out of 82 VLBWs i.e. 34.14% mortality during the neonatal period, thus making the survival rate equal to 65.86%.

Among the 34 ELBW neonates 18 (52.94%) did not survive the neonatal period thus having a survival rate of 47.06%. None of the neonates below 650 grams of birth weight survived during present study period and overall mortality rate was 39.65 % in the whole study group (Figure 11).



**Figure 11: Percentage of mortality in neonates.**

## DISCUSSION

It was a prospective study conducted in department of pediatrics and neonatology at GB pant hospital Srinagar



over a period of 1 year. The purpose of the study was to determine the morbidities and mortality suffered by VLBW and ELBW neonates during their neonatal period. The outcome of both ELBW and VLBW babies depends on many factors like optimized neonatal care, better knowledge of the pathophysiology of the premature infant, advent of exogenous surfactant therapy and neonatal intensive care unit to handle sick infants. In this study we found that the survival rates of both VLBW and ELBW infants in our neonatal intensive care unit (NICU) is low although comparable with other tertiary care hospitals of our country. These infants suffer a lot of morbidities and go through a very hard phase during the neonatal period due to the immaturity of the organs and inability to cope up with the outside hostile environment. All the neonatal setups in our state do not have a NICU, (level III center) and most of the health centers especially in the rural areas do not have a proper neonatal facility and most health care providing centers are far away from the level III centres. In case of a preterm delivery resulting in a VLBW or ELBW newborn, a referral to higher centre is needed. This referral after birth deprives these neonates of the immediate health care and hence makes these neonates at high risk for development of most of the morbidities. The transportation service also makes these neonates vulnerable to morbidities like hypothermia and hypoglycemia and this also worsens the final outcome. As the Prognosis depends not only on birth weight and gestational age but also on other perinatal factors and specialised intensive care in the first hours of life, these neonates have a bad outcome.

In this study the causes of morbidity were studied separately in VLBW and ELBW neonates. RDS was found in 53 out of 116 cases (45.69%). RDS was more common in the ELBW group and RDS is found to be inversely proportional to the birth weight of the baby. Neonates who received antenatal steroids were found to have less respiratory morbidities. Similar results were found by Mukhopadhyay et al, and Fanaroff AA, et al.<sup>18,19</sup> Neonatal sepsis was found in 43.9% of VLBW neonates and 67.7% of ELBW neonates. Culture proven sepsis was found in only 26.83% VLBW and 41.2% ELBW neonates. The most common organisms isolated were *Klebsiella* (sensitive to amikacin and meropenem), *Staphylococcus aureus* (sensitive to ampicillin and vancomycin) and *Escherichia coli* (sensitive to amikacin and imipenem). VLBW babies developed more sepsis than other neonates since their immune system and skin barrier are immature and they are also exposed to many invasive diagnostic and therapeutic procedures. Majority of the sepsis was hospital acquired as most of the neonates had late onset sepsis and did not have any feature of sepsis at the admission. Apneas occurred in 23 (28.04%) of VLBW and 29 (85.29%) ELBW neonates. As is evident apneas occur in significantly higher rates in ELBW neonates. Significant jaundice was found in 33 (40.2%) VLBW neonates and 25 (73.53%) ELBW neonates, out of which 18 (21.9%) VLBW neonates

required exchange transfusion while 10 (29.4%) ELBW required exchange.

Jaundice is much more common in these neonates as a result of increased red blood cell (RBC) turnover and destruction and in the context of an immature liver that has physiologically impaired conjugation and elimination of bilirubin. NEC was diagnosed in 15 (18.29%) VLBW neonates and in 12 (35.3%) ELBW neonates while as NEC stage II or higher was found in 6 (7.32%) VLBW and 7 (17.64%) ELBW neonates. Overall NEC II was found in 13 (11.20%) of the study population. IVH was found in 13 (15.85%) VLBW neonates and 18 (52.94%) ELBW neonates. As is evident IVH occurs at a significantly high rates in ELBW neonates. An IVH of grade II was found in 5(6.1%) VLBW and 10 (29.4%) ELBW neonates. PDA was found in 12(14.63%) VLBW neonates and 14 (41.17%) ELBW neonates and ROP occurred in 18 (21.95%) of VLBW neonates and 9 (26.47%) of the ELBW neonates. In present study hypoglycaemia was documented in 16 (19.5%) VLBW neonates and 14 (41.2%) ELBW neonates. Overall hypoglycemia occurred in 25.9% of the study population. Hypoglycemia occurred more in ELBW neonates who actually have poor reserve of carbohydrates and are mostly dependent on intravenous dextrose rather than enteral feeds as it is difficult to establish proper enteral feeds in these neonates. Hypothermia was a major finding in present study group as we found 30 (36.6%) VLBW neonates and 26(76.5%) ELBW neonates to be hypothermic at admission and was due to improper transportation means.

In present study 28 out of 82 VLBW neonates died (34.14%) during the neonatal period making the survival rate equal to 65.86%. Among the 34 ELBW neonates 18 (52.94%) did not survive the neonatal period thus having a survival rate of 47.06%. None of the neonates below 650 grams of birth weight survived during our study period.

## CONCLUSION

ELBW and VLBW neonates have a major contribution to mortality in our NICU and while most of the deaths in this group occur within the first week of life, the most at risk are the ELBW neonates and the major causes include sepsis, RDS, IVH and perinatal asphyxia. Appropriate referral of high risk pregnancy and delivery in centers with good neonatal facility should be encouraged. Authors postulate that in order to improve the survival and decrease morbidity all high risk pregnancies should be delivered at centers where neonatal ICU facility is available.

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