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Outcomes of Very Low Birth Weight Infants (<1.5 kg) and Preterm Infants (Gestational Age=32 Weeks) at tertiary care hospital in western Gujarat

[1]Harshkumar Bariya, [2]Dimple Vishnubhai Patel, [3]Ashvin Ishvarbhai Dave and [4]Chandan Narwani

[1,3]Department of Paediatrics, Shantaba Medical College and Hospital, Amreli, Gujarat, India

[2,4]Department of Pediatrics, Government Medical College, and Sir T. General Hospital, Bhavnagar, Gujarat, India

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Corresponding Author
Chandan Narwani,
Department of Pediatrics, Government Medical College, and Sir T. General Hospital, Bhavnagar, Gujarat, India
chandannarwani8@gmail.com

Author Designation
[1,2,3]Senior Resident
[4]Assistant professor

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Abstract
Very low birth weight (VLBW) infants, constituting approximately 4-8% of live births, account for a significant proportion of neonatal mortality. Both birth weight (BW) and gestational age (GA) are critical in determining neonatal outcomes, with lower values correlating with higher morbidity and mortality rates. This study investigates the mortality and morbidity rates among VLBW infants or those born at =32 weeks of gestation in the NICU, while exploring associated maternal risk factors. This prospective observational cohort study was conducted from January 1, 2017, to December 31, 2017. Data were collected on maternal demographics, antenatal care, mode of delivery, infant characteristics, and clinical outcomes including respiratory support, surfactant therapy and complications such as chronic lung disease (CLD), retinopathy of prematurity (ROP), necrotizing enterocolitis (NEC), and intraventricular hemorrhage (IVH). Definitions for clinical conditions were based on established criteria. The study included 307 VLBW infants or those born at =32 weeks. The overall mortality rate was 16%, with survival rates varying by GA: 68.1% for =28 weeks, 90.8% for 29-32 weeks, and 94.7% for >32 weeks. The incidence of bronchopulmonary dysplasia (BPD) was 9.1%, significantly lower than reported in other studies, which may be attributed to improved NICU practices. The incidence of patent ductus arteriosus (PDA) was 30.2% and retinopathy of prematurity (ROP) requiring treatment was 16.2%. Necrotizing enterocolitis (NEC) was observed in 4.2% of the infants and the incidence of germinal matrix hemorrhage/intraventricular hemorrhage (GMH/IVH) was 15.6%. The average length of NICU stay was 34.8 days. The survival rate of VLBW infants improved with increasing birth weight and gender was not a significant mortality risk factor. The study highlights the impact of enhanced NICU practices on reducing BPD and NEC rates. These findings underscore the importance of continued advancements in neonatal care to improve outcomes for VLBW infants.

INTRODUCTION

Infants with very low birth weight (VLBW) constitute approximately 4-8% of live births., however, they account for roughly one-third of neonatal period deaths[1,2]. Birth weight (BW) and gestational age (GA) are critical determinants in predicting both the short-term and long-term quality of life of neonates. Neonates with low BW and GA exhibit a higher incidence of morbidity and mortality during the neonatal period. Furthermore, premature births are correlated with an elevated risk of mortality and morbidity[2-5].

Infants with very low birth weight (VLBW <1500 g) or those born at=32 weeks gestation represent a distinctive patient population within the neonatal intensive care unit (NICU). These VLBW infants, particularly those weighing less than 1000 g (extremely low birth weight [ELBW]), exhibit profound physiological immaturity. This immaturity renders them exceedingly sensitive to minor variations in respiratory management, blood pressure regulation, fluid administration, nutrition and virtually every other aspect of medical care.

The underdeveloped biological and physiological systems of these premature infants frequently result in a range of pathologies. These include respiratory distress syndrome (RDS), symptomatic patent ductus arteriosus (PDA), necrotizing enterocolitis (NEC), retinopathy of prematurity (ROP), intraventricular hemorrhage (IVH), periventricular leukomalacia (PVL), and bronchopulmonary dysplasia (BPD). Each of these conditions significantly impacts the prognosis of VLBW infants. In addition to these immediate health concerns, VLBW infants are also at a heightened risk for adverse neurodevelopmental outcomes. The combination of their physiological vulnerability and the complex medical challenges they face necessitates meticulous and specialized care to optimize both their short-term survival and long-term development[5-11].

The advancement of technology in NICU facilities, the availability of experienced and specialized NICU staff, the application of appropriate neonatal mechanical ventilation modes, surfactant therapy, and the introduction of antenatal and postnatal corticosteroid treatments have collectively increased the survival rates of neonates born with a birth weight of <1500 g to up to 95%. However, these elevated survival rates have been accompanied by an increase in morbidity rates[11].

In this study, we aimed to determine the mortality and morbidity rates of VLBW infants or those born at =32 weeks gestation admitted to an NICU. Additionally, we explored the associated maternal risk factors.

MATERIALS AND METHODS

This study was designed as a prospective observational cohort study. The data collection period spanned from January 1, 2017-December 31, 2017. The following data were acquired prospectively from the medical case forms of the infants: gender, gestational age (GA), birth weight (BW), antenatal steroid therapy, need for active delivery room resuscitation, clinical diagnoses (such as respiratory distress syndrome [RDS] and sepsis), ventilatory support (including durations of mechanical ventilation, nasal continuous positive airway pressure [CPAP], heated humidified high-flow nasal cannula [HHHFNC] and free oxygen support), surfactant therapy, morbidities (including symptomatic patent ductus arteriosus [PDA], necrotizing enterocolitis [NEC], intraventricular hemorrhage [IVH], periventricular leukomalacia [PVL], bronchopulmonary dysplasia [BPD] and retinopathy of prematurity [ROP]), duration of hospital stay, discharge status and maternal demographic and clinical information (such as the mother's age, pregnancy records and presence of any obstetrical disease).

The study focused on gathering observational baseline data on both mothers and infants, including the therapies used and the outcomes of the infants. The information collected was generic and not specific to any disease or treatment. The data encompassed various aspects such as:

- **Mother's health:** Pregnancy history, complications and presence of any obstetrical disease.
- **Labor and delivery:** Rupture of the membranes, administration of steroids and antibiotics and mode of delivery.
- **Infant's health:** Gestational age, birth weight, need for delivery room resuscitation and types of respiratory support.
- **Infant's medical outcomes:** Status of the heart, lungs, nervous system, gastrointestinal system, vision, incidence of infections, mortality and number of days hospitalized.

The data collected were used to examine associations between baseline characteristics, treatments, and outcomes, track trends in disease incidence and therapy effectiveness and identify questions requiring further in-depth research.

Eligibility Criteria:

- Ages Eligible for Study: Any age
- Genders Eligible for Study: Both

Inclusion Criteria:

- Birth weight of less than 1500 grams, or
- Gestational age of 32 weeks or less

Study Protocol and Definitions[12-19]:
Gestational Age (GA): Gestational age was determined

based on the last menstrual period and/or earlier obstetrical ultrasound and was subsequently confirmed by neonatologists using the New Ballard Score.

Chronic Lung Disease (CLD): CLD was defined by the need for supplemental oxygen at 36 weeks postmenstrual age.

Retinopathy of Prematurity (ROP): Diagnosis of ROP was established through fundoscopic examination, and the condition was classified according to the International Classification of Retinopathy. All examinations were conducted by two trained ophthalmologists.

Necrotizing Enterocolitis (NEC): NEC diagnosis followed the modified Bell classification system and was based on clinical presentation, radiographic findings, and laboratory results.

Periventricular Leukomalacia (PVL): PVL, characterized by necrosis of white matter, was diagnosed using cranial ultrasonography. PVL was categorized into four grades based on the persistence and progression of periventricular echodensities: Grade 1, transient echodensities persisting for=7 days., Grade 2, echodensities evolving into small, localized fronto-parietal cysts., Grade 3, extensive periventricular cystic lesions and Grade 4, extensive cystic lesions extending into deep white matter. Diagnosis was confirmed by cranial magnetic resonance imaging if necessary.

Patent Ductus Arteriosus (PDA): Significant PDA, defined as a ductus arteriosus measuring more than 1.5 mm, was diagnosed via echocardiographic examination conducted by a cardiologist within the first 48 hours of life.

Germinal Matrix Hemorrhage (GMH)/Intraventricular Hemorrhage (IVH): GMH/IVH was classified according to the Papile staging system. Cranial ultrasound was performed on days 5-7, days 21-28 and at term corrected age. In some cases, additional imaging such as CT or MRI of the brain was conducted as needed. Classification included: Grade I, subependymal germinal matrix hemorrhage; Grade II, subependymal and intraventricular hemorrhage without ventricular dilatation., Grade III, subependymal and intraventricular hemorrhage with ventricular dilatation and Grade IV, periventricular hemorrhagic infarction (PVHI).

RESULTS AND DISCUSSIONS

A total of 307 very low birth weight (VLBW) infants or those born at=32 weeks' gestation were admitted to the NICU during the study period.

Perinatal Risks:

- **Mother's Age:** The mean age of the mothers was 28.5 years, with a range from 19 to 59 years.
- **Maternal Hypertension/Preeclampsia:** A history of maternal hypertension was reported in 35.8% (n=110/307) of the cases.
- **Gestational Diabetes Mellitus:** Gestational diabetes mellitus was reported in 4.5% (n=14/307) of the mothers.
- **Chorioamnionitis:** Chorioamnionitis was reported in 0.9% (n=3/307) of the cases.
- **Antenatal Steroids:** A total of 75.5% (n=232/307) of the mothers had received antenatal steroids prior to delivery.
- **Mode of Delivery:** Delivery by caesarean section occurred in 80.7% (n=248/307) of the cases, while vaginal deliveries accounted for 19.3% (n=59/307).
- **Multiple Births:** Among the VLBW or =32 weeks infants, 39.7% (n=122/307) were from multiple births.

Infant Characteristics:

- **Gender:** More males (56.1%, n=172/307) than females (43.9%, n=135/307) were admitted to the NICU.
- **Gestational Age:** The mean gestational age (GA) of the infants at admission was 30+1 weeks, with a range from 21+5 weeks to 39+4 weeks.
- **Birth Weight:** The mean birth weight at admission was 1198.40 g, with a range from 450 g-2430 g.

Survival to Discharge, DAMA, or Transfer from NICU:

- **Overall Mortality:** The mortality rate among VLBW infants was 16% (n=48/307).
- Survival Rates by Gestational Age: The survival rates were 68.1% for infants =28 weeks, 90.8% for those 29-32 weeks, and 94.7% for those >32 weeks.
- **Gender and Mortality:** There was no significant difference in mortality rates between male and female infants.
- **Extremely Preterm Infants (GA 21-24 weeks):** Infants born at 21-24 weeks exhibited a 100% mortality rate.
- **Very Preterm Infants (GA 25-28 weeks):** Survival rates varied significantly within this group, with a notable increase in survival as gestational age increased. At 25 weeks, the survival rate was 42%, while by 28 weeks, it rose to 97%.
- **Moderately Preterm Infants (GA 29-32 weeks):** This group displayed relatively high survival rates, with a gradual improvement from 84% at 29 weeks to 90% at 32 weeks.
- **Infants >32 weeks but <1.5 kg:** Despite their low birth weight, this group had a high survival rate of 95%.

Table 1. Mortality and survival analysis of Infants according to Gestational age

GA [Weeks]	Total	Death	Survival [%]	Mortality [%]
21	1	1	0	100
22	3	3	0	100
23	2	2	0	100
24	8	8	0	100
25	12	7	42	58
26	14	2	86	14
27	23	6	74	26
28	31	1	97	3
29	31	5	84	16
30	54	6	89	11
31	51	1	98	2
32	39	4	90	10
>32 wks but <1.5kg	38	2	95	5
Grand Total	307	48	84 %	16 %

Overall, the table indicates a direct correlation between higher gestational age and improved survival rates and lower gestational age and high mortality rate with an overall mortality rate of 16% across the entire cohort of 307 infants.

Recent advancements in perinatal and neonatal care over the past two decades have led to increasing survival rates for very preterm and very low birth weight (VLBW) infants. Minguez-Milio *et al.* reported that the mode of delivery did not affect survival; however, cesarean section (LSCS) was associated with lower morbidity and a better prognosis for neurodevelopmental outcomes in extremely low birth weight (ELBW) infants. Jakuskiene *et al.* also demonstrated that delivery via LSCS increased survival rates. In our study, the overall LSCS rate was 80.4% (n=247/307)[20].

Improvements in current obstetrical care have significantly contributed to better neonatal outcomes, with a greater number of infants receiving antenatal corticosteroids and fewer requiring resuscitation at birth. Warner *et al.* reported an antenatal steroid therapy rate of 53% in infants with a birth weight of 400 g-1500 g. In our study, the rate of antenatal steroid therapy was 75.2% (n=231/307)[22].

The incidence of bronchopulmonary dysplasia (BPD) among infants weighing less than 1500 g was reported by the American Academy of Pediatrics to be 23%. Zhang *et al.* reported an incidence of 48.3% in infants with a birth weight of =1500 g[9]. In our study, the incidence of BPD was 9.1%. This lower incidence may be attributed to NICU practices such as appropriate respiratory support with gentle ventilation, early weaning to nasal CPAP, careful oxygen administration, optimal fluid and nutrition management and stringent infection control measures.

In developed countries, the incidence of patent ductus arteriosus (PDA) is known to be around 30%. Jakuskiene[20] found a PDA incidence of 22% for infants with a gestational age (GA) of 22-27 weeks and 19% for those with a GA of 28-32 weeks. In our study, the PDA incidence was 30.2%, which was higher than in other studies. This higher incidence may be due to our practice of diagnosing PDA by echocardiography within the first 48 hours of life.

Regarding retinopathy of prematurity (ROP), Jakuskiene[20] reported that 9% of infants with a GA between 22 and 27 weeks and 2% of infants with a GA between 28 and 32 weeks required treatment such as laser or cryocoagulation. In our study, 16.2% (n=41/253) of infants required treatment for ROP.

The incidence of necrotizing enterocolitis (NEC) in VLBW infants was reported by Cole *et al.* to be 10%, while Wilson et al. reported the highest NEC incidence to be 42% in infants with a birth weight of <1000 g[25]. In our study, the NEC incidence was 4.2%. The use of early minimal enteral nutrition with human milk appears to be a contributing factor to this low incidence of NEC.

The incidence of germinal matrix hemorrhage/intraventricular hemorrhage (GMH/IVH) is known to be around 30% in developed countries. Jakuskiene[20] reported an IVH incidence rate of 39.1%. In our study, the GMH/IVH incidence was 15.6%.

Periventricular leukomalacia (PVL) is most common in infants with a GA between 26 and 29 weeks, peaking at 27 weeks. Jakuskiene[20] found a PVL incidence of 13% in infants with a GA of 22-27 weeks and 6% in those with a GA of 28-32 weeks. In our study, the PVL incidence was 4.2%.

In the literature, the length of hospital stay is reported to be 97 days for infants with a birth weight of less than 1000 g and 59 days for those with a birth weight of 1000 g to 1500 g. In our study, the average hospital stay was 34.8 days for infants with a birth weight of <1500 grams or a gestational age of=32 weeks.

CONCLUSION

Our study observed that the survival rate of very low birth weight (VLBW) infants improved with increasing birth weight. Gender did not emerge as a significant risk factor for mortality in this population. The decreased incidence of bronchopulmonary dysplasia (BPD) observed may be attributed to the implementation of appropriate respiratory support with gentle ventilation, early weaning to nasal continuous positive airway pressure (CPAP), a policy of safe oxygen administration, as well as optimal fluid and nutritional management and stringent infection control measures.

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