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Mortality and Outcomes of Very Low Birth Weight Infants in Faculty of Medicine Navamindradhiraj University

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ABSTRACT

OBJECTIVE: To determine the mortality and morbidity rate of very low birth weight infants (VLBW) who were admitted to the neonatal care unit of Faculty of Medicine Vajira Hospital, Navamindradhiraj University.

METHODS: A retrospective review of statistical data from the medical record of VLBW infants who were admitted between January 1, 2014 to December 31, 2020 (7 years). The statistical data include data collected until infants were discharged from hospital.

RESULTS: A total of 217 VLBW infants were analyzed. The mortality rate among VLBW infants during the 7-year study is 12%. The infant's mortality rates of birth weight (BW) 1,000-1,499 g and 500-999 g were 5% and 25%, respectively. The mean gestational age was 29.4 ± 2.7 weeks, the mean BW was 1079.8 ± 255.9 g . The common morbidities were respiratory distress syndrome (65%), bronchopulmonary dysplasia (34.1%), hemodynamic significant patent ductus arteriosus (41%) and culture positive late onset sepsis (35.9%). On the 28th day after birth, the survival rate of birth weight 1,000-1,499 g was 95.7% and significantly higher than birth weight 500-999 g extremely low birth weight (ELBW) (80.3%). In addition, when comparing BW in two groups, it was found that the mortality and morbidity rate were higher in ELBW group with statistically significant (p-value < 0.001). The trend of mortality rate for VLBW infants were 23.3%, 20.7% and 18.2% in 2015-2017. However, the mortality rate was decreased to 7.9%, 3% and 7.3% in 2018-2020.

CONCLUSION: The mortality and morbidity rates are significantly correlated to BW. The mortality and morbidity rate of VLBW infants tend to decrease each year.

KEYWORDS: morbidity rate, mortality rate, survival rate, very low birth weight infants

INTRODUCTION

In Southeast Asia, preterm neonatal morbidity accounts for 37% of the mortality of newborn[1] and is considered the most critical cause. In Thailand, first nationwide study showed the incidence of extremely low birth weight (ELBW) infants was 1.8 per 1,000 live births and mortality rate was 36.9% in hospital[2]. The risk factors contributing to the preterm labor and morbidity include teenage pregnancy, maternal under and overweight, long and short gestational intervals, chronic diseases, maternal infectious diseases, depression conditions, maternal smoking, etc[3].

The preterm infants account for 10% of all live newborns at Faculty of Medicine Navamindradhiraj University from data record in neonatal unit. The rates of mortality and morbidity are inversely proportional to the gestational age (GA) and birth weight (BW) of the preterm infants. Some preterm infants who survived have high risk of delayed growth development, chronic illness, and other long-term health issues[3-4].

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Nowadays, treatment modality and strategies include administration of prenatal corticosteroids, surfactants, use of non-invasive ventilator, and gentle ventilator techniques administration can reduce morbidity conditions such as necrotizing enterocolitis (NEC), nosocomial infection, severe intraventricular hemorrhage (IVH), retinopathy of prematurity (ROP), bronchopulmonary dysplasia (BPD), and hemodynamic significant patent ductus arteriosus (hsPDA). Despite these treatments, post-discharge complications such as chronic lung disease in infants can still be found . It is important that the health monitoring system for preterm infants after discharge from hospital is implemented to develop more comprehensive and holistic care measures and methods[3-5].

The health incidences related to preterm, very low birth weight infants (VLBW), remain alarmingly high. In addition to maternal physical condition, other factors such as family/living environment, socio-economic status, and community health conditions can contribute to these health incidences [5]. Therefore, a holistic research program that links various facets of preterm infant causes, preventions, and medical care together is warranted. Faculty of Medicine Vajira Hospital, Navamindradhiraj University is actively working towards being the center of excellence for preterm newborn health care. The study regarding mortality and morbidity rates of VLBW infants preterm is important to improve and develop health care strategies and quality of neonatal care. This study aims determine and analyze mortality rate, morbidity rate, and their related factors of VLBW infants at Vajira Hospital.

METHODS

This is a retrospective cohort study. The data were collected from the neonatal patients diagnosed as VLBW infant who were born in Vajira Hospital or were transferred from other hospitals and admitted into the neonatal unit from January 1, 2014 to December 31, 2020. Preterm patients with genetic abnormalities and major congenital anomalies, periviable infants (GA < 24 weeks or BW < 500 g and VLBW infants who were referred to the other hospitals before discharge were excluded.

Information collected from mothers with live VLBW infants includes age, underlying diseases, pregnancy history, antenatal risk factors including pregnancy induced hypertension (PIH), gestational diabetes mellitus (GDM), risk sepsis (preterm labor, prolonged preterm premature rupture of membrane (PPPROM) and inadequate intrapartum antibiotic prophylaxis), multiple pregnancy and no antenatal care (ANC), treatment received before delivery and methods of delivery , number of referral and number of birth before arrival (BBA). Information collected from VLBW infants includes gender, birth weight (categorized as small for gestational age (SGA) and appropriate for gestational age (AGA), gestational age determined by obstetric measures (eg, last menstrual period and ultrasonography) or by clinical assessment using Ballard score system, APGAR score, morbidities IVH as defined in Papile GM/IVH classification, which grade3/4 IVH was considered severe grade, periventricular leukomalacia (PVL), RDS, culture positive-late onset sepsis (LOS), central line-associated bloodstream infection (CLABSI) as defined in infectious diseases society of America 2020, septicemia/ meningitis, ventilator associated pneumonia (VAP), urinary tract infection (UTI), NEC as defined in Modified Bell's staging criteria for necrotizing enterocolitis, BPD as defined in national of health consensus conference (NIH) criteria, hsPDA which was diagnosed based on both echocardiogram and clinical findings by pediatric cardiologist, ROP as defined in International Classification of ROP, treatments received including surfactant therapy, hsPDA medical treatment and surgical intervention, ROP requiring intervention or surgical treatment/ severe ROP, and NEC medical and surgical treatment, and cause of death.

Statistical analyses for this study were performed using SPSS version 17.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics (n, mean

and standard deviation) were used in summarizing continuous variables. Frequency and percents were used in summarizing categorical variables. Comparisons between birth weight categories, t-test was used in comparisons for continuous variables. Chi-square test or Fisher's exact test was used in comparisons for categorical variables. Kaplan-Meier was used in estimating survival rates and log-rank test was used in comparison the survival curves between the two birth weight categories. When appropriate, logistic regression was used in analyzing binary categorical outcomes by adjusting for key prenatal variables. Unless otherwise indicated, the statistical significance level was 0.05.

The sample size calculation for this study was based on mortality rate of VLBW infants at Chaing Mai University in 2010 and 2015 with alpha level of 0.05 and estimation error of 0.05. The minimum sample size needed to achieve these criteria was 144 people. However, in this particular study, the number of participants was 239, which provides a more robust result. The larger sample size ensures that the results are more representative of the population being studied and reduces the risk of random error in the estimation of the proportion.

This study was approved by internal review board of Faculty of Medicine Vajira Hospital, Navamindradhiraj University. The COA number of this project is 200/64E. All information had been through the research ethics consideration and was used for research purposes only. No personal information is disclosed.

RESULTS

Between January 1, 2014 and December 31, 2020, there were 239 newborns diagnosed as VLBW infants (birth weight lower than 1,500 g) in Vajira Hospital. Of these 239, 22 were excluded due to major organ anomalies (9 cases), chromosome abnormalities (5 cases), periviable birth (1 case), and referral to other hospitals due to medicare (7 cases). The total number of VLBW infants admitted into Vajira's neonatal unit had increased over this study period. The ELBW (birth weight 500-999 g) infants represented a significant portion, with high records up to 42.4% (14 cases) in 2017 and 39.5% (15 cases) in 2018. In 2020, the incidence of BW 1,000–1,499 g was of the highest (28 cases) during these 7 years (figure 1). There are two categories of preterm infants, ELBW infants (500–999 g) and birth weight 1,000–1,499 g. The maternal ages of ELBW (28.7 ± 7.4 years) was not significantly different. There was no significant difference in terms of maternal risk complications and mode of delivery between two groups, however maternal of ELBW infants received completed prenatal dexamethasone lower than other group with statistically significant. Risk sepsis was the most common complication of preterm delivery. (table 1)

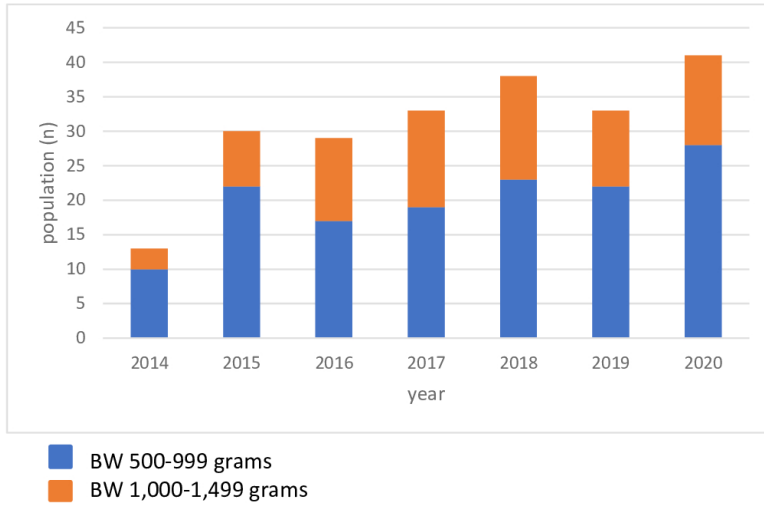

Figure 1 Total numbers of VLBW infants at Vajira Hospital

Table 1 Maternal characteristics (2014-2020; N = 217)

Characteristics	Total (N = 217)	Birth Weight (g)		P-value
		500-999 (N = 76)	1,000-1,499 (N = 141)	
Maternal age (years)	27.9 ± 7.2	28.7 ± 7.4	27.6 ± 7.1	0.267
Normal (21-34 years)	132 (60.8)	43 (56.6)	89 (63.1)	0.370
Teenage (≤ 20 years)	42 (19.4)	14 (18.4)	28 (19.9)	
Elderly (≥ 35 years)	43 (19.8)	19 (25.0)	24 (17.0)	
Maternal complication	135 (62.2)	41 (53.9)	94 (66.7)	0.065
Risk sepsis	165 (76.0)	60 (78.9)	105 (74.5)	0.461
PIH	61 (28.1)	16 (21.1)	45 (31.9)	0.090
GDM	12 (5.5)	4 (5.3)	8 (5.7)	1.000
Multiple pregnancy	33 (15.2)	10 (13.2)	23 (16.3)	0.537
No ANC	7 (3.2)	3 (3.9)	4 (2.8)	0.698
Dexamethasone	190 (87.6)	68 (89.5)	122 (86.5)	0.530
Complete course	87 (40.1)	20 (26.3)	67 (47.5)	0.002
Refer	40 (18.4)	16 (21.1)	24 (17.0)	0.465
BBA	10 (4.6)	4 (5.3)	6 (4.3)	0.743
Mode of delivery				
Cesarean section	127 (58.5)	37 (48.7)	90 (63.8)	0.031
Normal delivery	90 (41.5)	39 (51.3)	51 (36.2)	

Abbreviations: ANC, antenatal care; BBA, birth before arrival; g,gram; GDM, gestational diabetes mellitus; N, number; PIH, pregnancy-induced hypertension; PROM, premature rupture of membranes
Data are presented as number (%), mean ± standard deviation or median (interquartile range).
P-value corresponds to [t]Independent Samples T-Test, [m]Mann-Whitney U Test, [c]Chi-Square Test or [f]Fisher's Exact Test.

The survival rate in first 28 days of life of infants in BW 1,000-1,499 g group was significantly higher than ELBW infants as shown in figure 2. The GA means of BW 500-999 g (ELBW) and BW 1,000-1,499 g were 27.3 ± 2.4 weeks and 30.6 ± 2.0 weeks, respectively; however, the majority (61.8%) of ELBW had < 28 weeks while the majority (53.2%) of BW 1,000-1,499 g group had 28-30 weeks of GA (table 2). The infants in both groups were mostly AGA. Resuscitation at birth of ELBW infants had a significantly higher intubation rate than infants of BW 1,000-1,499 g (p-value < 0.001). The rate of birth asphyxia of ELBW infants (52.6%) was significantly higher than that of BW 1,000-1,499 g group (22.7%) (p-value < 0.001). The incidences of severe asphyxia were found in both groups but there was no significant difference.

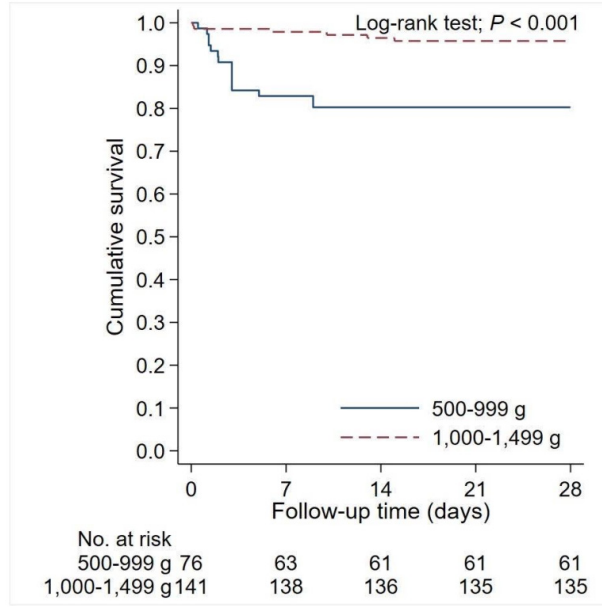

Figure 2 Cumulative survival rate according to BW (P < 0.001)

Table 2 Infant characteristics (2014 - 2020; N = 217)

Characteristics	Total (N = 217)	Birth Weight (g)		P-value
		500-999 (N = 76)	1,000-1,499 (N = 141)	
Gestational age (weeks)	29.4 ± 2.7	27.3 ± 2.4	30.6 ± 2.0	< 0.001
< 27	55 (25.3)	47 (61.8)	8 (5.7)	< 0.001
28-30	100 (46.1)	25 (32.9)	75 (53.2)	
31-32	35 (16.1)	1 (1.3)	34 (24.1)	
> 32	27 (12.4)	3 (3.9)	24 (17.0)	
Type				
AGA	176 (81.1)	61 (80.3)	115 (81.6)	0.817
SGA	40 (18.4)	15 (19.7)	25 (17.7)	
LGA	1 (0.5)	0 (0.0)	1 (0.7)	
Endotracheal intubation	125 (57.6)	69 (90.8)	56 (39.7)	< 0.001
Asphyxia	72 (33.2)	40 (52.6)	32 (22.7)	< 0.001
Severe asphyxia	21 (9.7)	9 (11.8)	12 (8.5)	0.428

Abbreviations: AGA, average for gestational age; g,gram; LGA, large for gestational age; N, number; SGA, small for gestational age
Data are presented as number (%), mean ± standard deviation or median (interquartile range).
P-value corresponds to [t]Independent Samples T-Test, [m]Mann-Whitney U Test, [c]Chi-Square Test or [f]Fisher's Exact Test.

On the 28th day after birth, the survival rate of infants in BW 1,000-1,499 g group (95.7%) was significantly higher than ELBW's (80.3%). BW is likely a good indicator of survival rate – the higher BW, the better survival rate. As for the final outcome, the total 19 out of 76 ELBW infants did not survive and 12 ELBWs (63.2%) died during the first 7 days after birth. The deaths of VLBW infants were more spread out during the first 28 days and were likely a result of many care treatment attempts to keep these infants alive (table 3). In 2014, there was no mortality case in VLBW infants because only 13 cases of VLBW infants. The trend of mortality rate for VLBW infants were 23.3%, 20.7% and 18.2% in 2015-2017, however, the mortality rate was decreased to 7.9%, 3% and 7.3% in 2018-2020. (figure 3)

The incidences of critical morbidity conditions RDS, ROP, IVH, BPD, hsPDA, CLABSI and VAP and intubation rate were significantly lower in infants of BW 1,000-1,499 g group compared to ELBW (figure 4, 5). There is no correlation in yearly morbidity conditions and care interventions.

Table 3 Mortality rate of VLBW infants categorized by birth weight (2014-2020; N = 217)

Variables	Total (N = 217)	Birth Weight (g)		P-value
		500-999 (N = 76)	1,000-1,499 (N = 141)	
Number of survival by day 28	196 (90.3)	61 (80.3)	135 (95.7)	< 0.001
Total number of death	26 (12.0)	19 (25.0)	7 (5.0)	< 0.001
Total number of survival	191 (88.0)	57 (75.0)	134 (95.0)	

Abbreviations: g,gram; N,number
Data are presented as number (%), mean ± standard deviation or median (interquartile range).
P-value corresponds to [t]Independent Samples T-Test, [m]Mann-Whitney U Test, [c]Chi-Square Test or [f]Fisher's Exact Test.

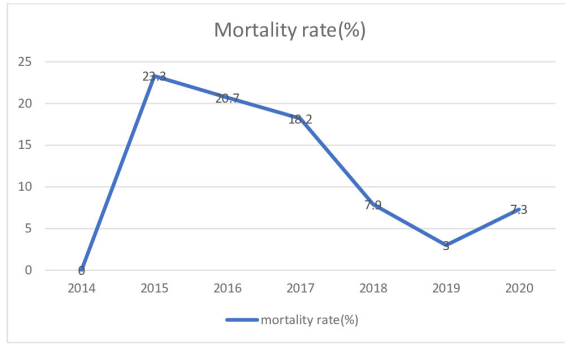

Figure 3 Trend of VLBW infants' mortality

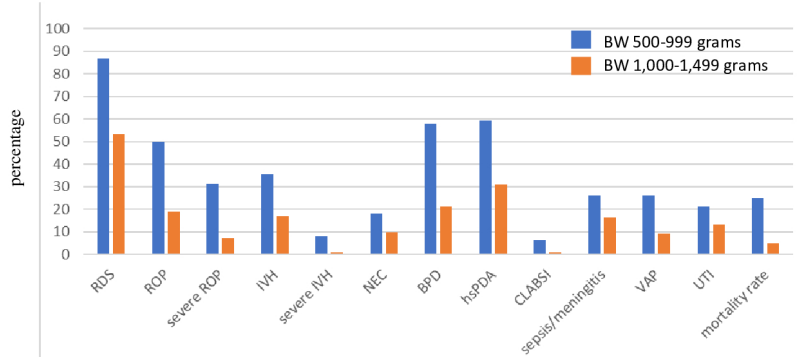

Figure 4 Mortality and morbidities of Infants

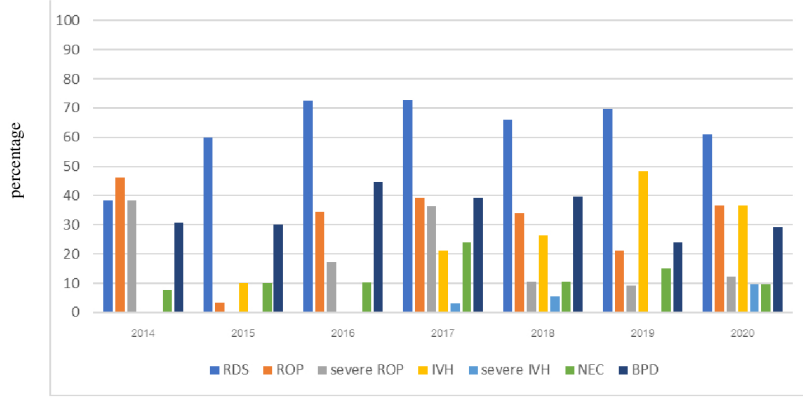

Figure 5 Morbidities by year of VLBW infants

DISCUSSION

The incidence of VLBW infants admitted to the neonatal unit of Vajira Hospital from January 1st, 2014, to December 31st, 2020, has increased every year. The infant mortality rate in this study accounted for 12%, which is similar to that reported by other institutions in Thailand[4-6] and developed countries such as Japan[7], Korean[8], Germany[9], and United State of America[10]. This study has shown that mortality and morbidities among VLBW infants significantly correlate with BW. ELBW infants had a higher mortality rate than BW 1,000-1,499 g group. The mortality rates of both groups were 25% and 5%, respectively. The mortality rate of ELBW infants in Faculty of Medicine Navamindradhiraj University is close to other tertiary hospital in Thailand[6], which are around 20-26%. Same as the mortality rate of VLBW infants that is around 5-10% from other tertiary care research[4-6]. Current study in mortality

rate of ELBW infant in Thailand, which data collected from National Health Coverage Scheme in 2015-2020 showed in-hospital mortality rate of ELBW infant was 36.9%. However, among all ELBW infants of this study, 65.1% were born at tertiary-level hospitals[2]. The most common cause of death in both groups was sepsis (76%), followed by PPHN (11.5%) and severe birth asphyxia (11.5%). Similar to other tertiary hospital in Thailand that found the survival rate of VLBW infants is higher than ELBW infants. We also found that on the 28th day after birth, the survival rate of BW 1,000-1,499 g infants was significantly higher.

The critical morbidities in the ELBW group were RDS, ROP, BPD, PDA and intubation rates and these were significantly higher than BW 1,000-1,499 g group. Based on the treatment results each year, it was found that there was no difference in mortality and morbidity rates in this study. However, the results showed a decreasing trend for both rates due to wildly used of surfactant treatment, non-invasive ventilators, t-pieces resuscitation in delivery room, peripheral inserted central catheter and protocol of infectious control in our unit started at year 2018. Despite of increasing in population of VLBW infants in 2018-2020, VLBW infants' mortality still declined. This correlates with the previous study, proving that better medical tools and technology reduce mortality and morbidity rate[8,11]. For this study, the morbidities such as RDS, ROP, IVH, PDA, and culture positive-late onset neonatal sepsis remained high. High incidence of RDS positively correlated with increased surfactant administration. However, there was a decrease in intubation rate due to current less invasive surfactant administration techniques and t-piece resuscitator in resuscitation room. The intubation rate's decline also reduced the incidence of BPD, moderate BPD, and VAP. ROP is still found in a large amount, about 37% of all VLBW infants in 2020, but the severe ROP or ROP that requires intervention were found to have reduced to 12.2%, which is consistent with the findings of research in Thailand[4-5]. The decline of severe ROP may be resulted from the decreased intubation rate and reduced exposure to high concentrations of oxygen. IVH and severe IVH are also found in large numbers, compared to about 7.5% found in studies in developed countries[9-10]. The risk factors of IVH are low GA, low BW, and asphyxia. From this study, the incidence of asphyxia and severe asphyxia accounted for 33% and 9.7%, respectively. PDA is still found to be high compared to those from Thai research[4-5]. The factors that contribute to increased hsPDA were low in GA, BW, low Apgar score for in-room resuscitation, and RDS requiring a surfactant therapy[12-13]. From this study, high incidence of hsPDA is likely associated with low GA and BW, high incidence of asphyxia, and high incidence of RDS requiring a surfactant therapy, which tends to increase every year.

Sepsis is another still very common condition, similar to research findings in Thailand[4-5]. The incidence of CLABSI and UTI is still high, while septicemia and pneumonia show a decreasing trend. Most common organisms were gram negative bacilli species such as *Escherichia coli* and *Klebsiella pneumoniae*. It may be necessary to find additional risk factors for CLABSI and UTI to reduce these problems therefore our unit set up the quality improvement team to management about infectious control in ICU. NEC is another condition that tends to decrease in both medically and surgically NEC. Currently, Vajira Hospital has a feeding protocol, that may improve this problem.

The strength of this study is that it is the first study to examine mortality and morbidity rates in VLBW infants at Vajira Hospital. For the limitations, since this is a retrospective cohort study, some data may be incomplete, such as maternal exposure to antibiotics and prenatal steroids, which, if completed, could more clearly reveal risk factors for morbidities. In addition, the population of this study was hospital based rather than population-based. For further study, we plan to assess the detailed causes of death during the NICU stay and after hospital discharge in each subject and consider the short and long-term financial burden in each patient. This study can be further used to assess the quality of care, such as infants who are referred versus infants who are treated at Vajira Hospital from birth.

CONCLUSION

The mortality and morbidity rates are significantly correlated to BW. The mortality in VLBW infants in Faculty of Medicine Vajira Hospital, Navamindradhiraj University are close to other tertiary hospitals in Thailand. The most common cause of death is neonatal sepsis. The morbidities; RDS, ROP, IVH, PDA and LOS were still high, requiring further study to identify risk factors to reduce these morbidities in VLBW infants.

CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose.

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DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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