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Study of Neonatal Morbidity and Mortality in Very Low Birth Weight Neonates Admitted in Neonatal Intensive Care Unit in a Tertiary Care Centre: An Observational Study

Pracheta Gupta[1], Suryakant Ingale[2], Gauri Parab[1], Poornima Pol[3*]

[1]Junior resident, Department of Pediatrics, BKL Walawalkar Rural Medical College and Hospital, Sawarde, India
[2]Professor and Head, Department of Pediatrics, BKL Walawalkar Rural Medical College and Hospital, Sawarde, India
[3]Assistant Professor, Department of Anesthesia, Ideal Institute of Medical Science and Hospital, Wada, Palghar District, Maharashtra, India

***Address for Correspondence:** Dr Poornima Pol, H4-302, 3rd floor, Cidco Valley Shilp CHS, Sector 37, Kharghar, Navi Mumbai, Maharashtra, 410210, India
E-mail: drpoornimapol@gmail.com

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ABSTRACT

Background: Thorough documentation of morbidity and mortality is crucial for understanding health trends in very low birth weight (VLBW) neonates. Morbidity and mortality in VLBW neonates represent significant health issues, making it essential to identify associated risk factors. The perinatal and neonatal periods are critical in highlighting the health conditions of at-risk populations. This study aims to examine intricate patterns of morbidity and mortality among VLBW neonates.

Methods: VLBW neonates admitted to the Neonatal Intensive Care Unit, BKL Walawalkar Hospital, from November 2022 to May 2024 were examined. We collected comprehensive maternal information, such as age, birth locality, gestational age, and various risk factors. The study focused on demographic profiles, clinical variables, and outcomes.

Results: Out of 203 VLBW neonates, 31% were appropriate for gestational age, 66% were small, and 6.4% were restricted Intrauterine growth. Common morbidities were respiratory distress syndrome (39.9%) followed by sepsis (25.6%). The majority of VLBW neonates were born of normal vaginal delivery (44.8%) with gestational age between 28-32 weeks (54.7%). A significant statistical association between gestational age and mortality outcomes was found(p-value=0.005)

Conclusion: Respiratory distress syndrome is the leading cause of morbidity and mortality in VLBW neonates. It is crucial to utilize surfactant therapy effectively and ensure timely transportation for neonates. To address these issues, it is essential to improve prenatal care, guarantee skilled attendance during childbirth, conduct regular screenings, implement infection control measures, and educate parents.

Key-words: Intrauterine growth restriction, Respiratory distress syndrome, Sepsis, Small for gestation age, Very low birth weight

INTRODUCTION

Preterm birth is a significant issue leading to low birth weight (LBW) in approximately 20 million infants globally each year, with India accounting for 40% of this figure. Preterm births frequently result in serious neonatal complications, including both morbidity and mortality and can contribute to disabilities in later childhood.[1] The World Health Organization (WHO) defines low birth weight as a birth weight of less than 2,500 grams, a classification that has existed for many years. LBW is categorized into very low birth weight (VLBW, less than 1,500 grams) and extremely low birth weight (ELBW, less than 1,000 grams).[2]

In India, nearly 8 million LBW infants are born each year, which represents about 28% of all live births in the country. Among these, around 8 million are VLBW infants, making India responsible for 40% of the global VLBW burden.[3] The National Family Health Survey indicates that the prevalence of VLBW infants in India stands at 21.5%. Recent reports from the WHO and United Nations

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Children's fund (UNICEF) reveal that infant mortality in India is significant, with VLBW infants accounting for 57% of all etiologies contributing to this statistic.[3,4]

Among the various factors contributing to VLBW babies, key elements include intrauterine growth restriction (IUGR), preterm delivery, and a combination of both pathological and physiological conditions. Infants with IUGR experience significantly higher rates of morbidity and mortality compared to appropriately grown, gestation-matched peers. Malnutrition in infancy is a major contributor to VLBW, with over 40% of such babies identified as malnourished during their first year.[5,6]

Additionally, LBW infants face a 2.3-fold increased risk of mortality from infections compared to those with normal birth weight. A recent study in India identified several factors strongly linked to VLBW, including maternal age (under 19 years), maternal weight (below 45 kg), a poor obstetric history, rural residency, gestational age (under 37 weeks), and pregnancy-induced hypertension. [5-7]

VLBW is a critical factor associated with morbidity in newborns and children, particularly linked to neurodevelopmental issues such as intellectual disabilities and learning difficulties. In low-income countries, VLBW has also been connected to a higher prevalence of stunting and is a significant contributor to chronic health conditions like diabetes, obesity, and cardiovascular diseases in adulthood.[8] This information is crucial for improving perinatal and neonatal care tailored to local needs.[9]

VLBW and prematurity are significant predictors of perinatal survival and postnatal complications, contributing to broader health challenges in developing regions. Most VLBW infants require intensive care to survive.[10] While advancements in pediatric care have led to improved survival rates and quality of life in higher-income countries-where 95% of VLBW infants survive and 90% do not face lasting harm, many low-income countries see a high mortality rate due to inadequate care.

Evaluating the impact of low birth weight on mortality and short-term and long-term health outcomes is vital for guiding prenatal and postnatal counseling for families, which can enhance decision-making and promote ongoing improvements in care. Despite numerous studies in this field, few adequately capture the local burden of preterm birth and its implications.[11,12] Therefore, this study aims to identify factors contributing to the increased morbidity and mortality among VLBW infants to implement measures to reduce these risks.

MATERIALS AND METHODS

Study Design, Period and Site- This prospective observational study was conducted on 203 very low birth weight neonates admitted to the Neonatal Intensive Care Unit of Pediatrics, BKL Walawalkar Hospital from November 2022 to May 2024.

Sample size calculation- The sample size was determined using a single population proportion formula considering the following assumptions: 95% confidence level, margin of error (0.05) and the rate of preterm mortality 22% from previous studies.

$$n=(Z\alpha/2)^2 \times p\,(1-p)/\,(d)^2$$

$$n= [1.96]^2 *0.22*0.78/ [0.05]^2 = 164 \text{ neonates.}$$

After adding a 10% loss to follow-up, the sample size was 191 neonates.

Eligibility criteria- All neonates diagnosed as VLBW neonates from the first day of life up to 28 days old, admitted to the neonatal intensive care unit, were eligible for the study. Neonates whose parents declined to participate in the study or were discharged against medical advice were excluded from the research.

Methodology- All participants' prenatal history, natal events, and neonatal course were thoroughly assessed. This included gathering information on the mother's obstetric history, and antenatal risk factors, and any relevant drug history. A comprehensive natal and postnatal history of each neonate was collected and documented. A complete clinical examination was performed, and relevant anthropometric measurements, investigations, and treatments were recorded using a pre-designed proforma.

Examination- A detailed general examination was conducted, noting vital parameters such as heart rate, respiratory rate, temperature, peripheral pulses, and any abnormalities like pallor, edema, jaundice, cyanosis, and congenital or craniofacial anomalies. A thorough head-to-toe examination was performed, and all neonatal reflexes were assessed for abnormalities. Systematic examinations were also conducted.

Anthropometry- The weight of the neonates, without clothing, was measured using a digital weighing scale, with an accuracy of 5 grams. Length was measured using an infantometer, and head circumference was assessed using

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a non-stretch measuring tape (cross-type method) from the occipital protuberance to the supraorbital ridges on the forehead.

Investigations were carried out as needed, including complete blood counts, blood cultures, blood sugar levels, C-reactive protein tests, and chest X-rays. All enrolled infants underwent examinations and investigations, including complete blood counts, blood sugar levels, C-reactive protein tests, chest X-rays, and blood cultures.

Statistical Analysis- The chi-square test and Fischer exact test were used to analyze the significance of the difference between the frequency distribution of the data. p-value<0.05 was considered statistically significant. The collected data was entered into Microsoft Excel and analyzed using the Statistical Package for the Social Sciences (SPSS© for windows™ IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp) and GraphPad Prism software version 8.4.2.

Ethical Approval- Institutional research ethical committee approval was taken before the research. Informed consent was taken from parents or guardians of all neonates included in this study.

RESULTS

Table 1 shows that of 203 VLBW neonates, 52.7% were males and 47.3% were females. Also, 61.6% were inborn and 38.4% were outborn. The total mean weight of the neonates with standard deviation (S.D) included in the study was 1.25±0.13 kilograms. Mean birth weight was 1.23±0.13 kg in males and 1.28±0.12 kg in females. Out of 203 VLBW babies, 44.8% were born out of normal vaginal delivery and 55.2% were born by cesarean section. Most neonates (54.7%) had a gestational age between 28-32 weeks, followed by 26.1% of the neonates had a gestational age between 32-34 weeks. Table 1 shows the gestational age-wise distribution. Furthermore, 76 (37.4%) were Small for Gestational Age (SGA), 31(15.3%) were appropriate for Gestational Age (AGA), 13(6.4%) were intrauterine Growth Restriction (IUGR). The percentage of SGA babies contributed to maximum numbers.

Table 1: Demographic and clinical variables in neonates

Parameters	VLBW Neonates	
	Number	Percentage (%)
Gender		
Male	107	52.7
Female	96	47.3
Birth Locality		
In-born	125	61.6
Out-born	78	38.4
Mode of delivery		
Normal vaginal	91	44.8
LSCS	112	55.2
Gestational age		
Less than 28 weeks	13	6.4
28-32 weeks	111	54.7
32-34 weeks	53	26.1
34-36 weeks	26	12.8
Birth weight compared with gestational age		
AGA	58	31
SGA	124	66
IUGR	21	6.4

LSCS: Lower segment caesarean section, AGA: Appropriate for Gestational Age, SGA: Small for Gestational Age, IUGR: Intrauterine Growth Restriction

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Table 2 shows the morbidity pattern and outcomes in VLBW neonates. In this study, the most common morbidities among VLBW neonates were RDS (n = 81, 39.9%), Sepsis (n=52, 25.6%) followed by Transient Tachypnoea of Newborn (n = 39, 19.2%). Out of 81 neonates suffering from RDS, 62 neonates required surfactant. Three neonates were given an exchange transfusion of 32 neonates suffering neonatal hyperbilirubinemia. 78.3% of VLBW neonates survived, and 21.7% did not (Table 2).

Table 2: Morbidities and outcomes of neonates

Variables	VLBW neonate	
	Number	Percentage (%)
Morbidities		
Pneumothorax	3	1.5
Pneumonia	3	1.5
Intraventricular Haemorrhage	3	1.5
Hydrocephalus	4	2.0
Meningitis	4	2.0
Retinopathy of Prematurity	4	2.0
Patent Ductus Arteriosus	4	2.0
Infant of Diabetic Mother	4	2.0
Necrotizing Enterocolitis	5	2.5
Meconium Aspiration Syndrome	6	2.9
Apnea of Prematurity	7	3.4
Congenital Anomaly	7	3.4
Shock	8	3.9
Asphyxia	10	4.9
Hypoglycaemia	20	9.8
Neonatal Hyperbilirubinemia	32	15.8
Transient Tachypnoea of Newborn	39	19.2
Sepsis	71	34.9
Respiratory Distress Syndrome	81	39.9
Outcomes		
Alive	136	67
Death	67	33

Table 3 shows a significant statistical association between the gestational age of the neonates and their outcome. The neonates with small gestational age were at higher risk of mortality. (p-value=0.005) However, no significant association between the gender, birth locality, mode of delivery of the neonate and their outcomes was established (p-value=0.88, 0.64, 0.23 respectively at 95%CI) (Table 3).

Table 3: Association of Demographic and clinical variables with outcomes

Variable	Outcome		Total	p-value
	Survival	Death		
Gender				
Male	71	36	107	0.88
Female	65	31	96	
Birth Locality			Total	p-value

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Inborn	82	43	125	0.64
Outborn	54	24	78	
Gestational Age			Total	p-value
<28 weeks	4	9	13	0.005*
28-32 weeks	75	36	111	
32-34 weeks	37	16	53	
34-36 weeks	20	6	26	
Mode of Delivery			Total	p-value
Normal Vaginal	71	41	112	0.23
LSCS	65	26	91	

*LSCS- Lower segment caesarean section. The data were analysed with Chi-Square test and Fischer's exact test. P value <0.05 was considered significant. *highly statistically significant*

Table 4 shows that on multiple regression analysis, only two morbidities i.e. respiratory distress syndrome and sepsis, were found as factors significantly associated with the risk of mortality. Diseases like pneumothorax, pneumonia, Retinopathy of prematurity, Necrotizing enterocolitis and meconium aspiration syndrome could not be analysed with multiple logistic regression due to perfect separation or because one or more predictors are linearly dependent (Table 4).

Table 4: Mortality patterns in VLBW Neonates according to morbidities and treatment given in neonates

Disease	Total	Survived	Death	OR	95% CI	p-value
Pneumothorax	3	3	0	-	-	-
Pneumonia	3	3	0	-	-	-
Intraventricular Haemorrhage	3	2	1	0.99	0.09-21.41	0.99
Hydrocephalus	4	2	2	0.48	0.05-4.11	0.86
Meningitis	4	3	1	1.49	0.18-30.40	0.93
Retinopathy of Prematurity	4	4	0	-	-	-
Patent Ductus Arteriosus	4	3	1	1.49	0.18- 30.40	0.93
Infant of Diabetic Mother	4	3	1	1.49	0.18- 30.40	0.93
Necrotizing Enterocolitis	5	5	0	-	-	-
Meconium Aspiration Syndrome	6	2	4	-	-	-
Apnea of Prematurity	7	3	4	0.36	0.06- 1.65	0.66
Congenital Anomaly	7	4	3	0.65	0.13- 3.36	0.85
Shock	8	7	1	3.581	0.61- 67.66	0.67
Asphyxia	10	7	3	1.16	0.31- 5.50	0.93
Hypoglycaemia	20	11	9	0.57	0.22-1.47	0.53
Neonatal Hyperbilirubinemia	32	22	10	1.1	0.49- 2.57	0.88
Transient Tachypnoea of Newborn	39	24	15	0.73	0.37- 1.07	0.56

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Sepsis	71	35	36	0.30	0.16- 0.54	0.001*
Respiratory Distress Syndrome	81	43	38	0.35	0.19-0.64	0.004*
Surfactant	63	34	29	0.44	0.23-0.81	0.034*
Exchange Transfusion	3	3	0	-	-	-

*Data were analysed using multiple regression analysis. *Shows statistically significant association*

Fig. 1 depicts that most neonates died between 48-72 hrs (25.37%) and 24-48 hrs (21.31%).

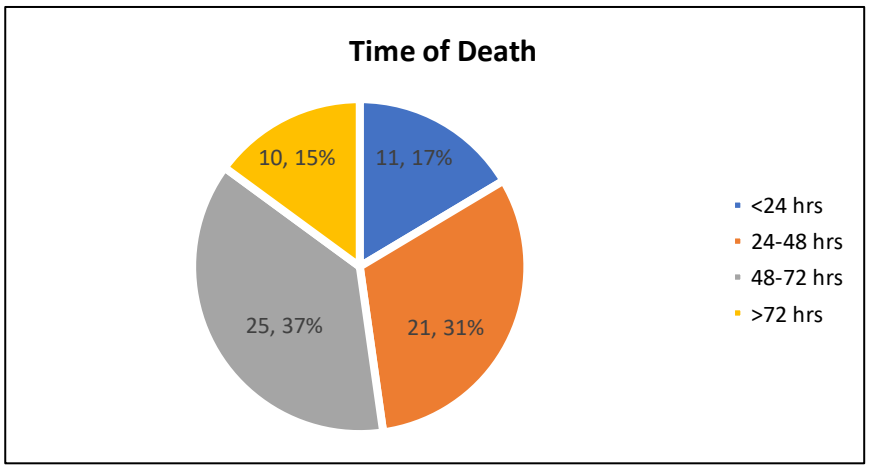

Fig. 1: Distribution of neonates according to time of death

DISCUSSION

Prenatal care and hospital deliveries have been shown to significantly lower mortality rates, highlighting their importance for the safety of both mothers and newborns. In countries with high home birth rates, efforts are being made to transition all deliveries to healthcare facilities to ensure that skilled birth attendants are present. Each year, over 40% of maternal stillbirths and premature deaths occur during childbirth, which underscores the necessity of hospital transfers in certain cases to mitigate the risk of premature deaths.[13] Regarding the birth locality in the present study, most neonates were inborn (61.6%), while 38.4% were outborn.

The gender analysis revealed a notable male predominance, with 52.7% males compared to 47.3% females. The mean birth weight was 1.23±0.13 kg for males and 1.28±0.12 kg for females, leading to an overall mean weight of 1.25±0.13 kg for all neonates included in the study.

Kabilan *et al.* found similar results to our study, with 98.7% of deliveries being inborn and only 1.2% outborn.[14] Guran's study also indicated a low rate of outborn deliveries, with only 10.7% in 2002–2006 and 5.3% in 2007–2011.[15] Genie *et al.* corroborated our findings regarding gender and place of delivery, reporting a male predominance of 63.57% and 93.81% of deliveries occurred in healthcare institutions, with just 6.19% at home.[16] These results align with our data findings. In contrast, Jeschke et al. reported a female predominance among VLBW neonates, with females constituting 51.2%.[17] Guran *et al.* noted a lower prevalence of male infants in their study from 2002 to 2011, with male rates of 43.8% from 2002 to 2006 and 46.7% from 2007 to 2011.[15] Similar to our findings, Genie et al. did not find a statistically significant relationship between gender and study outcomes (p-value = 0.307, 95%CI).

Regarding birth locality, 62.64% of the infants survived, while 37.36% did not. In contrast, of the 18 home deliveries, 55.56% survived and 44.44% did not. Consistent with our results, this study also found no statistically significant association between birth locality and study outcomes (p-value = 0.55 with 95%CI).[16]

Kusuda *et al.* corroborated our findings, as they also found no statistical association between demographic factors such as gender and birth locality with neonatal outcomes, including survival status (both p values > 0.05 with a 95%CI).[18] In the present study, 44.8% of neonates were delivered vaginally, while 55.2% were born via cesarean

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section. Among the study participants, 54.7% were born between 28 and 32 weeks, followed by 26.1% between 32 and 34 weeks. Our analysis revealed that 37.4% were small for gestational age, 15.3% were appropriate for gestational age, and 6.4% had IUGR.

The mean gestational age in our study was 31.9±3.095 weeks, aligning with findings from Kabilan *et al.* found that 1.9% of women had assisted vaginal deliveries, 61.7% had normal vaginal deliveries, and 36.4% had cesarean sections in their research. Most neonates were in the gestational age group of 33-36 weeks (44.2%), with 57.8% classified as small for gestational age, 81.8% being singletons, and 98.7% inborn.[14] Guran et al. evaluated mean gestational ages of VLBW infants from 2002-2006 and 2007-2011, reporting mean gestational ages of 29.8±3.0 weeks for 2002-2006 and 28.9±2.9 weeks for 2007-2011. They also observed an increase in the prevalence of cesarean sections among VLBW infants, which rose from 46% in 2002-2006 to 74.4% in 2007-2011.[15]

Kusuda *et al.* also supported our study findings as they could not establish a statistical association between the gestational age of the neonates and outcomes like the alive or dead status of neonates [p value >0.05 with 95%CI].[18] Ballot et al. compared the mode of deliveries in 2007 and 2013. They could not establish statistical significance between cesarean section and morbidity as well as mortality pattern in both years (55.4% 51.2–59.4) vs 51.4% (46.1–58.5) (p-value = 0.23 with 95%CI).[19]

Premature infants typically have underdeveloped lungs, which results in impaired alveolarization, type 2 cell differentiation and surfactant production. Furthermore, premature infants lack proper brain and lung self-regulation, along with immature immune systems, making them vulnerable to conditions such as shock, respiratory distress syndrome, and sepsis.[1] In the current study, we evaluated various morbidity patterns in VLBW neonates. The most commonly observed morbidity was respiratory distress syndrome (39.9%) and sepsis (25.6%). Another study found that respiratory distress was the leading cause of death in VLBW infants, accounting for 37.03% of all fatalities.

Sepsis and hypoxic-ischemic encephalopathy followed as the second and third leading causes, contributing to 34.56% and 13.58% of deaths, respectively.[1] According to data from the NIHDNRN Centre, approximately 93% of infants born before 28 weeks of gestation experience respiratory distress syndrome.[20] According to data from the Vermont Oxford Network, RDS was present in 90% of infants weighing less than 1000 grams, while this figure decreased to 60% for those weighing between 1000 and 1500 grams.[21] Guran et al. found that intraventricular hemorrhage occurred in 20% of VLBW infants, predominantly classified as grade 1-2 bleeds.[15]

Retinopathy of prematurity, a leading cause of vision loss and blindness in children, is a significant issue in preterm infants, especially those born before 28 weeks gestation and weighing less than 1000 grams in developed countries. In this study, the mean prevalence of advanced retinopathy of prematurity (grade III and above) in VLBW infants was 9.3%.

VLBW neonates diagnosed with RDS were found to have 4.6 times higher odds of mortality compared to those without RDS (AOR: 4.6; 95% CI 2.51 to 8.40). This finding is supported by studies from Aga Khan University Hospital in Pakistan by Khan *et al.* [22] and Telangan by Hasthi *et al.* [23]. From Mahatma Gandhi Memorial Government Hospital in India by Saminathan *et al.* [24] A potential explanation for this increased risk is that neonates with RDS frequently experience lung collapse, which can lead to higher mortality rates among preterm low birth weight infants.[22-24] Additionally, VLBW neonates with hypoglycemia exhibited 3.91 times greater odds of mortality compared to those without this diagnosis (OR: 3.91; 95% CI 1.09 to 10.52), as noted by Genie *et al.*[16] This aligns with findings from studies conducted in Telangana and at Mahatma Gandhi Memorial Government Hospital. This increased risk may be attributed to the immature organ systems in preterm neonates, which often lead to inadequate glycogen storage and subsequent mortality.[23,24]

Genie et al. also reported that VLBW neonates with sepsis had twice the odds of mortality compared to those without sepsis (AOR: 2.0; 95% CI 1.03 to 3.89).[16] This is consistent with results from research in Telangana and Mahatma Gandhi Memorial Government Hospital. The heightened risk may stem from the immature immune systems of preterm, low birth weight infants, making them more vulnerable to severe infections that can result in neonatal death.[23,24]

Additionally, Tripathy et al. found that RDS presented the greatest mortality risk, likely due to fewer infants receiving antenatal steroids and lower rates of continuous positive airway pressure and surfactant therapy in their settings. In their study, shock was reported in 35.8% of infants who did not survive, compared to 16.79% in those who did,

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indicating a significant correlation.[1] The narrow autoregulatory blood pressure range in premature neonates means that normal blood pressure levels are typically at the lower end of this range.[10] Sepsis, hypoxic-ischemic encephalopathy and RDS were identified as major causes of death in the study by Tripathy *et al.* and contributed to the onset of shock. The presence of congenital anomalies alongside low birth weight was found to increase mortality risk significantly. Sepsis remains the most common cause of mortality in developing countries, with prematurity significantly exacerbating this risk. Similarly, Tripathy et al. highlighted sepsis as a key morbidity contributing to mortality in their study.[1]

The current study had few limitations. Due to a small sample size, the findings of this study need to be corroborated in larger sample studies and a larger sample size of the population in the study could have given more conclusive findings. Since this institution serves as a tertiary healthcare and referral centre, factors such as inadequate transport and delays in transfer may influence the outcomes observed.

CONCLUSIONS

We can conclude that VLBW babies are significant contributors to neonatal mortality and morbidity. The primary causes of these outcomes were RDS and sepsis. VLBW neonates, who often face critical challenges related to their pulmonary and circulatory systems, are at a considerably higher risk of mortality. Most neonates survived in our study due to early interventions and appropriate care. Our findings identified gestational age as an independent predictor of neonatal mortality.

The primary goal should be to implement early interventions and appropriate care strategies for VLBW infants in the delivery room, enhancing healthcare starting from the perinatal period to improve survival rates. Preventing prematurity, enforcing infection control measures, and upgrading neonatal care across all levels are essential strategies to mitigate this issue. We also suggest conducting larger studies to validate our findings further.

CONTRIBUTION OF AUTHORS

Research concept- Dr Pracheta Gupta, Dr Suryakant Ingale, Dr Gauri Parab, Dr Poornima Pol

Research design- Dr Pracheta Gupta, Dr Suryakant Ingale, Dr Gauri Parab, Dr Poornima Pol

Supervision- Dr Suryakant Ingale, Dr Poornima Pol

Materials- Dr Pracheta Gupta, Dr Suryakant Ingale, Dr Gauri Parab, Dr Poornima Pol

Data collection- Dr Pracheta Gupta, Dr Gauri Parab

Data analysis and Interpretation- Dr Pracheta Gupta, Dr Suryakant Ingale, Dr Gauri Parab, Dr Poornima Pol

Literature search- Dr Pracheta Gupta, Dr Suryakant Ingale, Dr Gauri Parab, Dr Poornima Pol

Writing article- Dr Pracheta Gupta, Dr Suryakant Ingale, Dr Gauri Parab, Dr Poornima Pol

Critical review- Dr Pracheta Gupta, Dr Suryakant Ingale, Dr Gauri Parab, Dr Poornima Pol

Article editing- Dr Pracheta Gupta, Dr Gauri Parab, Dr Poornima Pol

Final approval- Dr Pracheta Gupta, Dr Suryakant Ingale, Dr Gauri Parab, Dr Poornima Pol

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