Determinants of Mortality in Preterm Newborns Admitted in a Neonatal Intensive Care Unit: Findings from a Tertiary Level Maternity Hospital in Nepal

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Abstract

Introduction: Prematurity is a major cause of admission in the NICU in most hospitals. Premature babies are likely to face complications. Understanding the factors contributing to preterm mortality is needed to identify interventions required to reduce neonatal mortality rate. This study aims to determine the causes of mortality in preterm babies.
Methods: A retrospective study was carried out in Paropakar Maternity and Women's Hospital, Thapathali, Kathmandu, Nepal. All the preterm babies admitted in the sick newborn units were included. Descriptive statistics were performed using frequency and percentage. The bivariate and multivariate analyses were performed to determine the causes of mortality in preterm.
Results: Total 205 (71.4%) admitted preterm babies had complications at the time of admission. LBW babies were three times more likely to have mortality among preterm admission (p – value < 0.0001). Co-morbidities such as sepsis (p - value < 0.05) and perinatal asphyxia (p – value < 0.0001) were significantly associated with preterm mortality. The duration of stay among preterm babies was higher compared to term babies. The mortality rate was higher among preterm admission compared to term admission (60% vs 40%).
Conclusions: Preterm babies with LBW, neonatal sepsis and perinatal asphyxia are at greater risk of mortality. Improved antenatal and perinatal care, quality newborn care and appropriate infection prevention measures can help reduce preterm birth, prematurity related complications and mortality among these vulnerable group of newborns.

Introduction

The neonatal period is the most vulnerable time for a child's survival as there is a high risk of death within the first month of life. In 2019, 2.4 million neonatal deaths occurred globally which is approximately 6,700 neonatal deaths every day.[1] World Health Organization (WHO) has depicted about 11% of the babies are born preterm which is nearly 15 million babies. Around 35% of these babies die before 28 days of life.[2] Prematurity related complications, birth asphyxia, neonatal sepsis, congenital anomalies are major causes of neonatal mortality.[3] However, it is not known which of these conditions contribute to what proportion of preterm mortality. Globally, preterm is the most frequent and leading cause of neonatal deaths.[4,5] There is a significant variation among causes of preterm mortality between countries and within countries and the burden of preterm birth and mortality is higher in Southeast Asia and sub Saharan Africa.[6]

There is an increased risk of death and serious disability when a baby is born preterm as compared to term infants. Respiratory problems such as a respiratory distress syndrome (RDS) and apnea of prematurity, sepsis, compromised immune systems are immediate consequences while delay in developmental milestones and lower performance in late life are the long-term consequences associated with preterm birth.[5] The mortality in preterm neonates could result either from preterm-related complications like apnea of prematurity, RDS, pulmonary hemorrhage, hypothermia, hypoglycemia or due to conditions such as congenital anomalies, sepsis and asphyxia.[6] As effective interventions become available to prevent some of the specific causes of preterm related mortality in low resource settings, there is a need to establish the major contributing factors.[6,7]

Globally from 1990 to 2016, mortality in children younger than five years was reduced by 56% and neonatal mortality by 49%.[7] Nepal has made a significant progress in reducing neonatal mortality gradually from 50 deaths per 1,000 live births in 1996 to 21 deaths per 1,000 live births which is still a slow decline as compared to the decline in infant and under five mortality rate over the same period.[8] Around 81,000 newborns are born preterm in Nepal and for 33% of all neonatal deaths is contributed by prematurity related complications.[9,10] The proportion of neonatal mortality among under five mortality has increased from 42% in 1996 to 54% in 2016.[8] A study conducted in western Nepal showed that preterm birth was a major cause for admission in the neonatal unit.
Common morbidities of preterm were sepsis, jaundice, RDS and necrotizing enterocolitis out of which case fatality rate was higher in RDS and perinatal asphyxia.[11,12] Different factors play role in increasing the risk of death in preterm but there are limited studies in Nepal. Hence, this study has been conceptualized to determine the causes of mortality in babies who were born preterm.

Methods

This retrospective study was carried out in Paropakar Maternity and Women's Hospital, Thapathali, Kathmandu, Nepal from 2019 March to Jan 2021. Babies admitted in NICU or SNCU were included for this study while stillborn babies were excluded from the study. The socio-demographic and intrapartum-related clinical information of the mothers were extracted from the sick newborn registers. Similarly, information regarding sick newborns' management and outcome were assessed from the data retrieval form. Clinicians involved in newborn care filled up these forms. The data were reassessed for completeness by a team of experts comprising of paediatricians.
Perinatal asphyxia-babies was defined with low one and five-minute APGAR scores as determined by attending clinician based on clinical status and arterial blood gas analysis report. We defined the various terminologies as follows.

- Preterm birth - Babies born before 37 completed weeks of gestation.
- Pre-discharge mortality - Death of the newborn before discharge from the hospital
- Low birth weight - Birth weight less than 2500 grams.

We noted the maternal demographic characteristics like age, ethnicity and obstetric characteristics like mode of delivery, parity etc. Neonatal data like sex of the baby, gestational age etc were noted. The entered data was cleaned and exported to Statistical Package for the Social Sciences (SPSS) version 23 for data analysis. Descriptive statistics were performed using frequency and percentage. For all categorical variables, bivariate analyses were performed using binary logistic regression. At 95% confidence interval (CI), $p < 0.05$ was considered to be significant. Variables with $p < 0.2$ from the bivariate analysis were considered for multiple regression analysis. Ethical approval was taken from our institutional review committee (Registration number 61/1967).

Results

Table 1. Background Characteristics among Term and Preterm babies

Variables	Preterm	Term n (%) p - value
Age (N = 2653)*	n (%)	0.450
15 - 19	109 (11.4%)	196 (11.6%)
20 - 35	793 (82.8%)	1419 (83.7%)
> 35	56 (5.8%)	80 (4.7%)
Ethnicity (N = 2751)		0.056
Brahmin / Chhetri	357 (31.6%)	555 (31.6%)
Madhesi	46 (3.5%)	62 (3.5%)
Muslim	9 (0.9%)	16 (0.9%)
Janajati	507 (56.6%)	992 (50.9%)
Dalit	78 (7.4%)	129 (7.8%)
Complication of mother during admission (N = 764)*		< 0.0001
No	82 (28.6%)	238 (45.2%)
Yes	205 (71.4%)	239 (54.8%)
Sex (N = 2737)*		0.259
Male	539 (54.2%)	984 (56.5%)
Female	455 (45.8%)	759 (43.5%)

*Variables with missing information

During this study, in total 2907 of the babies were admitted at the NICU out of which 2751 had information on preterm (n = 997) and term (n = 1754). The majority of the women aged 20 to 35 years of age had delivered the baby

at the hospital and 82.8% of preterm babies lies in this group. Those women who delivered preterm, as well as term babies, belonged to Janajati among the ethnic group. The majority of the preterm were male babies 539 (54.2%). Among the preterms, 205 (71.4%) had a complication of mother that led to their admission. (Table 1).

Table 2. Bi-variate analysis of the association among cause of mortality in admitted preterm babies

Variables	N	Preterm	Term	COR (95% CI)	P-Value
Sepsis					
No	307	192 (75.6%)	115 (69.3%)	1	
Yes	113	62 (24.4%)	51 (30.7%)	0.409 (0.255-0.657)	< 0.0001
Congenital Anomaly					
No	375	229 (90.2%)	146 (88.0%)	1	
Yes	45	25 (9.8%)	20 (12.0%)	0.797 (0.427-1.487)	0.476
LBW					
No	284	144 (56.7%)	140 (84.3%)	1	
Yes	136	110 (43.3%)	26 (15.7%)	4.11 (2.528-6.691)	< 0.0001
Perinatal Asphyxia					
No	294	203 (79.9%)	78 (47.0%)	1	
Yes	126	51 (20.1%)	88 (53.0%)	0.305 (0.198-0.474)	< 0.0001

In bi-variate analysis, LBW babies were four times more likely to have mortality among preterm admission (COR 4.11, 95% CI: 2.52 - 6.69, p - value < 0.0001). Similarly, co-morbidities such as sepsis (COR 0.409, 95% CI: 0.255 - 0.657, p – value < 0.0001) and perinatal asphyxia (COR 0.305, 95% CI: 0.198 - 0.474, p-value < 0.0001) were significantly associated with preterm mortality (Table 2).

Table 3. Multi-variate analysis of association among cause of mortality in preterm babies

Variables	N	Preterm	Term	AOR (95% CI)	P Value
Sepsis					
No	307	192(75.6%)	115(69.3%)	1	
Yes	113	62 (24.4%)	51 (30.7%)	0.429 (0.259-0.708)	0.001
LBW					
No	284	144(56.7%)	140(84.3%)	1	
Yes	136	110(43.3%)	26 (15.7%)	3.365 (2.007-5.641)	< 0.0001
Perinatal Asphyxia					
No	294	203(79.9%)	78 (47.0%)	1	
Yes	126	51 (20.1%)	88 (53.0%)	0.216 (0.134 -0.348)	< 0.0001

The multivariate analysis showed that babies diagnosed with sepsis (AOR0.429, 95% CI:0.259 - 0.708, p-value < 0.05), perinatal asphyxia (AOR 0.216, 95% CI:0.134 - 0.348, p-value < 0.0001) were significantly associated with preterm mortality. However, LBW babies had three times increased odds of having mortality among preterm admission (AOR 3.365, 95% CI: 2.007 - 5.641, p-value < 0.0001) after adjustment with babies having sepsis and perinatal asphyxia. (Table 3)

Table 4. Duration of stay among preterm and term admission

Duration of Stay (N = 2662)	Preterm	Term	P-Value
	N = 955	N = 1707	< 0.0001
0- 3 Days	232 (24.3%)	408 (23.9%)	
4 - 7 Days	335 (35.1%)	707 (41.4%)	
8 - 14 Days	312 (32.7%)	547 (32.0%)	
15 - 21 Days	54 (5.7%)	31 (1.8%)	
> 21 Days	22 (2.3%)	14 (0.8%)	

There was an increased duration of stay between 15 to 21 days and more than 21 days among preterm admission as compared with term admission (p value < 0.0001). The duration of stay among preterm and term babies was mostly four to seven days (Table 4).

Table 5. Discharge outcomes among Preterm and Term babies

Discharge Outcome among total admission	Preterm N (%)	Term N (%)	P-Value
N = 2751	N = 997	N = 1754	< 0.0001
Improved	645 (64.7%)	1468 (83.7%)	
Expired	254 (25%)	166 (9.5%)	
LAMA	22 (2.2%)	28 (1.6%)	
DOPR	8 (0.8%)	8 (0.5%)	
Referred	68 (6.8%)	84 (4.8%)	

Table 5 shows that 645 (64.7%) improved among the admitted preterm, whereas 1468 (83.7%) term babies improved during the stay. Among the preterms, 254 (25%) babies expired while among the admitted term babies, 166 (9.5%) babies died.

Figure 1. Distribution category of gestational age among admitted preterms in weeks

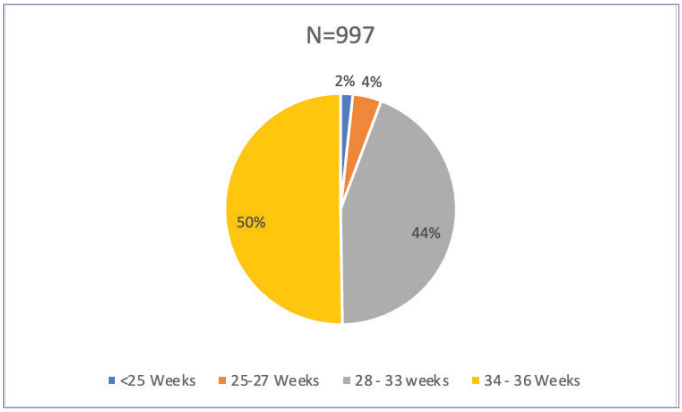
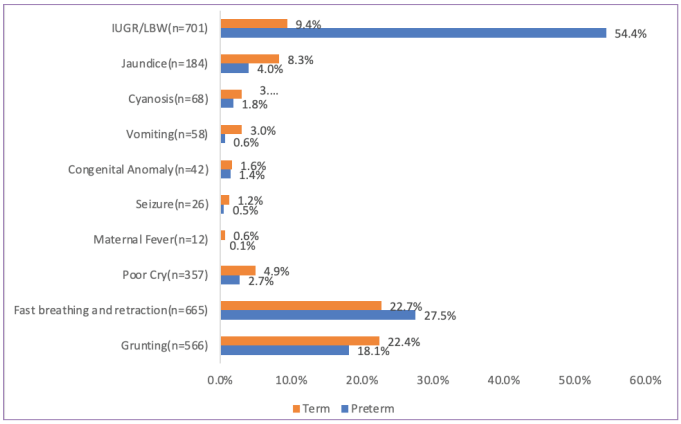


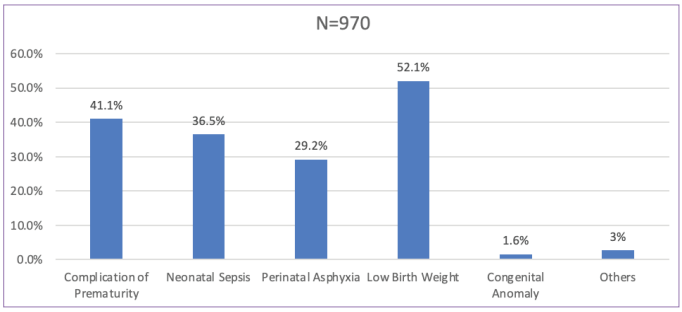
Figure 1. shows the distribution of gestational age among preterm admission. Majority of the preterm admission (50%) were of gestational age between 34 to 36 weeks. Similarly, 44% of the admitted preterms were 28 to 33 weeks of gestation and 4% of the admission were among 25 to 27 weeks and 2% of the preterm admission were below 25 weeks of gestation.

Figure 2. Factors associated with cause of admission among preterm and term babies



The proportion of causes of admission among preterm and term babes is shown in figure 2. The proportion of preterm babies admitted having LBW was 54.4% compared to term with 9.4%. The proportion of fast breathing and retraction among preterm admission was 27.5% whereas it was 22.7% among term admissions. The proportion of preterm babies having grunting was 18.1%. The proportion of preterm babies with jaundice was 4.0%. The proportion of preterm babies with cyanosis was 1.8% and preterm babies with vomiting was 0.6%. The proportion of preterm babies with congenital anomaly was 1.4%. The proportion of preterm babies having seizure was 0.5% and with maternal fever was 0.1%. The proportion of preterm babies with poor cry was 2.7%.

Figure 3. Problems in admitted preterm babies



There was a higher proportion of LBW 505 (52.1%) identified in admitted preterms. The proportion of complications of prematurity was 399 (44.1%), neonatal sepsis was 354 (36.5%) and perinatal asphyxia 283 (29.2%). The congenital anomaly was less among co-morbidities in the preterm admission 16 (1.6%). Other problems in preterm babies were 27 (3%) (Figure 3).

Discussion

This study determined the causes of mortality in preterm and LBW newborns and its associated problems. This study showed that the majority (54.2%) of the preterm babies were males. Similar findings were observed in the study conducted by Lao et al where male babies were found to be at higher risk for preterm births.[12] However, a study by Gurung et al which depicted female babies at higher risk of preterm births.[13] In the present study, conditions such as grunting, fast breathing and retraction, cyanosis, jaundice and were significantly associated with causes of admission among preterm babies (p-value < 0.005). Similar findings were observed in the study conducted by Aynalem et al.[14] The complications during preterm admissions were highly variable and prevalent (71.4%) in the current study. There was a higher proportion of LBW (505) (52.1%) identified in admitted preterm. However, this finding was contrasted in another study from our country done in the past.[15] This difference may have been resulted due to different study settings. In the present study, LBW was significantly associated with mortality among preterm babies (p < 0.0001). Similar findings were observed in another study done in our set up by Paudel et al.[16] LBW babies were four times more likely to have mortality among preterm admission in the present study. The study by Vilanova et al also showed similar findings where LBW who was born at 22 to 27 weeks had nearly two times greater risk of death in the first year of life.[17]

Besides LBW, various other associated comorbidities were present among prterem babies in this study. Among all the preterms, 354 (36.5%) had neonatal sepsis, 283 (29.2%) had perinatal asphyxia, and 16 (1.6%) had congenital anomaly as associated comorbidities. Similar findings were found in another study by Shrestha et al.[18] However, in the study by Ajao et al, congenital anomaly was observed to be higher (5.1%) as compared to our

study.[19] This variation could have been resulted as these two studies have been was conducted in different contexts.

The current study showed that co-morbidities such as sepsis and perinatal asphyxia were significantly associated with preterm mortality. Similar findings were observed in the study by Getabelew et al.[20] In this study, there was an increased proportion in mortality among preterm babies as compared to term babies. Similar findings were found in the study by KC et al where preterm infants had 12 times increased risk of neonatal death than term babies.[21] This study has tried to explore the factors related with preterm mortality. However, our study is limited by the fact that it is a retrospective study conducted in a single centre. This study should pave way further in the future for a larger, multi centric studies which would explore into the factors associated with preterm mortality and contribute to reduction of preterm mortality in our country.

Conclusions

Preterms form the major bulk of admissions in NICU. Along with prematurity, various determinants such as LBW, sepsis, perinatal asphyxia are related to preterm mortality. Thus, timely interventions such as early referral of pregnancy with high risk and improvement of antenatal care, quality perinatal and neonatal care, appropriate infection prevention measures can help in reducing preterm mortality in Nepal.

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