Original Research

Influence of Low Birth Weight and Preterm Birth on Morbidity, Mortality and Medication Use among Neonates in Resource Limited Settings: A Prospective Observational Study

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ABSTRACT

Introduction: The birth rate in India is estimated to be 26,932,586 per year. Of these 27 million babies born each year, 1 million babies die before the age of 1 month; India carries the highest share with 30% of global neonatal mortality. Three neonates are dying every minute in India and every fourth baby born has a low birth weight. Low birth weight directly or indirectly contributes to 60- 80% of all neonatal death.

Aim: We aimed to assess the impact of preterm birth and low birth weight on medical conditions, medications use and mortality among neonates in a resource-limited setting.

Methodology: A prospective observational study was conducted at the neonatal intensive care unit (NICU) over 6 months. Neonates of either sex admitted to NICU and who received at least one medication were enrolled in the study. Perinatal and demographic data, reasons for NICU admission, medications prescribed, and discharge status were documented and analysed.

Result: Four hundred and four neonates were included in the study: 61.1% were boys, 38.9% were girls. Respiratory distress syndrome (n=120, 29.7%), neonatal jaundice (60, 14.85%), and sepsis (44, 10.9%) were the most commonly observed conditions and were significantly more common among preterm and low birth weight neonates. Nearly half of the medications prescribed were antibiotics (n=1113, 49.6%). The mean number of medications prescribed to each neonate is 5.5. The mortality rate was significantly higher in extremely preterm and very preterm when compared to term neonates.

Conclusion: Medical conditions, medications prescribed and the mortality rate was significantly higher among preterm and low birth weight neonates admitted in the NICU that are included in the study.

Key Words: Low birth weight, Preterm birth, Mortality, Medication use, Neonates, Resource limited setting

INTRODUCTION

As per WHO, birth before 37 weeks of gestation is defined as preterm birth (PTB) and less than 2500 grams of body weight as low birth weight (LBW). PTB and LBW babies are more prone to severe morbidity and mortality in the neonatal stage.[1]As per WHO estimate globally, 15 million preterm births per year, and India ranked with the highest number of preterm births of 3.5 million approximately.[1,2] As per UNICEF estimate globally 3.9 million infant deaths per year, 1 million deaths (Approximately 25.6%) carried by India.[3,4]Preterm birth complications are the leading cause of death among children under 5 years of age, responsible for nearly one million deaths in 2015. Three neonates are dying every minute in India and every fourth baby born has a low birth weight.[5]directly or indirectly contributes 60–80% of all neonatal deaths. On average, 12% of babies are born preterm in low-income countries compared to 9% in high-income countries. WHO identified that half of the babies born at or below 32 weeks (2 months early) die due to a lack of feasi-

ble and cost-effective care in low-income countries, such as warmth, breastfeeding support, and basic care for infections and breathing difficulties.[2]There is a scantiness of research on outcomes of PTB and LBW in India and no studies in rural recourse limited settings of India. In this context, this study was conducted with an aim to assess the impact of PTB and LBW on morbidity, drug usage, and mortality among neonates in a rural resource-limited setting.

METHODS

A prospective observational study was conducted in a neonatal intensive care unit (NICU) at a rural recourse limited setting of Anantapur district, Andhra Pradesh, India over six months from April 2019 to September 2019. The study was initiated after clearance from the ethics committee (Approval No: RIPER/IRB/PP/2019/06). Irrespective of gender, neonates admitted in NICU were included in the study after taking consent from guardian/parent. Neonates under observation, fluid replacement, nutritional supplements, vaccination and phototherapy without one or more medication use were excluded from the study. The sample size was calculated as 404 using Epi-info 7 das software version 7.2.3.1 (CDSCO, Atlanta, USA) with the assumption of 50% probability, design effect 1, error 5%, CI 95% and 5% non-response rate. Study participants were categorised based on gestational age (GA) as extremely preterm (EPT: Less than 28 weeks), very preterm (VPT: 28-32 weeks), moderate to late preterm (MLPT: 33-37 weeks) and term (More than 37 weeks). Study participants were classified based on birth weight as extremely low birth weight (ELBW: Less than 1000 Grams), very low birth weight (VLBW: 1000-1499 Grams), low birth weight (LBW: 1500-2499 Grams) and normal birth weight (NBW: Equal or more than 2500 Grams). All required data was collected by using a data collection form which consists of demographic details which include name, age, gender, patient ID, birth weight, gestational age, medical condition, medications prescribed including dose, frequency, duration of therapy, route of administration and discharge status of the patient. Graph Pad Prism 3.0 software (San Diego, California, USA) software was used for the statistical analysis. Descriptive statistical analysis for categorical variables was performed by calculating the frequencies and percentages; the chi-square test was used to compare categorical variables. An unpaired t-test was used to compare continuous variables. *p*-value < 0.05 was considered statistically significant.

RESULTS

A total of 404 neonates were included in the study with the mean (SD) age of 8.06 (7.46) days and a median of 6 days. 66.1% were boys, preterm 35.15 %, and 40.1 % underweight as shown in Table 1.

A major reason for the NICU admission was respiratory distress syndrome (RDS) 29.7%, neonatal jaundice 14.85%, sepsis 10.9%, and birth asphyxia 8.4% as shown in Table 2.

Compared to term neonates, RDS and birth asphyxia were significantly higher in very preterm and moderate to late preterm neonates. Compared to normal birth weight neonates, RDS and seizures were significantly higher in very low birth weight and low birth weight, birth asphyxia was significantly higher in very low birth weight neonates as shown in Table 3.

At the time of discharge, out of 404 participants included in study 298 (73.8%) were clinically active and feeding well. The mortality rate was 32 (7.92%), 30 (7.4%) of neonates were discharged against medication and 44 (10.9%) neonates were discharged at a request. Overall death rates in extremely preterm (16.7%) and very preterm (4.34%) were significantly higher compared to term (10.7%) neonates as shown in Table 4.

A total of 2,243 medications were prescribed to all neonates included in the study, on average, each neonate has prescribed 5.5 medications. Of all the medications prescribed 1113 (49.6%) were antibiotics and the remaining 1130 (50.4 %) were non- antibiotics as shown in Table 5. According to the ATC classification system, most of the antibiotics were prescribed for systemic use followed by oral and topical use. Analysis based on the WHO core indicators revealed that an average of 5.5 medications was prescribed per encounter. Among all the medications prescribed 90% of medications were prescribed by generic name and all the medications prescribed among all the neonates included in the study were on the National essential medication list and on the WHO essential medicines list for children.

Table 1: Demographic details of neonates included in the study (N=404)

Variables	Values
Age (days) Mean (SD) Median	
Gender, n (%)	8.06 (7.46)
Boys	6
Girls	
Gestational age (wk)	247 (61.1)
	157 (38.9)
>37 (term) n (%)	
33-37 (moderate-late preterm) n (%)	262 (64.85)
	84 (20.7)
28-32 (very preterm) n (%)	46 (11.38)
<28 (extremely preterm) n (%)	12 (2.97)
Birth weight (g) n (%)	242 (59.9)
≥2500 (normal)	101 (25.0)
2499-1500(LBW)	49 (12.1)
1499-1000(VLBW)	12 (2.97)
<1000(ELBW)	

SD: Standard deviation, LBW: Low birth weight; VLBW: Very low birth weight, ELBW: Extremely low birth weight.

Table 2: Medical conditions of neonates in NICU included in the study (N=404)

Variables	n (%)
RDS (Respiratory Distress Syndrome) NNJ (Neonatal Jaundice)	120 (29.7)
Sepsis	60 (14.85)
Birth Asphyxia Hypoglycemia Tachypnea Seizures	44 (10.9)
MAS(Meconium aspiration syndrome) HIE (Hypoxic-ischemic encephalopathy) Prematurity care	34 (8.4)
Others	28 (6.9)
	26 (6.4)
	14 (3.5)
	12 (3.0)
	10 (2.5)
	33 (8.2)
	23 (5.7)

Table 3: Medical conditions for the NICU admission based on GA, Birth weight, Age

Demographics	N	RDS n (%)	P	NNJ n (%)	P	Sepsis n (%)	P	Birth Asphyxia n (%)	P	Seizures n (%)	P	MAS n(%)	P	HIE n (%)	P
Gestational Age (wks)															
Extreme preterm	12	4 (33.3)	0.123	2 (16.7)	0.5	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0
Very preterm	46	29 (69.6)	<0.001*	6(13.04)	0.6	8 (17.4)	0.15	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0
Moderate -late preterm	84	32 (50)	<0.001*	15 (20.02)	0.09	8 (9.52)	0.5	0 (0.0)	0	4 (4.8)	0.45	4 (1.5)	0.33	2 (0.8)	0.55
Term	262	55(16.03)	Ref	37(13.35)	Ref	28 (10.7)	Ref	34 (13.1)	Ref	10 (3.9)	Ref	8 (3.1)	Ref	8 (3.05)	Ref
Birth weight (g)															
ELBW	12	2 (16.7)	0.64	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0
VLBW	49	40 (81.6)	<0.001*	6 (12.2)	0.26	7 (14.3)	0.4	0 (0.0)	0.0	0(0.0)	0	0 (0.0)	0	0 (0.0)	0
LBW	101	34 (33.7)	0.001*	12 (11.9)	0.133	8 (7.9)	0.2	8 (8.02)	0.28	0 (0.0)	0	4 (1.6)	0.5	2 (0.8)	0.4
Normal	242	42(17.35)	Ref	42 (17.4)	Ref	29 (11.9)	Ref	26 (10.8)	Ref	14 (5.8)	Ref	8 (3.3)	Ref	8 (3.3)	Ref
Age (Days)															
1-10 days	294	98(33.3)	0.065	54 (18.4)	0.422	29 (10)	0.25	26(8.9)	0.9	14 (4.8)	0.47	10(62.5)	0.6	8 (50)	0.65
11-20 days	74	10 (13.5)	0.64	2 (2.7)	0.143	5 (6.75)	0.15	5 (6.8)	0.37	0 (0.0)	0	2 (12.5)	0.7	2 (12.5)	0.7
21-30 days	20	0 (0.0)	0.2	2 (10)	0.61	7 (35.0)	0.24	3 (15.0)	0.16	0 (0.0)	0	0 (0.0)	0.0	0 (0.0)	0
>30 days	16	2 (12.5)	Ref	2 (12.5)	Ref e	3 (18.75)	Ref	0 (0.0)	Ref	0 (0.0)	Ref	0 (0.0)	Ref	0 (0.0)	Ref

ELBW: Extremely low birth weight, VLBW: Very low birth weight, LBW: Low birth weight, GA: Gestational age
*Significant (<0.005)

Table 4: Discharge status based on GA, birth weight and age

Demographics	N	Death n	n%	P	Discharge against medication n	n%	P	Discharge at request n	n%	P	Active & feeding well n	n%	P
Gestational age (wks)													
Extreme preterm	12	2	16.7	<0.001*	0	0	0	10	83.33	<0.001*	0	0	0
very preterm	46	2	4.34	0.04*	15	32.6	<0.001*	10	21.73	<0.001*	19	41.3	<0.001*
moderate -late preterm	84	0	0	0	14	16.7	<0.001*	24	28.6	<0.001*	46	54.7	<0.001*
Term	262	28	10.68	Ref	1	0.38	Ref	0	0	Ref	233	88.9	Ref

Table 4: *(Continued)*

Demographics		Death			Discharge against medication			Discharge at request			Active & feeding well		
	N	n	n%	P	n	n%	P	n	n%	P	n	n%	P
Birth weight (g)													
ELBW	12	2	16.7	0.405	0	0	0.58	0	0	0.96	10	83.3	<0.001*
VLBW	49	0	0	0	19	38.8	<0.001*	28	57.1	<0.001*	2	4.08	0.015
LBW	101	2	2	0	0	0	0	16	15.9	<0.001*	83	82.2	<0.001*
Normal	242	28	11.6	Ref	11	4.54	Ref	0	0	Ref	203	83.9	Ref
Age(Days)													
1-10 days	294	30	10.2	0.19	16	5.44	0.42	24	8.2	0.002*	224	76.2	0.17
11-20 days	74	0	0	0	10	13.5	0.125	10	13.51	0.034*	54	72.9	0.3
21-30 days	20	2	10	0.301	4	20	0.08	4	20	0.214	10	50	0.34
>30 days	16	0	0	Ref	0	0	Ref	6	37.5	Ref	10	62.5	Ref

ELBW: Extremely low birth weight, VLBW: Very low birth weight, LBW: Low birth weight, GA: Gestational age

*Significant (<0.005)

Table 5: Medications prescribed based on GA, birth weight and age

Demographics	N	Medications prescribed		Antibiotics prescribed	
		Number	Percentage	Number	Percentage
Gestational age					
Extremely preterm	12	101	4.5	64	1.05
Very preterm	46	546	24.34	216	19.4
Moderate-late preterm	84	662	29.5	298	26.8
Term	262	934	41.6	535	48.1
Birth weight					
ELBW	12	152	16.8	79	7.1
VLBW	49	402	17.9	162	14.5
LBW	101	708	31.6	308	27.7
NBW	242	981	43.7	564	50.7
Age (days)					
1-10	294	1614	71.9	861	77.4
11-20	74	408	18.2	175	15.7
21-30	20	123	5.5	48	4.3
>30	16	98	4.4	29	2.6

ELBW: Extremely low birth weight, VLBW: Very low birth weight, LBW: Low birth weight, NBW: Normal birth weight
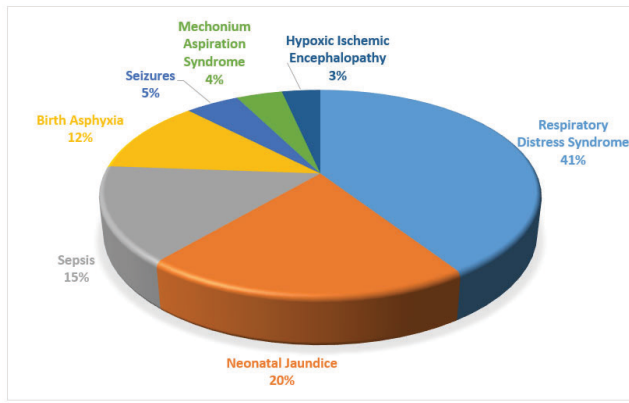
Figure 1: Disease wise distribution.

DISCUSSION

The main objective of this study is to assess the impact of preterm birth and low birth weight on medical conditions, medications use and mortality among neonates. Our study revealed that out of 404 patient's majority of them are baby boys 247(61.1%) and baby girls157 (38.9%). A similar pattern was observed in studies conducted in Central India (59.3%) baby boys and East India (62.5%) baby boys.[5,6] The prevalence of preterm (35.1%) and low birth weight (40.1%) babies in our study were lower compared to a study conducted in Central India (54.8% and 73%, respectively) and higher compared to a study conducted in east India.[5,6]

The most common condition for NICU admission was RDS (Respiratory distress syndrome), followed by sepsis and neonatal jaundice and the most reason was Tachypnoea. RDS was the commonly observed condition among all categories of neonates according to the GA and birth weight.

The majority of neonates in extremely preterm, very preterm and moderate to late preterm categories experience RDS and neonatal jaundice.

The mean number of medications prescribed to neonates in our study was 5.5 medications per neonate and was consistent with published data between 3.7 and 8.6 medications per neonate.[7,8] Majority of the medications prescribed to neonates included in our study were antibiotics. Gentamycin was the most commonly prescribed antibiotic among neonates and a similar pattern was observed in previous studies conducted in the UK, USA, Australia and Germany.[7,9]

The most commonly prescribed off label drugs in NICU were Gentamycin, Ampicillin, Amikacin, Cefotaxime etc. was observed in our study is similar to the studies conducted in NICU, Iran 2019. The choice of antibiotic regimens varies to different hospitals according to their hospital policies.

The overall neonatal mortality rate in our study was 7.9% (32/404). The babies born extremely preterm had the highest mortality rate (16.7%) compared to others. Systematic analysis of Indian data identified that preterm birth complications cause 43.7% of neonatal deaths.[10,11]

The strengths of the present study include the systematic follow up of neonates admitted in NICU to identify the medication utilization and to assess the prevalence and impact of preterm birth and low birth weight and medical conditions, medication use and neonatal mortality.[12,13] Our study provides data about health outcomes and medication use among neonates in NICU in a secondary care hospital serving patients mainly of low socio-economic backgrounds. As this study is a single centred study, our results may be different from outcomes at other hospitals of Andhra Pradesh and Telangana [8,14,15].

CONCLUSION

Respiratory distress syndrome was the most commonly observed medical condition among neonates and associated with the prescribing of more medications especially antibiotics. The mortality rate was higher in birth asphyxia. Medical conditions, medications prescribed and the mortality rate was significantly higher among preterm and low birth weight neonates compared to term and normal weight neonates.

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Conflict of Interest: Nil

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