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Original Article

Prevalence and Determinants of Mortality among Preterm Infants in Jos University Teaching Hospital, Jos, Nigeria

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Abstract

Background: Prematurity is a leading cause of child death globally, a burden that is higher in Sub-Saharan Africa. There is paucity of data on outcomes and trends in prematurity in North-Central Nigeria. This study aimed at determining the mortality rate and factors associated with mortality among preterm infants admitted in a tertiary hospital in Jos, North-Central Nigeria.

Materials and Methods: This was a retrospective cross-sectional study of neonatal admissions in Jos University Teaching Hospital, Jos over a 5 year period. Socio-demographic, obstetric, and neonatal variables were extracted from Unit records. Data analysis was done using SPSS version 21.

Results: A total of 646 (32.8%) preterms out of 1961 admitted neonates were studied. The gestational age ranged from 24 to 36 weeks at birth with 34 (5.6%) aged <28 weeks. The overall mortality rate among preterm was 18.7% (121/646). Sepsis (28.9%), respiratory distress syndrome (20.7%), congenital anomalies (13.2%), and asphyxia (9.9%) were the commonest cause of death. Being delivered at a gestational age <28 weeks (AOR 17.8, 95% confidence interval [CI] 4.7–67.8), 28–31 weeks (AOR 5.19, 1.7–15.9), 5 min APGAR score <7 (AOR=2.59, 95% CI=1.4–4.7), and birth weight <1000g (AOR 3.35, 95% CI=1.4–7.9) were associated with increased risk of mortality.

Conclusion: Prematurity is a major cause of neonatal mortality in our health facility. These deaths are associated with being delivered very premature. Measures aimed at improved infection control, respiratory support and effective neonatal resuscitation could reduce preterm deaths significantly.

Key words: Asphyxia, Birth weight, Cause of death, Infant, Newborn, Prematurity, Sepsis

INTRODUCTION

Globally, each year, an estimated 15 million preterm births (before 37 completed weeks) occur with 1.1 million deaths as a result of complications from prematurity.[1] Sub-Saharan Africa and Asia account for 60% of preterm births and 80% of preterm deaths.[2] The incidence of preterm births appears to be increasing and prematurity is now the leading cause of child death globally.[1] In spite of progress toward achieving global targets of reducing child mortality, prematurity significantly contributed to the non-actualization of the fourth millennial development goal and threatens success of the sustainable development goal. Common causes of mortality in preterm include: Respiratory distress syndrome (RDS), sepsis (including pneumonia), apnea, hypothermia, and jaundice.[3,4]

There exist high inequalities in preterm mortality rates between countries with about half of infants born before 32 weeks in low-income countries dying while half of infants delivered at 24 weeks in high-income countries survive, reflecting weak health systems.[5] Preterm infants born in Sub-Saharan Africa and South-east Asia are 12 times more likely to die than does in developed countries.[5]

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With an estimated 871,000 preterm births and 98,000 mortalities as a direct result of prematurity annually, Nigeria ranks 3rd as country with the highest number of preterm births globally.[6] Prematurity is the third leading cause of child death in Nigeria, after malaria and pneumonia.[6] There is a wide range (5.4–34%) of hospital-based preterm-related deaths in Nigeria which largely represents the method of calculation.[4,7-9] Studies reporting cumulative incidence reported lower values compared to point prevalence. Some studies included stillbirths, those who were discharged against medical advice, or calculated perinatal mortality while others excluded a significant proportion of the target population.[4,7,10] Other factors that may contribute to these differences include: Tier of health care facility, skills of healthcare workers, and availability of specialized facilities and interventions to manage complications such as continuous positive airway pressure (CPAP) machines, surfactants, and incubators for very preterm infants.

There is paucity of data on prematurity in North-Central Nigeria. The available reports included a small number of preterm limiting generalizability.[4] Therefore, this study aims at bridging this gap by determining the prevalence of mortality and evaluating factors associated with mortality amongst preterm in a tertiary hospital in Jos, North-Central, Nigeria.

MATERIALS AND METHODS

This was a retrospective cross-sectional study of all preterm neonates admitted into the Special Care Baby Unit (SCBU) of Jos University Teaching Hospital, Jos, Plateau state, Nigeria, over a 5 year period (between January 1, 2016, and May 31, 2021). During that period, there was a 5-month cumulative period of no neonatal admissions due to industrial actions by health workers. Therefore, 60 months were included in this analysis.

Jos University Teaching Hospital is a 600 bed spaces tertiary hospital located in Jos, Plateau State and serves as the foremost referral center in Plateau State. The hospital receives referral from neighboring states of Bauchi, Nasarawa, Taraba, Benue, and Southern Kaduna, and States with combined human populations of over 20 million (National population Commission). It has a 30 bed SCBU which is manned by three consultant pediatricians, one senior registrar and two pediatric resident. It also has 16 nurses with a minimum of two nurses per shift. The unit has five incubators and introduced improvised CPAP in 2016 for managing neonates with respiratory distress. Other facilities include ten low emission diode phototherapy devices that all provide intensive phototherapy and an irradiance meter.

Data extraction was done by trained research assistant. Data were entered into pre-coded Microsoft Excel spreadsheet. Variables of interest include socio-demographic variables such as maternal age, age, sex, obstetric variables (parity and place of birth), and other characteristics (type of gestation, gestational age, duration of admission, outcome of admission, and diagnosis at outcome). Outcome of admission was either discharge or died (mortality). Patients whose parents signed against medical advice and patients with no information about outcome were excluded from the study. Gestational age was determined by past menstrual period, early ultrasound scan or modified Ballard score. Prematurity was defined as a gestational age <37 completed weeks.

The minimum sample size was calculated using the prevalence formula for proportions of death. Assuming 29% of preterm deaths are due to one of the likely causes of preterm mortality, with a 5% precision and 95% level of confidence, power set at 80% and 15% for incomplete data, 364 preterm were required.[3]

Ethical approval was obtained from the institutional ethics review board of JUTH with ref JUTH/DCS/REC/127/XXX/2239. Dataset was de-identified before data analysis.

Statistical Analysis

Collected data were cleaned and checked for completeness. Data analysis was carried out using IBM's SPSS statistical software version 25 (2017). Baseline characteristics of the sampled population and causes of mortality were presented in frequency tables. Bivariate and multivariate logistic regression was used to determine factors associated with mortality. Independent variables with $P < 0.2$ following bivariate logistic regression were included in the multivariate logistic regression. Crudes odds ratio and adjusted odds ratio situated within 95% confidence interval (95% CI) were used to estimate effect size for bivariate and multivariate logistic regression, respectively. $P < 0.05$ was considered statistically significant.

RESULTS

A total of 1961 admitted neonates were studied of whom 646/1967 (32.8%) were preterm. (Figure 1) Of the 646 preterms hospitalized and treated for various medical and surgical conditions, 302 (50.9%) were male and 490 (75.9) were admitted within 24 h of birth. The gestational age ranged from 24 to 36 weeks with 34 (5.6%) with a gestational age <28 weeks. The modal gestational age was 32–33 weeks (274/603, 45.4%). The mean maternal age was 29.4 ± 6.5 years with 424 (71.3%) being aged 20–34 years. Table 1 describes the characteristics of the studied preterm babies.

Table 1: Characteristics of preterm neonates admitted in JUTH between 2016 and 2020

Variable	*n*	Frequency	Percentage
Age (day)	646		
<1		490	75.9
1–2		72	11.1
≥3		84	13.0
Gestational age (weeks)	603		
<28		34	5.6
28–31		167	27.7
32–33		274	45.4
34–36		128	21.2
Sex	593		
Male		302	50.9
Female		291	49.1
Birth weight (g)	620		
<1000		38	6.1
1000–1499		153	24.7
1500–2499		377	60.8
≥2500		52	8.4
Maternal age (years)	595		
<20		28	4.7
20–34		424	71.3
≥35		143	24.0
Maternal parity	613		
1		221	36.1
1–4		292	47.6
≥5		100	16.3
Type of gestation	639		
Singleton		521	81.5
Multiple		118	18.5
APGAR score at 5 min	412		
<7		108	26.2
≥7		304	73.8
Outcome	646		
Discharge		525	81.3
Death		121	18.7

The all-cause mortality rate in preterm infants was 121/646 (18.7%) and in term infants 114/1321 (8.6%). Complications of prematurity accounted for 51.5% of all neonatal deaths in studied infants. Causes of death were unrecorded in 15(12.4%) infants. Sepsis accounted for 35 (28.9%) deaths, excluding 5 (4.2%) deaths from congenital pneumonia. Other causes of mortality were RDS, asphyxia, and congenital anomalies with 25 (20.7%), 112 (9.9%), and 16 (13.2%), respectively [Table 2].

Bivariate analysis of factors associated with mortality [Table 3] showed that gestational age ($P \leq 0.001$), birth weight ($P \leq 0.001$), maternal parity ($P = 0.031$), and APGAR score at 5 min ($P = 0.001$) were significantly associated with mortality, respectively. There were 22 (64.7%) and 29 (76.3%) deaths in infants delivered at gestational age <28 weeks and 28–31 weeks, respectively. Being delivered at a gestational age of <28 weeks and 28–31 weeks was significantly associated with increased risk of death when compared to those delivered at 34–36 weeks (COR=16.22, 95%CI=6.5–40.2 and COR=2.7, 95% CI=1.4–5.3, respectively). Death was recorded in

Table 2: Causes of mortality in preterm infants in JUTH between 2016 and 2020

Causes of death	Number (*n*=121)	Percentage
Sepsis	35	28.9
Respiratory distress syndrome	25	20.7
Asphyxia	12	9.9
Congenital pneumonia	5	4.2
Congenital anomalies	16	13.2
Neonatal jaundice	3	2.5
Apnea	4	3.2
Anemia	2	1.6
Necrotizing enterocolitis	2	1.6
Disseminated intravascular coagulopathy	1	0.8
Hypoglycemia	1	0.8
Unrecorded	15	12.4

29 (76.3%) and 34 (22.2) infants delivered with a birth weight of <1000 g and 1000–1499 g, respectively. The risk of death was significantly higher in infants with a birth weight of <1000 g (COR=52.6 and 95%CI=13.2–210.2) and 1000–1499 g (COR=4.67 and 95%CI=1.4–15.9) when compared with those with a birth weight ≥2500 g. Infants delivered to multiparous mothers (1–4 deliveries) had a lower risk of death (COR=0.48 and 95%CI=0.3–0.8) when compared with grand multiparous mothers (≥5 deliveries). Infants delivered with an APGAR score of <7 at 5 min had a higher risk of death (COR=2.47 and 95%CI=1.4–4.2) when compared to those with APGAR score ≥7 at 5 min. Age, sex, maternal age, and type of gestation were not associated with mortality.

Multivariate logistic regression of factors with $P < 0.2$ in the bivariate analysis was done in two models [Tables 4A and B] ensuring that both gestational age and birth weight were not included in the same model. This is because gestational age had a high correlation with birth weight. Following multivariate logistic regression, being delivered at a gestational age <28 weeks (AOR 17.8 and 95%CI 4.7–67.8), 28–31 weeks (AOR 5.19 and 1.7–15.9), 5 min APGAR score <7 (AOR=2.59 and 95%CI=1.4–4.7), and birth weight <1000 g (AOR 3.35 and 95%CI=1.4–7.9) were associated with increased risk of mortality. Having a birth weight between 1500 and 2499 g was associated with the lower risk of mortality (AOR 0.71 and 95%CI=0.5–0.9).

DISCUSSION

Findings from our study suggest that prematurity contributes significantly to the burden of neonatal admissions and deaths. Prematurity accounted for nearly a third of neonatal admissions which is similar to reports from tertiary hospitals in India (28.5%), Cameroun (36.6%), Southern Nigeria (24%), and North-Eastern Nigeria (32.9%).[8,11-13] These values are generally higher than those

Table 3: Bivariate analysis of factors associated with mortality among preterm infants admitted in JUTH between 2016 and 2020

Variable	Discharge (%)	Death (%)	Crude odds ratio	95% Confidence interval	*P* value
Age (day)					0.232
<1	399 (81.4)	81 (18.6)	1.37	0.7–2.6	0.346
1–2	54 (75.0)	18 (25.0)	2.00	0.9–4.5	0.094
≥3	72 (85.7)	12 (14.3)	1.00 (Ref)		
Gestational age (weeks)					<0.001*
<28	12 (35.3)	22 (64.7)	16.22	6.5–40.2	<0.001
28–31	128 (76.6)	39 (23.4)	2.70	1.4–5.3	0.004
32–33	231 (84.3)	43 (15.7)	1.65	0.8–3.2	0.138
34–36	115 (89.8)	13 (10.2)	1.00 (Ref)		
Sex					
Male	247 (81.8)	55 (18.2)	1.17	0.8–1.8	0.459
Female	231 (79.4)	60 (20.6)	1.00 (Ref)		
Birth weight (g)					<0.001*
<1000	9 (23.7)	29 (76.3)	52.63	13.2–210.2	<0.001
1000–1499	119 (77.8)	34 (22.2)	4.67	1.4–15.9	0.014
1500–2499	333 (88.3)	44 (11.7)	2.16	0.6–7.2	0.212
≥2500	49 (94.2)	3 (5.8)	1.00 (Ref)		
Maternal age (years)					0.336
<20	24 (85.7))	4 (14.3)	0.97	0.3–3.1	0.956
20–34	340 (80.2)	84 (19.8)	1.44	0.9–2.4	0.174
≥35	122 (85.3)	21 (14.7)	1.00 (Ref)		
Maternal parity					0.031*
1	180 (81.4)	41 (18.6)	0.62	0.4–1.1	0.088
2–4	248 (84.9)	44 (15.1)	0.48	0.3–0.8	0.008
≥5	73 (73.0)	27 (27.0)	1.00 (Ref)		
Type of gestation					
Singleton	425 (81.6)	96 (18.4)	0.89	0.5–1.5	0.631
Multiple	94 (79.7)	24 (20.3)	1.00 (Ref)		
APGAR score at 5 min					
<7	78 (72.2)	30 (27.8)	2.47	1.4–4.2	0.001*
≥7	263 (86.5)	41 (13.5)	1.00 (Ref)		

Ref – reference category, * significant factor ($P < 0.02$)

reporting the cumulative incidence of preterm births which describe the burden of prematurity as a proportion of preterm births, not neonatal admissions.[7,14]

Our study observed a preterm mortality rate of 18.7% giving a survival rate of 81.3% at discharge. The survival rate is similar to 79.4% and 81.3% reported from studies in India and Cameroun but higher than figures from Nepal.[12,15,16] The major difference with the study from Nepal is that they included discharge against medical advice as an outcome which invariably reduced the percentage of infants that survived. Studies that report survival rate as a proportion of all preterm birth generally report higher survival rates.[17] This could be as a result of improved survival among late preterm infants who constitute about 70% of preterm births as a higher proportion of late preterm are expected to have normal extra-uterine transition and are usually discharged from nurseries without being admitted in NICUs or SCBUs.[18,19]

Sepsis, RDS, congenital anomalies, and asphyxia were the commonest identified causes of death in preterm infants studied. While respiratory problems and sepsis have been identified as major causes of mortality in preterm in most studies, fewer studies report asphyxia as a common cause.[8,12,15,16] Congenital anomalies were a common cause of mortality in our study which probably reflects the nature of our facility being a major referral center for Pediatric surgery in North-Central Nigeria. Infants delivered with major congenital anomalies are at higher risk of neonatal death with the risk being even higher if they are delivered premature.[20-22] In a recent study, having a major birth defect increased the risk of mortality ten-fold among very low birth weight infants.[20] Necrotizing enterocolitis (NEC) was identified as the cause of death in 2 (1.6%) of mortalities in our study. This is rather low compared to another study estimating about a quarter of deaths in preterm as a result of NEC.[16] This may be a reflection of a low incidence of NEC in this cohort of preterm infants because NEC has been reported to have one of the highest case fatality rates (up to 66%) in preterm infants.[8] The low incidence of NEC observed in this study may also be limited by the data extraction which underestimated incidence using reported causes of death.

In our study, mortality was significantly higher with decreasing gestational age, being extreme low birth weight and with a

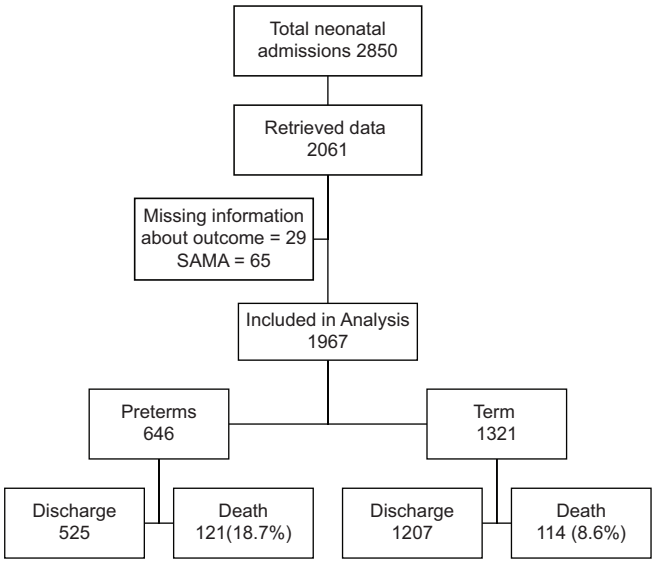

Figure 1: Flow chart of neonates in the study. SAMA: Signed against medical advice

Table 4: Multivariate logistic regression of factors associated with preterm mortality in JUTH between 2016 and 2020

A. (analysis without birth weight)			
Variable	**Adjusted odds ratio**	**95% Confidence Interval**	***P* value**
Gestational age (weeks)			<0.001*
<28	17.80	4.7–67.8	<0.001*
28–31	5.19	1.7–15.91	0.004*
32–33	2.44	0.8–7.5	0.119
34–36	1.00 (Ref)		
Maternal parity			0.021*
1	0.67	0.3–1.5	0.321
2–4	0.35	0.2–0.8	0.008*
≥5	1.00 (Ref)		
APGAR score at 5 min			
<7	2.59	1.4–4.7	0.002*
≥7	1.00 (Ref)		
B. (analysis without gestational age)			
Variable	**Crude odds ratio**	**95% Confidence Interval**	***P* value**
Birth weight (g)			<0.001*
<1000	3.35	1.4–7.9	0.005*
1000–1499	0.90	0.6–1.3	0.590
1500–2499	0.71	0.5–0.9	0.011*
≥2500	1.00 (Ref)		
Maternal parity			0.024*
1	0.71	0.3–1.6	0.390
2-4	0.37	0.2–0.8	0.010*
≥5	1.00 (Ref)		
APGAR score at 5 min			
<7	1.95	1.0–3.7	0.039*
≥7	1.00 (Ref)		

#Due to the strong correlation between birth weight and gestational age, two models (A and B) had to be produced to prevent the reducing effect of either on risk of mortality

5 min APGAR score <7. This is consistent with findings from different studies globally.[15,23-25] A study in East Africa reported that birth asphyxia was 3 times more likely to lead to mortality than RDS.[26] Low APGAR score at five minutes <5 has been used as a proxy for asphyxia and was a significant predictor of death in our study and in keeping with the previous reports.[13,25] Blundell and Chakraborty reported that low 1st and 5th min APGAR scores (<7) were significant predictors of mortality in infants delivered between 28 and 32 weeks but had limited prognostic value in those aged <28 weeks, possibly due to the high mortality in this group.[27] A multicenter study in Nigeria and Kenya identified being delivered very preterm and extreme low birth weight as independent predictors of neonatal mortality.[28] The 76.3% mortality rate reported among ELBW preterm infants was comparable to 80% reported previously among ELBW infants by Shrestha *et al.*[16] However, the mortality rate in extreme preterm infants of 65% obtained in our study was much higher than 28% obtained in South Wales.[29] Thus, reflecting the general observation that mortality in extreme preterm infants may be similar in different setting in LMICs but much higher than reported in high income countries.

Maternal parity of 2–4 was significantly associated with the lower risk of death when compared to being grand multiparous. Being primiparous was not significantly associated with increased mortality. The reason for our findings about parity is not immediate but seems not to differ from a previous report that found no significant association of mortality with sex, maternal age, and parity.[25]

The study was limited by its retrospective nature; therefore, data about certain possible factors such as place of birth, socio-demographic details of parents, and important obstetric history were not analyzed because they were largely unavailable. Furthermore, attributing only one cause of death is rather simplistic than often experienced in clinical practice.

CONCLUSION

Prematurity is a major cause of neonatal admissions and deaths in our facility. Neonatal infections, RDS, and asphyxia account for about half of deaths in the studied preterm infants. Decreasing gestational age, extreme low birth weight, low APGAR, and low APGAR scores are associated with mortality in studied preterm infants. Interventions targeted at preventing extreme prematurity and intrapartum complications are recommended to meet global targets in neonatal mortality.

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