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RESEARCH ARTICLE

Determinants and outcomes of preterm births in Nigerian tertiary facilities

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Abstract

Objective: To describe the incidence, and sociodemographic and clinical factors associated with preterm birth and perinatal mortality in Nigeria.

Design: Secondary analysis of data collected through the Maternal Perinatal Database for Quality, Equity and Dignity (MPD-4-QED) Programme.

Setting: Data from births in 54 referral-level hospitals across Nigeria between 1 September 2019 and 31 August 2020.

Population: A total of 69 698 births.

Methods: Multilevel modelling was used to determine the factors associated with preterm birth and perinatal mortality.

Outcome measures: Preterm birth and preterm perinatal mortality.

Results: Of 62 383 live births, 9547 were preterm (153 per 1000 live births). Maternal age (<20 years – adjusted odds ratio [aOR] 1.52, 95% CI 1.36–1.71; >35 years – aOR 1.23, 95% CI 1.16–1.30), no formal education (aOR 1.68, 95% CI 1.54–1.84), partner not gainfully employed (aOR 1.94, 95% CI 1.61–2.34) and no antenatal care (aOR 2.62, 95% CI 2.42–2.84) were associated with preterm births. Early neonatal mortality for preterm neonates was 47.2 per 1000 preterm live births (451/9547). Father's occupation (manual labour aOR 1.52, 95% CI 1.20–1.93), hypertensive disorders of pregnancy (aOR 1.37, 95% CI 1.02–1.83), no antenatal care (aOR 2.74, 95% CI 2.04–3.67), earlier gestation (28 to <32 weeks – aOR 2.94, 95% CI 2.15–4.10; 32 to <34 weeks – aOR 1.80, 95% CI 1.3–2.44) and birthweight <1000 g (aOR 21.35, 95% CI 12.54–36.33) were associated with preterm perinatal mortality.

Conclusions: Preterm birth and perinatal mortality in Nigeria are high. Efforts should be made to enhance access to quality health care during pregnancy, delivery and the neonatal period, and improve the parental socio-economic status.

KEYWORDS
clinical determinants, mortality, Nigeria, premature births, sociodemographics

For affiliations refer to page 39.

1 | INTRODUCTION

Preterm birth is a complication of pregnancy that incurs short- and long-term medical and financial burdens for affected children and their families, as well as the health-care system.[1,2] Globally in 2020, there were 13.4 million preterm births[3] and about 1.01 million deaths occurred in these preterm neonates.[4] Over 50% of deaths in the newborn period are attributable to preterm births and about two-thirds of the former occur in sub-Saharan Africa.[1,3] In 2020, Nigeria ranked third in global preterm births with 774 100 preterm births and a preterm birth rate of 9.9%%.[3]

Preterm births occur before 37 completed weeks of pregnancy and are sub-categorised into extremely preterm (<28 weeks of gestation), very preterm (28 to <32 weeks of gestation), moderate (32 to <34 weeks of gestation) and late preterm (34 to <37 weeks of gestation).[1] The underlying mechanisms of preterm birth are not clearly understood, but they have been associated with socio-clinical factors such as maternal age, parity, lack of maternal antenatal care (ANC), previous preterm birth, multiple gestation, hypertensive disorders in pregnancy, prolonged prelabour rupture of membranes, and malaria.[2,5,6,7,8] Other reported factors include genetic influences, environmental exposure and infertility treatments.[7] Perinatal deaths, including those attributable to prematurity, reflect poor quality of care received during pregnancy, labour and the early neonatal period.[2,4,9,10,11] Studies conducted in Nigeria have been mainly single-facility-based. Hence, it is necessary to investigate preterm births and their outcomes on a nationwide scale, to identify associated factors and inform the design of programmes to improve outcomes for preterm births.

This study aimed to describe the incidence, and sociodemographic and clinical determinants of preterm birth and mortality among preterm neonates in tertiary hospitals in Nigeria using maternal and perinatal data collected through the Maternal Perinatal Database for Quality, Equity and Dignity (MPD-4-QED) Programme established in 54 referral-level hospitals across Nigeria.

2 | METHODS

This paper is a secondary analysis of data from 76 563 pregnant women collected through the MPD-4-QED Programme.[12] The study was conducted in 54 tertiary hospitals across the six geopolitical zones in Nigeria (Northeast, Northcentral, Northwest, Southeast, Southwest and Southsouth zones) between 1 September 2019 and 31 August 2020. The consenting hospitals (48 public and six private) had in-house specialist obstetricians and neonatologists as well as equipment and appliances to provide tertiary-level care including incubators, monitors and oxygen therapy. The population of the programme comprised all women (and their babies) who were admitted for delivery or on account of complications within 42 days of delivery or termination of pregnancy between 1 September 2019 and 31 August 2020. Data from all women who met the inclusion criteria were collected by specially trained medical records officers using an electronic case report form with information collected from medical files. Audits of perinatal deaths were carried out by neonatologists. The detailed methodology has been published in the primary paper.[12] Relevant data on enrolled women who gave birth in the participating facilities at ≥28 weeks of gestation were extracted from the database and analysed.

2.1 | Statistical analysis

The incidence of preterm birth was calculated as the number of liveborn preterm neonates divided by the total number of live births,[13] at or after 28 weeks of gestation during the study period.

The maternal sociodemographic, and clinical characteristics of the births were described by the gestational age groups (preterm <37 weeks and term) by reporting the absolute and relative frequencies. To test the differences on the characteristics of those women with preterm and term pregnancy, a logistic mixed effect model was used. The model considered the binary outcome 'preterm pregnancy', the characteristic variables as the factor and the hospital as a random effect. The *p* value reported was obtained from the mixed effect model.

Univariable analysis and multivariable models were constructed to evaluate the risk factors associated with preterm birth and mortality on preterm babies (in separate models).

A conceptual hierarchical multivariable model was constructed by the obstetrician and neonatologists involved in the network to identify the possible factors associated with each outcome. According to this conceptual model, the sociodemographic characteristics of the mothers in the first level may directly or indirectly determine all the other factors under study. The second level of the model included previous obstetric characteristics that can be partially explained by sociodemographic factors. The third level gathered variables of the current pregnancy that may be affected by preceding variables. The fourth level included known associated characteristics that directly influence preterm birth (Box 1).

In the univariable analysis each variable of interest was tested one by one. For the multivariate model, all variables at the first level that had evidence of association ($p < 0.05$) with the outcome were kept. The next step was to evaluate which variables in the second level were associated with the outcome with the inclusion of the variables at the first level. Level 1 variables that were associated with the outcome remained in the model regardless of if they continued to be associated or not. Level 2 variables that were associated with outcome at the second level were kept. A similar procedure was repeated for the variables at the third level and the fourth. For both univariate and multivariate strategies, a logistic mixed effect logistic regression model considering the hospital as a random effect was performed.[14] The crude odds ratios (OR) and adjusted odds ratios (aOR) were reported.

BOX 1 Variables tested at each level of the model.

Level 1: maternal age, marital status, maternal level of education, woman's occupation, as well as her partner's occupation.

Level 2: parity, previous caesarean section, previous miscarriage, chronic medical disorder.

Level 3: hypertensive disorders in pregnancy, gestational diabetes, antenatal care booking, referral status.

Level 4: sex of neonate, status of membranes at admission, duration of ruptured membranes, onset of labour, mode of delivery.

3 | RESULTS

A total of 76 563 women were enrolled in the MPD-4-QED Programme. Of these, 69 698 women (and their 72 231 neonates) were admitted for delivery. The gestational ages at delivery were available for 64 189 women and 65 653 neonates. The outcome at 7 days after birth was not documented for four neonates (two preterm and two term), therefore only 65 649 (11 244 preterm and 54 405 term) neonates were included in this secondary analysis.

Of the 65 649 neonates included in the analysis, 3266 (1697 preterm and 1569 term) were stillborn, giving a stillbirth rate of 49.7/1000 total births. Preterm stillbirths accounted for 52% (1697/3266) of all stillbirths. The preterm stillbirth rate was 151 per 1000 preterm births (1697/11 244) and the term stillbirth rate was 29 per 1000 term births (1569/54 405).

From the total 62 383 live births, 9547 were preterm, giving a preterm birth rate of 153 per 1000 live births. A total of 762 neonates (451 preterm and 311 term) had died by day 7 after birth, giving an overall early neonatal mortality rate of 12.2 per 1000 total live births (762/62 383). The preterm neonatal mortality rate was 47.2 per 1000 live births (451/9547). The early neonatal deaths in addition to the stillbirths gave a total of 4028 (2148 preterm and 1880 term) perinatal deaths and a perinatal mortality rate of 61.4 per 1000 total births. Preterm perinatal deaths accounted for 53.3% (2148/4028) of all perinatal deaths. The preterm perinatal mortality rate was 191 per 1000 preterm births (2148/11 244) compared with term perinatal mortality rate of 34.6 per 1000 total term birth (1880/54 405).

Mothers of preterm neonates were more likely to be at the extremes of reproductive age (<20 or ≥35 years), without formal education and not gainfully employed compared with mothers of term neonates, as shown in Table 1. Table 2 shows the obstetric characteristics of the study population. More women with preterm babies had hypertensive disorders in pregnancy (17.9% versus 5.3%), had no ANC (16.7% versus 7.2%) and were referred (27% versus 8.7%) compared with women with term babies.

The clinical characteristics more common in the preterm births were twin pregnancy (8.6% versus 2.1%), emergency caesarean delivery (30.5% versus 19.0%) and duration of

TABLE 1 Maternal sociodemographic characteristics by gestational age at delivery for women who had a live birth ($n = 64\,189$ women).

Characteristics	Preterm births ($N = 10\,435$)		Term births ($N = 53\,754$)		*p* value
	n	%	*n*	%	
Age					
<20 years	569	5.5	1441	2.7	<0.001
20–34 years	8083	77.5	44 273	82.4	
>=35 years	1783	17.1	8040	15.0	
Marital status					
Single	150	1.4	528	1.0	<0.001
Married/cohabiting	10 236	98.1	52 977	98.6	
Separated/divorced	23	0.2	55	0.1	
Widowed	2	0.0	6	0.0	
Missing data	24	0.2	188	0.3	
Educational level					
No formal education	1450	13.9	4193	7.8	<0.001
Primary education	520	5.0	1613	3.0	
Secondary education	4199	40.2	20 577	38.3	
Completed post-secondary education	3627	34.8	24 307	45.2	
Missing data	639	6.1	3064	5.7	
Women's occupation					
Not gainfully employed	4146	39.7	18 546	34.5	<0.001
Professional/technical/managerial	2126	20.4	13 710	25.5	
Sales/trading	2428	23.3	12 838	23.9	
Manual labour/other	1541	14.8	7599	14.1	
Missing data	194	1.9	1061	2.0	
Partner's occupation					
Not gainfully employed	176	1.7	488	0.9	<0.001
Professional/technical/managerial	3554	34.1	24 630	45.8	
Sales/trading	2830	27.1	13 785	25.6	
Manual labour/other	3408	32.7	12 950	24.1	
Missing data	467	4.5	1901	3.5	

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TABLE 2 Obstetrics characteristics by gestational age at delivery for women who had a live birth ($n = 64\,189$ women).

Previous obstetric characteristics	Preterm delivery ($N = 10\,435$)		Term delivery ($N = 53\,754$)		p value[a]
	n	%	*n*	%	
Parity					
Nulliparous (0)	3096	29.7	16 322	30.4	<0.001
Multiparous (1–4)	6228	59.7	33 442	62.2	
Grand multipara (5 or more)	1111	10.6	3988	7.4	
Missing data	–	0.0	2	0.0	
Previous caesarean section[b]					
No	5481	74.7	28 647	76.5	0.150
Yes	1582	21.6	7706	20.6	
Missing data	276	3.8	1079	2.9	
Previous miscarriage					
No	7337	70.3	38 475	71.6	<0.001
Yes	2918	28	14 484	26.9	
Missing data	180	1.7	795	1.5	
Pre-existing medical disorder[c]					
No	9293	89.1	48 865	90.9	<0.001
Yes	1050	10.1	4331	8.1	
Missing data	92	0.9	558	1.0	
Current pregnancy					
Hypertensive disorders in pregnancy[d]					
No	8477	81.2	50 191	93.4	<0.001
Yes	1871	17.9	2873	5.3	
Missing data	87	0.8	690	1.3	
Gestational diabetes					
No	10 280	98.5	52 867	98.3	<0.001
Yes	68	0.7	197	0.4	
Missing data	87	0.8	690	1.3	
Antenatal care					
No antenatal care	1747	16.7	3874	7.2	<0.001
ANC at the same facility	5624	53.9	43 543	81	
ANC at another health facility	2925	28	5692	10.6	
ANC with traditional birth attendant or informal setting	61	0.6	164	0.3	
Missing data	78	0.7	481	0.9	
Booking gestational age					
<13 weeks	620	5.9	4061	7.6	<0.001
13–26 weeks	2972	28.5	22 432	41.7	
>26 weeks	1701	16.3	14 364	26.7	
Missing data[e]	5142	49.3	12 897	24	
Referral status					
Not referred or self-referred	7519	72.1	48 749	90.7	<0.001
Referred from public or private hospital	2816	27	4696	8.7	
Referred from informal setting	99	0.9	308	0.6	
Missing data	1	0.0	1	0.0	

[a] p-value obtained from the mixed model.

[b] Only multiparous women were considered.

[c] Pre-existing hypertension, pre-existing diabetes, asthma, sickle cell anaemia, tuberculosis, HIV/AIDS, hepatitis, cardiac disease, renal disease, thyroid disease, epilepsy or other medical disorder.

[d] Woman had at least one of the following: gestational hypertension, pre-eclampsia, eclampsia at time of admission.

[e] Missing data corresponded to women who did not have antenatal care at the same facility.

rupture of fetal membranes >18 hours (14.9% versus 7.2%). With regards to birthweight, 54.1% of preterm neonates compared with 6.2% of the term neonates were in the low birthweight category (<2500 g; as detailed in Appendix A in Appendix S1).

In the group of preterm neonates, the median gestational age and weights at birth (with interquartile range [IQR]) were 35 (IQR 32–36) weeks and 2300 (IQR 1700–2900) grams, respectively. Most of the deliveries were late preterm deliveries (64.6%), while 19% and 16.4% were moderate and very preterm deliveries, respectively. Appropriateness of growth by gestational age was assessed for neonates at ≥33 weeks of gestation ($n = 8158$) using INTERGROWTH-21st standards and 17.3% of these preterm neonates were small for gestational age while 18.7% were large for gestational age.[15]

The male:female ratio was 1.02:1 for preterm neonates and 1.08:1 for the term neonates. Of the live births, 3429 (36.0%) of the 9547 preterm live births compared with 4761 (9.1%) of the 52 426 term live births were admitted into special care baby units (410 term neonates had no information on special care baby unit admission; details in Appendix B in the Appendix S1).

As shown in Table 3, the odds of preterm birth were highest among mothers aged <20 years (aOR 1.52, 95% CI 1.36–1.71; $p < 0.001$) with no formal education (aOR 1.68, 95% CI 1.54–1.84; $p < 0.001$) and with a partner not gainfully employed (aOR 1.94, 95% CI 1.94–2.34; $p < 0.001$). Additionally, having a chronic medical disorder (aOR 1.29, 95% CI 1.19–1.39; $p < 0.001$), hypertensive disorders in pregnancy (aOR 2.48, 95% CI 2.31–2.66; $p < 0.001$), gestational diabetes (aOR 2.06, 95% CI 1.53–2.77; $p < 0.001$), lack of ANC (aOR 2.62, 95% CI 2.42–2.84; $p < 0.001$) or ANC outside the place of birth (aOR 2.6, 95% CI 2.39–2.83; $p < 0.0001$) and being referred from public or private hospital (aOR 1.43, 95% CI 1.32–1.55; $p < 0.001$) were significantly associated with preterm birth.

Table 4 shows the factors associated with early neonatal mortality in live-born preterm neonates. The multivariable model found that the mother's partner's occupation, her parity as well as hypertensive disorders in pregnancy, ANC booking, mode of delivery, gestational age and baby's birthweight were associated with early neonatal death. The odds of having an early neonatal death were higher among those who were very preterm as well as moderately preterm (aOR 2.94, 95% CI 2.15–4.01; $p < 0.001$; aOR 1.80, 95% CI −1.33 to 2.44; $p < 0.001$, respectively). The odds were also higher for mothers who had an instrumental vaginal delivery (aOR 5.15, 95% CI 2.22–11.96; $p < 0.001$), did not have ANC (aOR 2.74; 95% CI 2.04–3.67; $p < 0.001$) or had ANC outside the place of birth (aOR 2.67, 95% CI −2.08 to 3.42 and $p < 0.001$).

4 | DISCUSSION

4.1 | Main findings

The incidence of preterm births and preterm perinatal mortality in the current study was high, The identified factors that were associated with preterm births and associated perinatal mortality included extremes of maternal age (<20 and >35 years), no ANC, no formal maternal education, referral from other facility and father who was unemployed or an unskilled labourer.

Nigeria is the third highest contributor to preterm births globally after India and Pakistan,[4] and this is reflected in the findings in this study. The preterm birth rate in this study is higher than the global figure of 9.9%, and 10.1% in Sub-Saharan Africa in 2020.[4] The rate is also higher than the rates reported in a multi-country survey for Ghana (3.2%), Tanzania (4.9%), Zambia (7.4%) and Bangladesh (11.7%).[16] Earlier studies among singleton deliveries in Nigeria had reported comparable rates of 16.9% and 16.8%.[2,17] Possible factors responsible for the high preterm birth rate in Nigeria include poor use of ANC facilities and high incidence of hypertensive disorders in pregnancy.

Various risk factors for preterm birth have been reported.[18-20] Younger and advanced maternal ages were associated with preterm birth in this study and other studies.[21,22] Younger mothers can also be at risk due to the increased likelihood of factors identifiable with preterm labour such as low socio-economic status, unmarried, poor educational level and anaemia.[23] Other studies reported an association with advanced maternal age alone.[24-26] This has been associated with adverse obstetric outcomes such as hypertension and gestational diabetes, which are also risk factors for preterm birth.[27-29] Contrary to our study, Wagura et al. in Kenya reported that maternal age <20 years was protective for preterm birth.[6] However, the authors admitted that the small number of young women in their study may possibly explain their findings.

Preterm birth was higher among mothers who were unemployed and single or divorced compared with those who were employed or married/cohabiting. Employment may indicate a favourable socioe-conomic status contrary to unemployment which may limit access to health care due to financial constraints. These factors have been reported as maternal risk factors for preterm birth.[2,30] Female empowerment and health insurance will help ameliorate the effect of these factors on the neonate. Other factors associated with preterm birth in this study were hypertensive disorders and gestational diabetes, similar to findings in other studies.[31,32]

The overall perinatal mortality rate of 61.4 per 1000 births was higher than the 40.9 reported in a 2019 meta-analysis in Sub-Saharan Africa.[33] The present study was in referral hospitals, hence referrals of complex cases and late presentation could account for the high rate reported. About 80% of perinatal deaths in the current study were stillbirths with similar distribution among the preterm and term cohorts. Stillbirths are therefore an important contributor to perinatal mortality, and they must be audited as highlighted by the key global stakeholders.[34] The contribution of preterm neonates to the overall perinatal mortality (53.3%) recorded in this study is high. This may be due to the timing of preterm mortalities. Sankar et al.[35] in a systematic review reported that 83% of

TABLE 3 Associated maternal characteristics for preterm delivery (64 189 women).

	Unadjusted OR (95% CI)	*p* value[a]	Adjusted OR (95% CI)[b]	*p* value[a]
Age				
<20 years	1.89 (1.70–2.10)	<0.001	1.52 (1.36–1.71)	<0.001
20–34 years	1		1	
≥35 years	1.21 (1.15–1.28)		1.23 (1.16–1.30)	
Marital status				
Single/Separated/Divorced/Widowed	1	<0.001	–	–
Married/cohabiting	1.44 (1.21–1.71)			
Woman's education level				
No formal education	2.2 (2.02–2.39)	<0.001	1.68 (1.54–1.84)	<0.001
Primary education	1.88 (1.69–2.10)		1.52 (1.36–1.69)	
Secondary education	1.34 (1.28–1.41)		1.20 (1.14–1.27)	
Completed post-secondary education	1		1	
Woman's occupation				
Not gainfully employed	1.26 (1.19–1.34)	<0.001	–	–
Professional/technical/managerial	1			
Sales/trading	1.23 (1.16–1.31)			
Manual labour/other	1.32 (1.23–1.42)			
Partner's occupation				
Not gainfully employed	2.13 (1.78–2.56)	<0.001	1.94 (1.61–2.34)	<0.001
Professional/technical/managerial	1		1	
Sales/trading	1.37 (1.30–1.45)		1.29 (1.22–1.36)	
Manual labour/other	2.07 (1.96–2.19)		1.87 (1.76–1.98)	
Parity				
Nulliparous (0)	1.01 (0.97–1.06)	<0.001	–	–
Multiparous (1–4)	1			
Grand multipara (5 or more)	1.27 (1.17–1.37)			
Previous caesarean section[c]				
No	1	0.150	–	–
Yes	1.05 (0.98–1.11)			
Previous miscarriage				
No	1	<0.001	–	–
Yes	1.10 (1.05–1.16)			
Chronic medical disorder[d]				
No	1	<0.001	1	<0.001
Yes	1.26 (1.17–1.35)		1.29 (1.19–1.39)	
Hypertensive disorders in current pregnancy[e]				
No	1	<0.001	1	<0.001
Yes	3.44 (3.23–3.67)		2.48 (2.31–2.66)	
Gestational diabetes				
No	1	<0.001	1	<0.001
Yes	2.02 (1.55–2.64)		2.06 (1.53–2.77)	
Antenatal care booking (ANC)				
No antenatal care	3.56 (3.32–3.8)	<0.001	2.62 (2.42–2.84)	<0.001
ANC at the same facility	1		1	
ANC at another health facility	3.9 (3.69–4.12)		2.60 (2.39–2.83)	
ANC with TBA or informal setting	3.23 (2.4–4.36)		2.50 (1.80–3.46)	

(Continues)

TABLE 3 (Continued)

	Unadjusted OR (95% CI)	*p* value[a]	Adjusted OR (95% CI)[b]	*p* value[a]
Referral status				
Not referred or self-referred	1	<0.001	1	<0.001
Referred from public or private hospital	3.68 (3.48–3.88)		1.43 (1.32–1.55)	
Referred from informal setting	2.31 (1.83–2.90)		0.91 (0.71–1.18)	
Associated characteristics of preterm births				
Sex				
Male	0.93 (0.90–0.97)	0.001	–	–
Female	1			
Duration of ruptured of membrane[f]				
<18 h	1	<0.001	1	<0.001
>= 18 h	1.79 (1.50–2.14)		1.46 (1.20–1.78)	
Onset of labour				
Spontaneous	1	<0.001	–	–
Induction	1.51 (1.36–1.67)			
No labour	1.16 (1.08–1.24)			
Mode of delivery				
Spontaneous vaginal	1	<0.001	1	0.001
Assisted vaginal (instrumental)	1.71 (1.34–2.18)		1.03 (0.51–2.08)	
Emergency caesarean section	1.20 (1.12–1.28)		2.48 (1.56–3.93)	
Elective caesarean section	2.08 (1.98–2.19)		0.90 (0.76–1.08)	

[a]p-value obtained from the mixed model.

[b]The odds ratio reported is adjusted by the significant variables at the same level and the significant variables at the previous levels.

[c]Only multiparous women were considered.

[d]Pre-existing hypertension, pre-existing diabetes, asthma, sickle cell anaemia, tuberculosis, HIV/AIDS, hepatitis, cardiac disease, renal disease, thyroid disease, epilepsy or other medical disorder.

[e]Woman had at least one of the following: gestational hypertension, pre-eclampsia, eclampsia at time of admission.

[f]Only women with ruptured membrane at time of admission were included in denominator. In the multivariable model, the group with no rupture of membrane were included but the category for this variable was not shown.

prematurity-related deaths occurred in the first week of life in low- and middle-income countries. This highlights the need to improve the quality of care during the antenatal period, birth and first week of life as recommended in the Every Newborn Action Plan.[36,37]

Women who had ANC at the same facility as the birth had decreased odds of preterm birth and neonatal mortality. This finding may be a result of the benefits of ANC in the early detection and management of hypertensive disorders in pregnancy and other clinical conditions at risk of preterm birth. A cross-sectional analysis of the quality of ANC in Nigeria comparing primary, secondary and tertiary health facilities in the detection of hypertensive disorders showed a worse performance in the former compared with the latter.[38] Late referrals may explain the influence of ANC outside the participating hospitals, as many mothers in the main study who were referred presented with life-threatening conditions.[12] This brings to the forefront the need to strengthen the two-way referral systems that will be beneficial to reducing the preterm complications as well as continued training of healthcare professionals, especially at primary and secondary levels.

Hypertensive disorders in pregnancy are associated with poor outcomes for mother and newborn and proper management is required to mitigate these. The odds of perinatal mortality for instrumental delivery were five times more than for spontaneous delivery. This could be because most of the mothers were very ill and had pregnancy complications necessitating assisted delivery. In a similar survey that investigated the outcomes of preterm birth by mode of delivery, caesarean delivery compared with vaginal birth was associated with increased neonatal intensive care unit admission, but significantly decreased odds of intrapartum stillbirth and perinatal death.[39]

The association of lower birthweight and gestational age with higher perinatal mortality among the preterm neonates is expected as smaller and more immature neonates are prone to more complications. It is therefore necessary for the government to invest in low-cost, minimum package equipment such as bilirubinometer, continuous positive airway pressure devices, radiant warmer, neonatal suction machines, oxygen concentrators and multiparameter monitors, in addition to training of personnel for care of these neonates.[40]

TABLE 4 Associated maternal characteristics with neonatal deaths among live born preterm births ($N = 9547$).

	n/N	Mortality rate	Unadjusted OR (95% CI)	*p*-value[a]	Adjusted OR (95% CI)[b]	*p*-value[a]
Age						
<20 years	15/507	3.0%	0.60 (0.35–1.01)	0.119	–	–
20–34 years	347/7396	4.7%	1			
≥35 years	89/1644	5.4%	1.07 (0.84–1.37)			
Marital status						
Single/Separated/Divorced/ Widowed	4/149	2.7%	1	0.190	–	–
Married/cohabitating	447/9375	4.8%	0.52 (0.19–1.39)			
Missing data	23/9547	0.2%				
Woman's education level						
No formal education	57/1053	5.4%	1.38 (0.95–2.01)	0.369	–	–
Primary education	17/427	4.0%	1.02 (0.60–1.71)			
Secondary education	178/3920	4.5%	1.12 (0.89–1.40)			
Completed post-secondary education	168/3573	4.7%	1			
Missing data	574/9547	6.0%				
Woman's occupation						
Not gainfully employed	148/3541	4.2%	0.96 (0.72–1.28)	0.200	–	–
Professional/technical/ managerial	100/2121	4.7%	1			
Sales/trading	121/2324	5.2%	1.25 (0.95–1.65)			
Manual labour/other	72/1387	5.2%	0.95 (0.69–1.32)			
Missing data	174/9547	1.8%				
Partner's occupation						
Not gainfully employed	8/136	5.9%	1.34 (0.63–2.83)	0.007	1.34 (0.63–2.83)	0.007
Professional/technical/ managerial	140/3443	4.1%	1		1	
Sales/trading	109/2601	4.2%	1.17 (0.90–1.52)		1.17 (0.90–1.52)	
Manual labour/other	179/2945	6.1%	1.52 (1.20–1.93)		1.52 (1.20–1.93)	
Missing data	422/9547	4.4%				
Parity						
Nulliparous (0)	123/2943	4.2%	0.85 (0.68–1.05)	0.010	0.85 (0.68–1.06)	0.020
Multiparous (1–4)	275/5774	4.8%	1		1	
Grand multipara (5 or more)	53/830	6.4%	1.45 (1.05–1.99)		1.39 (1.00–1.93)	
Hypertensive disorders in pregnancy[c]						
No	335/7925	4.2%	1	<0.001	1	0.009
Yes	116/1528	7.6%	1.60 (1.28–2.00)		1.37 (1.02–1.83)	
Missing data	94/9547	1.0%				
Antenatal care booking (ANC)						
No antenatal care or informal setting	103/1363	7.6%	2.72 (2.07–3.57)	<0.001	2.74 (2.04–3.67)	0.000
ANC at the same facility	153/5640	2.7%	1		1	
ANC at another health facility	194/2468	7.9%	2.69 (2.13–3.40)		2.67 (2.08–3.42)	
Missing data	76/9547	0.8%				

(Continues)

TABLE 4 (Continued)

	n/N	Mortality rate	Unadjusted OR (95% CI)	*p*-value[a]	Adjusted OR (95% CI)[b]	*p*-value[a]
Referral status						
Not referred or self-referred	244/7137	3.4%	1	<0.001	–	–
Referred from public or private hospital	202/2335	8.7%	2.38 (1.93–2.93)			
Referred from informal setting or other	5/74	6.8%	1.75 (0.69–4.41)			
Missing data	1/9547	0.0%				
Duration of ruptured of membrane[d]						
<18 h	34/884	3.8%	1	0.030	–	–
≥18 h	17/208	8.2%	2.05 (1.07–3.92)			
Missing data	8455/9547	88.6%				
Onset of labour						
Spontaneous	241/6115	3.9%	1	0.035	–	–
Induction	18/225	8.0%	1.64 (0.99–2.73)			
No labour	42/1364	3.1%	0.77 (0.54–1.08)			
Missing data	1843/9547	19.3%				
Mode of delivery						
Spontaneous vaginal	159/4751	3.3%	1	<0.001	1	<0.001
Assisted vaginal (instrumental)	11/60	18.3%	5.9 (2.96–11.79)		5.15 (2.22–11.96)	
Emergency caesarean section	235/3247	7.2%	0.87 (0.61–1.24)		1.22 (0.82–1.83)	
Elective caesarean section	42/1363	3.1%	1.87 (1.51–2.32)		1.89 (1.48–2.40)	
Missing data	126/9547	1.3%				
Gestational age in weeks						
≥28 and <32	226/1507	15.0%	8.98 (7.12–11.32)	<0.001	2.94 (2.15–4.01)	<0.001
≥32 and <34	94/1517	6.2%	3.18 (2.42–4.18)		1.80 (1.33–2.44)	
≥34 and <37	131/6523	2.0%	1		1	
Birth weight in grams						
≥500 and <1000	55/151	36.4%	50.89 (32.51–79.66)	<0.001	21.35 (12.54–36.33)	<0.001
≥1000 and <1500	165/950	17.4%	18.35 (13.24–25.44)		7.51 (5.01–11.25)	
≥1500 and <2500	172/3733	4.6%	3.99 (2.92–5.45)		2.60 (1.85–3.64)	
≥2500 and <4000	56/4569	1.2%	1		1	
≥4000	3/140	2.1%	1.59 (0.50–5.09)		1.41 (0.43–4.58)	
Missing data	4/9547	0.0%				

[a]p-value obtained from the mixed model.
[b]The odds ratio reported is adjusted by the significant variables at the same level and the significant variables at the previous levels.
[c]Woman had at least one of the following: pregnancy induced hypertension, pre-eclampsia, eclampsia at time of admission.
[d]Only women with ruptured membrane at time of admission were included in denominator.

4.2 | Strengths and limitations

The major strengths of this study are the national coverage it has, with participating hospitals from all six geopolitical zones in the country, as well as the large number of study participants involved, which included all women admitted for birth (healthy women and women with complications). These give information that can be used for planning of interventions on a national basis.

One limitation of this study is that out-born neonates were excluded, potentially under-estimating the number of preterm neonates and the perinatal mortality. In addition to this, differences in clinical procedures between the large number of hospitals that participated in the study may have affected the preterm outcomes observed. This study was tertiary-hospital-based, so is not representative of lower levels of care where over 60% of deliveries occur outside the hospital.[41] There was around 8% missing data on gestational at birth and 0.003%

missing data on vital status at discharge (or 7 days after birth). Infants with missing gestational age may have been preterm, thus underestimating the true preterm rate.

4.3 | Interpretation

Hypertensive disorders in pregnancy, lack of ANC at tertiary and specialist hospitals, as well as late referrals are major contributors to the high preterm perinatal mortality in this study. Although the reasons for these were not studied, inadequate healthcare worker training at lower levels of care, and socio-economic factors like poverty may be contributory and ultimately affect neonatal outcomes.[42]

5 | CONCLUSION

Preterm birth and perinatal mortality rates in Nigeria are still unacceptably high. Concerted efforts should be put in place to increase access to quality antenatal, labour and delivery care, as well as neonatal care. In addition, training and re-training of healthcare providers particularly at the primary and secondary care levels on early identification of high-risk pregnancies to facilitate early referral for adequate care is of utmost importance. Finally, further studies to identify the cause of stillbirths, when and how they occur are important to reduce preterm perinatal mortality and ultimately reduce overall neonatal mortality. These are important in moving Nigeria towards achieving the Sustainable Development Goal 3 of reducing child deaths by 2030.

AUTHOR CONTRIBUTIONS

All authors were involved in data collection for the study, the development of the concept note for the analysis, and the interpretation of the results (through a series of virtual meetings). IF, ID and ZI wrote the first draft of the manuscript. All authors reviewed the draft and approved the final version of the manuscript for publication.

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CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY STATEMENT

All relevant data are within the manuscript and its Supporting information files.

ETHICS STATEMENT

The scientific content of the study was approved by the WHO Human Reproduction Programme (HRP) Research Project Review Panel (protocol ID, A65930, 06 May 2018). WHO Ethics review committee (ID A65930, 5 June 2018) and the Nigerian National Health Research and Ethics Committee approved the study (ID NHREC/01/01/2007, 5 September 2018). Authorities of all participating hospitals granted written institutional approval to participate in the programme's data collection, periodic analyses and reporting.

CONSENT FOR PUBLICATION

Individual-level written consent was not required as the study did not involve direct interaction with women or their babies, or interview of medical staff.

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The funders did not play any role in the study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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