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Original Article

Neonatal Outcomes of Preterm Pre-Eclampsia in a Tertiary Hospital in Northern Nigeria

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ABSTRACT

Background: Preterm birth and preeclampsia (PE) significantly contribute to neonatal mortality, which is unacceptably high in Nigeria. The risks faced by a neonate become compounded if delivered prematurely to halt the progression of PE. This study aimed to determine the neonatal outcomes and associated factors in preterm neonates of mothers with PE in a Nigerian tertiary hospital.

Materials and methods: A descriptive, retrospective one-year review of neonates born to women with preterm preeclampsia who were managed in the inborn Neonatal Unit of the Ahmadu Bello University Teaching Hospital, Zaria. The case folders were identified, and relevant information was extracted. The data were analyzed using SPSS version 21, and $p < 0.05$ was considered significant for test of association.

Results: Forty-seven neonates were studied. The mean birth weight of the neonates was $1.6\text{kg} \pm (0.43)$, mean gestational age at delivery was 32.9 weeks (± 2.2), and 83% were delivered via caesarean section. Neonatal jaundice (72.5%), neonatal sepsis (72.3%), respiratory distress syndrome (40.4%) and anaemia (36.2%) were the leading morbidities. Birth weight was associated with neonatal mortality ($p=0.004$). Mortality was increased by about three and eleven-fold in neonates born at <32 weeks of gestation and in those that weighed $<1500\text{g}$ (OR 3.1, 95% CI 0.7-

13.3; OR 10.8, 95% CI 1.9-59.8) respectively. Birth asphyxia and respiratory distress syndrome were more likely to occur in neonates delivered vaginally ($p=0.02$ OR 7.6, 95% CI 1.5-39.6 and $p=0.04$ OR 6.0, 95% CI 1.0-33.9) respectively.

Conclusion: Vaginal delivery among mothers with preeclampsia was associated with birth asphyxia and respiratory distress syndrome. Very preterm gestation, very low birth weight and vaginal delivery increased the risk of neonatal mortality. The study highlights the compounded risks faced by preterm neonates of mothers with PE and underscores the need for advanced neonatal care to improve survival rates.

Key words: preterm, preeclampsia, neonatal outcomes, mortality, pregnancy complications

INTRODUCTION

Globally, 13.4 million neonates are born preterm.^[1] Preterm birth complications are the leading cause of neonatal deaths globally and contribute significantly to under-5 mortality. These complications are associated with long-term physical, neurodevelopmental, and socio-economic problems as well as early onset of chronic diseases.^[2] Two-thirds of the world's births occur in Asia and Sub-Saharan Africa, with Nigeria ranking third among the countries with the highest number of preterm births globally.^[2] Prematurity accounts for over 40% of neonatal

deaths in Nigeria.^[3] The northwest zone in Nigeria has the highest neonatal death rate, reported at 47 per 1000 births in Kaduna state.^[4] The risk factors for preterm births include hypertensive disorders of pregnancy, multiple gestation, prolonged rupture of membranes, antepartum haemorrhage and maternal medical comorbidities.^[1]

Preeclampsia, which complicates about 13% of pregnancies in sub-Saharan Africa (SSA)^[5] is a globally recognised leading cause of maternal mortality and a significant contributor to neonatal morbidity and mortality and preterm birth.^{[6],[7]} Dassah et al reported PE doubled the odds of preterm birth in an African setting, and McKenzie et al found PE to increase the risk of all neonatal complications compared to neonates of mothers without PE.^{[8],[9]} Sule-Odu et al reported that more than half of neonates of mothers with PE were delivered prematurely in a tertiary hospital in southern Nigeria.^[10] Delivery is a cardinal principle in the management of PE; thus, when preterm, the neonates are faced with compounded risks due to both prematurity and the effects of PE which may result in intrauterine growth restriction and placental insufficiency, low birth weight, prematurity and complications such as respiratory distress syndrome, and increase need for neonatal intensive care.^[11]

Preterm neonates often require advanced neonatal care, which is not widely available in most healthcare facilities in resource-poor settings.^[12] Despite the recognized association between preeclampsia and adverse neonatal outcomes, there is limited research specifically focusing on the neonatal outcomes of preterm preeclampsia in Nigeria. Understanding the specific risks and outcomes may help healthcare providers optimize the care provided to both mothers and neonates, ultimately reducing the burden of neonatal morbidity and mortality in Nigeria. Thus, this study aimed to determine the neonatal outcomes and factors associated with neonatal morbidity and mortality in neonates of mothers with preterm PE in a Nigerian tertiary hospital.

MATERIALS AND METHOD

The study was a retrospective study of neonates of mothers with PE who delivered at the Ahmadu Bello University Teaching Hospital (ABUTH) Zaria and were admitted to the neonatal unit in the department of paediatrics from August 2020 to July 2021.

The neonatal unit is a 30-bed unit divided into inborn (neonates delivered in the facility) and outborn (neonates delivered outside ABUTH) sections. The facility serves the metropolis and receives referrals from other primary and secondary facilities in Zaria and its environs, Kaduna state capital and neighbouring states like Katsina, Kano and Zamfara. The neonatal unit offers a wide range of neonatal services, including continuous positive airway pressure (CPAP), exchange blood transfusion (EBT) and kangaroo mother care (KMC). The unit has an average monthly admission of 80 neonates.

The medical records of the neonates of mothers with PE who delivered at ABUTH and were admitted, were retrieved from the Hospital Medical Record Department, and relevant data, which included neonates' gestational age, sex, birth weight, morbidities, and outcomes, were recorded. Maternal age, parity, mode of delivery, and history of foetal lung maturation with corticosteroids were also extracted and recorded.

Ethical approval

Ethical approval was obtained from the hospital Health Research Ethical Committee. (ABUTH-HREC/29/08/23).

Results were presented as tables and charts. Data was analysed using SPSS version 21. Fisher's exact test was used to assess the association between variables. A p-value of < 0.05 was considered significant. Binary logistic regression was performed to determine the association between maternal and neonatal characteristics with neonatal mortality, and between mode of delivery and neonatal morbidity.

The primary outcomes of interest are neonatal mortality and composite neonatal morbidities (first- and fifth-minute APGAR scores, birth

weight, gestational age at delivery, need for oxygen therapy, neonatal jaundice, neonatal hypoglycaemia, neonatal sepsis, respiratory distress syndrome, necrotising enterocolitis, intraventricular haemorrhage and duration of hospital stay.

RESULTS

A total of 729 neonates were admitted within the period, of which 239 (32.8%) were preterm births. Forty-seven (19.7%) of the preterm births were due to pre-eclampsia and accounted for 6.4% of the total admissions into the unit.

Twenty-nine (61.7%) of the 47 preterm were females, 19(40.4%) had a birth weight of between 1500 -<2000g while two were of extreme low birth weight. The mean birth weight and gestational age were $1.6 \pm 0.43\text{kg}$ and 32.9 ± 2.2 weeks respectively. Most mothers (78.7%) had received at least a dose of dexamethasone for foetal lung maturation before delivery.

The mean maternal age was 30 ± 6.5 years, eighteen (38.3%)—were nulliparous while 25.5% were grand multiparas. The majority (83%) of the neonates were delivered via caesarean section. As shown in Table 1.

Table 1: Characteristics of neonates and their preterm preeclamptic mothers

Characteristic	Frequency (%)	Characteristic	Frequency (%)
Birthweight		Mode of delivery	
<1000g	2 (4.3)	CS	39 (83.0)
1000 - 1499g	16 (34.0)	VD	8 (17.0)
1500 - 1999g	19 (40.4)		
2000 - 2499g	8 (17.0)	Maternal age (years)	
2500 - 2999g	2 (4.3)	15-19	2 (4.3)
		20-24	10 (21.3)
Gestational age (weeks)		25-29	11 (23.4)
28-29 ⁺⁶	3 (6.4)	30-34	10 (21.3)
30-31 ⁺⁶	11 (23.4)	35-39	12 (25.5)
32-33 ⁺⁶	16 (34.0)	≥40	2 (4.3)
34-37 ⁺⁰	17 (36.2)		
		Parity	
Sex of baby		0	17 (36.2)
Female	29 (61.7)	1-4	18 (38.3)
Male	18 (38.3)	≥5	12 (25.5)
Use of Dexamethasone			
Yes	37 (78.7)		
No	10 (21.3)		

CS- caesarean section, VD-vaginal delivery

Neonatal jaundice (72.5%), neonatal sepsis (72.3%) and respiratory distress syndrome (40.4%) were the leading clinical presentations while intraventricular hemorrhage and necrotizing enterocolitis (NEC) were the least (8.5%) as seen in Figure 1.

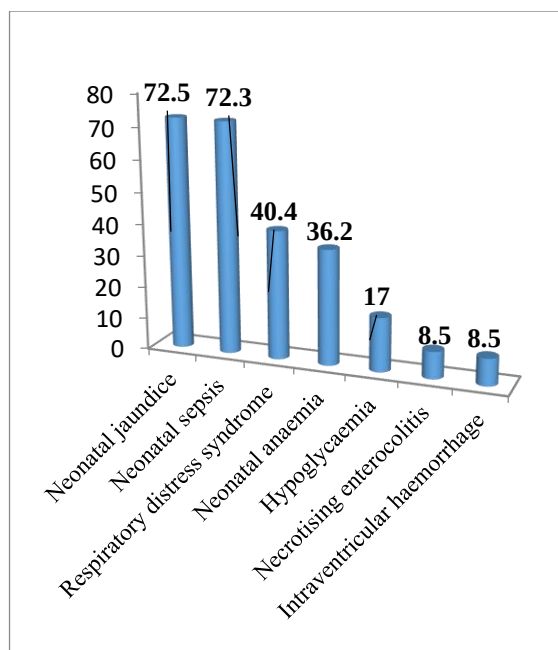


Figure 1: Frequency distribution of neonatal morbidity among neonates of mothers with preterm preeclampsia.

Death occurred in 21.3% of the neonates. Only birth weight was associated with neonatal mortality ($p=0.004$). There was no significant association between mode of delivery and survival, but neonates delivered vaginally had about a 30% higher odd of mortality ($p=1.00$, OR 1.29, 95% CI 0.2-7.6). Use of at least one dose of corticosteroids for fetal lung maturation had no effect on neonatal mortality. Mortality was increased by about three and eleven-fold in neonates that were born at <32 weeks of gestation and in those that weighed <1500 g (OR 3.1, 95% CI 0.7-13.3; OR 10.8, 95% CI 1.9-59.8), respectively. Neonatal mortality was 30% less likely to occur in neonates of nulliparous women (OR 0.7, 95% CI 0.15-3.18). These are depicted in Table 2.

Table 2: Association of Maternal and Neonatal Characteristics with Neonatal Mortality Among Preterm Infants Delivered Following Pre-eclampsia

Characteristic	Neonatal mortality		P-value	Odds ratio (CI)
Mode of delivery	Died	Alive		
VD	2	6	1.00	1.29 (0.2-7.6)
CS	8	31		
Birth weight				
< 1500 g	8	10	0.004	10.8(1.95-59.8)
≥ 1500 g	2	27		
Gestational age				
<32 weeks	5	9	0.12	3.1(0.7-13.3)
≥ 32 weeks	5	28		
Sex				
Male	4	14	0.90	1.0 (0.2-4.6)
female	6	23		
Parity				
0	3	14	0.65	0.7 (0.15-3.18)
≥ 1	7	23		
Dexamethasone use				
No	2	8	0.91	0.90(0.15-5.14)
Yes	8	29		
Age at admission				
≥ 6 hours	0	6	0.33	0.23(0.01-4.5)
<6 hours	10	31		

CI-confidence interval, VD-vaginal delivery, CS-caesarean section

Mode of delivery was associated with birth asphyxia and respiratory distress syndrome ($p<0.05$).

Birth asphyxia was about eight times and respiratory distress syndrome was six times more likely to occur in neonates delivered vaginally (OR 7.6, 95% CI 1.5-39.6 and OR 6.0, 95% CI 1.0-33.9) respectively. Mode of delivery was not associated with the need for respiratory support

and duration of hospital stay. These are shown in Table 3.

Table 3: Association Between Mode of Delivery and Neonatal Morbidities Among Infants Born to Mothers with Preterm Pre-eclampsia

Morbidity	Mode of delivery		p-value	Odds (CI)	ratio
	VD	CS			
Firstminute APGAR					
<7	6	18	0.15	3.5 (0.6-19.5)	
≥7	2	21			
Fifthminute APGAR					
<7	5	7	0.02	7.6 (1.5-39.6)	
≥7	3	32			
Need for oxygen					
Yes	5	24	1.00	1.0 (0.2-5.0)	
No	3	15			
Need for CPAP					
Yes	0	4	0.94	1.1 (0.04-25.5)	
No	8	35			
Hospital stay					
≥1 week	5	25	0.93	0.93 (0.19-4.5)	
<1 week	3	14			
RDS					
Yes	6	13	0.04	6.0 (1.0-33.9)	
No	2	26			
Neonatal sepsis					
Yes	6	28	1.00	1.17 (0.2-6.7)	
No	2	11			
Neonatal jaundice					
Yes	8	26	0.09	8.6 (0.5-161)	
No	0	13			
Anaemia					
Yes	4	13	0.43	2.0 (0.4-9.3)	
No	4	26			
Hypoglycaemia					
Yes	2	6	0.61	1.83 (0.2-11.3)	
No	6	33			
IVH					
Yes	2	2	0.09	6.1 (0.72-52.4)	
No	6	37			
NEC					

CI-confidence interval, CPAP-continuous positive airway pressure, RDS- respiratory distress syndrome, IVH- intraventricular haemorrhage, NEC- necrotising enterocolitis

DISCUSSION:

Preterm birth is a recognised complication of PE.^{[13],[14]} Preterm PE contributed to 17.6% of preterm births among neonates in this study and 6.4% of total neonatal admissions. In southern Nigeria, the risk of preterm birth among mothers with PE was increased by 17-fold.^[15] Sule-Odu *et al.* and Onyiruka *et al.* in other parts of Nigeria reported that more than half of neonates of mothers with PE were born preterm.^{[10], [16]} This higher proportion of prematurity reported from the latter studies included all neonates delivered by mothers with PE, not only neonates that required admission into SCBU as in this study. Several studies have reported higher admission rates among neonates of mothers with PE than our findings. This is due to the inclusion of term PE and longer study duration in these studies, while our study included only cases of preterm PE in a one-year period.^{[17]-[20]}

The mean gestational age in the study was similar to findings by Johnson *et al.* but higher than that found by Duramas *et al.* The mean birth weight in this study is comparable to findings from Turkey^[21] but higher than that reported from Romania.^[11] This difference is likely due to the gestational age of neonates recruited in the Romanian study, including only neonates less than 35 weeks, while we studied neonates born at less than 37 weeks. Most neonates in our study were delivered by caesarean section, which is consistent with several studies across the globe^{[7],[11],[22],[23]}.

This is likely due to unfavorable cervical status before term, the need to urgently halt disease progression in the mother and increased risk of obstetric complications like fetal distress and uteroplacental insufficiency posed by PE thereby making vaginal delivery unsuitable in many cases.^[24] In this study, about one-third of the neonates were born to nulliparous women, consistent with a Ghanaian study^[19] but in contrast to a Polish report of 81% which included mothers with term PE. The mean age of mothers in this study is similar to that of Iranian mothers in a similar study of preterm PE before 34 weeks' gestation.^[7]

Over half of neonates of mothers with preterm PE have been reported to have an adverse composite outcome in an African setting.^[19] About half of the neonates in our study had a first-minute Apgar score of less than 7, which is higher than that reported by Sharami *et al.*^[7] We found one-quarter of neonates to have a fifth-minute Apgar score of less than 7, which is consistent with findings in other Nigerian settings.^{[10],[24]} However, other studies have reported lower rates of birth asphyxia in such neonates.^{[7],[11],[22],[25],[26]} The commonest neonatal morbidity found was neonatal jaundice, which contrasts with findings from a systematic review on neonatal outcome of PE where respiratory morbidity was the commonest.^[6] There was no eligible Nigerian study included in the systematic review, reflecting the paucity of studies on neonatal morbidities of PE in Nigeria. Neonatal sepsis was seen in over two-thirds of neonates in our study, which is higher than that reported in other non-African settings.^{[7],[21],[24]} Tian *et al.* reported PE to be an independent risk factor for RDS^[27], and respiratory distress was reported to be a leading morbidity among neonates of mothers with preterm PE.^{[6],[11],[23]} However, less than half of the neonates in this study were diagnosed with RDS. Few neonates in this study required CPAP, which contrasts with findings from Romania where more than half of neonates needed CPAP.^[11] The inclusion of late preterms in this study likely resulted in a lower incidence of RDS when compared to studies that recruited only early preterms. IVH was the least common morbidity found in this study similar to an Iranian study^[7] but contrasts with the report by Matyas *et al.* where 45% of the neonates had IVH.^[11] Our finding of low incidence of IVH lends credence to the evidence suggested by Bossung *et al.* in a large population based cohort study of neonates delivered before 32 weeks where PTB due to PE was found to be associated with reduced risk of IVH.^[28] Compared to the study by Matyas *et al.*, we found a lower incidence of hypoglycaemia in the studied neonates, though what this study found was higher than that reported by Sharami *et al.*^[7] The study found a neonatal mortality rate similar to that reported in a systematic review but higher

than reports from other settings.^{[7],[21],[23],[29]} The studies reporting lower neonatal mortality were not conducted in sub-Saharan Africa, which is generally characterized by high neonatal mortality rates driven by a weak health care system.

Neonates delivered vaginally had an increased odds of having birth asphyxia and RDS. This, though expected, further suggests health system challenge and may have been a consequence of limited access to timely or emergency caesarean delivery. Timely caesarean delivery can help prevent some of the maternal and neonatal complications associated with vaginal delivery. Route of delivery did not affect the other neonatal morbidities studied and is similar to finding by Coviello *et al.*^[30] The absence of an association between mode of delivery and neonatal mortality in the present study is consistent with the findings of Tuhrahmi *et al.* in Jakarta^[31]. In contrast, a multicenter survey from China^[32] demonstrated a significant protective effect of caesarean delivery on neonatal survival, possibly reflecting differences in patient characteristics, obstetric practices, and access to timely perinatal care.

The odds of neonatal mortality were increased in neonates born before 32 weeks, similar to a study by Geidam *et al.*^[33]

Van Esch *et al.* reported higher mortality among preterm neonates of mothers with PE before 32 weeks when compared to neonates of women without PE.^[34] This can be explained by the fact that prematurity alone is a significant cause of mortality, coupled with inadequate neonatal care that is prevalent in many low-resource settings. The current study found vaginal delivery to increase the odds of neonatal mortality, similar to a finding consistent with that reported by Tuhrahmi *et al.* in Jakarta.^[31] This association may be attributable to the increased risk of intrapartum complications, birth asphyxia, and delayed delivery of high-risk fetuses in pregnancies complicated by severe pre-eclampsia. Very low birth weight was also found to be significantly associated with neonatal mortality in this study. Being preterm and very low birth weight further increases vulnerability to death largely driven by

physiological immaturity, increased susceptibility to infection, respiratory complications, and limited physiological reserves. Given the high burden of prematurity and constrained neonatal intensive care resources in many sub-Saharan African.^[35] settings, very low birth weight continues to be a major determinant of neonatal survival.

This study provides a valuable insight into neonatal outcomes of preterm PE in Nigeria, which is relatively under-researched. It also provides useful information about the effect of delivery mode on neonatal outcome, thereby will help to guide obstetricians and the woman in deciding the mode of delivery when PE occurs. However, it is limited by its retrospective study design and single-centre nature, which can limit generalizability, and it excluded out-born neonates of mothers who had PE.

CONCLUSION

Vaginal delivery among mothers with pre-eclampsia was significantly associated with an increased occurrence of birth asphyxia and respiratory distress syndrome. In addition, very preterm gestation, very low birth weight, and vaginal delivery were identified as significant predictors of neonatal mortality. These findings highlight the heightened vulnerability of preterm infants born to mothers with pre-eclampsia and underscore the need for timely obstetric interventions, enhanced perinatal monitoring, and advanced neonatal care services to improve neonatal outcomes and survival.

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