

# Comparing the risk of adverse effects of intrapartum and postpartum versus antepartum preeclampsia/eclampsia among women admitted at federal teaching hospital, Birnin Kebbi, northwest Nigeria

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## ABSTRACT

**Introduction:** Preeclampsia is a multi-organ system disorder that is responsible for a significant rate of maternal and perinatal morbidity and mortality worldwide. Though many studies have worked on the risk factors, there is a limited study on the adverse maternal outcomes highlighting the comparison between antepartum preeclampsia/eclampsia (APE/E), intrapartum preeclampsia/eclampsia (IPE/E) and postpartum preeclampsia/eclampsia (PPE).

**Materials and Methods:** A retrospective cohort study was conducted by reviewing records of gestational induced hypertension patients who progressed to having preeclampsia/eclampsia at admitted at the Federal Teaching Hospital, Birnin Kebbi, between January 2009 and December 2019.

**Results:** The multinomial logistic final model identified six maternal adverse outcomes of preeclampsia/eclampsia: stillbirth, (ARR 0.86 and 0.31, respectively), preterm delivery (ARR 8.55 and 3.10, respectively), induction of labour (ARR 0.39 and 0.36, respectively), maternal death (ARR 12.28 and 8.75, respectively), low birth weight (ARR 0.09 and 0.11, respectively) and convulsion (ARR 8.17 and 8.22, respectively).

**Conclusion:** These study findings offer valuable insights into the adverse maternal outcomes of preeclampsia and eclampsia within the Nigerian context. It serves as a potential research project that can be applied to the clinical setting to help clinicians manage preeclamptic and eclamptic patients better.

## KEYWORDS:

*Antepartum preeclampsia/eclampsia, intrapartum preeclampsia/eclampsia, postpartum preeclampsia/eclampsia, multinomial logistic regression, adverse maternal outcome*

## INTRODUCTION

Pre-eclampsia is a pregnancy disorder; it is one of the most serious acute complications of pregnancy, which is the most serious of the hypertensive disorders of pregnancy.<sup>1-3</sup>

Pre-eclampsia (PE) is a common disorder that particularly affects first pregnancies, though the causes, placental and maternal factors, vary among individuals. It has various types of clinical presentation, and most women are asymptomatic. The disease is often diagnosed during routine antenatal care; it is also one of the complications of pregnancy that results in foetal and maternal morbidity and mortality.<sup>4-7</sup>

Preeclampsia is characterised by new onset of hypertension and proteinuria or by hypertension accompanied by significant end-organ dysfunction with or without proteinuria after 20 weeks of gestation or postpartum in a previously normotensive patient. However, it is important to note that a diagnosis can still be made in the absence of proteinuria if the new-onset hypertension presents with specific signs or symptoms of significant end-organ dysfunction.<sup>8</sup>

The International Society for the Study of Hypertension in Pregnancy (ISSHP) in 2021 defined Pre-eclampsia (de novo) as gestational hypertension accompanied by one or more of the following new onset conditions at  $\geq 20$  weeks of gestation: (i) Proteinuria, (ii). Other maternal end-organ dysfunction, including: a) Neurological complications (e.g., eclampsia, altered mental status, blindness, stroke, clonus, severe headaches, or persistent visual scotomata), (b) Pulmonary oedema, (c) Haematological complications (e.g., platelet count  $< 150,000/\mu\text{L}$ , DIC, haemolysis), (d) AKI (such as creatinine  $\geq 90 \mu\text{mol/L}$  or  $1 \text{ mg/dL}$ ), (e) Liver involvement (e.g., elevated transaminases such as ALT or AST  $> 40 \text{ IU/L}$ ) with or without right upper quadrant or epigastric abdominal pain).<sup>9</sup>

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Preeclampsia could progress to eclampsia, characterised by seizures, and other complications such as kidney or liver damage and ultimately death of the mother and/or foetus if left untreated, and it is one of the serious obstetric emergencies.<sup>10,11</sup>

<sup>2,10,12,13</sup> observed that 10% of all pregnancies globally are complicated by hypertension, with preeclampsia and eclampsia (PE and E) being the major causes of maternal and perinatal morbidity and mortality, with an expected 62,000–77,000 deaths per year.<sup>3</sup> also noted that the global prevalence of all pre-eclampsia in the years 2002–2010 was approximated at 4.6% of deliveries. Preeclampsia and eclampsia have an incidence ranging from 2–5% of pregnancies in Western Europe and North America to as high as 18% in parts of Africa.<sup>14,15</sup> With a prevalence range of 1.8 to 16.7% in developing countries, and an occurrence of 10% of pregnancies in African women.<sup>3</sup>

Furthermore<sup>16</sup> acknowledged that PE is a major cause of almost a third of a million maternal deaths in low and middle-income settings and also causes more than six million perinatal deaths, approximately eight million preterm births and almost 20 million low birthweight infants in developing nations; Additionally, pre-eclampsia and its adverse outcomes have been linked to higher risks of chronic non-communicable diseases (NCDs) in later life, thus creating a huge challenge within the context of double burden and limited resources in the developing world.

In West Africa, PE and E account for 15–25% of maternal deaths in Ghana, while in Nigeria, they account for a high maternal mortality ratio of 512 per 100,000 live births and a high infant mortality rate (67 deaths per 1000 live births).<sup>1</sup>

Despite the high rate of pre-eclampsia and eclampsia-related maternal and perinatal morbidity and mortality in developing countries like Nigeria, there are limited studies on its maternal outcome, especially in the northern part of Nigeria. Researchers have attempted to examine the global trend, severity and risk factors of PE and E, but almost all these studies used binary logistic regression and other statistical analyses.

In this study, preeclampsia/eclampsia (PE/E) was classified according to the study by<sup>17</sup>, which stated that PE/E has been traditionally divided into three groups: antepartum preeclampsia/eclampsia (APE/E), intrapartum preeclampsia/eclampsia (IPE/E), and postpartum preeclampsia/eclampsia (PPE/E). APE/E occurs during pregnancy. Intrapartum PE begins when labour starts and ends following the third stage of labour, while postpartum PE, which has traditionally been defined as new-onset PE 48 hours after delivery to 6 weeks postpartum

Thus, the multinomial logistic regression analysis is used in this study to investigate maternal outcomes comparing IPE/E and PPE/E versus APE/E.

## MATERIALS AND METHODS

A retrospective cohort study research design was used to comprehensively review 131 preeclampsia/eclampsia (PE/E) patients in Federal Teaching Hospital (FTH), formerly known as the Federal Medical Centre (FMC), Birnin Kebbi, between January 2009 and December 2019. Data analysed included demographic data, clinical presentation, medical treatment received, method and outcome of delivery, maternal outcome and discharge data. Data was filled in a data proforma anonymously. All confirmed preeclampsia and eclampsia patients who had no previous history of hypertension were included in the study. Gestational Induced Hypertension (GIH) patients who did not have PE/E and PE/E patients who died before they got to the hospital were excluded from the study. All the patients included in the study were not less than 17 years old at diagnosis.

Data was collected from the Health Information Management department based on the patient's demographics, booking status, parity and adverse outcomes of preeclampsia/eclampsia. FTH is the main tertiary health centre in Kebbi State, and it serves as a referral centre to all primary and secondary health centres in the state. The calculation of sample size was done using G Power Sample size calculation software, with a significance level (alpha) of 0.05 and a power of the study (1- $\beta$ ) of 90%. An estimated 10% was added in anticipation of missing data or loss to follow-up. The final sample size was calculated as 131 patients. The Multinomial logistic regression is one of the generalised linear models, which shows an extension of the binary logistic regression model. It is generally used in cases where response variables have more than two categories or levels. The explanatory variable (s) of the regression model can be either continuous, categorical or both.

### Statistical Analysis

The statistical analysis was done using STATA SE version 14.0.<sup>18</sup> Descriptive statistics were used to examine the distribution of patients' demographic characteristics. The multinomial logistic regression (MLOGIT) model was applied to estimate the relationship between the adverse maternal outcomes and preeclampsia/eclampsia (antepartum, intrapartum and postpartum), the univariable and multivariable analyses, respectively. For the univariable analysis step of (MLOGIT), simple MLOGIT was used to identify potential adverse maternal outcomes. Covariates with a significant level (p-value)  $\leq 0.25$  were selected for inclusion in subsequent multivariable modelling.<sup>19</sup>

The multivariable MLOGIT model was applied to estimate the relationship between adverse maternal outcomes and preeclampsia/eclampsia (antepartum, intrapartum and postpartum). The parsimonious model, including the statistically significant and clinically plausible variables, was chosen in this study. Linearity was not done due to the absence of numerical variables, though multicollinearity was done by evaluating the correlation matrix, standard errors, p-value and confidence interval. Omission of correlated variables (PPH and placenta abruptio) with high confidence intervals was done. Subsequently, potential two-way biologically or clinically meaningful interaction terms between significant independent variables were evaluated,

**Table I: Demographic characteristics of preeclamptic/eclamptic patients in FTH Birnin Kebbi for multinomial regression analysis**

Demographic variables	Frequency (n)	Percentage (%)	Mean (SD)
Age*			23.45 (5.42)
Tribe / Ethnicity			
HAUSA	78	59.54	
IBO	17	12.98	
YORUBA	11	8.40	
OTHERS	25	19.08	
SOCIO-ECONOMIC STATUS			
Low	98	74.81	
Medium	33	25.19	
EDUCATION LEVEL			
Illiterate	95	73.28	
Literate	35	26.72	
BOOKING STATUS			
Booked	44	33.59	
Unbooked	87	66.41	
PARITY			
Nulliparous	89	67.94	
Multiparous	42	32.06	
MULTIPLE PREGNANCY			
Yes	11	8.40	
no	120	91.60	
PE/E DIAGNOSIS			
APE	88	67.18	
IPE	15	11.45	
PPE	28	21.37	

SD = standard deviation, \*normally distributed

and no interaction was found. The overall fitness of the model was assessed, and the model was found to be fit.

Model adequacy was done using the Hosmer-Lemeshow test, Pearson chi-square, classification table and Area under ROC curve. Statistical results were reported as adjusted Relative Risk Ratios (ARRs) and corresponding 95% confidence intervals (CIs). A p-value of <0.05 was regarded as significant.<sup>19</sup>

#### *Ethics Approval*

This study was approved by the ethics committee of the Federal Medical Centre (FMC), now known as Federal University Teaching Hospital (FTH), Birnin Kebbi and the Universiti Zainal Abidin Human Research Ethics Committee (UHREC). The patient consent form was not mandatory for the ethics approval from FTH Birnin Kebbi, due to the non-interventional nature of the study and secondary data collection, with all data being anonymous.

## **RESULTS**

The results from Table I, which presents the characteristics of PE/E patients in FTH, Birnin Kebbi, show that respondents numbering 131 had a mean (standard deviation) age of 23.45 (5.42) years. 78(59.54%) were Hausas, 98(74.81%) had low socioeconomic status, 35(26.72%) were literate, 89(67.94%) were nulliparous, 11 (8.4%) had multiple pregnancies, and only 44 (33.59%) were booked in the antenatal clinic (ANC). 88 (67.94%) had APE, 15 (11.45%) had IPE, and 28 (21.37%) had PPE.

The univariable analysis of the multinomial regression model of maternal adverse outcomes of preeclampsia/eclampsia in FTH Birnin Kebbi, Kebbi State, results show the adverse outcomes of preeclampsia/eclampsia: logit one (intrapartum preeclampsia/eclampsia versus antepartum preeclampsia/eclampsia) and logit two (postpartum preeclampsia/eclampsia versus antepartum preeclampsia/eclampsia). The adverse outcomes of preeclampsia/eclampsia included in the univariable analysis are: Blurring of vision, PPH, stillbirth, preterm delivery, induced labour, maternal death, placenta abruptio, low birth weight and convulsion. All the factors that had a p-value ≤ 0.25 in both logit one and logit two were included in the multivariable analysis.

Results from the fitted model of multinomial regression for adverse maternal outcomes of PE/E in the FTH Birnin Kebbi are presented in Table II. The table reports adjusted relative risk ratios (ARRs), associated 95% confidence intervals (CIs) and p-values. APE was used for the baseline or reference category in the logit models one and two. IPE and APE were paired in the first logit, and PPE and APE were paired in the second logit; this resulted in two equations in one model fit. Six statistically significant variables from the multinomial regression univariable model were analysed, and all were found to be statistically significant based on p-value <0.05 and have been reported in the paper.

**Table II: Adverse maternal outcome of Preeclampsia/eclampsia (intrapartum and postpartum preeclampsia/eclampsia) logit function 1 and 2**

Logit function	Variable	Regression coefficient ( $\beta$ )	Adjusted rrr (95% CI)	P value
1	PPH			
	no	1	0.00	
	yes	3.07	0.05 (0.01, 0.44)	0.007
	STILLBIRTH			
	no	1	0.00	
	yes	0.15	0.86 (0.29, 2.55)	0.791
	PRETERM			
	no	1	0.00	
	yes	2.14	8.55 (2.93, 24.96)	<0.001
	INDUCED LABOUR			
	no	1	0.00	
	yes	0.95	0.39 (0.18, 0.85)	0.018
	MATERNAL DEATH			
	no	1	0.00	
yes	2.51	12.28 (3.72, 40.46)	<0.001	
2	LOWBIRTH WEIGHT			
	no	1	0.00	
	yes	2.46	0.09(0.03, 0.29)	<0.001
	CONVULSION			
	no	1	0.00	
	yes	2.10	8.17 (3.24, 20.62)	<0.001
	PPH			
	no	1	0.00	
	yes	2.64	0.07 (0.01, 0.67)	0.02
	STILLBIRTH			
	no	1	0.00	
	yes	1.16	0.31 (0.10, 0.93)	0.04
	PRETERM DELIVERY			
	no	1	0.00	
yes	1.13	3.10 (1.35, 7.15)	0.008	
INDUCED LABOUR				
no	1	0.00		
yes	1.00	0.36 (0.17, 0.80)	0.012	
MATERNAL DEATH				
no	1	0.00		
yes	2.17	8.75 (2.61, 29.32)	<0.001	
LOW BIRTH WEIGHT				
no	1	0.00		
yes	2.23	0.11(.03, 0.37)	<0.001	
CONVULSION				
no	1	0.00		
yes	2.11	8.22 (2.91, 23.17)	<0.001	

- Multinomial logistic regression was applied
- Interaction was not reported
- RRR= relative risk ratio, CI = confidence interval, b: Regression coefficient; Adjusted RRR= Adjusted relative risk ratio.
- Overall fitness of the model was checked and reported to be Hosmer-Lemeshow test (logit function 1=P = 0.783; logit function 2 = P = 0.827), Pearson chi square test (logit function 1: P = 0.886; logit function 2: P = P = 0.884), overall correctly classified percentage (logit function 1: 82.01%; logit function 2; 82.76%), Area under the ROC curve (logit function 1: 0.879; logit function 2: 0.837).

**Table III: Overall Fit of the Model**

	Logit function 1	Logit function 2
Hosmer –Lemeshow test	P = 0.783	P = 0.827
Pearson chi-square test	P = 0.886	P = 0.884
Classification table correctly classified	82.01%	82.76%
Area under the ROC curve	0.879	0.837

## DISCUSSION

Pre-eclampsia is the most severe form of hypertensive disorders in pregnancy and is a major contributor to maternal and fetal morbidity and mortality worldwide.<sup>3</sup> It remains one of the most serious causes of adverse pregnancy outcomes, particularly in developing countries where access to timely and adequate healthcare is often limited.<sup>1,2</sup>

This hospital-based retrospective study was performed to identify the adverse maternal outcomes among Preeclamptic/eclamptic patients, and the results obtained above show that most patients (82.25%) were Hausa by tribe. The majority of the women (88.75%) had low socioeconomic status, 85.4% were illiterate, and 81.7% of the women had no antenatal care (ANC) booking. This may be because most of the patients are from low-resource settings with financial constraints. This gives an indication that most women having a high risk of the adverse outcome of preeclampsia/eclampsia in Kebbi State are Indigenous young, uneducated women, mostly from rural areas, on referral to FTH Birnin Kebbi.<sup>20,21</sup>

Adverse maternal outcomes of preeclampsia/eclampsia can be severe, leading to maternal and perinatal morbidity and mortality.<sup>4,22</sup> This study identified stillbirth as one of the adverse maternal outcomes of PE/E. Similarly, studies by<sup>12,23-26</sup> have all confirmed stillbirth as an adverse maternal outcome of PE/E. The findings of this study also noted preterm delivery as another adverse maternal outcome of PE/E. This result was corroborated by<sup>24</sup>, which attests that the high prenatal mortality of PE/E mothers was a result of preterm delivery.<sup>26</sup> also affirmed preterm delivery as an adverse outcome of PE/E. The following were other adverse maternal outcomes of PE/E as found out in this study, which were consistent with the results of previous works: Induction of labour<sup>26,27</sup>, maternal death<sup>12, 24, 25, 27</sup>, low birth weight<sup>26</sup> and convulsion.<sup>12,26</sup>

### *Comparison of IPE and PPE VERSUS APE*

Studies have consistently shown that stillbirth is a major adverse outcome associated with Preeclampsia/eclampsia globally.<sup>28-30</sup> In line with these inclinations and previous local research in Nigeria.<sup>31,32</sup> This study finds that IPE and PPE have a lower risk of stillbirth compared to APE (RRR 0.86 and 0.31, respectively). This comparison indicates that pregnant women with APE face a higher risk of stillbirth than those with IPE and PPE.

This study compared the results of IPE and PPE versus APE as it relates to the outcome of preterm delivery. Globally, most studies emphasised preterm delivery or prematurity as an adverse outcome of preeclampsia/eclampsia.<sup>33</sup> Consistent with these trends and previous local studies in Nigeria and other Sub-Saharan countries<sup>4,24,26</sup>, our study found that women with IPE and PPE had a higher risk of preterm than women with APE (ARRR 8.55 and 3.10, respectively). Thus, the outcome of this research is emphasising preterm delivery as an adverse maternal outcome of PE/E

There is increasing evidence suggesting that most eclamptic mothers undergo induction of labour to terminate their pregnancy due to foetal distress.<sup>26,27</sup> In this study, women with

IPE and PPE who experienced induced labour had a lower risk of induction compared to women with APE (ARR 0.39 and 0.36, respectively). This indicates that pregnant women with APE face a higher risk of requiring induction of labour compared to those with IPE and PPE. The difference in the likelihood of undergoing induction of labour as an IPE or PPE mother is 3% according to this study.

In our study, women with IPE and PPE had a higher risk of maternal death than women with APE (ARRR 12.28 and 8.75, respectively). Though the direct risk comparison of APE, IPE, and PPE has not been observed in literature, a study conducted in Canada revealed that PPE was strongly associated with pregnancy complications, which could lead to maternal mortality.<sup>33</sup> Other studies from East and Northern Africa also noted maternal death as an outcome of PE/E, a Nigerian study indicated that maternal death could be due to lack of early presentation at the hospital.<sup>10,21,27</sup>

The issue of low birth weight in babies is a global phenomenon. It was noted in a study that 50% of the newborns have a low birth weight (1.5 - 2.5 kg), which was consequent with their premature birth and intrauterine growth retardation (IUGR).<sup>34</sup> This suggests that low birth weight in PE/E mothers is not only subsequent to the disease as a primary cause, but also other associated factors like prematurity/preterm delivery and IUGR. It was observed in this study that women with IPE and PPE had a lower risk of low-birth-weight babies compared to APE (ARRR 0.09 and 0.11, respectively). Although no comparison of IPE and PPE mothers has been observed in the literature, a study reported that nearly half (40.1%) of babies born to eclamptic mothers had low birth weight.<sup>26</sup>

Convulsion in a non-epileptic pregnant woman is a sign of eclampsia, as observed by.<sup>8</sup> This study observed that IPE and PPE had a higher risk of convulsion compared to APE (ARR 8.17 and 8.22, respectively). This reflects that eclampsia could be antepartum, intrapartum or postpartum and the difference in the risk of convulsing as an IPE mother and a PPE mother in FTH Birnin Kebbi is 0.05 times, which is a small difference, emphasising that there are almost equal chances of having eclampsia at any stage of pregnancy. Though a study observed different findings from this study, among 250 patients diagnosed with eclampsia, 148 patients had the seizures antenatally, 2 patients had the seizures intra-partum, and 100 patients had the seizures after delivery.<sup>27</sup> Another study from Tanzania, which differs from our findings, recorded that Convulsions in patients with eclampsia were classified as antepartum (44%), intrapartum (42%) and postpartum (15%) convulsions most commonly occurred after the onset of labour or within 24 hours after birth of the eight women (15%) with postpartum convulsions, seven women (88%) developed eclampsia within 24 hours, one woman (1%) had convulsions 1 week after delivery (late post-partum eclampsia).<sup>35</sup>

## CONCLUSION

This retrospective cohort study reported adverse maternal outcomes of preeclampsia/eclampsia patients in FTH, Birnin Kebbi, comparing the risk of IPE and PPE versus APE. It was

observed that women with IPE and PPE had a lower risk of stillbirth, induction of labour and low birth weight and a higher risk of preterm delivery, maternal death and convulsion than women with APE. The findings represent Kebbi state, as FTH, Birnin Kebbi, is the major tertiary hospital in Kebbi state, North West, Nigeria. This study suggests policy interventions to enhance health and medical interventions for women in the childbearing age group in the less developed areas of the northern states and the country at large. Awareness of preeclampsia should be raised by healthcare providers and policy makers in the antenatal clinics and through the mass media, focusing on younger women, low wealth status, and those living in rural areas, emphasising on preceding symptoms, high complication and mortality rate.

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