

Risk factors for hypertensive disorders of pregnancy in Abuja, Nigeria: A prospective case-control study

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ABSTRACT

Background: Hypertensive disorders of pregnancy (HDP) are an important cause of maternal and perinatal morbidity and mortality throughout the world, particularly in developing countries like Nigeria. The study determined the risk factors for the development of HDP among women who booked early for antenatal care.

Materials and Methods: This was a prospective case-control study conducted from March 2015 to March 2016 involving pregnant women with gestational age less than 20 weeks at booking and were followed up until delivery and 6 weeks postpartum. Information on gestational age at recruitment, at diagnosis of HDP, mode of delivery, and fetal outcome were recorded. Risk factors for HDP were compared between women who developed HDP (cases) and those who did not develop HDP (controls) by Fisher's exact test, Chi-square, and student's t-tests. Univariate and multivariate logistic regression analysis was used to test the relationship between certain risk factors and the development of HDP. A *P* value of less than 0.05 was considered statistically significant.

Results: The prevalence of HDP in the study was 19.4%. Family history of preeclampsia (OR: 5.339, 95% CI: 1.149–24.818, *P* = 0.033); previous history of preeclampsia (OR: 10.819, 95% CI: 3.570–32.792, *P* < 0.001); multifetal gestation (OR: 13.275, 95% CI: 2.899–38.127, *P* = 0.010); chronic hypertension (OR: 3.431, 95% CI: 1.778–8.710, *P* < 0.001) and diabetes; (OR: 2.846 95% CI: 0.460–17.584, *P* < 0.251) were the risk factors associated with the development of HDP among the study population while nulliparity (OR: 0.726, 95% CI 0.366–1.440, *P* = 0.395); body mass index (BMI) (mean ± SD), (OR: 0.405, 95% CI: 0.173–0.945, *P* < 0.037); and low educational level (OR: 0.582, 95% CI: 0.070–4.857, *P* = 0.613) were not.

Conclusion: The prevalence of HDP in the study group was high. Risk factors for HDP included family history of hypertension, previous history of preeclampsia, multifetal gestation, and chronic hypertension.

Key words: Abuja; hypertensive disorders of pregnancy; Nigeria.

Introduction

Hypertensive disorders of pregnancy (HDP) are among the main public health issues worldwide and are comprised a spectrum of disorders typically classified into categories that include chronic (preexisting) hypertension, gestational hypertension, preeclampsia (PE) (including chronic (preexisting) hypertension with superimposed PE), and eclampsia.^[1-5]

Hypertension in pregnancy is defined as a systolic blood pressure of 140 mmHg or greater or diastolic blood pressure of 90 mmHg or greater.^[6,7]

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It is also defined as a diastolic blood pressure of 90 mmHg or greater on two occasions more than 4 h apart or a single diastolic blood pressure above 110 mmHg.^[8]

Hypertensive diseases of pregnancy are associated with severe maternal obstetric complications and contribute significantly to maternal and perinatal morbidity and mortality.

Hypertensive diseases of pregnancy can also trigger some severe forms of maternal complications, such as cardiovascular and cerebrovascular diseases, liver and kidney failure, placental abruption, disseminated intravascular coagulation (DIC), and hemolysis, elevated liver enzymes, and low platelet (HELLP) syndrome. Under these circumstances, placenta dysfunction may occur, leading to fetal growth restriction, fetal distress, preterm birth, intrauterine fetal demise, stillbirth, and neonatal asphyxia.^[9] They are also known as the second commonest cause of perinatal mortality in industrialized countries.^[1,10] While HDP has been described as a maternal complication over the last several decades, its true etiology and pathophysiology remain unknown; HDP-related complications are still threatening maternal and fetal life and health. The prognosis of HDP is associated with the severity of the disease process.^[11]

Available evidence suggests that some risk factors and conditions are linked to HDP. These include a family history of hypertension, PE in a previous pregnancy, chronic hypertension, extremes of maternal age, obesity, nulliparity, gestational diabetes, and multifetal gestation.^[12-15] Therefore, early identification and definition of the relationship between such risk factors and HDP may be useful in preventing complications associated with HDP.

Despite the available literature on risk factors for HDP particularly in developed countries, there is a paucity of information regarding the prevalence of HDP as well as risk factors for HDP amongst pregnant women in Nigeria.

A previous study in Nigeria on the subject matter was limited by the fact that they were conducted in homogenous communities with similar sociocultural and socioeconomic characteristics.^[15] The current study which was conducted in Abuja, Nigeria's Federal Capital which has a cosmopolitan environment and a population under rapid social, economic, and structural changes may allow for generalization of the result findings.

The study aimed to identify risk factors that are associated with the development of HDP among early booked women at a Nigerian Teaching hospital.

Materials and Methods

Study location

The study was conducted at the University of Abuja Teaching Hospital, Abuja between 1st March 2015 and 1st March 2016. This tertiary public health institution provides specialized health care services to the inhabitants of Nigeria's Federal Capital Territory and its neighboring states. The territory covers an area of about 8000 square kilometers. The obstetric unit undertakes an average of 2500 deliveries annually.

Booking clinic is on Mondays during which an average of 70 women are booked for antenatal clinics. Follow-up antenatal clinics take place from Tuesdays to Fridays except during national public holidays.

Study design

This was a prospective case-control study to describe and identify risk factors and the proportion of early booked women that developed hypertensive disorders during pregnancy and 6 weeks following delivery at a Nigerian Teaching Hospital.

Study population

The sample population comprised all pregnant women that booked early and, for the purpose of this study before 20 weeks of gestation, attended the antenatal clinic and were followed up till delivery and 6 weeks postpartum.

Inclusion criteria

All the consenting normotensive women who booked at gestational age less than 20 weeks.

Exclusion criteria

Pregnant women with gestational ages of 20 weeks or more at booking,

Pregnant women with elevated blood pressure at booking.

Sample size determination

The sample size for the study was calculated using the formula for calculation of sample

size for cross-sectional studies ($n = \frac{z^2 pq}{d^2}$) where,

n = minimum sample size

z = the standard normal deviation usually set at 1.96.

p = prevalence of HDP of 17% (0.17) from a previous study.^[15]

$q = 1.0 - p$

d = degree of accuracy set at 0.05

Therefore, the minimum sample size for a simple proportion with 5% accuracy and 95% level of confidence was calculated as below:

$$n = \frac{1.96 \times 1.96 \times 0.17 \times 0.83}{0.05 \times 0.05}$$

$n = 216.8$

Considering an attrition rate of 10% the calculated sample size was rounded up to 240.

Data collection method

Awareness about the study was created among hospital staff including the nurses and doctors at the antenatal clinic, labor ward, and maternity ward.

Every eligible woman was counseled on the objectives of the study and an informed consent form was signed by participants. They were subsequently enrolled into the study and followed up till 6 weeks after delivery using the routine antenatal clinic schedule of 4 weekly visits till 28 weeks, then two weekly visits till 36 weeks and subsequently weekly visits till delivery except when there is a pregnancy complication during which the women are seen earlier for treatment and close follow-up.

The primary outcome was the development of any of the HDP (gestational hypertension, PE/eclampsia, chronic hypertension with superimposed PE).

The secondary outcomes included mean birth weight and mode of delivery between normotensive and those that developed HDP.

At enrollment, a standardized questionnaire was used to provide information on age, parity, weight, height, educational status, previous history of diabetes, previous history of PE, family history of hypertension, and multifetal gestation.

The gestational age of the pregnancy of participants was deduced from their last menstrual period in combination with an early ultrasound scan estimate.

Body mass index (BMI) was calculated from weights obtained at booking using digital scale and height that was obtained in meters using a stadiometer. BMI ≥ 30 kg/m² was considered as obese.

Blood pressures were measured at each visit from participants' right arm using standard mercury sphygmomanometers after

they were seated at rest for 3–5 min. Proper cuff size on the basis of right midarm circumference was selected for each participant and blood pressure readings that coincided with the timing of the first (systolic) and fifth (diastolic) Korotkoff sounds were recorded. Korotkoff phase I and V (disappearance) were used, rather than phase IV (muffling), since it is more reproducible and shows better correlation with true diastolic blood pressure in pregnancy.^[7] However, Korotkoff IV was chosen where Korotkoff V failed to be recorded. Urine protein was routinely measured using dipsticks at every antenatal checkup (ANC) visit.

All participants were given a dedicated phone number which they could contact if they have any complaints regarding their pregnancy.

Statistical analyses

The frequencies of risk factors were compared between groups of women who developed HDP (cases) and those who did not develop HDP (controls) by Fisher's exact test, Chi-square, or student's t-tests. A multivariate logistic regression analysis was performed to assess the independent role of clinical, social, and demographic variables if significantly associated with hypertensive disease in pregnancy in the univariate analysis, using the SPSS 20.0 for windows (SPSS Inc. Chicago, IL). The variables tested in the univariate analysis included the family and previous history of PE, current multifetal gestation, BMI, nulliparity, diabetes mellitus, chronic hypertension, parity, and educational level. P value < 0.05 was considered statistically significant. Ethical approval for the study was obtained from the health research and ethics committees of the University of Abuja Teaching Hospital, Gwagwalada.

Results

Out of 240 women recruited for the study, only 221 of them completed the study and were therefore used for data analysis. Regarding the remaining 19, 4 (1.7%) women had miscarriages, 11 (4.6%) women did not deliver in our facility, 4 (1.7%) women delivered at home.

Forty-three (19.5%) of the 221 women that were recruited during the antenatal period and longitudinally followed up till 6 weeks postpartum were diagnosed to have HDP while 178 (80.5%) were normotensive.

Gestational hypertension, PE, chronic hypertension, and chronic hypertension superimposed with PE accounted for 19 (8.6%), 14 (6.3%), 6 (2.7%), and 4 (1.8%), respectively for HDP. Therefore, the most common type of HDP found among participants was gestational hypertension and the least common was chronic hypertension superimposed with PE. This is shown in Table 1.

There was no statistically significant difference between sociodemographic and reproductive characteristics of women that developed HDP (cases) and those who did not develop HDP (controls). This is reflected in Table 2.

Following univariate analysis, [Table 3] the study showed that there was a statistically significant higher odds of having hypertension during pregnancy in women with chronic hypertension (OR: 46.853, 95% CI: 5.747–381.969, $P < 0.001$), twin gestation (OR: 13.275, 95% CI: 1.346–130.963, $P = 0.024$); previous history of PE (OR: 10.586, 95% CI: 3.904–28.700, $P < 0.001$); and a family history of PE (OR: 8.458, 95% CI: 2.352–30.416, $P = 0.001$). This implied that those with chronic hypertension had a 47 times higher chance of having hypertension later in pregnancy compared to those

who were not previously hypertensive before pregnancy, also twin gestation, previous history of PE and family history of PE increased the chances for developing HDP by 13, 11, and 9 times, respectively. Contrastingly, there was no increased chance of HDP in relation to BMI ≥ 30 kg/m² rather the odds of developing HDP was 64% lower among hypertensives than in the controls and this was statistically significant (OR: 0.363, 95% CI: 0.183–0.717, $P < 0.006$). Although, diabetes was associated with a higher chance of developing hypertensive disorder of pregnancy this increase was not statistically significant (OR: 2.846, 95% CI: 0.460–17.584, $P = 0.251$).

Twin gestation (OR: 24.056, 95% CI: 2.899–38.127, $P = 0.010$); previous history of PE (OR: 10.819, 95% CI: 3.570–32.792, $P < 0.001$); women with family history of PE (OR: 5.339, 95% CI: 1.149–24.818., $P = 0.033$) and chronic hypertension (OR: 3.431, 95% CI: 1.778–8.710, $P < 0.001$) following multivariate regression analysis while controlling for cofounders still had higher odds of 24, 10, 5, and 3 times, respectively, in developing hypertensive disorder of pregnancy. BMI did not show any higher chance of hypertensive disorder of pregnancy but rather a decreased

Table 1: Occurrence of hypertensive disorders in pregnancy

Types of Hypertensive disorders in pregnancy	Frequency	Percent
Gestational hypertension	19	8.6
Preeclampsia	14	6.3
Chronic hypertension	6	2.7
Chronic hypertension superimposed with preeclampsia	4	1.8
Total	43	19.4%

Table 2: Sociodemographic and reproductive characteristics

Sociodemography and reproductive characteristics	HDP n=43 n (%)	Normotensive n=178 n (%)	Total n=221 n (%)	P
Age				
Mean (SD)	32.6 (5.6)	29.4 (4.5)		0.092*
<20	1 (2.3)	0 (0.0)	1 (0.5)	
20-24	1 (2.3)	21 (11.8)	22 (10.0)	
25-29	11 (25.6)	80 (44.9)	91 (41.2)	
30-34	14 (32.6)	51 (28.7)	65 (29.4)	
35-39	11 (25.6)	23 (12.9)	34 (15.4)	
≥ 40	5 (11.6)	3 (1.7)	8 (3.6)	
Marital status				
Married	43 (100.0)	173 (97.2)	216 (97.7)	0.586**
Single	0 (0.0)	5 (2.8)	5 (2.3)	
Husband occupation				
Civil servant	19 (44.2)	93 (52.2)	112 (50.7)	0.082***
Trader	9 (20.9)	47 (26.4)	56 (25.3)	
Farmer	0 (0.0)	2 (1.1)	2 (0.9)	
Artisan	13 (30.2)	21 (11.8)	34 (15.4)	
Unemployed	1 (2.3)	5 (2.8)	6 (2.8)	
Professional	1 (2.3)	10 (5.6)	11 (5.0)	
Educational level				
None	1 (2.3)	0 (0.0)	1 (0.5)	0.119***
Primary	0 (0.0)	7 (3.9)	7 (3.2)	
Secondary	14 (32.6)	59 (33.1)	73 (33.0)	
Tertiary	28 (65.1)	112 (62.9)	140 (63.3)	
Number of deliveries				
0	16 (37.2)	80 (44.9)	96 (43.4)	0.763***
1	11 (25.6)	38 (21.3)	49 (22.2)	
2-4	14 (32.6)	55 (30.9)	69 (31.2)	
≥ 5	2 (4.7)	5 (2.8)	7 (3.2)	

*t-test. **Fisher's exact test. ***Chi-square

Table 3: Characteristics of women with the hypertensive disorder in pregnancy compared with normotensive women (univariate analysis)

Characteristics	HDP n=43 n (%)	Normotensive n=178 n (%)	Odds ratio (95% CI)	P
Chronic hypertension	9 (20.9)	1 (0.6)	46.853 (5.747-381.969)	<0.001**
Twin gestation	3 (7.0)	1 (0.6)	13.275 (1.346-130.963)	0.024**
Previous PE history	13 (30.2)	7 (3.9)	10.586 (3.904-28.700)	<0.001**
Family history of PE	7 (16.3)	4 (2.2)	8.458 (2.352-30.416)	0.001**
BMI (mean±SD)	31.1±10.3	26.9±9.4	0.363 (0.183-0.717)	0.006*
Nulliparity	16 (37.2)	80 (44.9)	0.726 (0.366-1.440)	0.395**
Diabetes	2 (4.7)	3 (1.7)	2.846 (0.460-17.584)	0.251**
Low educational level	1 (2.3)	7 (3.9)	0.582 (0.070-4.857)	0.613**

*t-test. **Fisher's exact test. PE: preeclampsia; HDP: hypertensive disorders of pregnancy

Table 4: Characteristics of women with hypertensive disorder in pregnancy compared with normotensive women (A multivariate logistic regression analysis)

Characteristics	HDP n=43 n (%)	Normotensive n=178 n (%)	Odd ratio (95% CI)	P
Twin gestation	3 (7.0)	1 (0.6)	24.056 (2.899-38.127)	0.010
Previous PE history	13 (30.2)	7 (3.9)	10.819 (3.570-32.792)	<0.001
Family history of PE	7 (16.3)	4 (2.2)	5.339 (1.149-24.818)	0.033
Chronic hypertension	9 (20.9)	1 (0.6)	3.431 (1.778-8.710)	<0.001
BMI	31.1±10.3	26.9±9.4	0.405 (0.173-0.945)	0.037*

*t-test

Table 5: Mode of delivery in both groups

Mode of Delivery	HDP n=43 n (%)	Normotensive n=178 n (%)	Total n=221 n (%)	P
SVD	14 (32.6)	134 (75.3)	148 (67.0)	<0.001**
Induction of labor	8 (18.6)	5 (2.8)	13 (5.9)	0.001**
Instrumental Delivery	3 (7.0)	2 (1.1)	5 (2.3)	0.052**
Caesarean section	18 (41.9)	37 (20.8)	55 (24.9)	0.006**

**Fisher's exact test. SVD: singular value decomposition

Table 6: Fetal outcome

Variables	HDP n=43 Mean (SD)	Normotensive n=178 Mean (SD)	dF	T	P
Birth weight (kg)	2.9 (6.5)	3.2 (8.4)	46	4.936	<0.001*
APGAR score (1 min)	7.0 (2.5)	8.3 (1.2)	8	1.644	0.139*
APGAR score (5 min)	8.4 (2.4)	9.6 (1.2)	6	1.245	0.260*

*t-test

odd of about 60% for cases compared to controls (OR: 0.405, 95% CI: 0.173–0.945, $P < 0.037$). This is shown in Table 4.

With regards to the mode of delivery and fetal outcome, women with hypertensive disorders were more likely to have a cesarean section (41.9% vs 20.8%); $P < 0.006$, and a higher rate of induction of labor (18.6% vs 2.8%); $P = 0.001$. The mean birth weight of babies of the women with HDP was 2.9 kg compared with that of normotensives 3.2 kg. This difference was also statistically significant ($P < 0.001$). There were no statistically

significant differences between the two groups regarding APGAR scores at 1 and 5 min.

Discussions

The prevalence of the hypertensive disorders in pregnancy of 19.4% found in this study is comparable to findings of 17% reported previously in Sokoto, North-Western Nigeria^[15] but was higher than 10.3% reported from a community study in Ogun state in Southern Nigeria.^[16] The fact that this study and the quoted study from Sokoto where conducted at a University Teaching Hospital where high-risk pregnancies are usually managed may have resulted in the recruitment of women with increased risk for development of HDP when compared to those presenting to primary health centers.

This high prevalence portends great danger for pregnant women especially for those in communities devoid of antenatal services. There is, therefore, a need for continued research into ways of preventing HDP as well as early detection and management to prevent possible complications.

In this study, a family history of PE, previous history of PE, twin gestation, and chronic hypertension were significantly more frequent in the HDP group when compared to the normotensive group. These results are similar to findings from other studies in different populations.^[1,6,8,9,12,13,15]

The family history of PE and the previous history of PE significantly increased the risk for HDP by 7.5 and 7.7-fold,

respectively, compared to the normotensives. This work confirms the strong associations of the family and the previous history of PE with an increased risk of HDP. These findings of a strong association between family and previous history of PE have been reported in other studies.^[1,6,9,12,13,15] Indeed, the genetic component in pathophysiological abnormalities of PE has been suggested.^[12,17-19] Therefore, pregnant women with this history should be carefully monitored both prenatally and in the postpartum period.

Although previous studies^[9,11,18] had found a higher risk of PE in obese women when compared with those with normal BMI, our findings did not support such even though the mean BMI was higher in hypertensive women.

Some studies have shown that twin pregnancy is an important risk factor for HDP.^[9,15,20] However, in other studies this association was not established.^[12,21]

Generally, PE is regarded as a disease of first pregnancy and its frequency ranges between 2% and 7% in healthy nulliparous women.^[22] Nulliparity is well established as a risk factor for hypertensive disorders in pregnancy.^[1,9,13,15,21] Contrary to these reports our study did not find nulliparity as a risk factor for women presenting with PE and gestational hypertension despite its accounting for 37.2% cases of HDP group. The lack of association between nulliparity and risk of PE in this study is, however, consistent with findings from two other studies.^[12,23] Although the mechanism for this lack of association cannot be fully explained, it has been proposed that the degree to which PE would be a disease of nulliparity would depend on the percentage of patients seen who were nulliparous.^[23] Thus, this finding is likely to be due to the low percentage of nulliparous women who developed HDP.

Previous studies had suggested that pregnant women with diabetes are more likely to develop HDP than those without diabetes.^[9,10,15,21] However, our study did not show an increased risk. This could be attributed to the good glycemic control recorded among the diabetics enrolled in the study.

Personal history of chronic hypertension is one of the reported risk factors for hypertensive diseases in pregnancy.^[13,20,21,24] This agrees with our findings which confirmed a strong association between history of chronic hypertension and risk of PE.

Evidence suggests that women with a low level of education are more likely to develop HDP than those who have received a higher level of education.^[13,21] In our study, 96%

attained at least secondary education which could be the reason for the lack of association between level of education and risk of HDP.

Regarding the mode of delivery, [Table 5] the frequency of cesarean section among the hypertensive group in the present study was 41.9% compared to 20.8% among the normotensive, $P = 0.006$. This finding is nearly similar to 45.8% reported by Zibaenezhad *et al.*^[11] It is, however, lower than a cesarean section rate of 76.95% reported in another study.^[9] The reason advanced for increased cesarean section includes the concern that opting for induction of labor and vaginal delivery may result in worsening maternal and perinatal outcomes.^[4,9,15]

Concerning fetal outcome, [Table 6] lower birth weight, and perinatal mortality are higher in a hypertensive group than the normotensive.^[11] This observation was consistent with our finding where the mean birth weight of babies of the women with hypertensive was lower (2.9 kg vs 3.2 kg). This was found to be statistically significant with P value < 0.001 . This also conforms to findings from previous studies.^[15,25]

The inclusion of pregnant women with chronic hypertension is a possible limitation to the study but this was necessary to accurately determine the prevalence of HDP.

Findings from this study suggest that a family history of PE and previous history of PE, diabetes, twin gestation, and chronic hypertension are more probable risk factors for hypertensive disorders in pregnancy. Identification of these risk factors for HDP would be useful for early diagnosis of HDP as well as instituting measures to prevent complications of HDP especially the modifiable factors.

The high prevalence of 19.4% of HDP in this study also portends great danger for pregnant women especially for those in communities devoid of antenatal services. Early booking and antenatal care could offer a unique platform for the provision of cost-effective health interventions which will ensure healthy outcomes for pregnant women. It is, therefore, recommended that HDP prevention interventions should start before pregnancy and target women of childbearing age by reinforcing the adoption of healthy lifestyle practices (i.e. dietary changes, weight loss, and exercise).

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Conflicts of interest

There are no conflicts of interest.

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