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Original Article

A Cross-Sectional Study about Demographic and Medical Characteristics of Hypertensive Pregnant Women in Two Secondary Healthcare Facilities, in Ilorin, Nigeria

Assessment of Medications Used in the Management of Hypertension in Pregnancy in Two Secondary Healthcare Facilities, Ilorin

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Abstract

Background Hypertension is one of the major causes of related maternal deaths worldwide and it is one of the most common medical disorders encountered during pregnancy.

Aim This study aimed at assessing the demographic and medical characteristics of hypertensive pregnant women in two secondary healthcare facilities, in Ilorin, Nigeria

Method This was a cross-sectional study among 104 pregnant women with hypertension attending the outpatient department of General Hospital and Civil Service Clinic, Ilorin between March and May 2021. A validated self-administered questionnaire was used to obtain information on sociodemographics. Data on the medical characteristics of the respondents and their medications were extracted from the respondent's medical files. Ethical approval was obtained from the Ministry of Health and General Hospital, Ilorin. For statistical analysis for categorical measurements, the frequencies and percentages were computed.

Results Seventy-five percent of the correspondents were below 36 years old, 97% were married, 79% had tertiary education, and 74% were above 24 weeks of gestation. About 68% of the correspondents had blood pressure more than or equal to 140/90 and 10% had blood pressure more than 160 mm Hg systolic or more than 100 mm Hg diastolic. About 78.8% of the correspondents had a family history of hypertension, 13.5% had a family history of diabetes mellitus, and 22.1% had a family history of obesity. About 27.9% had pre-existing hypertension, 61.5% developed hypertension before the end of 20 weeks of gestation, and 10.6% developed hypertension after 20 weeks of gestation. About 24% had their antihypertensive medication changed during pregnancy, 38.5% were treated with methyldopa, 31.7% with nifedipine, and

27% with nifedipine and methyldopa. Majority (83.6%) of the respondents were not adherent to their medications.

Conclusion   Two-third of the patients had poor blood pressure control irrespective of the fact that all were under drug therapy. Family history and large body mass index are the main risk factors for the development of hypertension during pregnancy. Non-compliance may play a significant role in no drug response.

ملخص المقال باللغة العربية

دراسة مقطعية حول الخصائص الديموغرافية والطبية للنساء الحوامل المصابات بارتفاع ضغط الدم في اثنين من مرافق الرعاية الصحية الثانوية، في إيلورين، نيجيريا.

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الخلفية: يعد ارتفاع ضغط الدم أحد الأسباب الرئيسية لوفيات الأمهات في جميع أنحاء العالم وهو أحد الاضطرابات الطبية الأكثر شيوعًا أثناء الحمل.

الهدف: تهدف هذه الدراسة إلى تقييم الخصائص الديموغرافية والطبية للنساء الحوامل المصابات بارتفاع ضغط الدم في اثنين من مرافق الرعاية الصحية الثانوية، في إيلورين، نيجيريا.

الطرق: هذه دراسة مقطعية شملت 104 نساء حوامل مصابات بارتفاع ضغط الدم يراجعن قسم العيادات الخارجية بالمستشفى العام وعيادة الخدمة المدنية في إيلورين بين مارس ومايو 2021م. تم استخدام استبيان متحقق منه ذاتياً للحصول على معلومات حول المعلومات الاجتماعية. تم استخراج البيانات المتعلقة بالخصائص الطبية للمريضات وأدويتهن من الملفات الطبية. تم الحصول على الموافقة الأخلاقية من وزارة الصحة والمستشفى العام، إيلورين. للتحليل الإحصائي للبيانات، تم حساب التكرارات والنسب المئوية.

النتائج: 75% من الحوامل كانت أعمارهن أقل من 36 سنة، و97% متزوجات، و79% حصلن على تعليم جامعي، و74% تجاوزن 24 أسبوعًا من الحمل. كان ضغط الدم لدى حوالي 68% من النساء ≤140/90، وكان ضغط الدم عند 10% أكبر من 160 ملم زئبقي ضغطًا انقباضيًا أو أكبر من 100 ملم زئبقي انبساطيًا. 78.8% من النساء لديهن تاريخ عائلي لارتفاع ضغط الدم، و13.5% لديهن تاريخ عائلي لمرض السكري، و22.1% لديهن تاريخ عائلي للسمنة. 27.9% أصبن بارتفاع ضغط الدم قبل الحمل، و61.5% أصبن بارتفاع ضغط الدم قبل نهاية الأسبوع 20 من الحمل، و10.6% أصبن بارتفاع ضغط الدم بعد 20 أسبوعًا من الحمل. تم تغيير الأدوية الخافضة للضغط أثناء الحمل لحوالي 24% من النساء، وتم علاج 38.5% بميثيل دوبا، و31.7% بالنيفيديبين، و27% بالنيفيديبين وميثيل دوبا. الأغلبية (83.6%) من النساء لم يكونوا ملتزمين بأدويتهم.

الاستنتاج: لم يكن ضغط الدم تحت السيطرة لثلثي المريضات بغض النظر عن حقيقة أنهن كن تحت العلاج الدوائي. يعد التاريخ العائلي ومؤشر كتلة الجسم عاملان أساسيان لنشؤ ارتفاع ضغط الدم أثناء الحمل. قد يلعب عدم الامتثال للعلاج دورًا مهمًا في عدم الاستجابة للأدوية.

الكلمات المفتاحية: ارتفاع ضغط الدم أثناء الحمل، الحمل، ارتفاع ضغط الدم المزمن، تسمم الحمل، الالتزام بالأدوية

Introduction

When the systolic blood pressure (SBP) level is 140 mm Hg or higher or a diastolic blood pressure (DBP) level of 90 mm Hg or higher, it is called hypertension.[1] Hypertension in pregnancy is classified into three major categories: pre-existing (chronic) hypertension, gestational hypertension, and pre-eclampsia (which includes eclampsia).[2] The National High Blood Pressure Education Program Working Group has recommended that the term "gestational hypertension" should be used instead of "pregnancy-induced hypertension" to describe situations in which elevated blood pressure without proteinuria develops in a woman after 20 weeks of pregnancy and blood pressure levels return to normal after delivery[1] The World Health Organization (WHO) Multi-country Survey on Maternal and Newborn Health—a cross-sectional hospital-based survey in 29 countries across Africa, Asia, Latin America, and the Middle East reported 0.21% of women in Africa to have chronic hypertension, and 0.55% had pre-eclampsia.[3] An unacceptably high number of maternal deaths occur in Nigerian public tertiary hospitals annually with obstetric hemorrhage and hypertensive disorders being the most frequent causes of organ dysfunctions.[4] The effectiveness of medical treatment is influenced not only by the patients' commitment (adherence) to the prescribed regimen but also important is the safety, effectiveness, and appropriateness of the drugs used.[5] The goal of chronic and gestational hypertension treatment during pregnancy is to prevent maternal hypertension-related problems, maintain a healthy pregnancy, and lower the risk of preterm birth. Conversely, to prevent fetal dysplasia or congenital malformations caused by a rapid decrease in uterine–placental perfusion to the fetus due to antihypertensive medication treatment, the amount and duration of drug exposure should be reduced.[6]

Recommended antihypertensive medications include hydralazine, labetalol, nifedipine, methyldopa, and magnesium sulfate.[7] Angiotensin-converting enzyme inhibitors, (ACEIs) on the other hand, should be avoided during pregnancy due to the risk of fetal renal dysfunction, oligohydramnios, fetal growth restriction, skeletal deformity, limb contracture, patent ductus arteriosus, lung hypoplasia, and neonatal death.[8] ACEIs should also be avoided in women of childbearing age.[9] In addition, thiazide, a diuretic, if utilized for chronic hypertension in patients prior to pregnancy, can also be used as a second antihypertensive agent in consideration of renal function.[7] Labetalol is a nonselective α-1 and β-blocker that is supplied intravenously at a dose of 20 mg and then analyzed within 10 minutes.[10,11] Although methyldopa, an oral medicine, can be used safely during pregnancy because it does not cause any issues in the fetus or newborn, it does induce side effects in pregnant women such as lethargy or depression. The objective of this study was to evaluate the demographic and medical characteristics of hypertensive pregnant women in two secondary healthcare facilities, in Ilorin, Nigeria.

Methods

Study Design
A cross-sectional study among pregnant women attending the ante-natal clinic was recruited from General Hospital and Civil Service Hospital, Ilorin. Inclusion criteria included pregnant women with pre-existing hypertension, pregnant women with pregnancy-induced hypertension, pregnant women with hypertension and type 2 diabetes mellitus (DM). The exclusion criteria included pregnant women with mental illness that could interfere with their response, and pregnant women with other disease conditions apart from hypertension and type 2 DM.

Sampling Size Determination
The sample size for the pregnant women involved in the study was determined using the statistical formula by Fischer $n = Z^2pq/d^2$. With regard to this study, the prevalence of hypertension in pregnancy in Nigeria is 17%.[12]

Data Collection
The study was conducted by interviewing the respondents using structured questionnaires and by extracting the respondents' medication records from the patients' files. Selected patients' files were serialized to avoid repetition. The questionnaires consisted of three sections. Section A contained sociodemographic and health characteristics of the respondents. Section B contained questions relating to the risk factors of the disease condition. Section C contained the medications used in the management of hypertension and section D was on medication adherence. Medication adherence was assessed using the four-item medication adherence questionnaire (MAQ). Respondents answering "No" to all items on MAQ were identified as "adherent." Answering "Yes" to at least one of the MAQ was said to be "non-adherent." MAQ was selected because it has been globally

validated to identify adherence behaviors in chronic disease populations. It included the following questions:

1. Do you ever forget to take your medications?
2. When you feel better do you sometimes stop to take your medications?
3. When you travel do you sometimes forget to take along your medications with you?
4. Do you sometimes feel inconvenient taking your medications?

The questionnaires were administered to the eligible respondents by the researcher. Research ethics such as freedom to decline or consent to participate in the study were observed. Anonymity of participant and confidentiality of responses were also ensured.

Data Analysis
The Statistical Package for Social Sciences (SPSS) version 20.00 was used for data entry and data analyses. Percentages and tables were used to present summarized data. For categorical measurements, the frequencies were computed.

Ethical approval: Ethical approval was obtained from the Ministry of Health, Kwara State, Ilorin, Nigeria with Ethical No: MOK/KS/EU/777/425

Results

►**Table 1** shows that 75.0% of the respondent were within the age group 18 to 36 years, while 25.0% were above 37 years old. About 97% were married. About 78.8% had a tertiary level of education, and 20.2% had secondary education. Majority of the respondents (74.0%) were within 25 to 36 weeks of gestation (third trimester).

►**Table 2** shows that majority of respondents (68.3%) had poor blood pressure control, while 10.5% had a sever hypertension. About 78.8% of the respondents had a family history of hypertension, 17.3% had a history of chronic hypertension, while 13.5% had a family history of DM and 22.1% a family history of obesity. Most of the respondents have normal body mass index (BMI; 39.4%), with 28.8% were overweight, and 17.4% were obese.

►**Table 3** shows the history of morbidity. About 28% of the patients had pre-existing hypertension, while 61.5% developed hypertension before 20 weeks gestation and 10.6% developed hypertension after 20 weeks of gestation. In total, 98.1% of the patients had hypertension only, and 1.9% had hypertension and DM.

►**Table 4** shows the antihypertensive medications taken by the respondents during pregnancy. About 38.5% of the respondents were on methyldopa only, 31.7% were on nifedipine only, while 26.9% were on nifedipine and methyldopa.

►**Table 5** shows medication adherence score. Majority (83.65%) of the respondents were not adherent to their medications, while 16.35% were adherent to their medication.

Discussion

The main objective of this study was to evaluate the health condition of pregnant women diagnosed with hypertension

Table 1 Sociodemographic characteristics of respondents

Variables	Responses	Frequency	Percentage
Age	18–36 years	78	75.0
	37–55 years	26	25.0
Marital status	Single	1	1.0
	Married	101	97.1
	Divorced	2	1.9
Educational qualification	Primary education	1	1
	Secondary education	21	20.2
	Tertiary education	82	78.8
Age of gestation	Less than 12 weeks	2	1.9
	12–24 weeks	25	24.1
	25–36 weeks	77	74.0

Table 2 Blood pressure and risk factors of the disease condition

	Variable	Frequency	Percentage
Blood pressure (mm Hg)	$\leq 140/80$	22	21.1
	$\geq 140/90$	71	68.3
	(SBP$\geq$ 160 or DBP$\geq$100)	11	10.5
Risk factors	Family history of HTN	82	78.8
	Family history of DM	14	13.5
	Family history of obesity	23	22.1
Body mass index (kg/m^2)	Under weight <18.5	15	14.4
	Normal weight 18.5–24.9	41	39.4
	Overweight 25–29.9	30	28.8
	Obese > 30	18	17.4

Abbreviations: DBP, diastolic blood pressure; DM, diabetes mellitus; HTN, hypertension; SBP, systolic blood pressure.

Table 3 History of disease conditions

Variables	Responses	Frequency	Percentage
Previously on antihypertensive medication.	Yes	29	27.9
Previously on ACEI	Yes	4	3.8
Changed antihypertensive medications after conception	Yes	25	24
Trimester of diagnosis of hypertension.	Pre-existing	29	27.9
	< 20 weeks	64	61.5
	>20 weeks	11	10.6
Morbid/comorbid condition in pregnancy	Only hypertension	102	98.1
	Both hypertensive and diabetic	2	1.9

Abbreviation: ACEI, angiotensin-converting enzyme inhibitor.

in relation to blood pressure control, risk factors, drug treatment, and adherence to therapy.

We found that about 68% of the correspondents in this study had blood pressure more than or equal to 140/90.

Globally, high blood pressure (one of the criteria for pre-eclampsia) occurs in 6 to 8% of all pregnancies and contributes significantly to maternal, fetal, and neonatal morbidity.[11] A study in Nigeria showed a prevalence of

Table 4 The present medications history

Medications	Frequency	Percentage
Methyldopa	40	38.5
Nifedipine	33	31.7
Nifedipine and methyldopa	28	26.9
Nifedipine, methyldopa, and hydralazine	1	1.0
Amlodipine	2	1.9

Table 5 Medication adherence score

MAQ score	Frequency	Percentage
1–4	87	83.65
0	17	16.35
Total	104	100.00

Abbreviation: MAQ, medication adherence questionnaire.

pre-eclampsia in pregnant hypertensive women to be 6%.[12] One of the possible risk factors for pre-eclampsia is maternal ages, and the mean age in this study was 35 ± 2.27. Women over 35 years old have four to fivefold risk of suffering pre-eclampsia compared to women aged between 25 and 29 years.[13] On the other hand, 10% of the pregnant women in our study had sever hypertension (an SBP$\geq$170 mm Hg or DBP $>$ 110 mm Hg). It was reported that severe chronic hypertension increases the risk of pre-eclampsia to as high as 46% with resultant raised maternal and fetal risks.[14] About 79% of the pregnant women had tertiary education; this suggests that the study population is relatively well-educated. However, it appears that their education does not necessarily translate into positive outcomes in terms of their health welfare. Similarly, it was reported that high literacy level has not impacted positively on pregnant women health-seeking behavior.[14] It was suggested that the outcomes for pregnancy complicated by hypertension range from uneventful pregnancy in women with chronic, controlled hypertension to death in cases of pre-eclampsia–eclampsia. The major adverse outcomes include central nervous system injuries such as seizures (eclampsia), hemorrhagic and ischemic strokes, hepatic damage ranging from transaminase elevation, the so-called "HELLP syndrome" (hemolysis, elevated liver enzymes, and low platelets), hepatic failure, renal dysfunction as well as increased frequency of cesarean delivery, preterm delivery, and abruptio placentae.[15–17]

When we looked for risk factors related to gestational hypertension, we found that 78.8% of the patients had family history of hypertension, 22.1% family history of obesity, and 17.3% family history of DM. These findings suggest that there may be a genetic predisposition or familial influence contributing to the development of gestational hypertension in these individuals. It has been suggested that the presence of hypertension in first-degree relatives increases the risks of pre-eclampsia.[18]

Another factor we studied was the BMI. We found that 46.2% of respondent had a BMI more than 25 mg/kg. A study carried out at the University of Jos Teaching Hospital, Nigeria shows that BMI more than 25 mg/kg is a risk factor for developing pre-eclampsia,[18] gestational diabetes, gestational hypertension, cesarean section, and postpartum hemorrhage.[19,20] Another documented risk factor for gestational hypertension is the presence of hypertension, diabetes, and obesity in first-degree relatives which increases the risks of gestational hypertension or pre-eclampsia.[21] Delays in diagnosis and access to adequate treatment are major contributors to pre-eclampsia-related maternal and neonatal mortality.[22]

In terms of drug therapy, we found that 27.9% were already on antihypertensive therapy, only 3.8% were on ACEIs. Twenty-four percent of all patients had their antihypertensive therapy changed during pregnancy. Although the British Hypertension Society publish a guideline in 2004 recommend the use of ACEIs as first line for nonblack younger patients, it should be avoided in women of childbearing age,[9,23] as these drugs can cause fetotoxicity and could be teratogenic.

American Congress of Gynecology (ACOG) recommends methyldopa, labetalol, and nifedipine as first-line medications in the treatment of hypertension in pregnancy, and the use of diuretics only as a second-line medication in situations that specifically call for such a mechanism of action.[11] In our study, all respondents were prescribed antihypertensive that are considered safe in pregnancy by the ACOG.[1] These included methyldopa (38.5%), nifedipine (31.7%), or a combination of both (26.9%).

Nonadherence is a global issue among patients taking frequent medications, particularly in primary care and could be as high as 65%.[24] Noncompliance with chronic medications during pregnancy may have a negative impact on both the mother's and fetus's health.[5] There is paucity of data on medication adherence in pregnant women in Nigeria. It has been recognized that poorly treated conditions such as diabetes or chronic hypertension can result in unfavorable pregnancy outcomes if such health conditions are suboptimally treated. Therefore, appropriate clinical care of women's chronic disorders during pregnancy is critical for maternal–fetal health.[23] Majority of patients in our study (83.6%) were not adherent to their medications. Lupatteli et al noted that 32.9% of pregnant women had low medication adherence with cardiovascular disorder, 40.0% for epilepsy, 55.6% for rheumatic disorder, and 36.1% for bowel disorder, whereas only 17.1% of pregnant women with diabetes had the least in adherence.[23]

The high rate of low adherence may be due to apprehension about the teratogenic risks of these medications in pregnancy.[23] Other reasons for nonadherence include having prior children and lack of folic acid use increases the chances of low adherence during pregnancy by two to fivefolds.[23] Also having a previous experience with nonadherence in pregnancy without consequences, a general lack of awareness about hazards, and/or a lack of motivation to follow

healthcare professionals' advice are all factors that have contribute to non-adherence in pregnant women.[23]

Conclusion

Two-third of the patients had poor blood pressure control irrespective of the fact that all were under drug therapy. Family history and large BMI are the main risk factors for the development of hypertension during pregnancy. Noncompliance may play a significant role in no drug response. These findings suggest that hypertension is a significant concern during pregnancy, and there is a need for improved adherence to medication and early intervention strategies to manage hypertensive disorders effectively.

References

1 ACOG Committee on Practice Bulletins. ACOG Practice Bulletin. Chronic hypertension in pregnancy. Obstet Gynecol 2001;98(01): 177–185

2 Magee LA, Sharma S, Nathan HL, et al; CLIP Study Group. The incidence of pregnancy hypertension in India, Pakistan, Mozambique, and Nigeria: a prospective population-level analysis. PLoS Med 2019;16(04):e1002783

3 Abalos E, Cuesta C, Carroli G, et al; WHO Multicountry Survey on Maternal and Newborn Health Research Network. Pre-eclampsia, eclampsia and adverse maternal and perinatal outcomes: a secondary analysis of the World Health Organization Multicountry Survey on Maternal and Newborn Health. BJOG 2014;121 (Suppl 1):14–24

4 Oladapo OT, Adetoro OO, Ekele BA, et al; Nigeria Near-miss and Maternal Death Surveillance Network. When getting there is not enough: a nationwide cross-sectional study of 998 maternal deaths and 1451 near-misses in public tertiary hospitals in a low-income country. BJOG 2016;123(06):928–938

5 Sawicki E, Stewart K, Wong S, Leung L, Paul E, George J. Medication use for chronic health conditions by pregnant women attending an Australian maternity hospital. Aust N Z J Obstet Gynaecol 2011; 51(04):333–338

6 Yeonhee K, Jongcheul S, Yeon-Hee K, Jong Chul S. Management of chronic hypertension in pregnancy. J Korean Med Assoc 2015;58 (10):897–904

7 Foo L, Tay J, Lees CC, McEniery CM, Wilkinson IB. Hypertension in pregnancy: natural history and treatment options. Curr Hypertens Rep 2015;17(05):36

8 Martinovic J, Benachi A, Laurent N, Daïkha-Dahmane F, Gubler MC. Fetal toxic effects and angiotensin-II-receptor antagonists. Lancet 2001;358(9277):241–242

9 Shotan A, Widerhorn J, Hurst A, Elkayam U. Risks of angiotensin-converting enzyme inhibition during pregnancy: experimental and clinical evidence, potential mechanisms, and recommendations for use. Am J Med 1994;96(05):451–456

10 Schroeder BMAmerican College of Obstetricians and Gynecologists. ACOG practice bulletin on diagnosing and managing preeclampsia and eclampsia. Am Fam Physician 2002;66(02): 330–331

11 American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 125: chronic hypertension in pregnancy. Obstet Gynecol 2012;119(2 Pt 1):396–407

12 Singh S, Ahmed EB, Egondu SC, Ikechukwu NE. Hypertensive disorders in pregnancy among pregnant women in a Nigerian Teaching Hospital. Niger Med J 2014;55(05):384–388

13 Tessema GA, Tekeste A, Ayele TA. Preeclampsia and associated factors among pregnant women attending antenatal care in Dessie referral hospital, Northeast Ethiopia: a hospital-based study. BMC Pregnancy Childbirth 2015;15:73

14 Onoh RC, Onyebuchi KA, Mamah JE, Anozie BO, Kenneth EC, Chidi EO. Obstetric outcome of pregnancies complicated by hypertensive disorders of pregnancy. Sahel Med J. 2020;23(03):141

15 Shan D, Qiu PY, Wu YX, et al. Pregnancy outcomes in women of advanced maternal age: a retrospective cohort study from China. Sci Rep 2018;8(01):12239

16 MacKay AP, Berg CJ, Atrash HK. Pregnancy-related mortality from preeclampsia and eclampsia. Obstet Gynecol 2001;97(04):533–538

17 Heard AR, Dekker GA, Chan A, Jacobs DJ, Vreeburg SA, Priest KR. Hypertension during pregnancy in South Australia, part 1: pregnancy outcomes. Aust N Z J Obstet Gynaecol 2004;44(05):404–409

18 Musa J, Mohammed C, Ocheke A, Kahansim M, Pam V, Daru P. Incidence and risk factors for pre-eclampsia in Jos Nigeria. Afr Health Sci 2018;18(03):584–595

19 Chiu M, Austin PC, Manuel DG, Shah BR, Tu JV. Deriving ethnic-specific BMI cutoff points for assessing diabetes risk. Diabetes Care 2011;34(08):1741–1748

20 Rahman MM, Abe SK, Kanda M, et al. Maternal body mass index and risk of birth and maternal health outcomes in low- and middle-income countries: a systematic review and meta-analysis. Obes Rev 2015;16(09):758–770

21 English FA, Kenny LC, McCarthy FP. Risk factors and effective management of preeclampsia. Integr Blood Press Control 2015; 8:7–12

22 Cooper WO, Hernandez-Diaz S, Arbogast PG, et al. Major congenital malformations after first-trimester exposure to ACE inhibitors. N Engl J Med 2006;354(23):2443–2451

23 Webster LM, Reed K, Myers JE, et al. Quantifying adherence to antihypertensive medication for chronic hypertension during pregnancy. Pregnancy Hypertens 2019;17:12–14

24 Lupattelli A, Spigset O, Nordeng H. Adherence to medication for chronic disorders during pregnancy: results from a multinational study. Int J Clin Pharm 2014;36(01):145–153