

International Journal of Preclinical & Pharmaceutical Research

Journal homepage: <u>www.preclinicaljournal.com</u>

PRESCRIPTION PATTERN AND ADHERENCE TO ANTIHYPERTENSIVES AMONG PREGNANT WOMEN IN CENTRAL HOSPITAL WARRI, DELTA STATE, NIGERIA.

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ABSTRACT

Pregnancy induced hypertension poses a threat to both mother and the foetus as it is a reason for increased risk of perinatal complications including the death of a mother or the child. Aim to evaluate the pattern of prescription of antihypertensives and the rate of adherence to these medications in pregnancy. Using both retrospective and prospective approaches, the study carried out in Central Hospital Warri, Delta State covered the assessment of 198 case folders of patients from October, 2009 to December, 2012 and interview of 100 patients within a six month period. Data were collected from the case files into a data collection form while the interview was conducted with the administration of a validated, closed ended 16-item questionnaire. Data were entered into a statistical table and analysed using the SPSS version 17.0 statistical package. Hypertension in pregnancy was prevalent among women carrying their first pregnancy (32.8%) and child bearing age of between 28-32 years (34.3%). The prescribed drugs included methyldopa (50.7%), Nifedipine (42.1%), Hydralazine (1.9%), Lisinopril (0.8%), and Furosemide (0.8%). The most prescribed drug was Methyldopa (91.9%). Poor adherence (33%) was evident among the patients. Methyldopa was the most prescribed drug in the management of hypertensive disorder with forgetfulness ranking the highest reason for poor adherence.

Key Words: Hypertension, Pregnancy, Antihypertensives, Prescription, Adherence.

INTRODUCTION

Maternal mortality is unacceptably high. About 800 women die from pregnancy- or childbirth-related complications around the world every day. In 2010, 287 000 women died during and following pregnancy and childbirth. Almost all of these deaths occurred in lowresource settings, and most could have been prevented [1] Women die as a result of complications during and following pregnancy and childbirth. The major complications that account for 80% of all maternal deaths are: severe bleeding (mostly bleeding after childbirth), infections (usually after childbirth), unsafe abortion and high blood pressure during pregnancy (pre-eclampsia and eclampsia] [1]. Pre-eclampsia usually occurs after 20 weeks gestation and is a multi-system disorder.

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John E. Arute Email: arute4john@yahoo.com It was classically defined as a triad of hypertension, oedema, and proteinuria, but a more modern definition of pre-eclampsia concentrates on a gestational elevation of blood pressure together with > 0.3 g proteinuria per 24 hours. Oedema is no longer included because of the lack of specificity [2]. Preeclampsia and related hypertensive disorders of pregnancy impact 5-8% of all births in the United States [3, 4].

Incidence rates for preeclampsia alone - in the United States, Canada and Western Europe, range from 2-5%. [3,4]. In the developing world, severe forms of preeclampsia and eclampsia are more common, ranging from a low of 4% of all deliveries to as high as 18% in parts of Africa [3]. The variation in incidence rates is driven by the diversity of definitions and other criteria (including procedures, tests and their methodologies). In Latin America, preeclampsia is the number one cause of maternal death [5].

Ten million women develop preeclampsia each year around the world. Worldwide about 76,000 pregnant women die each year from preeclampsia and related hypertensive disorders. And, the number of babies who die from these disorders is thought to be on the order of 500,000 per annum [6].

In developing countries, a woman is seven times more likely to develop preeclampsia than a woman in a developed country. From 10-25% of these cases will result in maternal death [7]

Consequent upon this, pregnant women are a special group of individuals and hypertension among these set of people should be of utmost concern. Pregnancy induced hypertension (PIH) possess a threat to both the mother and the foetus as it is a reason for increased risk of perinatal complications including death of a mother or the child [8].

Another problem that could arise as a result of PIH is placental abruption (premature detachment of the placenta from the uterus). PIH can also lead to fetal problems including intrauterine growth restriction thereby resulting to poor fetal growth and stillbirth.

More evidently, is the fact that hypertension in pregnancy might lead to pre-eclampsia which could be life threatening as a study affirmed that offspring of women with this hypertensive disorder of pregnancy are at increased risk of cardiovascular complications later in life [9]. If untreated, severe PIH may cause dangerous seizures and even death in the mother and fetus. Because of these risks, it may be necessary for the baby to be delivered early, before 37 weeks gestation.

No wonder according to the United nations summit held in 2000, the 4th and 5th goal among the millennium development goals is to reduce child death and improve maternal health by three quarters between 1990 and 2015 [10].

Consistent control of blood pressure requires that pregnant women with hypertension follow medication and dietary regimen. However, the pharmacological effect of antihypertensive therapy may seem to be little if attention is not paid to adherence.

OBJECTIVES OF THE STUDY Main Objective

To evaluate the pattern of prescription of antihypertensives and the rate of adherence to these medications among the pregnant women in Central Hospital Warri, Delta State.

Specific Objectives

• To determine the age bracket of pregnant women who are commonly hypertensive

• To determine the different type of antihypertensives used during this period

• To determine the most commonly prescribed antihypertensive

• To determine the design of therapy be it single or combined

• To determine the degree of adherence to the antihypertensives prescribed

• To determine the causes of non-adherence among these group of patients

METHODS

This was both a retrospective and a prospective study used to evaluate the pattern of antihypertensive prescription and the level of adherence to the prescribed medication among pregnant women respectively in Central Hospital Warri, Delta State.

For the retrospective, a pre-tested data collection form prepared in English language was used to access 198 patients' case folders. Information included in the form were Age, tribe, gestational age, blood pressure, type of hypertension, names of drug prescribed, route of administration, dosage and frequency of drug, and no of pregnancy.

For the prospective, a validated, closed ended 16item questionnaire prepared using the Morisky 8-item medication adherence questionnaire as a template was used to interview 100 hypertensive pregnant women attending antenatal clinics during the period of the study. Additional information to the 8-items was about the patient's sociodemographic profile which includes: age, marital status, educational qualification, religion, ethnic group, occupation, and monthly income. In order to maintain patients' confidentiality, patients' name were not included.

In order to maintain accuracy and precision, patients were informed of the benefits of the research and an informed consent was obtained before the questionnaires were filled. The patients were assured of confidentiality. For patients with low or no educational skill, questions were read, explained and duly filled for them after answers had been supplied by them.

The data collected were carefully entered into a statistical table and analyzed using the SPSS version 17.0 statistical package. Absolute numbers and simple percentages were used to describe categorical variables while quantitative variables were described using measures of central tendency and measures of dispersion. The Chi-square test was used in assessing the significance of associations between categorical groups. A p-value of \leq 0.05 was considered statistically significant.

RESULTS

The tables below represent the result obtained in this study. 198 case files were accessed for the retrospective study. Of the 198 patients, their ages range between 18 and 57 years. They were of different ethnic groups with Urhobo ranking the highest giving a value of 92(46.5%), 21(10.6%) were Ijaw, Itsekiri accounted for 19(9.6%), 22(11.1%) were Igbo, 13(6.6%) were Edo while others comprising of Isoko, Yoruba, Ibibio, Kwale, Ika and

Hausa accounted for 31(15.6%). The patients were all married. All except 6 of the patients were Christians. The socio-demographic features of the patients' are represented in table 1 below.

Table 2 shows the prevalence of pregnancy induced hypertension based on the type of hypertension and number of pregnancy at Warri Central Hospital during the period of the study. Patients that had their first pregnancy for the different type of hypertension (Mild/ pre-eclampsia, severe, Chronic and superimposed) accounted for 48(61.5%), 6(10%), 10(23.8%) and 1(5.9%) respectively. The second pregnancy accounted for 14(17.9%), 13(21.7%), 15(35.7%), and 6(35.3%). The third pregnancy accounted for 4(5.1%), 22(36.1%), 5(11.9%), and 4(23.5%). The fourth pregnancy accounted for 5(6.4%), 8(13.3%), 6(14.3%) and 2(11.8%). The fifth pregnancy gave 4(5.1%), 8(13.3%), 4(9.5%) and 1(5.9%). The sixth, seventh, eighth, ninth and tenth pregnancy accounted for 1(1.3%), 0(0%), 1(2.4%) and 1(5.9%), 1(1.3%), 0(0%), 1(2.4%) and 0(0%), 1(1.3%), 3(5%),0(0%) and 0(0%), 0(0%), 0(0%), 0(0%) and 2(11.8%), 0(0%), 1(1.7%), 0(0%) and 0(0%)

Table 3 below highlights the frequency of the prescribed antihypertensives and their route of administration. Centrally acting adrenergic drugs (Methyldopa) was found to be mostly prescribed which accounted for 182(50.7%). Next to it was the Calcium (Ca²⁺) Channel blocker (Nifedipine) which accounted for 151(42.1%). 13(3.6%) had vasodilators (Hydralazine), 7(1.9%) had Beta blockers (Atenolol), 3(0.8%) had Angiotensin Converting Enzyme Inhibitors (ACEI) while 3(0.8%) were prescribed diuretics (Furosemide). Also the oral route recorded the highest frequency accounting for 90.2%

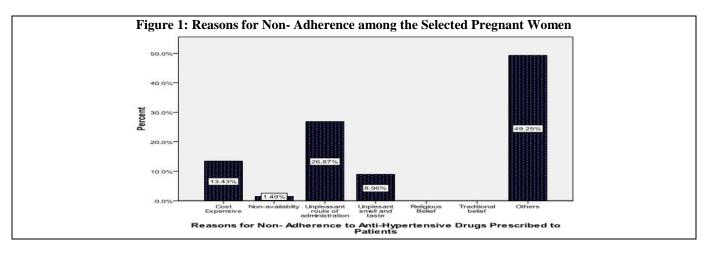
Table 4 shows the pattern of drug prescribed. 12(6.1%) of the 198 patients had lifestyle modification. 20(6.1%) patients were placed on a single therapy. 114(57.6%) were on two combination of drugs. 45(22.7%) had three combination of drugs while 7(3.5%) were prescribed a combination of four drugs.For the prospective,

100 patients were interviewed. The socio-demographics is presented in table 5. The ages range between 18years and above 58 years. Majority of the patients were between 33 and 37 years. All except one of the patients interviewed were married at the time of the study. Less than half of the respondents (42%) had tertiary education as the highest level of education attained and only 8% of the respondents had no educational qualification. Majority of the population were Christian (95%) while others were of the Islamic religion. A higher percentage of the respondents were traders (44%), followed by those who were self employed (29%), 15% civil servants, 5% students while others made up 7%. Of the 100 patients, majority were Urhobo giving a value of 44%, 19% were Ijaw, Itsekiri accounted for 11%, 9% were Igbo, 4% were Edo while others comprising of Isoko, Yoruba, and Hausa accounted for 16%. 57% of the entire population had their monthly income between N5, 000 to N30, 000 while 6% had their income above N100, 000

Table 6 presents the level of adherence. More than half of the respondents were non-adherent to their blood pressure medications (67 %), while (33%) of the respondents were adherent to their blood pressure medication.

Table 7 displays the correlational analysis of Socio-Demographic variable of pregnant women to the degree of adherence to antihypertensive drugs prescribed using the chi-square analysis. Ethnic group was significantly associated with adherence ($x^2=14.114$, df=5, p<0.05). Factors found not to be significantly associated with adherence were, age ($x^2 = 6.652$, df=6, p>0.05), marital status ($x^2=0..498$, df=1, p>0.05), educational qualification ($x^2=3.943$, df= 3, p>0.05), religion ($x^2=0.117$, df=1, p>0.05), occupation ($x^2=5.664$, df=4, p>0.05), and Monthly income ($x^2=3.042$, df=3, p>0.05).

Fig 1 shows that the major factor why respondents did not adhere to their medication is forgetfulness (49.25%), while only a small percent of respondents miss their medication as a result of non-availability (1.49%). 26.87% was due to unpleasant route of administration while 13.43% complained of cost.



Ethnic Group	Frequency	Percentage (%)
Age (years)		
18-22	14	7.1%
23-27	25	12.6%
28-32	68	34.3%
33-37	55	27.8%
38-42	28	14.1%
43-47	4	2.1%
48-52	3	1.5%
53-57	1	0.5%
Above 58	0	0%
Ethnic group		
Urhobo	92	46.5%
Ijaw	21	10.6%
Itskeri	19	9.6%
Igbo	22	11.1%
Edo	13	6.6%
Other	31	15.7%
Religion		
Christian	192	96.9%
Islam	6	3.0%
Marital Status		
Married	198	100%
Divorced	0	0%

 Table 1. Socio-demographic characteristics of patient

Table 2. Prevalence of Pregnancy- induced hypertension

		Type of Hy	ypertension		
Nth No. of Pregnancy	Mild/Pre- Eclampsia	Severe Hypertension	Chronic Hypertension	Superimposed HTN	Total
	Frequency (%)	Frequency (%)	Frequency (%)	Frequency (%)	Frequency (%)
1	48(61.5)	6(9.8)	10(23.8)	1(5.9)	65(32.8)
2	14(17.9)	13(21.3)	15(35.7)	6(35.3)	48(24.2)
3	4(5.1)	22(36.1)	5(11.9)	4(23.5)	35(17.7)
4	5(6.4)	8(13.1)	6(14.3)	2(11.8)	21(10.6)
5	4(5.1)	8(13.1)	4(9.5)	1(5.9)	17(8.6)
6	1(1.3)	0(.0)	1(2.4)	1(5.9)	3(1.5)
7	1(1.3)	0(.0)	1(2.4)	0(.0)	2(1.0)
8	1(1.3)	3(4.9)	0(.0)	0(.0)	4(2.0)
9	0(.0)	0(.0)	0(.0)	2(11.8)	2(1.0)
10	0(.0)	1(1.6)	0(.0)	0(.0)	1(0.5)
Total	78(100.0)	61(100.0)	42(100.0)	17(100.0)	198(100.0)

Table 3. Frequency on the Different type of Anti-hypertensive Drugs Prescribed and their Route of Administration

		Frequency	Percent		
	Centrally acting	182	50.7%		
	Ca ²⁺ Channel blockers	151	42.1%		
	Vasodilator	13	3.6%		
Name of Drug	Beta Blockers	7	1.9%		
	ACE inhibitors 3		0.8%		
	Diuretics	3	0.8%		
	Total	359	100.0%		
Doute of	Oral	370	90.2%		
Route of Administration	Intravenous (IV)	40	9.8%		
Aummistration	Total	410	100.0%		

Combination of Drugs	Frequency	Percentage (%)
Life Style Modification	12	6.1%
One drug	20	10.1%
Two drugs	114	57.6%
Three drugs	45	22.7%
Four drugs	7	3.5%

Table 4. Frequency of Combination of Anti – hypertensive Drugs

Table 5. Patients' Socio-demographics

Characteristics		Frequency (%)									
Age (years)	18-22	23-27	28-32		33-37	38-42	43-47	48-52	53-57	Above 58	
Total (100)	5(5)	8(8)	31(3)	1)	33(33)	20(20)	2(2)	0(0)	0(0)	1(1)	
Marital status	Marrieo	l D	ivorced								
Total (100)	99(99)		1(1)								
Educational Qu	alification	Noi	ne	Pri	imary	Secon	dary	Tert	iary		
Total (1	.00)	8(8	8(8) 15(1		5(15)	35(3	35)	42(4	42(42)		
Religion	Christian	Isla	m								
Total (100)	95(95)	5(5	5)								
Ethnic group	Urhobo	Ijaw	Itsek	iri	Igbo	Edo	Otl	hers			
Total (100)	41(41)	19(19)	11(1	1)	9(9)	4(4)	16	(16)			
Occupation	Student	Civil	Servant	bervant		mployed Trader		ader	Others		
Total (100)	5(5)	15	(15)	5) 2		9(29) 44		44(44) 7(7)			
Monthly Income	Below	v N5,000	5,000 N5,000-N		30,000	N30,000-N	N30,000-N100,000		Above N100,000		
Total (100)	15	15(15) 57(57)		7)	22(2	22(22) 6(6)					

Table 6. Level of Adherence

Level Of Adherence	Frequency	Percentage (%)
Non adherence	67	67%
Adherence	33	33%
Total	100	100%

Table 7. Correlational analysis of Socio-Demographic Variable of Pregnam	Women to the Degree of Adherence to
Antihypertensive Drugs Prescribed (Chi-square Analysis)	

Variables		Adhere	ence	Non Adherence				
Variables		Frequency	%	Frequency	%	X ²	Df	P-Value
	18-22	0	.0%	5	7.5%	6.652	6	0.354
	23-27	3	9.1%	5	7.5%			
	28-32	8	24.2%	23	34.3%			
	33-37	13	39.4%	20	29.9%			
Af D	38-42	9	27.3%	11	16.4%			
Age of Pregnant Women	43-47	0	.0%	2	3.0%			
	48-52	0	.0%	0	.0%			
	53-58	0	.0%	0	.0%			
	Above 59	0	.0%	1	1.5%			
	Total	33	100.0%	67	100.0%			
	Single	0	.0%	0	.0%	0.498	1	0.481
	Married	33	100.0%	66	98.5%			
	Divorced	0	.0%	1	1.5%			
Marital Status	Seperated	0	.0%	0	.0%			
	Widowed	0	.0%	0	.0%			
	Total	33	100.0%	67	100.0%			
	Primary	2	6.1%	13	19.4%	3.943	3	0.268
Educational Qualification	Secondary	13	39.4%	22	32.8%			

	Tertiary	14	42.4%	28	41.8%			
	None	4	12.1%	4	6.0%			
	Total	33	100.0%	67	100.0%			
	Christian	31	93.9%	64	95.5%	0.117	1	0.733
D -1:-:	Islam	2	6.1%	3	4.5%			
Religion	Others	0	.0%	0	.0%			
	Total	33	100.0%	67	100.0%			
	Uhrobo	8	24.2%	33	49.3%	14.114	5	0.015
	Ijaw	7	21.2%	12	17.9%			
	Itskeri	2	6.1%	9	13.4%			
Ethnic Group	Igbo	7	21.2%	2	3.0%			
	Edo	2	6.1%	2	3.0%			
	Other	7	21.2%	9	13.4%			
	Total	33	100.0%	67	100.0%			
	Student	2	6.1%	3	4.5%	5.664	4	0.226
	Civil Servant	3	9.1%	12	17.9%			
Occupation	Self employed	14	42.4%	15	22.4%			
	Trader	13	39.4%	31	46.3%			
	Others	1	3.0%	6	9.0%			
	Total	33	100.0%	67	100.0%			
Monthly Income	Below N5, 000	7	21.2%	8	11.9%	3.042	3	0.385
	N5, 000-N30, 000	15	45.5%	42	62.7%			
	N30, 000- N100, 000	9	27.3%	13	19.4%			
	Above N100, 000	2	6.1%	4	6.0%			
	Total	33	100.0%	67	100.0%			

(Note: X^2 is Significant when P-value is less than 0.05)

DISCUSSION

In this study, it was observed that hypertension in pregnancy was most prevalent among those carrying their first pregnancy (32.8%) and women between the childbearing age of 28 to 32 years old (34.3%), thus posing a major risk or predisposing factor to hypertensive disorder.

The result was comparable with the findings that the first pregnancy accounted for the highest percentage of patients with pre-eclampsia [11, 12], and that the hypertension in the first pregnancy constitutes a very important risk factor. Those with their second to the tenth pregnancy accounted for 24.2%, 17.7%, 10.6%, 8.6%, 1.5%, 1.0%, 2.0%, 1.0% and 0.5% respectively. First pregnancy is thus observed as a predisposing factor to preeclampsia since the first foetus is seen as a hostile graft which the mother's immune system tries to fight as a foreign body [13].

Therefore women carrying their first pregnancies should be encouraged to regularly visit antenatal clinics

and meet their care givers so as to prevent the complications associated with first pregnancies as a crucial factor for gestational hypertension. There are reports that there is a multifactorial condition involving some sorts of immune response to pregnancy as a foreign material just as in tissue graft rejection and that the varying intensities of the rejection are probably responsible for the numerous ways the hypertension presents itself in different women [13].

More evidently, is the study carried out which affirmed that offspring of women with this hypertensive disorder of pregnancy are at increased risk of cardiovascular complications later in life [9]. No wonder, it is stated among the Millennium development goals to reduce child death and improve maternal health by 2015 as the fourth and fifth goals respectively [10].

In addition, it was revealed that methyldopa of the centrally acting adrenergic class was the most frequently

prescribed antihypertensive because it was prescribed to more than half (50.7%) hypertensive pregnant women. This could be due to the fact that methyldopa has a long history of use in treating hypertension in pregnancy, and using methyldopa as reported increases fetal survival rates and decreases mid-trimester fetal loss [14]. According to Ludwina, methyldopa has been an antihypertensive drug of first choice in case of pregnancy as it has tolerable or no side effects to the foetus and has been shown to be safe in every trimester. Nifedipine from the Ca²⁺ channel blocking class was administered to 42.1% patients. It has been found useful as well in the management of hypertensive disorder in pregnancy as it acts within 10-20 minutes from oral administration [15].

Hydralazine, a vasodilator was prescribed to 3.6% patients intravenously. The intravenous form of hydralazine is used usually in combination with other antihypertensive as it has been found useful when treating severe hypertension due to pre-eclampsia. Another drug employed in the management of hypertensive disorder in pregnancy is atenolol, a beta blocker. Although it is more effective than methyldopa in the treatment of mild to severe hypertension [15] as it was prescribed to 1.9% of the patients, it is worthy of note that it is given from the third trimester of pregnancy and should be avoided in the first trimester. Diuretics such as Furosemide used as an antihypertensive was not left out in the management of hypertensive disorders as it has been reported to compliment the effect of other antihypertensives. The common regimens of therapy administered on the patients were in the order combination of two drugs> combination of three drugs> single therapy> life style modification, then the use of four drugs. The combinations used were methyldopa and nifedipine (for two), methyldopa, nifedipine and hydralazine or methyldopa, nifedipine and atenolol in case of three combinations of drugs. It was observed that methyldopa was the most frequently used drug as it appeared in almost all the different combinations of the drug therapy. In addition to the use of drugs in the management of hypertensive disorders, life style modification was also employed in some patients (6.1%). This could be due to the fact that the prescriber must have believed the patient needs healthy life style such as having a nutrient-rich diet, limit alcohol intake, stop smoking and engage in aerobic exercises at least 30minutes daily.

This study revealed that less than half (33%) of the patients adhered to their prescribed medication. Poor adherence was found to be mainly due to forgetfulness (49.25%) which could be due to busy schedule on the side of the patients as a predisposing factor to them forgetting to adhere to their prescribed regimen. Other factors include unpleasant route of administration (26.87%) as some pregnant women feel uncomfortable with the oral route of administration, cost/expenses (13.43%) as this was shown with almost half of the patients receiving less than N30, 000 monthly income when after settling their individual monthly expenses as both mothers and wives might be left with little or nothing to purchase the prescribed drugs. Unpleasant smell and taste (8.96%) was recorded as another factor for poor adherence. This could be due to the fact that as pregnant women, nausea and vomiting are observed at the first trimester of pregnancy. Lastly, nonavailability (1.49%).

CONCLUSION

The study revealed prevalence of pre-eclampsia as a hypertensive disorder in pregnancy among women carrying their first pregnancy while Methyldopa still remains the drug of choice in the management of hypertension as shown where it was administered to 91.9% patients. Poor adherence was also evident due to forgetfulness, unpleasant route of administration, unpleasant smell and taste, cost/expenses and nonavailability.

ETHICAL CONSIDERATION

Informed consent was obtained from all one hundred participants of the prospective study. The consent was obtained after the aims of the study had been explained. Ethical approval to carry out the study was obtained from Delta State Hospital management Board, Warri medical Zone through a letter for appropriate approval prior to the study. Relevant guidelines for maintaining the confidentiality of information were strictly adhered to.

ACKNOWLEDGEMENT

We the authors wish to acknowledge the members of staff of the obstetrics and gyneacology department of central hospital Warri, Delta State.

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