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PRESCRIPTION PATTERN OF ANTIHYPERTENSIVE DRUGS IN ENUGU: A REPORT OF THE ESUT RESEARCH GROUP

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ABSTRACT
Over the years many antihypertensive medications have become available; however, there is a need for early, effective and rational combination of medications. Limited data exist in South East Nigeria to give a clear picture of prescription patterns. The main objective of the present study, therefore, is to assess the prescribing patterns of antihypertensives in outpatients attending a teaching hospital in Enugu, South East Nigeria. This is a cross-sectional study conducted in the medical out-patient clinic of the Enugu State University of Science and Technology Teaching Hospital (ESUTH) in Enugu, Enugu State, South East Nigeria. The SPSS version 17 (IBM Corporation, New York, USA) was used for database management and statistical analysis. Three hundred and sixty one subjects were recruited and their case notes were reviewed. During the period under review 25.5% (93/361) were on monotherapy and 67.6% (243/361) were on combination therapy. Most combinations were made up of 2 medications 75.7% (184/243). Diuretics 59.8% (216/361), calcium channel blockers 43.2% (156/361) and angiotensin converting enzymes inhibitors 42.8% (153/361) were commonly prescribed. Diuretics were the most commonly used drug 54.6 % (197/361) in combination therapy. Blood pressure was normal (<140/90mmHg) in 31% (112/361) individuals. Number of medications prescribed positively correlated with systolic and diastolic blood pressure levels and negatively with the number of co-morbidities. In conclusion, most hypertensive subjects attending the outpatient clinic at ESUTH, Enugu used diuretic based combination therapy. Prescription pattern correlated with blood pressure levels and not number of co-morbidities. The overall level of blood pressure control among hypertensive subjects remains low at 31% despite the fact that 74.5% were on combination therapy. Public health educational measures promoting primary and secondary prevention of hypertension should be encouraged with emphasis on adherence

KEYWORDS: Antihypertensive drugs, Hyprtension, Nigeria, Prescription pattern.

INTRODUCTION
Hypertension has increased in prevalence for individuals of all races and ethnicities[1] with more than 35% of the adult population currently hypertensive in many African countries[2]. In most studies less than 30% of hypertensives were on drug treatment and less than 20% had blood pressure within the defined normal range[2]. Over the years many antihypertensive medications have become available, however, there is a need for early, effective and rational combination of medications in poor countries such as ours[3].

The 7th report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC7)[4] recommended what can be described as rational drug combination in the treatment of hypertension based on established clinical trials. Survey of prescription presents an indirect way to ascertain the assimilation of modern recommendation of hypertensive treatment among practising physicians in a tertiary hospital[5]. This is particularly true in the elderly with multiple pathologies and co-morbidities where the added burden of poly-pharmacy and high rates of adverse drug reactions[6] may lead to greater likelihood of non- adherence. Limited data exist in South East Nigeria to give a clear picture of prescription patterns. This is the first study, to the best of our knowledge, from South East Nigeria to address prescription pattern of antihypertensives and blood pressure control in a hospital setting.

MATERIALS AND METHODS
Study Design
This is a cross sectional study conducted in the medical out-patient clinic of the Enugu State University of Science and Technology Teaching Hospital (ESUTH) in

Enugu, Enugu State, South East Nigeria. Case notes of all consecutive out-patients being managed for hypertension were reviewed. Patients were recruited from different sub-specialties. Exclusion criteria were less than 3 clinic visits in the last 6 months. Ethical clearance was obtained from the Ethics Review Committee of ESUTH. Ethical conduct was maintained during data collection and throughout the research process. Study duration was 6 months (June –November 2013).

Prescription Pattern

Current prescription (drugs used by the patient before the index visit) and other cardiovascular co-morbidities were recorded from the case file.

Blood Pressure Measurement

Participants were interviewed in the clinic between 9:00 and 10:30 am to ensure steady state. After they had rested in a sitting position for 2-5minutes, the blood pressure was recorded twice by means of mercury sphygmomanometer according to the guidelines of the European Society of Hypertension[7]. Blood pressure was measured by one of the investigators or a doctor not below the rank of a registrar in the department of medicine using mercury sphygmomanometer and stethoscope (Kris-Alloy®, Wuxi Medical Instrument Factory, Wuxi City Jiangsu, China). All blood pressure measurements were obtained at the non-dominant arm. A standard cuff with an inflatable bladder of 22 × 12 cm was used if arm circumference is less than 32 cm and cuffs with a 35 × 15 cm bladder on larger arms. High blood pressure was defined using the WHO/ISH criteria of systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic blood pressure (DBP) ≥ 90 mmHg[7]. Weight was measured using a standard bathroom scale in kilograms. Height was measured in centimetres using a straight metre rule with the patient standing erect on a flat surface. The blood pressure measurements were averaged for analysis.

Statistical Methods

The SPSS version 17 (IBM Corporation, New York, USA) was used for database management and statistical analysis. Data were presented in tables. The statistical methods also included Student's *t*-test for unpaired observations. Normal blood pressure (or high blood pressure) was calculated as percentage of participants with SBP, DBP and SBP/DBP below WHO/ISH criteria[11]. In all, *p < 0.05 was regarded as statistically significant. Conclusions were drawn at this level of significance at 95% confidence level.

RESULTS

Three hundred and sixty one (226 women, 135 men) case notes were reviewed. The characteristics of the studied population are presented in Table 1. Most subjects were 45-64 years. The mean age was 59.8±12.2 years. Men were significantly older than women (**p<0.0001). Most of the subjects were married (70.1%) and came from urban settings 69.3% (250/361). The majority of the subjects were in business or civil servants 44.3% (160/361) and had some tertiary education 47.6% (172/361). Regular use of herbal medicine was reported in 71.2% (257/361) cases.

During the period under review, 6.9% (25/361) were not on medication (stopped their medication at home), 25.5% (93/361) were on monotherapy and 67.6% (243/361) were on combination therapy. Most combinations were made up of 2 medications 75.7% (184/243). Diuretics 59.8% (216/361), calcium channel blockers 43.2% (156/361) and angiotensin converting enzyme inhibitors 42.8% (153/361) were commonly prescribed. Diuretics were the most commonly used drug 54.6 % (197/361) in combination therapy. Beta blockers were the least prescribed 3.6% (13/361) as depicted in Tables 2a and 2b.

Most patients had only hypertension (HBP) 53.7% (194/361) while the rest also had diabetes (HBP/DM)34.1% (123/361), stroke (HBP/Stroke) 7.2% (26/361) or both (HBP/DM/Stroke) 5% (18/361). The prescription pattern in hypertensives with various comorbidities is shown in Table 3. Diuretics were the most commonly prescribed drug in all sub groups reaching as high as 80% in HBP/Stroke. CCB and ACEI were evenly prescribed in HBP and HBP/DM. CCB was prescribed twice as much in HBP/Stroke as ACEI. The least prescribed drugs were Beta blockers (3.6-4.8%). The highest proportion of patients who were not on medication were in patients with HBP/DM/Stroke.

The mean systolic blood pressure was 141.0±21.8mmHg (140.9±22.3mmHg women, 141.3±21.1mmHg men, p=0.86) and diastolic blood pressure was 85.0±13.5mmHg (84.6±13.4mmHg women, 85.7±13.7mmHg men, p=0.43). The distribution of prescription pattern and blood pressure is shown in Tables 4 and 5. Systolic blood pressure was normal (<140mmHg) in 40.2% (145/361) of the subjects; 40% (54/135) men, 40.3% (91/226) women, *p=0.97. Diastolic blood pressure was normal in 52.4% (189/361); 48.1% (65/135) men, 54.9% (124/226) women, *p=0.137. Overall, blood pressure (SBP/DBP <140/90mmHg) was controlled in 31% (112/361) of the subjects; women 30.1% (68/226), men 32.6% (44/135), *p=0.62.

The distribution of blood pressure and prescription pattern is shown in Tables 4 and 5.

Number of medications prescribed positively correlated with systolic (r=0.252) and diastolic blood pressure (r=0.176) and negatively with the number of medical co-morbidities.

Table 1: Characteristics of Participants

Characteristic	Total	Women	Men	*P*-value
Anthropometrics				
Gender, n(%)	361(100)	226(62.6)	135(37.4)	<0.0001
Age, years	59.8±12.2	57.5 ± 12.8	63.7 ±10.1	<0.0001
Height, cm	159.5±7	157.2 ± 5.6	163.3 ± 7.4	<0.0001
Weight, kg	74.4±15.4	75.0 ± 17.3	73.0 ± 12.5	0.24
Body mass index, kg/m^2	29.3±6.5	30.3 ± 6.5	27.5±6	<0.0001
Age group (years)				
<45, n(%)	37(10.2)	32(14.2)	5(3.7)	<0.0001
45-64, n(%)	190(52.6)	127(56.2)	63(46.7)	<0.0001
≥65, n(%)	134(37.1)	67(29.6)	67(49.6)	<0.0001
Peripheral haemodynamics				
Systolic pressure, mm Hg	142.4±21.8	142.5 ± 22.3	142.2 ±20.9	0.90
Diastolic pressure, mm Hg	84.2±13.7	84.0 ± 13.3	84.4 ±14.5	0.84
Lifestyle	66(31.4)	37 (36.3)	29 (26.9)	0.14
Herbal medicine n(%)	257(71.2)	154(68.1)	103(76.3)	0.10

Table 2: Prescription Pattern of Antihypertensive Drugs

	N (%)
Table 2a.	
Diuretics	216(59.8)
CCB	156(43.2)
ACEI	153(42.4)
ARB	86 (23.8)
Aldomet	18(5)
ß-blockers	13(3.6)
No medication	25(6.9)
Monotherapy	93(25.8)
Combination therapy	*243(67.3)*
Two drugs	184(51)
≥Three drugs	59(16.3)
Table 2b..	
ACEI	39(10.8)
ACEI+CCB	24(6.6)
ACEI+Diuretics	51(14.1)
ACEI + Aldomet	2(0.6)
ACEI+CCB+Diuretics	26(7.2)
ACEI+CCB+ Aldomet	1(0.3)
ACEI+CCB+Diuretics + Aldomet	2(0.6)
ARB	10(2.8)
ARB +CCB	15(4.2)
ARB + Diuretics	41(11.4)
ARB +CCB+ Diuretics	17(4.7)
ARB + Diuretics + ß-blockers	1(0.3)
ARB+CCB + ß-blockers+ Diuretics	1(0.3)
ARB +CCB+ Diuretics + Aldomet	1(0.3)
CCB	21(5.8)
CCB+Diuretics	41(11.4)
CCB+ ß-blockers	1(0.3)
CCB+ ß-blockers +Diuretics	1(0.3)
CCB+ Diuretics + Aldomet	5(1.4)

ß-blockers	5(1.4)
ß-blockers + Aldomet	1(0.3)
Diuretics	22(6.1)
Diuretics + ß-blockers	2(0.6)
Diuretics + Aldomet	4(1.1)
Aldomet	2(0.6

Table 3: Distribution of Antihypertensive Drugs among Patients with Hypertension

Disorder	Hypertension	HBP/DM	HBP/stroke	HBP/DM/Stroke	Total
Diuretics	135(69.6)	53(43.1)	21(80.8)	7(38.9)	216(59.8)
CCB	85(43.8)	51(41.5)	13(50)	7(38.9)	156(43.2)
ACEI	86(44.3)	53(43.1)	7(26.9)	7(38.9)	153(42.4)
ARB	50(25.8)	30(24.4)	5(19.2)	1(5.6)	86(23.8)
ß-blockers	9(4.6)	3(2.4)	1(3.8)	-	13(3.6)
Aldomet	11(5.7)	4(3.3)	1(3.8)	2(11.1)	18(5)
No medication	4(2.1)	15(12.2)	2(7.7)	4(22.2)	25(6.9)
Monotherapy	48(24.7)	34(27.6)	3(11.5)	7(38.9)	93(25.5)
Combination therapy	142(73.2)	74(60.2)	21(80.8)	7(38.9)	243(67.6)
Total	194(53.7)	123(34.1)	26(7.2)	18(5)	361(100)

Table 4. Distribution of Antihypertensive and Blood Pressure Control

Disorder	SBP<140	DBP<90	SBP/DBP< 140/90
ACEI	61(39.9)	83(41.3)	47(30.7)
ARB	32(37.2)	53(26.4)	28(32.6)
CCB	39(25)	75(37.3)	31(19.9)
ß-blockers	4(30.8)	8(4)	4(30.8)
Diuretics	77(35.6)	116(57.7)	64(29.6)
Aldomet	3(16.7)	6(3)	2(11.1)
No medication	14(56)	17(8.5)	12(48)
Monotherapy	42(45.7)	53(26.4)	35(38)
Combination therapy	82 (33.6)	131(65.2)	66(27)
Total	138(38.2)	201(55.7)	113(31.3)

Table 5: Blood Pressure Control and Other Variables

Variable	SBP (mmHg) (<140mmHg)	DBP(mmHg) (<90mmHg)	SBP/DBP(mmHg) (<140/90 mmHg)
Co-morbidity			
HBP	74(38.1)	102(52.6)	62(32)
HBP+diabetes	55(44.7)	66(53.7)	36(29.3)
HBP+stroke	12(46.2)	12(46.2)	10(38.5)
HBP+diabetes+stroke	4(22.2)	9(50)	4(22.2)
Prescription			
No medication	11(44)	20(80)	10(40)
Monotherapy	44(47.3)	50(53.8)	35(37.6)
Combination therapy			
Two drugs	81(42.9)	102(54)	61(32.3)
Three drugs+	9(16.7)	17(31.5)	6(11.5)
Total	145(40.2)	114(54.3)	112(31)

Table 6: Correlation between Systolic Blood Pressure, Diastolic Blood Pressure, Presence of Comorbidity and Number of Medication

	SBP (mmHg)		DBP(mmHg)			
Co morbidity	**r**	**p-value.**	**r**	**p-value**	**r**	**p-value**
No medication	0.252	<0.001	0.176	0.001	-0.382	<0.001
Co-morbidity	0.024	0.65	0.049	0.35	-	-

DISCUSSION

The major findings in this study are: firstly, the frequent use of combination therapy (67.6%); secondly, frequent use of diuretics 59.8%, calcium channel blockers 43.2% and angiotensin converting enzyme inhibitors 42.8 %; thirdly, the number of drugs prescribed positively correlated with blood pressure level and negatively with the number of co-morbidities in a patient. The most prescribed antihypertensives in this study were diuretics, ACEI/ARB and CCB. Although older antihypertensive drugs are cheaper, in the long run they may contribute to the development of side effects such as metabolic syndrome, diabetes mellitus, gout and dyslipidemia. More importantly, treatment with newer drugs results in lower risk of morbidity and mortality[8-10]. The low rate of prescription of cheaper drugs such as beta blockers and central acting drugs such as alpha methyl dopa, as well as the overall prescription pattern is similar to previous reports in Nigeria[5,11-13]. Tamuno and Fadare reported that 62% of the patients were on ACEI while 14.5% and 15.5% were on beta blockers and alpha methyl dopa respectively[11]. A report from East Africa showed that diuretics and beta blockers were the most prescribed antihypertensives[14] which is different from the index report where diuretics and ACEI/ARB were the most prescribed.

The most commonly used combinations were ACEI + diuretics (14.1%), ARB+ diuretics (11.4%) and CCB + diuretics (11.4%) respectively. Anticipated advantages of this approach include tighter and earlier blood pressure control, simplification of the therapeutic regimen and therefore better adherence; avoidance of dose dependent adverse effects experienced with higher doses of single agents and attenuation of adverse effects of some agents. The proportion of patients on combination therapy (67.6%) in this study is consistent with reports from other teaching hospitals in Nigeria and Africa where 56%-80% were on combination therapy[11-13]. We found a positive correlation between systolic and diastolic blood pressure levels and the number of prescriptions used and a negative correlation with the number of co-morbidities. This suggests that blood pressure levels rather than the presence of co-morbidity was the most likely determinant of prescription pattern. The frequent prescription of diuretics either as monotherapy or in combination therapy is similar to previous studies[11-13] and may also be linked to the documented efficacy of diuretics in blacks[3,4].

Undoubtedly, cost containment is important in the management of a common disease, such as hypertension, especially in Nigerian settings where out-of-pocket medical expenditure is the usual practice, hence the high patronage given to cheap unbranded drugs. It is important therefore, that the cost implication of combination therapy be considered in South East Nigeria because of rampant poverty. The cost of ARB, ACEI and CCB are known to be much higher than the older drugs. The high prescription rates of combination therapy using these drugs may contribute to poor adherence because of poverty. The relative high proportion of those who were not on medication during the study period may support this assumption.

Prescription pattern in patients with co-morbidities revealed some interesting trends. About 22% of those with hypertension/diabetes/stroke were not on medication. Apart from high cost of medications, pill burden, drug side effects and other patient (or physician) related factors may be contributory. Many community dwellers do not accept hypertension as a lifelong disorder (mainly due to poor patient education), hence may feel that they are 'cured' as soon as the blood pressure drops and come to hospital soon after it rises. Many people still seek care from spiritual and herbal healer as was seen in this study where 71.2% were using herbal (alternative) medicine; most of which have doubtful efficacy.

Diuretics was prescribed in 38.9% in patients with HBP/DM/Stroke. The reason may be the metabolic side effect of diuretics especially the thiazides. Most combination therapy was prescribed in those with stroke also suggesting that these patients may have higher levels of blood pressure at onset.

This study shows that blood pressure (SBP/DBP) was controlled in 31.3% similar to 30.5% obtained in another study[13] and 29% obtained in Ibadan[15]. Epidemiological data show that 0.9%-47.8% of hypertensive patients in SSA achieve blood pressure control[2]. The low rate of control may suggest non adherence among the patients.

This is the first study in South East Nigeria, to the best of our knowledge, to study the prescription pattern of antihypertensive drugs in a teaching hospital setting in SE Nigeria. However, the sample may not strictly be representative, as most patients in the community do not attend government hospitals due to long waiting time. This limitation makes it difficult to generalize our findings to other populations. Prescription pattern in some categories such as those with co-morbid diabetes and stroke may have been overestimated because of small number of patients in the study. Another limitation of the study was the teaching hospital setting which is

likely to make subjects with severe hypertension to be over represented.

CONCLUSION

Most hypertensive subjects attending the outpatient clinic at ESUTH in Enugu used diuretic based combination therapy. Prescription pattern positively correlated with blood pressure levels but negatively with the number of co-morbidities. The overall level of blood pressure control among hypertensive subjects remains low at 30.1% despite the fact that 74.5% were on combination therapy. Public health educational measures promoting primary and secondary prevention of hypertension should be encouraged with emphasis on adherence.

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