*Full Length Research Paper*

# Evaluation of the prescription pattern of antihypertensive agents in a tertiary health institution in Nigeria

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**Hypertension is a cardiovascular disease with high morbidity and mortality. Effective blood pressure control can be achieved in patients with lifestyle modifications and by the use of antihypertensive agents. The objective of this study was to determine the prescribing pattern of antihypertensive medications in a tertiary health institution in South-Eastern Nigeria and also to determine the prescribers' compliance to recognised treatment guidelines. This was a retrospective cross sectional study and a total of 848 prescriptions generated from 202 hypertensive case files were used. Data extracted from the case files of hypertensive patients who attended the hospital from January to December, 2010 were coded and analysed using Statistical Package for Social Sciences (SPSS). The mean age of the patients consisting of mainly females (n=119, 59%) and then, males (n=83, 41%) was 59 years. Stage 2 hypertension was the most common class seen among the patients followed by stage 1 and then, the prehypertension with antihypertensive agents prescribed at all the stages. Co-morbid conditions increased with increase in blood pressure with type 2 diabetes being the most common, followed by congestive heart failure (CHF). The study also showed that the two most commonly prescribed agents either as monotherapy or as combination therapy were diuretics (D) and calcium channel blockers (CCBs) followed by angiotensin converting enzyme inhibitors (ACEIs) with angiotensin receptor blockers (ARBs) being the least prescribed. This study showed that there were reductions in the mean systolic and diastolic blood pressures with a decrease in mean arterial pressure (MAP) from 118 to 104 mmHg after initiation of therapy. This study shows a good adherence to current evidence based treatment guidelines and hypertension treatment guidelines.**

**Key words:** Hypertension, antihypertensives, prescription pattern, tertiary health institution, Nigeria.

## INTRODUCTION

Hypertension is the most common worldwide cardiovascular disease which is especially prevalent in
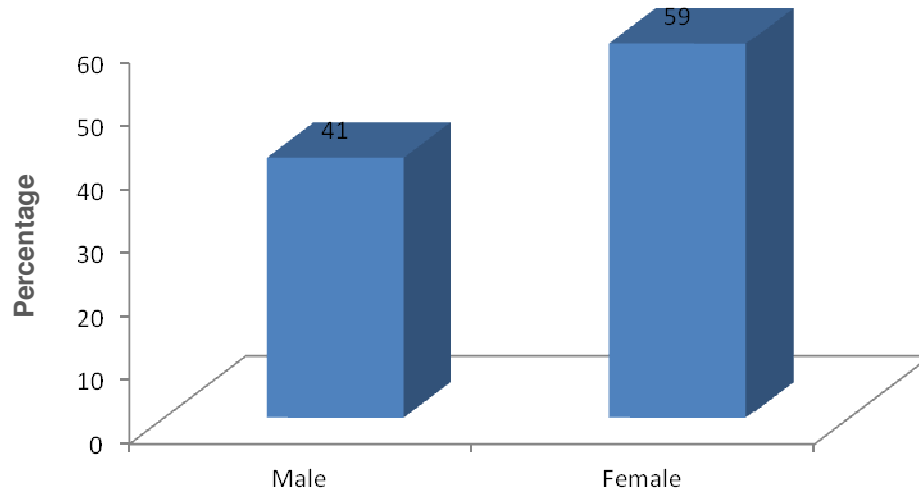
**Figure 1.** Percentage of gender distribution.

many developing countries (Benowitz, 2007) and it has been estimated to cause 4.5% of current global disease burden. Increased age is associated with increased prevalence of hypertension especially systolic hypertension after 60 years (Anderson, 1999). Most people do not know that they are hypertensive, while some have misconceptions about it. Several community-based investigations have served to emphasize that hypertension is rapidly emerging as a major public health problem in developing countries (Fuentes et al., 2000). The prevalence of hypertension in Nigeria, which was 15.3% (urban) and 10.6% (rural) in the general population (Akinkugbe, 2002; FMOH, 1997), was later estimated in hospital setting to be 17 to 20% (Kadiri et al., 1999). Hypertension has been implicated as a major factor in the development of stroke, coronary artery disease, heart failure and atrial fibrillation (Angeli et al., 2014).

Treating hypertension has been associated with about 40% reduction in the risk of stroke and about 15% reduction in the risk of myocardial infarction (Collins et al., 1990). Hence, lifelong management and life style modifications, and pharmacotherapy (Seseen, 2009) are needed for its treatment and management, and the ultimate goal is to reduce morbidity and mortality through a reduction in hypertensive associated complications.

Meanwhile, evidence based hypertension treatment guidelines are widely available for the management of hypertension with the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure in 2003 (JNC 7) (Chobanian et al., 2003) and the currently released, Eight Joint National Committee (JNC 8) report on Evidence-Based Guideline for the Management of High Blood Pressure in Adults (James et al., 2014) being widely recognized as the gold standards for hypertension management. Recent evidence suggests that adherence to these treatment guidelines with little or no modifications results in good control and meaningful reductions in blood pressure and also results in substantial reduction in prescription cost. However, as more new generation drugs are now available for the management of hypertension and combination therapies in most cases are showing better treatment outcomes; drug utilization studies intended to evaluate and analyze prescribing attitude of physicians are very important. They are enabling the achievement of rational and cost effective medical care, as well as, achievement of the effective blood pressure control.

This study is therefore aimed at determining the prescribing pattern of antihypertensive medications in a tertiary health institution in South-Eastern Nigeria and also to determine the prescribers' compliance to recognised treatment guidelines.

## METHODOLOGY

This was a cross sectional retrospective study carried out at Nnamdi Azikiwe University Teaching Hospital (NAUTH), in the South-East Nigeria between January and December, 2010. The medical records of hypertensive African Blacks who attended the hospital within the specified period were used for the study. Eight hundred and forty eight prescriptions from two hundred and two folders were selected and the patients' demographic data, dates of visits, antihypertensive agents used both as monotherapy and as combination therapy were recorded and analysed using Statistical Package for Social Sciences application (SPSS version 18, USA).

## RESULTS

A total of 848 prescriptions from 202 patients were used for the study. The mean age of the patients was 59 years with male to female ratio of approximately 1:1.5 as shown in Figure 1.

**Table 1.** Classification of the antihypertensive patients with respect to severity of hypertension using JNC 7 classification (n: 202).

| Category | BP level (mmHg) | No. of patients (%) |
|---|---|---|
| Prehypertension | 120-139/80-89 | 12  (5.9) |
| Stage 1 hypertension | 140-159/90-99 | 75  (37.1) |
| Stage 2 hypertension | ≥160/100 | 115 (56.9) |

BP: Blood pressure, No.: Number.

**Table 2.** Frequency of occurrence of co-morbidities in hypertensive patients.

| Co-morbidities | Frequency | Percentage |
|---|---|---|
| Type 2 diabetes mellitus | 38 | 19 |
| Congestive cardiac failure | 12 | 6 |
| Nephropathy | 6 | 3 |
| Haemorrhagic stroke | 1 | 0.5 |
| Aortic aneurysm | 1 | 0.5 |
| Angina | 1 | 0.5 |
| Hypertensive encephalopathy | 1 | 0.5 |

Antihypertensive agents were prescribed to patients at all stages of hypertension, namely, prehypertensive stage, stages 1 and 2 using the JNC 7 classification system. Fifty seven percent of the patients had stage 2 hypertension, 37.1% had stage 1 hypertension while 5.9% of the patients were on the prehypertensive stage as shown in Table 1.

The mean systolic and diastolic blood pressures prior to treatment were 163.6 and 94.9 mmHg, while they were respectively, 138.9 and 87.2 mmHg after the treatment.

Prevalence of co-morbidity increased with the hypertensive stage ranging from 2.5% in prehypertensive stage to 12.4% in stage 1 and, 22.3% in stage 2 hypertension.

Table 2 shows that type 2 diabetes mellitus was the most common co-morbid condition (19.0%) followed by CHF (6%) and nephropathy (3%). Other co-morbidities with prevalence of 0.5% respectively were: haemorrhagic stroke, aortic aneurysm, angina pectoris and hypertensive encephalopathy.

The agents' prescription pattern and frequency are as shown in Table 3. The most frequently prescribed agent was the thaizide diuretics (54.7%) followed by calcium channel blockers (53.0%), then angiotensin converting enzyme inhibitors (ACEIs) (27.2%). Central acting agents (19.7%), beta blockers (BB) (9.8%) with angiotensin receptor blockers (ARBs) (5.3%) were the least prescribed. The most frequently prescribed drug as a monotherapy was calcium channel blockers (CCBs) (17.3%) followed by diuretics (10.9%).

Similarly, the most frequently prescribed 2-drugs combination therapy was CCB + Diuretics (D) and ACEI + D with 16.8 and 11.9%, respectively. The most frequently prescribed 3 drugs combination therapy were CCB+ACEI+D with 3.5%   and BB+Methyldopa (M)+D with 2.0%, and CCB+BB+M and CCB+Hydralazine (H)+D being the least having 0.5%, respectively. About 1% of the patient population were on 4 drugs combination which included ACEI+BB+CCB+D and ACEI+BB+M+D with each having 0.5% each.

A hundred and fifty one patients (74.8%) were on a low dose aspirin. However, 101 (50.0%) of the patients had aspirin prescribed initially.

## DISCUSSION

A prescription based survey is considered to be one of the most effective methods to assess and evaluate the prescribing attitude of physicians and dispensing attitude of pharmacists. This type of survey helps in monitoring and evaluating, and also indicates necessary modifications in prescribing practices directed to achieve rational and cost effective medical care (Suheela et al., 2011).

In this study, it was registered that the mean age of the patients was 59 years and that hypertension was more prevalent in the female population than in the male population. This finding of hypertension being more prevalent in the female population is similar to results of the study conducted in North India by Bajaj et al. (2012). They have registered that 58% of the hypertensive patients were female and 42% were male. However, Ukwe and Ubaka (2012) and Suheela et al. (2011) found the disease to be more prevalent in the male population than the female population in their respective areas of study.

Advanced age has been an established risk factor in

**Table 3.** Antihypertensives prescription pattern.

| Antihypertensive class | Frequency (%) |
|---|---|
| **Classes of antihypertensives prescribed** | |
| Thiazide diuretics | 464 (54.7) |
| Calcium channel blocker (Nifedipine Amlodipine Felodipine) | 441 (53.0) |
| ACEI'S (Lisinopril, Captopril, Enalapril, Ramipril) | 231 (27.2) |
| Centrally acting agents (Methylolopa) | 167 (19.7) |
| Beta blockers (Propranolol, Atenolol) | 83 (9.8) |
| Loop diuretics (furosemide) | 66 (7.8) |
| ARB'S (Losartan) | 45 (5.3) |
| Aldesterone antagonist (Spironolactone) | 35 (4.2) |
| Lipid lowering drugs (Statins) | 11 (1.3) |
| Direct vasodilator (Hydralazine) | 5 (0.6) |
| | |
| **Agents prescribed as monotherapy** | |
| CCB | 35 (17.3) |
| Diuretic | 22 (10.9) |
| Methyldopa | 5 (2.5) |
| ACEI | 6 (3.0) |
| Beta blocker | 2 (1.0) |
| No drug record | 1 (0.5) |
| | |
| **Agents prescribed as 2- drug combination** | |
| CCB + Diuretic (D) | 34 (16.8) |
| ACEI + D | 24 (11.9) |
| Methyldopa (M) + D | 14 (6.0) |
| Beta Blocker (BB) + D | 1 (0.5) |
| ARB + D | 2 (1.0) |
| CCB + ACEI | 6 (3.0) |
| CCB + BB | 4 (2.0) |
| ACEI + M | 9 (4.5) |
| ACEI + M | 3 (1.5) |
| ACEI + BB | 2 (1.0) |
| BB + M | 4 (2.0) |
| | |
| **Agents prescribed as 3-drug combination** | |
| CCB + ACEI + (D) | 7 (3.5) |
| CCB + ARB + D | 2 (1.0) |
| CCB + ACEI + M | 2 (1.0) |
| CCB + ACEI + BB | 2 (1.0) |
| CCB + BB + M | 1 (0.5) |
| CCB + M + D | 3 (1.5) |
| CCB + H + D | 1 (0.5) |
| ACEI + M + D | 3 (1.5) |
| BB+ M + D | 4 (2.0) |
| BB + M + ACEI | 1 (0.5) |
| | |
| **Agents prescribed as 4-drug combination** | |
| ACEI + CCB + BB + D | 1 (0.5) |
| ACEI + BB + M + D | 1 (0.5) |

D: Diuretics; ACEI: angiotensin converting enzyme inhibitors; CCB: calcium channel blocker; BB: beta blocker; M: methyldopa; ARB: angiotensin receptor blocker; H: hydralazine.

hypertension and other cardiovascular diseases. In India for instance, blood pressure has been shown to increase with age with a prevalence rate of 51.8% in the elderly (Augustine et al., 2010).

This study also revealed that antihypertensive agents were prescribed to patients at the three classes of hypertension, namely, prehypertension, stages 1 hypertension and 2 hypertension. The JNC 7 guidelines, classified hypertension into prehypertension which is when the systolic and diastolic blood pressure are between 120 to 139 and 80 to 89, respectively, stage 1 when they are 140 to 159 and 90 to 99 mmHg, respectively and stage 2 when ≥160 and ≥100 mmHg, respectively. According to the guideline, individuals in the prehypertensive stage should be considered for lifestyle modifications to prevent cardiovascular disease (CVD) with no antihypertensive drug indicated unless with compelling indications. This study failed to record if the antihypertensives were indicated for compelling indications or not. However, the study revealed that there was about 2.5% prevalence of co-morbid conditions in the prehypertensive stage which may likely be the reason for the antihypertensive drugs administered in this class of patients. Greater percentage of the patients was diagnosed stage 2 hypertension (57%) compared to those with stage 1 (37.1%) and those with prehypertensive stage (5.9%).

Hypertension often coexists with other cardiovascular risk factors like diabetes, hyperlipidemia and obesity which compound the cardiovascular risks attributable to hypertension and this results in high morbidity and mortality especially, when inadequately managed (Godley et al., 2001; Klungel et al., 1998; Trillings and Froom, 2000). From the result of this study, hypertension coexisted with other CVDs in the three stages with type 2 diabetes mellitus being the most common co-morbid condition followed by CHF and then, nephropathy. This result is similar to the findings reported by Ukwe and Ubaka (2012) in a study conducted in a tertiary hospital in Enugu State Nigeria. They reported that diabetes was the most common co-morbid condition seen with hypertension. However, hypertension is a highly prevalent risk factor for CVD throughout the world (WHO, 2003). Hypertension and diabetes frequently coexist and this increases more with age (Sandozi and Emani, 2010). It is about twice as common in patients with diabetes as in those without (McInnis et al., 2008). Furthermore, hypertension also leads to stroke, intermittent hemodialysis (IHD) and renal failure; hence, the high prevalence of these conditions in these patients is to be expected (Heart Disease and Pervention Program, 2003). Globally, it has been indicated that 62% of cerebrovascular disease and 49% of IHD are attributable to suboptimal blood pressure (WHO, 2002).

Our study showed that the patients were well managed, as shown by the mean reduction in both the systolic and diastolic blood pressure after treatment in comparison to the levels registered before treatment.

We have established that thaizide diuretics is the most frequently prescribed agent either as a monotherapy or combination therapy for the management of hypertension in our study site. This finding was similar to the results of the studies from Britain, Italy, Spain, South Africa and Canada where diuretics have been shown to be the most popular medication for the treatment of hypertension (Ford and Asghar, 1995; Wallenius et al., 1988; Edward et al., 1998). This practice is in line with the JNC 7 report which have placed emphasize on the use of thaizide type diuretics as first line agent for the management of hypertension. Diuretics have been increasingly recognized as essential for blood pressure control due to their ability to reduce blood volume and cardiovascular resistance (Suheela et al., 2011).

The high use of thiazide diuretics was closely followed by calcium channel blockers with its percentage use being 53%. This is in agreement with the study by Bajaj et al. (2012) and other studies which have favoured the use of CCB in most countries as a first line agent for the management of hypertension. The 2014 evidence-based guidelines for the management of high blood pressure in adults (JNC 8) also favoured the use of thiazide diuretics and CCBs as initial therapies in blacks (James et al., 2014). In countries like Taiwan and the United States, CCB were the most prescribed medication for the management of hypertension (Ford and Asghar, 1995; Chou et al., 2004). Meanwhile, many studies support the use of CCB and diuretics in the elderly and black Africans (ALLHAT Collaborative Research Group, 2002; Adigun et al., 2003) in line with the newly published guidelines. Adigun et al. (2003) in a study conducted in Nigeria reported that diuretics were the most prescribed agents either as monotherapy or in combination with other agents and that more patients on CCB monotherapy achieved normotensive than any other group followed by diuretics. Therefore, since our study showed a mean age of 59 years for the patients and they were blacks, the high use of CCB and diuretics may be justified. This is also in line with the study in Taiwan by Chou et al. (2004) that found CCBs as the most frequently prescribed antihypertensive medication for patients ≥55 year old, and also recognised to be effective and safe in adult blacks as a whole (Fadayomi et al., 1986).

Our study also found angiotensin receptor blockers to be the least prescribed class of antihypertensive agents. This is contrary to other reports in which ARBs were found to be the second most prescribed class of antihypertensive drugs after diuretics (Bajaj et al., 2012) and these two classes were included as first line agents in both JNC 7 and JNC 8. The lower use of this class which may be probably due to high price associated with this class of agents is not in accordance with the principles of providing the best possible medical care for the patients.

Most of the patients were on combination therapy with

2, 3 and even 4-drug regimen with diuretics being included in almost all the combination therapy. This is in line with the JNC 7 and JNC 8 guidelines which stated that combination therapy using antihypertensive drugs of different mechanisms of actions has been used to produce optimal control of blood pressure where monotherapy fails (Chobanian et al., 2003; James et al., 2014). These guidelines also stated that controlling blood pressure should be initiated with two agents one of which should be a thaizide diuretics. Furthermore, the frequent use of thaizide diuretics may be due to the fact that diuretics have been found to work synergystically with other hypertensive agents (Aguwa, 2004). However, most other studies have shown that combination therapy gives significant reductions in systolic and diastolic blood pressure compared to those on monotherapy (Yusuff and Balogun, 2005; Gavras and Rosenthal, 2004). Hence, combination therapy has been shown to reduce mortality and morbidity in hypertension.

Although the use of combination therapy has been shown to be beneficial, its excessive use may pose some negative effects like increased adverse drug reactions and negative drug interactions to the patient. Hence, Flack et al. (2010) advised that though combination therapy may be logical especially when systolic blood pressure is greater than 15 mmHg and or diastolic blood pressure greater than 10 mmHg above targeted goal, care should be taken to avoid unnecessary combinations. They further identified some undesirable antihypertensive combinations which include ACEI+ARB, BB+ACEI, BB+CCB (nondihydropyridine type), BB+central adrenergic inhibitor, and alpha-blocker+adrenergic inhibitors (Flack et al., 2010), some of which have been identified in this study.

The most common combination therapy identified in this study with CCB+D (16.8%) may be due to the fact stated ealier that these two drugs has been proven to be effective in the elderly and Africans (ALLHAT Collaborative Research Group, 2002).

## Conclusion

This study showed that hypertension in this hospital is being treated with good conformity to the gold standard rule; however, care should be taken to avoid undesirable combinations. Diuretics and calcium channel blockers are the most prescribed agents both as monotherapy and as combined therapy. Significant reduction in both systolic and diastolic blood presures was acheived with prescribed treatment patterns.

## Conflict of Interest

The authors have not declared any conflict of interest.

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