DYSLIPIDAEMIA IN HYPERTENSION - ARE WE TREATING ENOUGH?

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ABSTRACT

INTRODUCTION: The coexistence of dyslipidaemia and hypertension results in enhanced atherosclerosis. Adequate treatment of dyslipidaemia in hypertensive patients is thus essential for reducing the burden of cardiovascular diseases.

OBJECTIVE: To determine the prevalence of dyslipidaemia among hypertensives and evaluate lipid treatment status of patients with dyslipidaemia in a tertiary hospital in Nigeria.

METHODS: This cross-sectional comparative study was done between May, 2015 and June, 2016 in a tertiary hospital in Nigeria. The serum lipid levels of adult patients with hypertension and controls without hypertension were determined. Lipid treatment status of patients with dyslipidaemia were also reviewed. Serum lipid levels were analyzed using spectrophotometric methods.

RESULTS: The study included 200 adult hypertensive patients and 100 control participants. The mean age (SD) was 56.3 (6.9) years and 54.9 (8.3) years with range 41-68 and 44-69 years for patients and controls respectively. Eighty-eight (44.0%) hypertensive patients and 23(23.5%) of the control group were found to have dyslipidaemia. Out of the 60(68.2%) patients with elevated LDL-C, 32(53.3%) had LDL-C >4.1mmol/L, out of which only 8(25%) were on antilipid medication.

CONCLUSION: Over one-third of studied hypertensive patients had dyslipidaemia and only a quarter of those who needed antilipids were on the medication. Greater awareness is needed both in the medical and patient communities in order to effectively manage dyslipidaemic hypertension, and hence aid in ameliorating the burden of cardiovascular diseases.

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INTRODUCTION

Dyslipidemia and hypertension are recognized as prominent risk factors in the development of cardiovascular disease (CVD). Studies have consistently indicated that hypertension and hypercholesterolemia frequently coexist, causing what is known as dyslipidaemia in hypertension.[1] It is known that lipids play a pivotal role in the development of atherosclerosis starting from initial changes. Oxidized-LDL, is particularly atherogenic and has been suggested to affect endothelium-dependent vascular tone through a decreased biological activity of endothelium-derived nitric oxide (NO).[2,3] Hypertension equally affects endothelial function, thus when these two conditions coexist, the endothelium is not spared and the individual is at a greater risk for atherosclerosis.

The prevalence of dyslipidemia as seen among patients with hypertension vary from region to region. In a study on abdominal adiposity and atherogenic dyslipidaemia among geriatric Nigerians, dyslipidaemic hypertensive patients constituted 44.3%[4] of their study population. And among newly diagnosed hypertensive patients, a prevalence of 58.9%[5] was reported. Another study[6] in the South-West Nigeria also reported a positive

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correlation between hypertension and hyperlipidaemia. In the United States, the prevalence has been estimated to range from 15 to 31%[7] and estimated to be inherent in over 5 million Turkish adults.[8] Globally, raised cholesterol is estimated to cause 2.6 million deaths and 29.7 million disability adjusted life years.[9]

Cardiovascular disease, the primary clinical outcome of dyslipidaemia among hypertensive s is no longer merely an emerging problem in Africa, and while the risk factors and the pattern of diseases causing CVD may differ from those in Europe and North America, the impact is greater in Africa.[10] Age-specific mortality and morbidity associated with CVD and chronic diseases are higher in sub-Saharan Africa than in established market economies.[11]

Several medications exist for the treatment of dyslipidemia. Among these are the HMG-CoA reductase inhibitors (statins), fibrates, bile acid sequestrants, lipoprotein lipase inhibitors and cholesterol absorption inhibitors. These medications either exist singly or in combination.

Though both Eighth Joint National Committee (JNC 8)[12] and the National Cholesterol Education Program's series of Adult Treatment Panel (NCEP ATP) [13] reports have been developed to provide healthcare professionals with recommendations pertinent to detecting and managing dyslipidemia, it has been reported that the quality of care for dyslipidemia is still suboptimal in general.[14] The consequences of under treatment (or no treatment) contributes to the rising cardiovascular disease burden.

The aim of this study is to contribute to existing data on the prevalence of dyslipidaemia among hypertensive patients receiving treatment and to determine the level of lipid treatment among dyslipidaemic hypertensive patients in the study setting in order to highlight the unmet need for lipid control in our patients.

MATERIALS AND METHODS

Study design and location

This cross-sectional comparative study was carried out at University of Nigeria Teaching Hospital (UNTH), Enugu, Nigeria, between May, 2015 and June, 2016. UNTH, Enugu is the pioneer teaching hospital in the Southeastern Nigeria and is owned by the Federal government of Nigeria. It is currently located at Ituku-Ozalla, at the outskirt of Enugu city and majorly serves about 5 states in its vicinity.

Study Population

Study participants included patients with essential hypertension attending medical out-patient clinic at the University of Nigeria Teaching Hospital. A total of 200 adult hypertensive patients aged 18 years and above who have been on treatment for at least 3 months were recruited using systematic sampling. This was done using a sampling interval of 2, thus the first patient who presented at the clinic was selected, followed by the 3rd, 5th, till sample size was completed. Patients with secondary hypertension, pregnant women and those declining consent were excluded from the study. Also, another age and sex matched 100 control participants without hypertension were recruited from hospital staff and patients' relatives for the study. Individuals on oral contraceptives, antipsychotics, anticonvulsants, steroids and other medications that might affect lipid levels were also excluded.

Definition of Hypertension and Dyslipidaemia

Blood pressure readings were based on the JNC VII classification and guidelines. Normal blood pressure was defined as a systolic blood pressure of <120 mmHg and a diastolic blood pressure of < 80 mmHg.

Dyslipidaemia was defined using the National Cholesterol Education Program Adult Treatment panel III (NCEP-ATP III)[13] criteria as follows: Total Cholesterol (TC) $\geq$ 5.2 mmol/L, Low Density Lipoprotein-cholesterol (LDL) > 3.4 mmol/L, Triglycerides (TG) > 1.7 mmol/L and High Density lipoprotein-cholesterol (HDL) < 1.0mmol/L.

NCEP-ATP III also identified other risk factors for the development of coronary heart disease (CHD) which includes Hypertension, Cigarette smoking, Diabetes, Age Male $\geq$ 45 years, Female $\geq$ 55 years, family history of premature CHD, Obesity

Sample collection and analysis

After at least a ten minutes rest, blood pressure was measured twice with 5 minutes interval, using a sphygmomanometer (Omron, Japan). This was done on the left hand while sitting, and the mean of

the two readings of the systolic and diastolic pressures recorded. Blood samples (5mls) were collected aseptically after 10 -14 hours of fasting into lithium heparin bottles, centrifuged for 10 minutes at 1500 rpm and plasma separated into plain tubes. These were stored at -18°C and analyzed a day after collection. Total cholesterol was measured using Enzymatic Endpoint (CHOD-PAP) method[15] (Randox, UK). Triglycerides were measured using the GPO-PAP method[16] (Randox, UK).

High density lipoprotein-cholesterol (HDL-C) was measured using the precipitation technique[17] (Randox,UK) while Low density lipoprotein-cholesterol (LDL-C) was calculated using the Friedewald equation.[18] Friedewald equation was not used for patients with plasma triglyceride concentration greater than 400mg/dL (4.52 mmol/L). Quality control was ensured by the use of commercially prepared quality control materials (Levels 1 and 3) included in every batch of samples analyzed. Inter-assay and intra-assay Coefficient of variation were recorded as shown in Table 6.

Data regarding duration of treatment, antihypertensive and lipid lowering medications, age, sex and race were also collected from the participants.

Ethical considerations

Informed consent was obtained from participants after the purpose of the study was explained to them. Ethical clearance was obtained from UNTH Health Research and Ethics Committee.

Statistical analysis

Data was double-entered into a Microsoft Excel spreadsheet and analysis was carried out using Epi Info 3.5.1(CDC, Atlanta, GA, USA). Continuous variables were summarized as means (standard deviation [SD]), number and percentages while Categorical variables were presented only as proportions (number) and percentages. Student's t-test was used to compare continuous variables and chi square used for categorical values. All tests were two-tailed with $p < 0.05$ taken as statistically significant.

RESULTS

Two hundred (200) adult hypertensive patients and 100 controls without hypertension were included in the study. All patients and controls were 40 years and above and of Igbo tribe. The mean (SD) age was 56.3 (6.9) years and 54.9 (8.3) years with range 41-68 and 44-69 years for patients and controls respectively. There were 64 male and 136 female patients; while controls consisted of 40 males and 60 females. Male to female ratio was 1:2 and 1:1.5 for patients and controls respectively.

Based on ATP III criteria, a statistically greater number of hypertensive patients 88 (44.0%) were found to have dyslipidaemia when compared to the control group (P = 0.0004). Out of the 88 patients with dyslipidaemia, 60 (68.2%) had elevated LDL-cholesterol ≥3.4 mmol/L, 44(50.0%) had elevated Total Cholesterol ≥5.2mmol/L, 8 (9.1%) had elevated triglygerides ≥1.7mmol/L and 44(50.0%) had reduced HDL-cholesterol levels less than 1.0mmol/L. Out of the 60 (68.2%) with elevated LDL-cholesterol, 32 (53.3%) had LDL-C ≥4.1mmol/L.

Among the control group, 23 (23.0%) had dyslipidaemia. Out of the 23 controls with dyslipidaemia, 10(43.5%) had elevated LDL-cholesterol ≥3.4 mmol/L, 14(60.9%) had elevated Total Cholesterol ≥5.2mmol/L, 3(13.0%) had elevated triglygerides ≥1.7mmol/L and 10(43.5%) had reduced HDL-cholesterol levels less than 1.0mmol/L. None had elevated LDL-cholesterol ≥4.1mmol/L.

A significantly greater proportion of females 81(41.3%) had dyslipidaemia when compared with 30(28.8%) of males, P=0.03. Among the hypertensive group, 64(47.0%) of the females and 24(37.5%) of the males had dyslipidaemia, whereas in the control group, 17(28.3%) of the females and 6(15.0%) of the males had dyslipidaemia. This gender distribution is shown in Figure 1.

Hypertensives with dyslipidaemia had significantly higher mean values of total- and LDL-cholesterol with lower value of HDL-cholesterol when compared with hypertensives without dyslipidaemia as shown in Table 2. This pattern was also seen when comparing hypertensives with dyslipidaemia with controls without dyslipidaemia (Table 4), but among control subjects, the values in individuals with dyslipidaemia were higher but not significant (Table 3). Differences in triglyceride levels were however significant among controls but not among hypertensive patients.

When compared with controls with dyslipidaemia, hypertensives with dyslipidaemia had higher mean values of total and LDL-cholesterol though these differences were not statistically significant as depicted in Table 5.
In terms of lipid treatment status, out of the 32 (53.3%) hypertensive patients with LDL-C ≥4.1mmol/L, only 8(25%) were on antilipid medication (Fig 2). Six (75%) patients were on statin alone while 2(25 %) were on a combination of niacin and statin.

DISCUSSION

The overall prevalence of dyslipidaemia among adult hypertensive patients in this study was 44.0%. This figure is comparable to a prevalence rate of 44.3%[4] obtained in another study in 2012 in a South-Eastern Nigerian hospital, though the study was carried out among geriatrics. It is however lower than the prevalence of 58.9%[5] obtained in South-West Nigeria and higher than the prevalence of 30.7% recorded in the 2004 study in the United States[19] and 35% recorded in Turkish adults.[8] The South-Western Nigeria study was carried out among newly-diagnosed hypertensives and that may account for the differences. The lower prevalences seen in the western countries may be attributed to greater awareness among patients and consequently earlier presentation to health facilities, and earlier commencement of treatment. Other factors include, more inclusive health insurance cover, better access to healthcare and greater compliance to medication.

Among female patients, however, the prevalence of 47.0% of dyslipidaemia in hypertensive women seen in this study is consistent with the rate of 49.5% recorded in the Genoa study[20] among black hypertensive females but is greater than 21% recorded among Turkish adult hypertensive females.[8] The 37.5% prevalence seen among hypertensive men also differed from 56.7% recorded in the Genoa study among black hypertensive males and 20% among Turkish adult hypertensive males.

These figures buttress the fact that dyslipidaemia is commonly associated with hypertension hence increasing the risk of atherosclerosis and cardiovascular disease as each of them represents an independent major risk factor, and their co-existence represents a synergism enhancing the development of atherosclerosis. However, the higher proportion of females with dyslipidaemia in the present study contrasts with documented findings that men generally have higher prevalence of dyslipidaemia than females. [20, 21, 22] While this remains true, the higher proportion of females with dyslipidaemia in the present study may be due to the age of female participants most of who are in the menopausal age group. The mean menopausal age in Nigeria is documented to be 49.4[23] and 46.16[24] years by two different researchers, and the mean age of female participants in the present study was 55.4 years which is quite higher than the documented age of menopause. Menopause has been reported to be associated with dyslipidaemia[25] and could therefore account for the findings in this study.

In this study also, dyslipidaemia was found in 23.0% of the healthy control group. Though this figure is lower than the 60% reported by Oguejiofor *et al*[26] in apparently healthy Nigerians, it is deemed high because it is higher than prevalences reported in some developed countries. Among Latin American populations, the prevalence of hypercholesterolaemia varied from 6% to 20%[27] depending on the city, and is quoted as 22% in Australia.[28]

This high prevalence of dyslipidaemia can partly be attributed to urbanization, western diet, and sedentary lifestyle. Indeed, a report has demonstrated a higher prevalence in urban versus rural areas in Nigeria.[29]

This elevated lipid levels in apparently healthy individuals is also worthy of note because dyslipidaemia alone is a major risk factor for development of atherosclerosis. More so, since it causes no symptoms, the individual remains ignorant of the condition and takes no precaution especially in a developing country like Nigeria where the culture of regular and routine medical evaluation is yet to be entrenched.

According to NCEP ATP recommendations, LDL-c levels of ≥4.1 mmol/L in the presence of no Coronary Heart Disease and multiple (2 or more) risk factors necessitates drug therapy.[13]
In this study, hypertension, age (mean age of 56.5 years), and 22% of dyslipidaemic patients with HDL-c < 1.0mmol/L are all coronary heart disease risk factors.

The 75% of patients with multiple risk factors (hypertension, mean age of 56.5 years, abnormal lipid profile) who are not at goal and not on antilipids is worrisome as they are at increased risk of cardiovascular diseases. The finding of 25% dyslipidaemic drug-treated patients in this study is however higher than 16.4% and 12.8% reported respectively for black women and men in the Genoa study.[20]

The 75% of patients (LDL-c ≥4.1 mmol/L) who are neither at goal nor on antilipids recorded in this study is lower than the 80.3%[30] of patients with dyslipidemia who were either undiagnosed, untreated or under-treated recorded in Germany. This difference may be due to fact that the German study included not only hypertensive patients but all patients seen in the primary care setting.
The reasons for this poor treatment level in our study may not be unconnected with out-of-pocket financing as national health insurance is yet to be all-encompassing and adequately utilized by patients. Others reasons may be low level of literacy among patients, poor patient compliance with medication and inadequate patient monitoring of lipid levels by clinicians.

STRENGHTS AND LIMITATIONS OF STUDY

Being a cross-sectional study, causality of the low lipid treatment level cannot be determined. Again, this study was conducted in one tertiary health facility, hence the findings may not be representative of the entire country of study. Hence, further research possibly a multi-center study in this area is needed. Despite these limitations, the present study contributes to the growing body of literature on dyslipidaemia in hypertension. It equally identifies important gaps and existing misalignment between internationally acknowledged treatment guidelines and practice of clinicians in the study location at the time of study. The current study can indeed provide support for further research in this area geared towards improved clinical care.

CONCLUSION

High prevalence and poor treatment level of dyslipidaemic hypertension seen in this study requires prompt attention and concerted efforts from clinicians and other stakeholders in the health sector in order to reduce the risk of cardiovascular diseases among patients. There is a need to increase the awareness, both in the medical and patient communities, so that these two conditions can be adequately targeted and treated.

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