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Prevalence and risk factors for peripheral arterial disease in adults with systemic hypertension in Southern Nigeria

Boma Oyan [1,*] and Sarah Tonye Abere [2]

[1] *Cardiology unit, Department of Internal Medicine Rivers State University Teaching Hospital, 6-8 Harley Street, Port Harcourt, Rivers State, Nigeria.*

[2] *Gastroenterology/Hepatology unit, Department of Internal Medicine Rivers State University Teaching Hospital, 6-8 Harley Street, Port Harcourt, Rivers State, Nigeria*

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Abstract

Aims: Atherosclerotic peripheral arterial disease affects quality of life and is used as a marker for atherosclerosis in the coronary and cerebral arteries. The ankle brachial pressure index can be used for identifying persons with peripheral arterial disease. This study aims to determine the prevalence of peripheral arterial disease in a cohort of hypertensive patients using the ankle brachial pressure index as well as identify the risk factors associated with PAD.

Methods: One hundred and sixty hypertensive subjects and a commensurate number of age and sex matched apparently healthy controls were evaluated. Assessment of PAD was made using the history, physical examination and measurement of the ankle brachial pressure index. Chi square (χ^2) and Student t tests were used to assess statistically differences between categorical and continuous variables respectively. Correlation and regression analysis was used to assess the risk factors for PAD in hypertension.

Results: The mean age of the cases with systemic hypertension was 56.3 ± 8.2 years with a range of 42-72 years. There was a female preponderance with a female: male ratio of 1.8:1 as 64.4% of the cases were females and 35.6% were males. The prevalence of PAD using the ABPI was 11% in hypertensives and risk factors were determined to be increasing age (p=0.026), duration of hypertension (p=0.011), and BMI (p=0.008).

Conclusion: This study highlights the presence of PAD in adult hypertensive patients and identifies the risk factors associated with PAD.

Keywords: PAD; Hypertension; ABPI; Intermittent claudication

1. Introduction

The term Peripheral Arterial Disease (PAD) refers to a disorder that obstructs the blood supply to the lower or upper extremities. It is most commonly caused by atherosclerosis but may also result from thrombosis, embolism, vasculitis, fibromuscular dysplasia, or entrapment [1].

Atherosclerotic PAD has been associated with long term morbidity and mortality and is an indicator of widespread atherosclerosis in other vascular territories as studies following up patients with PAD and have shown that it strongly correlates with risk of major cardiovascular events in the coronary and cerebral arterial circulations [2,3].

* Corresponding author: Boma Oyan
Cardiology unit, Department of Internal Medicine Rivers State University Teaching Hospital, 6-8 Harley Street, Port Harcourt, Rivers State, Nigeria.

The prevalence of a PAD varies depending on the population under review and the diagnostic method utilized. Intermittent claudication (IC) is said to be the most common symptomatic manifestation of PAD [4]. However, although intermittent claudication and rest pain have a high specificity for the diagnosis of PAD, they are not sensitive enough when compared to angiographically identifiable obstruction of lower limb arteries [5]. The ankle brachial pressure index is a the non-invasively assessed ratio of ankle to brachial systolic blood pressures. An ABPI of ≤0.90 is used for the diagnosis of PAD [6].

Hypertension is a well-documented risk for the development of vascular diseases including PAD; as hypertension is associated with the development and progression of atherosclerosis [7]; however, the prevalence of PAD in this subset of patients has not been fully elucidated in the literature especially in developing countries where the disease has been well documented in diabetes mellitus [8].

The well-known traditional risk factors associated with atherosclerotic arterial disease of the coronary and cerebral arteries have been previously documented for the development of PAD. These factors include hypertension, diabetes mellitus, dyslipidaemia, obesity, tobacco smoking [7,9]; with diabetes mellitus and cigarette smoking noted to have the strongest association [7].

2. Material and methods

We retrospectively analysed data collected from 160 patients with systemic hypertension and 160 non hypertensives (controls) attending the Cardiology Clinic of the Medical outpatient department at the University of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria (2011-2012). We collected the demographic information, physical examination findings, with emphasis on anthropometric measurements, blood pressure and volume of peripheral pulses palpated in both lower limbs. Information from the administered Edinburgh Claudication questionnaire [10] as well as the ankle brachial pressure index (ABPI) using a handheld doppler with a vascular probe with a frequency of 8megaHertz was obtained. Laboratory results of fasting lipid profile were also analysed.

The ankle brachial pressure index was calculated for each leg, and the lower value was the patient's overall ABPI. An abnormal value in either leg indicated peripheral artery disease. Subjects with ABPI ≤0.90 were diagnosed to have PAD. The ankle brachial pressure index was used to evaluate the severity of peripheral arterial disease as individuals with ABPI between 0.80-0.90 were considered to have mild arterial disease, 0.50-0.79 was considered as moderate arterial disease and <0.50 as severe arterial disease [11].

Ethical approval was obtained from the ethical board of the hospital and documented Informed consent was given by the participants.

2.1. Participants

We included 160 patients above the age of 40 years on management for systemic hypertension seen in the Cardiology clinic. Patients who use tobacco in any form, persons living with diabetes mellitus, chronic kidney disease as well as pregnant women were excluded from the study. One hundred and sixty controls were matched for age and sex.

2.2. Data collection

We extracted the demographic (age, sex, prior history of cardiovascular disease); anthropometric (WC, WHR, BMI); and examination (BP, examination of lower limb peripheral pulses, ABPI) findings of hypertensive patients as well as their fasting lipid profile parameters.

2.3. Outcome measures

The primary aim of the study was to determine the prevalence and risk factors of PAD using the ABPI in hypertensive patients.

2.4. Statistical analysis

All data were analyzed using the commercially available statistical package for social sciences (SPSS) version 21 analytic software. Data were expressed as mean ± standard deviations and percentages. Continuous variables were compared with the students t-test, or one-way analysis of variance as considered appropriate. Proportions or categorical parameters were compared with the chi-square test. Relations among continuous variables were assessed using Pearson correlation test and multiple linear regression analysis. All tests were considered to be statistically significant at the p-value < 0.05.

3. Results

A total of 320 subjects were included in this study of which 160 constituted the participants with systemic hypertension (cases) and 160 were the controls with normal blood pressure.

3.1. Comparison of demographic variables in cases and controls

The mean age of the cases with systemic hypertension was 56.3 ± 8.2 years with a range of 42-72 years while the mean age of the control population was 56.2 ± 8.3 years with a range of 41-73 years (p=0.96).

There were more females than males among the cases in a ratio of 1.8:1 as 103 (64.4%) of the cases were females and 57 (35.6%) were males. Among the controls also, there was a female preponderance with 51 (63.8%) being female, giving a female to male ratio of 1.8:1 (p=0.92)

The median duration of hypertension among the cases was 3 years, (ranging from 6 months to 18 years), with 104 (65.0%) having been hypertensive for less than 5 years, while 41 (25.6%) and 10 (6.2%) had been hypertensive for 5-9 years and 10-14 years respectively. Only 5 (3.2%) of the cases had been hypertensive for 15-20 years.

There was a prior history of coronary artery disease in only one (0.6%) case, however, 8 (5%) persons had a prior history of stroke. None of the controls gave a prior history of cardiovascular disease. (p=0.001)

There was a positive family history of Cardiovascular disease in a first degree relative in 77 (48.13%) cases. Among the controls, a positive family history in a first degree relative of CVD was present in 28 (17.5%) persons (p=0.248).

General characteristics of the study population is given in table 1.

Table 1 Clinical and laboratory characteristics of the study population

Variable	Subjects (n=160) Mean (±SD)	controls (n=160) mean (±SD)	p value
Age (years)	56.3 ± 8.2	56.2 ± 8.3	0.960
Women (%)	64.4%	63.8%	0.924
BMI (kg/m2)	28.9 ± 5.2	26.2 ± 2.9	<0.001
WC (cm)	97.0 ± 13.0	87.0 ± 7.9	<0.001
WHR	0.9±0.1	0.8±0.1	<0.001
SBP (mmHg)	142.0 ± 16.9	117.5 ± 7.8	<0.001
DBP (mmHg)	88.7 ± 9.0	76.2 ± 5.8	<0.001
ABPI	1.02 ± 0.11	1.07 ± 0.07	<0.001
PAD (%)	11.0%	0.0%	0.002
TC (mmol/l)	5.2 ± 0.9	4.9 ± 0.6	0.001
TG (mmol/l)	1.3 ± 0.5	1.2 ±0.4	0.012
HDL-c (mmol/l)	1.3 ± 0.4	1.4 ± 0.4	0.001
LDL-c (mmol/l)	3.4 ± 0.9	3.0 ± 0.7	0.118

Key: Data expressed as mean ± standard deviation. BMI= body mass index; WC= waist circumference; WHR= waist- hip ratio; SBP= systolic blood pressure; DBP= diastolic blood pressure; ABPI= ankle brachial pressure index; TC= total cholesterol, TG= triglycerides, HDL-c= high density lipoprotein cholesterol, LDL-c= low density lipoprotein cholesterol

3.2. Prevalence of PAD

The mean ankle brachial pressure index among the cases was 1.02 ± 0.11 with a range of 0.71 to 1.33. The mean ABPI among the controls was 1.07 ± 0.07 (range 0.92 to 1.23). There was a statistically significant difference in the mean ABPI among the cases and controls (p<0.001).

IC was present in 3 (1.9%) of the hypertensive population and none of the controls (p=<0.001); while based on palpation of lower limb peripheral pulses PAD was identified in 10 (6.5%) cases versus 1 (0.63%) control (p=0.023).

Among the cases, 18 (11.0%) had an ABPI ≤0.90 while none of the controls had an ABPI ≤0.90. Eleven cases had mild PAD; seven cases had moderate PAD while there was no case with severe PAD. Eight cases with abnormal ABPI (44.4%) were male while 10 (55.5%) were female (p=0.924).

Using the ABPI as the reference for the diagnosis of PAD, the sensitivity of the Edinburgh claudication questionnaire in this study was 16.7% and the specificity was 100%.

3.3. Risk factors for PAD in hypertension

The was a significant difference in the mean age, BMI and WC in hypertensive patients with peripheral arterial disease compared to those without PAD (table 2).

Table 2 Clinical and laboratory characteristics of hypertensive subjects

Variable	PAD present (n=18) MEAN (±SD)	PAD absent (n=142) MEAN (±SD)	p VALUE
Age (years)	64.2 ± 7.4	55.3 ± 7.8	<0.001
BMI (kg/m2)	24.6 ± 4.1	29.4 ± 5.1	<0.001
WC (cm)	89.7± 15.1	97.9 ± 10.5	0.011
WHR	0.9±0.1	0.9±0.4	0.191
SBP (mmHg)	143.8 ± 20.3	141.8 ± 16.5	0.639
DBP (mmHg)	89.6 ± 7.0	88.7 ± 9.2	0.692
ABPI	0.80 ± 0.05	1.04 ± 0.08	<0.001
TC (mmol/l)	5.3 ±0.5	5.2 ± 0.9	0.636
TG (mmol/l)	1.3 ± 0.5	1.2 ± 0.5	0.735
HDL-c (mmol/l)	1.4 ± 0.4	1.3 ± 0.4	0.268
LDL-c (mmol/l)	3.4 ± 0.5	3.3 ± 1.0	0.974

Key: Data expressed as mean ± standard deviation. BMI= body mass index; WC= waist circumference; WHR= waist- hip ratio; SBP= systolic blood pressure; DBP= diastolic blood pressure; ABPI= ankle brachial pressure index; TC= total cholesterol, TG= triglycerides, HDL-c= high density lipoprotein cholesterol, LDL-c= low density lipoprotein cholesterol

There was a significant positive correlation between ABPI and BMI (r=0.243; p=0.002), and a significant negative correlation with age (r=-0.332; p<0.001) and duration of hypertension (r=-0.328; p<001). However, the correlation of ABPI with SBP (r=-0.79; p=0.319), DBP (r=-0.059; p=0.459), WC (r=0.110; p=0.166), WHR (r=0.038; p=0.667) and lipid parameters were not significant (TC: r=-0.134, p=0.092; TG: r=0.138, p=0.083; LDL-c: r=-0.116, p=0.144; HDL-c: r=-0.106, p=0.183).

Binary logistic regression shows increasing age (OR=1.74; 95%CI=1.18-2.63; p=0.026), duration of hypertension (OR=2.63; 95%CI=1.57-5.02; p=0.011) and BMI (OR=1.52; 95%CI=1.08-3.58; p=0.008) as risk factors for PAD in this cohort of hypertensives.

4. Discussion

The progression of the pathophysiology of atherosclerotic PAD is much the same as for coronary artery disease and cerebrovascular disease [2]. Given this, it is essential for risk factor modification if disease is present in one arterial territory to prevent its development and/or progression in other arterial territories.

The prevalence of peripheral arterial disease among the cases with systemic hypertension in this study was 11.0%. This figure is much lower than that reported in other African countries with a prevalence of 42.6% in Angola [12], despite similar age and gender distribution. This may be due to inclusion of patients with diabetes mellitus and smokers in their study which are well recognized risk factors for the development of PAD [7]. However, population-based studies give a much lower prevalence of PAD in hypertensives of 8.7% [9], although ethnicity may account for this difference. In

another study to determine the prevalence of PAD among male hypertensive subjects, the prevalence was 17.5% which is similar to the prevalence among the males in this study of 14.0% [13].

The prevalence of PAD increases with age and this study showed that the mean age was significantly higher in the cases with peripheral arterial disease compared to those without PAD and there was a significant correlation between increasing age and decreasing ABPI. This agrees with most literature where age is an important predictor for PAD [14,15]. It is also important to note that age is an important risk factor for the development of atherosclerosis in all vascular beds [3], therefore it is important to evaluate elderly patients for symptoms and signs of coronary as well as cerebral artery disease. The effect of gender on the presence of PAD has not reached a consensus as there are large scaled studies which report a higher prevalence in men [16] while other studies report a higher prevalence in women [15]. However, these studies were done on different races which may explain the disparity in their results. In this study, there were more females than males with PAD (55.6% were female).

There was a strong correlation between duration of hypertension and decreasing ABPI and after regression analysis, duration of hypertension was the strongest contributor to decreasing ABPI. This may be due to the fact that with longer duration of hypertension, coupled with the other cardio-metabolic risk factors, there will be more target organ damage, atherosclerosis and thus PAD [2]. There was a non-significant negative correlation between both the systolic BP and the diastolic BP with the ABPI. Wright et al [17] also reported that the ABPI did not correlate with office blood pressure, but with ambulatory blood pressure monitoring, there was a significant relationship between blood pressure and the ABPI. However, the international guidelines still recommend clinic or office measurements as a standard diagnostic tool [3]. This study showed that subjects with PAD had significantly lower BMI and waist circumference while the waist-hip ratio was non-significantly lower than in subjects without PAD, however, after correlation analysis, there was a significant relationship between ABPI and a lower BMI but not waist circumference or waist-hip ratio. Although Farkas et al [16] reported that 71% of cases with PAD had increased waist circumference, the waist circumference did not correlate with ABPI, whereas other studies actually reported significantly lower BMI among hypertensive subjects with PAD [15]. Although PAD has been associated with the traditional cardiovascular risk factors, the differences in these studies may indicate that PAD may have its own unique risk factors which will need to be elucidated in future studies.

Dyslipidemia was present in 88.8% of the cases with PAD but the mean lipid profile parameters did not differ significantly between the cases with PAD compared with the cases without PAD. Correlation analyses also did not reveal a significant relationship between any of the lipid profile parameters and the ABPI. Most studies also report a high prevalence of dyslipidemia [15,16] in PAD but the predominant lipid abnormalities range from raised total cholesterol [15] to reduced HDL-c [16].

5. Conclusion

Hypertension is the commonest risk factor for the development of cardiovascular disease and is associated with increased morbidity and all-cause mortality. Screening for PAD can identify individuals at high risk of vascular events so as to target them for aggressive risk reduction interventions. The ABPI is an important cardiovascular disease diagnostic test that can be applied in a clinical population with a high detection rate, low to no risk and low cost to ameliorate overall cardiovascular risk.

Limitations of the study

- The ABPI does not detect occlusive disease distal to the ankle.
- This was a hospital based cross sectional study which limits conclusions about causality.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare no conflict of interest.

Statement of ethical approval

Ethical approval was given by the University of Port Harcourt Teaching Hospital Ethical Committee and the Research Ethics group of the Centre for Medical Research and Training, College of Health Sciences, University of Port Harcourt. (UPTH/ADM/90/S.II/VOL.X/61).

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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