Annals of African Medicine Vol. 9, No. 2; 2010:62-7
DOI: 10.4103/1596-3519.64750

Original Article

Microalbuminuria and its relations with serum lipid abnormalities in adult Nigerians with newly diagnosed hypertension

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Abstract

Background: Microalbuminuria (MA) has been associated with increased risk of adverse cardiovascular events in nondiabetic hypertensive patients. This may be partly due to increased serum lipid abnormalities in these patients. The objective was to evaluate the association between MA and serum lipid abnormalities in nondiabetic adult Nigerians with hypertension.
Materials and Methods: A prospective study which recruited 96 consecutive newly diagnosed adult Nigerian hypertensive met the study criteria. These patients were compared with the same number of age- and sex-matched healthy normotensive individuals.
Results: 52 (54.2%) and 44 (45.8%) of patients were males and females, respectively. Mean ± SD ages were 51.2 ± 10.1 and 48.2 ± 8.8 years for male and female patients, respectively. Microalbuminuria was more than five times more prevalent in the patients than in the controls. The means ± SD serum total cholesterol (5.0 ± 0.56 vs. 4.05 ± 0.50 mmol/L, *P* = 0.04) and low-density lipoprotein cholesterol (3.99 ± 0.49 vs. 2.84 ± 0.58 mmol/L, *P* = 0.001) were significantly higher, while the mean ± SD for high-density lipoprotein cholesterol was (0.91 ± 0.16 vs. 1.04 ± 0.13 mmol/L, *P* = 0.03) significantly lower in microalbuminuric patients than in non-microalbuminuric patients.
Conclusion: This study has shown that adult nondiabetic Nigerians with MA are significantly more likely to have dyslipidemia than patients without MA. Hence, this subset of hypertensive patients constitutes a high risk group. Screening for MA, and early recognition and prompt treatment of serum lipid abnormalities in these patients may reduce the risk of adverse cardiovascular events.

Keywords: Hypertension, microalbuminuria, nondiabetic adult Nigerians, serum lipid abnormalities

Résumé

Arrière-plan: Microalbuminurie (MA) a été associée à un risque accru d'événements indésirables cardiovasculaires chez nondiabetic hypertendu. Cela peut être en partie en raison d'anomalies de lipides sérum accrue chez ces patients. L'objectif était d'évaluer l'association entre MA et le sérum anomalies de lipides dans nondiabetic Nigérians adultes avec l'hypertension.
Matériel et méthodes: Étude un éventuel dont 96 recruté consécutives nouvellement diagnostiquée adulte hypertendues moins satisfait aux critères de l'étude. Ces patients ont été comparés avec le même nombre d'âge et sexe-correspond à des individus normotensive sains.
Résultats: 52 (54.2%) et 44 (45.8%) des patients étaient les hommes et les femmes, respectivement. Moyenne ± SD âges ont 51,2 ± 10.1 et 48,2 ± 8,8 ans pour les patients masculins et féminins, respectivement. MICROALBUMINURIE a été plus que cinq fois plus fréquents chez les patients que dans les contrôles. Le cholestérol total moyen ± SD sérum (± 5.0 0,56 VS 4,05 ± 0,50 mmol/L, *P* = 0,04) et le taux de cholestérol lipoprotéines de basse (3,99 ± 0.49 VS 2,84 ± 1.58 mmol/L, *P* = 0.001) ont été considérablement plus élevés, tandis que la moyenne ± SD pour high-density lipoprotéine cholestérol était (0,91 ± 0,16 VS 1.04 ± 0,13 mmol/L, *P* = 0,03) diminuer de manière significative chez les patients microalbuminuric que chez les patients non-microalbuminuric.

Conclusion: Cette étude a montré que nondiabetic adultes Nigérians avec MA sont beaucoup plus susceptibles d'avoir des dyslipidemia que les patients sans MA. Par conséquent, ce sous-ensemble de hypertendu constitue un groupe à risque élevé. Dépistage pour MA et le traitement de reconnaissance et invite précoce des anomalies de lipides sérum chez ces patients peuvent réduire le risque d'événements indésirables cardiovasculaires.

Mots-clés: L'hypertension, microalbuminuria, nondiabetic adultes Nigérians, les anomalies de lipides sérum

Introduction

Microalbuminuria (MA) is a condition in which albumin excretion in the urine is above the 'normal' range but below the clinically detectable level, by standard screening tests i.e. urine dipsticks. It is defined as the presence of 20–200 μg/min or 30–300 mg/day of albumin excretion in the urine.[1] Microalbuminuria occurs in nondiabetic hypertensive populations[2-5] and it has prognostic implication in these patients as it has been associated with increased cardiovascular morbidity and mortality.[6,7]

The excess cardiovascular morbidity and mortality associated with MA in nondiabetic hypertensive patients may partly be related to their serum lipid abnormalities, particularly, reductions in high-density lipoprotein cholesterol (HDL-c) and elevations in low-density lipoprotein cholesterol (LDL-c) and lipoprotein(a). Some lipid components can directly injure the kidneys.[8] Thus adverse lipid profile may contribute not only to the development of MA in hypertension (HT) but also to its ultimate correlate, cardiovascular morbidity and mortality.[9] The objective of the study was to determine the prevalence of MA in nondiabetic adult Nigerians with essential HT and to evaluate its association with serum lipid abnormalities

Materials and Methods

Ninety-six adult Nigerians with newly diagnosed HT were compared with age- and sex-matched healthy normotensive controls. The study was done at the Cardiology Unit of the University of Ilorin Teaching Hospital, Ilorin, Nigeria. Both oral and written consent was obtained from all the participants. Patients with previous use of antihypertensives, diabetes mellitus, obesity, overt proteinuria or congestive heart failure were excluded from the study. The study protocol was approved by the Ethical and Research Committee of the University of Ilorin Teaching Hospital, Ilorin, Nigeria.

Clinical evaluation, definitions and measurements

All participants had a detailed history and a thorough physical examination, including anthropometry. Blood pressure was measured using mercury column sphygmomanometer and a cuff of appropriate size. A standardized protocol was followed, in which systolic (SBP) and diastolic blood pressure (DBP) was measured on the left arm after participants had been seated for at least 5 min. The phase I Korotkoff's sounds were taken as SBP. The disappearance of these sounds (phase V) was the criterion for DBP. Three measurements were done at least 2 min apart and the mean value used for the study. Hypertension was defined as SBP ≥140 mmHg and/or DBP ≥90 mmHg, or use of antihypertensive drugs.[10-12] Pulse pressure (PP) was calculated as the difference between SBP and DBP while the mean arterial pressure (MAP) was derived with the formula:

MAP (mmHg) = DBP (mmHg) + (1/3 PP) mmHg

Microalbuminuria testing

Microalbuminuria was determined using the Micra Test strips (Boehringer Mannheim, Germany) urine dipstick. This dipstick has been found to be a rapid, accurate and cheap mean to screen the presence of MA.[13] There are four colour blocks corresponding to negative (or 0), 20, 50 and 100 mg/L of albumin. The test was done on three consecutive first morning voided urine samples of both patients and controls. Microalbuminuria was considered to be present when two of the three urine samples tested produce a reaction color corresponding to 20 mg/L or more. The mean value of the MA was recorded for each participant.

Laboratory evaluation

Blood samples were collected and analyzed in the laboratory for electrolytes, urea (BUN), creatinine (Cr) and fasting plasma glucose (FPG). Blood samples were also analyzed for fasting lipid profile; serum TC and triglyceride (TG) were determined using the standard colorimetric enzymatic methods, while serum LDL-c and HDL-c were precipitated by the polyvinyl sulfate and phosphotungstic acid method, respectively. Atherogenic index (AI) was calculated from the formula:

AI = LDL-c (mmol/L)/HDL-c (mmol/L)

Estimated glomerular filtration rate (eGFR) was derived using Cockcroft Gault formula:[14]

eGFR = (140-age [years]) / serum creatinine (μmol/L) × 0.85 (if female) × BSA/1.732 m^2

(where BSA is the body surface area estimated with the formula:[15] BSA (m^2) = 0.20247 × height $(m)^{0.725}$ × weight $(kg)^{0.425}$. Some previous studies in Africa have showed a good correlation between eGFR derived from Cockcroft Gault formula and GFR measured using endogenous creatinine clearance and Cr-ethylenediaminetetra-acetic acid (Cr-EDTA)[16,17]

Data analysis

Statistical analysis was performed using SPSS version 9. Descriptive data were presented as mean ± standard deviation. Continuous variables were compared using *t* test. *P* value <0.05 was considered significant.

Results

The characteristics of both patients and controls are shown in Table 1. Fifty-two (54.2%) of the hypertensive patients were male while 44 (45.8%) were females. The mean ± SD ages for patients were 51.2 ± 10.1 and 48.2 ± 8.8 years for males and females, respectively. The mean age for patients was not significantly different when compared with that of the controls (49.7 ± 12.7 vs. 46.1 ± 13, *P* = 0.054). Twenty seven (27.1%) were petty traders, 33 (34.4%) were civil servants and 11 (11.5%) pensioners. Others were 3 (3.1%) students, 8 (8.3%) farmers, 8 (8.3%) artisans and 7 (7.3%) business persons.

MAL was more than five times more prevalent in hypertensive patients than in the normotensive controls. Thus, the proportion of MA positivity in the patients was significantly more than in the controls (32.3 vs 6.25%, *P* < 0.001). The serum lipid parameters of the hypertensive patients with and without MA are shown in Table 2. In the hypertensive patients, the mean ± SD serum TC was significantly higher in those with MAL than in their counterparts without MA (5.0 ± 0.56 vs. 4.05 ± 0.5 mmol/L, *P* = 0.04). The mean ± SD serum LDL-c was also significantly higher in the MA hypertensive patients (3.99 ± 0.49 vs. 2.84 ± 0.58 mmol/L, *P* = 0.001). On the other hand, the mean ± SD serum HDL-c in patients with MA was lower than in patients without MA (0.91 ± 0.16 vs. 1.04 ± 0.13 mmol/L). The difference was statistically significant (*P* = 0.001). There was no statistically significant difference in the mean ± SD of serum TG between these subgroups of hypertensive patients. Also, the mean ± SD of

Table 1: Clinical and laboratory characteristics of patients and controls

	Patients			Controls			*P* value
	MFTMFT			MFTMFT			
	(n = 52)	(n = 44)	(n = 96)	(n = 49)	(n = 47)	(n = 96)	
Mean age (years)	51.2 ± 10.1	48.2 ± 8.8	49.7 ± 12.7	49.6 ± 12.3	42.6 ± 10.4	46.1 ± 13.0	0.3
Mean SBP (mmHg)	164.5 ± 14.2	155.5 ± 15.1	160.0 ± 15.0	132.4 ± 9.7	125.6 ± 8.2	129.0 ± 10.0	0.01
Mean DBP (mmHg)	111.5 ± 10.1	103.3 ± 11.8	107.4 ± 10.5	82.1 ± 5.9	78.3 ± 7.1	80.2 ± 6.9	0.01
Mean PP (mmHg)	53.0 ± 10.7	52.2 ± 12.9	52.6 ± 8.6	50.3 ± 6.5	47.3 ± 7.6	48.8 ± 7.1	0.08
Mean MAP (mmHg)	129.2 ± 9.5	120.7 ± 10.5	124.9 ± 9.0	98.9 ± 9.2	94.1 ± 8.7	96.5 ± 8.6	0.01
TC (mmol/L)	4.55 ± 0.76	4.37 ± 0.81	4.46 ± 0.79	3.50 ± 0.41	3.28 ± 0.38	3.39 ± 0.42	0.01
TG (mmol/L)	1.28 ± 0.27	1.24 ± 0.29	1.26 ± 0.32	1.23 ± 0.12	1.17 ± 0.11	1.20 ± 0.18	0.6
LDL-c (mmol/L)	3.29 ± 0.68	3.11 ± 0.79	3.20 ± 0.77	2.52 ± 0.42	2.36 ± 0.39	2.44 ± 0.38	0.02
HDL-c (mmol/L)	1.10 ± 0.22	1.02 ± 0.26	1.06 ± 0.25	1.27 ± 0.17	1.2 ± 0.19	1.24 ± 0.13	0.0
CR (μmol/L)	95.9 ± 12.1	90.9 ± 13.2	93.4 ± 11.5	88.7 ± 10.6	85.3 ± 11.2	87.0 ± 10.8	0.06
eGFR (mL/min)	84.8 ± 8.7	86.6 ± 9.2	85.7 ± 10.1	91.3 ± 7.9	93.9 ± 8.2	92.6 ± 6.8	0.03

Table 2: Clinical and serum lipid characteristics of patients with and without MAL

	Patients with MAL			Patients without MAL			*P* value
	MFTMFT			MFTMFT			
	(n = 18)	(n = 13)	(n = 31)	(n = 37)	(n = 18)	(n = 65)	
Mean age (year)	54.9 ± 8.8	50.6 ± 9.2	52.5 ± 11.9	49.5 ± 10.1	47.8 ± 8.7	48.3 ± 13.0	0.1
Mean SBP (mmHg)	185.2 ± 18.4	179.5 ± 20.1	182.2 ± 20.4	162.8 ± 17.9	168.1 ± 18.3	168.3 ± 22.1	0.07
Mean DBP (mmHg)	120.3 ± 20.5	119.7 ± 17.0	120.5 ± 18.7	100.8 ± 15.1	100.4 ± 12.1	102 ± 14.9	0.03
Mean PP (mmHg)	64.7 ± 10.9	80.1 ± 12.4	81.8 ± 11.7	60.3 ± 13.1	66.5 ± 105	66.4 ± 10.2	0.06
Serum TC (mmol/L)	5.05 ± 0.87	4.94 ± 0.78	5.0 ± 0.56	4.11 ± 0.62	3.99 ± 0.53	4.05 ± 0.5	0.04
Serum TG (mmol/L)	1.47 ± 0.21	1.35 ± 0.24	1.41 ± 0.35	1.39 ± 0.25	1.25 ± 0.29	1.32 ± 0.29	0.2
Serum LDL-c (mmol/L)	4.08 ± 0.51	3.90 ± 0.49	3.99 ± 0.49	2.92 ± 0.71	2.76 ± 0.69	2.84 ± 0.58	0.001
Serum HDL-c (mmol/L)	0.93 ± 0.18	0.89 ± 0.17	0.91 ± 0.16	1.06 ± 0.16	1.03 ± 0.14	1.04 ± 0.13	0.03
AI	4.39 ± 0.36	4.38 ± 0.42	4.39 ± 0.31	2.75 ± 0.25	2.68 ± 0.29	2.73 ± 0.30	0.001
Serum CR (μmol/L)	96.4 ± 14.1	95.9 ± 13.7	94.3 ± 10.6	94.1 ± 13.2	93.1 ± 12.9	93.5 ± 11.7	0.5
eGRF (mL/min)	81.8 ± 7.9	75.5 ± 8.1	78.9 ± 8.5	87.3 ± 6.8	78.9 ± 9.2	83.1 ± 7.7	0.2

LDL-c/HDL-c ratio was higher in MA than in non-MA subgroups (4.38 ± 0.31 vs. 2.43 ± 0.42, $P = 0.02$).

Tables 3 and 4 compare patients with MA and those without MA with the control group. The pattern of dyslipidemia in the hypertensive patients with and without MA is shown in Table 5. Dyslipidemia was more common in patients with MA than in those without MA (67.7 vs. 23.1%, $P = 0.002$). Low HDL-c and high TC were the most common types of dyslipidemia in hypertensive patients with MA.

Discussion

This study shows that MA is a common finding in newly diagnosed adult Nigerians with HT. Although the reported prevalence of MA in 32.3% of the patients is higher than what Akinsola *et al.*[4] found in their study, it is still within the range of 4.7–40% documented in some other previous studies.[18-22] The variability in prevalence may be due to factors such as patient selection procedures, duration of hypertension, existence of prior antihypertensive treatment and method of estimation or detection of MA.[23,24]

The study also reveals that MA is a coronary risk factor in adult Nigerian with HT, compatible with previous documentation.[4,6,25,26] This is due to the fact that hypertensive patients with MA were more likely to have serum lipid abnormalities when compared with the hypertensives without MA and with the normotensive controls. The hypertensive patients with MA had significantly higher mean serum TC, LDL cholesterol and AI and significantly lower mean serum HDL than their counterparts without MA. Microalbuminuria was also significantly and positively correlated with serum TC and LDL cholesterol and significantly and negatively correlated with serum HDL. This is consistent with the report of other studies that have been done before.[26-28] Bigazzi *et al.*[26,29] reported that dyslipidemia was associated with MAL and adds to the cardiovascular risk in HBP.

The reason for the association between MA and serum lipid abnormalities has not been established. Lundman *et al.*[30] demonstrated an association between mild-to-moderate HBP and endothelial dysfunction and increased plasma asymmetric dimethylarginine. Microalbuminuria has been well recognized as a marker of endothelial dysfunction in HBP.[7,31] However, the serum lipid abnormalities may precede and possibly be responsible for the development of MA.[26] It is known that cholesterol-rich diet may cause albuminuria and glomerulosclerosis, and pharmacological agents that lower serum lipids may ameliorate renal injury in different animal species.[8,9,32,33] On the other hand, MA may be an early manifestation or even precede the development of HBP and be responsible for serum lipid abnormalities. Fauvel[34] and Grunfeld[35] have shown that MA could be found in normotensive offspring of hypertensive parents. Proteinuria or MA may increase serum levels of TC, LDL-cholesterol and lipoprotein(a).[36,37]

Limitations of the study

There is no doubt that this study has some limitations. Fasting plasma glucose alone is not enough to classify individuals as not having cardiovascular

Table 3: Serum lipid profiles of patients with MAL and the control group

	Patients with MAL			Controls			*P* value
	MFTMFT			MFTMFT			
	(n = 18)	(n = 13)	(n = 31)	(n = 49)	(n = 47)	(n = 96)	
Serum TC (mmol/L)	5.05 ± 0.87	4.94 ± 0.78	5.0 ± 0.56	3.50 ± 0.41	3.28 ± 0.38	3.39 ± 0.42	<0.001
Serum TG (mmol/L)	1.47 ± 0.21	1.35 ± 0.24	1.41 ± 0.35	1.23 ± 0.12	1.17 ± 0.11	1.20 ± 0.18	0.09
Serum LDL-c (mmol/L)	4.08 ± 0.51	3.90 ± 0.49	3.99 ± 0.49	2.52 ± 0.42	2.36 ± 0.39	2.44 ± 0.38	<0.001
Serum HDL-c (mmol/L)	0.93 ± 0.18	0.89 ± 0.17	0.91 ± 0.16	1.27 ± 0.17	1.21 ± 0.19	1.24 ± 0.13	0.02
AI	4.39 ± 0.36	4.38 ± 0.42	4.39 ± 0.31	1.98 ± 0.25	1.95 ± 0.31	1.97 ± 0.29	<0.001

Table 4: Serum lipid profiles of patients without MAL and the control group

	Patients without MAL			Controls			*P* value
	MFTMFT			MFTMFT			
	(n = 37)	(n = 28)	(n = 65)	(n = 49)	(n = 47)	(n = 96)	
Serum TC (mmol/L)	4.11 ± 0.62	3.99 ± 0.53	4.05 ± 0.5	3.50 ± 0.41	3.28 ± 0.38	3.39 ± 0.42	0.03
Serum TG (mmol/L)	1.39 ± 0.25	1.25 ± 0.29	1.32 ± 0.29	1.23 ± 0.12	1.17 ± 0.11	1.20 ± 0.18	0.1
Serum LDL-c (mmol/L)	2.92 ± 0.71	2.76 ± 0.69	2.84 ± 0.58	2.52 ± 0.42	2.36 ± 0.39	2.44 ± 0.38	0.06
Serum HDL-c (mmol/L)	1.06 ± 0.16	1.03 ± 0.14	1.04 ± 0.13	1.27 ± 0.17	1.21 ± 0.19	1.24 ± 0.13	0.7
AI	2.75 ± 0.27	2.68 ± 0.25	2.73 ± 0.20	1.98 ± 0.25	1.95 ± 0.31	1.97 ± 0.29	0.05

Table 5: Pattern of dyslipidemia in patients with and without MAL

Dyslipidemia	Patients with MAL (%) (n = 31)	Patients without MAL (%) (n = 65)	*P* value
High TC	6 (19.4)	4 (6.2)	0.1
High LDL-c	2 (6.5)	2 (3.1)	0.8
Low HDL-c	6 (19.4)	2 (3.1)	0.02
High TG	1 (3.2)	3 (4.6)	0.8
High LDL-c plus low HDL-c	3 (9.7)	1 (1.5)	0.2
High TC plus high LDL-c	2 (6.5)	2 (3.1)	0.8
High TC plus high TG	1 (3.2)	1 (1.5)	

risk associated with glucose intolerance. This is because some form of glucose intolerance such as impaired glucose intolerance is also associated with increased cardiovascular risk as in diabetes mellitus. Also, the presence of MA was detected using a semi-quantitative method in a setting where a quantitative measurement would have been more appropriate. However, a number of previous studies have documented a close correlation between this albumin measurement for overnight or 24-hour urine collections.[38,39] In addition this study was designed to assess association between MA and lipid abnormalities and not to elucidate information on the possible mechanism(s) of this association

Conclusion

This study has shown that adult Nigerian hypertensive patients with MA are significantly more likely to have dyslipidemia than patients without MA. This study provides evidence that in nondiabetic patients with HBP, MA signals presence of serum lipid abnormalities with atherogenic potential. Hence this subset of adult Nigerian hypertensive with MA constitutes a high risk group. We suggest that screening of MA be made part of routine investigation and follow-up assessment for all patients with HT. Early recognition and prompt treatment of serum lipid abnormalities in this subset of patients may reduce the risk of adverse cardiovascular events.

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Source of Support: Nil, **Conflict of Interest:** None declared.