Original Article

PREVALENCE OF CHRONIC KIDNEY DISEASE IN PATIENTS WITH METABOLIC SYNDROME: A SINGLE CENTRE EXPERIENCE IN NIGERIA

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ABSTRACT

BACKGROUND

The prevalence of metabolic syndrome (MS) is increasing worldwide, not sparing developing countries like Nigeria. Chronic kidney disease (CKD) is also assuming epidemic proportions globally. Metabolic syndrome has been associated with CKD in several reports, most of which are foreign based. Given that data on CKD in MS patients is rare in this part of the world, the study was undertaken with the aim of determining the prevalence of CKD in patients with MS.

METHODS

Two hundred and twenty two subjects completed the study out of the two hundred and thirty that met the criteria for MS as defined by the harmonized criteria for definition of MS. CKD was defined as eGFR less than 60 ml/min/1.73 m^2 as determined by the Modification of Diet for Renal Disease (MDRD) formula. Proteinuria was defined as presence of at least 1+ of protein in urine in absence of leukocyturia or nitrituria.

RESULTS

Elevated blood pressure, elevated fasting glucose and central obesity were the commonest traits of MS. The prevalence of CKD in participants with MS was 20.3% while proteinuria was found in 121(54.5%) of them. The prevalence of CKD increased with additional traits of the syndrome.

CONCLUSION

CKD and proteinuria are prevalent in patients with metabolic syndrome. Prevalence of CKD in MS increases with additional component of the syndrome.

KEY WORDS

Blood pressure, cholesterol, diabetes, glucose, lipid, obesity

INTRODUCTION

The metabolic syndrome (MS) has evolved from a vague association of common chronic diseases to a formally defined cluster of clinical traits with adverse impact on cardiovascular risk. It may be characterized by abdominal

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obesity, hyperglycaemia, hypertension, hypertryglyceridemia and reduced HDL cholesterol.

Several criteria have been put forward over time to aid in diagnosis of this condition. These include those by the World Health organization (WHO),[1] European Group for the Study of Insulin resistance,[2] the National Cholesterol Education Program Adult Treatment Panel (NCEP ATP) III,[3] the American Association of Clinical Endocrinologists,[4] the International Diabetes Federation(IDF) criteria.[5] However in October 2009, a joint statement was issued by the International Diabetes Federation; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity to standardize the diagnostic criteria for the metabolic syndrome.[6] Agreed cut-points for all the components of metabolic syndrome were published and the diagnosis defined as the presence of any three or more abnormal findings: Elevated waist circumference(WC): population and country-specific; Serum triglycerides(TG) > 150mg/dl/ (1.7 mmol/l) or drug treatment for elevated triglycerides; Serum HDL cholesterol < 40mg/dl (1.0mmol/l) in men and < 50mg/dl (1.3mmol/l) in women or drug treatment for low HDL-C; Blood pressure > 130/85mmHg or drug treatment for elevated blood pressure(BP) and Fasting plasma glucose (FPG) >100mg/dl (5.6mmol/l) or drug treatment for elevated blood glucose.

About a quarter of the world population is estimated to suffer from metabolic syndrome.[7] Its prevalence in developing countries has been observed to be on the increase lately and this may be related to changes in lifestyle and diet.[8,9] Although it is widely known that the metabolic syndrome is a major risk factor for the development of cardiovascular disease and type 2 diabetes, evidence linking MS with CKD has also emerged.[10,11] CKD has become a major public health problem, with a growing burden and significant impact on morbidity, mortality, quality of life, use of health services and health expenditure.

Mechanism by which the metabolic syndrome initiates or accelerates renal disease remains unclear but there are postulations that it may be related to the presence of obesity itself. Obesity has been shown to be an independent risk factor for CKD and has been associated with a type of focal segmental glomerulosclerosis called 'obesity-related glomerulopathy.[12] Insulin resistance may have a direct role in the pathogenesis of renal injury, as a consequence of stimulating the sympathetic nervous system and renin-angiotensin system.[13] Dyslipidaemia, a feature of the metabolic syndrome may induce toxic and inflammatory tubulo-interstitial injury.[14] Treating end stage renal disease (ESRD) imposes a large economic burden on the patients, the health care delivery system and the society at large. Considering the magnitude of the morbidity, mortality and huge cost of management of CKD and ESRD patients, it becomes imperative to adopt preventive strategies. Subjects with MS are thus candidates for CKD screening.

Studies on prevalence of CKD in metabolic syndrome patients are rare in developing countries like Nigeria. The aim of the study was to determine the prevalence of CKD in patients with metabolic syndrome in Benin City, Nigeria.

METHODS

The study was carried out in the University of Benin Teaching Hospital (UBTH), a tertiary health care centre in Benin City. Benin City is an ancient city and a cosmopolitan town located in Edo State in the South-Southern geo-political zone of Nigeria. UBTH is a 600 bedded hospital and runs specialist hypertensive and diabetic clinics amongst other specialized services.

Consecutive hypertensive and diabetic patients attending the medical outpatient clinic of UBTH from September 2010 to May 2011 were screened for features of MS as defined by the harmonized criteria for definition of MS.[6]

A WC cut off of 94 cm for males and 80cm for females was used according to the current recommended threshold for abdominal obesity in Sub-Saharan Africa.[6]

Patients that had at least three of the MS traits were recruited for the study. However, patients less than 18 years old, patients with CKD from other causes, apart from hypertension and diabetes, pregnant women, HIV patients and other wasting diseases, as well as patients with obvious ascites were excluded. Those with urinary tract infection as evidenced by leukocyturia or presence of nitrites in urine were also excluded from the study.

The sample size was determined using the formula, $N=Z^2pq/d.^2$ [15]

Where N = minimum sample size, Z = normal standard deviate at 95% confidence Interval = 1.96, P = prevalence, q = 1-p, d = precision set at 0.05

In a study of a group of Nigerians with metabolic syndrome by Ulasi et al, the overall prevalence of metabolic syndrome was 15.9%.[16]

Applying this as "p" in the Fischer's formula, $N=Z^2pq/d^2$ gives 205.

However, to make allowances for drop-outs, 230 patients with MS were enrolled.

Using interviewer – administered questionnaire, socio-demographic data such as age, sex, marital status and ethnicity were obtained.

Blood pressure was taken using the Accoson mercury sphygmomanometer. For uniformity of measurement, the first sound (Korotkoff 1) was taken as the systolic blood pressure and the extinction of all sounds (Korotkoff 5) as the diastolic blood pressure. Blood pressure was recorded to the nearest 2mmHg. Elevated blood pressure as a

component of MS was defined as BP of 130/85mmHg or use of anti-hypertensives. [6]

Waist circumference (WC) was measured at a level midway between the lower rib margin and the iliac crest with the tape around the body in a horizontal position at the end of gentle expiration. Abdominal obesity was defined as waist circumferences of > 80cm and > 94cm for females and males respectively.[6]

Mid-stream urine was collected and analyzed for proteinuria with a combi 9 dipstix. For the purpose of this study, proteinuria was considered positive in the presence of at least 1+ of protein in the absence of leukocyturia or nitrituria. Six mls of venous blood were collected from the participants and used for analysis of urea and creatinine and serum lipid profile after an overnight fast. The abbreviated version of the Modification of Diet in Renal Disease (MDRD) equation[17] was used in estimating the glomerular filtration rate (GFR) viz: eGFR= 186.3x (serum creatinine) exp [-1.154] age exp [0.203] x [0.724 if female] x (1.21 if African). CKD was defined as eGFR< 60mls/min/1.73m.[2]

An HDL-C value of less than 50mg/dl (1.3mmol/l) for females and 40mg/dl (1.0 mmol/l) for males was considered a significant component of MS.[6] For serum triglycerides, significantly elevated values were those > 150mg/dl.[6] FPG was determined using the accucheck glucometer and values > 100mg/dl considered elevated.[6] Individuals who were already on medications for elevated blood glucose irrespective of their present blood glucose readings were also enlisted.[6]

ETHICAL CONSIDERATION

Ethical approval was obtained from the Ethics and Research Committee of UBTH before commencement of the study. After a thorough explanation of the details of the study, the history to be obtained from participants as well as procedures to be performed, informed consent was obtained from those that were willing to partake in the study.

DATA ANALYSIS

Data was entered, stored and analyzed using the Statistical Package for Social Sciences for windows software version 17.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were presented as mean, standard deviation and range while categorical variables were presented as frequencies and percentages. Fisher's exact test was used in testing for significant differences between groups. Results were presented in tabular forms. Confidence interval was at the 95% limit and p values of < 0.05 were accepted as being statistically significant.

RESULTS

A total of five hundred and thirty hypertensive and diabetic patients were screened for metabolic syndrome. Out of this, two hundred and thirty (43.4%) met the criteria for diagnosis of the syndrome. One hundred and sixty two of those that met the criteria were females while sixty eight were males. There was no significant difference in the proportion of male and female subjects with MS (p = 0.572). However, eight patients did not have complete data. Two hundred and twenty two participants had complete data which were the ones used in analysis.

Characteristics of participants

Out of the 222 participants that completed the study, 64(28.8%) were males while 158(71.2%) were females.

The mean age of the participants was 60.0+11.4 years. Majority (80.2%) of them were married. Bini (54.5%) was the dominant tribe. The socio-demographic data of the participants are shown in table1.

Two hundred and three (91.4%) patients were either known hypertensives or had BP> 130/85 on presentation. One hundred and ninety (85.6%) patients were either known diabetic patients or had an FPG > 100mg/dl (5.6 mmol/l). One hundred and seventy two (77.5%) participants had abdominal obesity. Ninety four (42.3%) participants either had TG > 50mg/dl (mmol/l) or were already on drug treatment for high TG while 117(52.7%) participants had low HDL or were on drug treatment for low HDL. Participants had various combinations of these components ranging from three to all five.

Prevalence of CKD

The overall prevalence of CKD in the study was 20.3%. The prevalence of CKD in patients with 3, 4 and 5 MS traits were 15.3%, 27.0% and 40.0% respectively showing an increasing prevalence with an increasing number of traits. This difference was observed to be statistically significant (P = 0.02) as reported in table 2.

Positive dipstick proteinuria was found in 121 (54.5%) of the participants.

DISCUSSION

Most of the patients in this study were of Edo State Origin (Bini and Esan). This is to be expected, considering that the hospital is located in Edo state.

Among the five diagnostic traits for the metabolic syndrome, elevated blood pressure, hyperglycemia and abdominal obesity were the most prevalent in the patients. Similarly, these three traits were the most common components reported in Ervin's report among metabolic syndrome cohorts in the US though obesity had the highest frequency in that report.[18] Hypertriglyceridemia and low HDL cholesterol were the least frequent traits among the metabolic syndrome patients. This is in agreement with documented reports of relatively low triglycerides and high HDL cholesterol

conc entrations especially among Africans.[19, 20] In Ulasi's series, hypertriglyceridemia was virtually non-existent in the patients.[16]

The prevalence of CKD in the MS patients in this series was 20.3%. Unfortunately, there is a paucity of data on prevalence rates of CKD in MS patients to allow for adequate comparison with the findings from this study. However, Emem-Chioma et al reported low prevalence rates of CKD in MS patients of 4.8% in Rivers State, Nigeria, [21] This is markedly lower than the findings of this study. Differing patient characteristics and methodology may have contributed to some of the observed differences. Their population was younger and the sample size was smaller. A Chinese study found a prevalence rate of 15.4% which is also less than the rate we found.[22] Apart from possible ethnic and other demographic differences, the IDF criteria for MS was used in that study while we used the harmonized criteria.

Also, increased incidence rates of CKD with increased odds have been reported severally in prospective studies of patients with MS compared with the normal population [10,23,24]

There was a significant relationship between the number of components of MS and CKD. The prevalence of CKD was highest in those with all traits and least in those with only three components. Similar observations have been reported severally in literature.[9, 10, 25] According to Lea of the Emory University, the individual components of the MS do not seem to have much effect on kidney disease progression but when taken together, the syndrome does seem to have a significant impact.[26] There may thus be a synergistic effect among the various components in their association with CKD.

Over half of the patients had proteinuria. Although there was no control group for comparison, the prevalence of proteinuria in this study was indisputably high. Data in prevalence of proteinuria in metabolic syndrome is also rare. Jutilainen et al found a high prevalence of proteinuria in diabetic patients; 75.5% in men and 65.0% in women[27] Another Central African study reported a prevalence of 23.8%.[28] Even though only 5.7% of Korean subjects with the metabolic syndrome had proteinuria, proteinuria was still more in metabolic syndrome patients compared with 2.7% in patients without the syndrome.[29] This low rate is however not in agreement with our findings. The reason for this difference is not clear but differences in demographic characteristics may also be contributory.

It is therefore likely from our study that metabolic syndrome has a positive association with renal disease. The exact mechanism by which the metabolic syndrome initiates or causes progression of kidney disease remains unclear and is beyond the scope of the study but may however warrant further studies.

This study had some limitations. Serum creatinine assay was not repeated for the patients during the study. Since accurate diagnosis of CKD entails persistence of abnormalities for at least 3 months, there may have been some over-estimation in this regard. In addition, diagnosing hyperglycaemia using a finger-prick glucose meter has limitations. Blood glucose meters measure the glucose in whole blood which is actually lower than plasma glucose. Fortunately however, the glucometer used in this study gave results in plasma equivalent.

Also, this study was a hospital based one where the sample tested were patients who were already attending a specialist clinic. A population based study where the general population is screened would probably have been more apt. Also, the cohort in our study was voluntary and could have been biased by the health worker effect. A younger population may probably have been more appropriate since older patients are more likely to have other co-morbidities, which themselves, predispose to CKD. Since women made up a vast majority of the participants, there may be need for some caution in generalization of results.

Despite the above limitations, the findings of this study remain valid. The study has revealed a high prevalence of CKD in the metabolic syndrome which may be contributed to by a synergistic effect of all the components of the syndrome. There is therefore need for regular screening of patients with MS for CKD.

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Tables
Table 1: Socio-demographic data of the MS patients

Variable	Mean ±SD (yrs)	Range (yrs)	Frequency n (%)
Age	60.0 ± 11.4	29 – 91	
Sex			
Male			64 (28.8)
Female			158(71.2)
Total			222(100.0)
Marital status			
Single			4(1.8)
Married			178(80.2)
Widowed			39(17.6)
Separated			1(0.4)
Total			222(100.0)
Tribe			
Bini			121(54.5)
Esan			35(15.8)
Delta Ibo			19(8.6)
Urhobo			8(3.6)
Etsako			8(3.6)
Ika			6(2.7)
Others			25(11.2)
Total			222(100.0)

Table 2: Relationship between number of metabolic syndrome traits and CKD

Chronic kidney disease

No of MS Traits	Yes	No	Total
3	22(15.3%)	122(84.7%)	144(100.0%)
4	17(27.0%)	46(73.0%)	63(100.0%)
5	6(40.0%)	9(60.0%)	15(100.0%)
Total	45(20.3%)	177(79.7%)	222(100.0%)

Fisher's exact p = 0.02

LIST OF ABBREVIATION

ATP	Adult treatment panel
BP	Blood pressure
CKD	Chronic kidney disease
eGFR	Estimated glomerular filtration
ESRD	end stage renal disease
FPG	Fasting plasma glucose
HDL	High density lipoprotein
HDL-C	High density
HIV	Human immunodeficiency virus Lipoprotein cholesterol
HTN	Hypertension
LDL	Low density lipoprotein
LDL-C	Low density lipoprotein Cholesterol
MDRD	`Modified diet in renal disease
MS	Metabolic syndrome
NCEP	National cholesterol education Program
TG	Triglyceride
UBTH	University of Benin Teaching Hospital
WC	Waist circumference