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Metabolic Syndrome and Kidney Damage: Prevalence and Assessment of Risk among Apparently Healthy Resident of Ado Ekiti, South West Nigeria

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Authors' contributions

This work was carried out in collaboration between all authors. Authors ASD, DDA and EEE contributed to conception and design of the study. Data collection and write-up of the manuscript by authors DDA, ASD and OEG. Authors EEE, ASD and MOR performed the statistical analysis and interpretation. Authors ASD, JGO, MOR, EEE, OEG and DDA revised the manuscript and approved version to be published.

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ABSTRACT

Background: Individuals with metabolic syndrome are at increased risk of developing chronic kidney disease.
Objective: There is limited information on the relationship between metabolic syndrome and CKD

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among Nigerian population. Data from few available studies are contradictory.
In this study, we set out to determine the prevalence of CKD and associated metabolic risk factors among selected apparently healthy resident of Ado Ekiti, Nigeria.
Methods: Data for this study were collected during the year 2016 edition of an annual religious outreach program at Ado-Ekiti, Nigeria. A total of 336 adult males and females participated in the study.
Metabolic syndrome was defined according to National Cholesterol Education Program Adult Treatment Panel III. Glomerular filtration rate was estimated using the abbreviated Modification of Diet in Renal Disease formula. CKD was defined as eGFR ≤ 30–59 ml/min/1.73 m^2 and /or ≥2+ dipstick proteinuria.
Results: The mean age of the participants was 51.71 ± 10.44 years. The overall prevalence of chronic kidney disease and metabolic syndrome was 7.4% and 24.7% respectively.
In multivariate models, elevated blood pressure OR 3.217 (95% CI 1.144-9.051, P = 0.026) and elevated Triglyceride level OR 3.292 (95% CI 1.245-8.701, *P*=0.016) were significantly association with an increased odds of chronic kidney disease.
There was a significant difference in the prevalence of CKD among persons with (15.7%) and without (4.7%) metabolic syndrome (*P*= 0.001). Logistic regression showed that metabolic syndrome is associated with risk of CKD, OR 2.969 CI 1.589-5.545.
Conclusion: This study showed that metabolic syndrome was associated with chronic kidney disease

Keywords: Glomerular filtration rate; hypertension; kidney disease; metabolic syndrome; obesity.

1. INTRODUCTION

Metabolic syndrome (MetSyn) refers to a cluster of related risk factors that include abdominal obesity, diabetes, hypertension, and elevated cholesterol [1].

The occurrence of this risk markers has been shown to increase an individual's likelihood of developing chronic disease [2]. These chronic diseases include cardiovascular disease (CVD) [3], cancers [4], type 2 diabetes mellitus (DM) [5] and chronic kidney disease (CKD) [6,7]. Chronic kidney disease (CKD) is increasingly being recognized as an important public health problem [8]. It is a major risk factor for ESRD, cardiovascular disease, and premature death [9].

The prevalence of the metabolic syndrome varies among populations so does the prevalence of the individual components of the syndrome [10-13].

Cross-sectional as well as longitudinal studies have suggested a relationship between the metabolic syndrome and risk for CKD [6,7,14, 15]. Kurella et al. in their analysis of dataset from the Atherosclerosis Risk in Communities study demonstrated a strong independent link between metabolic syndrome and increased risk of CKD in non-diabetic adults [14].

In a report from NHANES III, the metabolic syndrome in multivariate analysis significantly increased the risk of both chronic kidney disease and microalbuminuria. The risk of both complications was documented to increase with the number of components of the metabolic syndrome [6].

2. MATERIALS AND METHODS

This is a cross-sectional study conducted among Christian faithful during the year 2016 edition of their regular annual religious outreach program at Ado-Ekiti, Nigeria. Adult males and females were the participants in this study. The investigators utilized the opportunity of providing medical services support for the participants to collect data for the study. Among the screened 450 participants, 336 healthy individuals had complete data for analysis.

Written informed consents were signed by all participants. Ethical clearance was obtained from the ethical review committee of the Ekiti State University Teaching Hospital, Ado Ekiti.

The participants were instructed to come fasting on the day of the medical check-up. However, only the consenting apparently healthy adults above 18 years of age were included in the study.

An interviewer administered semi-structured questionnaire was used to collect information

on respondent's socio-demographic characteristics, past medical history and nutritional status.

The anthropometry measurements including the height, weight, waist and hip circumferences were taken using standard procedures [16].

The body mass index (BMI) in kg/m^2 was calculated as weight in kilograms divided by the square of height in meters. We classified subjects on the basis of cutoff points commonly used in clinical practice as follows: underweight <18.5; normal 18.5-24.9; overweight 25-29.9; obese ≥30.

The blood pressure was measured with Accusson's mercury sphygmomanometer attached with appropriate cuff sizes on the left upper arm in sitting position.

Venous blood samples were analyzed at the laboratory department of Ekiti State University Teaching Hospital, Ado Ekiti. The total cholesterol was determined using enzymatic CHOD-POD method while the Triglyceride was estimated using GPO-POD enzymatic method. The HDL-C was determined by precipitation with heparin-manganese chloride reagent followed by enzymatic colorimetric procedure. The LDL-C was calculated using the friedewald formula [17]. The fasting plasma glucose was determined by using the colorimetric glucose oxidase-peroxidase method [18].

The metabolic syndrome was defined according to National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) (i.e. the presence of at least 3 of the following: HDL-cholesterol <1.04 mmol/L for men or 1.29 mmol/L for women, fasting glucose ≥ 6.1 mmol/L or glucose lowering medication, triglycerides level ≥ 1.69 mmol/L or lipid lowering medication, BP ≥ 130/85 mmHg or use of antihypertensive medication, waist circumference ≥ 102 cm for men or ≥ 88 cm for women [19].

Urinalysis was done using Multistix 10SG by Bayer diagnostic. Dipstick proteinuria of at least 2+ was taken as significant and represents markers of kidney injury. Plasma creatinine was measured using Jaffe's reaction. The estimated glomerular filtration rate (eGFR) was calculated using the modified Modification of Diets in Renal Disease formula [20]. GFR = 186 x $(Cr)^{-1.154}$ x $(Age)^{-0.203}$ x 0.742 (if female) x 1.210 (if black).

According to the National kidney foundation using the Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines,[21] patients were classified into five stages based on eGFR as follows; Stage 1 (Normal or increased eGFR) = ≥90 ml/min/1.73 m^2; Stage 2 (Mildly decreased eGFR) = 60–89 ml/min/1.73 m^2; Stage 3 (Moderately decreased eGFR) = 30–59 ml/min/1.73 m^2; Stage 4 (Severely decreased eGFR) = 15–29 ml/min/1.73 m^2 and Stage 5 (Kidney failure) = <15 ml/min/1.73 m^2.

CKD was defined in this study as eGFR ≤ 30–59 ml/min/1.73 m^2 and /or ≥2+ dipstick proteinuria.

2.1 Statistical Analysis

Data for a continuous variable were presented as mean (±SD) and for categorical variables as number and percentages. The prevalence of the metabolic syndrome and its individual components namely; high triglyceride level, elevated blood pressure level, low HDL cholesterol level, high plasma glucose level and abdominal obesity were determined.

Chi-square and student's T test were used for comparison of individual with and without metabolic syndrome. The ORs (95% CI) of CKD by the number of metabolic syndrome risk factors were determined by logistic regression.

Multivariable logistic regression models, adjusting for all baseline factors, were constructed to examine predictors of CKD. A p value of <0.05 was taken as significant.

3. RESULTS

3.1 Clinical Characteristic and Bio-chemical Profile of the Participants

Table 1 gives the population characteristics in the entire group of 336 subjects. The mean age of the participants was 51.71 ± 10.44 years with a minimum and maximum age of 18 and 80 years respectively. The majority of the respondent were female 250 (74.4%). About half (53.3%) were active government worker while the proportion of traders, clergy and farmers were 89(26.5%), 40(11.9%) and 14(4.2%) respectively. Table 1 presents the general characteristic of study participants by metabolic syndrome status. Participants with metabolic syndrome were found to be older with a higher mean value of both biochemical and clinical profiles.

Table 1. Socio-demography characteristic of the participants n=336

Characteristic	MetSyn Absent	MetSyn Present	P-value
Age (years)	50.58±10.56	54.95±9.43	0.001
Female N %	194(77.9)	56(64.4)	0.013
Active working class N (%)	130(72.6)	49(27.4)	0.225
Hip Circumference, cm	103.87±13.99	105.21±15.71	0.457
Waist Circumference, cm	88.48 ±9.84	98.21±13.71	0.000
Blood pressure (mmHg)			
Systolic	123.64±16.02	147.47±31.62	0.000
Diastolic	75.89±9.40	84.05±17.25	0.000
Total cholesterol (mmol/L)	5.22±1.55	5.61±1.25	0.035
HDL-chol (mmol/L)	1.64±0.82	1.42±0.66	0.000
Triglycerides (mmol/L)	1.18±0.47	1.68±0.54	0.000
LDL Chol (mmol/L)	3.46±0.98	3.31±1.03	0.360
FPG (mmol/L)	4.74±0.87	5.99±31.31	0.000
Albumin creatinine ratio (mg/g)	26.04±14.01	40.23±26.70	0.001
eGFR (ml/min/1.73m^2)	109.87±32.25	84.34±31.64	0.001
Dipstick proteinuria N %	11 (4.4)	15 (17.2)	0.001
CKD, N %	12(4.7)	13(15.7)	0.001

Overall the prevalence of low HDL, elevated TG, high BP and fasting blood sugar was 44.9%, 30.1%, 31.8%, and 27.7% respectively Table 2. The overall prevalence of CKD was 7.4% while metabolic syndrome was present in 24.7% of the participants as shown in Table 2.

Table 2. Prevalence of clinical characteristic of the study participant

Characteristics	No %
HDL	151(44.9)
Blood pressure	107(31.8)
Abdominal obesity	72(21.4)
Impaired fasting plasma sugar	93(27.7)
Triglyceride	101(30.1)
Metabolic syndrome	83(24.7)
CKD	25(7.4)

The prevalence of dipstick proteinuria and the mean urinary albumin–creatinine ratio were higher, while estimated glomerular filtration rate was lower among participants with the metabolic syndrome compared with those without the metabolic syndrome as illustrated in Table 1.

3.2 Prevalence and Association of CKD with Metabolic Syndrome

There was a significant difference in the prevalence of CKD among persons with (15.7%) and without (4.7%) metabolic syndrome. *P*= 0.001. Logistic regression showed that metabolic syndrome is associated with risk of CKD, OR 2.969 CI 1.589-5.545. About one-third of the participants have at least one component of Metsyn, while only 1.8% had all the five components present. Fig. 1.

3.3 Association of Components of Metabolic Syndrome with Chronic Kidney Disease

Table 3 shows the multivariate adjusted odds ratio of CKD associated with individual components of metabolic syndrome. In multivariate models, elevated blood pressure OR 3.217 (95% CI 1.144-9.051,P = 0.026) and elevated Triglyceride level OR 3.292 (95% CI 1.245-8.701, *P*=0.016) were significantly associated with an increased odds of chronic kidney disease.

4. DISCUSSION

This study evaluated the association of metabolic syndrome with chronic kidney disease.

In exploring this relationship, we identified a significant positive association between the metabolic syndrome and risk for chronic kidney disease.

The findings in this study showed that among the 336 apparently healthy participants, the prevalence rate of CKD was 7.4%. There is a significant difference in the prevalence between participants with (15.7%) and without (4.7%) MetSyn.

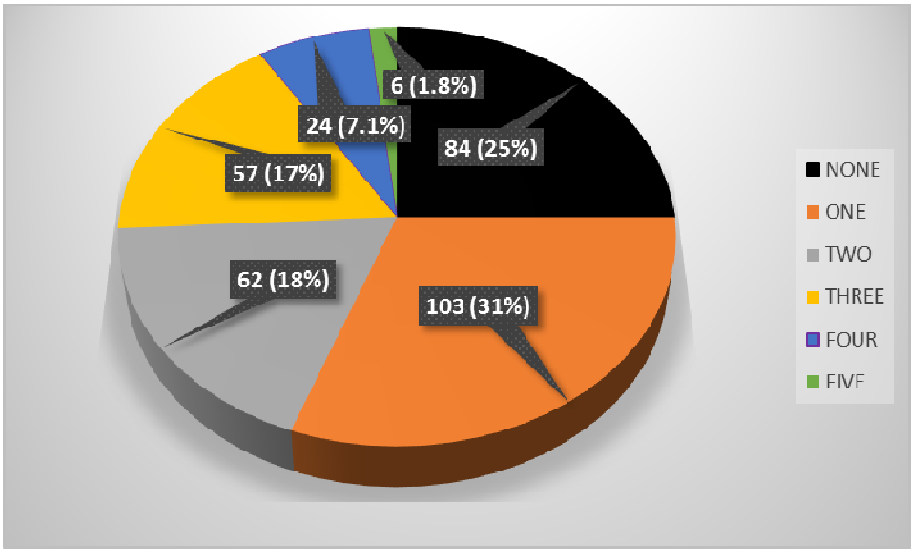

Fig. 1. Distribution of the number of components of metabolic syndrome among participants

Table 3. Association of component of metabolic syndrome with chronic kidney disease

Components	OR	95%CI	P-value
Abdominal obesity	1.225	0.472-3.181	0.676
Elevated Blood Pressure	3.217	1.144-9.051	0.026
Elevated fasting plasma sugar	1.067	0.412-2.759	0.893
Elevated Triglyceride	3.292	1.245-8.701	0.016
Low HDL	0.585	0.226-1.517	0.271

HDL= high density lipoprotein

Our finding is similar to a Chinese study [22] in which participants with MetSyn had a higher prevalence of CKD (15.4% vs 8.3%; *P* < 0.001) than those without MetSyn.

A Japanese study [23] reported a higher prevalence of 21.4% with CKD among participants with MetSyn. Their study revealed that MetSyn is a significant determinant of CKD among participants who were 60 years or younger. They also found a linear relationship between the number of MetSyn components and CKD.

Toshiharu Ninomiya et al. in the Hisayama study followed up 1,440 community-dwelling individuals without CKD aged 40 years or older and examined the effects of metabolic syndrome on the development of CKD. They found a significant difference in the incidence of CKD in individual with than without MetSyn (10.6% versus 4.8%; P < 0.01) [15].

Among the few studies done in our country, Emem-Chioma et al. [24] reported a higher but non significance prevalence of CKD among individuals with MetSyn compared with those without.

Oghenekaro Egbi et al. [25] in South eastern part of Nigeria documented a higher prevalence of CKD (20.3%) among patients with metabolic syndrome.

Chen et al. [6] analyzed a data from the National Health and Nutrition Examination Survey (NHANES III) database of 7800 subjects followed for 21 years. The subjects with normal renal function at baseline were found to have an OR of 2.6 (95%CI: 1.68-4.03) for CKD if MetSyn was present.

In the Iranian population, a group that has a high prevalence of CKD and obesity, Maleki et al [26] showed that CKD was present in 14.8% patients with MetSyn and 8.3% individuals without MetSyn. They also found that MetSyn was associated with an increased odds ratio for a glomerular filtration rate <60 ml/min/1.73 m^2. 1.91; (1.22-2.99), P = 0.004).

In another study, Kurella et al. [14] found that non-diabetic adults with the metabolic syndrome had an increased risk for developing CKD over 9 years of follow-up. This risk was found to be independent of baseline confounding factors.

Ryu et al. [27] followed 10,685 Korean men without diabetes mellitus or high blood pressure over 3.8 years for development of CKD. Participants with pre-existing metabolic syndrome (n = 787) were found to be at increased risk for CKD (hazard ratio 1.99 [95% CI 1.46–2.73]). Similarly, among participants without metabolic syndrome at baseline, development of metabolic syndrome during follow-up was also associated with an increased risk of incident CKD (hazard ratio 1.75 [95% CI 1.28–1.39]) [28].

The glomeruli in individual with metabolic syndrome are exposed to several injurious factors. The combined effect of obesity, insulin resistance, hypertension and inflammation among others all of which result in hyperfiltration-induced renal injury.

Previous studies [29,30] have established a relationship between the risk conferred by individual components of the syndrome and development of CKD. Our study showed that hypertension and high triglyceride levels are associated with an increased risk for chronic kidney disease among the subjects with metabolic syndrome.

Hypertension has been demonstrated to have adverse effects on the kidney and is strongly associated with initiation of renal disease and accelerated loss of kidney function [31-34]. The normal age related physiological decline in renal function is further heightened by high blood pressure [35-37]. Similarly, dyslipidemia has been suggested to be a risk factor in the development of renal injury [38-40].

The Third National Health and Nutrition Examination Survey in the US as analyzed by Chen et al. [6] showed that high blood pressure was the most powerful predictor of CKD in patients with MetSyn.

Similarly, analysis of data from a prospective population-based study, the ‘‘Tehran Lipid and Glucose Study’’ showed that hypertension is a strong risk factor for development of CKD among individuals with MetSyn [41].

Our finding was consistent with studies that concluded that high TG levels had association with CKD and appeared to be a risk factor for developing CKD [42,43]. However, we found no significant association between low HDL levels with CKD.

Reports from the Atherosclerosis Risk in Communities (ARIC) study found high triglycerides and low HDL cholesterol to predict an increased risk of renal dysfunction [43].

The mechanisms whereby dyslipidemia contributes to renal injury in individuals with metabolic syndrome are incompletely understood. Reports from animal study showed that the development of focal segmental glomerular sclerosis was correlated with serum triglyceride, but not serum cholesterol level [44, 45].

Nishida Y et al found that LDL and TG-rich lipoproteins caused proliferation of mesangial cells, the mechanism which is possibly mediated via cytokines [46]. Lipoproteins have also been found to stimulate production of fibronectin and monocyte chemo-attractant protein-1 expression in mesangial cells [47]. The observed association between the metabolic syndrome and the risk for renal disease call for concerted efforts not only in finding potential strategies for preventing the attendant complication but also in focusing on early treatment of metabolic syndrome.

Our study is important as it shows that the relationship observed between metabolic syndrome and CKD documented in previous studies outside our environment may equally hold true in our setting. It is equally noteworthy that in individuals without MetSyn and CKD, there may be some other important prevailing CKD risk factors that are non- metabolic in nature apart from the effect of aging.

5. CONCLUSION

The consequences of the rising prevalence of CKD in the developing countries of the world are devastating. Diagnosing MetSyn in its earlier stages may contribute to slowing down the progression of CKD as well as improving the patient’s quality of life. Proven preventive measures include; regular health check and awareness campaign, lifestyle interventions such as weight reduction, low salt intake and exercise. Of equal importance is treatment of blood pressure and blood sugar to target level as well

as controlling other metabolic risk factors associated with development of CKD.

6. LIMITATIONS

The cross sectional nature of the study and the fact that estimated GFR was used instead of a directly measured GFR to define CKD. Equation based estimation of GFR has been found to be limited in their usefulness as CKD screening tools for the general population. Similarly, because our study population was not randomly selected from the general population, the possibility for bias cannot be ruled out.

CONSENTS

All authors declare that 'written informed consent was obtained from all the participants.

ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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