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Prevalence of Kidney Dysfunction and Its Relationship with Components of Metabolic Syndrome in a Hospital Setting

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Abstract

Metabolic syndrome (MetS) is defined by a set of components including hyperglycemia, dyslipidemia, hypertension, and central obesity. Despite the well-established association between MetS and chronic kidney disease (CKD) whose prevalence is on the increase, significant gap remains in our understanding of the relationship between kidney dysfunction and individual components of MetS, particularly in Nigeria. The objectives were to determine the prevalence of kidney dysfunction among adults with MetS and to examine the relationship of key components of MetS with kidney dysfunction using a cross-sectional study of randomly selected hospital outpatients with MetS. Kidney function was assessed using estimated glomerular filtration rate (eGFR). Descriptive and inferential statistical analyses were performed and statistical significance was set at $p < .05$. The mean age of the 75 study participants with MetS was 53.33 ± 13.94 years. Females constituted 65.3% and males, 34.7%. The prevalence of kidney dysfunction (eGFR < 60 mL/min/1.73 m²) was 36.0%, with no significant difference between genders. The key components of MetS that significantly correlated with kidney function were blood pressure, serum high density lipoprotein-cholesterol, and triglyceride. The same components independently predicted kidney function. To conclude, the study highlights the considerable burden of kidney dysfunction among adults with metabolic syndrome in Nigeria. Hypertension and dyslipidemia were the components of metabolic syndrome significantly associated with kidney dysfunction. Screening, early detection and targeted interventions including lifestyle modification and appropriate drug management are crucial to mitigate the impact of metabolic syndrome on kidney health, to improve health outcomes and to reduce CKD burden.

Keywords: Central Obesity, Chronic Kidney Disease, Dyslipidemia, Hyperglycemia, Hypertension, Metabolic Syndrome, Nigeria.

1. INTRODUCTION

The rising prevalence of metabolic syndrome (MetS) and kidney disease is a major global health concern, particularly in resource-constrained countries who have the highest mortality rates (Bikbov B *et al.*, 2020). MetS, a set of conditions including hyperglycemia, atherogenic dyslipidemia, hypertension, and central obesity, increases the risk of cardiovascular events and overt diabetes. Research has shown some association between MetS and chronic kidney disease (CKD), though the mechanistic relationship between metabolic syndrome and kidney injury is not yet well understood (Singh AK & Kari JA, 2013). Persons with MetS have at least 2.5 fold higher risk of developing CKD (Singh AK & Kari JA, 2013; Chen J *et al.*, 2004). World-wide, the prevalence of metabolic syndrome has been reported to be between 12.5% to 32.4% in adults, depending on the diagnostic criteria and said to be increasing in the developing world (Bowo-Ngandji A *et al.*, 2023; Nashar K & Egan BM, 2014).

The diagnostic criteria for MetS have evolved over time since it was first named Syndrome X by Gerald Reaven in 1988 (Reaven GM, 1988). Over the years, different diagnostic criteria for MetS have been proposed by groups, beginning with the World Health Organization (WHO) in 1998 (Alberti KG & Zimmet PZ, 1998), then the European Group for the Study of Insulin Resistance in 1999 (Alberti KG & Zimmet PZ, 1999), the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) in 2002 (National Cholesterol Education Program [NCEP], 2002), the American Association of Clinical Endocrinologists in 2003 (Bloomgarden ZT, 2003), the National Cholesterol Education Program Revised Adult Treatment Panel III (NCEP-ATP III Revised) in 2005 (NCEP-ATP III, 2005), and the International Diabetes Federation (IDF) in 2005 (Zimmet P *et al*., 2005). The criteria differed mostly in the emphasis and cut-off values of the components of MetS. These led to lack of comparability between research findings with the use of different criteria for diagnosis of metabolic syndrome. To address these challenges, a consensus group of several experts and stakeholder organizations was set up, comprising the IDF, American Heart Association (AHA), National Heart, Lung, and Blood Institute (NHLBI), World Heart Federation, International Atherosclerosis Society, and International Association for the Study of Obesity culminating in the release of the Joint Interim Statement (JIS) in 2009 (Alberti KG *et al*., 2009). The JIS harmonized the existing criteria, which became a generally accepted definition of MetS. According to the JIS criteria, a diagnosis of MetS can be made when any three of the following conditions are present: central obesity, dyslipidemia, elevated blood pressure, or impaired fasting glucose. Furthermore, no single component is considered more significant than the others.

The components of MetS, are major risk factors for CKD. While the exact mechanistic pathway of MetS-associated kidney dysfunction remains uncertain, insulin resistance, chronic inflammation, and oxidative stress have been shown to be contributing factors (Singh AK & Kari JA, 2013; Chen J *et al*., 2004; Nashar K & Egan BM, 2014). MetS can lead to functional and structural abnormalities in the kidneys, including activation of the renin-angiotensin-aldosterone system (RAAS), glomerular hyperfiltration, albuminuria, podocyte injury, and fibrosis. However, the relationship between MetS and CKD is bidirectional and complicated. Incident MetS has also found in patients with established CKD (Nashar K & Egan BM, 2014). CKD is a significant public health issue, especially in low- and middle-income countries with limited resources for diagnosis and management, potentially leading to unmitigated consequences (Bikbov B *et al.*, 2020; Francis A *et al.*, 2024). Currently, at least 850 million persons are living with CKD world-wide, while Africans are said to be at higher risk of developing kidney disease and at a younger age with greater propensity to progress to kidney failure (Francis A *et al*., 2024). The ranking of CKD in the contribution of diseases to disability-adjusted life-years (DALY) rose in almost a decade, from the 29th position in 1990 to 18th in 2019 (Francis A *et al.*, 2024).

Despite the growing evidence linking MetS to CKD, research in developing countries including Nigeria is limited. The role of individual components of MetS in kidney dysfunction remains elusive. This study aims to address this knowledge gap by investigating the prevalence of kidney dysfunction and its relationship to the individual components of MetS in a hospital setting in Nigeria, an African country. Specifically, the study will determine the prevalence of kidney dysfunction as assessed by estimated glomerular filtration rate (eGFR) among adults with a diagnosis of MetS based on the harmonized JIS criteria (Alberti KG *et al*., 2009). Additionally, the study will examine the association between individual components of MetS and kidney dysfunction. A better understanding of the relationship between MetS components and kidney dysfunction can contribute valuable insights for identifying individuals at higher risk for kidney complications from MetS and for developing more accessible, affordable and effective strategies for prevention, early detection, and management of both CKD and MetS in resource-limited settings.

2. MATERIAL AND METHODS

2.1 Study Design

This study was a cross-sectional, observational study conducted at the Medical Out-Patient Clinic of the Igbinedion University Teaching Hospital Okada, Edo State in the South-South geopolitical zone of Nigeria. Adult patients presenting to the Medical Out-Patient Clinic (MOPC) with at least one component of the Metabolic Syndrome were selected through random integer generator using the RAND function in Excel, for further investigations to ascertain if they meet the criteria for the diagnosis of Metabolic Syndrome. Subjects were selected over a 16-month period when the desired sample size was obtained.

2.2 Study Population

The study population consisted of adults (≥18 years old) with newly diagnosed MetS using the 2009 Joint Interim Statement (JIS) of IDF/AHA/NHLBI definition (Alberti KG *et al*., 2009). The JIS defines MetS as the presence in an individual of any three or more of the following: waist circumference ≥102 cm in males or ≥88 cm in females indicative of central obesity, serum triglycerides ≥ 150 mg/dL or specific drug treatment for hypertriglyceridemia, high density lipoprotein cholesterol (HDL-C) < 40 mg/dL in men and < 50 mg/dL in women or drug treatment for reduced HDL-C, systolic blood pressure ≥ 130 mmHg and/or diastolic blood pressure ≥ 85 mmHg or on antihypertensive medication, fasting glucose ≥ 100 mg/dL or drug treatment for elevated fasting glucose.

2.1.1 Inclusion criteria: Subjects were included if they were 18 years or older, of either sex with a new diagnosis of metabolic syndrome based on the JIS criteria, were relatively stable clinically and if they provided informed consent.

2.1.2 Exclusion criteria: Participants were excluded if they were under 18 years of age, did not meet JIS criteria for metabolic syndrome, were pregnant, had ascites, or had life-threatening conditions that would interfere with study participation. In addition, patients who did not give consent were excluded.

2.3 Sample Size Calculation

The sample size was calculated using the following formula (Wang X & Ji X, 2020):

$$n = \frac{Z^2 \times P \times (1 - P)}{d^2}$$

Where, n is sample size, Z is 1.96 for alpha 0.05, P is the prevalence of the condition/disease, d is precision or margin of error, which is 0.05 for this study.

We assumed a 4.8% prevalence of kidney dysfunction in patients with metabolic syndrome based on a similar study in Nigeria (Emem-Chioma PC *et al.*, 2011) using single-population proportion formula with a confidence level of 95% and a 5% margin of error. After sample size adjustment to account for attrition, 75 patients were enrolled to participate in this study.

2.4 Data Collection

Data were collected with questionnaire and laboratory tests.

The questionnaire was used to collect information on sociodemographic characteristics (age in years at last birthday, sex, education, occupation, religion), medical history, physical examination, assessment of central obesity using waist circumference (WC) in cm, systolic blood pressure (SBP) and diastolic blood pressure (DBP), both in mmHg.

One of the authors (HUI) measured the waist circumference (WC) of subjects with a standard tape. The tape was applied to the exposed abdomen devoid of clothing, at a level halfway between the lowest costal margin and iliac crest. The tape was applied to the abdomen while the participant was standing with the arms hanging loosely by the sides and feet together. The measurement was taken to the nearest 0.1 cm in mid-expiration when the participant was breathing gently with the abdominal muscles relaxed.

Blood pressure (BP) was measured using the auscultatory method with a validated manual mercury sphygmomanometer, following the American Heart Association guidelines (Pickering TG *et al*., 2005). The subjects were made to sit comfortably on a chair with a back rest and legs dependent and uncrossed. After a 5-minute rest, the appropriate cuff size was applied to the bared and supported upper arm at heart level. Talking was discouraged during the measurement. The first and last audible sounds corresponding to the SBP and the DBP respectively were taken to the nearest 2 mm Hg. The BP was taken in both arms, initial readings were discarded. The average of the subsequent two readings in the arm with the higher reading was recorded as the BP for each participant. The mean arterial pressure (MAP) was calculated using the following formula:

MAP (mmHg) = (1/3 * SBP) + (2/3 * DBP).

2.4.1 Clinical Laboratory Investigation

2.4.1.1 Sample collection

Venous blood samples were collected according to ethical guidelines, from the subjects in the morning after an overnight fast. Fast was defined as abstinence from caloric intake for 8 hours. Drinking of water was allowed. The blood samples were placed in a sodium fluoride/potassium oxalate container and in lithium heparin tube for chemical analysis. The labelled samples were mixed to ensure anticoagulation, centrifuged and the plasma was stored at -20°C pending analysis.

2.4.1.2 Analysis of biochemical parameters

Each subject's sample was analyzed for serum creatinine, triglyceride (TG), High-Density Lipoprotein-Cholesterol (HDL-C), and fasting plasma glucose (FPG) using Beckman Coulter AU5400 Chemistry System (Beckler Coulter, Brea, CA).

The assay for serum creatinine concentration was based on Jaffe's test involving the reaction of creatinine with alkaline picrate to form a colored complex and absorbance measured at 520 nm (Lamb EJ & Prince CP, 2012) Serum creatinine was employed to estimate the glomerular filtration rate (eGFR) in ml/min/1.73 m^2 body surface area. The eGFR was calculated using the Modification of Diet in Renal Disease (MDRD) GFR equation (Levey AS *et al.*, 2002).

The triglyceride estimation involved using triglyceride reagents and absorbance measured at 500 nm (Bucolo G & David H, 1973). HDL-C was measured directly by precipitating non-HDL lipoproteins and then enzymatically analyzing the remaining HDL (Warnick GR *et al*., 2001). Triglyceride concentration ≥ 150 mg/dL and/or HDL-C < 40 mg/dL in men or < 50 mg/dL in women is referred to as dyslipidemia.

The fasting plasma glucose assay was based on the glucose oxidase method, where glucose is oxidized to gluconic acid and hydrogen peroxide, which reacts with chromogen to form a colored product. After diluting the blood samples from the patients with phosphate buffer, they were mixed with glucose oxidase and peroxidase reagents, incubated at 37°C, and absorbance was measured at 500 nm (Sacks DB *et al*., 2011).

Hyperglycemia refers to elevated blood glucose levels including prediabetes (impaired fasting glucose-IFG, impaired glucose tolerance-IGT) and diabetes.

2.5 Variables:

The dependent variable in this study was eGFR and the independent variables were sociodemographic factors and the components of MetS (WC, SBP, DBP, TG, HDL-C, FPG), in addition to MAP.

2.6 Ethical Considerations

Ethical approval for the study was obtained from the Igbinedion University Teaching Hospital Ethical Research Committee. All the participants provided informed consent before enrollment to the study. The participants were assured of confidentiality of their data and this was maintained throughout the course of the study, which adhered to the Helsinki Declaration regarding medical research involving human subjects (World Medical Association, 2001).

2.7 Statistical Analysis

The data were entered into Excel Spreadsheet (Microsoft Office 2019), cleaned, imported into and analyzed using IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp. (2020). The characteristics of the study population were summarized with descriptive statistics as frequencies, percentages, and means with standard deviation. Inferences based on analyses of the data were made using Independent-Samples T test to compare the means of continuous variables and Chi-square tests or Fisher's exact tests when appropriate, to compare the association between categorical variables in 2x2 contingency tables. Pearson correlation analysis was conducted to assess the linear relationship between eGFR and components of MetS, having confirmed that the data fulfilled the assumptions for the test. However, the independent variables SBP and DBP were highly correlated with each other. So, SBP and DBP were computed into a new variable, mean arterial pressure (MAP) as described earlier, for the correlation test. Effect size or correlation coefficient (*r*), was interpreted thus: 0.10, small, 0.30 moderate, and 0.50 large (Cohen J, 1992). The independent effects of the independent variables on eGFR were evaluated with multiple linear regression. A two-tailed $p < 0.05$ was considered statistically significant.

3. RESULTS AND DISCUSSION

3.1 Characteristics of participants

Majority of the 75 participants who had a diagnosis of metabolic syndrome (MetS), were female (65.3%), Christian (98.7%), had primary school education (53%), or were farmers (73.3%). The mean age of the study population was 53.33 ± 13.94 years and the age range was from 19 years to 80 years. The most common individual components of MetS were SBP (82.7%) and DBP (78.7%). The least common was low HDL-C (36%), consisting of 29.3% females and 6.7% males. Further, among MetS patients, the prevalence of central obesity assessed with Waist Circumference (WC) was 41.3%, comprising 28% females and 13.3% males. Twenty-seven (36%) of the participants had kidney dysfunction with estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73 m^2. Table I below shows the sociodemographic and other characteristics of the study population.

Table I: Characteristics of Participants

Characteristic	N (75)	% (100)
Age (years at last birthday)		
≤ 45	21	28
> 45	54	72
Sex		
Female	49	65.3
Male	26	34.7
Religion		
Christianity	74	98.7
Islam	1	1.3
Level of Education		
Primary	39	52
Secondary	24	32
Tertiary	12	16
Occupation		
Banker	1	1.3
Farmer	55	73.3
Lecturer	11	14.7
Hair dresser	1	1.3
Carpenter	2	2.7
Petty trader	3	4.0
Student	1	1.3
Secretary	1	1.3

Waist Circumference (WC, in cm)*		
No central obesity	44	58.7
Central obesity	31	41.3
Systolic Blood Pressure (mmHg)		
< 130	13	17.3
≥ 130	62	82.7
Diastolic Blood Pressure (mmHg)		
< 85	16	21.3
≥ 85	59	78.7
High Density Lipoprotein-Cholesterol (HDL-C, in mg/dL)†		
Low	27	36
Normal	48	64
Triglyceride (mg/dL)		
< 150	23	30.7
≥ 150	52	69.3
Fasting Plasma Glucose (mg/dL)		
<100	45	60
≥ 100	30	40
Estimated Glomerular Filtration Rate (ml/min/1.73 m^2)		
< 60	27	36
≥ 60	48	64

* No central obesity, WC in Males < 102 cm. WC in Females < 88 cm
Central obesity, WC in Males ≥ 102 cm. WC in Females ≥ 88 cm

† Low HDL-C in Males < 40 mg/dL and in Females < 50 mg/dL Normal HDL-C in Males ≥ 40 mg/dL and in Females ≥ 50 mg/dL

3.2 Prevalence of Kidney Dysfunction among Components of Metabolic Syndrome

The eGFR of the study population ranged from 28.4 to 168.9 ml/min/1.73 m^2 with a study population mean of 90.3 ± 39.0 ml/min/1.73 m^2. Females had a non-significantly higher prevalence of kidney dysfunction than males (36.7% versus 34.6% respectively, $\chi 2 = .033$, df = 1, p = .856). There were also no significant differences in the prevalence of kidney dysfunction between other sociodemographic groups based on age, education, religion and occupation. Unexpectedly, the younger age group ≤ 45 years had a higher prevalence of kidney dysfunction compared to the older age group > 45 years, though the difference was not statistically significant (38.1% vs. 35.2% respectively, $\chi 2 = .056$, df = 1, p = .814).

More than half (57.1%) of the adults who had central obesity had kidney dysfunction. The next highest prevalence of kidney dysfunction (42.9%) was among those with low HDL-C (< 40 mg/dL in men and < 50 mg/dL in women). Participants with IFG (≥ 100 mg/dL) had the lowest prevalence of kidney dysfunction (30%). All the study participants had either three or four components of the diagnostic criteria for MetS. None had more than four of the criteria. Though the prevalence of kidney dysfunction was higher among participants who had co-existent four components of MetS compared to three components, the difference was not significant (54.6% vs. 34.4% respectively, $\chi 2 = 1.924$, df = 1, p = .165). The prevalence of kidney dysfunction within each component of MetS is illustrated in Figure I below.

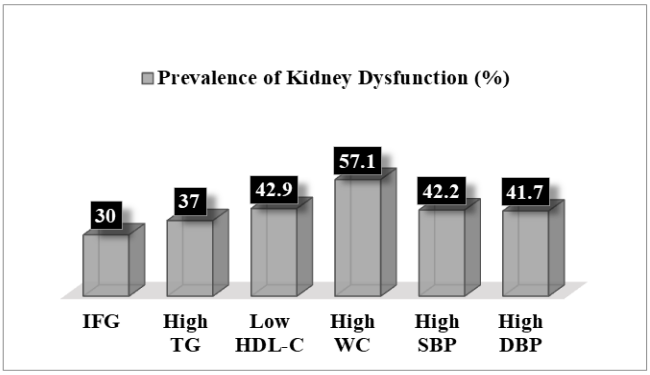

Figure I: Prevalence of kidney dysfunction among individual components of Metabolic Syndrome
Key: WC, **W**aist **C**ircumference. **HDL-C**, **H**igh **D**ensity **L**ipoprotein-**C**holesterol. **TG**, **Tri**glyceride. **SBP**, **S**ystolic **B**lood **P**ressure. **DBP**, **D**iastolic **B**lood **P**ressure**. IFG**, **I**mpaired **F**asting **G**lucose.
Note: Kidney Dysfunction = eGFR < 60 ml/min/1.73 m^2

3.3 Relationship between Components of Metabolic Syndrome and Kidney Function

Some components of MetS were significantly correlated with kidney function, while others were not. The MAP, TG and HDL-C levels had significant correlation with eGFR, representing kidney function. MAP and TG had a moderate, negative correlation with eGFR (r = -.301, p = .009 and r = -.343, p =.003, respectively), while HDL-C had a moderate, positive correlation with eGFR (r =.325, p = .004). On the other hand, the correlation of eGFR with Age, WC, and FPG was not statistically significant (p > .05) as indicated in Table II, below.

Table II. Correlation between eGFR and Components of the Metabolic Syndrome (N=75)

Variables	Pearson Correlation, *r*	Significance (2-tailed)	95% Confidence Intervals (2-tailed)	
			Lower	Upper
eGFR - AGE	-.034	.772	-.194	.259
eGFR – WC	-.038	.744	-.263	.190
eGFR – HDL-C	.325**	.004	.106	.514
eGFR – TG	-.343**	.003	-.529	-.126
eGFR – FPG	-.214	.066	-.014	.420
eGFR – MAP	-.301**	.009	-.494	-.080

**. Correlation is significant at the 0.01 level (2-tailed)

Key: WC = Waist Circumference, HDL-C = High Density Lipoprotein-Cholesterol, TG = Triglyceride, FPG = Fasting Plasma Glucose, MAP = Mean Arterial Pressure

Having fulfilled the assumptions to ensure valid results, multiple linear regression assessed the impact of the predictor variables: age and the individual components of MetS (WC, HDL-C, TG, FPG, and MAP) on the dependent variable: eGFR (kidney function).

The regression model was significant, $F(5, 69) = 6.072$, $p < .001$ indicating at least one of the predictor variables significantly affects kidney function. The predictor variables explained 30.6% of the variance in kidney function with an adjusted R^2 of 0.306. While the model had a good fit, it is important to note that it does not prove causation, and external factors not included in the model may also affect kidney function.

Table III below shows that indeed, HDL-C, TG, and MAP, were independently and significantly predictive of eGFR in the participants, after controlling for confounding factors. Higher MAP and TG levels were associated with lower eGFR suggesting damaging effect of increased levels of MAP and TG on the kidney function. Hence, for each unit increase in MAP, eGFR was expected to decrease by 0.871 ml/min/1.73 m^2 and for every unit increase in TG, eGFR was expected decrease by 0.179 ml/min/1.73 m^2. However, higher HDL-C levels were associated with higher eGFR, suggesting protective effect of higher HDL-C levels on kidney function. So, for each unit increase in HDL, eGFR was expected to increase by 0.571 ml/min/1.73 m^2. Age, WC, and FPG did not show a significant linear relationship with eGFR and were not predictive of eGFR.

Table III: Independent Predictors of Kidney Dysfunction in Metabolic Syndrome Patients

Predictor Variables	B	t	Sig	95% Confidence Intervals for B	
				Lower	Upper
Constant	216.055	5.993	.000	144.130	287.981
AGE	-.277	-.937	.352	-.867	.313
WC	-.864	-1.110	.271	-2.418	.689
HDL	.571	2.767	.007	.159	.982
TG	-.179	-3.085	.003	-.294	-.063
FBG	-.025	-.668	.507	-.101	.050
MAP	-.781	-2.733	.008	-1.350	-.211

Dependent Variable: eGFR

To summarize the results of this study, the participants were mostly female, middle aged or elderly with limited education in an agrarian community. The most common component of metabolic syndrome was hypertension (SBP and DBP). Over one-third of the study population had kidney dysfunction. Participants with central obesity (WC) had the highest prevalence of kidney dysfunction. Dyslipidemia (low HDL-C, high TG) and Hypertension (MAP) were significantly associated with kidney dysfunction.

3.4 DISCUSSION

The rising prevalence of metabolic syndrome and its potential consequences for kidney health pose significant challenges in low-resource settings, where healthcare resources are limited and high mortality rates continue unabated (Francis A *et al.*, 2024). The

relationship between metabolic syndrome and kidney dysfunction is poorly understood in low- and middle-income countries. This study aimed to fill this research and knowledge gap by examining the relationship between kidney function and key components of metabolic syndrome among adults in low-resource settings, with the goal of informing health policies and clinical practice.

The majority of participants were middle-aged and elderly, a demographic at higher risk for metabolic syndrome, chronic kidney disease, and increased mortality from cardiovascular diseases (Bikbov B *et al.*, 2020; Singh AK & Kari JA, 2013; Chen J *et al*., 2004; Bowo-Ngandji A *et al*., 2023; Nashar K & Egan BM, 2014; Francis A *et al.*, 2024). This finding emphasizes the need for preventive strategies targeting this growing population, particularly in developing countries like Nigeria. Though sociodemographic factors appeared not to have a discernible impact on the association between metabolic syndrome and kidney function in this study, the younger-aged adults with metabolic syndrome had a higher prevalence of kidney dysfunction compared to the older adults. Although the difference was not statistically significant, the clinical relevance cannot be overlooked, particularly as incident CKD appears to affect younger age groups in black Africans and to progress faster to kidney failure (Francis A *et al.*, 2024). Apart from the co-morbid metabolic syndrome in these persons, factors such as genetics, lifestyle and environment may have contributed to this finding. However, it would be expedient to further investigate the relatively high prevalence of kidney dysfunction among the younger age group from an agrarian community in this study, given the increasing incidence of chronic kidney disease of unknown etiology (CKDu) or of multifactorial origin (CKD mfo) involving mainly young farmers (Fiseha T *et al*., 2024; Wimalawansa SJ, 2015).

This study yielded several notable findings. Notably, over one-third of adults with metabolic syndrome demonstrated evidence of kidney dysfunction. A few of the studies conducted in Nigeria some years ago, reported much lower prevalences of CKD associated with MetS compared to the 36% prevalence in the present study. A 2011 study (Emem-Chioma PC *et al.*, 2011) at a general hospital in Okrika, South-South Region of Nigeria reported a prevalence of 4.8% among adult patients in a general outpatient clinic. Another study, which was community-based in Ado-Ekiti, South-West Region of Nigeria reported a 15% prevalence in 2017 among apparently healthy adults in the community (Dada A *et al*., 2017). Despite variations in study populations, including location, diagnostic criteria, and methodology, the increasing prevalence of metabolic syndrome in Nigeria over a 13-year period has to be alarming. This trend necessitates concerted and evidence-based public health policies and clinical practice strategies to reduce the disease burden. Unfortunately, developing countries like Nigeria have limited healthcare infrastructure to address the heavy and increasing burden of kidney complications and metabolic syndrome. Furthermore, the economic consequences of the chronic conditions can be dire. The burden of disease is usually disproportionately borne by the marginalized even in resource-limited communities, thereby aggravating existing health disparities.

Some components of metabolic syndrome were linked to kidney dysfunction in this study. Dyslipidemia (raised serum triglyceride and low high density lipoprotein-cholesterol) and elevated blood pressure were significantly associated with kidney dysfunction and they also emerged as independent predictors of decreased kidney function. The mechanisms underlying the effect of dyslipidemia on kidney function are still not well understood. Nevertheless, some of the proposed mechanistic pathways may include atherosclerosis, oxidative stress, chronic inflammation, hemodynamic change and endothelial dysfunction, though high TG specifically, may directly promote glomerulosclerosis (Singh AK & Kari JA, 2013; Chen J *et al*., 2004; Nashar K & Egan BM, 2014). The putative mechanisms through which hypertension in the context of metabolic syndrome causes kidney dysfunction includes action through angiotensin II, which stimulates reactive oxygen species (ROS) production, thereby decreasing nitric oxide synthase production, leading to renal microvascular injury, ischemia, and tubulointerstitial damage (Nashar K & Egan BM, 2014).

Further studies are required to further elucidate the impact of dyslipidemia and hypertension on kidney dysfunction in persons with metabolic syndrome. The metabolic syndrome is a known risk factor for kidney dysfunction, but the role of the individual components of metabolic syndrome in metabolic syndrome-associated kidney disease is still not well-defined and vary in different contexts and at different times.

Although fasting plasma glucose and waist circumference (WC), an indicator of central obesity, were not significantly associated with kidney dysfunction in this study, the highest prevalence of kidney dysfunction was observed among individuals with central obesity. This discrepancy is difficult to explain but may be due to other kidney-related risk factors, such as medications, that were not investigated in this study Contrary to some of our findings, a 2007 study of non-diabetic black Africans found a significant association between kidney dysfunction and obesity using the NCEP-ATP III criteria (Okpechi IG *et al*., 2077). However, a study in Ghana, another developing country in West Africa, reported similar findings to this present study (Owiredu WK *et al*., 2012). Consistent with the present study, the Ghanaian study showed that elevated triglycerides and systolic blood pressure were associated with CKD, though unlike this study, waist circumference was also a contributing factor in the Ghanaian study.

However, hypertension has been consistently identified as the most significant predictor of chronic kidney disease (CKD) in individuals with metabolic syndrome (Chen J *et al*., 2004). Given the significant association between dyslipidemia and hypertension in this study, the need to prioritize screening, monitoring, and strategies to manage these and other components of metabolic syndrome cannot be overstated.

This study aimed to investigate the chain connecting metabolic syndrome and kidney disease, both of which contribute to cardiovascular risk (Singh AK & Kari JA, 2013; Nashar K & Egan BM, 2014; Francis A *et al.*, 2024). The concept of cardiovascular-kidney-metabolic (CKM) syndrome has gained recognition due to the increasing understanding of their interconnectedness (Sebastian SA *et al*., 2023). Effective interventions are essential to disrupt this chain and improve outcomes for affected individuals. A comprehensive approach is needed to enhance capacity and to improve access to equitable healthcare services, promote public health initiatives for awareness and prevention of metabolic dysregulation and its complications and to support research on effective interventions for metabolic syndrome and kidney disease in resource-limited countries.

This study confirms the link between metabolic syndrome and kidney dysfunction. However, inconsistent diagnostic criteria for metabolic syndrome can hinder comparisons across different settings. Adopting standardized criteria like the JIS is essential for comparability between study findings to enhance our understanding. Further research is needed to explore the specific contributions of individual components of the metabolic syndrome to kidney dysfunction. The findings highlight the urgent need for early screening and management of metabolic syndrome and kidney disease in developing countries to address the rising burden of these conditions.

The findings of this study should be considered within the context of its limitations. Due to its cross-sectional design, the study only established an association, not causation, between metabolic syndrome and kidney dysfunction. The temporal relationship between these conditions remains unclear, as they share common risk factors and they have a bidirectional, albeit complex relationship. This often leads to their coexistence, making it challenging to definitively determine causality, which was not the primary objective of this study. A longitudinal study, which is generally more expensive, would be better suited to investigate the temporal relationship between metabolic syndrome and kidney dysfunction. Another limitation due to cost implications, was the relatively small sample size and the single-hospital setting, which may limit the generalizability of the findings to the broader population. Furthermore, this study did not investigate lifestyle factors such as diet, medications, smoking, and other morbidities that can confound the relationship between metabolic syndrome components and kidney function. However, potential confounders like age and sex were considered. Additionally, the definitive diagnosis of CKD was not made, as eGFR was assessed only once, and the diagnosis of CKD requires evidence of reduced kidney function and/or markers of kidney damage such as urine albumin-creatinine ratio for at least three months. Nevertheless, the study's strengths include the use of the harmonized 2009 JIS criteria for diagnosing metabolic syndrome and its focus on a growing area of importance in developing countries.

4. CONCLUSION

This study contributes to the limited literature on the association between kidney dysfunction and the components of metabolic syndrome, particularly in resource-limited settings. By highlighting the significant burden of kidney disease among individuals with metabolic syndrome, the study emphasizes the compelling need for early detection and intervention. Identifying key risk factors such as hypertension, low HDL cholesterol, and elevated triglycerides may have important clinical and public health implications in terms of risk stratification, prevention and management strategies.

The substantial burden of metabolic syndrome and kidney complications, warrants targeted interventions and cost-effective public health initiatives to protect kidney health. Longitudinal studies are recommended to further investigate any causal relationship between metabolic syndrome and kidney disease and to evaluate the effectiveness of interventions to prevent and manage the dual burden of metabolic syndrome and kidney damage. Policymakers and healthcare providers can play a pivotal role in implementing these recommendations to reduce the prevalence of kidney dysfunction and improve the health outcomes of adults with metabolic syndrome.

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