

Journal of Clinical Nephrology and Renal Care

ORIGINAL ARTICLE

Magnitude of Metabolic Syndrome and its Associated Factors among Patients with Chronic Kidney Disease: Laboratory-Based Cross-Sectional Study in Northwest Ethiopia

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Abstract

Background: Chronic kidney disease (CKD) is a noncommunicable disorder that causes a progressive decline in kidney function, leading to complications such as metabolic disorders that can increase the risk of heart diseases. Metabolic syndrome (MetS) is a significant global health issue characterized by a combination of factors like high blood pressure, central obesity, abnormal lipid levels, and elevated blood sugar levels. As such, this research conducted in Northwest Ethiopia sought to determine the prevalence of MetS and its related factors among CKD patients within the Ethiopian population.

Method: An institutional cross-sectional study was carried out at the renal clinic in FHCRH located in Bahir Dar, Ethiopia. Data collection was done through face-to-face interviews using a structured questionnaire. Blood pressure and anthropometric parameters were measured following standard procedures. Approximately 5 ml of serum was exploited for analyzing lipid profiles and fasting blood glucose levels using an automated chemistry analyzer. Statistical analysis of all data was conducted using the Statistical Package for the Social Sciences (SPSS) software version 25. A significance level of P < 0.05 was considered statistically significant. **Result:** A total of one hundred CKD patients participated in the study, resulting in a response rate of 100%. The findings indicated that approximately 16.1% (95% CI: 8.02-27.67) of males and 21.1% (95% CI: 9.55-37.32) of females were found to have MetS, with an overall prevalence of around 18% (95% CI: 11.03-26.95). Analysis of the individual components of MetS revealed that most components were more prevalent in females, except for elevated fasting blood glucose, which was higher among males. The most common component among all participants was increased waist circumference (21%), while elevated triglycerides had the lowest prevalence at 14%.

Conclusion: In conclusion, this study underscores the significant prevalence of MetS among CKD patients in Northwest Ethiopia. It emphasizes the critical need for early detection, prevention, and effective management strategies for MetS in CKD patients, particularly those with a family history of these conditions and older age.

Keywords

CKD, MetS, Central obesity, Dyslipidemia, Hypertension, Ethiopia



Citation: Agidew MM, Teklemaryam AB, Mengstie MA, Bayafers AM, Muche ZT, et al. (2024) Magnitude of Metabolic Syndrome and its Associated Factors among Patients with Chronic Kidney Disease: Laboratory-Based Cross-Sectional Study in Northwest Ethiopia. J Clin Nephrol Ren Care 10:095. doi.org/10.23937/2572-3286.1510095

Accepted: May 09, 2024: Published: May 11, 2024

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Abbreviations

BP: Blood Pressure; BMI: Body Mass Index; TG: Triglyceride; HDL-C: High Density Lipoprotein Cholesterol; FBG: Fasting Blood Glucose; CKD: Chronic Kidney Disease; eGFR: Estimated Glomerular Filtration Rate; ESRD: End-Stage Renal Disease; EPHI: Ethiopian Public Health Institute; FHCSH: Felege Hiwot Comprehensive Specialized Hospital

Introduction

Globally, more than 750 million people are affected by chronic kidney disease (CKD), a non-communicable condition that results in a gradual deterioration of kidney function characterized by various indications of kidney damage. The decline in renal function is evaluated by lower estimated glomerular filtration rate (eGFR) levels, which are determined from serum creatinine levels using the CKD epidemiology collaboration (CKD-EPI) equation calculator [1-3]. Lower eGFR levels are crucial markers of CKD for diagnosis and categorization [4,5]. CKD is identified if either of the following criteria is met: (1) Persistent kidney damage for a minimum of 3 months, featuring structural or functional irregularities in the kidneys with or without reduced eGFR, abnormal blood or urine composition, kidney imaging, and biopsy; or (2) An eGFR level below 60 mL/min/1.73 m² for at least 3 months, irrespective of other signs of kidney damage [6]. CKD is a significant contributor to poor health outcomes and mortality, primarily due to its link with a range of complications, notably with metabolic syndrome (MetS) that in turn leads to cardiovascular conditions [7,8].

MetS is a growing global health concern that is increasingly linked to CKD. The prevalence of MetS is on $the rise in regions such as the Middle \, East and \, sub-Saharan$ Africa [9,10]. MetS is characterized by a combination of disorders and risk factors for heart disease, including high blood pressure (BP), central obesity defined by waist circumference (WC), dyslipidemia, and fasting blood glucose (FBG) [11]. Studies have shown that all these components of MetS are significantly associated with CKD [9,12]. Individuals with CKD are more likely to have MetS due to metabolic imbalances [13]. Lifestyle choices and genetic factors also contribute to the development of MetS in CKD patients [14]. There is a clear connection between MetS and kidney damage [9], although the exact mechanism by which CKD leads to the occurrence of MetS components remains unclear. Factors such as high-calorie diets, poor nutrition, lack of physical activity, and obesity are common risk factors for MetS among CKD patients in developed and developing countries [15]. While CKD may contribute to the development of components of MetS [16], its impact on the individual components varies [9].

Moreover, the lack of extensive data on the prevalence of MetS in individuals with CKD in Ethiopia is apparent, mainly due to the limited scope of research. This knowledge gap has spurred our interest in exploring the occurrence of MetS in CKD patients. Therefore, the main aim of this study is to ascertain the prevalence of MetS and associated factors among CKD patients in the Ethiopian population.

Methods and Materials

Study area, period, and design

An institutional cross-sectional study was carried out at the renal clinic in FHCSH located in Bahir Dar Ethiopia, situated 560 kilometers northwest of Addis Ababa, from September to November 2020.

Population

A purposive non-probability sampling technique was applied to assess the prevalence of MetS among 100 CKD patients receiving treatment at the renal clinic during the study period. These patients were identified as chronically ill and presented with CKD [17].

Eligibility criteria

The study included CKD patients aged between 18 and 65 years who were diagnosed based on their eGFR levels and were actively receiving treatment at the renal clinic. Excluded from the study were patients with liver diseases, patients outside the age range of 18 to 65 years, pregnant women, and postpartum individuals.

Study variables

Socio-demographic characteristics, behavioral factors, anthropometric measurements, and clinical indicators were considered as independent variables, while MetS and its diagnostic criteria were treated as the dependent variable.

Data collection

Sociodemographic, medical, and related information was gathered through structured questionnaires administered via face-to-face interviews. Various data required for this study were collected using different methods as outlined below.

Measurement of Blood Pressure (BP)

BP was measured directly using a digital sphygmomanometer after the participant had been stabilized for 10 minutes. Two readings of BP were taken, and the average of these readings was used for analysis for each participant.

Anthropometric measurements

Anthropometric measurements including waist circumference, weight, and height were measured using standard equipment. WC was measured directly, and Body Mass Index (BMI) was calculated by dividing weight in kilograms by height in square meters using the formula: BMI = Weight (kg)/Height (m²). The calculated BMI values were then categorized according to the World Health Organization (WHO) guidelines as underweight (BMI < 18.5 kg/m²), normal weight (BMI

18.5-24.9 kg/m²), overweight (BMI 25.0-29.9 kg/m²), and obese (BMI > 30 kg/m^2) [18].

Laboratory tests

Blood samples were obtained following an overnight fast of at least 8 hours to measure levels of FBG, triglycerides (TG), and high-density lipoprotein cholesterol (HDL-C).

Blood sample collection and laboratory analysis

After obtaining informed consent, 5 ml of blood was collected from each participant and placed in a serum separator tube (SST). The blood sample was then centrifuged at 5,000 rpm for 5 minutes within 40 minutes to separate the serum. The separated serum was transferred to a Nunc tube using a micropipette and stored in a refrigerator at -70 °C until laboratory analysis. All biochemical parameters were analyzed according to the guidelines of the International Federation of Clinical Chemistry (IFCC) expert panel. The measurements were performed using a fully automated Roche Cobas[®] C 502 Chemistry Analyzer [19].

Data processing and statistical analysis

Following data entry, coding, and cleaning, statistical analysis was conducted using Statistical Package for the Social Sciences (SPSS) software version 25.0. Categorical variables were reported as frequencies and percentages, while continuous variables were described using means and standard deviations (SD). Statistical significance was defined as p-values less than 0.05.

Definition of CKD

As previously stated, individuals are diagnosed with CKD if they meet one of the following criteria: (1) They exhibit kidney damage lasting at least 3 months, characterized by structural or functional abnormalities in the kidneys, with or without a decreased eGFR, abnormal blood or urine test results, abnormal kidney imaging findings, or biopsy results; or (2) They have a consistently decreased eGFR level (eGFR < 60 mL/min/1.73 m²) for a minimum of 3 months, regardless of other indicators of kidney damage [6].

Definition of MetS

Patients with CKD were assessed for MetS using the modified National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) [20]. According to the NCEP guidelines, individuals can be diagnosed with MetS if they exhibit three or more of the following conditions: (1) Central obesity (WC \geq 94 cm in males and \geq 80 cm in females); (2) TG level \geq 150 mg/dL; (3) Reduced HDL-C < 40 mg/dL for males and < 50 mg/dL for females; (4) High BP (systolic BP \geq 130 or diastolic BP \geq 85 mmHg); (5) Elevated FBG levels \geq 100 mg/dL.

Results

Sociodemographic and behavioral characteristics

This study involved 100 participants diagnosed with CKD. Of these participants, 62 were male and 38 were female. The average ages of the male and female participants were 46.9 \pm 13.45 and 41.5 \pm 14.20 years, respectively. Approximately 51.6% of males and 65.8% of females were residents of urban areas. In terms of education, 65.8% of males had completed primary education, while 14.5% had completed secondary education. Similarly, 79% of males and 71.1% of females were not office workers. Regarding educational attainment, 36.8% of males were illiterate, while 7.9% of females had completed higher education. Additionally, 85.5% of males and 100% of females did not have a history of alcohol intake, and 90.3% of males and 100% of females did not have a history of cigarette smoking (Table 1).

Variables		Male (n = 62)	Female (n = 38)
Age (year)	Mean + SD	46.9 ± 13.45	41.5 ± 14.20
Residence	Rural	30 (48.4%)	13 (34.2%)
	Urban	32 (51.6%)	25 (65.8%)
Educational status	Illiterate	19 (30.6%)	14 (36.8%)
	Primary Education	22 (65.8%)	9 (23.7%)
	Secondary Education	9 (14.5%)	12 (31.6%)
	College/ University	12 (19.4%)	3 (7.9%)
Occupational status	Office worker	13 (21%)	11 (28.9%)
	Not office worker	49 (79%)	27 (71.1%)
Alcohol use	Yes	9 (14.5%)	-
	No	53 (85.5%)	38 (100%)
Smoking status	Active smoker	6 (9.6%)	-
	Nonsmoker	56 (90.3%)	38 (100%)

Continuous variables are expressed as mean ± SD, whereas categorical variables are expressed in frequency and percent; n, the number of participants

Anthropometric parameters and BP in male and female participants

In this study, the average BMI values for male participants were 21.14 \pm 3.36 Kg/m², while for female participants, it was 20.16 \pm 3.39 Kg/m². The mean SBP was 118.77 \pm 10.73 mmHg for males and 117.92 \pm 10.58 mmHg for females. Similarly, the mean DBP was 77.13 \pm 9.02 mmHg for males and 76.76 \pm 6.67 mmHg for females. Here, the study found that weight and height were statistically significantly correlated with the sex of the participants (Table 2).

Clinical characteristics of the study participants

The study revealed that 11.3% of male participants and 13.2% of female participants reported a family

history of CKD. Among the CKD patients in the study, approximately 16.1% of males and 21.1% of females were identified to have MetS. Additionally, a family history of MetS was reported by 6.5% of male participants and 13.2% of female participants (Table 3).

Magnitudes of MetS and its components among the study participants

The data in the table below showed that the prevalence of MetS is higher in females [21.1% (95% CI: 9.55-37.32)] compared to males [16.1% (95% CI: 8.02-27.67)] with an overall prevalence of around 18% (95% CI: 11.03-26.95). Analysis of the individual components of MetS revealed that most components were more common in females than in males. However, elevated

Table 2: Anthropometric	parameters and BF	of study participants.
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Variables	Male (n = 62)	Female (n = 38)	P-value
Weight (kg)	58.6 ± 8.3	49.97 ± 8.96	0.000
Height (m)	1.67 ± 0.06	1.58 ± 0.05	0.000
BMI (kg/m²)	21.14 ± 3.36	20.16 ± 3.39	0.164
Systolic BP (mmHg)	118.77 ± 10.73	117.92 ± 10.58	0.699
Diastolic BP (mmHg)	77.13 ± 9.02	76.76 ± 6.67	0.829

All the variables are continuous and expressed as mean \pm SD n (%). BMI: Body Mass Index; BP: Blood Pressure; p-value is significant at < 0.001.

Variables		Males (n = 62)	Females (n = 38)
Family history of CKD	Yes	7 (11.3%)	5 (13.2%)
	No	55 (88.7%)	33 (86.8%)
	Yes	10 (16.1%)	8 (21.1%)
MetS	No	52 (83.9%)	30 (78.9%)
Family history of MetS	Yes	4 (6.5%)	5 (13.2%)
	No	58 (93.5%)	33 (86.8%)

Table 3: Clinical characteristics of CKD patients.

Variables are expressed in frequency and percent. CKD: Chronic Kidney Disease; MetS: Metabolic Syndrome

Table 4: Components of MetS among the study participants.

Parameter		Male (n = 62)	Female (n = 38)	Total (n = 100)
Presence of MetS	Yes	10 (16.1%)	8 (21.1%)	18 (18%)
	No	52 (83.9%)	30 (78.9%)	82 (82%)
Presence of HTN	Yes	9 (14.5%)	6 (15.8%)	15 (15%)
	No	53 (85.5%)	32 (84.2%)	85 (85%)
Increased WC	Yes	12 (19.4%)	9 (23.7%)	21 (21%)
	No	50 (80.6%)	29 (76.3%)	79 (79%)
Increased TG	Yes	6 (9.7%)	8 (21.1%)	14 (14%)
	No	56 (90.3%)	30 (78.9)	86 (86%)
Decreased HDL-C	Yes	8 (12.9%)	7 (18.4%)	15 (15%)
	No	54 (87.1%)	31 (81.6%)	85 (85%)
Increased FBG	Yes	12 (19.4%)	4 (10.5%)	16 (16%)
	No	50 (80.6%)	34 (89.5%)	84 (84%)

Variables are expressed in frequency and percent. HTN: Hypertension; WC: Waist Circumference; TG: Triglyceride; HDL-C: High Density Lipoprotein Cholesterol; FBG: Fasting Blood Glucose

FBG was more prevalent in males (19.4%) than in females (10.5%). Among all participants, increased WC had the highest prevalence (21%), while elevated TG had the lowest prevalence (14%) (Table 4).

Comparison of factors of MetS among CKD patients with and without MetS

The table below demonstrated that the prevalence of all recognized components of MetS was significantly higher in CKD patients with MetS compared to those without MetS. The prevalence of hypertension (HTN), increased WC, elevated TG, decreased HDL-C, and elevated FBG in participants with MetS were 77.8%, 94.4%, 77.8%, 72.2%, and 50%, respectively (p < 0.001 for all components) (Table 5).

Furthermore, this study revealed that age group, occupational status, BMI, and family history of MetS were significantly linked to the occurrence of MetS. Individuals aged 56-65 years-old had a higher prevalence of MetS at 29.6%, while those who were overweight (75%) and obese (100%) exhibited a greater magnitude of MetS. Besides, the prevalence of MetS was significantly higher (72.2%) among participants

engaged in office work compared to non-office workers. Furthermore, individuals with a family history of MetS had a substantially higher prevalence of MetS (55.6%) compared to those without a history of MetS (14.3%) (Table 6).

Analysis of MetS factors using binary and logistic regression

The results presented in the table below confirmed that HTN [AOR: 95% CI: 0.004 (0-0.034)], increasing WC [AOR: 95% CI: 0.003 (0-0.029)], decreased levels of HDL-C [AOR: 95% CI: 0.01 (0.002-0.055)], and elevated FBG [AOR: 95% CI: 0.093 (0.028-0.312)] were statistically significantly associated with MetS when analyzed using binary logistic regression. Subsequently, these variables were included in a multivariable logistic regression model to determine if they were independent predictors of MetS, assessed by adjusted odds ratios (AOR) with 95% confidence intervals.

The results of the multivariable logistic regression revealed that only an increased WC and decreased HDL-C levels remained statistically significant predictors of MetS. Specifically, the study showed that CKD

Table 5: Two-Tailed Pearson's Correlation Analysis of MetS components among the participants.

Parameters	Patients v	vith MetS (n = 18)	Patients without MetS (n = 82)	P-value	
Presence of HTN	Yes	14 (77.8%)	1 (1.2%)	0.000	
	No	4 (22.2%)	81 (98.8%)		
Increased WC	Yes	17 (94.4%)	4 (4.9%)	0.000	
	No	1 (5.6%)	78 (95.1%)		
Increased TG	Yes	14 (77.8%)	0	0.000	
	No	4 (22.2%)	82 (100%)		
Decreased HDL-C	Yes	13 (72.2%)	2 (2.4%)	0.000	
	No	5 (27.8%)	80 (97.6%)		
Increased FBG	Yes	9 (50%	7 (8.5%)	0.000	
	No	9 (50%)	75 (91.5)		

Variables are expressed in frequency and percent. p-value is significant at < 0.001.

Table 6: Two-tailed pearson's correlation analysis of MetS components among CKD patients.

Parameters	Patients with MetS (n = 18)		Patients without MetS (n = 82)	P-value	
Age category	18-35	2 (7.1%)	26 (92.9%)		
	36-45	1 (5.3%)	18 (94.7%)		
	46-55	7 (26.9%)	19 (71.3%)	0.009	
	56-65	8 (29.6%)	19 (70.4%)		
Occupational status	Office workers	13 (72.2%)	11 (13.4%)	0.000	
	Not Office workers	5 (27.8%)	71 (86.6%)		
	Under weight	4 (16.7%)	20 (83.3%)		
BMI	Normal weight	5 (7.7%)	60 (92.3%)	0.000	
	Over weight	6 (75%)	2 (25%)		
	Obesity	3 (100%)	-		
Family history of MetS	Yes	5 (55.6%)	4 (44.4%)	0.002	
	No	13 (14.3%)	78 (85.7%)		

Variables are expressed in frequency and percent. p-value is significant at < 0.01

Table 7: Binary and multivariable logistic regression	n analysis of components of MetS among CKD patients.
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Parameters	Patients with MetS (n = 18) Patients without MetS (n = 82) COR (95% CI) Yes 77.8% 1.2% 1		Patients without MetS (n = 82)	COR (95% CI)	AOR (95% CI)	P-value
HTN			1			
	No*	22.2%	98.8%	0.004 (0-0.034)	0.098 (0.005-2.023	0.133
High WC	Yes	94.4%	4.9%	1	1	
	No*	5.6%	95.1%	0.003 (0-0.029)	0.029 (0.002-0.545)	0.01 8
Low	Yes	72.2%	2.4%	1	1	
HDL-C	No*	27.8%	97.6%	0.01(0.002-0.055)	0.052(0.003-0.841)	0.037
High FBG	Yes	50%	8.5%	1	1	
	No*	50%	91.5	0.093(0.028-0.312)	0.278(0.023-3.387)	0.315

Variables are expressed in frequency and percent. Categories having variables marked by strikes (*) are reference categories while those categories having variables that are not marked contain significant variables to which the COR and AOR was done. p-value is significant at < 0.05

patients with elevated WC were more likely to have MetS compared to CKD patients with normal WC [AOR: 95% CI: 0.029 (0.002-0.545)]. Similarly, CKD patients with lower HDL-C levels were at higher risk of developing MetS compared to those with higher HDL-C levels [AOR: 95% CI: 0.052 (0.003-0.841)] (Table 7).

Discussion

CKD has various concurrent medical conditions. One such condition is MetS, that can lead to cardiovascular complications in CKD patients [7,8]. It is important for healthcare providers to regularly monitor CKD patients for MetS and its components in order to detect any concomitant diseases early on. Previous researches have shown a significant relationship between MetS and CKD [9,12], with CKD patients being more likely to have MetS due to lifestyle choices and genetic factors [14] that contribute to metabolic imbalances [13]. While the exact mechanism linking CKD and MetS is not fully understood, there is a strong association between the two conditions.9Factors like poor nutrition, lack of physical activity, and obesity are common risk factors for MetS among CKD patients both in developed and developing countries including Ethiopia [15]. Besides, there is a lack of concrete data signifying the consequence of CKD on the magnitude of MetS in Ethiopia, due to limited full-fledged study. This alarms us to assess the magnitude of MetS and its contributing factors among CKD patients in Ethiopia.

The aim of this study was to determine the prevalence of MetS and its associated factors among CKD patients. The study found that the prevalence of MetS was higher in females (21.1%, 95% CI: 8.09-34.01) compared to males (16.1%, 95% CI: 6.97-25.28), which is consistent with a previous study conducted among working adults in Eastern Ethiopia [21,22]. The higher magnitude of MetS in females than males is more likely due to a combination of biological, hormonal, and lifestyle factors. The overall magnitude MetS among the participants was 18% (95% CI: 10.47-25.53) which aligns with other previous studies conducted in Ethiopia

ther previous studies conducted in Ethiopia

among different populations [21,23,24]. The finding of this study is also consistent with the finding of the study conducted in Sudan that found MetS was higher (19%) which is almost similar with our finding [10].

However, our study found a higher overall prevalence of MetS compared to a national survey in Ethiopia, possibly due to a larger proportion of rural participants in the survey [22]. On the other hand, the finding of this research showed that the prevalence of MetS is lower than the pooled prevalence of MetS in Ethiopia found by the systematic review and meta-analysis [25]. The difference might be due to the inclusion of many and different studies in that review. Likewise, this study found that the prevalence of MetS among CKD patients was lower compared to a previous study in Thailand that focused on hypertensive CKD patients, possibly due to differences in the study participants' health conditions (being hypertensive) [26].

When we assessed the components of MetS, the study results suggest that HTN, higher WC, lower levels of HDL-C, and elevated FBG are significantly linked to MetS (p < 0.05) based on binary logistic regression analysis. These factors were subsequently assessed in a multivariable logistic regression model to determine their individual predictive value for MetS, as shown by adjusted odds ratios (AOR) with 95% confidence intervals. The analysis revealed that only increased WC [p = 0.018, AOR = 0.029 (95% CI: 0.002-0.545)] and decreased HDL-C levels [p = 0.037, AOR = 0.052 (95% CI: 0.003-0.841)] remained as statistically significant predictors of MetS. Specifically, the study found that CKD patients with higher WC were more likely to have MetS compared to those with normal WC. This reflection is supported by various previous studies, including a research conducted in Sudan specifically among CKD patients [10,21,27]. Similarly, CKD patients with lower HDL-C levels were at a higher risk of developing MetS compared to those with higher HDL-C levels, aligning with findings from studies conducted in different countries [10,21,27].

Evaluation of the individual components of MetS showed that most components were more frequently observed in females compared to males. However, elevated FBG was more common in males (19.4%) than in females (10.5%). Among all participants, increased WC had the highest prevalence (21%), while elevated TG had the lowest prevalence (14%). Our results are consistent with a previous study conducted in Ethiopia, which reported that WC had the highest prevalence and dyslipidemia had the lowest prevalence [27]. However, our findings differ from a study conducted in Sudan, which found that HTN was highly prevalent and high WC had a lower prevalence [10]. The incongruity might be due to the difference in the population under the study.

Additionally, this study identified several contributing factors to the development of MetS among CKD patients. The research revealed a significant correlation between age group, occupational status, BMI, and family history of MetS with the severity of MetS (p < 0.001 for all factors). These findings align with previous studies, such as one conducted in Eastern Ethiopia on MetS among working adults, which demonstrated an increase in MetS prevalence with age [21,28]. Furthermore, a study in Malaysia also indicated that advancing age was linked to a higher prevalence of MetS [29]. Additionally, other studies have reported a connection between a family history of MetS and the development of MetS, consistent with the results of our study [28,30-32].

Strength and Limitation of the Study

The study's key strength lies in its originality, as it sheds light on the prevalence and risk factors of MetS among CKD patients. This serves as a foundational reference for future in-depth investigations. However, the study encountered certain limitations. Firstly, financial constraints hindered sample collection at FHCSH, restricting the study to only 100 participants. Consequently, this limited sample size may not fully represent the entire CKD population in Ethiopia. Furthermore, the study's cross-sectional design prevented the observation of prospective trends, thereby impeding the establishment of causal relationships between various factors examined.

Conclusion

In conclusion, this study confirms that MetS poses a significant health threat to CKD patients in Ethiopia. Consequently, individuals with CKD face an elevated risk of developing cardiovascular complications that can lead to premature mortality. Among CKD patients, various factors contribute to the development of MetS, including its individual components, age, occupation, BMI, and a family history of MetS. Therefore, healthcare providers should implement tailored interventions for high-risk CKD patients to mitigate the risk of cardiovascular complications.

Ethical Approval and Consent to Participate

Prior to commencing data and sample collection, ethical clearance was obtained from the Research Ethical Committees of the Biochemistry Department at Addis Ababa University, College of Health Sciences. Additionally, an official collaboration letter was obtained from the Department of Biochemistry for data collection and analysis. Written informed consent was obtained from each eligible study participant, and all ethical principles were strictly adhered to throughout the study.

Funding

The study was funded by Addis Ababa University.

Conflict of Interest

No conflict of interest was reported by the authors.

Availability of Data and Materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Author Contributions

All authors had a significant contribution to this study, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas. They took part in drafting, revising, or critically reviewing the article; gave final approval of the manuscript to be published; have agreed on the journal to which the article has been submitted, and are accountable for all aspects of the work.

Acknowledgments

We would like to express our wholehearted gratitude to Addis Ababa University for its supports for this study. We are also grateful to FHCSH and the EPHI for their collaboration in data collection and laboratory analysis. Lastly, we would like to acknowledge the patients participated in the study, data collectors, and laboratory professionals for their precious support.

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