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Evaluation of the relationship between xanthine oxidase activity and metabolic syndrome in a population group in Bangladesh

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Xanthine oxidase (XO) is an enzyme that converts hypoxanthine into xanthine and xanthine into uric acid, which is then eliminated by the kidneys. Serum XO has been linked to diabetes, hypertension, liver dysfunction, and cardiovascular diseases. However, limited information exists on the relationship between serum XO activity and MetS. This study aimed to analyze the relationship between XO activity and metabolic syndrome (MetS) and its components in an adult population group in Bangladesh A total of 601 participants aged ≥18 years were included in the study. MetS was defined based on the criteria set by the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III). Serum XO activity was measured using the enzyme-linked immunosorbent assay (ELISA), while other biochemical parameters were measured using colorimetric methods. The relationship between serum XO and MetS levels was determined through multivariate logistic regression analysis. Serum XO activity was found to be significantly higher in females (6.17 ± 3.77 U/L) as compared to males (4.00 ± 2.77 U/L) ($p < 0.001$). Furthermore, participants with MetS had significantly higher mean levels of serum XO (5.34 ± 3.39 U/L) than those without MetS (3.86 ± 2.90 U/L) ($p < 0.001$). The prevalence of MetS and its components, such as blood pressure and blood glucose increased across the XO quartiles ($p < 0.001$). Regression analysis indicated that XO activity was significantly and independently associated with the prevalence of MetS (at least $p < 0.05$ for all cases) and its components, including elevated blood pressure, high blood glucose, and low HDL-C (at least $p < 0.05$ for all cases). In conclusion, individuals with MetS had significantly higher XO levels than those without MetS. Serum XO activity showed an independent association with MetS and some of its components. Therefore, XO might serve as a useful marker of MetS. Prospective studies are needed to determine the underlying mechanisms linking XO and MetS.

Keywords Xanthine oxidase, Association, Metabolic syndrome, Bangladeshi adults

Xanthine oxidase (XO) is a type of enzyme that belongs to the xanthine oxidoreductase (XOR) family. It generates reactive oxygen species (ROS) and catalyzes the oxidation of hypoxanthine to xanthine and xanthine to uric acid[1]. Another form of XOR is xanthine dehydrogenase (XDH). Both XDH and XO are single-gene products that exist in separate but inter-convertible forms[2]. XDH is mostly present inside the cell, whereas XO is found in biological fluids like milk and blood plasma[3,4]. Apart from the significant role of XO in producing uric acid in the human body, it is also responsible for producing a considerable amount of reactive oxygen species (ROS) such as H_2O_2 and $O_2^{\cdot-}$[5,6] in mammalian cells. ROS are linked to increased blood pressure through endothelial dysfunction, vascular inflammation, and structural remodeling[7]. In recent years, there has been increasing attention given to XO. Animal studies have demonstrated that oxidants produced by XO have a greater impact on arterial blood pressure in spontaneously hypertensive rats[8].

It has been reported that XO activity is significantly elevated in the vasculature of patients with coronary artery disease[9]. Additionally, XO activity has been linked to cardiovascular events and an increased risk of future events in patients with chronic heart failure[10].

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Metabolic syndrome (MetS) is a complex medical condition that results from the presence of multiple metabolic disorders[11]. These disorders include obesity, particularly visceral obesity, dyslipidemia with high triglycerides and/or low levels of high-density lipoprotein cholesterol (HDL-C), hypertension, and fasting hyperglycemia[11]. A person is diagnosed with MetS if they have three or more of these conditions[11,12]. The risk factors associated with MetS are predictive of both cardiovascular diseases and type 2 diabetes.

It has long been recognized that high levels of uric acid in the blood also called hyperuricemia can increase the risk of various cardiometabolic diseases[13,14]. However, some previous studies have suggested that hyperuricemia may not be an independent risk factor for such diseases, but rather a marker for other underlying conditions[15,16]. As a result, there is still ongoing debate about whether hyperuricemia should be considered an independent risk factor for cardiometabolic diseases. In contrast, XO has been suggested to be linked with diabetes and cardiovascular events in humans[17,18]. A study conducted in Japan showed that plasma XOR activity was positively linked with BMI, liver enzymes, TG and fasting plasma insulin[19]. Serum XO activity has been suggested to be related to obesity, hypertension, and diabetes in the general population[18,20–22]. However, there is limited information on the relationship between XO and metabolic parameters and MetS, which needs further clarification. Therefore, we hypothesize that serum XO activity could be a useful marker for MetS. In this study, we measured serum XO activity and determined its associations with MetS in an adult cohort in Bangladesh.

Materials and methods

Study population

The study was conducted at the Department of Biochemistry and Molecular Biology of Shahjalal University of Science and Technology, Sylhet, Bangladesh. It was a cross-sectional design carried out between December 2019 and November 2020. A simple random sampling technique was used to select participants from different backgrounds such as local city people, students, and academic and non-academic staff from the Sylhet and Dhaka regions of Bangladesh. A total of 601 participants, aged 18 years and above, were included in the study. The inclusion criteria for the study were being above 18 years of age, willing to participate and free from severe chronic illness. The study excluded pregnant women, lactating mothers, and those with a history of hepatotoxic drug intake, kidney disease, alcohol intake, and acute or chronic hepatitis. Also, participants with missing anthropometric data or blood samples were excluded. The study was approved by the Internal Ethics Committee at the Department of Biochemistry and Molecular Biology of Shahjalal University of Science and Technology, Bangladesh (Reference no 02/BMB/2019). Prior to being included in the study, all participants provided written informed consent. All methods were performed in accordance with the relevant guidelines and regulations.

Data collection

The participants' demographic and lifestyle information were collected using a standard questionnaire. The questionnaire included recording age, gender, weight, and height, following a standard procedure described elsewhere[23–29]. The participant's systolic and diastolic blood pressure (SBP and DBP) were measured twice in the left arm using an automated sphygmomanometer (Omron M10, Omron Corporation, Tokyo, Japan) while seated after resting for at least 10 min. Body weight (BW) was measured using a calibrated digital weighing machine (Beurer 700, Germany) to the nearest 0.1 kg, and body height (BH) was recorded to the nearest 0.1 cm using a height measuring tape. The body mass index (BMI) was calculated as weight in kg divided by height in square meters (kg/m^2). Waist circumference (WC) was measured using a general tape midway between the lowest border of the ribs and the iliac crest. Hip circumference (HC) was measured at the largest circumference of the buttocks to the nearest 0.5 cm. Measurements were taken without shoes and with minimal clothing.

Sample collection and laboratory analysis

Venous blood samples were collected from each subject after an overnight fast. The samples were then centrifuged and the isolated serum was stored at − 20 °C until laboratory analysis. XO activity in the serum was measured using an enzyme-linked immunosorbent assay (ELISA) with a plate reader (ELISA reader, Apollo 11 LB 913, Berthold, Germany). The Human XO ELISA Kit was purchased from MyBioSource company, USA (Cat No: MBS774009). In addition, other biochemical markers such as serum uric acid (SUA), fasting blood glucose (FBG), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were measured using a colorimetric method and a semi-automatic biochemistry analyzer (Humalyzer 3000, Medicon Services, Germany), following the manufacturer's protocol (HUMAN Gesellschaft für Biochemica und Diagnostica mbH, Germany). The measurements were carried out according to the standard manufacturer's protocols provided within the kit, and the precision of the measurements was maintained regularly by method standard calibration.

Serum XO measurement

The level of Serum XO was measured as per the manufacturing protocol. In brief, standards and serum samples were added to the micro-wells that had previously been coated with antibodies. Subsequently, HRP-conjugate solution was added to these wells to form an immune complex. After an incubation period of 1 h at 37 °C, the unbound enzyme was removed by washing the wells. Substrates were then added, causing the solution to turn blue and eventually yellow. The intensity of the yellow colour was directly proportional to the levels of XO present in the serum sample. After 15 min, the absorbance (OD) of each well was measured at 450 nm using an ELISA reader (Apollo 11 LB 913, Berthold, Germany). Finally, XO activity in the samples was calculated based on the standard graph prepared in an excel sheet.

Diagnostic criteria

MetS was defined using the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) criteria[12]. It is characterized by having at least three of the following components: WC of ≥ 90 cm in men or ≥ 80 cm in women; TG levels of ≥ 150 mg/dl; HDL-C levels of < 40 mg/dl in men and < 50 mg/dl in women; blood pressure levels of ≥ 130/85 mmHg or taking antihypertensive medication; FBG levels of ≥ 110 mg/dl or taking antidiabetic medicines. All participants were divided into four quartiles based on their serum XO concentrations, with Q1: ≤ 2.23 U/L, Q2: 2.24–3.72 U/L, Q3: 3.73–6.15 U/L, and Q4: > 6.15 U/L. Hyperuricemia was defined as SUA concentration of > 7.0 mg/dL (416.4 µmol/L) in men or > 6.0 mg/dL (356.9 µmol/L) in women[30]. Physical activity was classified into three groups: inadequate (comfortable office work and housework), medium (walking, swimming), and adequate (carrying, lifting, jogging, and/or sports). The smoking status was divided into two categories: never smokers and current smokers.

Statistical analysis

Statistical data analyses were conducted using IBM SPSS statistics (version 23), Chicago, IL, USA. We have plotted Q-Q plot and histogram to check the normality of the data set. The data is presented as mean ± SD. The baseline characteristics of the volunteers in the gender group were compared using an independent sample t-test, while one-way ANOVA was used for the XO quartiles. To differentiate the proportions of the categorical variables, a Chi-square test was applied. The association between XO activity and MetS was assessed using multivariate logistic regression models. MetS was categorized as either "yes" (presence) or "no" (absence). In the regression analysis, MetS (yes) was considered the dependent variable, while XO served as the independent variable. Reference category was XO level Q1. Three models were used in the regression analysis. Model 1 was adjusted for age (years) and gender (male and female). Model 2 was adjusted for model 1 and SUA (mg/dL). Model 3 was adjusted for variables in model 2 and physical activity (low vs medium/adequate), and smoking (yes vs no). A p-value of less than 0.05 was considered statistically significant.

Results

Participant's characteristics in the MetS and non-MetS group

Table 1 presents the baseline characteristics of the participants in the MetS and non-MetS groups. Out of the total 601 participants, 271 individuals (198 male and 73 female) were diagnosed with MetS based on the diagnostic criteria. The MetS group had significantly higher mean values of age, WC, HC, BMI, SBP and DBP as compared to the non-MetS group ($p < 0.001$ for all cases). Additionally, the mean level of XO was significantly higher in the MetS group (5.34 ± 3.39 U/L) in contrast to the non-MetS group (3.86 ± 2.90 U/L) ($p < 0.001$). There was also

	Non-MetS	MetS	P-value
N	330	271	
Gender, m/f	244/86	198/73	–
Age (years)	36.89 ± 13.59	42.76 ± 12.38	0.000
WC (cm)	82.57 ± 9.81	88.42 ± 11.54	0.000
HC (cm)	91.22 ± 8.34	93.33 ± 8.68	0.009
BMI (kg/m^2)	23.72 ± 3.63	25.62 ± 3.62	0.000
SBP (mmHg)	119.30 ± 12.48	134.48 ± 14.77	0.000
DBP (mmHg)	77.16 ± 8.12	88.07 ± 8.83	0.000
FBG (mmol/L)	6.11 ± 2.92	8.06 ± 4.17	0.000
TG (mg/dL)	151.94 ± 92.50	225.34 ± 122.98	0.000
TC (mg/dL)	182.16 ± 53.80	223.95 ± 85.21	0.000
HDL-C (mg/dL)	35.00 ± 12.31	31.70 ± 11.76	0.003
LDL-C (mg/dL)	117.72 ± 48.58	151.61 ± 78.60	0.000
XO (U/L)	3.86 ± 2.90	5.34 ± 3.39	0.000
SUA (mg/dL)	6.09 ± 1.92	5.69 ± 1.93	0.014
Hyperuricemia (%)	29.2	25.6	0.327
Diabetes (%)	24.5	53.1	0.000
Hypertension (%)	19.1	64.6	0.000
Physical activity (%)			
Low	20.9	24.2	0.402
Moderate/adequate	79.1	75.8	0.470
Smoking (%)			
Yes	23.0	18.8	0.208
No	77.0	81.2	0.247

Table 1. Baseline characteristics of the participants based on the presence of MetS. MetS: Metabolic Syndrome. Values are presented as mean ± SD. P-values for continuous and categorical variables are obtained from independent sample t-test and chi-square test, respectively.

a significant difference in the mean level of other biochemical parameters such as FBG, lipid profile (TG, TC, HDL-C, LDL-C), and SUA (at least $p < 0.05$ for all cases). However, no significant difference was found between the MetS and non-MetS groups for smoking and physical activity.

Prevalence of MetS and its components by gender

The prevalence of MetS and its components are displayed in Table 2 and Fig. 1. Overall, 45.1% of the subjects had MetS, with 44.8% in males and 45.9% in females. The prevalence of MetS components such as increased WC, elevated SBP, and TG levels was significantly higher in males than in females ($p < 0.05$ for all cases). Conversely, the levels of elevated FBG and HDL-C were significantly higher in females than in males ($p < 0.01$ for both cases). The prevalence of hyperuricemia was 27.6%, with a significant difference between males (30.5%) and females (19.5%) ($p < 0.01$). There was no significant difference in the prevalence of MetS between males (44.8%) and females (45.9%). Males were more likely to engage either in moderate or adequate physical activity than females ($p < 0.01$). Only male subjects were habitual smokers.

Prevalence of MetS and its components across the XO quartiles

The levels of XO were categorized into four groups, based on quartiles. The first group, Q1, had levels of ≤ 2.23 U/L, the second group, Q2, had levels ranging from 2.24 to 3.72 U/L, the third group, Q3, had levels ranging from 3.73 to 6.15 U/L, and the fourth group, Q4, had levels greater than 6.15 U/L (as shown in Table 3). The prevalence of MetS increased significantly across the quartiles of XO, with percentages of 38.6%, 39%, 61.1%, and 67.1% ($p < 0.001$). There was also a significant increasing trend observed for elevated SBP and FBG across the quartiles of XO. However, there was a significant decreasing trend observed for low HDL-C across the quartiles of XO ($p < 0.05$).

Association of XO with the prevalence of MetS and its components

Multivariate logistic regression was applied to investigate the relationship between XO and MetS, with XO as the independent variable and MetS as the dependent variable. The results of the regression analysis are presented in Table 4. In all four models, there was a positive and significant association between XO and MetS (at least $p < 0.05$ for all cases). We also examined the relationship between XO and individual components of MetS (Table 5). After adjusting for age and sex, a significant association was found between XO and three MetS components, namely high blood pressure ($p < 0.01$), hyperglycemia ($p < 0.01$), and low HDL-C ($p < 0.05$).

	Total	Female	Male	P-value
N	601	159	442	–
Age (year)	39.44 ± 13.37	39.24 ± 13.87	39.51 ± 13.20	0.833
WC (cm)	84.99 ± 10.96	82.44 ± 10.79	86.08 ± 10.88	0.001
HC (cm)	92.13 ± 8.54	91.52 ± 8.75	92.39 ± 8.45	0.323
BMI (kg/m^2)	24.55 ± 3.74	24.43 ± 4.46	24.59 ± 3.45	0.637
SBP (mmHg)	126.16 ± 15.51	123.92 ± 17.57	126.96 ± 14.64	0.034
DBP (mmHg)	82.09 ± 10.04	88.93 ± 10.68	82.50 ± 9.78	0.091
FBG (mmol/L)	6.99 ± 3.66	7.77 ± 4.07	6.71 ± 3.48	0.002
TG (mg/dL)	187.31 ± 114.21	171.09 ± 124.68	193.11 ± 109.81	0.046
TC (mg/dL)	201.42 ± 73.02	215.34 ± 86.71	197.14 ± 67.81	0.019
HDL-C (mg/dL)	33.48 ± 12.16	36.61 ± 10.06	32.52 ± 12.59	0.002
LDL-C (mg/dL)	133.34 ± 66.31	151.01 ± 83.71	127.90 ± 59.02	0.001
XO (U/L)	4.62 ± 3.24	6.17 ± 3.77	4.00 ± 2.77	0.000
SUA (mg/dL)	5.91 ± 1.94	4.82 ± 1.92	6.29 ± 1.79	0.034
MetS (%)	45.1	45.9	44.8	0.853
Hyperuricemia (%)	27.6	19.5	30.5	0.008
Diabetes (%)	37.5	53.8	31.7	0.000
Hypertension (%)	39.7	40.3	39.5	0.860
Physical activity (%)				
Low	23.3	31.6	18.3	0.002
Moderate/adequate	77.7	68.4	81.7	0.003
Smoking (%)				
Yes	21.1	0.0	28.7	0.000
No	78.9	100.0	71.3	0.000

Table 2. Baseline characteristics of the participants according to the sex groups. MetS: Metabolic Syndrome. Values are presented as mean ± SD. P-values for continuous and categorical variables are obtained from independent sample t-test and chi-square test, respectively.

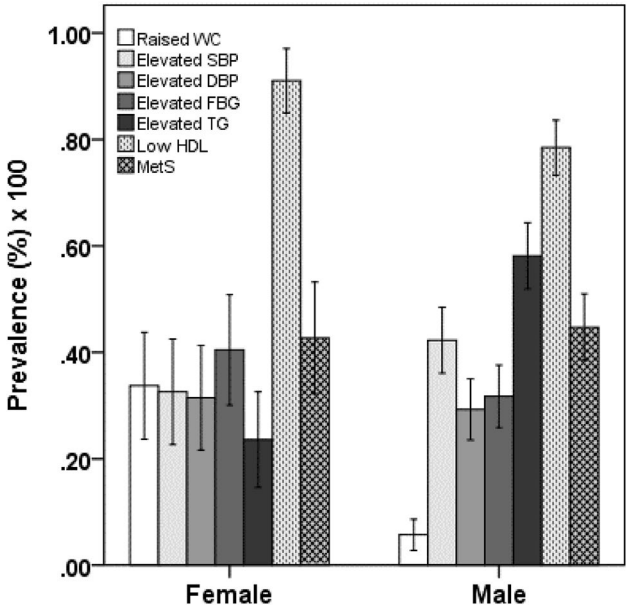

Fig. 1. Prevalence of MetS and its components in the gender group. P < 0.001 when the prevalence of raised WC, elevated FBG and elevated TG is compared between the sex groups. P < 0.05 when the prevalence of low HDL-C is compared between the sex groups. P-values are obtained from chi-square test.

Parameters	Serum XO				
	Q1	Q2	Q3	Q4	P-value
Raised WC (%)	11.6	23.2	12.7	15.8	0.335
Elevated SBP (%)	31.7	39.0	65.5	61.0	0.000
Elevated DBP (%)	42.7	43.9	46.4	46.3	0.952
Elevated FBG (%)	24.1	40.2	60.7	73.2	0.000
Elevated TG (%)	55.4	45.6	62.5	65.8	0.074
Low HDL-C (%)	92.8	79.1	73.0	85.1	0.021
MetS (%)	38.6	39.0	61.1	67.1	0.000

Table 3. Prevalence of MetS and its components in the XO quartile groups. XO quartiles, Q1: ≤ 2.23 U/L, Q2: 2.24–3.72 U/L, Q3: 3.73–6.15 U/L, Q4: > 6.15 U/L. P-values are obtained from chi-square test.

	OR (95% CI)				
	Q1	Q2	Q3	Q4	P-value for trend
Model 1	1	0.880 (0.448–1.729)	2.129 (1.082–4.188)	2.565 (1.082–5.216)	< 0.05
Model 2	1	0.890 (0.443–1.788)	2.063 (1.027–4.145)	2.881 (1.374–6.039)	< 0.05
Model 3	1	0.863 (0.428–1.740)	2.052 (1.020–4.126)	2.893 (1.377–6.075)	< 0.05

Table 4. logistic regression analysis to assess the relationship between XO and MetS. XO quartiles, Q1: ≤ 2.23 U/L, Q2: 2.24–3.72 U/L, Q3: 3.73–6.15 U/L, Q4: > 6.15 U/L. Dependent variable is MetS (yes) and independent variable is XO (U/L). Reference category is XO level Q1. Model 1: adjusted for age (years) and gender (male and female). Model 2: model 1 + SUA (mg/dL). Model 3: model 2 + physical activity (low vs medium/adequate) and smoking (Yes vs No). OR, odds ratio; CI, confidence interval.

Discussion

The present study evaluated the potential relationship between XO activity and MetS in a cohort of adult individuals in Bangladesh. Previous studies have demonstrated a possible link between XO and hypertension and cardiovascular disease, yet there is currently a scarcity of information pertaining to the relationship between SUA and MetS in the adult population at large. Our investigation shows a significant association between XO activity and MetS, as well as its individual components, among Bangladeshi adults.

	OR (95% CI)				P-value for trend
	Q1	Q2	Q3	Q4	
Abdominal obesity	1	1.662 (0.466–5.921)	0.673 (0.181–2.506)	0.405 (0.110–1.495)	> 0.05
High blood pressure	1	1.164 (0.585–2.314)	3.314 (1.652–6.647)	3.001 (1.463–6.158)	< 0.01
Hyperglycemia	1	1.003 (0.478–2.105)	2.812 (1.329–5.949)	3.839 (1.730–8.520)	< 0.01
High TG	1	0.618 (0.299–1.276)	1.204 (0.588–2.465)	1.731 (0.806–3.718)	> 0.05
Low HDL-C	1	0.422 (0.140–1.269)	0.333 (0.112–0.993)	0.663 (0.193–2.274)	< 0.05

Table 5. Age and sex-adjusted multivariate logistic regression analysis to assess the relationship between XO and the components of MetS. XO quartiles, Q1: ≤ 2.23 U/L, Q2: 2.24–3.72 U/L, Q3: 3.73–6.15 U/L, Q4: > 6.15 U/L. The dependent variable is MetS components (yes) and the independent variable is XO (U/L). Reference category is XO level Q1. The model is adjusted for age (years) and sex (male and female). OR, odds ratio; CI, confidence interval.

Our study found that females have significantly higher serum XO activity than males. The participants with MetS had significantly higher serum XO activity than those without MetS. We also observed an increased prevalence of MetS and its components across the XO quartiles. Regression analysis showed a significant association between serum XO activity and MetS and its components, including elevated blood pressure, high blood glucose, and low HDL-C. Our findings align with some previous studies conducted on general individuals and type 2 diabetes patients[17,19,31,32]. A study conducted in Brazil included 17 participants, consisting of 9 healthy individuals and 8 individuals with MetS[17]. The study showed that the MetS group had higher XO activity compared to the healthy control group and XO activity was positively correlated with SOD, hs-CRP, WC, and BMI. Similarly, a study in a general population group in Japan (n = 627) reported a positive correlation between plasma XOR activity and various factors such as BMI, WC, blood pressure, and liver enzyme[31]. Another study showed that participants (n = 98) with type 2 diabetes had a positive correlation between XOR and TG and a negative correlation with HDL-C[19]. The study also indicated that XOR activity was positively associated with BMI, liver enzymes, plasma insulin, and insulin resistance. XO activity was also found to be independently associated with albuminuria in patients with type 2 diabetes[33] and MetS[34] in other population groups. In a further study conducted in Japan, plasma XO activity was found to be correlated with indices of insulin resistance and liver dysfunction in participants (n = 60) with type 2 diabetes mellitus and MetS[32]. It is worth mentioning that most of the previous studies had a small number of participants and a history of diabetes, which limits their generalizability. Additionally, the studies did not establish a direct association between XO and MetS. In our study, we included a moderate number of participants, including healthy, hypertensive, and diabetic subjects, and our findings suggest an independent association of XO activity with MetS.

The two main mechanisms that cause metabolic derangement are insulin resistance and an abundance of circulating free fatty acids[35]. Adipose tissue produces pro-inflammatory cytokines that cause insulin resistance, lipolysis, and liver production of pro-thrombotic factors[35]. This abnormal production leads to an inflammatory chronic state, resulting in endothelial dysfunction and a pro-thrombotic state (reviewed in Ref.[36]). High levels of free fatty acids and impaired insulin activity can lead to hyperglycemia and insulin resistance (reviewed in Refs.[37,38]. Insulin resistance may indue hypertension due to increased renal sodium reabsorption and the secretion of angiotensinogen, leptin, and resistin by adipose tissue[39]. Insulin resistance also impairs endothelial function by reducing nitric oxide-dependent vasodilation (reviewed in Ref.[37]). MetS and hyperinsulinemia are associated with inflammation and oxidative stress, which can lead to high levels of oxidized LDL and increase the risk of atherosclerosis[40,41]. Hyperinsulinemia can also cause urate reabsorption, leading to hyperuricemia, commonly observed in MetS (reviewed in Refs.[42,43]).

As discussed above, XOR activity in human blood is positively correlated with insulin resistance, BMI, and liver dysfunctions. In a study, allopurinol treatment has been found to improve insulin resistance and lower SUA and systemic inflammation in subjects with asymptomatic hyperuricemia[44]. Women who have Polycystic Ovary Syndrome (PCOS) have a higher likelihood of developing MetS. For women with PCOS (n = 45), high serum XO activity was shown to be correlated with high serum levels of C-reactive protein, fasting glycemia, fasting insulinemia, and insulin resistance index[45]. These findings imply that XOR activity may play a role in the development of these metabolic disorders.

The role of XOR in MetS has been indirectly demonstrated in animal models and clinical studies. Inhibiting XOR with allopurinol in a mouse model of MetS has been found to reduce inflammation, insulin resistance, and increase adiponectin production[46]. In a rat model with MetS, allopurinol's XO inhibition reversed hypertension and proteinuria without changing body weight gain, hyperinsulinemia, or fasting hyperglycemia[47]. XO inhibition also reversed kidney factors linked to hypertension and proteinuria, including TGF-β, collagen deposition, and angiotensin II and receptor expression[47]. Studies demonstrated that elevated XOR activity may raise blood pressure through multiple mechanisms including (1) the endothelial dysfunction caused by ROS, RNS and uric acid-derived free radicals, (2) the remodeling of arterioles, (3) the up-regulation of the renin/angiotensin pathway, and (4) the inflammatory reactions (reviewed in Refs.[16,48]). Increased XOR activity leads to oxidative stress, impairing NO-mediated vasodilation, whereas, inhibition of XOR by allopurinol, has been found to improve vascular function and myocardial function in some clinical trials. This suggests a direct link between XOR-generated ROS and endothelial dysfunction, which can lead to MetS[49].

There are certain limitations to our study. First, the sample size was relatively small. Second, our data was collected in a cross-sectional manner, which makes it difficult to establish a causal relationship between XO activity and MetS. Thirdly, participants with type 2 diabetes had taken some medications that could have influenced metabolic markers. For example, one study showed that taking metformin decreased plasma XO activity and thiobarbituric acid reactive substances[50], while another study found no statistical difference between plasma XO activities and taking metformin or not[31]. While we took into account some potential confounding factors, there may be others that we did not consider. For example, we did not have access to data on renal function tests, which can also impact XO activity. Therefore, we should be cautious when extrapolating our findings to other populations. Although there are some limitations, our findings can serve as a valuable reference point for future studies.

Conclusions

The present study indicates that the prevalence of MetS and its components increases with higher levels of XO across the quartile groups. Elevated levels of XO were significantly associated with MetS and its components, including elevated blood pressure, blood glucose, and low HDL-C levels. The measurements of XO activity in blood may provide clues about the risk of developing MetS. However, further studies are necessary to examine the role of XO in the pathogenesis of MetS.

Data availability

All data generated or analysed during this study are included in this published article

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Author contributions

N.A., played a major role in the conception and design of the study, data analysis and interpretation and wrote the manuscript. A.T., N. I., and N.Z.S., contributed to sample collection and laboratory experiments. F.I. helped in the result analysis and revision of the manuscript draft. All authors read the manuscript and approved the final version.

Competing interests

The authors declare no competing interests.

Additional information

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