

RESEARCH NOTE

Open Access



The association between lipid profile, oxidized LDL and the components of metabolic syndrome with serum mineral status and kidney function in individuals with obesity

Abnoos Mokhtari Ardekani¹, Zahra Hamidi Nava², Burhan Abdullah Zaman³, Sahar Vahdat⁴, Amir-Hossein Lame-Jouybari⁵ and Azam Mivefroshan^{6*}

Abstract

Background Metabolic syndrome (MetS) is presented with a cluster of cardio-metabolic risk factors with widespread prevalence. In the present case-control study, we aimed to examine the relationship between several minerals and renal function tests with the components of MetS in individuals with obesity.

Methods This study included 127 individuals with obesity of both gender with or without MetS as the case and control, respectively. MetS was characterized based on the Adult Treatment Panel III (ATP III) criteria. Anthropometric variables and blood pressure were recorded. Mineral status including serum magnesium, copper, calcium, phosphorous, and iron were measured using standard colorimetric methods. Also, the serum lipid levels, concentrations of oxidized low-density lipoprotein (Ox-LDL), and renal function tests, including total protein, albumin, urea, creatinine, and uric acid were evaluated using commercial enzyme-linked immunosorbent assay (ELISA) kits.

Results According to our results, individuals with obesity and MetS had higher levels of waist circumference (WC) and diastolic blood pressure ($P < 0.05$) compared to individuals with obesity and without MetS. Moreover, individuals with obesity and MetS had higher levels of serum total cholesterol (TC), triglyceride (TG), insulin, and iron ($P < 0.05$). In individuals with obesity and MetS, iron and albumin showed a positive relationship with LDL cholesterol and TG concentrations, respectively ($P < 0.05$ for all of them). Also, there was a positive association between serum magnesium and Ox-LDL in individuals with obesity with MetS. While, in individuals with obesity and without MetS, only a positive association between urea and uric acid with WC was observed ($P < 0.05$).

Conclusion Our results suggest that disturbed serum lipids in obesity-metabolic syndrome is associated with homeostatic changes in the level of minerals or proteins that are involved in their metabolism. Although, further studies are needed to better explain and clarify the underlying mechanism of observed relationships.

*Correspondence:
Azam Mivefroshan
mivefroshanazam@gmail.com

Full list of author information is available at the end of the article



© The Author(s) 2023. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

Keywords Metabolic syndrome, Obesity, Mineral hemostasis, Renal function

Background

Metabolic syndrome (MetS) is characterized by various risk factors such as hypertension, central obesity, glucose intolerance, insulin resistance (IR), and dyslipidemia [1–3]. It is highly prevalent worldwide, with a prevalence ranging from 20 to 25% in the adult population [4–7]. In Iran, a high prevalence of MetS has been recognized. According to the results of a recent meta-analysis study, the prevalence among the Iranian population is 26% [8]. Several studies have revealed that not only MetS increases the risk of cardiovascular disease, but also the incidence of type 2 diabetes mellitus (T2DM) and chronic kidney disease (CKD) in the general population [9–12].

The relationship between MetS and CKD is garnering increased attention in medicinal research. Several studies have demonstrated the association between MetS and CKD indicators such as microalbuminuria, proteinuria, glomerular filtration rate, interstitial fibrosis, and tubular atrophy [13–15]. Hyperinsulinemia in MetS, results in excessive renal sodium maintenance and increased blood pressure [16, 17], which in turn can cause several renal diseases by activation of the renin-angiotensin-aldosterone system, adipokine imbalance, and endothelial dysfunction [13, 14].

Dietary minerals such as magnesium, copper, calcium, phosphorous, and iron have a potential role in growth, immunity, neurological functions and metabolism in the human body and are hypothesized to be involved in diabetes and MetS [18–22]. Some of these minerals have an important role in the pathogenesis of metabolic syndrome; several studies have revealed that metabolic syndrome is associated with lower serum magnesium concentrations and that magnesium supplementation will be effective to compensate for this deficiency [23, 24]. Also, copper deficiency in metabolic syndrome and its role in the development of coronary heart disease (CHD) in these patients [25, 26]. Evidence has emphasized the particular role of excess iron and iron overload in the incidence of metabolic disorders like non-alcoholic fatty liver disease or heart attacks in patients with MetS [27, 28]. And this is also true about calcium-phosphorous products and the incidence of coronary artery disease (CAD) in patients with MetS [29].

Moreover, clinical symptoms of MetS might also be indirectly or directly associated with changes in the metabolism of minerals [19, 20]. IR or oxidative stress might also be associated with mineral metabolism [30]. Taking MetS and minerals into consideration, dietary consumption of copper and iron was related to an increased risk of MetS [19, 28, 31]. Song et al. revealed

an inverse association between dietary magnesium intake and MetS prevalence among healthy American women [32]. Moreover, as reported previously, excess body iron is possibly associated with the development of MetS and T2DM [33, 34]. There is little evidence about the relationship between serum levels of minerals and MetS, and most of the existing findings are not statistically significant [35, 36].

MetS is associated with many comorbidities such as chronic kidney disease (CKD). This association might be through mechanisms related to excessive renal perfusion and hyperfiltration [37, 38]. Lea et al. revealed that every single component of MetS may not have a serious effect on kidney disease, but the combination of components might alter kidney function [39]. Inconsistent with this finding, in a Southeast Asian Cohort study, among five MetS components, high blood pressure was related to the higher prevalence of CKD [40]. In one study by Maric C et al., high blood pressure and slight hyperglycemia were associated with an increased risk of CKD and microalbuminuria [41]. Prior studies have reported a relationship between MetS and renal disease, defined as low creatinine clearance or proteinuria and increased risk for micro-albuminuria, a marker of kidney disease [37, 42]. This highlights the importance of the link between MetS and mineral status and kidney function.

Several pieces of evidence have emphasized the importance of maintaining adequate levels of these minerals in the prevention and management of MetS and its associated complications; in the current case-control study, we aimed to investigate the association between mineral status and renal function tests with MetS components in individuals with obesity and MetS compared with individuals with obesity but without MetS.

Materials and methods

Study design

This case-control study included 62 individuals with obesity and MetS and 65 individuals with obesity and without MetS from August to October 2020. The sample size was obtained based on the results of a previous study [43], considering a power of 80%, and a type I error of 5% using power analysis and sample size software (Statistica software, version 10). There were 62 cases (individuals with obesity and MetS) and 65 control samples (individuals with obesity and without MetS) with an approximately 1:1 ratio. Groups were matched based on gender, body mass index (BMI), and age. The subjects were recruited with public announcement and the randomization procedure was used to avoid any selection or volunteer bias. In this procedure, the volunteers that

met our inclusion criteria were assigned each a random number. Then, study participants were chosen randomly based on these numbers.

Inclusion criteria were as follows: individuals with obesity and with or without MetS, aged 20–50 years, and $BMI \geq 30 \text{ kg/m}^2$. The exclusion criteria were: participants that used vitamin and mineral supplements in the last three months; those with any type of diabetes, bone problems or osteopenia/osteoporosis, those who were under hormonal drugs, antidepressants, glucocorticoids, anti-diuretics, antibiotics medications; patients with any history of atherosclerosis, cancer, chronic liver disease, kidney diseases, acute infections, and recent acute illness; menopausal, pregnant, and lactating women. Patients were informed about the study aims and completed a written informed consent before participating in the study.

Anthropometric measurements

Body weight was measured at fasting state by calibrated Seca scale (Dubai, United Arab Emirates) with light clothes and without shoes and an accuracy of 100 g, and height was measured using stadiometer at approximately 0.5 cm. A non-stretchable tape was used to measure waist circumference (WC) at the narrowest area of the waist approximately 0.5 cm. BMI was defined as weight divided by height squared and obesity was defined as BMI more than 30 kg/m^2 .

Appetite measurements

The Visual Analogue Scale (VAS) was used for appetite assessments. This questionnaire includes questions about satiety, desire to eat sweet/salty/fatty foods, hunger, fullness, and prospective food intake. Individuals were asked to mark their senses on a 100 mm line and quantification of appetite was done by measuring the distance from the beginning to the marked point (Supplementary material 1) [44].

Criteria of metabolic syndrome (MetS)

The MetS was defined according to the criteria of the Adult Treatment Panel III (ATP III) [45] as the presence of three or more of the following characteristics: (a) $WC \geq 102 \text{ cm}$ for men and $\geq 88 \text{ cm}$ for women, (b) serum HDL-C $\leq 40 \text{ mg/dl}$ for men and $\leq 50 \text{ mg/dl}$ for women, (c) serum TG $\geq 150 \text{ mg/dl}$, (d) fasting blood glucose (FBG) $\geq 100 \text{ mg/dl}$, and (e) hypertension (systolic blood pressure (SBP) $\geq 130 \text{ mmHg}$ or diastolic blood pressure (DBP) $\geq 85 \text{ mmHg}$ that includes the Stage 1 of HTN as blood pressure ≥ 130 and $\leq 139/\geq 80$ and $\leq 89 \text{ mmHg}$ and Stage 2 HTN as blood pressure $\geq 140/\geq 90 \text{ mmHg}$ [46].

Biochemical assessments and blood pressure

In this study, 5 ml of fasting blood samples were collected from all participants after 12–14 h of fasting. Serum was extracted from blood samples by centrifugation at 2500 rpm at room temperature for 10 min (Beckman Avanti J-25, USA) and immediately transferred to -70°C until assay. Mineral status, including serum magnesium, copper, calcium, phosphorous, and iron was measured using standard colorimetric methods (kits from Ziest Chem Co., Tehran-Iran). The intra- and inter-assay coefficients of variation (CVs) were 0.92 and 1.09 for magnesium; 1.9 and 6.9 for copper; 1.4 and 2.7 for calcium; 1.9 and 3.1 for phosphate; and < 10 for iron, respectively. Kidney function tests including blood creatinine (Man company, Cat No: 613,027, Iran. Intra- and inter-assay CVs were $< 3.5\%$ both), urea (Man company, Cat No: 613,020, Iran. Intra- and inter-assay CVs were 1.1 and 1.4 respectively), uric acid (Man company, Cat No: 613,028, Iran. Intra- and inter-assay CVs were 1.3 and 1.6 respectively) albumin (Man company, Cat No: 613,040, Iran Intra- and inter-assay CVs were 2 and 1.8 respectively), and total protein (Bioassay Technology Laboratory, Shanghai Korean Biotech, Shanghai City, Cat No: E1149Hu, China. Intra- and inter-assay CV were 1.5 and 2.6 respectively), serum FSG (glucose oxidase, phenol, 4-amino antipyrine peroxidase method, Pars Azmoon, Cat No: 1,500,017, Karaj, Iran. Intra- and inter-assay CV were 1.63 and 2.2 respectively), were measured using the commercial kits.

Serum Ox-LDL was measured by Bioassay Technology Laboratory ELISA kit with the intra-assay (CV of $< 8\%$) and inter-assay (CV of $< 10\%$). Serum insulin level was evaluated by ELISA kit (DiaMetra, Milano, Italy) with the intra-assay (CV of $\leq 5\%$) and inter-assay ($\leq 10\%$). Furthermore, serum lipid profiles, including TG (kit No. 1,500,032), TC (kit No. 1,500,010), and HDL-C (kit No. kit No. 0121500) were assessed by Abbott ALCYON™ 300 using ELISA kits (Pars Azmoon, Tehran, Iran, kit No. 031 500). The mean intra- and inter-assay CVs were 1.53 and 1.60 for TG; < 4 for HDL-C; and 0.061 and 1.14 for TC, respectively. All these assessments were done in a blinding status to group assignments. Blood pressure was measured with a standard mercury sphygmomanometer twice in the same arm after at least 15 min of rest and the mean of the two measurements was used for analysis. All the tests were conducted according to the directions of the manufacturers.

Statistical analyses

SPSS software (version 24, SPSS Inc., USA) was used for statistical analyses. We reported quantitative data as mean \pm standard deviation and qualitative variables were reported as frequency (%). Independent sample t-test and partial correlation analysis were used for data analysis, and the effects of confounders, including age, gender, and

Table 1 The baseline characteristics of the study subjects

Variables	The study subgroups		P-value
	Obese adults without MetS (n = 62)	Obese adults with MetS (n = 65)	
Age (Year)	35.46 ± 8.01	32.15 ± 9.97	0.33*
Gender			
Female [n(%)]	15 (24)	17 (26)	0.21**
Male [n(%)]	47 (76)	48 (74)	
Appetite	190.00 ± 34.01	204.23 ± 46.43	0.36*
WC	95.13 ± 7.01	102.07 ± 8.55	0.02*
BMI (kg/m ²)	32.60 ± 2.49	33.70 ± 3.51	0.34*
SBP (mmHg)	122.00 ± 6.76	126.10 ± 9.60	0.19*
DBP (mmHg)	79.33 ± 4.57	83.84 ± 5.06	0.02*

*P-value was reported based on Independent Sample T test. ** P-value was reported based on Chi-square test. BMI: Body Mass Index; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; MetS: Metabolic Syndrome. Data are presented as mean ± SD. WC and DBP are significantly higher among obese adults with MetS. No significant difference was observed for other variables.

Table 2 The comparison of biochemical parameters among study groups

Variables	The study sub-groups		P-value*
	Obese adults without MetS (n = 62)	Obese adults with MetS (n = 65)	
TG (mg/dl)	128.46 ± 57.67	186.08 ± 73.65	0.028*
HDL (mg/dl)	34.00 ± 11.26	31.61 ± 8.62	0.540*
LDL (mg/dl)	115.82 ± 24.65	126.33 ± 27.28	0.134*
Total cholesterol (mg/dl)	177.13 ± 31.81	195.69 ± 31.40	0.022*
FSG (mg/dl)	89.22 ± 9.16	99.88 ± 35.95	0.33
Insulin (μIU/l)	5.77 ± 2.42	11.96 ± 9.40	0.017*
Total Protein (g/dl)	9.68 ± 2.51	8.27 ± 3.11	0.12
Albumin (g/dl)	5.94 ± 1.60	5.80 ± 1.61	0.78
Urea (mg/dl)	17.75 ± 5.56	15.95 ± 4.53	0.30
Creatinine (mg/dl)	2.05 ± 0.60	2.17 ± 0.83	0.59
Uric acid (mg/dl)	5.77 ± 1.78	4.67 ± 1.69	0.049*
Magnesium (mg/dl)	1.81 ± 0.18	1.87 ± 0.33	0.38
Copper (μg/dl)	91.54 ± 21.51	90.45 ± 19.23	0.32
Iron (mcg/dL)	68.3 ± 18.28	75.35 ± 22.83	0.047*
TIBC (μg/dl)	291.26 ± 19.81	299.75 ± 13.17	0.18
Calcium (mg/dl)	8.61 ± 0.63	8.81 ± 0.64	0.22
Phosphorus (mg/dl)	4.45 ± 2.20	3.71 ± 1.11	0.29

*P-value was reported based on Independent Sample T test and the values less than 0.05 were considered as statistically significant. TG: triglyceride; HDL: high density lipoprotein; LDL, low density lipoprotein; FSG, fasting serum glucose; TIBC, total iron binding capacity. TG, total cholesterol, insulin and iron concentrations were significantly higher among obese adults with MetS. While obese adults without MetS had higher uric acid values.

BMI were adjusted. P-values less than 0.05 were considered significant.

Results

The present study included 127 individuals with obesity (62 with MetS and 65 without MetS).

The results are as follows:

Demographic findings of the study subgroups

Demographic information of the participants is provided in Table 1. WC (P=0.02) and DBP (P=0.02) were significantly lower in subjects without MetS compared to those with MetS. No significant difference was observed between the groups regarding gender, age, BMI, and SBP (P>0.05). Appetite was non-significantly higher among obese adults with MetS compared with obese adults without MetS (P=0.35).

Biochemical variables in study subgroups

Table 2 presented the biochemical values, including mineral status and renal function test compared between the two groups. Individuals with obesity and MetS represented significantly higher levels of serum TC, TG, insulin, and iron, but lower uric acid values (P<0.05 for all of them).

The association between MetS components, mineral status and kidney function tests

The association between mineral statuses with the components of MetS is shown in Table 3. In individuals with obesity and MetS, serum magnesium was in positive association with ox-LDL (r=0.44; P=0.037) and serum iron was positively associated with LDL (r=0.48; P=0.05). No significant association between serum minerals and MetS components was observed in individuals with obesity but without MetS and also in combined groups. Table 4 represents the association between kidney function tests and components of MetS. In individuals with obesity and MetS, albumin showed a positive relationship with TG concentrations (r=0.49; P=0.04). While in individuals with obesity but without MetS, urea (r=0.86; P=0.05) and uric acid (r=0.88; P=0.04) were positively associated with WC. Furthermore, in combination of both groups, albumin was positively associated with TG (r=0.45, P=0.02), and negatively associated with HDL-C (r= -0.41; P=0.04), while uric acid was positively associated with WC values (r=0.43; P=0.03).

Discussion

In the current study, we evaluated the association between metabolic risk factors, including Ox-LDL, lipid profile and components of MetS with mineral status and renal function tests among individuals with obesity and with or without MetS. We found higher levels of serum TC, TG, insulin, and iron in individuals with obesity and MetS (Table 2). In subjects with MetS, iron and albumin showed a positive relationship with LDL-C and TG concentrations, respectively. Also, a positive association was observed between urea and uric acid values with WC in subjects without MetS. In both groups, albumin was positively associated with TG and negatively associated with HDL-C; moreover, uric acid was positively

Table 3 The correlation between magnesium, copper, calcium, phosphorous, and iron with components of metabolic syndrome in study groups

Study groups	Variables	Variables									
		Magnesium		Copper		Calcium		Phosphorous		Iron	
		r	P	r	P	r	P	r	P	r	P
Obese adults with MetS	TC	0.03	0.9	-0.04	0.86	-0.23	0.37	0.1	0.68	-0.27	0.31
	TG	-0.37	0.15	0.34	0.19	-0.37	0.15	0.18	0.5	0.24	0.35
	HDL	0.35	0.17	-0.15	0.57	0.18	0.48	0.09	0.72	-0.02	0.92
	WC	0.33	0.2	-0.34	0.19	-0.04	0.87	-0.25	0.34	-0.32	0.22
	LDL	-0.05	0.84	-0.35	0.17	-0.3	0.24	0.2	0.45	0.48	0.049
	OX-LDL	0.44	0.037	-0.05	0.84	0.16	0.53	-0.45	0.07	-0.26	0.33
Obese adults without MetS	TC	0.38	0.61	-0.01	0.98	0.1	0.9	-0.04	0.96	-0.09	0.9
	TG	0.25	0.75	0.64	0.35	-0.48	0.52	-0.71	0.28	-0.9	0.1
	HDL	-0.88	0.12	0.2	0.79	-0.38	0.61	-0.1	0.9	0.46	0.53
	WC	0.22	0.77	0.19	0.8	-0.1	0.89	-0.23	0.76	-0.64	0.34
	LDL	0.46	0.53	-0.36	0.63	0.41	0.58	0.32	0.67	0.22	0.77
	OX-LDL	-0.79	0.2	0.01	0.98	-0.2	0.79	0.09	0.91	0.76	0.23
Combination of the two groups	TC	-0.05	0.79	0.1	0.64	-0.16	0.47	0.008	0.97	-0.23	0.28
	TG	-0.1	0.65	0.06	0.77	-0.19	0.38	-0.06	0.76	0.08	0.71
	HDL	0.15	0.5	0.02	0.92	0	0.99	0.09	0.68	-0.04	0.84
	WC	0.001	0.99	-0.005	0.98	-0.12	0.56	-0.29	0.19	-0.36	0.09
	LDL	-0.02	0.9	-0.1	0.63	-0.1	0.63	0.17	0.44	-0.34	0.11
	OX-LDL	0.28	0.2	-0.04	0.83	0.04	0.84	-0.21	0.33	-0.16	0.45

Data analysis was done by partial correlation. MetS: Metabolic Syndrome; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; TG: triglyceride; HDL: High-Density Lipoprotein; WC: Waist Circumference; LDL: Low-Density Lipoprotein. In obese adults with MetS, ox-LDL was positively associated with serum magnesium and iron concentrations. No other association was observed for obese adults without MetS or the combination of both groups.

Table 4 The correlation between total protein, albumin, urea, creatinine, and uric acid with the components of metabolic syndrome in study groups

Study groups	Variables	Variables									
		Total Protein		Albumin		Urea		Creatinine		Uric acid	
		r	P	r	P	r	P	r	P	r	P
Obese adults with MetS	TC	-0.21	0.93	-0.19	0.45	-0.13	0.6	-0.14	0.58	0.17	0.49
	TG	0.29	0.24	0.49	0.04	-0.18	0.48	0.17	0.5	0.27	0.91
	HDL	-0.1	0.68	-0.41	0.1	0.38	0.13	0.23	0.36	0.27	0.28
	WC	-0.25	0.31	-0.36	0.15	-0.07	0.97	-0.15	0.55	0.28	0.27
	LDL	-0.12	0.64	0.34	0.17	-0.03	0.88	-0.05	0.84	0.33	0.18
	OX-LDL	-0.12	0.64	-0.19	0.44	-0.39	0.11	-0.13	0.61	-0.2	0.44
Obese adults without MetS	TC	0.41	0.48	-0.61	0.27	0.03	0.95	0.25	0.68	-0.45	0.44
	TG	-0.14	0.82	0.39	0.51	0.18	0.77	0.06	0.91	-0.005	0.99
	HDL	0.15	0.8	-0.43	0.46	0.18	0.76	-0.39	0.5	0.48	0.4
	WC	0.63	0.24	0.3	0.61	0.86	0.049	0.41	0.48	0.88	0.04
	LDL	0.46	0.42	-0.7	0.18	-0.1	0.87	0.34	0.57	-0.58	0.3
	OX-LDL	-0.77	0.12	-0.36	0.54	-0.8	0.1	-0.84	0.07	-0.41	0.48
Combination of the two groups	TC	0.03	0.89	-0.26	0.21	-0.17	0.41	-0.012	0.57	0.06	0.77
	TG	0.003	0.99	0.45	0.02	0.001	0.99	0.17	0.4	-0.09	0.64
	HDL	0.1	0.63	-0.41	0.04	0.25	0.22	0.06	0.76	0.38	0.06
	WC	-0.03	0.87	-0.14	0.5	0.08	0.68	-0.09	0.66	0.43	0.03
	LDL	-0.03	0.86	0.14	0.5	-0.14	0.51	-0.02	0.89	0.15	0.47
	OX-LDL	-0.01	0.95	-0.24	0.24	-0.37	0.07	-0.15	0.46	-0.09	0.66

Data analysis was done by partial correlation. MetS: Metabolic Syndrome; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; TG: triglyceride; HDL: High-Density Lipoprotein; WC: Waist Circumference; LDL: Low-Density Lipoprotein. In obese individuals with MetS, albumin was in a positive relationship with TG. In obese individuals without MetS, urea and uric acid were positively associated with WC. In combination of both groups, albumin was positively associated with TG, and negatively associated with HDL-C, while uric acid was in positive association with WC values.

associated with WC. In addition, serum magnesium was non-significantly higher among the MetS group, and serum magnesium values had a relatively strong significant association ($r=0.44$; $P=0.037$) with Ox-LDL-C concentrations (Tables 3 and 4).

A cross-sectional study by Xie et al. [47] showed that MetS was independently related to CKD, especially the components of raised TG, FBG, and blood pressure. Similar to our results, in a study that was carried out by Gohari-Kahou et al., there was no significant difference between serum magnesium levels among individuals with MetS and without MetS, and no significant relationship was detected with MetS components [48]. In another cross-sectional study among 11,686 women, an inverse association was reported between MetS prevalence and dietary magnesium intake [32]. Many studies have established a positive association between low dietary magnesium consumption and MetS risk independently from other risk factors, such as BMI, gender, age, exercise, energy, and alcohol intake [49, 50]. Several studies highlighted the role of magnesium as a cofactor of several enzymes involved in the regulation of cellular glucose metabolism [51, 52] and interactions with cellular calcium homeostasis improving insulin sensitivity [53, 54]. It should be noted that serum magnesium does not necessarily reflect body magnesium stores as do intracellular magnesium measurements and is also a poor indicator of intracellular magnesium level. Evidence suggests that magnesium can affect body weight, but the underlying mechanism is still unknown. The hypothesis is that magnesium cooperates with fatty acids to form soaps in the intestine, thus reducing obtained energy from fats [52]. The results of some studies showed that, in magnesium deficiency, serum HDL-C levels were significantly lower and TG levels were significantly higher [55–57]. Magnesium intake may likely contribute to increasing lipoprotein lipase activity [58, 59].

In our study, serum iron concentration was significantly associated with LDL-C levels in individuals with obesity and MetS (Table 3). The suggested mechanism was that iron-induced IR, which in turn led to unfavorable LDL-C, and hepatic IR increased the secretion and synthesis of apoB by protein-tyrosine phosphatase 1B [60]. Consistent with previous studies, body iron stores were associated with MetS components [61–63]. Similar to our results, in a cross-sectional study conducted on 7,540 adults, after adjusting for covariates, the levels of LDL-C were positively related to iron levels [64]. The results of another cross-sectional study showed that serum iron concentration was positively associated with HDL-C, LDL-C, and TC, but was inversely associated with TG in female students [65].

The level of serum iron does not necessarily show a lack of iron stores. While serum iron is commonly used

as an indicator of efficient iron, serum ferritin is a more sensitive indicator of iron stores. Caution is necessary when assessing patients with metabolic disorders as a low serum iron may not represent iron insufficiency. In our study, individuals with obesity and MetS showed higher serum iron levels compared to the non-MetS group (Table 2). Iron affects insulin secretion and synthesis in the pancreatic gland and leads to metabolic abnormalities that may augment the production of free radicals [66, 67]. Similar to our results, in a cohort study in Japan, Honda et al. did not find a relationship between iron concentrations and WC in 2,322 CKD patients [68]. However, In a study with 1,130 participants, Choma et al. showed that BMI was inversely related to ferritin level, but WC was positively and non-significantly related to ferritin level [69].

In our findings, serum copper was not significantly different between the two groups, and the association between serum copper and the components of MetS was not significant. Lima et al. [70] indicated a negative correlation between serum copper with LDL-C and TC. However, Obeid et al. reported a positive association between serum copper with TC, LDL-C, and HDL-C levels [25]. These inconsistencies might be due to the difference in general characteristics of study participants, as well as the difference in measurement tools.

In the current study, no significant difference was reported between the two groups in serum calcium. Also, there was no significant association between serum calcium and metabolic risk factors (Tables 3 and 4). Contrary to our findings, a cross-sectional study showed that serum calcium level was related to all the MetS components except HDL-C [71]. However, some previous studies demonstrated that an increased level of intracellular calcium exerts its effects by reducing the number of glucose receptors (e.g. glucose transporter (GLUT) –4) and reduces insulin receptor's activity [72, 73]. In a study in Canada, altered calcium homeostasis was associated with adverse changes in IR, beta-cell function, and fasting serum glucose [74]. It should be noted that these studies were performed at the cellular level while we measured serum calcium concentrations that are roughly under homeostatic control. Therefore, its serum change might be minimal as shown in our results. Moreover, blood calcium level is not a good indicator because it is strongly regulated. Only in extreme conditions, such as severe hyperparathyroidism or malnutrition, the serum ionized calcium level is above or below the normal range.

As expected, in our study, serum TC and TG levels were significantly higher in subjects with MetS (Table 2). The prominent role of dyslipidemia in developing CKD has been confirmed in numerous studies. In a study among 2,380 American Indians, Lucove et al. reported a positive association between MetS occurrence and

elevated CKD risk after ten years of follow-up [75]. In another study by Ninomiya et al., after five years of follow-up in 1,440 Japanese adults, 10.6% of participants with MetS developed CKD [76]. In our study, we also observed positive associations between renal function tests and serum lipid profile that confirm previous findings (Table 4). These associations were diverse between groups; for example, albumin was in positive association with TG in individuals with obesity and MetS and combination analysis, while serum urea and uric acid were positively associated with WC in individuals with obesity and without MetS and in combination analysis. Ming et al. [77] also revealed that large WC is related to CKD to a less extent after adjusting the components of MetS.

Similarly, other studies reported positive associations between MetS components and renal function tests. For example, in a study by Wang et al., serum TG level was associated with reduced renal function only in patients with T2DM [78, 79]. In the current study, serum creatinine was non-significantly higher among individuals with MetS, which was partially in accordance with the findings of a previous study that reported a negative relationship between creatinine clearance and the prevalence of MetS [80]. In another study, a high LDL/HDL ratio was associated with elevated serum creatinine values [81]. The exact mechanism explaining the association between MetS and renal disease has not been completely clarified; however, the suggested pathophysiological factors include IR, oxidative stress, endothelial dysfunction, hyperfiltration, and renin–angiotensin–aldosterone-system activation [82]. A prior study by Lee et al. revealed that early intervention in MetS could make the CKD progression slower in patients with early-stage CKD, and help to recognize the risk of MetS change on kidney function in patients [82].

The observed results might be due to the role of IR in the induction of oxidative stress and inflammation and consequently reduced renal function [83]. IR exacerbates kidney disease through such mechanisms as sodium maintenance, increased glomerular filtration rate (GFR), and reduced Na^+ , K^+ -ATPase activity [84, 85]. IR can also cause excessive production of very low-density lipoprotein (VLDL) and the development of hypertriglyceridemia [86].

Limitations of the current study

This study has some limitations; first of all, the assessment of renal function tests was limited, and no information on GFR, and blood electrolytes was available. Second, since the sample size was relatively small, the findings should be generalized with caution. So, large-scale prospective studies are still required to confirm the findings. Third, the effect of dietary intake on the relationship between MetS and renal function tests was not considered and we lacked data on mineral consumption

from the diet. Finally, because this was a case–control study, there was a possibility of confounding and recall bias. However, the strengths of the current study should also be mentioned, it is the first study that emphasized the possible role of some important micro-element and kidney function tests in the pathogenesis of obesity-related disorders and MetS. These findings have some clinical importance; first, the results of the current study suggest that change in mineral status could be a good prognostic biomarker in obesity and its related comorbidities like CVD, T2DM and CKD that could be used in clinical practice. Moreover, from the clinical point of view, chronic disturbed mineral status can be a predictor of the development of cardiovascular disease or diabetes in the future. Also, the inverse association can be considered well; in patients with obesity, metabolic syndrome or related diseases, the mineral balance might prevent some adverse effects related to the disease status.

Future directions

Further longitudinal studies are required to infer the causality. Also, it is suggested that for the future studies, more sensitive and reliable renal function tests be applied and also, other obesity-related conditions like diabetes and cardiovascular disease be examined.

Conclusion

Our results suggest that disturbed serum lipids in obesity-metabolic syndrome is associated with homeostatic changes in the level of minerals or proteins that are involved in their metabolism. The current findings highlight the possible clinical importance of these elements or proteins as possible prognostic markers in obesity and its related comorbidities. Although, further studies are needed to better explain and clarify the underlying mechanism of observed relationships.

List of abbreviations

ATP III	Adult Treatment Panel III
BMI	Body mass index
CAD	Coronary artery disease
CHD	Coronary heart disease
CKD	Chronic kidney disease
DBP	Diastolic blood pressure
ELISA	Enzyme-linked immunosorbent assay
FBS	Fasting blood glucose
GFR	Glomerular filtration rate
HDL	High density lipoprotein cholesterol
LDL	Low density lipoprotein cholesterol
MetS	Metabolic syndrome
SBP	Systolic blood pressure
T2DM	Type 2 diabetes mellitus
TC	Total cholesterol
TG	Triglyceride
VAS	Visual Analogue Scale
WC	Waist circumference

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s13104-023-06472-2>.

Supplementary Material 1: Visual analogue scale for appetite measurement

Acknowledgements

We thank all of the study participants. We also are thankful to the Research Undersecretary of Tabriz University of Medical Sciences for their financial support.

Author' contributions

AMA and AM supervised the project and analyzed data, AMA also generated the study hypothesis and was involved in patients' recruitment. ZHN and BAZ were involved in data collection and manuscript writing. ZHN also conceptualized the first hypothesis of work and was also involved in writing the first draft of the paper. SV, ALJ and ZH were involved in data collection and analysis. ALJ also performed the lab works.

Funding

The present study has been financially supported by a grant from Tabriz University of Medical Sciences. (Code: IR.TBZMED.REC.1400.650 and grant number: 67573). The funders had no role in hypothesis generation, recruiting and designing the study. Their role was only financial supporting.

Data Availability

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

Declarations

Ethics approval and consent to participate

This study protocol has been approved by the ethics committee of the Tabriz University of Medical Sciences, Code: IR.TBZMED.REC.1400.650 and grant number: 67573). Written informed consent was obtained from all of the participants before participation in the study. All methods in the current research were performed in accordance with the declaration of Helsinki's guidelines and regulations.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

¹Endocrinology and Metabolism Research Center, Institute of Basic and Clinical Physiology Science, & Physiology Research Center, Kerman University of Medical Sciences, Kerman, Iran

²Department of Internal Medicine, Faculty of Medical Science, Mazandaran University of Medical Science, Sari, Iran

³Medical Physiology, Basic Sciences Department, College of Pharmacy, University of Duhok, Kurdistan, Iraq

⁴Isfahan Kidney Diseases Research Center, School of Medicine, Khorshid Hospital, Isfahan University of Medical Sciences, Isfahan, Iran

⁵Student Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran

⁶Department of Internal Medicine, School of Medicine, Urmia University of Medical Sciences, Urmia, Iran

Received: 25 December 2022 / Accepted: 23 August 2023

Published online: 05 September 2023

References

1. Li X, et al. Impact of metabolic syndrome and its components on prognosis in patients with Cardiovascular Diseases: a Meta-analysis. *Front Cardiovasc med.* 2021;10:739.
2. Guembe MJ, et al. Risk for cardiovascular disease associated with metabolic syndrome and its components: a 13-year prospective study in the RIVANA cohort. *Cardiovasc Diabetol.* 2020;19(1):1–14.
3. Ulaganathan V, Kandiah M, Shariff ZM. *A case-control study on the association of abdominal obesity and hypercholesterolemia with the risk of colorectal cancer.* *J Carcinog.* 2018. 17.
4. Ranasinghe P, et al. Prevalence and trends of metabolic syndrome among adults in the asia-pacific region: a systematic review. *BMC Public Health.* 2017;17(1):1–9.
5. Belete R, et al. Global prevalence of metabolic syndrome among patients with type I diabetes mellitus: a systematic review and meta-analysis. *Diabetol Metab Syndr.* 2021;13(1):1–13.
6. Schroeder K, et al. Sleep is inversely associated with sedentary time among youth with obesity. *Am J Health Behav.* 2020;44(6):756–64.
7. Tang D, et al. Differences in overweight and obesity between the North and South of China. *Am J Health Behav.* 2020;44(6):780–93.
8. Fatahi A, Doosti-Irani A, Cheraghi Z. Prevalence and incidence of metabolic syndrome in Iran: a systematic review and Meta-analysis. *Int J Prev Med.* 2020;11:64–4.
9. Thomas G, et al. Metabolic syndrome and kidney disease: a systematic review and meta-analysis. *Clin J Am Soc Nephrol.* 2011;6(10):2364–73.
10. Ninomiya T, et al. Impact of metabolic syndrome on the development of cardiovascular disease in a general japanese population: the Hisayama study. *Stroke.* 2007;38(7):2063–9.
11. Guerra ZC, et al. Associations of Acculturation and gender with obesity and physical activity among Latinos. *Am J Health Behav.* 2022;46(3):324–36.
12. Rottapel RE, Hudson LB, Folta SC. Cardiovascular health and african-american women: a qualitative analysis. *Am J Health Behav.* 2021;45(4):735–45.
13. Prasad GR. Metabolic syndrome and chronic kidney disease: current status and future directions. *World J Nephrol.* 2014;3(4):210.
14. Wondmkun YT. Obesity, insulin resistance, and type 2 diabetes: associations and therapeutic implications. *Diabetes Metab Syndr Obes.* 2020;13:3611–6.
15. Gallegos-Gonzalez G, et al. Association between stress and metabolic syndrome and its mediating factors in University students. *Am J Health Behav.* 2021;45(6):1091–102.
16. Irsik DL, Brands MW. Physiological hyperinsulinemia caused by acute hyperglycemia minimizes renal sodium loss by direct action on kidneys. *Am J Physiol Regul Integr Comp Physiol.* 2018;315(3):R547–r552.
17. Naghibi D, Mohammadzadeh S, Azami-Aghdash S. Barriers to evidence-based practice in Health System: a systematic review. *Evid Based Care.* 2021;11(2):74–82.
18. Prashanth L, et al. A review on role of essential trace elements in health and disease. *J Dr NTR Univ Health Sci.* 2015;4(2):75–85.
19. Aguilar M, et al. Plasma mineral content in type-2 diabetic patients and their association with the metabolic syndrome. *Annals of Nutrition and Metabolism.* 2007;51(5):402–6.
20. Vajdi M, Farhangi MA, Nikniaz L. Diet-derived nutrient patterns and components of metabolic syndrome: a cross-sectional community-based study. *BMC Endocr Disord.* 2020;20(1):1–13.
21. Zhuang T, Han H, Yang Z. Iron, oxidative stress and gestational diabetes. *Nutrients.* 2014;6(9):3968–80.
22. Al-Turfi SM. Z., et al., Evaluation of the Effect of Alcoholic Extract of Laurus Nobilis Leaves on blood biochemical parameters and histological changes in the liver and kidney among female Wistar rats treated with depakene (Sodium Valproate). Volume 77. *Archives of Razi Institute;* 2022. pp. 981–9. 3.
23. He K, et al. Magnesium intake and incidence of metabolic syndrome among young adults. *Circulation.* 2006;113(13):1675–82.
24. Guerrero-Romero F, Jaquez-Chairez FO, Rodríguez-Morán M. Magnesium in metabolic syndrome: a review based on randomized, double-blind clinical trials. *Magnes Res.* 2016;29(4):146–53.
25. Obeid O, et al. Plasma copper, zinc, and selenium levels and correlates with metabolic syndrome components of lebanese adults. *Biol Trace Elem Res.* 2008;123(1):58–65.
26. Arnaud J, et al. Gender differences in copper, zinc and selenium status in diabetic-free metabolic syndrome european population—the IMMIDIET study. *Nutr Metabolism Cardiovasc Dis.* 2012;22(6):517–24.
27. Dongiovanni P, et al. Iron in fatty liver and in the metabolic syndrome: a promising therapeutic target. *J Hepatol.* 2011;55(4):920–32.

28. de Oliveira Otto MC, et al. Dietary intakes of zinc and heme iron from red meat, but not from other sources, are associated with greater risk of metabolic syndrome and cardiovascular disease. *J Nutr.* 2012;142(3):526–33.
29. Kim WS, Lee D-H, Youn H-J. Calcium–phosphorus product concentration is a risk factor of coronary artery disease in metabolic syndrome. *Atherosclerosis.* 2013;229(1):253–7.
30. Dubey P, Thakur V, Chattopadhyay M. Role of minerals and trace elements in diabetes and insulin resistance. *Nutrients.* 2020;12(6):1864.
31. Song C, et al. Associations of serum minerals with body mass index in adult women. *Eur J Clin Nutr.* 2007;61(5):682–5.
32. Song Y, et al. Magnesium intake, C-reactive protein, and the prevalence of metabolic syndrome in middle-aged and older US women. *Diabetes Care.* 2005;28(6):1438–44.
33. Tofano RJ, et al. Association of metabolic syndrome and hyperferritinemia in patients at cardiovascular risk. *Diabetes Metab Syndr Obes.* 2020;13:3239.
34. Shim YS, et al. Association of serum ferritin with insulin resistance, abdominal obesity, and metabolic syndrome in Korean adolescent and adults: the Korean National Health and Nutrition Examination Survey, 2008 to 2011. *Medicine.* 2017;96(8):e6179.
35. Sobczak AI, et al. Total plasma magnesium, zinc, copper and selenium concentrations in type-I and type-II diabetes. *Biomaterials.* 2019;32(1):123–38.
36. Seo J-A, et al. The associations between serum zinc levels and metabolic syndrome in the Korean population: findings from the 2010 Korean National Health and Nutrition Examination Survey. *PLoS ONE.* 2014;9(8):e105990.
37. Chen J, et al. The metabolic syndrome and chronic kidney disease in US adults. *Ann Intern Med.* 2004;140(3):167–74.
38. Grundy SM. *Metabolic syndrome scientific statement by the American heart association and the national heart, lung, and blood institute.* 2005, Am Heart Assoc. p. 2243–4.
39. Lea J, et al. Metabolic syndrome, proteinuria, and the risk of progressive CKD in hypertensive African Americans. *Am J Kidney Dis.* 2008;51(5):732–40.
40. Kitiyakara C, et al. The metabolic syndrome and chronic kidney disease in a Southeast Asian cohort. *Kidney Int.* 2007;71(7):693–700.
41. Maric C, Hall JE. Obesity, metabolic syndrome and diabetic nephropathy. *Contrib Nephrol.* 2011;170:28–35.
42. Pinto-Sietsma S-J, et al. A central body fat distribution is related to renal function impairment, even in lean subjects. *Am J Kidney Dis.* 2003;41(4):733–41.
43. Zeinalian R, et al. The effects of *Spirulina Platensis* on anthropometric indices, appetite, lipid profile and serum vascular endothelial growth factor (VEGF) in obese individuals: a randomized double blinded placebo controlled trial. *BMC Complement Altern Med.* 2017;17(1):1–8.
44. Flint A, et al. Reproducibility, power and validity of visual analogue scales in assessment of appetite sensations in single test meal studies. *Int J Obes.* 2000;24(1):38–48.
45. Grundy SM, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute scientific statement. *Circulation.* 2005;112(17):2735–52.
46. Srivastava A, Mirza TM, Sharan S. *Prehypertension 2019.*
47. Xie K, et al. The association of metabolic syndrome components and chronic kidney disease in patients with hypertension. *Lipids Health Dis.* 2019;18(1):1–6.
48. Gohari-Kahou M, et al. The association between serum and dietary magnesium with cardiovascular disease risk factors in Iranian adults with metabolic syndrome. *Transl Metab Syndr Res.* 2020;3:42–8.
49. Dibaba D, et al. Dietary magnesium intake and risk of metabolic syndrome: a meta-analysis. *Diabet Med.* 2014;31(11):1301–9.
50. Choi M-K, Bae Y-J. Relationship between dietary magnesium, manganese, and copper and metabolic syndrome risk in Korean adults: the Korea National Health and Nutrition Examination Survey (2007–2008). *Biol Trace Elem Res.* 2013;156(1):56–66.
51. Morakinyo AO, Samuel TA, Adekunbi DA. Magnesium upregulates insulin receptor and glucose transporter-4 in streptozotocin-nicotinamide-induced type-2 diabetic rats. *Endocr Regul.* 2018;52(1):6–16.
52. Fiorentini D, et al. Magnesium: biochemistry, nutrition, detection, and social impact of diseases linked to its deficiency. *Nutrients.* 2021;13(4):1136.
53. Liu H, et al. Magnesium supplementation enhances insulin sensitivity and decreases insulin resistance in diabetic rats. *Iran J Basic Med Sci.* 2020;23(8):990–8.
54. Zhao B, et al. Association of magnesium intake with type 2 diabetes and total stroke: an updated systematic review and meta-analysis. *BMJ open.* 2020;10(3):e032240.
55. Gãman MA, et al. Crosstalk of magnesium and serum lipids in dyslipidemia and associated disorders: a systematic review. *Nutrients.* 2021;13(5):1411.
56. Farhangi MA, Ostadrahimi A, Mahboob S. Serum calcium, magnesium, phosphorous and lipid profile in healthy Iranian premenopausal women. *Biochemia Med.* 2011;21(3):312–20.
57. Nasiri A. Parental Care Challenges in Childhood obesity management: a qualitative study. *Evid Based Care.* 2022;11(4):7–15.
58. Zamora-Ginez I, et al. Relationship of the low-density lipoprotein (LDL)/high-density lipoprotein (HDL) index with antioxidant enzymes and with the oxLDL/HDL index. *Gaceta médica de México.* 2019;155(5):453–7.
59. Dos Santos LR, et al. Cardiovascular diseases in obesity: what is the role of magnesium? *Biol Trace Elem Res.* 2021;199(11):4020–7.
60. Sung HK, et al. Iron induces insulin resistance in cardiomyocytes via regulation of oxidative stress. *Sci Rep.* 2019;9(1):1–13.
61. Muñoz-Ruiz MA, et al. Metabolic syndrome may be associated with a lower prevalence of iron deficiency in Ecuadorian women of reproductive age. *J Nutr Sci.* 2021;10:e4–e4.
62. Wang M, et al. Association of serum ferritin with metabolic syndrome in eight cities in China. *Food Sci Nutr.* 2020;8(3):1406–14.
63. Gasmí A, et al. Lifestyle Genetics-Based reports in the treatment of obesity. *Arch Razi Inst.* 2021;76(4):707.
64. Zhou B, et al. Associations of iron status with apolipoproteins and lipid ratios: a cross-sectional study from the China Health and Nutrition Survey. *Lipids Health Dis.* 2020;19(1):1–12.
65. He L, et al. Serum iron levels are negatively correlated with serum triglyceride levels in female university students. *Ann Palliat Med.* 2020;9(2):414–9.
66. Blesia V et al. *Excessive Iron induces oxidative stress promoting Cellular perturbations and insulin secretory dysfunction in MIN6 Beta cells.* Cells, 2021. 10(5).
67. Altamura S, et al. Iron aggravates hepatic insulin resistance in the absence of inflammation in a novel db/db mouse model with iron overload. *Mol Metab.* 2021;51:101235.
68. Honda H, et al. Association of adiposity with hemoglobin levels in patients with chronic kidney disease not on dialysis. *Clin Exp Nephrol.* 2018;22(3):638–46.
69. Choma SSR, Alberts M, Modjadji SEP. Conflicting effects of BMI and waist circumference on iron status. *J Trace Elem Med Biol.* 2015;32:73–8.
70. Lima S, et al. Assessment of copper and lipid profile in obese children and adolescents. *Biol Trace Elem Res.* 2006;114(1):19–29.
71. Saltevo J, et al. Serum calcium level is associated with metabolic syndrome in the general population: FIN-D2D study. *Eur J Endocrinol.* 2011;165(3):429–34.
72. Pomytkin I, Pinelis V. *Insulin receptors and intracellular Ca²⁺ form a double-negative Regulatory Feedback Loop Controlling insulin sensitivity.* F1000Research, 2020. 9: p. 598–8.
73. Idevall-Hagren O, Tengholm A. Metabolic regulation of calcium signaling in beta cells. *Seminars in Cell & Developmental Biology.* 2020. Elsevier.
74. Sun G, et al. Altered calcium homeostasis is correlated with abnormalities of fasting serum glucose, insulin resistance, and β -cell function in the Newfoundland population. *Diabetes.* 2005;54(11):3336–9.
75. Lucove J, et al. Metabolic syndrome and the development of CKD in American Indians: the strong heart study. *Am J Kidney Dis.* 2008;51(1):21–8.
76. Ninomiya T, et al. Metabolic syndrome and CKD in a general Japanese population: the Hisayama Study. *Am J Kidney Dis.* 2006;48(3):383–91.
77. Ming J, et al. Metabolic syndrome and chronic kidney disease in general Chinese adults: results from the 2007–08 China National Diabetes and Metabolic Disorders Study. *Clin Chim Acta.* 2014;430:115–20.
78. Wang C et al. *Poor Control of Plasma Triglycerides Is Associated with Early Decline of Estimated Glomerular Filtration Rates in New-Onset Type 2 Diabetes in China: Results from a 3-Year Follow-Up Study* J Diabetes Res., 2020. 2020: p. 3613041.
79. Aghajani R, et al. Effect of Aerobic Program in the morning and afternoon on Obestatin and the body composition of overweight and obese women. *J Chem Health Risks.* 2020;10(2):117–25.
80. Tao J et al. *Serum uric acid to creatinine ratio and metabolic syndrome in postmenopausal Chinese women.* Medicine, 2020. 99(17).
81. Schaeffner ES, et al. Cholesterol and the risk of renal dysfunction in apparently healthy men. *Clin J Am Soc Nephrol.* 2003;14(8):2084–91.
82. Lee SJ, et al. Metabolic syndrome status over 2 years predicts incident chronic kidney disease in mid-life adults: a 10-year prospective cohort study. *Sci Rep.* 2018;8(1):1–7.
83. Rapa SF, et al. Inflammation and oxidative stress in chronic kidney disease-potential therapeutic role of Minerals, Vitamins and Plant-Derived Metabolites. *Int J Mol Sci.* 2019;21(1):263.

84. Spoto B, Pisano A, Zoccali C. Insulin resistance in chronic kidney disease: a systematic review. *Am J Physiol Renal*. 2016;311(6):1087–108.
85. Gorjao R et al. *Molecular mechanisms involved in inflammation and insulin resistance in chronic diseases and possible interventions* J Biomed Biotechnol, 2012. 2012: p. 841983.
86. Tsimihodimos V, Dounousi E, Siamopoulos KC. Dyslipidemia in chronic kidney disease: an approach to pathogenesis and treatment. *J Am Soc Nephrol*. 2008;28(6):958–73.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.