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Research Article

ASSOCIATION BETWEEN TRACE ELEMENTS AND METABOLIC SYNDROME AMONG TYPE 2 DIABETES MELLITUS PATIENTS IN GORGAN

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ABSTRACT

Objective: Metabolic syndrome changes in different ethnic and age group. Trace elements are associated with metabolic syndrome. The present study was aimed to assess the serum levels of iron, zinc, and copper in Gorgan and their association with the metabolic syndrome components.

Methods: The present study was carried out in the Metabolic Disorders Research Center of Gorgan Faculty of Medicine. There were 152 Type 2 diabetic subjects who were referred to the Department of Diabetes Center in 5th Azar Educational Hospital in Golestan University of Medical Sciences, Iran, 2014.

Results: The mean waist circumference, systolic blood pressure (SBP) and diastolic blood pressure (DBP), total cholesterol, triglyceride, and fasting blood glucose levels were significantly higher in the Type 2 diabetic patients with metabolic syndrome, but the mean HDL-cholesterol was significantly lower ($p<0.05$). Mean serum level of copper was slightly higher, and mean serum level of zinc and iron were lower in patients with metabolic syndrome than that of subjects without metabolic syndrome. There were significant differences in the mean of SBP and DBP, triglyceride, high-density lipoprotein (HDL)-cholesterol, and fasting blood glucose in men and women with metabolic syndrome when compared with subjects without metabolic syndrome. There were also significant differences in the mean of body mass index and waist circumference in women with metabolic syndrome. Serum zinc positively correlated with HDL-cholesterol level (in all and in women Type 2 diabetic patients), SBP (in all Type 2 diabetic patients), and DBP (in men Type 2 diabetic patients) ($p<0.05$).

Conclusion: Differences of our results with other studies emphasize further research on trace elements and metabolic syndrome and their relationship with different diseases are necessary.

Keywords: Iron, Copper, Zinc, Metabolic syndrome, Type 2 diabetic patients.

INTRODUCTION

Metabolic syndrome is explained as a cluster of risk factors, which may expose subjects to diabetes and cardiovascular diseases [1]. Differences in genetic diversities, age, and sex influence the prevalence of metabolic syndrome and its components [2]. Studies of Marjani *et al.* have been shown that metabolic syndrome change in different ethnic and age groups and postmenopausal women [3-7]. The trace elements such as zinc (Zn), copper (Cu), and iron (Fe) are associated with metabolic syndrome [8,9]. It has been shown that zinc level is associated with total cholesterol and low-density lipoprotein (LDL) cholesterol [8]. A study has indicated that metabolic syndrome is associated with the metabolism of zinc [9]. Some other studies have shown that the level of zinc changed in different conditions like obesity and Type 2 diabetic patients as observed in animal and human patterns [10-15]. Zinc as a trace element participates in the metabolism of proteins, carbohydrates, lipids, and nucleic acids [16,17]. Zinc deficiency may cause insulin resistance, hyperglycemia, impaired glucose tolerance [9], and the development of diabetes [18]. Studies have indicated that zinc trigger lipogenesis and glucose transport in adipocytes of rat [19] and glucose uptake in skeletal muscle of mouse [20]. There is a relationship between metabolic syndrome and insulin resistance. Another important trace element is iron. Many studies have shown that there is a link between insulin resistance and hepatic iron overload (elevated serum ferritin level) [21,22]. Some different studies have indicated that there are an association between elevated serum ferritin and serum alanine transaminase, hypertension, and myocardial infarction, respectively [23-25]. Bozzini *et al.* showed an association between metabolic syndrome and excess of body iron [26]. Evidence shows that the accumulation of body iron is related to the metabolic syndrome and Type 2 diabetes in general populations [27]. Studies on middle-aged or older men and of postmenopausal women have revealed that there is an association between iron metabolism and disorders of glucose metabolism [28,29]. Many studies have indicated that higher iron stores are associated with the progress of diabetes and coronary heart disease while lower iron stores decrease the prevalence of these diseases [30,31]. Some studies have indicated mildly high levels of body iron stores are shown as a risk factor for cardiovascular disease [25,32-35]; whereas other study has shown that there was no relation between iron level and coronary heart disease [35]. It has been reported that there is an association between iron stores and risk of diabetes, hepatic damage, and cardiovascular diseases [36]. Few studies have shown an association of trace element levels in subjects with or without metabolic syndrome in different populations [37,38]. Trace elements take part in metabolism, growth, immunological, and neurological functions [39]. Copper is another essential trace element that catalyzes oxidation - reduction reactions, detoxification, transport, production, and formation reactions [40]. A study has been shown that there is a relationship between copper level and total cholesterol, LDL cholesterol, and triglyceride levels [41]. Epidemiological studies have revealed that there is a positive association between low zinc and copper levels and elevated risk of cardiovascular disease [42]. Another study has shown an association of copper, zinc, and iron levels and scope of myocardial damage [43]. The present study was aimed to assess the serum levels of zinc, iron, and copper in Gorgan (South East of Caspian Sea) and their association with the metabolic syndrome components Type 2 diabetic patients.

METHODS

The present study was carried out in the Metabolic Disorders Research Center of Gorgan Faculty of Medicine, Iran in 2014. There were 152 Type 2 diabetic subjects. All diabetic patients, aged 56.35±3.94 years who were referred to the Department of Diabetes Center (the only

Diabetes Center in Gorgan) in 5th Azar Educational Hospital in Golestan University of Medical Sciences participated in this study, 2014. Subjects with chronic liver disease, chronic renal disease, chronic and acute infections, recent acute illness, cirrhosis, hyperthyroidism, recent blood donation or transfusion, and recent intake of iron therapy were excluded. A ten ml venous blood sample was collected from all subjects after 12 hrs overnight fast. The serum fasting blood glucose, triglycerides, LDL-cholesterol, and high-density lipoprotein (HDL)-cholesterol levels were measured by commercial kit using spectrophotometer techniques (Model JENWAY 6105 UV/VIS) in the Metabolic Disorders Research Center. Weight was measured, while subjects were minimally clothed without shoes, using digital scales. Height was measured in standing position using tape meter while the shoulder was in a normal position. Body mass index (BMI) was defined as weight in kilograms divided by height in meters squared. Overweight was defined as BMI 25.0-29.9 kg/m^2 and obese as BMI ≥30 kg/m^2 [44]. Waist circumferences were measured at the point halfway between the lower border of ribs and the iliac crest in a horizontal plane [45]. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured in sitting position on the right hand. Metabolic syndrome identified if Type 2 diabetic subjects had any three or more of the following criteria, according to the adult treatment Panel III [46]: (1) Abdominal obesity: Waist circumference >102 cm in males and >88 cm in females, (2) hypertriglyceridemia: Serum triglycerides level ≥ 150 mg/dl, (3) Low HDL-cholesterol: < 40 mg/dl in males and < 50 mg/dl in females, (4) High blood pressure: SBP ≥ 130 mmHg and/or DBP ≥ 85 mmHg or on treatment for hypertension, and (5) High fasting glucose: Serum glucose level ≥110 mg/dl or on treatment for diabetes. Serum copper, iron, and zinc were determined by flame atomic absorption spectrometry (Perkin Elmer 560, Norwalk, CT, USA). The results are shown as means and standard deviations and percentages. All statistical analysis was calculated with SPSS - 16 version software. The results were evaluated by using independent sample t-test and Associations between parameters were evaluated by Spearman correlation coefficients. A $p<0.05$ was considered as statistically significant.

RESULTS

A total of 152 Type-2 diabetic patients were studied. The mean age of the subjects was 56.36±3.94 years. The mean duration of diabetes was 4.09±1.75 years. Table 1 shows the clinical and biochemical data of the subjects with and without the metabolic syndrome in Type 2 diabetic patients. The mean waist circumference, SBP and DBP, total cholesterol, triglyceride, and fasting blood glucose levels were significantly higher in the Type 2 diabetic patients with metabolic syndrome, but the mean HDL-cholesterol was significantly lower as ($p<0.05$). Mean serum level of copper was slightly higher, and mean serum level of zinc and iron were lower in patients with metabolic syndrome than that of subjects without metabolic syndrome. Table 2 shows clinical and biochemical data of Type 2 diabetic men and women with and without metabolic syndrome. There were significant differences in the mean of SBP and DBP, triglyceride, HDL-cholesterol, and fasting blood glucose in men and women with metabolic syndrome when compared with subjects without metabolic syndrome. There were also significant differences in the mean of BMI and waist circumference in women with metabolic syndrome. Mean serum level of trace elements in men and women with metabolic syndrome were not significant when compared with that of subjects without metabolic syndrome. Correlation between serum iron, zinc, and copper levels and characteristics of study subjects in Type 2 diabetic patients, in men and women with the metabolic syndrome, are summarized in Tables 3 and 4. Serum zinc positively correlated with HDL-cholesterol level (in all and in women Type 2 diabetic patients), SBP (in all Type 2 diabetic patients), and DBP (in men Type 2 diabetic patients) ($p<0.05$). There was no significant correlation between copper or iron and components of the metabolic syndrome and other subjects.

DISCUSSION

The aim of this study was to assess the association between metabolic syndrome and trace elements in Type 2 diabetics. Among Type 2 diabetic patients with metabolic syndrome, the mean BMI was in the range of obesity (BMI>30 kg/m^2), the mean triglyceride (209 mg/dl), fasting blood glucose (181 mg/dl), and waist circumference (100 cm) were above the normal range, and the mean HDL was low (33 mg/dl). Serum triglycerides are as risk factors for ischemic heart disease [26]. It is one of the components of metabolic syndrome. We found no significant association between serum iron concentration and metabolic syndrome components. Mean fasting serum iron and zinc levels were found to be slightly lower whereas copper level was higher in Type 2 diabetic patients with metabolic syndrome than that of without metabolic syndrome. A role of iron was for the 1st time described by Sullivan in 1981. Iron stores were shown to be decreased in women after menopause in comparison with premenopausal iron stores [47]. According to our results, all subjects and women with metabolic syndrome show lower serum iron level (not significant) when compared to those without metabolic syndrome. Serum iron level was higher in men. Elevated body iron may show an important role in the development of diabetic complications. Increased body iron may cause to metabolic abnormalities, which may increase free radicals formation. These radicals can take part in oxidative damage and lead to diabetic complications development [29,31,48].

Some studies have shown that increased iron level could affect insulin synthesis and secretion in the pancreas [49,50]. Increased iron also could elevate lipid peroxidation (especially have an effect on free fatty acids) which decrease glucose consumption and activate gluconeogenesis pathway in the liver. These lead to the development of insulin resistance [49,50]. Our study demonstrates that increased serum iron in men were not significantly associated with metabolic syndrome components in Type 2 diabetic patients. Studies have shown that progressive iron accumulation in the pancreatic cell is a disorder of glucose tolerance in patients with iron overload [51]. It has been also shown that iron metabolism is related to the component of the metabolic syndrome [30] which is not in agreement with our results. There was significant no correlation between iron and the component of the metabolic syndrome, however, a significant correlation was observed between zinc and metabolic syndrome components. Many studies revealed that metabolic syndrome is associated with elevated body iron stores in Western and Eastern countries [27,30,52,53]. Recent studies on healthy Chinese women have shown that higher iron stores were associated with Type 2 diabetes [54]. Several studies have reported the association between iron stores and component of metabolic syndrome, including hypertension [25], dyslipidemia [55,56], elevated fasting insulin and blood glucose [28], and central obesity [57]. No one of these parameters was in line with our findings. Acute zinc deficiency is not frequent in diabetic patients while some studies have shown that there is a zinc deficiency in Type 2 diabetes [58-61] but some other studies were not found significant differences with healthy subjects [62,63]. Recent studies indicated decreased levels of zinc in obese, insulin-resistant subjects [64]. A decreased zinc level seems to have a relationship with elevated risk for coronary artery disease [61] and mortality [65]. Some of these studies are in agreement with our results [58-61,64]. Copper and zinc are cofactors of different antioxidant enzymes. Many studies have revealed that there are conflicting results in these trace element levels in subjects with or without metabolic syndrome [38,39,65-67]. The present study showed that serum zinc was associated with the components of metabolic syndrome. A study in Europe indicated that zinc was negatively associated with metabolic syndrome components [68]. The association between zinc and metabolic syndrome in our study are in agreement with the results of other study [68]. Serum copper was not associated with the components of metabolic syndrome in our findings. The study showed that copper was negatively associated with metabolic syndrome components [68]. The lack of association between copper and metabolic syndrome in our study subjects are in agreement with the results of other study [38,39]. Studies on Chinese men with metabolic syndrome have shown that serum zinc levels were higher in subjects with metabolic syndrome than in control group, which was different to subjects with metabolic syndrome in Western

Table 1: Clinical and biochemical data of Type 2 diabetic subjects with and without metabolic syndrome

Parameters	Total number of subjects with Type 2 diabetes	Type 2 diabetic subjects with metabolic syndrome	Type 2 diabetic subjects without metabolic syndrome	P-value
Number of patients (%)	152 (100)	28 (18.42)	124 (81.58)	
Age (years)	56.36±3.94	56.38±3.83	56.20±4.45	0.842
Waist circumference (cm)	98.52±11.43	100.36±11.07	90.68±9.63	0.001
Height (cm)	162±0.11	160±0.12	167±0.09	0.005
Weight (kg)	74.83±0.38	75.72±13.65	71.00±12.23	0.074
BMI (kg/m^2)	29.20±12.65	30.10±13.83	25.36±3.17	0.001
SBP (mmHg)	130.78±19.48	133.33±1.96	120.0±1.48	0.001
DBP (mmHg)	78.23±12.03	79.35±1.22	73.44±0.97	0.007
Triglyceride (mg/dl)	197.61±84.10	209.99±87.40	144.68±35.51	0.001
Cholesterol (mg/dl)	173.37±50.82	176.65±53.11	159.37±37.16	0.044
HDL-cholesterol (mg/dl)	35.11±10.65	33.15±9.94	43.51±9.55	0.001
LDL-cholesterol (mg/dl)	90.71±47.11	92.65±48.95	82.44±37.93	0.225
Glucose (mg/dl)	171.85±76.80	181.79±77.47	129.34±57.81	0.001
Fe (mg/L)	1.03±0.58	1.01±0.37	1.08±0.62	0.443
Zn (mg/L)	0.94±0.22	0.93±0.22	0.96±0.21	0.506
Cu (mg/L)	1.35±0.38	1.37±0.38	1.26±0.34	0.147

HDL: High-density lipoprotein, LDL: Low-density lipoprotein, BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure

Table 2: Clinical and biochemical data of Type 2 diabetic men and women with and without metabolic syndrome

Parameters	Total number of subjects with Type 2 diabetes	Type 2 diabetic subjects with metabolic syndrome	Type 2 diabetic subjects without metabolic syndrome	p-value
Men				
Number of patients (%)	53 (100)	35 (66)	18 (34)	
Age (years)	57.33±4.31	57.33±4.31	55.81±3.64	0.869
Waist circumference (cm)	96.90±9.69	99.90±9.69	96.41±12.23	0.229
Height (cm)	170±0.08	170±0.08	157±0.11	0.562
Weight (kg)	78.20±13.49	78.20±13.49	72.98±13.18	0.272
BMI (kg/m^2)	26.77±3.62	30.77±3.62	26.53±15.37	0.084
SBP (mmHg)	133.8±1.94	133.8±1.94	129.0±1.93	0.011
DBP (mmHg)	80.1±1.09	80.1±1.09	77.1±1.25	0.040
Triglyceride (mg/dl)	189.12±79.07	202.12±79.07	189.24±86.76	0.006
Cholesterol (mg/dl)	169.61±42.43	175.61±42.43	169.43±54.96	0.258
HDL-cholesterol (mg/dl)	34.61±10.87	34.61±10.87	35.39±10.57	0.01
LDL-cholesterol (mg/dl)	87.44±44.48	92.44±44.48	87.51±48.63	0.836
Glucose (mg/dl)	182.87±81.01	182.87±81.01	165.84±74.13	0.003
Fe (mg/L)	1.03±0.38	1.07±0.38	1.02±0.67	0.745
Zn (mg/L)	0.91±0.16	0.90±0.16	0.98±0.24	0.491
Cu (mg/L)	1.17±0.29	1.27±0.29	1.49±0.41	0.844
Women				
Number of patients (%)	99 (100)	89 (89.9)	10 (10.10)	
Age (years)	55.81±3.64	56.04±3.69	53.80±2.44	0.749
Waist circumference (cm)	99.41±12.23	101.25±11.14	83.00±9.06	0.001
Height (cm)	157±0.11	157±0.11	158±0.06	0.579
Weight (kg)	72.98±13.18	74.20±13.06	62.20±8.94	0.002
BMI (kg/m^2)	30.53±15.37	31.18±16.05	24.75±3.39	0.002
SBP (mmHg)	129.0±1.93	131.3±1.89	109.0±0.99	0.001
DBP (mmHg)	77.1±1.25	78.2±1.24	68.0±0.91	0.007
Triglyceride (mg/dl)	202.24±86.76	209.79±88.14	135.00±20.52	0.009
Cholesterol (mg/dl)	175.43±54.96	177.55±56.66	156.60±32.59	0.098
HDL-cholesterol (mg/dl)	35.39±10.57	34.49±10.44	43.40±8.54	0.010
LDL-cholesterol (mg/dl)	92.51±48.63	94.37±49.92	76.10±32.63	0.137
Glucose (mg/dl)	165.84±74.13	172.22±73.77	109.10±51.48	0.004
Fe (mg/L)	1.02±0.67	1.01±0.69	1.10±0.41	0.422
Zn (mg/L)	0. 95±0.24	0.99±0.23	1.11±0.25	0.073
Cu (mg/L)	1.39±0.41	1.41±0.42	1.34±0.24	0.141

HDL: High-density lipoprotein, LDL: Low-density lipoprotein, BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure

countries [69]. The same study showed that serum Zn and Zn/Cu were elevated in metabolic syndrome when compared to subjects without metabolic syndrome.

Serum Zn levels were positively correlated with SBP and DBP [69]. Another study has indicated that Zn and Zn/Cu were increased in study model of a rat with hypertension and low level of serum Cu [70]. On the other hand, their conclusion showed that an increased Zn and decreased Cu may be involved in higher blood pressure. Some studies have shown that there were no association between copper or zinc and metabolic syndrome in both genders [67,71]. Our findings showed that serum levels of zinc decreased in all, men and women Type 2 diabetic patients, which are in agreement with other studies [69-71]. In our study, the correlation between serum copper and metabolic syndrome components was not seen to reach significant value. In inconsistent to our study, a study indicated that the level of serum copper correlated negatively with total and LDL cholesterol [72]. Studies have shown that small weight loss normalizes the plasma zinc and decreases risk factors

Table 3: Correlation between serum iron, zinc, and copper levels and components of metabolic syndrome

Parameters	Iron		Zinc		Copper	
	r	P	r	P	r	P
Glucose	−0.131	0.148	−0.024	0.789	−0.026	0.778
Triglyceride	−0.111	0.221	0.058	0.525	−0.125	0.167
Cholesterol	0.010	0.915	−0.048	0.597	0.013	0.889
HDL-cholesterol	−0.137	0.128	0.236	0.008	−0.034	0.708
LDL-cholesterol	0.068	0.456	−0.069	0.446	0.048	0.595
Waist circumference	0.054	0.555	−0.076	0.399	0.116	0.201
SBP	0.073	0.422	0.184	0.041	0.071	0.431
DBP	0.068	0.454	0.112	0.216	−0.063	0.484
BMI	0.024	0.788	−0.052	0.563	0.026	0.777

HDL: High-density lipoprotein, LDL: Low-density lipoprotein, BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure

Table 4: Correlation between serum iron, zinc, and copper levels and characteristics of study subjects in men and women with metabolic syndrome

Parameters	Iron		Zinc		Copper	
	r	p	r	p	r	p
Men						
Glucose	−0.258	0.135	−0.119	0.496	0.052	0.768
Triglyceride	−0.264	0.125	0.138	0.430	−0.327	0.055
Cholesterol	−0.127	0.467	0.106	0.544	0.039	0.825
HDL-cholesterol	−0.092	0.600	0.105	0.547	−0.262	0.128
LDL-cholesterol	−0.048	0.782	0.099	0.570	0.161	0.354
Waist circumference	−0.053	0.763	−0.088	0.617	0.138	0.428
SBP	0.134	0.441	0.307	0.073	0.319	0.062
DBP	0.199	0.251	0.408	0.015	0.175	0.314
BMI	0.071	0.686	−0.144	0.408	0.099	0.570
Women						
Glucose	−0.110	0.306	0.011	0.919	−0.006	0.958
Triglyceride	−0.080	0.458	0.037	0.733	−0.089	0.408
Cholesterol	0.033	0.756	−0.081	0.448	0.004	0.971
HDL-cholesterol	−0.148	0.167	0.262	0.013	−0.041	0.706
LDL-cholesterol	0.094	0.382	−0.116	0.283	0.018	0.870
Waist circumference	0.079	0.461	−0.079	0.459	0.093	0.388
SBP	0.061	0.573	0.160	0.134	0.053	0.623
DBP	0.042	0.695	0.045	0.677	−0.083	0.438
BMI	0.023	0.827	−0.053	0.624	0.002	0.982

HDL: High-density lipoprotein, LDL: Low-density lipoprotein, BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure

for metabolic syndrome. [73]. Low plasma zinc levels were indicated in obese [62,63], Type 2 diabetic [18], and obese-Type 2 diabetic subjects [15,70]. A study found that there was no statistical correlation between plasma zinc and metabolic syndrome components [74]. In this study, decrease in serum zinc in patients with metabolic syndrome was shown to be negatively correlated with HDL and blood pressure.

CONCLUSION

The results of the study show that only the concentration of zinc affected by HDL, SBP, and DBP as components of the metabolic syndrome, respectively. There is no relationship between copper and iron concentration and metabolic syndrome components. Differences of our results with other studies emphasize on further researches on trace elements and metabolic syndrome and their relationship with different diseases.

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