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THE RELATION OF OMENTIN-1 LEVELS AND SOME TRACE ELEMENTS AS A POTENTIAL MARKERS FOR DIAGNOSIS OF PREDIABETIC OBESE PATIENTS

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Abstract: The obesity is one of the most common physiological disorders, also it is linked with a variety of circumstances like hypertension, dyslipidemia, T2DM, non-alcoholic fatty liver disease, and cardiovascular diseases. The aim of this study was to check the changes and compare serum omentin-1, lipid profile (TC, TG, VLDL-C, LDL-C, and HDL-C), trace elements (Mg, Zn, Cu, Fe) and insulin resistance between the prediabetic obese patients, healthy obese, and control subjects and assess the correlation between omentin-1, lipid profile, trace elements (Mg, Zn, Cu, Fe) levels and insulin resistance in prediabetic obese patients. Correlation analysis between omentin-1 levels with the biochemical parameters in the prediabetic obese patients with WC, body mass index, FBG, Insulin, HOMA-IR, HbA1c, TG, TC, LDL-C, VLDL-C, and copper was found to be negative; while significant positive correlation of omentin-1 with HDL-C, Mg, Zn, and Fe was noticed. Omentin-1 serum concentration level decrease and insulin resistance increased in prediabetic obese patients compared to healthy obese and control individuals. Omentin-1 inversely associated with obesity and insulin resistance, therefore can be used as a biomarker for obesity related metabolic disorders.

Keywords: Obesity, Type2 diabetes mellitus, Trace elements, glycemic indices.

Introduction

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Obesity has become a major health problem, being defined as the abnormal or excess fat accumulation in adipose tissue. The amount of fat differs in distribution in body of individuals. This high distribution of fat in the body leads to weight gain and increase the risks of obesity and other diseases types that caused by obesity. It is present to both genders of all age, diverse socio economic and ethnic groups. The number of obese adults has reached 3.3 billion worldwide.[1]

The equilibrium or homeostatic energy between energy inputs and outputs is controlled by a different relation between the central nervous system (CNS) and a number of organs in the hypothalamus. This is a key region for energy homeostasis that receives multiple adiposities, and nutrient connected signals from peripheral systems that reflect the energy status of the body. The hypothalamus reads these signals and transforms the information, which leads to change in the behavior such as food intake, and physical activity in addition to changes in energy spending, and metabolic processes.[2]

Impaired glucose tolerance (IGT) was prediabetic state of hyperglycemia that is linked with insulin resistance and enlarged risk of cardiovascular pathology. IGT can precede T2DM by many years. IGT was also the risk factor of mortality. Diabetes can be diagnosed based on plasma criteria, ether the fasting plasma glucose (FPB) or the 2-h plasma glucose (2-hPG) value during a 75g oral glucose tolerance test (OGTT), or HbA1c criteria.[3]

Type 2 diabetes mellitus was firstly associated with insulin secretary defects related to inflammation and metabolic stress among other contributors, including genetic factors. Additional classification scheme for

diabetes will likely center on the pathophysiology of the fundamental β-cell dysfunction and the stage of disease as indicated by glucose category: normal, impaired or diabetes.[4] The type2 diabetes mellitus (T2DM) risk was increased with BMI. Different studies illustrate the effect of overweight and obesity on T2DM. An association between obesity and T2DM recognizes certain characteristics of obese persons. This category displays an additional increase the risk of developing diabetes mellitus even after the control T2DM.[4]

Lifestyle modification which improve insulin sensitivity and β-cell function is very important in the running of glucose intolerance.[5] Several studies showed lifestyle interaction can decrease conversion to T2DM.[6,7]

Omentin-1 (interlectin-1) is a recently identified protein consists of 313 aminoacids, it is ant-inflammatory adipokine expressed in stromal vascular-cells of visceral adipose tissue. It is recommended that this protein plays an important role to the physiological difference between visceral, and subcutaneous adipose tissue. Also it is found in human vasculature comprising heart, thymus, small intestine, and colon.[8] Omentin-1 was the main circulating form, and it has a homologue namely omentin-2. Its genes are local neighboring to each other at 1q22-q23 in the area connected to T2DM. Together omentin homologues in circulating form are joined with expression in visceral fat tissue.[9] Omentin-1 was known to control the immune-reactions of the organisms, and have anti-inflammatory effect therefore have a significant relation with markers of inflammatory. They are also involved in defense mechanisms through binding to galacto-furanoses on bacteria and inhibits the TNF-α that mediate introduction of proinflammatory molecules in vascular endothelial- cells.[10]

Omentin-1 elevates insulin signal transduction, controls insulin stimulated glucose transport in human adipocytes (the uptake of basal glucose), and participates in regulation of lipid metabolism. Obesity elevates the danger of multiple metabolic diseases like hyperlipidemia, T2DM, atherosclerosis, and cardiovascular complications.[11] The anti-inflammatory functions of adipose tissue, could be included through various bioactive mediators, known as adipocytes like Omentin-1. This protein is affecting the variance of endothelium dependent vasodilatations. The enhance of endothelium via omentin-1 occurs by suppression of monocytes adhesion to TNF-α stimulated endothelial cells. Thus, ICAM-1 and VACAM-1 gene expression is stopped via inhibition of NF-Kb signaling pathway.[12,13]

Omentin-1 concentration is lower in obesity and DM. This low concentration of omentin-1 is seen in overweight and insulin resistance female patients with polycystic ovary syndrome.[14] Previous studies demonstrated that circulating omentin-1 has the important role in preventing atherosclerosis and has also cardio prolific effect.[15,16] They have been noticed that reduction in weight, increases the circulating omentin-1 concentration. Two reports found that circulating omentin-1 concentration correlates negatively with obesity and insulin resistance, but positively correlates with adiponectin and HDL-Cholesterol.[17,18]

The aim of the study was to investigate and compare serum omentin-1 concentrations between prediabetic obese patients, healthy obese, and control individuals, and to explore correlation of omentin-1 with measures of obesity and insulin resistance. The other goal was to detect its relation with insulin resistance, trace elements, glycemic control and metabolic parameters.

Materials and methods

Subjects

The case control study included three groups: Group 1 (60) prediabetic obese patients, Group 2 (60) healthy obese subjects, and Group 3 (58) control subjects. Diabetes was defined as a fasting plasma glucose value126 mg/dL (≥7mmol/L). The collection of samples was carried out during the period between March 2018 and the end of September 2018. Patients were diagnosed by specialist physicians at AL-Sader Teaching hospital in al-Najaf province, Iraq. Group 1 was formed by prediabetic obese who attended the diabetes center at medical city. The study exclusion criteria included (Cardiac diseases, Hypertension, renal disease, malignancies. The patients were using drugs such as glucocorticoid, infection and inflammation), all these three groups were matched for age.

All subjects were subjected to clinical examination included anthropometric measurements and blood pressure readings. Body mass index (BMI) was calculated as body weight in kilograms divided by square of height in meters (Kg/m^2). Waist circumference (WC) was measured using a non-stretchable measuring tape midway between the interior margin of the ribs and the superior border of the iliac crest during mid expiration, the subjects were asked to stand erect in a relaxed position with both feet together on a flat surface with one layer of clothing. Hip circumference was measured as the maximum circumference around the buttocks posteriorly at the level of greater trochanters and reported in centimeters.

An overnight fasting venous blood sample was obtained from all participants to assess omentin-1 levels and other biochemical parameters.

All samples were stored at room temperature for at least 30 minutes to allow the blood to clot, followed by centrifugation (2000 rpm) for 15 min to separated serum. Serum specimens were aliquoted and stored at -20 ^{o}C until further analysis. The Oral Glucose Tolerance Test (OGTT) was performed in overnight fasting subjects. All subjects received a dose of 75 g glucose in 250 ml of water. Blood Fasting blood samples were collected again after one hour and after two hour of glucose load. Glucose levels during OGTT were measured with the hexokinase method using a commercially available kit (Biolab, France). Lipid profile {Total Cholesterol (TC), Triglycerides (TG), and High-density lipoprotein cholesterol (HDL-C)} were determined by colorimetric method for the quantitative in vitro diagnostic measurement using kits from Biolab, France. Very low density lipoprotein cholesterol (VLDL-C) assay was measured by dividing the triglycerides concentration by five and it represent the concentration in milligram per deciliter,[21] and Low density lipoprotein cholesterol (LDL-C) was measured by the indirect method using Friedewald equation[21].

LDL-C= total cholesterol – (HDL-cholesterol + VLDL cholesterol).

LDL-C = total cholesterol - (HDL-cholesterol + TG/5)

Serum omentin-1 was estimated by ELISA using kits from Elabscience, Germany. Insulin levels were determined using a chemiluminescent assay (USA), and glycosylated hemoglobin (HbA1c) levels were determined using commercially available kits (Biolab, France). Homeostatic model assessment of insulin resistance (HOMA-IR) was calculated using the following formula:

HOMA- IR = [fasting Glucose (mg/dl) x Insulin (μU/ml) / 405].[19]

Statistical analysis

The data were translated into a computerized database structure, and the statistical analyses were carried out using the computer programmed SPSS version 24 (Statistical Package for Social Sciences).

These variables are conveniently described as Mean ± Standard deviation (S.D.), and the ANOVA (analysis of variance) was the parametric statistical analysis to test the significance of difference in means between more than two groups.

The statistical significance, direction and linear strength correlation between two quantitative variables, one of which being a non-normally distributed variable, was measured by Spearman's rank linear correlation coefficient, and a probability (P) value less than the 0.05 was considered statistically significant.

Results

In table 1, the base line characteristics of the study are presented. That includes the data of prediabetic obese patients group, healthy obese group and control group. They contain the number of individuals, age, BMI, WC, WHR, SBP, and DBP. It was found that significant ($P< 0.0005$) elevation of the BMI level in the prediabetic obese group when compared with control group and significant ($P<0.0005$) elevation of the BMI level in the healthy obese group when compared with control group. Also it was significant ($P<0.001$) elevations of the WC and WHR levels in the prediabetic obese patients group when compared with control group and significant ($P<0.001$) elevation of the WC and WHR levels in healthy obese group when compared with control group. On the other hand, no significant variations were indicated in the levels of the age, SBP and DBP in the

groups of prediabetic obese and healthy obese with respect to the group of control subjects.

Table 1. Anthropometric data measurements of the study population.

Parameters	Control Group (Mean ± SD)	Healthy obese Group (Mean ± SD)	Prediabetic obese Group (Mean ± SD)
No (M/F)	58(30/28)	60(35/25)	60(20/40)
Age (years)	42.29 ± 9.20	42.00 ± 7.58	44.00 ± 7.29
BMI (Kg/m^2)	23.71 ± 2.17	35.53 ± 2.73 [a](P<0.0005)	34.03 ± 6.84 [b](P<0.0005)
WC (cm)	70.80 ± 7.50	96.61 ± 4.89 [a](P<0.001)	98.54 ± 3.08 [b](P<0.001)
WHR	0.82 ± 0.04	0.92 ± 0.06 [a](P<0.001)	0.98 ± 0.05 [b](P<0.001)
SBP (mmHg)	110 ± 8.90	120 ± 14.80	125 ± 19.52
DBP (mmHg)	78 ± 1.8	78 ± 2.43	80 ±2.20

[a]Significant difference between values in Group2 and Group1. [b]Significant difference between values in Group3 and Group1, P<0.05 is considered significant. **No**: Number of subjects, **BMI**: Body mass index, **WC**: Waist circumference, **WHR:** ratio of waist to Hip, **SBP**: Systolic blood pressure**, DBP**: Diastolic blood pressure, **SD**: Standard deviation.

In table 2, fasting blood glucose, OGTT after one hour, OGTT after two hour, HbA1c, fasting insulin, and HOMA-IR were measured in 60 prediabetic obese patients group, 60 healthy obese patients group and 58 control patients group. The present study found a significant (p<0.001) increases in the FBG, OGTT, HbA1c, FI, and HOMA-IR levels in prediabetic obese patients group when compared with the control group and healthy obese group. On the other hand significant (P<0.05) increase in HOMA-IR levels in the healthy obese group when compared with control

group. Also significant (P<0.001) increase in FI levels in healthy obese group when compared with control group.

Table 2. Fasting Blood glucose, OGTT, glycosylated hemoglobin, fasting serum insulin, and HOMA-IR in the study subjects.

Parameters	**Control Group (Mean ± SD)**	**Healthy obese Group (Mean ± SD)**	**Prediabetic obese Group (Mean ± SD)**
FBG (mg/dl)	80.05 ± 9.70	83.81 ± 6.30	100.1 ± 15.80 [b](P<0.001) [c](P<0.001)
OGTT (mg/dl) 1 hour	98.7 ± 16.32	100.92 ± 20.5	144.52 ± 10.32 [b](P<0.001) [c](P<0.001)
OGTT (mg/dl) 2 hour	80.23 ± 9.5	83.41 ± 6.72	103.30 ± 16.27 [b](P<0.001) [c](P<0.001)
HbA1c (%)	5.00 ± 0.20	5.1 0± 0.50	6.60 ± 0.60 [b](P<0.001) [c](P<0.001)
FI (μU/ml)	5.32 ± 2.73	8.54 ± 5.98 [a](P<0.001)	11.35 ± 3.24 [b](P<0.001) [c](P<0.001)
HOMA-IR	1.10 ± 0.65	2.45 ± 0.95 [a](P<0.05)	5.36 ± 1.31 [b](P<0.001) [c](P<0.001)

[a]Significant difference between values in Group2 and Group1. [b]Significant difference between values in Group3 and Group1. [c]Significant difference between values in Group3 and Group2, P<0.05 is considered significant. **OGTT:** Oral Glucose Tolerance Test, **FBG:** Fasting blood glucose, **HbA1c:** Glycated hemoglobin, **FI:** Fasting Insulin.

In table 3 the results of TC, LDL-C, VLDL-C, and TG demonstrated significantly (P<0.0005) higher levels in prediabetic obese patients group when compared with the control group and significant (P<0.0005) elevation levels of healthy obese group when compared with the control group.

Whereas non-significant variation in levels of TC, LDL-C, VLDL-C, and TG in prediabetic obese patients group when compared with those of healthy obese group. The decrease in the mean value of serum HDL-C of prediabetic obese patients group and of healthy obese group when compared with mean value for control group, showed no significant variation of HDL in all these three groups.

Table 3. Lipid profile parameters in prediabetic obese, healthy obese and control groups.

Parameters	Control Group (Mean ± SD)	Healthy obese Group (Mean ± SD)	Prediabetic obese Group (Mean ± SD)
TC (mg/dl)	142.08 ±10.23	241.03 ± 7.4 [a](P<0.0005)	244.76 ± 6.64 [b](P<0.0005)
HDL-C (mg/dl)	56.07 ± 4.58	53.11±4.74	48.66 ± 5.27
LDL-C (mg/dl)	84.53 ± 12.22	151.78 ± 6.36 [a](P<0.0005)	153.68 ± 5.83 [b](P<0.0005)
VLDL-C (mg/dl)	27.52 ± 3.73	47.10 ± 7.61 [a](P<0.0005)	50.29 ± 5.22 [b](P<0.0005)
TG (mg/dl)	103.49 ± 21.20	241.93 ± 9.18 [a](P<0.0005)	246.08 ± 12.25 [b](P<0.0005)

[a]Significant difference between values in Group2 and Group1. [b]Significant difference between values in Group3 and Group1, P<0.05 was considered significant. **TC:** Total cholesterol, **HDL-C:** High density lipoprotein- Cholesterol, **LDL-C:** Low density lipoprotein- Cholesterol, **VLDL-C:** Very low density lipoprotein-Cholesterol, **TG:** Triglycerides.

In table 4 shows that omentin-1 levels were significantly (P<0.0005) lower in prediabetic obese group (11.18 ± 3.21 ng/ml) and healthy obese group (33.97 ± 5.77 ng/ml) when compared with control group (44.98 ± 3.2 ng/ml). Also prediabetic obese group showed significantly (P<0.0005) lower levels of serum omentin-1 in compared to healthy obese group.

Table 4. Anti-inflammatory marker in prediabetic obese, healthy obese and control subjects.

Parameters	Control Group (Mean ± SD)	Healthy obese Group (Mean ± SD)	prediabetic obese Group (Mean ± SD)
Omentin-1(ng/ml)	44.98 ± 3.2	33.97 ± 5.77 [a](P<0.0005)	11.18 ± 3.21 [b](P<0.0005) [c](P<0.0005)

[a]Significant difference between values in Group 2 and Group 1. [b]Significant difference between values in Group 3 and Group 1. [c]Significant difference between values in Group 3 and Group 2, P<0.05 was considered significant.

In table 5 that shown four trace elements (magnesium, zinc, copper, and iron) were evaluated of prediabetic obese patients group, healthy obese group and control group.

Table 5. Trace elements parameters in the study subjects.

Parameters	Control Group (mean ± SD)	Healthy obese Group (mean ± SD)	prediabetic obese Group (mean ± SD)
Mg (mg/dl	2.12 ± 0.24	1.63 ± 0.13 [a](P<0.001)	1.48 ± 0.12 [b](P<0.001)
Zn (µg/dl	96.79 ± 3.94	67.24 ± 2.73 [a](P<0.001)	65.76 ± 2.20 [b](P<0.001) c (P<0.01)
Cu (µg/dl	83.28 ± 4.48	145 ± 3.04 [a](P<0.001)	148.72 ± 3.98 [b](P<0.001) [c](P<0.001)
Fe (µg/dl	70.11 ± 2.64	60.21 ± 3.64 [a](P<0.001)	57.54 ± 2.50 b (P<0.001) c (P<0.001)

[a]Significance difference between values in Group 2 and Group 1. [b]Significant difference between values in Group 3 and Group 1. [c]Significant difference between values in Group3 and Group2, P<0.05 is considered significant. **Mg**: Magnesium; **Zn**: zinc; **Cu**: copper; **Fe**: Iron.

The concentration of magnesium was significantly (P<0.001) lower in prediabetic obese patients group when compared with control group and significantly (P<0.001) lower in healthy obese group when compared with control group. Also non-significant variation was seen in the magnesium levels of prediabetic obese patients group when compared with healthy obese group **(Figure 1).**

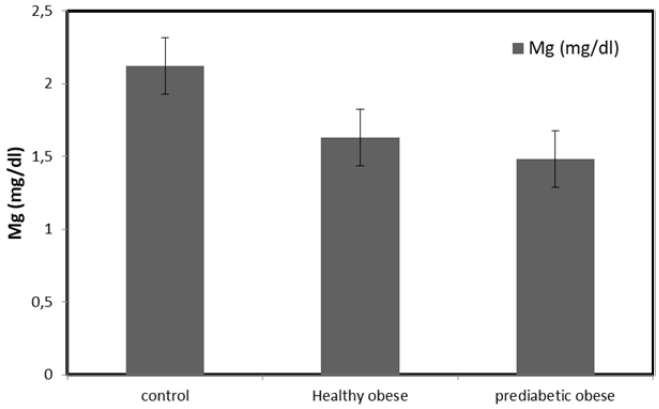

Figure 1. Mean distribution of Magnesium (mg/dl).

Also serum zinc levels were significantly (P<0.001) lower in prediabetes obese patients group when compared with control group, and significant (P<0.01) lower of Zn levels in prediabetic obese patients group when compared with healthy obese group. In addition, significant (P<0.001) lower in Zn levels of healthy obese group when compared with control group (**Figure 2**).

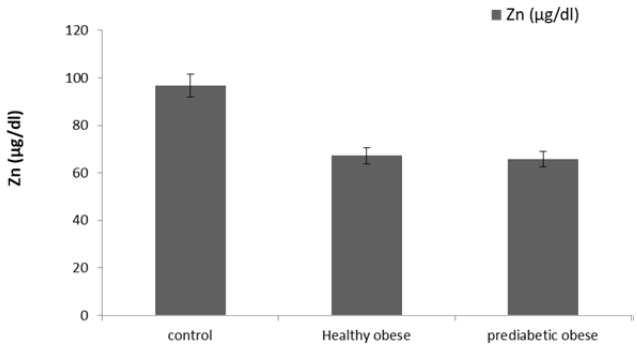

Figure 2. Mean distribution of Zinc (µg/dl).

Serum iron level was significantly (P<0.001) lower in prediabetic obese patients group when compared with healthy obese group and control group. In addition the level of iron was significantly (P<0.001) lower in healthy obese group when compared with control group (**Figure 3**).

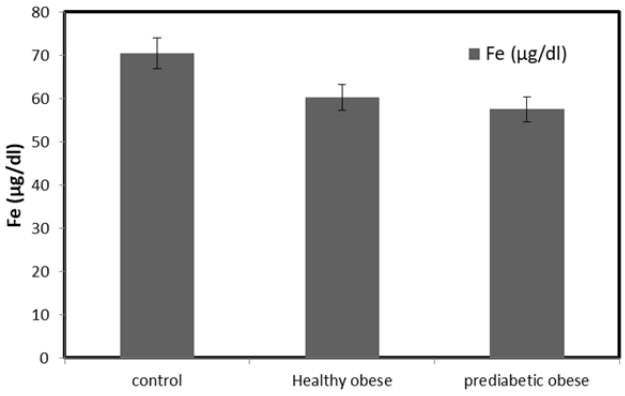

Figure 3. Mean distribution of Iron (µg/dl).

On the other hand, significant (P<0.001) elevation was indicated in the levels of copper in the group of prediabetic obese patients with respect to the group of healthy obese and control. Also the copper shows significant (P<0.001) elevation in the healthy obese group when compared with those of control group (Figure 4).

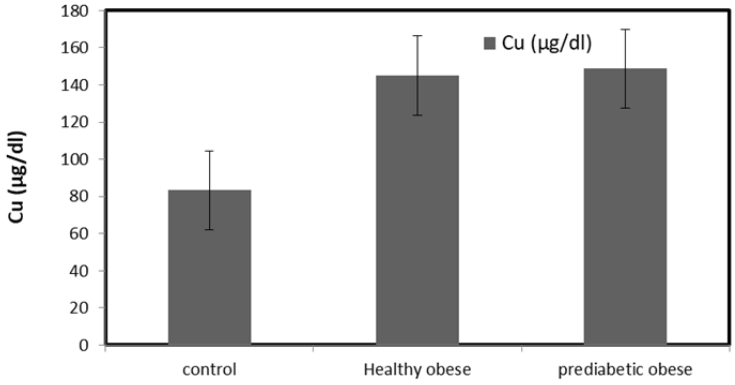

Figure 4. Mean distribution of Copper (µg/dl).

A significant positive correlations of prediabetic obese patients were obtained for HDL, Mg, Zn, Fe, while significant negative correlations were obtained for WC, BMI, FBG, insulin, HOMA-IR, HbA1c, TG, cholesterol, LDL, VLDL and Cu (Table 6).

Table 6. The relevance of omentin-1 with the biochemical parameters in the prediabetic obese patients.

Parameters	Omentin-1	
	r	P
WC (cm)	-0.855	0.0005
BMI(Kg/m^2)	-0.784	0.0005
FBG (mg/dl)	-0.925	0.0001
Insulin (µu/ml)	-0.938	0.0005
HOMA-IR	-0.970	0.0005
HbA1c (%)	-0.775	0.0001
TG (mg/dl)	-0.932	0.0005
Cholesterol (mg/dl)	-0.938	0.0005
HDL (mg/dl)	0.619	0.0001
LDL mg/dl)	-0.939	0.0005
VLDL (mg/dl)	-0.901	0.0005
Mg (mg/dl)	0.872	0.0005
Zn (µg/dl)	0.921	0.0005
Cu (µg/dl)	-0.975	0.0005
Fe (µg/dl)	0.771	0.0001

WC: Waist Circumference, **BMI**: Body mass index, **FBG**: Fasting blood glucose, **HOMA**: Homeostatic model assessment, **IR**: Insulin resistance, **HbA1c**: Glycosylated hemoglobin, **TG**: Triglycerides, **HDL**: High density lipoprotein **LDL**: Low density lipoprotein, **VLDL**: Very low density lipoprotein, Mg: Magnesium, Zn: Zinc, Cu: copper, Fe: Iron.

Discussion

On the one hand omentin-1 is an anti-inflammatory adipokine, on the other hand, it plays a significant role in modulating insulin sensitivity by paracrine and endocrine factor which controls the insulin sensitivity and glucose metabolism on the restricted level of omental adipose tissue, and also the increasing of the insulin signal transduction through activation of

the protein kinase (AKT/protein kinase B). Therefore, the distribution of fat in the body between the visceral and fat depot in subcutaneous it was enhanced.[20] Omentin-1 accelerated insulin to control glucose transport but has no effect on the basal glucose transport, which was an indication that is not possessing intrinsic insulin activity. Secreted omentin-1 in blood human leads to an accelerated insulin sensitivity and glucose metabolism at remote sites like muscle, liver and subcutaneous fat.[21]

Various studies reported that omentin-1 concentration decreased in T2DM, impaired glucose tolerance and obesity[21,22] hypothesized the abnormalities in circulating omentin-1 levels may be reflected by metabolic disorder that take place in the adipose tissue. Therefore, in the present study serum omentin-1 level in 60 prediabetic obese patients, 60 healthy obese patients and 58 control subjects was measured.

Our data support a statistically significant ($P<0.0005$) decrease in serum omentin-1 in prediabetic obese patients group and healthy obese group in compared with control group and also show significant ($P<0.0005$) decrease in serum omentin-1 in prediabetic obese patients when compared with healthy obese subjects.

The present study is in agreement with Catoi, *et al*.[23] study on the morbid obesity subjects which was demonstrated that serum omentin-1 levels was decreased in morbid obese subjects when compared with normal weight healthy subjects and the results were inversely linked with chronic inflammation. There was no known mechanism that leads to decrease omentin-1 levels in overweight and T2DM. Nevertheless, there were some reports that concluded insulin and glucose significantly reduce the omentin mRNA expression and omentin protein biosynthesis *in vitro* omential adipose tissue. Therefore, hyperinsulinemia leads to decrease the circulating

omentin-1 level in normal subjects and this supports the idea that insulin and glucose are directly or indirectly involved in the regulation of omentin-1 synthesis.[24,25]

This study is in agreement with study done by Moreno-Navarrete *et al.*[26] demonstrating that circulating omentin-1 concentrations were negatively correlated with WC, BMI, HOMA-IR, FBG and insulin, also positively correlated to HDL. Another study done by Catoi, *et al*[23] established that lower serum omentin-1 levels in obese children could be negatively correlated with BMI, WC, HOMA-IR and insulin levels, suggesting that omentin-1 might be a biomarker for metabolic dysfunction in childhood. El-Mesallamy, *et al*.[27] indicated a significant decrease in serum omentin-1 levels in T2DM, even after the adjustment for the effect of age or BMI. Moreover, the authors proposed a simple linear analysis and significant negative correlation between omentin-1 and BMI, FBG and HOMA-IR.

Several studies found that decreased serum omentin-1 in obese and non-obese females with polycystic ovary syndrome who have increased serum insulin concentrations.[16,27] The physiological role of omentin-1 in homeostasis of glucose is still unknown but Yang RZ, *et al*.[28] observed insulin stimulated glucose transport by increased protein kinase b (AKT) phosphorylation in human adipocytes, suggested that omentin may improve insulin sensitivity. Some researchers also observed that omentin-1 enhanced only insulin mediated glucose transport and didn't stimulated basal glucose transport on its own. Further, omentin-1 increased the activity of insulin receptor substrate (IRS) due to inhibition of mammalian target of rapamycin, which in turn was a consequence of Amp protein kinase (Amppk) activation.[29]

A very important observation of the present study is that significant negative correlation of omentin-1 with WC, FBG, insulin, HOMA-IR, cholesterol and triacylglyceride and significant positive correlation with HDL. The positive correlation of omentin-1 with HDL has been previously described in obesity, metabolic syndrome and cardiovascular disease.[30] However, the mechanism that explain these results was not clear. Most probably, omentin-1 might affect insulin signaling and regulation of lipoprotein metabolism by insulin and later impairs HDL production.

Trace elements are essential nutrients with regulatory, immunologic, and antioxidant functions resulting from their action as essential components or cofactors of enzymes throughout metabolism. Trace elements and minerals influence the pathogenesis of obesity and diabetes and their complications, mainly through their involvement in peroxidation and inflammation.[31]

Copper is an essential micronutrient required for the activity of many enzymes, with important role in the human body, copper is involved in the function of several copper enzymes, such as ceruloplasmin. Circulating levels of copper were reported to be significantly higher in obese patients compared to normal body weight controls. Some reports showed a negative correlation between serum copper and high density lipoprotein-cholesterol. The mechanism for its elevation in obese patients was unclear but it was thought to be due to pro-inflammatory cytokines released from adipose tissue such as 1L-1 enhance intra-cellular zinc accumulation with intra-cellular copper efflux, and when released to blood it binds to ceruloplasmin.[32]

While zinc was important a trace element has a role in enhance appetite. It was playing an important role in integrity of the immune system

and wound healing. Also it was found to enhance insulin synthesis, storage and release**.** Zinc deficiency in obese subjects causes resistance to insulin and intolerance of glucose but has also shown to be linked to obesity. As insulin resistance lead to pathological conditions such as metabolic disorder and obesity.[33] However, the exact mechanism is unclear. It may be due to zinc accumulation in adipose tissue as result of increased production of adipokines, increased leptin production. They induce chronic inflammation and expression of metallothionein and zinc-copper transporter in hepatocytes. The presence of these proteins results in accumulation of these metals in hepatocytes and adipose tissue and decreased serum concentration[34]. Therefore decreased serum zinc concentration in obese patients plays a role in insulin resistance. In the present study, lower serum zinc level was detected in prediabetic obese patients group when compared with control group and healthy obese group. Also lower serum zinc levels in healthy obese group in compared to control group. Zavala, *et al*.[35] has indicated that serum zinc concentration in obese children was associated with lipid, inflammation and insulin resistance. Another study done by Kelishadi, *et al*.[36] has demonstrated that zinc supplement administered to patients with T2DM can reduced triglyceride and increase High density lipoprotein cholesterol.

In a case control study done by Azab, *et al*.[37] serum iron levels was lower in obese compared to non-obese children was noticed. Zittermann, *et al*.[38] estimate a moderate iron absorption rate in women with obesity and this lead to iron deficiency. In contrast, Menzie, *et al*.[39] has found that the iron consumption is linked with the absorption of iron and not related with obesity linked hypoferremia.

Magnesium was the most abundant intracellular cation, approximately 50% of total body magnesium is found in bones. The other 50% is found inside cells of body. Magnesium is necessary for absorption and utilization of nutrients; carbohydrates, fats and proteins. Also it is a critical cofactor for hundreds of enzymes especially those involved in glucose metabolism and a direct antagonist of intracellular calcium. In hypomagnesaemia, when magnesium levels were reduced, insulin sensitivity of peripheral tissue through reduced auto-phosphorylation of tyrosine kinase, a component of β-subunit of the insulin receptor for which magnesium is a co-factor. Also, hypomagnesaemia may be associated with reduced β-cells proliferation and thus affecting insulin production.[40]

The findings of the present study, there were significant decrease in concentrations of zinc, magnesium and iron in prediabetic obese patients when compared to healthy obese and control subjects. Also decrease serum concentrations of zinc, magnesium and iron in healthy obese in compared to control subjects was noticed. All these findings support a correlation between zinc, magnesium and iron deficiency and obesity. The prediabetic obese patients may be at a greater risk of developing imbalance and deficiencies of trace elements compared to healthy obese and control subjects. Further studies need to elucidate the relationship between the trace elements and obesity.

In the present study the positive correlation between omentin-1 and Mg, Zn, and Fe; while the negative correlation between omentin-1 and Cu in prediabetic obese patients was found. The mean serum levels of magnesium, zinc, copper, and iron between the three groups were significantly different. For defining the role of serum trace elements in prediabetic obese patients more research is necessary. The results of the present study showed that these elements did play a prominent role in the pathogenesis of prediabetic obese patients.

Conclusions

Serum omentin-1 levels of prediabetic obese patients are significantly lower compared with healthy obese and control subjects. The present results suggest that serum omentin-1 levels might be used as a novel marker for prediabetic obese patients, with decreased levels of omentin-1 being asymptomatic of prediabetic obese, and revealed that these trace elements such as Mg, Zn, Cu, Fe play a prominent role in the pathogenesis of prediabetic obese.

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