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Reduced Omentin-1 Concentrations in the Serum of Normoglycemic First-Degree Relatives of Individuals with Type 2 Diabetes

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ABSTRACT

Type II diabetes mellitus (T2DM) is characterized by insulin resistance (IR) and impaired insulin secretion. First-degree relatives (FDRs) of T2DM patients are at higher risk of developing insulin resistance and T2DM. Omentin-1 an adipokine, plays a role in insulin sensitivity and glucose metabolism. This study aimed to evaluate serum omentin-1 levels in normoglycemic FDRs and its correlation with various parameters. This cross-sectional study included 96 participants 48 normoglycemic FDRs (cases) and 48 age and sex-matched controls. Cases were further divided into normal-weight and obese/overweight subgroups based on body mass index (BMI) and waist circumference (WC). Serum omentin-1 levels, physical parameters (BMI and WC) and biochemical parameters (fasting blood sugar (FBS) total cholesterol (TC) triglycerides (TG) were measured. Statistical analyses included t-tests, Spearman's rank correlation and Mann-Whitney u-test. Serum omentin-1 levels were significantly lower in FDRs compared to controls ($p<0.001$). Among FDRs, omentin-1 levels were lower in the obese/overweight subgroup compared to the normal-weight subgroup ($p = 0.016$). There was a significant negative correlation between omentin-1 levels and BMI in FDRs ($rs = -0.38$, $p<0.001$). TC levels negatively correlated with omentin-1 in FDRs ($rs = -0.219$, $p = 0.032$). No significant correlation was found between omentin-1 levels and FBS, WC or TG in any group. Gender did not significantly affect omentin-1 levels. This study reveals reduced serum omentin-1 levels in normoglycemic FDRs, especially in those who are obese/overweight, suggesting a potential role for omentin-1 in the patho-physiology of T2DM. Omentin-1 may play a role in glucose metabolism and insulin sensitivity. Strategies to maintain healthy body weight and promote physical activity could help improve omentin-1 levels and reduce the risk of T2DM in FDRs. Type II diabetes mellitus, omentin-1, first-degree relatives, insulin resistance, obesity, glucose metabolism, adipokines.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a multifactorial disease marked by compromised pancreatic insulin production and resistance to insulin across critical tissues, such as liver, muscle and fat. This condition is significantly influenced by environmental determinants, particularly those contributing to obesity. With an estimated 65.1 million individuals diagnosed, India ranks as the second-highest nation globally in terms of diabetes prevalence[1].

Individuals who are first-degree relatives (FDRs) of patients with T2DM have a higher susceptibility to insulin resistance[2]. Notably, research has indicated that even in the absence of insulin resistance (IR) beta cell dysfunction is observable in T2DM patient's progeny. These FDRs carry an approximate 40% risk of developing T2DM over their lifetime[3]. Additionally, the association between obesity, particularly an increased body mass index and waist-hip ratio (WHR), and the rise in conditions such as impaired glucose tolerance, dyslipidemia, notably hypertriglyceridemia and hypertension has been well-documented in population studies[4].

Omentin is a recently identified adipokine, expressed specifically in fat depots and was first discovered in a visceral omental adipose tissue CDNA library. The gene encoding Omentin is found in the 1q22q23 chromosomal region which has shown linkages to T2DM in various demographics[5]. Omentin MRNA is primarily expressed in the stromal vascular component of visceral fat tissue and is minimally present in subcutaneous fat and mature adipocytes[6]. There are two isoforms of Omentin. Omentin-1 and Omentin-2 with Omentin-1 being the predominant form in human plasma[6]. In vitro studies demonstrate that recombinant Omentin-1 enhances insulin-mediated glucose uptake and AKT phosphorylation in human subcutaneous and visceral adipose cells but it does not influence basal glucose uptake. Recent research has established a negative correlation between plasma levels and gene expression of Omentin-1 with obesity and insulin resistance and a positive correlation with adiponectin and HDL cholesterol levels[7].

There is a scarcity of studies addressing the role of omentin-1 in the pathophysiology of T2DM among FDRs. Thus, this study is designed to assess serum omentin levels in normoglycemic FDRs and to establish correlations with various health parameters. This investigation specifically focuses on Serum Omentin-1 Levels in normoglycemic first-degree relatives of individuals with type 2 diabetes.

MATERIALS AND METHODS

The present study was carried out in Department of Biochemistry, Mamata Medical College and General Hospital. The study was approved by human ethical committee. Informed consent was obtained from the subjects selected. This cross-sectional study enrolled a total of 96 participants, out of this, 48 normoglycemic persons, who were first degree relatives of T2DM patients were selected as cases and 48 age and sex matched healthy persons with no history of diabetes in parents or siblings were selected as controls for the study. Among the cases, 24 will be of normal weight and the remaining 24 will be obese/overweight. The subjects for the present work were selected based on following criteria.

Inclusion criteria:

- First degree relatives of diabetic patients
- Age group of 20-45 years of both sexes
- Non-smoker
- Non-alcoholic
- Informed written consent given by subject or their guardians

Exclusion criteria:

- Patients not giving written consent to participate in the studies
- Type 1 diabetes mellitus
- Cardiovascular diseases
- Renal and hepatic dysfunction
- Diseased persons or those taking medications for some illness

Sample collection and preparation: 5 mL of blood sample was collected from the subjects as well as controls after overnight fasting (12 hrs) by venipuncture and then centrifuged, aliquots of serum were stored at-80°C until assayed.

Total cholesterol and triglycerides were measured using cholesterol oxidase/peroxidase, glycerol phosphate oxidase/peroxidase methods. Serum Omentin levels were measured using raybio omentin enzyme immunoassay. Body mass index (BMI kg m^{-2}) and waist circumference (cm) were measured in each subject.

Statistical analysis: All values were expressed as Mean±SEM. The results obtained were analysed statistically using the unpaired student t-test to evaluate the significance of difference between the mean values. Spearmann's rank correlation coefficient was used for correlation. All data analysis was done using Microsoft Excel and the statistical package for the Social Sciences (SPSS, Version, 16.0) software for Windows. Differences were considered statistically significant at a level of $p<0.05$.

RESULTS

The serum omentin levels were estimated and compared among different groups in the study population. Also, the correlation between omentin

Table 1: Comparison of serum omentin 1 levels between males and females

Total (n = 96)	No	Mean±SD	Mann whitney U	p-value
Male	38	50.42±28.09	927.5	0.191
Female	58	43.96±27.24		
Cases (n = 48)				
Male	18	27.41±21.23	232	0.418
Female	30	23.37±18.12		
Controls (n = 48)				
Male	20	71.13±13.42	216.5	0.18
Female	28	66.03±15.4		

Table 2: Comparison of biochemical parameters among cases and controls. (Mean±SD)

Variables	Cases (n = 48)	Controls (n = 48)	p-value
Serum omentin	24.88±19.22	68.15±14.68	<0.001
FBS	88.88±7.525	86.23±6.656	0.086
Cholesterol	177.56±13.855	172.58±10.73	0.052
TG	103.42±21.296	85.31±11.346	<0.001

Table 3: Comparison of physical parameters among cases and controls. (Mean±SD)

Variables	Cases (n = 48)	Controls (n = 48)	p-value
BMI	23.18±1.534	22.19±0.63	<0.001
WC	81.84±6.07	75.15±4.72	<0.001

Table 4: Comparison of serum omentin 1 levels between obese/overweight and normal weight groups

Total (n = 48)	No	Mean±SD	Mann whitney U	p-value
Obese/overweight	24	18.73±16.69	171	0.016
Normal weight	24	31.03±19.95		

Table 5: Correlation between Serum Omentin 1 levels and physical and biochemical parameters (FBS, Total Cholesterol, TG, BMI, and WC)

	Total sample		Cases		Controls	
Variables	Spearman's rho (r) s	p-value	Spearman's rho (r)s	p-value	Spearman's rho (r)s	p-value
Omentinv/s BMI	-0.38	0	-0.33	0.02	-0.09	0.56
Omentinv/sWC	-0.42	0	-0.17	0.25	0.1	0.52
Omentinv/sFBS	-0.12	0.26	0.02	0.89	0.05	0.76
Omentinv/sTC	-0.219	0.032	-0.308	0.033	0.09	0.545
Omentinv/sTG	-0.375	0	-0.281	0.053	0.069	0.64

Table 6: Comparison of serum Omentin levels in different groups

Variable	Cases	Controls	Males	Females	Obese	Non-obese
Mean±SD	24.88±19.22	68.15±14.68	50.42±28.09	43.96±27.23	18.73±16.69	31.03±19.95
Median	20.8	66.35	57.36	48.05	11.86	25.45
Omentin						
Max	79.68	98.94	98.94	98.94	64.85	79.68
Min	3.39	45.5	5.91	3.39	3.39	5.68

levels with various physical and biochemical parameters was done. The results are presented in the form of tables and graphs.

A cross sectional study was conducted among 96 subjects with females comprising 60.42% and males 39.58% of the age group 20-45 years the mean age being 30.15±5.13 years and was grouped into two. The first group included 48 subjects who were first degree relatives of type 2 diabetic patients and were normoglycemic (cases) and the second group included 48 age and sex matched apparently healthy individuals, with no history of diabetes in parents or siblings (control).

In group one (n = 48) 37.5% are males and 62.5% are females with the mean age being 30.77±5.11 years. In group two (n = 48) 58.3% were females and 41.67% males. The age group included was 20-45 years with mean age being 29.52±5.11 years (Table 1 and 2).

The physical parameters measured include BMI and WC and based on these physical parameters group 1 is partitioned again into 2 groups. First group included 24 subjects who are obese/overweight (BMI >23 Kg m^2, WC >90 cm for males and >80cm for females) and second group included 24 normal weight subjects. The Serum Omentin levels are estimated and compared among these two groups also (Table 3 and 4).

Based on these physical parameters group 1 is partitioned again into 2 groups. First group ssincluded 24 persons, who are obese/overweight (BMI >23 Kg m^2, WC >90 cm for males and >80 cm for females) and second group included 24 normal weight persons. The Serum Omentin levels are estimated and compared between these two groups also.

The table 5 displays correlations between serum Omentin 1 levels and different health parameters in a study's total sample, as well as in two groups (cases and controls). It uses Spearman's rho (rs) values and p-values for statistical significance. Notable findings include a negative and significant correlation between Omentin 1 levels and body mass index (BMI) and waist circumference (WC) in the total sample but these correlations vary in strength and significance within the case and control groups. There's no significant correlation between Omentin 1 levels and fasting blood sugar (FBS) or triglycerides (TG) in any group. However, there is a significant negative

correlation between Omentin 1 levels and total cholesterol (TC) in both the total sample and the cases group but not in the controls group. These findings suggest potential relationships between Omentin 1 and certain health parameters, which may vary depending on the individual's health status.

Table 6 presents a comparison of serum Omentin levels across different groups. It includes cases, controls, males, females, obese individuals and non-obese individuals. The table provides statistics like mean (average) standard deviation (a measure of variation) median (middle value) maximum (highest value) and minimum (lowest value) Omentin levels for each group. These statistics help understand how Omentin levels vary within and between the groups. For example, it shows that cases have lower mean Omentin levels compared to controls and there is variability in Omentin levels within each group. Additionally, it highlights the range of Omentin levels, from the lowest to the highest, in each group, giving insights into the overall distribution of Omentin levels among these different categories of individuals.

DISCUSSIONS

Impaired glucose metabolism is a common finding in first-degree relatives (FDRs) of individuals with type 2 diabetes mellitus (T2DM) who also tend to display compromised β-cell functionality. This impairment affects their insulin and amylin secretory responses following glucose stimulation[8]. Both diminished insulin sensitivity and β-cell dysfunction are predictive of the progression to diabetes[9] placing FDRS at an elevated risk for developing insulin resistance and T2DM when compared to the general population.

Omentin-1 a novel adipokine expressed in a depot-specific manner, appears to modulate insulin sensitivity through its paracrine or endocrine effects[5]. Inverse correlations between omentin-1 levels, obesity measures, insulin resistance and positive correlations with adiponectin levels have been documented[7]. Conditions such as polycystic ovary syndrome, associated with obesity and insulin resistance have been shown to exhibit reduced omentin-1 mRNA and protein levels. Notably, increases in circulating omentin-1 levels have been linked to weight loss and enhancements in insulin sensitivity[10]. Furthermore, aerobic exercise in overweight and obese men resulted in elevated omentin-1 levels[11] and individuals with metabolic syndrome have been reported to have lower omentin-1 levels than controls[12], supporting omentin-1's involvement in insulin resistance pathophysiology. Our study observed notably lower circulating omentin-1 levels in FDRs compared to controls, mirroring findings by Akbarzadeh *et al*.[13] who also suggested that these reduced levels might indicate a predisposition to T2DM. Similarly, serum omentin levels were found to be lower in patients with T2DM and impaired glucose regulation compared to those with normal glucose tolerance[14].

These findings underscore omentin's significance in glucose metabolism. In vitro experiments have shown that Omentin augments insulin signal transduction through protein kinase B activation, improving insulin-mediated glucose transport in adipocytes. The observed decrease in serum Omentin-1 in patients with impaired glucose regulation may lead to reduced insulin-stimulated glucose uptake in adipose tissue or other insulin-responsive tissues, potentially contributing to insulin resistance and diabetes onset.

In our research a marked decrease in serum omentin levels was noted in the obese/overweight group versus the non-obese group, aligning with reports of diminished omentin MRNA expression in those with T2DM and obesity. Studies like those by Batista *et al*.[15] indicate a correlation between omentin-1 mRNA and plasma levels, suggesting that visceral fat's omentin-1 gene expression may predict circulating omentin-1 levels[6]. Dostalova study reported decreased serum omentin in both obese individuals and T2DM patients compared to controls, yet found no significant correlation with fasting glucose levels a finding consistent with our results[16]. Our study also established a significant negative correlation between omentin and BMI in FDRs but did not find a significant association with waist circumference (WC).

Cholesterol levels showed no significant variation between cases and controls, however, in FDRS a negative correlation with omentin levels was noted. While triglyceride (TG) levels differed significantly, no correlation with serum omentin was observed. Other studies have reported inverse relationships between omentin-1 and lipid parameters, suggesting omentin-1's role in lipid metabolism, potentially through the stimulation of 5-AMP-activated protein kinase, a known inhibitor of cholesterol synthesis[17,18]. Additionally a positive correlation between omentin-1 and HDL has been shown in other research[19]. Batista's study further supports the association between higher omentin levels with a leaner phenotype and suggests that elevated omentin may counteract the pathophysiological implications of obesity, specifically diabetes[6].

Regarding gender differences, our study found higher serum omentin levels in males compared to females, albeit not statistically significant. This finding could be attributed to the negative correlation between omentin-1 and adiposity and the higher adiposity generally found in females, with omentin-1 also being inversely related to ß-estradiol. This is in line with reports of higher serum omentin-1 levels in males and supports de Souza Batista's findings of women exhibiting higher circulating omentin-1 levels with a broader variation in relation to BMI[6].

CONCLUSION

In summary, our study revealed lower serum omentin-1 levels in first-degree relatives of type 2 diabetes patients, especially in the obese group. No gender differences were observed. We found a negative correlation between omentin levels, BMI and TC in FDRs but no significant associations with FBS, WC or TG. These findings suggest a potential role for omentin-1 in diabetes patho-physiology. Lower omentin levels may contribute to increased diabetes risk, especially when combined with other risk factors. Promoting healthy body weight through regular exercise may help improve omentin levels and potentially reduce diabetes risk in FDRS.

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