STUDY OF RELATIONSHIP BETWEEN THE PROTEIN OXIDATION MARKERS AND ADIPOKINES IN OBESE TYPE 2 DIABETIC PATIENTS

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ABSTRACT

Objective: This study was done to explore the correlation if any, between obesity markers adiponectin, leptin, and protein oxidative stress (OS) status in obese with and without type 2 diabetic mellitus (T2DM) patients.

Methods: In the present study, 30 healthy subjects, 30 obese non-diabetics, and 30 obese T2DM patients were enrolled. Protein OS parameters such as advanced oxidation of protein products (AOPPs) and protein carbonyl (PC) were estimated. Serum leptin, adiponectin, and insulin levels were measured by ELISA.

Results: The AOPP, PC, leptin, leptin adiponectin ratio (LAR), insulin, and homeostasis model assessment of insulin resistance (HOMA-IR) levels were significantly higher in obese non-diabetic and obese T2DM as compared to healthy control (p<0.001). However, serum adiponectin levels were significantly lower in obese non-diabetic and obese T2DM as compared to control (p<0.001). HOMA-IR and LAR both the index of IR were increased in obese non-diabetic and obese T2DM. Positive correlations were observed for AOPP with body mass index, PC in obese non-diabetic and with fasting blood glucose, postprandial blood glucose, HOMA-IR, and PC in obese T2DM. A negative correlation was found between PC and adiponectin in obese non-diabetic and obese T2DM. A significant inverse correlation was obtained between leptin and adiponectin in obese T2DM only.

Conclusion: The present study suggested that increased protein OS, hyperinsulinemia, and hyperleptinemia may lead to hypoadiponectinemia in obese with and without T2DM. Moreover, determination of protein oxidation markers can be useful for monitoring the dysregulation of adipokines and glucose metabolism in obesity and T2DM.

Keywords: Obesity, Type 2 diabetes, Adiponectin, Leptin, Protein carbonyl.

INTRODUCTION

Obesity is an epidemic and worldwide complication that represents a major health issue of the 21st century. Many studies have shown that obesity, especially visceral obesity is linked to chronic low-grade inflammation in hypertrophied adipose tissue that leads to initiation and progression of metabolic disorders such as dyslipidemia, hypertension, atherosclerosis, insulin resistance (IR), and type 2 diabetic mellitus (T2DM) [1]. Adipose tissue is not only a major source of energy for the human body but also inert storage reservoir for lipids [2]. The term adipokines can be defined as a biologically active substance released by adipose tissue [3]. It is now considered as a largest endocrine organ of the body that helps in the regulation of glucose and lipid metabolism, insulin sensitivity and secretion, inflammatory process, appetite, satiety, energy expenditure, endothelial function, blood pressure, and neuroendocrine regulation [4]. Most of the adipokines are proinflammatory and less the number of anti-inflammatory adipokines [5,6].

Adiponectin is an anti-inflammatory 30 kDa plasma protein and abundantly expressed in white adipose tissue [7]. A large number of experimental studies on rodent and cell culture model have demonstrated that adiponectin has a protective role in cardiovascular diseases [8]. In human studies decreased circulating levels of adiponectin in patients with cardiovascular disease give support to these findings [9]. A decrease in the level of adiponectin has been associated with IR, dyslipidemia, and atherosclerosis in human and rodents [6, 9]. It has a protective role against metabolic diseases and promotes insulin sensitivity [10]. It also maintains and widespread healthy adipose tissue by preventing ectopic lipid accumulation in an animal model and enhances insulin sensitivity [9,11].

In contrast, leptin is proinflammatory, a product of obese (*ob*) gene is a 16-kDa circulating protein hormone produced by adipocytes. It is an adipokines and a key molecule that regulates food intake and body weight [12]. The level of plasma leptin is directly proportional to the mass of body fat [13]. It also plays an important role in the regulation of body metabolism, energy homeostasis, and neuroendocrine function [14]. It acts by binding to circulating receptors, triggers Janus kinase, and induces signal transducer and activator of transcription pathway [15]. Increased leptin directly modulates pancreatic beta cells functions and indirectly through central neural pathways leading to progression of IR and T2DM [4,16]. Dysregulation of adipokines occurs through the generation of reactive oxygen species (ROS) in adipose tissue induces systemic oxidative stress (OS) in obesity. Moreover, the following OS is, directly and indirectly, related to the pathogenesis of obesity-associated IR [17].

Advanced oxidation of protein products (AOPPs) are ROS generated chloraminated oxidants, mainly hypochlorous acid and chloramines, derived by myeloperoxidase in activated neutrophils [18]. They are defined as dityrosine-containing cross-linked protein products and are a reliable marker to measure the degree of protein oxidation [19,20], whereas determination of plasma protein carbonyl (PC) is most stable and commonly used as an early marker of protein oxidation [21,22]. Increased level of carbonyl content has been found in several diseases such as rheumatoid arthritis, Alzheimer's disease, diabetic mellitus, and muscle damage due to strenuous exercise. With the binding of metal cations to protein and further attack of ROS, especially hydrogen peroxide and oxygen species modify amino acid lead to the formation

of carbonyls [23]. Increased level of AOPP and PC has been found in obesity and diabetes [20,23].

From extensive literature study, we found that there is a lack of data to clearly explain the relationship between circulating metabolic homeostasis adipokines and protein OS parameters in North India population specifically from Chandigarh region and its surroundings. This study evaluates the comparative and relative relationship between leptin, adiponectin, leptin adiponectin ratio (LAR), insulin, homeostasis model assessment of IR (HOMA-IR), and protein OS markers in obese subjects as well as in obese T2DM patients.

MATERIALS AND METHODS

This case-control study included 90 subjects, of which 30 healthy controls (body mass index [BMI] ≤25 kg/m^2), 30 obese non-diabetics (BMI ≥30 kg/m^2), and 30 obese T2DM patients (BMI ≥30 kg/m^2) were enrolled.

Anthropometric parameters and subject selection
The anthropometric parameters included weight and height measurements for determination of BMI. Each subject was provided a questionnaire for information about age, sex, height, weight, smoking status, and alcohol consumption. Care was taken to select healthy control subjects with BMI (≤25 kg/m^2) and had no family history of diabetes mellitus. The inclusion criteria for age in all groups were 30–50 years. For diabetic patients duration of diabetes was at least 5 years or more, fasting glucose ≥ 126 mg/dl and level of glycated hemoglobin (HbA1C) ≥6.5%. The criteria for selection of type 2 diabetic patients were in accordance with the World Health Organization, and all were under diabetic treatment with oral hypoglycemic drugs. This study excluded the patients taking antioxidants supplements, anti-inflammatory drugs, antiobesity therapies, inflammatory or malignant disease, history of hospitalization in preceding 6 months, pregnant and lactating women, Type I diabetic patients, and exogenous insulin. The study was approved by the Government Multispecialty hospital, Chandigarh (MS-II-2015/4631), India. All the participants were informed about the objectives of the study and written informed consent was obtained from all subjects involved in this study.

Sample collection
Venous peripheral blood sample of each subject was collected after 10–12 h of overnight fasting. Samples were collected into plain sterile and ethylenediaminetetraacetic acid (EDTA) anticoagulant Vacutainers tubes. For estimation of HbA1C whole blood collected in EDTA was used. Plasma samples were used for the measurement of AOPP and PC. The fasting serum samples were used for the measurement of fasting blood glucose (FBG), lipid profile, insulin, leptin, and adiponectin. Serum and plasma were stored at −80°C until further use.

Biochemical measurements
HbA1C was measured using commercially available kits (Erba Diagnostics Mannheim, Germany) by ion exchange resin method. Serum leptin and insulin level were measured quantitatively using solid phase enzyme-linked immunosorbent assay ELISA kit (DRG International, Inc., USA) and serum adiponectin was measured by human Acpro 30 ELISA kit (Ray Biotech Inc., USA). AOPP level was measured by the spectrophotometric method of Witko-Sarsat *et al*. 1998 [18]. PC level was measured by the method of Reznick and Packer 1994 [21]. Blood glucose, total cholesterol (TC), triglycerides (TG), and high-density lipoprotein (HDL) cholesterol were measured by Erba Transasia diagnostic kits. Low-density lipoprotein (LDL) cholesterol and very LDL (VLDL) cholesterol were calculated indirectly by Friedewald's formula [24]. IR was calculated by the HOMA-IR [25].

$$\text{HOMA-IR} = \text{Fasting insulin } (\mu U/ml) \times \text{Fasting glucose } (mmol/L)/22.5$$

Statistical analysis
IBM SPSS statistics 25.0.0 was used for data analysis. Data (quantitative) variable were presented as a mean ± standard deviation. Parametric one-way ANOVA for normally distributed variables to compared between groups followed by *post hoc* test. Nonparametric Kruskal–

Table 1: Clinical and demographical details of the subjects in groups

Parameters	Healthy control	Obese non-diabetic	Obese T2DM
	BMI≤25	BMI≥30	BMI≥30
n	30	30	30
Age (years)	40.23±6.89	41.30±6.48	47.40±3.50
p		<0.504*	<0.001*, <0.001**8
Gender (male/female)	18/12	20/10	15/15
BMI (kg/m^2)	22.67±2.04	32.63±2.73	32.83±2.56
p		<0.001*	<0.001*, <0.464**
FBG (mmol/L)	4.47±0.20	4.64±0.35	10.47±0.77
p		<0.026*	<0.001*, <0.001**
PPBG (mmol/L)	6.37±0.71	6.75±0.69	14.91±2.54
p		<0.617*	<0.001*, <0.001**
HbA1c (%)	4.54±0.36	4.60±0.38	8.92±0.96
p		<0.908*	<0.001*, <0.001**
Cholesterol (mg/dl)	156.47±22.55	184.57±29.45	195.17±32.17
p		<0.001*	<0.001*, <0.204**
Triglycerides (mg/dl)	110.37±32.31	167.01±45.00	246.89±48.55
p		<0.001*	<0.001*, <0.001**
HDL-cholesterol (mg/dl)	51.23±5.32	48.34±5.16	39.85±4.42
p		<0.069	<0.001*, <0.001**
LDL-cholesterol (mg/dl)	83.17±19.40	102.83±31.63	105.94±32.57
p		<0.011*	<0.003*, <0.756**
VLDL-cholesterol (mg/dl)	22.07±6.46	33.40±9.00	49.38±9.71
p		<0.001*	<0.001*, <0.001**
Insulin (µIU/ml)	6.78±2.01	13.17±4.31	13.58±3.85
p		<0.001*	<0.001*, <0.728**
HOMA-IR	1.35±0.42	2.74±0.99	6.17±1.72
p		<0.001*	<0.001*, <0.001**

Data are represented as mean±SD. p<0.05 statistically significant. *p significance versus Healthy control, **p significance versus obese nondiabetic. BMI: Body mass index, FBG: Fasting blood glucose, PPBG: Post-prandial blood glucose, T2DM: Type 2 diabetes mellitus, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, HOMA-IR: Homeostasis model assessment of insulin, HbA1c: Glycated hemoglobin, SD: Standard deviation

Wallis followed by Mann–Whitney U-tests for not normally distributed variables. Correlation analysis between variables for all groups was analyzed by Spearman's correlation test. p<0.05 (two-tailed) was studied statistically significant.

RESULTS

The demographical and clinical parameters studied in all groups were classified by BMI

In Table 1, FBG, TC, TG, LDL-cholesterol, VLDL-cholesterol, insulin, and HOMA-IR were found to be with significantly higher in obese-non diabetic and obese T2DM groups as compared to healthy control (p<0.05 or p<0.001). Age, postprandial blood glucose (PPBG), HDL-cholesterol, and HbA1c significantly higher in obese T2DM as compared to obese non-diabetic and healthy control (p<0.001). In Table 2, leptin showed

significantly increased whereas adiponectin significantly decreased in both obese non-diabetic and obese T2DM as compared to healthy control (p<0.001). LAR, AOPP, and PC significantly higher in obese non-diabetic and obese T2DM groups as compared to healthy control (p<0.001).

Correlation analysis studied among different parameters in all groups

In healthy control, AOPP showed positive correlation with HbA1c (r=0.411, p<0.024), between insulin and HOMA-IR (r=0.977, p<0.001). LAR showed positive correlation with leptin (r=0.914, p<0.001) but negative correlation with adiponectin (r=−0.547, p<0.002) and HbA1c (r=−0.383, p<0.037) (Table 3).

In obese non-diabetic, a positive correlation was found between age and PPBG (r=0.381, p<0.038). BMI was positively correlated with LAR

Table 2: Adipokines and oxidative stress parameters details of the subjects in groups

Parameters	Healthy control	Obese non-diabetic	Obese T2DM
Leptin (ng/ml)	6.82 ± 3.59	25.67 ± 8.13	26.89 ± 4.45
p		<0.001*	<0.001*, <0.544**
Adiponectin (ng/ml)	15.53 ± 3.42	8.93 ± 1.77	7.56 ± 1.66
p		<0.001*	<0.001*, <0.079**
Leptin/adiponectin ratio	0.47 ± 0.27	3.02 ± 1.38	3.81 ± 1.38
p		<0.001*	<0.001*, <0.007**
AOPP (μmol/l)	165.35 ± 41.79	208.84 ± 42.32	302.67 ± 57.64
p		<0.001*	<0.001*, <0.001**
PC (nmol/mg protein)	0.72 ± 0.07	0.98 ± 0.22	1.46 ± 0.24
p		<0.001*	<0.001*, <0.001**

Data are represented as mean ± SD. p<0.05 statistically significant. *p, significance versus healthy control, **p, significance versus obese nondiabetic. AOPP: Advanced oxidation of protein products; PC: Protein carbonyl, T2DM: Type 2 diabetic mellitus

Table 3: Spearman's correlation among measured parameters in healthy control

Parameters	Age	BMI	FBG	PPBG	HbA1c	Insulin	HOMAIR	Leptin	Adiponectin	LAR	AOPP
BMI											
r	0.168	1.000									
p	0.375										
FBG											
r	0.295	−0.131	1.000								
p	0.113	0.491									
PPBG											
r	−0.022	−0.109	0.173	1.000							
p	0.908	0.567	0.361								
HbA1c											
r	0.230	−0.237	0.099	0.240	1.000						
p	0.222	0.207	0.602	0.200							
Insulin											
r	0.053	−0.176	0.050	0.118	0.120	1.000					
p	0.780	0.352	0.794	0.536	0.526						
HOMA-IR											
r	0.120	−0.115	0.196	0.150	0.133	0.977**	1.000				
p	0.528	0.545	0.300	0.428	0.484	0.001					
Leptin											
r	0.042	0.121	−0.112	0.219	−0.350	0.073	0.072	1.000			
p	0.826	0.523	0.555	0.244	0.058	0.700	0.707				
Adiponectin											
r	−0.042	−0.163	0.169	0.081	0.205	0.107	0.125	−0.219	1.000		
p	0.824	0.389	0.372	0.670	0.276	0.574	0.510	0.245			
LAR											
r	0.070	0.228	−0.130	0.186	−.383*	0.019	0.021	0.914**	−0.547**	1.000	
p	0.712	0.226	0.492	0.325	0.037	0.921	0.914	0.001	0.002		
AOPP											
r	−0.043	−0.232	0.191	0.091	0.411*	0.180	0.204	−0.069	0.265	−0.189	1.000
p	0.823	0.216	0.312	0.634	0.024	0.341	0.281	0.717	0.157	0.316	
PC											
r	0.082	−0.221	0.209	0.007	0.117	0.069	0.080	−0.009	−0.126	0.021	0.170
p	0.668	0.241	0.268	0.969	0.536	0.719	0.676	0.962	0.509	0.914	0.370

*Correlation is significant at the 0.05 level (two-tailed). **Correlation is significant at the 0.01 level (two-tailed). BMI: Body mass index, FBG: Fasting blood glucose, PPBG: Postprandial blood glucose, HbA1c: Glycated hemoglobin, HOMA-IR: Homeostasis model assessment of insulin resistance, LAR: Leptin/adiponectin ratio, AOPP: Advanced oxidation of protein products, PC: Protein carbonyl

(r=0.375, p<0.041). LAR positively correlated with leptin (r=0.909, p<0.001) but negatively correlated with adiponectin (r=−0.384, p<0.036). HOMA-IR positively correlated with FBG (r=0.429, p=0.018) and insulin (r=0.968, p=0.001). AOPP positive correlation was found among BMI (r=0.429, p<0.018) and PC (r=0.702, p=0.001) whereas a negative correlation was found between PC and adiponectin (r=−0.412, p<0.024) (Table 4).

In obese T2DM, FBG positive correlation found among PPBG, HbA1c, insulin, and HOMA-IR (r=0.502, p<0.005; r=0.373, p<0.042; r=0.437, p=0.016; and r=0.670, p=0.001), respectively. HOMA-IR positive correlation found among PPBG, HbA1c, and insulin (r=0.528, p=0.001; r=0.536, p=0.002; and r=0.867, p=0.001), respectively. A negative correlation between leptin and adiponectin (r=−0.402, p<0.028). LAR positively correlated with leptin (r=0.731, p<0.001) but negatively correlated with adiponectin (r=−0.879, p<0.001). AOPP positively correlated with FBS, PPBG, HOMA-IR, and PC (r=0.385, p<0.036; r=0.422, p<0.020; r=0.497, p=0.005; and r=0.482, p=0.007) whereas PC negatively correlated with adiponectin (r=−0.371, p<0.043) (Table 5).

DISCUSSION

This study was done to examine protein oxidative markers (AOPP, PC) and major metabolic homeostasis markers (adiponectin, leptin, and LAR) in obese subjects with and without T2DM. Obese T2DM and obese non-diabetic had a significantly lower level of serum adiponectin as compared to lean T2DM and healthy control, respectively. Serum adiponectin level was decreased in obese subjects with and without diabetes, a similar trend was also seen in this study [26,27]. Decreased level of adiponectin has been strongly associated with IR and inflammation was seen as the main cause of the link between obesity and T2DM [28]. Adiponectin was negatively correlated with leptin in obese T2DM which is in accordance with previous reports [29]. This was due to increased HOMA-IR and leptin level and decreases adiponectin level which strongly predicts IR [30].

In contrast to adiponectin, leptin levels increase in obesity which is proportional to the degree of adiposity [13,31]. In this study, serum leptin and LAR were higher in both obese T2DM and obese non-diabetic patients with respect to healthy control. From this study, we observed that serum leptin and LAR were higher in obese patients whether obese patients were diabetic or not which is consistent with a previous study [16,32]. An earlier report showed that serum leptin was negatively correlated with serum adiponectin; this study also showed similar trends in obese T2DM patients [33]. As reported by Al-Hamodi *et al.* [13], an inverse association between leptin and adiponectin was observed which highlight the recent findings that indicated that the two adipokines interact with each other in the inflection of T2DM risks. Both leptin and adiponectin play an important role in the maintenance of metabolic homeostasis and fat accumulation in adipose tissue [9]. In central obesity, disturbance of their level leads to increase appetite and reduced energy expenditure results in IR by the accumulation of fat in adipose tissue [1].

In this study, HOMA-IR and LAR both indexes of IR were increased in obese non-diabetic and obese T2DM as compared to healthy control. As suggested by Satoh *et al.* [34], Kotani *et al.* [35], and LAR represented as a potential marker of an atherogenic index in obese type 2 diabetic patients. LAR is the most reliable marker of IR than HOMA-IR to leptin or adiponectin alone in obesity with and without type 2 diabetes [30]. It is also reported LAR to be associated with central obesity and metabolic syndrome subjects [35]. In this study, we observed LAR be positively correlated with BMI in obese non-

Table 4: Spearman's correlation among measured parameters in obese nondiabetic

Parameters	Age	BMI	FBG	PPBG	HbA1c	Insulin	HOMA-IR	Leptin	Adiponectin	LAR	AOPP
BMI											
r	−0.204	1.000									
p	0.279										
FBG											
r	−0.152	0.251	1.000								
p	0.422	0.180									
PPBG											
r	0.381*	0.012	−0.109	1.000							
p	0.038	0.949	0.565								
HbA1c											
r	−0.187	0.217	0.149	0.307	1.000						
p	0.323	0.249	0.433	0.098							
Insulin											
r	0.120	0.143	0.252	0.282	0.051	1.000					
p	0.527	0.452	0.180	0.131	0.787						
HOMA-IR											
r	0.054	0.177	0.429*	0.254	0.106	0.968**	1.000				
p	0.776	0.350	0.018	0.176	0.577	0.001					
LEPTIN											
r	0.095	0.287	0.185	−0.173	0.109	0.187	0.183	1.000			
p	0.616	0.124	0.328	0.361	0.565	0.322	0.334				
Adiponectin											
r	−0.127	0.018	−0.049	−0.287	−0.319	−0.078	−0.106	−0.116	1.000		
p	0.504	0.925	0.797	0.124	0.086	0.681	0.577	0.541			
LAR											
r	0.064	0.375*	0.283	−0.075	0.203	0.295	0.321	0.909**	−0.384*	1.000	
p	0.736	0.041	0.130	0.694	0.283	0.113	0.084	0.001	0.036		
AOPP											
r	−0.006	0.429*	−0.059	0.151	0.165	−0.151	−0.105	0.025	−0.312	0.196	1.000
p	0.973	0.018	0.756	0.427	0.384	0.426	0.582	0.897	0.093	0.300	
PC											
r	−0.034	0.335	−0.084	0.013	0.102	−0.191	−0.159	−0.181	−0.412*	−0.015	0.702**
p	0.857	0.071	0.661	0.945	0.593	0.312	0.403	0.340	0.024	0.936	0.001

*Correlation is significant at the 0.05 level (two-tailed), **Correlation is significant at the 0.01 level (two-tailed). BMI: Body mass index, FBG: Fasting blood glucose, PPBG: Post-prandial blood glucose, HbA1c: Glycated hemoglobin, HOMA-IR: Homeostasis model assessment of insulin resistance, LAR: Leptin/adiponectin ratio, AOPP: Advanced oxidation of protein products, PC: Protein carbonyl

Table 5: Spearman's correlation among measured parameters in obese type 2 diabetes mellitus

Parameters	Age	BMI	FBG	PPBG	HbA1c	Insulin	HOMA-IR	Leptin	Adiponectin	LAR	AOPP
BMI											
r	−0.075	1.000									
p	0.695										
FBG											
r	−0.186	0.142	1.000								
p	0.325	0.453									
PPBG											
r	−0.077	−0.024	0.502**	1.000							
p	0.685	0.899	0.005								
HbA1c											
r	−0.204	0.114	0.373*	0.330	1.000						
p	0.279	0.549	0.042	0.075							
Insulin											
r	−0.242	0.071	0.437*	0.279	0.527**	1.000					
p	0.197	0.711	0.016	0.136	0.003						
HOMA-IR											
r	−0.276	0.073	0.670**	0.528**	0.536**	0.867**	1.000				
p	0.139	0.702	0.001	0.003	0.002	0.001					
Leptin											
r	0.191	0.062	−0.070	−0.138	−0.032	−0.209	−0.216	1.000			
p	0.313	0.744	0.715	0.469	0.865	0.268	0.252				
Adiponectin											
r	−0.151	−0.138	0.102	0.201	−0.190	−0.021	0.037	−0.402*	1.000		
p	0.427	0.467	0.593	0.287	0.315	0.914	0.848	0.028			
LAR											
r	0.126	0.104	−0.106	−0.209	0.170	−0.056	−0.111	0.731**	−0.879**	1.000	
p	0.509	0.586	0.577	0.268	0.369	0.768	0.559	0.001	0.001		
AOPP											
r	−0.073	0.351	0.385*	0.422*	0.317	0.321	0.497**	−0.201	−0.045	−0.029	1.000
p	0.703	0.057	0.036	0.020	0.088	0.084	0.005	0.287	0.813	0.880	
PC											
r	−0.045	0.069	0.142	0.105	−0.090	0.227	0.289	−0.336	−0.371*	0.084	0.482**
p	0.813	0.716	0.454	0.580	0.635	0.228	0.121	0.070	0.043	0.658	0.007

*Correlation is significant at the 0.05 level (two-tailed). **Correlation is significant at the 0.01 level (two-tailed). BMI: Body mass index, FBG: Fasting blood glucose, PPBG: Post-prandial blood glucose, HbA1c: Glycated hemoglobin, HOMA-IR: Homeostasis model assessment of insulin resistance, LAR: Leptin/adiponectin ratio, AOPP: Advanced oxidation of protein products, PC: Protein carbonyl

diabetic such relation was also seen in postmenopausal women with metabolic syndrome [36]. In previous studies, it was also found that HOMA-IR and LAR have a significant positive correlation [36]. However, this study does not find such relation this might be due to a small sample population studied. IR state is linked to chronic low-grade inflammation in hypertrophied adipose tissue that promotes the initiation and progression of metabolic disorders and T2DM.

It is well studied that obesity induces OS that plays an important role in the pathogenesis of diabetes. AOPP had a significantly higher level in obese T2DM and obese non-diabetic in contrast to lean healthy control. AOPPs increased level is reported to be associated with obesity and diabetes [20,37]. Increased AOPPs may be an independent risk factor for coronary artery disease [19] and early marker of endothelial dysfunction in T2DM patients [38]. In this study, AOPP positively correlated with BMI, PC in obese non-diabetic subjects and with FBG, PPBG, HOMA-IR, and PC in obese T2DM which was in accordance with previous studies [39]. Li *et al.* [40] also reported that at 32–36 weeks gestational diabetes mellitus showed a significant relationship between AOPP and FBG level compared to normal pregnancies. Increase in levels of AOPP and PC may lead to development in the growth of diabetic complications and cardiovascular diseases.

In this study, we found a significant increase in PC level in obese T2DM patients as compared to obese non-diabetic and healthy control which was in accordance with previous reports [41,42]. According to Frohnert *et al.* [43], human obesity OS is linked to protein carbonylation which is directly correlated to adiposity and serum free fatty acids that may eventually lead to the development of IR. Studies have shown that in aging proteome accumulated OS-related post-translational modification including glycation, lipid peroxidation, and carbonylation observed in chronic inflammation, metabolic syndrome, and diabetes [44]. This study found an inverse correlation with increased PC level and decreased adiponectin in obese non-diabetic and obese T2DM which is in accordance with previous studies [45]. Therefore, this study supports the relation of obesity between protein OS markers and circulating adipokines.

CONCLUSION

Present the study suggests that an increase in levels of leptin, insulin, AOPP, and PC in obese non-diabetic subjects and obese T2DM patients play an important role in reducing the level of adiponectin. A significant increase in the level of HOMA-IR and LAR in obese suggests in the development of T2DM and IR. Moreover, obese subjects have increased OS that may contribute to the dysregulation of adipokines and altered glucose metabolism.

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DISCLOSURE STATEMENT

The authors declare that there are no conflicts of interest.

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