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The relationship between visfatin, resistin and CRP parameters and insulin resistance in obese and non-obese type 2 diabetic individuals

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ABSTRACT

Objectives: Inflammation caused by adipokines such as adiponectin, leptin, resistin, visfatin, interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α) released by fat cells and immune cells within fat tissue is a significant factor in the onset of insulin resistance and Type 2 diabetes mellitus (T2DM). This study explores the relationship among these adipokines and insulin resistance in T2DM patients, focusing on the impact of abdominal obesity.

Methods: The study involved 73 adult T2DM patients who were seperated into two groups based on their body mass index (BMI): 47 were classified as obese (BMI ≥30 kg/m²), and 26 were classified as non-obese (BMI <25 kg/m²). Additionally, 42 healthy controls were included, comprising 18 obese and 24 non-obese individuals. Adipokine concentrations (resistin, leptin, adiponectin, visfatin, IL-6 and TNF-α) were measured with the ELISA method.

Results: The concentrations of adiponectin were substantially lower in T2DM patients relative to the control group (P<0.0125). Leptin concentrations did not show significant differences between the groups, but there was a notable increase in obese controls compared to non-obese controls (P<0.0125). TNF-α concentrations were significantly higher in obese controls than in non-obese controls (P<0.001). Resistin concentrations were significantly correlated with C-reactive protein (CRP) and IL-6 in both groups, independent of BMI (P=0.001 and P<0.0125, respectively). We found that CRP levels were significantly higher in both obese diabetics compared to non-obese diabetics and in obese controls compared to non-obese controls (P<0.0001).

Conclusions: Adipose tissue is a crucial determinant of circulating inflammation markers. Elevated CRP concentrations in obesity may result from insulin resistance rather than being a cause. Further research is required to comprehend the connection between fatty tissue, insulin resistance, and elevated inflammatory markers.

Keywords: Obesity, Type 2 diabetes mellitus, resistin, visfatin, adiponectin, leptin

Diabetes is stated that affects more than 463 million people worldwide today and type 2 diabetes mellitus (T2DM) represents 90-95% of the total instances [1]. T2DM is associated with microvascular issues like retinopathy, nephropathy, and neuropathy, in addition to macrovascular problems in-

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cluding myocardial infarction, stroke, and peripheral vascular disease [2]. Conditions associated with obesity, including hypertension, elevated cholesterol levels, T2DM, fatty liver disease, heart disease, and certain cancers, resulted in roughly 3.4 million adult fatalities in 2016, as reported by the WHO [3].

tissue is an important organ that helps regulate glucose and lipid metabolism by producing adipokines [4]. Adipokines, create a low-grade chronic inflammatory state believed to lead to insulin resistance and T2DM [5]. Among these adipokines, interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) are cytokines that promote inflammation. Specifically, IL-6 is crucial in the liver by regulating the production of inflammatory proteins like C-reactive protein (CRP) [5]. TNF-α is a homotrimer protein composed of 157 amino acids that is primarily synthesized by activated macrophages, natural killer cells and T-lymphocytes [6]. Many autoimmune diseases, such as rheumatoid arthritis, psoriatic arthritis, psoriasis, non-infectious uveitis and inflammatory bowel disease, are triggered by abnormal secretion of TNF-α [6]. Leptin is present in the bloodstream in both its free and protein-bound states. The biologically active form is the free leptin, and the balance between free and bound forms regulates leptin bioavailability [3].

Adiponectin plays an important role in regulating lipid and carbohydrate metabolism and promotes the breakdown of fatty acids and the use of carbohydrates to reduce lipids and blood glucose levels [7]. Individuals suffering from DM, coronary heart disease and obesity have been observed to have significantly lower serum adiponectin concentrations compared to healthy individuals, suggesting that adiponectin levels are closely related to these diseases [7]. A hormone secreted from adipose tissue, Resistin leads to the development of T2DM by increasing insulin resistance and disrupting glucose homeostasis [8]. Resistin appears to be a link between visceral obesity and diabetes. Visfatin has been shown to be strongly associated with visceral adiposity [9]. Despite ongoing uncertainty regarding the connections among visfatin, lipid profiles, and glucose metabolism, meta-analysis findings continue to indicate that elevated visfatin levels are more common in individuals with obesity, T2DM, cardiovascular disease, and metabolic syndrome [10].

In this research, to contribute to the discussion on whether the relationship between insulin resistance, T2DM, and inflammation markers is independent of increased adipose tissue or is caused by obesity, we examined the relationship between adipokines such as resistin, leptin, adiponectin, visfatin, IL-6, TNF-α, and insulin resistance.

METHODS

This study follows the principles of the Declaration of Helsinki. The study was conducted with approval from Istanbul University Faculty of Medicine Clinical Research Ethics Committee dated 28.08.2006 and numbered 1745. All participants provided their informed consent.

The research took place between January 10, 2007, and September 15, 2007. Patients meeting the ADA criteria for type 2 diabetes and attending the Diabetes Polyclinic at Istanbul University Medicine Faculty, Endocrinology and Metabolic Diseases Department, were included in the study. These patients were divided into two groups based on their body mass index (BMI): obese (BMI ≥30 kg/m², 23 men and 24 women) and non-obese (BMI <25 kg/m², 18 men and 8 women). Additionally, 42 non-diabetic individuals were included as the control group (obese: BMI ≥30 kg/m², 7 men and 11 women; non-obese: BMI <25 kg/m², 9 men and 15 women).

Height, weight, waist and hip circumference measurements were taken for both patient and control groups. Patients using insulin and TZD as antidiabetic medications were excluded. Data on age, gender, medication history, diet, smoking, alcohol consumption, and any existing diseases other than diabetes were also collected for both groups.

Blood samples were collected after a fasting period of 8-12 hours to measure glucose, BUN, creatinine, triglyceride, total cholesterol, HDL-cholesterol, LDL-cholesterol, ALT, AST, HbA1c, fructosamine, insulin, hs-CRP, and C-peptide concentrations. Serum samples were prepared by centrifuging blood at 2500 rpm at +4 degrees Celsius for 10 minutes. Adiponectin, IL-6, leptin, resistin, TNF-α, and visfatin concentrations were determined using the ELISA method from serum samples stored at -80 degrees Celsius until the analysis day. Insulin resistance was as-

sessed using the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) formula, which is derived from fasting glucose and insulin levels.

Data Collection and Analysis

Glucose, cholesterol and triglyceride levels were measured by colorimetric enzymatic methods. BUN concentrations were determined using the kinetic UV method, while LDL-cholesterol and HDL-cholesterol were measured using homogeneous enzymatic colorimetric methods. Creatinine concentrations were measured using the kinetic colorimetric method, and AST and ALT concentrations were determined using the kinetic UV method. Fructosamine was analyzed colorimetrically on the Modular System DPP Autoanalyzer (Roche Diagnostics, Indianapolis, USA). HsCRP concentrations were measured using the immunoturbidimetric method on the Cobas Integra 800 (Roche Diagnostics, Indianapolis, USA, reference range; 0.5-5 mg/L) analyzer in the hospital central laboratory.

HbA1c concentrations were measured in whole blood hemolyzed with detergent using the turbidimetric inhibition immunoassay (TINIA) method on the Modular System P module (Roche Diagnostics, Indianapolis, USA). C-peptide concentrations were determined with the electrochemiluminescence immunoassay (ECLIA) method on the Modular System E170 module (Roche Diagnostics, Indianapolis, USA), and insulin levels were measured using the chemiluminescence microparticle immunoassay (CMIA) method on the Architect System i2000 (Abbott Diagnostics, USA) module. Serum resistin, adiponectin and leptin levels were determined by sandwich ELISA (Enzyme-linked immunosorbent assay) method using a commercial kit (ImmunAssayPro, Missouri, USA). TNF-α and IL-6 determination in serum was performed by sandwich ELISA (Enzyme Linked Immunosorbent Assay) method using a commercial kit (Biosource International, Inc., Human TNF-α and Human IL-6, California, USA), and visfatin determination in serum was performed by sandwich ELISA (Enzyme Linked Immunosorbent Assay) method using a commercial kit (Alpco Diagnostics, USA).

Statistical Analysis

In the study, the data distribution of the evaluated parameters was assessed, and skewness and kurtosis values were found to exceed 2. Consequently, statistical comparisons between groups were performed using the non-parametric Mann-Whitney U test. Given that four groups were compared, the Bonferroni correction was applied, and the significance level was set at $P< 0.0125$. The relationships between the evaluated parameters were assessed using Spearman's correlation analysis.

RESULTS

Table 1 presents the physical characteristics of the patient and control groups. The groups included 47 obese

Table 1. Age, body mass index, waist/hip ratio and HOMA-IR values of the patient and control groups.

	Obese DM (n=47)	Obese Control (n=18)	Non-Obese DM (n=26)	Non-Obese Control (n=24)
Age (years)	57.5 (38-70)	58 (36-65)	57 (42-70)	55.1 (35-60)
BMI (kg/m^2)	32.4 (30-58.8)	32.3 (30.2-35.8)	24.25 (21-24.9)	23.4 (19-24.9)
Waist-Hip Ratio	0.91 (0.74-1.14)	0.88 (0.72-0.99)	0.90 (0.75-0.95)	0.78 (0.68-0.91)
HOMA-IR	3.89 (0.97-17)	2.01 (0.66-4.58)	2.02 (0.76-8.6)	1.34 (0.63-3.2)

Data are shown as median (minimum-maximum). DM=Diabetes Mellitus, BMI=Body Mass Index, HOMA-IR= Homeostatic Model Assessment for Insulin Resistance

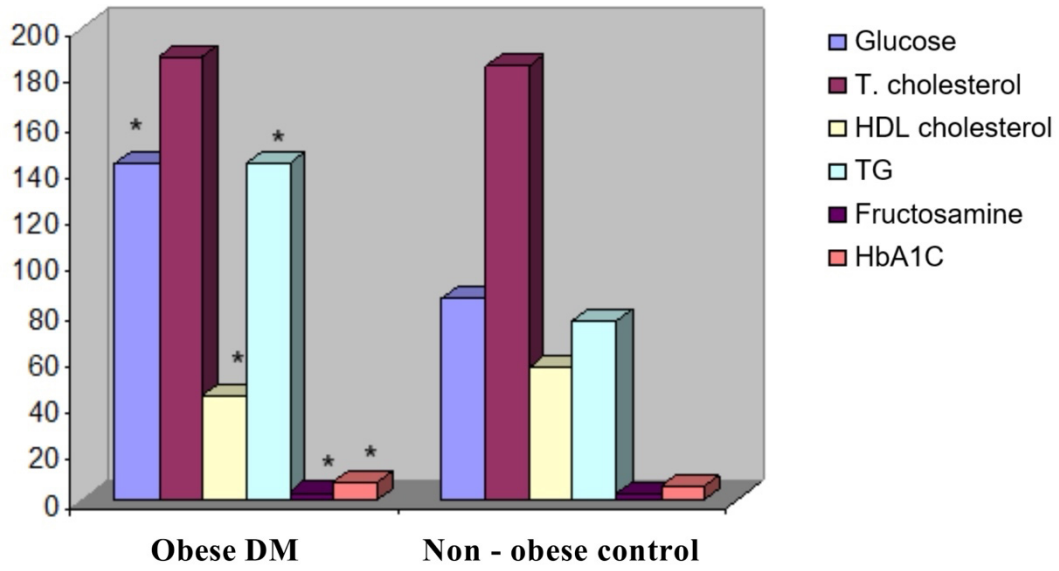

Fig. 1. Glucose, total cholesterol, HDL cholesterol, triglyceride, fructosamine and HbA1C values in obese diabetic and non-obese control groups (median), *P<0.001.

diabetic patients (24 women and 23 men), 26 non-obese diabetic patients (8 women and 18 men), 18 obese controls (11 women and 7 men), and 24 non-obese controls (15 women and 9 men). These groups were compared based on median (distribution range) values for age, BMI, HOMA-IR, and waist/hip ratio.

There was no statistical difference between the patient and control groups in terms of age. Significant differences were observed in waist/hip ratio. Particularly in the comparisons between the obese diabetic group and the obese control group and the obese diabetic group and the non-obese diabetic group, P values were found to be less than 0.0125. When the biochemical parameters of the obese diabetic group and the non-obese control group, the non-obese diabetic group and the non-obese control group, and the obese control group and the non-obese diabetic group were compared, the results were also found to be significant

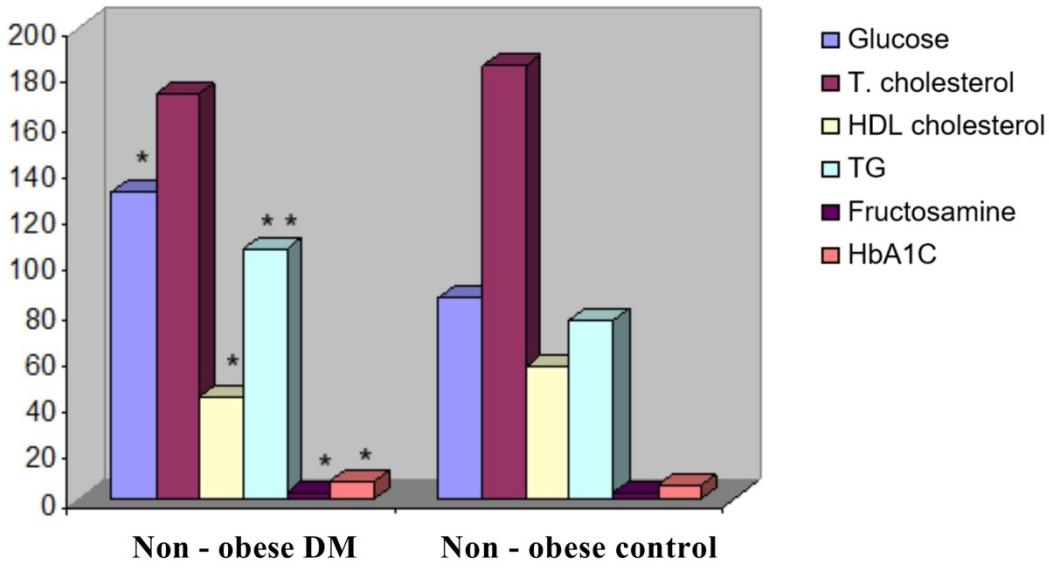

Fig. 2. Glucose, total cholesterol, HDL cholesterol, triglyceride, fructosamine and HbA1C values in non-obese diabetic and non-obese control groups (median), * P<0.001, **P<0.0125.

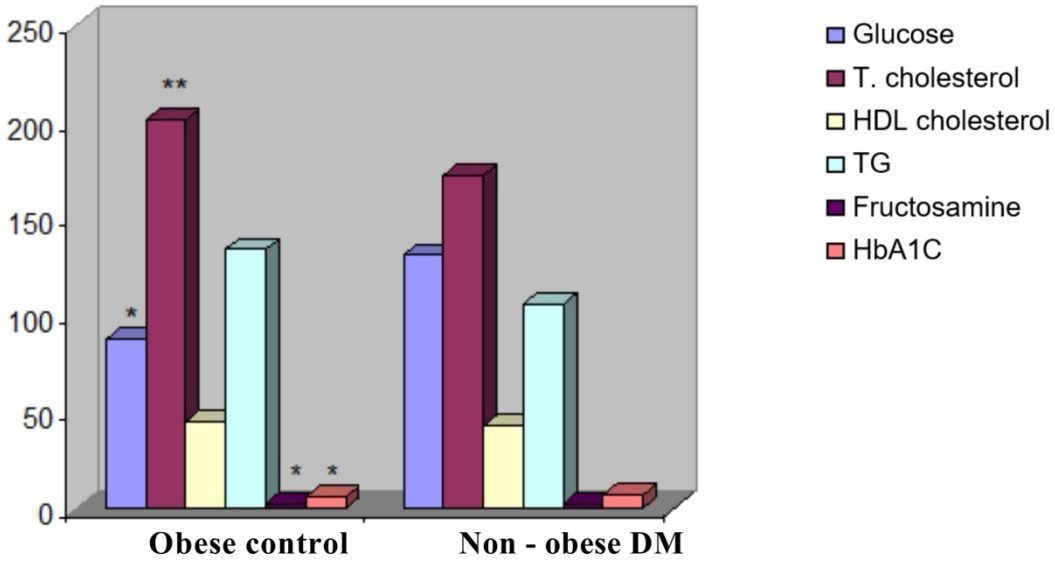

Fig. 3. Glucose, total cholesterol, HDL cholesterol, triglyceride, fructosamine and HbA1C values in non-obese diabetic and obese control groups (median), *P<0.001, **P<0.0125.

(Figs 1, 2 and 3).

Routine biochemical parameters of control groups and the patients are described in Table 2. Resistin, adiponectin, leptin, visfatin, Tnf-α, IL-6 and hsCRP values of patients and group controls are in Table 3 (Figs. 4, 5, 6, 7, 8 and 9). Correlations of resistin and vistatin with other parameters in the patient and control groups are in Tables 4 and 5.

DISCUSSION

Type 2 diabetes (T2DM) is a metabolic condition associated with obesity and impaired fat tissue storage. Insulin resistance (IR), which is considered to be a relative pancreatic β-cell deficiency with a disturbed balance between abnormal cellular response and insulin actions, is one of the leading causes of T2DM [11].

Table 2. Glucose, total cholesterol, HDL cholesterol, triglyceride, fructosamine and HbA1c values of the patient and control groups

	Obese DM	Obese Control	Non-Obese DM	Non-Obese Control
Glucose (mg/dL)	143 (83-341)	87.5 (72-100)	131 (79-287)	86 (73-98)
Total cholesterol (mg/dL)	188.3 (82-281)	201.5 (164-256)	172.5 (121-243)	184.5 (134-245)
HDL cholesterol (mg/dL)	44 (30-71)	45 (27-66)	43 (33-70)	56 (35-73)
Triglyceride (mg/dL)	143 (53-400)	134 (86-374)	106 (49-284)	76 (34-223)
Fructosamine (mmol/L)	2.99 (2.19-4.44)	2.32 (2.1-2.52)	2.88 (2.18-4.61)	2.38 (1.94-2.97)
HbA1C (%Hb)	7.2 (5.4-10.8)	5.75 (5.5-6.2)	6.8 (5.5-11.4)	5.6 (5-6.1)

Data are shown as median (minimum-maximum). DM=Diabetes Mellitus, HDL=High-density lipoprotein, HbA1c=Glycated Hemoglobin

Table 3. Resistin, adiponectin, leptin, visfatin, TNF-α, IL-6 and hsCRP values of patient and control groups

	Obese DM (n=47)	Obese Control (n=18)	Non-Obese DM (n=26)	Non-Obese Control (n=24)
Resistin (ng/mL)	9.72 (4.86-19.63)	12.4 (5.39-19.68)	8.22 (3.6-18.5)	10.33 (5.38-18.84)
Adinopectin (µg/mL)	6.8 (3.9-32.4)	9 (3.4-40.6)	5.7 (2.7-12.6)	8.99 (3-44.6)
Leptin (ng/mL)	55.5 (4.6-436.8)	78.99 (24.6-316)	46.94 (5.84-214.7)	49.31 (8.86-147.2)
Visfatin (ng/mL)	3.37 (1.35-24)	3.83 (0.75-10.8)	3.78 (0.25-11)	3.62 (0.83-17.25)
TNF-α (ρg/mL)	15.69 (6.32-73.74)	34.96 (11.09-153.6)	17.7 (3.31-67.43)	14.04 (0.6-60.67)
IL-6 (ρg/mL)	14 (10.2-25.35)	14.45 (10.2-19.97)	14.8 (9.18-30.66)	17.38 (10-33.6)
HsCRP (mg/L)	2.95 (0.7-78.5)	3.25 (0.73-13.4)	0.955 (0.12-7.6)	0.8 (0.3-4.1)

Data are shown as median (minimum-maximum). DM=Diabetes Mellitus, TNF=Tumor Necrosis Factor, IL=Interleukin, HsCRP= High-sensitivity C-reactive protein

Additionally, IR is closely linked to other metabolic conditions such as hypertension, hyperinsulinemia, dyslipidemia, obesity and fatty liver disease, which are key components of metabolic syndrome. Overweight and obese individuals exhibit a range of oxidative stress, metabolic abnormalities, immune dysfunction, mitochondrial dysfunction, and chronic low-grade inflammation [12].

Recent studies suggest that triglycerides accumulated in muscle tissue and impaired mitochondrial ox-

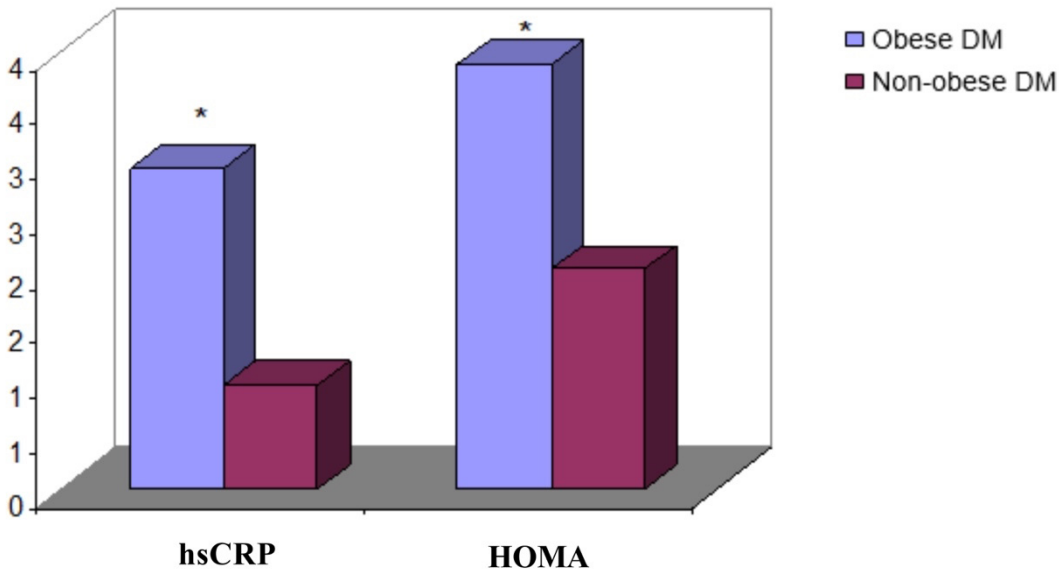

Fig. 2. HsCRP and HOMA-IR values in obese diabetic and non-obese diabetic groups (median), *P<0.001.

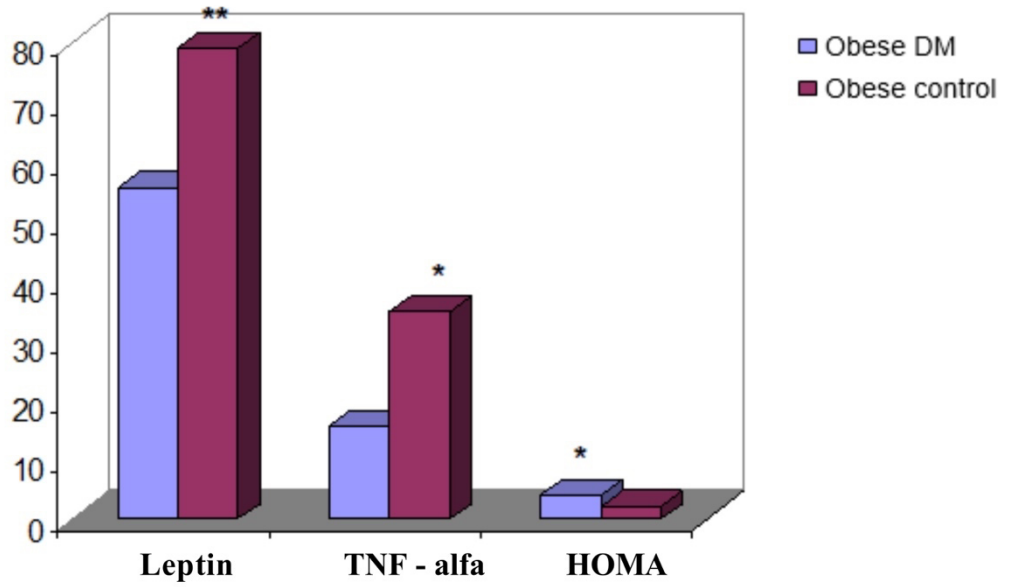

Fig. 5. Leptin, TNF-α and HOMA-IR values in obese diabetic and obese control groups (median), *P<0.001, ** P<0.0125.

idative phosphorylation in genetically predisposed individuals contribute to insulin resistance [13]. Adipose tissue, the primary source of circulating fatty acids, has been linked to impaired insulin action when there is an increase in abdominal fat tissue, as opposed to peripheral or gluteofemoral fat tissue [14,15].

Inflammation, particularly CRP, is regarded as a key contributor to the pathogenesis of glucose intolerance, insulin resistance, and T2DM [16,17]. Numerous studies have reported a strong relationship

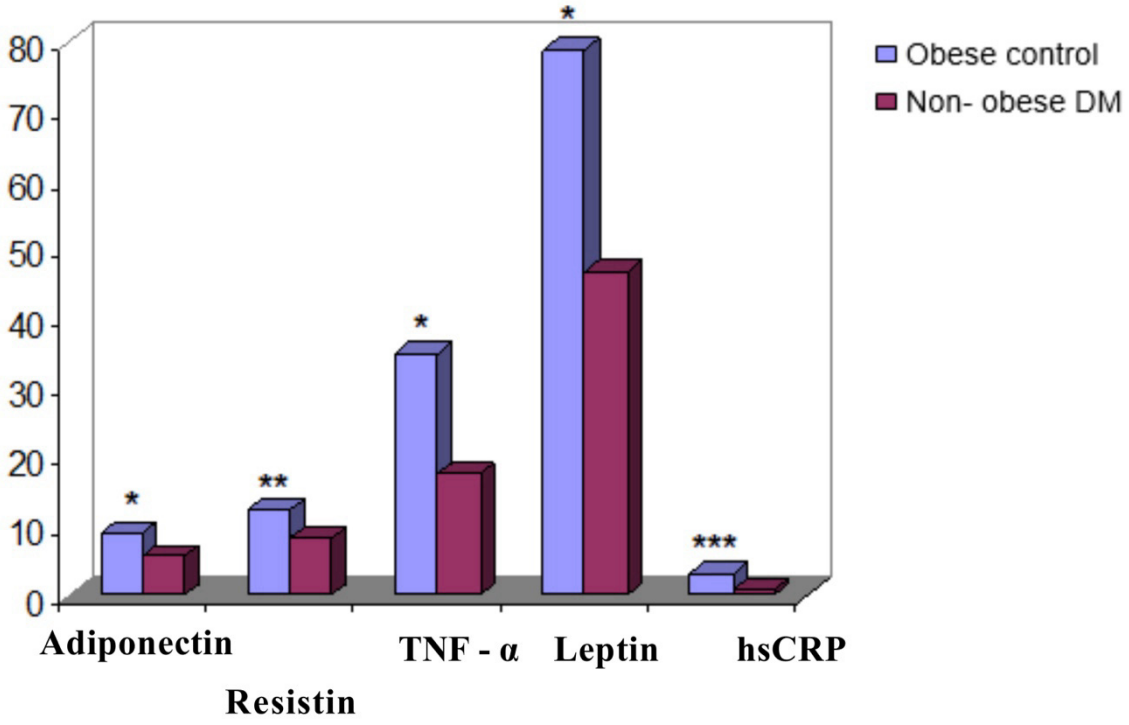

Fig. 6. Adiponectin, resistin, TNF-α, leptin and hsCRP values in obese control and non-obese diabetic groups (median), *P<0.01, **P<0.0125, ***P<0.001.

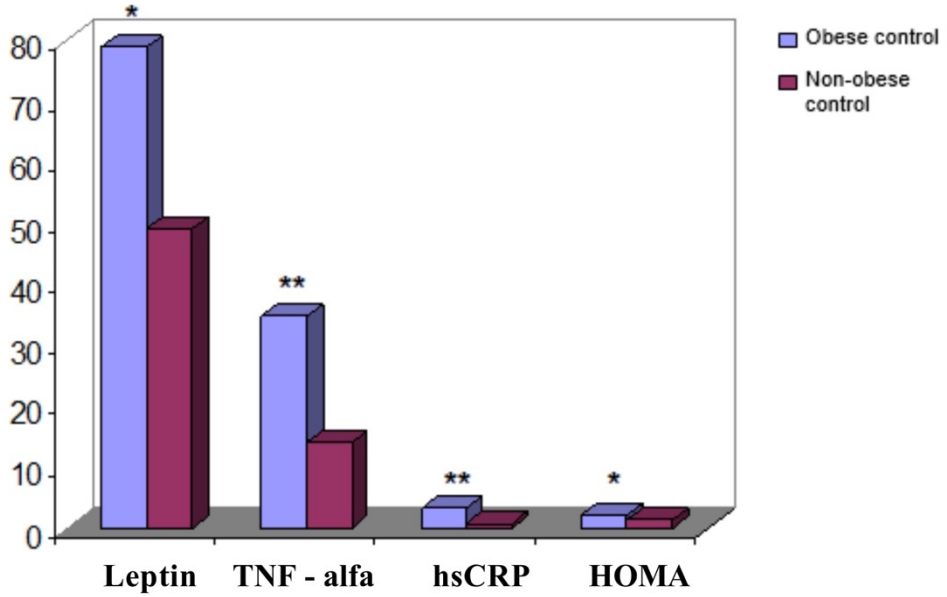

Fig. 7. Leptin, TNF-α, hsCRP and HOMA-IR values in obese control and non-obese control groups (median), *P<0.0125, ** P<0.001.

between circulating inflammatory markers and the development of T2DM [18-19]. Different markers, such as cytokines, chemokines, IL-6, and fibrinogen, have been examined, but results have been inconsistent.

Adipose tissue, traditionally known for storage and heat insulation, plays an active role in maintaining energy balance and in immune and inflammatory processes. Weight gain and obesity cause phenotypic changes in white adipose tissue characterized by the infiltration of inflammatory, dysfunctional fat cells into the stromal vascular fraction, and these inflammatory fat cells secrete proinflammatory cytokines that impair the function of adipose tissue and distant organs, both locally and systemically [12]. These adipokines affect insulin sensitivity and are vital in developing inflammation, insulin resistance, diabetes,

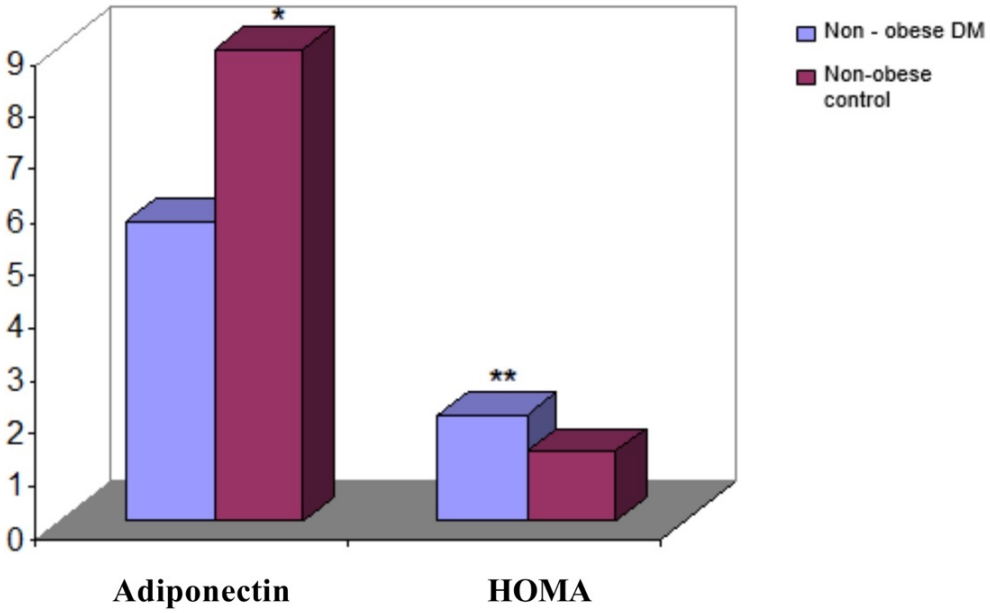

Fig. 8. Adiponectin and HOMA-IR values in non-obese diabetic and non-obese control groups (median) *P<0.0125, **P<0.01.

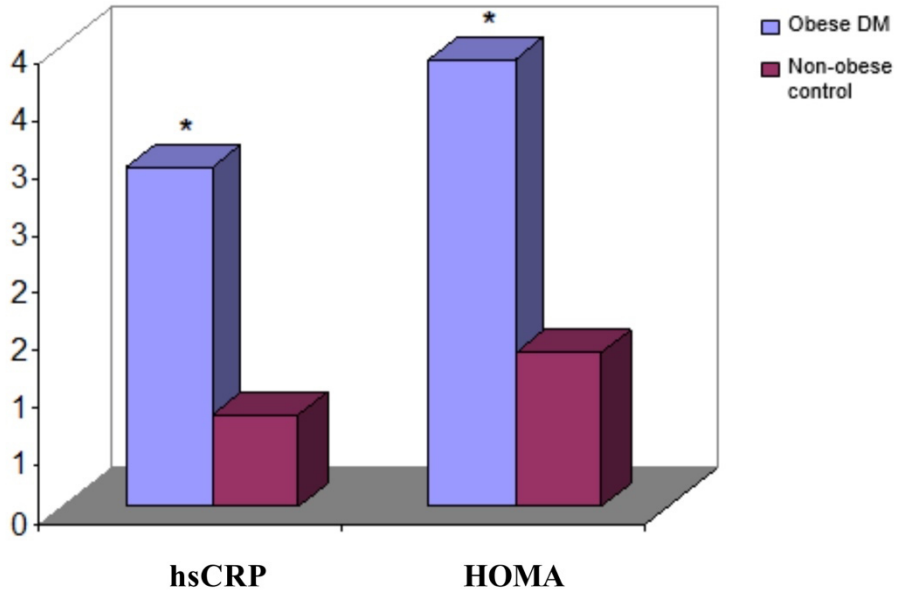

Fig. 9. HsCRP and HOMA-IR values in obese diabetic and non-obese control groups (median), *P<0.001.

dyslipidemia, and atherosclerosis [20].

While there is ongoing debate about whether the connection between T2DM and inflammatory markers is independent of increased adipose tissue or mediated by obesity, some studies argue that this debate is partly due to the indirect assessment of the amount and distribution of adipose tissue using anthropometric measures such as BMI and waist/hip ratio [21].

Our study analyzed T2DM patients diagnosed with the ADA criteria. Patients were divided into two groups according to BMI: obese (n=47) and non-obese (n=26). We investigated serum adipokine concentrations (leptin, adiponectin, resistin, visfatin, TNF-α, IL-6) and hs-CRP and their correlations with HOMA-IR-calculated insulin resistance. Additionally, we studied 42 healthy individuals with similar BMIs for comparison.

We found that, despite similar body mass indexes,

Table 4. Correlation of resistin with other parameters in patient and control groups.

Resistn	Obese DM		Obese Control		Non-Obese DM		Non-Obese Control	
	Correlation coefficient (r)	P value	Correlation coefficient (r)	P value	Correlation coefficient (r)	P value	Correlation coefficient (r)	P value
Adiponectin	-0.218	0.147	0.297	0.232	-0.002	0.993	-0.07	0.743
Leptin	0.045	0.766	0.301	0.226	-0.205	0.315	0.282	0.182
Visfatin	-0.085	0.574	0.439	0.068	0.614	**0.0008***	0.495	**0.014**
TNF-α	0.11	0.459	0.27	0.277	0.528	**0.006***	0.106	0.623
Il-6	0.235	0.112	0.245	0.328	0.398	**0.044**	-0.115	0.592
HsCRP	0.036	0.814	0.327	0.185	0.046	0.825	0.252	0.234
Homa-IR	-0.007	0.96	-0.458	0.055	-0.054	0.793	0.234	0.272
BMI	0.203	0.177	-0.145	0.567	0.202	0.322	0.217	0.308

DM=Diabetes Mellitus, TNF=Tumor Necrosis Factor, IL=Interleukin, HsCRP= High-sensitivity C-reactive protein, BMI=Body Mass Index, HOMA-IR= Homeostatic Model Assessment for Insulin Resistance

*P<0.0125

Table 5. Correlation of visfatin with other inflammatory parameters in patient and control groups

Visfatin	Obese DM		Obese Control		Non-Obese DM		Non-Obese Control	
	Correlation coefficient (r)	P value	Correlation coefficient (r)	P value	Correlation coefficient (r)	P value	Correlation coefficient (r)	P value
TNF-α	0.03	0.836	0.05	0.845	0.132	0.522	0.111	0.606
Il-6	0.148	0.314	0.486	**0.04**	0.274	0.176	-0.179	0.401
HsCRP	0.189	0.198	-0.331	0.179	-0.014	0.945	0.406	**0.04**
Homa-IR	0.239	0.101	-0.218	0.385	0.101	0.623	0.576	**0.0032***
BMI	-0.112	0.448	-0.056	0.826	-0.043	0.835	0.346	0.097

DM=Diabetes Mellitus, TNF=Tumor Necrosis Factor, IL=Interleukin, HsCRP= High-sensitivity C-reactive protein, BMI=Body Mass Index, HOMA-IR= Homeostatic Model Assessment for Insulin Resistance

*P<0.0125

the waist-hip ratios of diabetics in both groups were significantly higher than their controls, indicating abdominal obesity (P<0.0125 and P<0.0001, respectively). Studies have demonstrated that plasma concentrations of adiponectin, produced by specialized fat cells, are reduced in T2DM [22-23]. Our study also observed an important decrease in adiponectin concentrations in T2DM patients compared to the control group, with this significant difference persisting in non-obese diabetics (P<0.0125). However, adiponectin concentrations were not different between obese diabetics and their controls. The amount of food consumed, overall body fat, and various hormones all contribute to regulating leptin secretion [3]. Insulin is the main factor in regulating the production of leptin. Prolonged elevated insulin levels in the blood result in an increased concentration of leptin in the plasma, whereas short-term elevated insulin levels do not cause this change [24]. The effects of leptin resemble those of other acute-phase reactants; it stimulates the secretion of various inflammatory cytokines (e.g., IL-12, IL-6 and TNF-α) [25]. An increase in fat mass leads to higher concentrations of leptin in the blood, directly related to obesity [26]. Our study found higher leptin concentrations in obese T2DM patients than in non-obese T2DM patients, though the difference was insignificant. In the non-diabetic group, obese individuals had higher leptin concentrations than non-obese individuals (P<0.0125).

IL-6, which is secreted by some cells, endothelial cells, monocytes, including fibroblasts, and adipocytes, is crucial in regulating the production of inflammatory proteins like CRP in the liver [27]. There is a positive correlation among circulating IL-6 and CRP levels in adipose tissue [28]. Studies have shown that IL-6 may be linked to insulin resistance and complications [29]. However, our study found no significant differences in IL-6 levels among groups.

TNF-α is suspected to play a role in obesity-related insulin resistance, with increased expression in the adipose tissue of obese individuals [30]. Studies have found conflicting results regarding the relationship between TNF-α concentrations and human insulin resistance [31,32]. However, a study conducted between 1998 and 2001 in 2356 individuals (children of Framingham Study participants) showed that TNF-α has an association with insulin resistance [33]. In our study, TNF-α concentrations of obese controls were significantly higher than lean controls (P<0.001). Although non-obese diabetics had higher TNF-α concentrations than non-obese controls, the difference was insignificant. TNF-α concentrations in obese controls exceeded those in obese diabetics (P<0.001).

Resistin functions through autocrine, paracrine, and endocrine modes of action, affecting various cell types and tissues [34]. Circulating resistin levels positively correlate with common inflammatory and fibrinolytic biomarkers such as CRP, IL-6 and TNF-α in conditions including type 2 diabetes, chronic kidney disease, rheumatoid arthritis, coronary atherosclerosis and sepsis [34]. Inconsistent results have been obtained from human studies. Macrophages that infiltrate adipose tissue are believed to be humans' primary source of resistin [35]. Circulating resistin is positively

associated with adiposity and may have a role in pro-inflammatory signaling [5]. Our study found no difference in resistin concentrations among obese or non-obese diabetics or control groups. Furthermore, no significant correlation was found between resistin and insulin resistance. But there was a correlation between resistin concentrations and CRP concentrations in T2DM patients, independent of BMI (P<0.001). Visfatin, recently identified and synthesized primarily by visceral adipose tissue, has metabolic effects similar to insulin and shows a strong relationship with adipose tissue mass [36]. Although plasma visfatin concentrations are high in type 2 diabetes in some studies, no relationship between circulating visfatin and insulin resistance has been shown [37,38]. Our study found no significant difference in visfatin concentrations between type 2 diabetic patients and no relationship between visfatin and insulin resistance, BMI, or insulin concentrations.

CRP, typically produced by the liver in reaction to cytokines like IL-6, has also been found to have its mRNA expressed in adipose tissue [39]. This suggests that adiposity may be an important source of inflammatory cytokines in healthy individuals. The increased CRP concentrations detected in the presence of insulin resistance might be attributed to an increase in adipose tissue [40]. In our study, hs-CRP concentrations were significantly higher in obese diabetics than in non-obese diabetics, and in obese controls compared to non-obese controls (P<0.0001). This supports the hypothesis that increased adipose tissue mediates the slightly elevated CRP concentrations. It remains unclear whether inflammation triggers insulin resistance in obesity or if pro-inflammatory cytokines and inflammation markers like IL-6 and CRP are elevated in obese individuals as a result of insulin resistance. Our study found higher hs-CRP concentrations in non-obese diabetics than their controls, but the difference was not significant.

CONCLUSION

To sum up, our findings indicate that insulin resistance in the absence of obesity may not be associated with known inflammatory processes. It is clear that there is a link between obesity and insulin resistance, and that adipokines probably contribute to lipid and carbohydrate metabolism. Although new studies have made significant progress, more detailed studies on insulin resistance and obesity are needed.

Ethical Statement

This study follows the principles of the Declaration of Helsinki. The study was conducted with approval from Istanbul University Faculty of Medicine Clinical Research Ethics Committee dated 28.08.2006 and numbered 1745. All participants provided their informed consent.

Authors' Contribution

Study Conception: AT, AGST; Study Design: AY, AGST; Supervision: AY, AGST, AKÜ; Funding: N/A; Materials: AY, AKÜ; Data Collection and/or Processing: AY, AKÜ; Statistical Analysis and/or Data Interpretation: AY, AGST, AKÜ; Literature Review: AY, AGST; Manuscript Preparation: AY and Critical Review: AY, AGST.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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Editor's note

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