Serum Lipid Peroxidation And Leptin Levels In Male And Female Type 2 Diabetic Patients In Gorgan (South East Of Caspian Sea), Iran

MARJANI A *, VEGHARI G **, BADELEH MT ***

ABSTRACT

Background: The aim of the present study was to determinate the possible relationship between serum leptin and lipid peroxidation in male and female type 2 diabetic patients in Gorgan, Iran.

Methods: The subjects consisted of fifty type 2 diabetic patients and fifty age and sex-matched control subjects. The concentration of leptin, malondialdehyde, lipid parameters and insulin were measured in all subjects. The results were evaluated by using independent sample ‘t’ test and Spearman’s correlation coefficient test.

Results: Leptin was correlated with BMI (male: r=0.339 and female: r=0.426, p<0.05) and malondialdehyde levels (male: r=0.124 and female: r=0.271, p<0.05) in the type-2 diabetic patients. In the control subjects, only a correlation between leptin and BMI was found (male: r=0.165, female: r=0.037, p<0.05).

Conclusions: In the correlation analysis using leptin as the dependent variable, BMI was found to be the predictor of leptin in males and females. Increased lipid peroxidation and hyperleptinaemia may play a role in the beginning and development of type 2 diabetes mellitus in this area.

Key Words: Leptin, Lipid peroxidation, Type 2 diabetes mellitus, Gorgan
Marjani A, Veghari G, et al; The Relationship Between Serum Leptin And Lipid Peroxidation Of Male And Female Type 2 Diabetic Patients In Gorgan, Iran

The relationship between serum leptin and serum lipid peroxidation in male and female patients with type 2 diabetes was investigated in Gorgan, Iran. The study was conducted at the Biochemistry and Metabolic Disorder Research Center of Gorgan, Iran, in 2008. The study included 50 type 2 diabetes patients and 50 age and sex-matched healthy controls. Leptin levels were measured using a human leptin ELISA test kit, and serum lipid peroxidation was assessed using the level of malondialdehyde (MDA). The results showed a significant correlation between serum leptin and lipid peroxidation in both male and female patients. The study suggests that leptin may play a role in the pathogenesis of type 2 diabetes and lipid peroxidation.
chromogen was extracted with 4 ml of n-butyl alcohol by vigorous shaking. Separation of the organic phase was facilitated by centrifugation at 3000 rev./min for 10 min and its absorbance was determined at a wavelength of 530 nm.

**Results**

The clinical characteristics of the type-2 diabetic patients and control subjects are described in [Table/Fig 1]. The mean duration of diabetes mellitus in type-2 diabetes mellitus patients was 1.5 years (range 1-3 years). The mean age of male and female patients in the type-2 diabetic and control subjects were 50.38±10.78 (18 males) and 50.46±9.53 (32 females), and 48.40±10.49 years (20 females) and 48.46±10.65 years (30 females), respectively. A number of obvious differences were found between the two subjects. The female type 2 diabetes mellitus patients had higher levels of fasting blood sugar, total cholesterol, LDL-cholesterol, HDL-cholesterol, VLDL-cholesterol, triglycerides, malondialdehyde, leptin and insulin as compared to the male subjects. Notably, the BMI (32.88±5.82 kg/m²), malondialdehyde (2.57±1.38 nmol/ml) and leptin levels (34.99±10.19 ng/ml) were significantly higher in female type-2 diabetes mellitus patients than in diabetic male subjects (25.05±1.85 kg/m², 2.10±0.67 nmol/ml and 11.04±7.76 ng/ml) (P<0.05) [Table/Fig 1]. The data shown in Table 1 reveals that the BMI (30.60±5.50 kg/m²) and leptin levels (26.34±12.02 ng/ml) was significantly higher in female type-2 diabetes mellitus patients than in male subjects (25.97±4.36 kg/m² and 11.26±5.46 ng/ml) (P<0.05). There was no significant difference in other parameters in female type-2 diabetes mellitus patients and male subjects. The data of [Table/Fig 1] shows that the levels of fasting blood sugar, total cholesterol, LDL-cholesterol, VLDL-cholesterol, triglycerides, malondialdehyde and insulin were significantly higher in male and female (leptin was also higher) type-2 diabetes mellitus patients than in diabetic male and female controls (P<0.05). But this is not the same for HDL-cholesterol, age and BMI in female type-2 diabetes mellitus patients [Table/Fig 1]. There were no significant differences in age, BMI, HDL-cholesterol and leptin in male type-2 diabetes mellitus patients and in male control subjects. Leptin correlated positively and significantly with the BMI of diabetic and control males (r=0.339 and r=0.165, p<0.05) and females (r=0.426 and r=0.037, p<0.05). Leptin also correlated positively and significantly with malondialdehyde (MDA) in the male and female type-2 diabetes mellitus patients (r=0.124, r=0.271, p<0.05) [Table/Fig 2].

**Discussion**

In the present study, we have observed that the levels of malondialdehyde (MDA), a lipid peroxidation product and a marker
of oxidative stress, is increased significantly in male as well as in female diabetic patients [Table/Fig 1]. This apparently shows that diabetic patients are exposed to an increased oxidative stress via lipid peroxidation. Some other researchers have also reported elevated lipid peroxidation products in the blood samples of type 2 diabetic patients [20],[21]. Several studies have shown that lipid peroxidation is increased in diabetes, particularly in type 2 diabetes mellitus [22],[23],[24]. Jain [25] demonstrated that hyperglycaemia stimulates the lipid peroxidation of RBC and Kannan and Jain [26] later showed that it increases oxidative stress in cells in vitro. Contrary to our observations and to that of others, there are several studies which did not find increased oxidative stress in type 2 diabetes mellitus patients [27].

In an animal study, Midaoui and Champlain [28] suffered the rat from type 2 diabetes mellitus and examined oxidative stress in the model of rat. Notably, they observed that hyperglycaemia alone does not induce oxidative stress unless it was accompanied by insulin resistance; thereby, implying that the involvement of reactive oxygen species is selectively related to insulin resistance [29].

Our results reveal a significant increase in the concentration of MDA in type 2 diabetic patients as compared to the control subjects [Table/Fig 1]. This is in agreement with the other published reports [22],[23],[24],[25],[26]. Our results show that BMI, MDA and leptin are statistically increased in female diabetic patients as compared to male subjects [Table/Fig 1].

Many investigators have demonstrated that leptin has a major relationship with BMI [30],[31],[32],[33],[34],[35]. In our study, also, leptin showed a correlation with BMI, both inmales and females with diabetes and in control subjects. Leptin showed a correlation with MDA in both males and females with diabetes. A clear tendency towards being obese and overweight was apparent in female and male diabetic patients (BMI, 30.07±6.08 and 25.05±1.85 kg/m²) and in control subjects (BMI, 30.60±5.50 and 25.97±4.36 kg/m²). Some of the type 2 diabetes mellitus patients suffered from Hyperlipidaemia. Therefore, our results apparently showed that being obese and overweight gave rise to increased oxidative stress in type 2 diabetes mellitus patients. Being obesity and overweight did not change the oxidative stress in the control subjects. Our study focussed on the association between serum leptin concentration and lipid peroxidation in type 2 diabetics. Recent studies have showed that leptin significantly increases intracellular reactive oxygen species in microvascular endothelial cells, particularly in diabetics [36]. According to our study, increased leptin levels observed in male and female diabetics may be related to increased lipid peroxidation [Table/Fig 2].

Literature findings on the role of leptin in diabetes is conflicting. Investigators have reported either increased [37], decreased [38],[37],[38],[39] or unchanged [40],[41] leptin levels in diabetics. As Wauters et al. [42] have pointed out, adiposity and gender are the main determinants of leptin levels in normal controls and diabetic patients. Therefore, part of the controversy among previous reports could be related to the difference in the adiposity or the gender of the patients. Many investigators have described leptin alterations only in obese or overweight patients [38],[37],[40]. Few workers have studied only men [37] or women [39]. The mechanism by which leptin stimulates oxidative stress conditions is unclear, but it may be related to the fact that leptin stimulates mitochondrial fatty acid oxidation and the increased generation of reactive radicals [43]. Sebnem et al. [44] have observed a significant decrease in the leptin levels in the plasma of streptozotocin-induced diabetic rats. Streptozotocin-induced hypolectinaemia may be related to a reduced adipose tissue mass and to the reduced assimilation and storage of energy substrates in the fat tissue in insulin deficiency and/or to the direct toxic effect of streptozotocin on the adipose tissue [45]. Panarotto et al. [46] has described lower leptin concentrations in females with diabetes as compared to those in the
control subjects. Our data only appear to be in contrast with this finding; our patients actually had higher leptin levels and higher fasting serum glucose concentrations than those studied by Panarotto's group. Moreover, in correlation analysis, BMI is considered to be a significant predictor of hyperleptinaemia [Table/Fig 2]. In the correlation analysis using leptin as the dependent variable, BMI and MDA were found to be significant predictors of leptin.

In the present study, it was found that there was a correlation between serum leptin and BMI in males and females in normal and diabetic subjects. Gender specific correlation showed an association between leptin and MDA in diabetic patients. Serum leptin showed a significant relationship to MDA in male and female diabetic patients (r = 0.124 and r = 0.271, p < 0.05). This trend reflects the increased MDA in males and females. Therefore, serum MDA levels are confounded by leptin or vice versa, such that in diabetes.

Nakanishi et al. [47] have investigated the association between leptin and oxidative stress and have explained this association exclusively through obesity. Many investigators demonstrated that leptin had a major correlation with BMI [48],[49],[50],[51],[52]. There is still a controversy that leptin concentrations are affected by type 2 diabetes. Surveys of Mexican-American [53] and German [54] subjects showed that leptin did not differ between normal subjects and subjects with type 2 diabetes, with matched BMI in males and females. In another report, it was found that baseline plasma leptin levels in subjects with newly diagnosed or long-standing type 2 diabetes were not significantly different from nondiabetic controls matched for BMI [54]. Other reports comparing plasma leptin levels between controls and weight-matched subjects with type 2 diabetes have led to discrepant conclusions, showing no effect [55],[56] or a decrease in leptin [57],[58].

Our present study shows a similar relationship between leptin and oxidative stress in obese and overweight type 2 diabetes mellitus hyperleptinaemic patients. Finally, our study on individuals who were referred to the Department of Diabetes Center in 5th Azar Hospital in the Golestan University of Medical Sciences on the South East of the Caspian Sea indicated that Type 2 diabetes was associated with higher leptin and MDA levels and BMI. In the correlation analysis, we found a significant relation between leptin levels and BMI in males and females. Increased lipid peroxidation and hyperleptinaemia may play a role in the beginning and in the development of type 2 diabetes mellitus.

References
[29] Houstis N, Evans D, Rosen, Lander ES. Reactive oxygen species have a causal role in multiple forms of


[39] Sayeed MA, Khan AKA, Mahtab HM, Ahsan KA, Banu A, Khanam PA, Ahren B: Leptin is reduced in lean subjects with Type 2 diabetes in Bangladesh. Diab Care 2000; 26: 547.


[47] Nakanishi S, Yamane K., Kamei N., Nojima H., Okubo M., Kohno N. A protective effect of adiponectin against oxidative stress in Japanese Americans: the association between
adiponectin or leptin and urinary
isoprostane, Metabolism 2005;
[48] Wei M, Stern HM, Haffner SM.
Serum leptin levels in Mexican
American and non-Hispanic whites:
association with body mass index and
cigarette smoking. Ann Epidemiol
Serum leptin concentrations in
moderate and severe obesity:
relationship with clinical,
antropometric and metabolic factors.
Int J Obes Relat Metab Disord 1999;
23: 1066–73.
JA, et al. Involvement of leptin in the
association between percentage of
body fat and cardiovascular risk
Insulin and body fat distribution have
no direct effect on plasma leptin levels
in obese Caucasian women with and
without type 2 diabetes mellitus.
Diabetes Metab 1998; 24: 229-34.
[52] Hodge AM, Boyko EJ, de Courten M,
et al. Leptin and other components of
the metabolic syndrome in
Mauritius⁎ a factor analysis. Int J
Obes Relat Metab Disord 2001; 25:
126-31.
[53] McGregor GP, Desaga JF, Ehlenz K,
Fischer A, Heese F, Hegele A,
Lammer C, Peiser C, Lang RE.
Radiommunological measurement of
leptin in plasma of obese and diabetic
human subjects. Endocrinology 1996;
[54] Dagogo-Jack S, Liu J, Askari H,
Tykodi G, Umamaheswaran I.
Impaired leptin response to
glucocorticoid as a chronic
complication of diabetes. J Diabetes
Complications 2000; 14:327–32.
M, Tamaya N, Iwata F, Muraguchi M,
Ohmoto Y, Iguchi A. Gender-related
difference in relationship between
insulin resistance and serum leptin
level in Japanese type 2 diabetic and
non-diabetic subjects. Endocr J 2000;
47:615–21.
[56] Guler S, Cakir B, Demirbas B, Gursoy
G, Serter R, Aral Y. Leptin
concentrations are related to
glycaemic control, but do not change
with short-term oral antidiabetic
therapy in female patients with type 2
diabetes mellitus. Diabetes Obesity
Metab 2000; 2:313–16.
[57] Abdelgadir M, Elbagir M, Eltom M,
Berne C, Ahren B. Reduced leptin
concentrations in subjects with type 2
diabetes mellitus in Sudan. Metab Clin
[58] Roden M, Ludwig C, Nowotny P,
Schneider B, Clodi M, Vierhapper H,
Roden A, Waldhausl W. Relative
hypo leptinemia in patients with type 1
and type 2 diabetes mellitus. Int J
Obesity Relat Metab Disord 2000;
24:976–81.