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TO DETERMINE THE ASSOCIATION BETWEEN SERUM LEPTIN LEVEL AND BODY MASS INDEX (BMI) IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Abstract:
Background: *Leptin is polypeptide protein 16 kDa released from adipocytes, and plays a key role in energy expenditure which helps in the control of bodyweight. Leptin plays an important role in regulating appetite and metabolism whereas obesity promotes a number of cellular processes which lead to weakening of the leptin signaling processes and increases the chances of weight-gain induced by genetic and environmental factors. Normally, leptin reduces bodyweight, and increased blood leptin levels with obesity are an indication of leptin resistance. Decrease in appetite is indicated by reduced leptin levels.*
Objective: *To correlate serum leptin levels in obese and non-obese type 2 diabetic patients and compare them with healthy individuals.*
Study Design: *This is a case-control study, conducted in the Endocrinology Department of Services Hospital, Lahore, for six months, from November 2019 to April 2020.*
Methods: *The study included type 2 diabetic patients and an equal number of healthy controls. Fasting blood glucose, glycated haemoglobin, serum leptin, and body mass index were assessed in obese and non-obese subjects. Relation between body mass index and serum leptin level was explored. Data was analyzed using SPSS 20.*
Results: *Of the 96 subjects, 48(50%) were in each of the two groups. Among the cases, there were 23(48%) men and 25(52%) women with an overall mean age of 51.27±11.7 years. The control group had 28(58%) men and 20(42%) women with an overall mean age of 49.3±12.1 years. Serum leptin levels were significantly higher in obese 9.42±1.87ng/ml and non-obese 7.21±3.78 ng/ml patients than the controls 5.38±2.20 ng/ml ($p<0.05$). Serum leptin concentration was significantly correlated with body mass index, fasting blood glucose and BMI, FBG and glycated haemoglobin ($p<0.001$ each).*
Conclusion: *Increased levels of serum leptin could be used as a risk factor in the development of type 2 diabetes mellitus.*
Keywords: *Serum leptin, BMI, Diabetes mellitus.*

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INTRODUCTION:

Diabetes mellitus (DM) is still one of the complicated health problems and is an issue of major concern for healthcare provider's worldwide[1] and is associated with high risk of developing coronary artery diseases (CADs). [2] Leptin is polypeptide protein 16 kDa released from adipocytes, and plays a key role in energy expenditure which helps in the control of bodyweight. [3,4]Leptin plays an important role in regulating appetite and metabolism[5] whereas obesity promotes a number of cellular processes which lead to weakening of the leptin signaling processes and increases the chances of weight-gain induced by genetic and environmental factors. Normally, leptin reduces bodyweight, and increased blood leptin levels with obesity are an indication of 'leptin resistance'. [6]Decrease in appetite is indicated by reduced leptin levels. However, in obese people, not only leptin concentration is raised but also there is variation among obese people in leptin levels which indicates that the control of synthesis and secretion of leptin may involve other factors than fatty tissues. [7]Leptin could be the potential and beneficial alternative modality that could be considered with the support of clinical trials for its safety and efficacy[7] because leptin has a potential role in regulating appetite and can reverse DM by improving glucose tolerance. Although insulin is the main support for the regulation of blood sugar level, it is time to look for alternative therapies for controlling DM. In a study, serum leptin concentration was significantly high in non-insulin-dependent DM patients and the correlation between body mass index (BMI) and leptin concentration with regards to gender was similar.[8] The current study was planned to evaluate the variation in serum leptin levels in obese and non-obese type 2 DM (T2DM) patients and to compare them with healthy controls.

MATERIALS AND METHODS:

This is a case-control study, conducted in the Endocrinology Department of Services Hospital, Lahore, for six months, from November 2019 to April 2020 and comprised diagnosed T2DM cases of either gender aged 40-60 years with or without diabetic complications. Those excluded were patients with conditions that could affect erythrocyte turnover (hemolysis, blood loss) and haemoglobin variants, patients having acute liver diseases, renal failure and pregnancy, and patients using lipid-lowering drugs, oral contraceptives and hormonal replacement therapy (HRT). The study was approved by the RMC ethics committee, and written informed consent was obtained from all the subjects. All the subjects were screened with a detailed questionnaire. Demographic data was collected through a self-administered questionnaire, and BMI was measured independently by using weighing machine and measuring tape. World Health Organization (WHO) classification for obesity was adopted used for BMI purposes.9 Blood samples were collected between 7am and 9am after an overnight fast of 12h. Serum leptin concentrations were measured by enzyme-linked immune sorbent assay (ELISA) kits for human leptin. Fasting blood sugar (FBS) was estimated using glucose oxidase method. The concentration of glycated haemoglobin (HbA1c) was measured immune turbid metrically, using a micro particle agglutination inhibition method. In addition to using structure proforma for data collection, document review was done to observe the diagnosis and treatment taken by the patients for diabetes management. Data was analyzed using SPSS 20 . Mean standard deviation (SD) was calculated for numerical variables like age, BMI, serum leptin level, HbA1c levels. Frequencies and percentages were calculated for categorical variables like gender, high leptin levels, and high HbA1c. Chi square test was used to compare categorical variables like gender, high HbA1C levels and high leptin levels between obese and non-obese diabetic patients while taking $p<0.05$ as significant. Bivariate Pearson's correlation test was used to see the relationship between BMI and leptin levels in both the groups.

RESULTS:

Of the 96 subjects, 48(50%) were in each of the two groups. Among the cases, there were 23(48%) men and 25(52%) women with an overall mean age of 51.27±11.7 years. The control group had 28(58%) men and 20(42%) women with an overall mean age of 49.3±12.1 years (Table 1).

Table I: baseline characteristics

	Control (48)	Cases (48)	*p*-value
Gender (F/M)	28/20	23/25	NS
Mean Age (years)	49.3±12.1	51.27±11.7	NS
Height (meters)	1.62±4.7	1.63± 8.3	NS
Weight (kg)	61.4 ± 2.2	72.1±8.1	<0.001
BMI (kg/m^2)	21.6 ± 2.1	24.03±3.3	<0.001
Systolic BP (mmHg)	114.5±10.4	121.8±6.4	<0.001
Diastolic BP (mmHg)	76.32±3.6	81.6±7.3	<0.001
Fasting glucose (mg/dl)	79.3 ± 2.1	152±4.2	<0.001
HbA1c (%)	4.1 ± 2.2	8.7±3.1	<0.001
Leptin (ng/ml)	4.87±3.19	8.65±2.6	<0.001

Based on BMI, 12(25%) among the patients were non-obese and 36(75%) were obese. Mean BMI in the patients group was significantly high compared to the controls (p<0.05) (Table 2).

Table-2: Variation in levels of different parameters in normal healthy controls and obese and non-obese patients of type 2 diabetes mellitus.

	Controls (Mean ± SD)	Obese T2DM (Mean ± SD)	*p*-value	Nonobese T2DM (Mean ± SD)	*p*-value
Age	49.3±12.1	50.42±7.2	0.176	52.12±5.5	0.081
Height (meters)	1.62±4.7	1.63±8.3	0.063	1.62±6.3	0.142
Weight (kg)	61.4 ± 2.2	73.5±3.5	<0.001	63.7±7.3	<0.001
BMI (kg/m^2)	21.6 ± 2.1	27.8±1.3	<0.001	23.7±2.1	<0.001
Systolic BP (mmHg)	114.5±10.4	135.4±12.7	<0.001	130.78±11.4	<0.001
Diastolic BP (mmHg)	76.32±3.6	83.41±4.1	<0.001	75.14±2.2	<0.001
Fasting glucose (mg/dl)	79.3 ± 2.1	180.4±4.2	<0.001	161.1±2.3	<0.001
HbA1c (%)	4.1 ± 2.2	9.7±4.3	<0.001	7.9±4.4	<0.001
Leptin (ng/ml)	4.87±3.19	9.42±1.87	<0.001	7.21±3.78	<0.001

BP: Blood pressure, HbA1c: Glycated haemoglobin, BMI: Body mass index, T2DM: Type 2 diabetes mellitus.

Mean systolic blood pressure (SBP) was 135.4±12.7 mmHg in obese and 130.78±11.4 mmHg in non-obese patients compared to 114.5±10.4 mmHg in the controls. HbA1c was significantly higher in the patients compared to the controls (p<0.05). Mean serum leptin level was significantly higher in obese diabetics 9.42±1.87 compared to the controls 4.87±3.19 (p<0.05). Serum leptin concentration was significantly correlated with BMI, FBS and HbA1c (p<0.001 each) (Table 3).

Table-3: Correlation of serum leptin with other parameters.

	R	P value
Age	0.24	>0.05
BMI	0.54	<0.001
FBG	0.67	<0.001
HbA1c	0.62	<0.001

HbA1c: Glycated haemoglobin, FBG: Fasting blood glucose, BMI: Body mass index.

DISCUSSION:

The major finding in the current study was positive correlation between serum leptin level and HbA1c. Leptin is a vital adipose tissue-derived hormone involved in pathophysiological mechanisms related to DM. The present study showed that serum leptin levels were significantly elevated in obese T2DM patients. The findings are supported by a study which observed that elevated leptin levels could confound an association with diabetes.[10] Another study found that increased levels of serum leptin were associated with increased risk of T2DM. [11] Serum leptin levels were observed to be higher in the obese group and positively correlated with BMI. [12] Reports regarding the role of leptin in diabetes are inconsistent, with some studies reporting increased[13] or decreased[14]or unchanged[15] serum leptin levels in diabetics. One study showed that serum leptin was related with diabetes (p=0.001) and highly correlated with waist circumference in obese compared to non-obese diabetics. [16] The current study observed higher leptin levels in women than in men in both cases and controls. The findings are supported by studies citing various causes of elevated serum leptin levels in women than in men, including high adiposity and subcutaneous fat, existence of a negative correlation between leptin and testosterone levels. [17] In the current study, HbA1c and FBG was higher in obese diabetics than non-obese diabetics and healthy controls. Analysis intimated that there is relevant affiliation among HbA1C, obesity and lipid distribution in diabetic patients. [18] The study also showed a positive relationship between insulin resistance (IR) and serum HbA1c levels of obese children. Another study reported no difference between obese and non-obese groups in terms of HbA1c values. [19] The present study has its limitations. Primarily it is a preliminary study which does not display any effect of medication or time variation on the subjects. Secondly, the sample size is too small to allow any credible inferences. Thirdly, to correspond with leptin levels we did not evaluate / measure fat distribution of the subjects.

CONCLUSION:

There was an association between increased serum leptin levels and T2DM patients. The levels of HbA1c and FBS were high in obese diabetic compared to non-obese diabetics and healthy controls. Higher leptin levels may be considered an additional risk factor in T2DM patients with high BMI.

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