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A comparative study of serum leptin levels among type 2 diabetes mellitus patients and non-diabetic individuals – hospital based cross-sectional study in Thiruvanthpuram, Kerala

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ABSTRACT

Introduction

Type 2 Diabetes mellitus (DM) is a global health problem with its rapidly rising prevalence. Although insulin resistance is a prominent feature, there are abnormalities in secretion of adipokines like leptin. Leptin, an adipokine coded by ob gene plays a major role in islet cell growth and insulin secretion. It regulates appetite, increase the expression of key enzymes of carbohydrates metabolism and can reverse diabetes by improving glucose tolerance. Administration of recombinant leptin can abolish hyperglycemia by stimulating glucose disposal to the peripheral tissues. Although insulin is still the ultimate choice of treatment in diabetic patients, long-term therapy can produce ectopic lipid deposition and life threatening hypoglycemia.

Aim

To compare serum leptin levels among Type 2 DM patients and non-diabetic individuals.

Methodology

This hospital based cross-sectional study was conducted among 41 Type 2 diabetic patients and 41 nondiabetic individuals of both sexes between the age group of 40 - 70 years. The study groups were selected among those who visited the centralized clinical biochemistry laboratory under the Department of Biochemistry, Government Medical college Hospital, Thiruvananthapuram, during the study period of one year from February 2013- January 2014. Patients who are clinically diagnosed as diabetics and with FBS $\geq$126 mg/dl were included. Those with FBS <126 mg/dl were included in the non-diabetic group. People with liver disease, renal disease, heart failure, stroke, obesity (BMI $\geq$ 25 kg/m^2), pregnancy and lactation were excluded from the study. Serum leptin was assayed using ELISA method and FBS by hexokinase method. Difference in means of quantitative variables between the two groups were compared by student t test. Pearson correlation coefficient was obtained to study correlation between serum leptin and fasting blood glucose.

Results

The mean serum leptin levels among diabetic patients was (2.7 $\pm$ 0.9) lower than the non-diabetic individuals (7.9 $\pm$ 3.2) and this difference in mean was statistically significant ($p < 0.001$). Leptin levels was found to be low among both diabetic males and females than the nondiabetics.

Conclusion- The study results showed that serum leptin levels were lower among the diabetic patients compared to non-diabetics individuals.

Key Words: Leptin, Type 2 diabetes mellitus, Fasting blood sugar

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INTRODUCTION

Diabetes Mellitus (DM) is a group of metabolic disorders that share the phenotype of hyperglycemia.[1] Ethnicity plays a major role in determining its prevalence and India has the highest number of patients worldwide. Hence it is named the diabetes capital of the world [2] Insulin resistance is a prominent feature of type 2 DM which preceedes the insulin secretory defect.[3]But diabetes results only when insulin secretion becomes inadequate.[4]Both visceral and subcutaneous adipose tissue secrete a group of bioactive substances called adipocytokines like leptin which are involved in regulation of glucose and lipid metabolism. Evidence has suggested that insulin and leptin are closely related partners in physiological and pathophysiological conditions.[5] Leptin is the most powerful regulator through which the fat stores speak brain how much energy is available and what to do with it. Leptin stimulates glucose uptake by brown adipose tissue (BAT), brain, heart and all splanchnic tissues and increases glucoseturnover. High leptin levels are seen after a carbohydrate rich meal and is due to the effect of increased levels of insulin and glucose. The activity of phosphoenolpyruvate carboxykinase (PEPCK), an enzyme in gluconeogenic pathway is diminished by leptin. Hepatic insulin receptor substrate 1 (IRS-1) associated phosphatidylinositol 3 kinase activity is slightly elevated by leptin to enhance glucose utilization. All these mechanisms help to lower blood glucose levels. Leptin is also essential for the regulation of expression of glucose transporter, Glut-2 in pancreatic cells.[6] Leptin improves glucose tolerance by increasing the expression of key enzymes of metabolic pathways of carbohydrates by influencing the rate of glycogenolysis and gluconeogenesis via melanocortin-dependent and independent pathways. Leptin may play a key role in controlling and potentially reversing diabetes. It has been postulated that in individuals predisposed to diabetes, hypothalamic resistance to multiple signals, such as leptin, insulin and fattyacids could contribute to the susceptibility to weight gain and insulin resistance. Leptin deficiency can lead to hyperphagia, decreased metabolic rate and significant changes in insulin action which can alter carbohydrate and lipid metabolisms. A study by Retnakaran R, Cull C A et al suggest that alteration in serum leptin level is a risk factor for kidney function decline in patients with type 2 DM.[9] Patients with low leptin levels have a significantly elevated risk of progression of albuminuria as compared with those with high leptin levels. The antidiabetic effect of leptin is the result of profound alteration of glucose metabolism in liver, BAT, heart and consequently affect glucose turnover.[9] Insulin is still the ultimate choice of treatment in diabetic patients. Though insulin-based therapies are life-saving, they cannot completely restore metabolic homeostasis and instead lead to serious side effects. Thus better anti diabetic approaches are needed urgently. Leptin administration has impressive effects in improving insulin action and maintaining glucose homeostasis. Administration of recombinant leptin arrests hyperphagia and declines the body weight. Restoration of leptin sufficiency in the hypothalamus can abolish hyperglycemia and impose euglycemia to an extended period by stimulating glucose disposal to the peripheral tissues.[10] Studies by Abdelgadir M etal and Fischer S etal demonstrated that leptin concentration in type 2 diabetic patients, compared with healthy subjects, is different among different ethnic groups. [11] [12] A study by Tatti P etal indicate that leptin levels are similar in people with and without diabetes.[13] As there is difference in leptin concentration, among type 2 diabetic patients of different ethnicities compared with healthy subjects, the leptin concentration in South Indian diabetic patients need to be elucidated. Therefore the present study was aimed to investigate the serum leptin levels among Type 2 diabetes mellitus patients in comparison to non-diabetic individuals.

METHODOLOGY

The hospital based cross-sectional study was conducted among people who visited the centralized clinical biochemistry laboratory under the Department of Biochemistry, Medical college Hospital, Thiruvananthapuram, during the period from February 2013- January 2014. 41 diabetic patients and 41 nondiabetic individuals were included according to the formula for 95% confidence limits and 80% power

$$N = \frac{2 \times (Z\alpha \pm Z\beta)^2 \delta^2}{(\mu_1 - \mu_2)^2}$$

$(Z\alpha \pm Z\beta)^2 = 7.849$ $\delta = 3.4$ [standard deviation of leptin levels in the population [14]] $(\mu_1 - \mu_2) = 2.1$ (expected difference in mean). By simple random sampling 41 Type 2 diabetic patients and 41 nondiabetic individuals between 40 and 70 years of age of both sex were selected. Diabetic patients were selected based on clinical diagnosis and FBS values ≥126 mg/dl. Those individuals with FBS <126 mg/dl were included in non-diabetic group. Patients with liver disease, renal disease, heart failure, stroke, obesity (BMI ≥ 25 kg/m^2), pregnancy and lactation were excluded. The study was conducted after approval of the ethical committee (IEC No: 02/7/2012MCT). Only those individuals who gave written consent were included in the study. Blood pressure was recorded using Sphygmomanometer and >140/90 mm of Hg was taken as hypertension. Estimation of fasting blood glucose was done in fully automated analyser (EM360) from Transasia Biomed. Serum Leptin assay was done using ELISA kit from Labor Diagnostika on EL_x 800MS, ERBA MICROSCAN ELISA machine.

Statistical analysis was performed using SPSS for windows version 16.The mean and standard deviation for quantitative variables and percentage for qualitative variables were calculated for the study subjects. Difference in means of quantitative variables between the two groups were compared by student t test. The association between serum leptin and fasting blood glucose of the study subjects were assessed using Pearson correlation. A p value of less than 0.05 is considered significant.

Results

The study results found out that diabetic patients practiced a sedentary life style compared to non-diabetic individuals. The mean systolic blood pressure among the diabetics and non-diabetics were 141.8 ± 11.4 & 130.2 ± 8 mm of Hg while diastolic blood pressure were 87.6 ± 4.9 & 82 ±7.5 mm of Hg respectively (Table 1).

Table 1: Various study parameters among diabetic patients and non-diabetic individuals

Variables		Mean	Standard deviation	Median	Minimum	Maximum
Age(years)	Diabetic	53.6	8.2	54	42	69
	Non-diabetic	52.1	8.9	50	42	70
Diastolic BP(mm of Hg)	Diabetic	87.6	4.9	90	80	98
	Non-diabetic	82	7.5	84	60	92
Systolic BP(mm of Hg)	Diabetic	141.8	11.4	140	120	160
	Non-diabetic	130.2	8	130	110	146
FBS(mg/dl)	Diabetic	335.5	85.7	308	222	538
	Non-diabetic	81.7	6.9	82	60	90
Leptin(ng/ml)	Diabetic	2.7	0.9	2.6	1.4	4.8
	Non-diabetic	7.9	3.2	8.7	2	11.0

(BP- Blood Pressure, FBS- Fasting blood sugar)

The mean serum leptin level was 2.7 in diabetic patients while it was 7.9 among the non-diabetic individuals. This difference was found to be statistically significant (p value <.05).(Table 2).

Table 2 Comparison of mean serum Leptin levels between diabetic patients and non-diabetic individuals

		N	mean	sd	t	p
LEPTIN(ng/ml)	Diabetic	41	2.7	0.9	-9.934	<0.001
	Non diabetic	41	7.9	3.2		

The mean serum leptin levels among males and females in diabetic patients and non-diabetic individuals were compared and the difference was found to be statistically significant (p value <.05) (Table 3).

Table 3 Comparison of mean serum Leptin levels in both gender

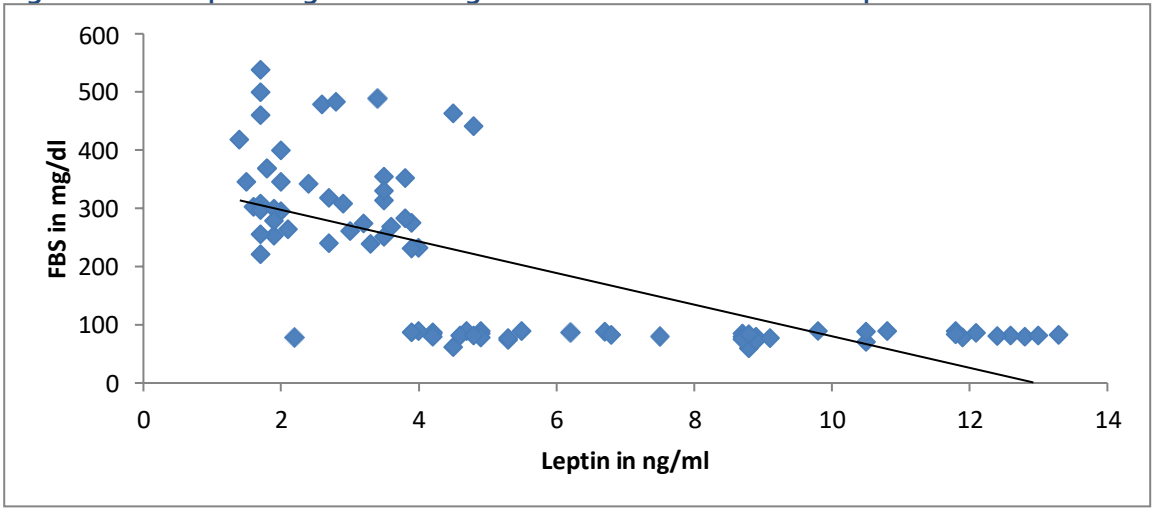
LEPTIN(ng/ml)		N	Mean	Std	t	p
Male	Diabetic	22	2.1	0.8	-7.366	<0.001
	Non diabetic	23	5.6	2.1		
Female	Diabetic	19	3.3	0.7	-16.765	<0.001
	Non diabetic	18	10.8	1.8		

The mean serum leptin levels in different age groups of 41-50, 51-60 & 61-70 years were 5.4 ± 4 ng/ml, 5 ± 3.1 ng/ml and 5.4 ± 3.5 ng/ml respectively. ANOVA test was done to compare the mean leptin levels in three age groups and the difference was not statistically significant Serum leptin showed statistically significant negative correlation with fasting blood sugar (p value <.05) (Table 4, Graph 1).

Table 4: Correlation of serum Leptin with FBS

	Leptin(ng/ml)	
FBS(mg/dl)	Pearson correlation (r)	-0.679
	p Value	<0.001

Figure 1 Scatter plot diagram showing correlation between serum Leptin and FBS



The equation obtained after simple regression analysis between leptin and FBS was Serum Leptin (y) = 5.769 – 0.016 FBS

Discussion

The study results showed that mean serum leptin levels among diabetic patients was 2.7±0.9 ng/ml and in non-diabetic individuals was 7.9±3.2 ng/ml. Thus low serum leptin levels were observed in diabetic patients compared to non-diabetic individuals Student t test was done to analyse the difference in mean leptin levels between these groups and the difference was found statistically significant A study by Moriya et al found out that serum leptin levels were low among poorly controlled Type 2 DM [15] On the other hand Tuominen et al found fasting plasma leptin levels is high in DM than in controls.[16] Haffner et al reported that leptin concentrations were not different in diabetic and non-diabetic subjects.[17] The comparison of serum leptin levels among different age groups do not show statistically significant relation. Thus we can conclude that there is not much variation in serum leptin levels as age advances. A study conducted by Alberto Verrotti et al also found no significant differences in leptin concentration in the three age groups of diabetic and non-diabetic subjects. [18] A statistically significant difference in mean serum leptin levels was observed in males and females among the diabetic patients and non-diabetic individuals. Among the diabetic males mean leptin was 2.1 ± 0.8 ng/ml and among diabetic females it was 3.3 ± 0.7 ng/ml. The mean leptin levels among non-diabetic males and females were 5.6± 2.1 ng/ml and 10.8 ± 1.8 ng/ml respectively. This shows that females have higher serum leptin compared to males in both groups. Pearson correlation was done to analyse

the correlation between serum leptin and FBS levels. There was strong negative correlation between these two variables (r = -.679) (Table 4)

This shows that as FBS levels increase, leptin levels decrease. The equation obtained on performing bivariate analysis by student t test, for predicting serum leptin levels show that one unit increase in leptin is produced by 0.016 times decrease in FBS. So we can conclude that the low serum leptin levels observed among the diabetic patients in the present study can be due to high FBS levels. However population based studies are needed to validate our study results in a broader aspect. Follow up studies are also needed to find out whether there is deterioration in leptin levels with progression of DM.

CONCLUSION

The study results showed that serum leptin levels were lower among the diabetic patients compared to non-diabetics individuals. Though insulin is still the mainstay for treatment of diabetes, leptin administration has impressive effects in improving insulin action and glucose homeostasis.

Units of Measurements	
BP	mm of Hg
FBS	mg/dl
Leptin	ng/ml

Abbreviations	
BP	Blood pressure
BAT	Brown Adipose Tissue
DM	Diabetes Melfitus
DKD	Diabetes Kidney Disease
FBS	Fasting Blood Glucose
Glut	Glucose transporter
INS	Insulin
IRS	Insulin Receptor Substrate
mRNA	Message RNA
OB	Obesity
PEPCK	Phosphoenol Pyruvate Carboxykinase

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