Original Research Article

Analysis of serum leptin levels as a biomarker in metabolic syndrome in type 2 diabetic patients in Okhla industrial area

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ABSTRACT

Background: Metabolic syndrome is a progressive disorder which includes a wide array of disorders i.e. central obesity, hypertension, dyslipidemia, hyperglycemia, and insulin resistance. In patients with metabolic syndrome there is an increased risk of mortality due to coronary heart disease, stroke, vascular dysfunction etc. Obesity is one of the most crucial epidemics of modern times and hormone leptin plays an important role in regulation of body weight and energy balance.
Methods: A total of 355 individuals were selected from the OPD, Department of general medicine at ESIC hospital, Okhla and it comprised of 196 males and 159 females suffering from type 2 diabetes mellitus with metabolic syndrome. The data was collected over a year i.e. June 2018 to July 2019. After baseline clinical and anthropometric evaluation, Fasting Blood Sugar (FBS), Post Prandial Blood Sugar (PPBS), lipid profile, Insulin (fasting), and leptin levels of the patients were analyzed.
Results: Blood sugar fasting, blood sugar post prandial, lipid profile, leptin and insulin levels were increased significantly in female patients as compared to male patients with type 2 diabetic patients and metabolic syndrome.
Conclusions: Based on the study results, it was found that leptin correlate significantly with metabolic syndrome and could be used as a biomarker for the early detection of the disease.

Keywords: Leptin, Metabolic syndrome, Obesity, Type 2 diabetes mellitus

INTRODUCTION

Leptin was discovered in 1994 and it is a 16-kDa product of the obese gene which is mainly produced by white adipose tissue. It belongs to long chain class I cytokines with four helix bundle conformation. Leptin is an important factor related to the regulation of food intake and it plays a vital role in the pathophysiology of the obesity as well.[1] Leptin reaches the hypothalamus through the blood–brain barrier and acts to reduce food intake and increase metabolism. It is observed that leptin acts through the increase in the effect of Cholecystokinin (CCK) which is released after meal intake from the small intestine. It is done through the receptor mediated activation.[2]

It also acts on the hypothalamus to signal when the body has sufficient energy stores, thus inhibiting appetite (i.e. it functions as an 'adipostat') and regulating the energy metabolism. The actions of leptin occur over both short and long time frames. In the short term, plasma leptin serves as a satiety signal, and over longer periods, daily

mean plasma leptin concentration communicates long-term energy status to the brain.[3]

Central leptin signaling plays a role in the regulation of metabolic activity by peripheral tissue. There is dysregulation of leptin due to disruption of melanocortin action which reduces the food intake by either physical injury to hypothalamus, by pharmacological agents or by genetic alterations of this protein and its receptors. Hence, due to the rising prevalence of human obesity and type 2 diabetes has generated extreme interest in the physiological roles that leptin plays in energy balance and food intake regulation.[4]

Leptin is important for body weight regulation. In mice, due to nonfunctional obese gene and mutations of this gene on chromosome seven, that encodes the leptin protein and results in obesity and type 2 diabetes. Leptin secreted by white adipose tissue is proportional to the volume of body of adipose tissue; therefore, adiposity greatly influences leptin levels. In addition, other factors, including rapid or excessive food intake, sleep, body temperature, gender, circadian rhythm, and other hormones such as insulin, growth hormone, glucocorticoids, testosterone, and thyroid hormone, impact leptin secretion and expression.[5]

Metabolic syndrome (MetS) is a group of metabolic disorder which is also known as Syndrome X. It is diagnosed with increased blood pressure, raised blood sugar, excess body fat around the waist.[6] According to National Heart, Lung and blood Institute, people with metabolic syndrome is twice likely to develop heart disease and five times more prone to develop diabetes without metabolic syndrome .The primary target of intervention of metabolic syndrome are lifestyle changes and weight loss and the secondary intervention is medication to treat existing risk factors like blood pressure, blood glucose and lipid levels.[7]

Although metabolic syndrome seems to have only attention of the medical community, the concept that an interrelated group of metabolic abnormalities is often present in people who develop cardiovascular disease and/or type 2 diabetes mellitus (DM) has been recognized for decades. In Northern India of urban community reported a prevalence of 22.37% for metabolic syndrome. On the contrary, a lower prevalence of 19.52% was reported in an urban population in western India.[8]

Although the predictive and clinical utility of metabolic syndrome has been debated in some circles, it is generally accepted that metabolic syndrome serves as a construct to identify individuals who have an increased and long-term risk of atherosclerotic cardiovascular disease (ASCVD) with or without type 2 DM.[9]

The aim of our study was to assess the relationship between serum leptin levels and metabolic syndrome in type 2 diabetic patients and to assess its role as a biomarker for metabolic syndrome.

METHODS

This study was conducted on the type 2 diabetic patients with metabolic syndrome with the age group of 65-75 years in the Department of Biochemistry, ESIC Hospital, Okhla. It comprised of total of 355 individuals i.e. male and female subjects are 196 and 159 respectively. The study period duration was from October 2018 to July 2019. The subjects with any acute and chronic disease i.e. thyroid diseases, chronic hepatitis, liver cirrhosis, those who were severely anemic (<6.0 gm% of Hb) and those suffering from any other systemic disorder were excluded from the study. Well informed written consent was obtained from all the enrolled subjects. Institutional ethical committee was also taken into the account. Inclusion criteria of the patients were as follows: Hypertension defined as BP $\geq$140/90 mmHg, Type 2 Diabetes Mellitus will be diagnosed in any person with diabetes mellitus on oral hypoglycemic drugs for control of blood sugar and FBS-110-125 mg/dL) WHO NCEP-ATP III, central obesity (defined by the WHO, NCEP-ATP III), hypertriglyceridemia-fasting serum triglyceride level $\geq$150 mg/dl.

A detailed clinical history including age, sex, occupation, socio-economic status, duration of diabetes and any associated risk factor contributing for the illness was elicited from the subjects.

Anthropometric parameters of the subjects i.e. Blood pressure was measured using a mercury sphygmomanometer to the right arm while the individuals were in a sitting position. The participant's weight and height was measured without shoes. BMI was calculated as weight (kg) divided by the square of height (m2). The waist circumference measurement was taken at the end of expiration and in between the midpoint of the last rib and superior iliac crest.

Under all aseptic precautions and after 12 hours fasting state, blood samples (5 ml) were drawn by venipuncture and collected in plain tube to measure Fasting Blood Sugar (FBS), Post Prandial Blood Sugar (PPBS), Total cholesterol, high-density lipoprotein cholesterol (HDL-C), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), Insulin (fasting), and leptin levels were measured using an enzymatic colorimetric method (Modular P; Roche Diagnostics).

Statistical analysis

The results are presented in Mean±SD. All the biochemical parameters were compared by using unpaired t-test between cases and controls. The Pearson's correlation coefficient was calculated among the study parameters. The p-value<0.05 was considered significant. All the analysis was carried out by using SPSS version.

RESULTS

A total of 355 diabetic patients suffering from metabolic syndrome were enrolled in the study. There were 196 male and 159 female patients of 65-75 years age group. The anthropometric parameters in both male and female subjects suffering from metabolic syndrome were studied in (Table 1). There was significant difference in BMI and waist circumference of the female subjects as compared to the male subjects.

Table 1: Anthropometric parameters in metabolic syndrome patients.

Parameters	Metabolic syndrome (males)	Metabolic syndrome (females)
Age (yrs)	73.6±4.5	72.8±3.8
Height (cms)	151.0±5.82	155.4±4.33
Weight (kgs)	72.3±8.41	79.6±9.20
BMI (kg/m^2)	33.5±4.46	39.4±5.23
Waist circumference (cms)	91.2±9.84	98.4±8.53
Systolic blood pressure (mm/Hg)	152±16.33	158±9.81
Diastolic blood pressure (mm/Hg)	118±6.42	120±6.28

Table 2: Biochemical parameters in metabolic syndrome patients.

Parameters	Metabolic syndrome (males)	Metabolic syndrome (females)	p-value
Fasting blood sugar (mg/dl)	128.3±15.4	138.2±20.7	<0.001
Post prandial blood sugar(mg/dl)	152±13.2	165.3±21.6	<0.001
S. total cholesterol (mg/dl)	163.2±42.2	175.3±40.4	<0.001
S. HDL-C (mg/dl)	52±38.2	54±36.3	<0.001
S. LDL-C(mg/dl)	41±20.7	46±21.3	<0.001
S.Triglyceride (mg/dl)	123.4±36.9	140.3±42.4	<0.001
S. Insulin (mIU/L)	2.6±1.50	3.2±1.43	<0.001
S. Leptin (ng/ml)	10.5±16.2	19.5±21.33	<0.001

Table 2 shows the biochemical parameters in metabolic syndrome patients. The level of FBS and PPBS was observed to be higher among female cases with respect to male cases. The lipid profile, insulin and leptin levels were also higher in the female cases with metabolic syndrome. The values of FBS, PPBS, lipid profile, leptin and insulin were found to be significantly increased with p-value <0.001.

DISCUSSION

Yun et al, reported that in a Korean population, it was observed that regardless of obesity status of the study subjects, the decrease in serum leptin levels reduces the cardiovascular risk factors and hence, the rate of metabolic syndrome.[10]

During 8-year follow-up done in Olivetti Heart Study (OHS) by Galleti et al, it was suggested that increase in leptin levels were strongly associated with increase in development of hypertension and impaired fasting glucose which points to rise in cases of metabolic syndrome.[11] In a prospective population based study in 2005, it was observed that glucose intolerance and insulin resistance are specific factors related to the development of metabolic syndrome.[12]

Considine et al, state that serum leptin levels and the mRNA content of adipocytes are elevated in obese patients as compared with non-obese controls and strongly positively correlated with the amount of body fat. Treating leptin deficiency with recombinant leptin resulted in reduced food intake and body weight, again demonstrating the role of leptin in mediating basal energy expenditure.[13]

Myers MG shown that high levels of leptin are usually observed in obese patients. The possible mechanisms include decreased sensitivity to elevated leptin levels, which is called leptin resistance, caused by defects at or downstream of the leptin receptor, induction of inhibitors of leptin signaling, and alterations in the transport of leptin across the blood-brain barrier.[14]

According to Zhao YF et al, Leptin, insulin concentrations, β-cell dysfunction and body weight all are inter-related to the course of development of obesity and type2 diabetes mellitus. Also, leptin resistance might occur in β-cells thus inducing hyperinsulinemia observed in obese patients.[15] Scuteri A state that serum leptin and high-sensitivity C-reactive protein were significant determinants of arterial stiffness independent of age, sex, and other traditional CV risk factors, indicating an association between inflammatory status and arterial stiffness.[16]

Stallmeyer et al, showed the importance of leptin as a mitogenic factor in skin repair and also topically administered leptin improved re-epithelialization. They investigated the regulation of leptin system during normal repair in healthy animals and found that highly proliferative keratinocytes of the wound margin epithelia strongly expressed the functional leptin receptor subtype.[17]

Different studies were done which revealed an association between leptin and regional adiposity. Leptin is more dependent on subcutaneous adipose tissue than on abdominal visceral tissue, since subcutaneous

adipocytes secrete more leptin than omental fat tissue. Abdominal subcutaneous fat volume was relatively more in males and post-menopausal females as compared to pre-menopausal subjects.[18] The BMI of the study population showed significant positive correlations with their insulin and leptin levels which were in agreement with the findings of the study done by Chung Jo et al, in Korean patients suffering from type 2 diabetes mellitus.[19]

The positive correlation between leptin and BMI were also established in a study done by Das et al and it was verified that HOMA-IR, insulin resistance and abdominal circumference and leptin levels were inter- related with type 2 diabetes mellitus.[20] In a prospective study done by Boyko et al it was found that leptin levels increases with increase in blood fasting glucose and triglycerides in patients of metabolic syndrome.[21] Mohiti et al, stated that leptin and insulin go hand in hand with respect to blood glucose regulation. The concentration of leptin in obese diabetic subjects was directly proportional to BMI.[22] McNeely et al, also found in their study that higher leptin levels suggested an increased risk for T2DM only in male patients during the follow up study.[23] Though in an interesting study done by Fogtello et al, leptin was found to be less useful tool for weight loss therapy in obese subjects with reduced food intake.[24] In a study done by Wen-Cheng Li et al, in 2011 it was shown that serum leptin levels were associated with metabolic syndrome as well as cardiovascular risk in an adult Taiwanese population.[25]

CONCLUSION

In the above study, it was observed that serum leptin levels were significantly associated in females as compared to males with the metabolic syndrome. It is directly related with the serum insulin and lipid profile levels. Leptin acts as an important link between obesity, insulin resistance, metabolic syndrome and cardiovascular complications. There is dearth of data to confirm if reduction of leptin can reduce cardiovascular complications in diabetic subjects. Since this study offers a small sample size, the statistical difference can vary in other large group populations. The effect of decreased leptin by dietary or pharmacological intervention in obese subjects with metabolic syndrome can surely decrease the burden of non-communicable disease.

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