# **Original Article**

#### SERUM LEPTIN IN OBESE TYPE 2 DIABETES MELLITUS

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## **ABSTRACT**

Leptin, a protein hormone expressed and released by adipocytes, is considered to have a role in the regulation of body weight and associated energy metabolism. The aim of this study was to investigate the serum leptin levels in obese type 2 diabetes mellitus individuals. Twenty obese male with type 2 diabetes mellitus (group A) and twenty obese male without type 2 diabetes mellitus (group B) were enrolled in the study. In both groups the body mass index (BMI), HbA1c and serum leptin levels were assessed. Serum leptin concentration of Group A was significantly lower than of group B;  $34.38\pm15.56$  ng/ml versus  $46.29\pm/13.51$  ng/ml, respectively; p<0.01. Serum leptin level was also significantly lower in a studied group of poorly controlled diabetes mellitus individuals compared to the one of well-controlled diabetics;  $29.49\pm11.82$  ng/ml versus  $37.89\pm10.54$  ng/ml, respectively; p<0.05. We also found a lower serum leptin level in obese male with type 2 diabetes mellitus than that of non diabetic obese. Serum leptin was lower in poorly controlled diabetes than of well controlled diabetes. We suggest that further studies are required to make clear the issue for lower leptin level and its role in the development of insulin resistance.

Key words: Leptin, Type 2 diabetes mellitus, Obesity

## Introduction

Leptin, a protein hormone expressed and released by adipocytes and encoded by obese gene. It is considered to have a role in the regulation of body weight and associated energy metabolism<sup>1</sup>. Leptin functions primarily as an antiobesity hormone. Obesity is a well known risk factor for the development of diabetes mellitus. Leptin has been implicated in the regulation of adipose mass<sup>2</sup> and has been reported to alter both insulin sensitivity <sup>3,4</sup> and insulin secretion<sup>5</sup>. Although it is clear that circulating leptin is positively correlated with body fat mass<sup>6</sup> Serum leptin levels were studied in hypothyroid females<sup>7</sup>, infertile patients<sup>8</sup>, pre-eclampsia patients <sup>9</sup> and patients with liver disease <sup>10</sup>. There is controversy about the level of circulating leptin whether it is reduced<sup>11</sup>, raised <sup>12,13</sup> or remains unchanged <sup>14–16</sup> in type 2 diabetes.

In this study we aimed to investigate leptin levels in obese male subjects with type 2 diabetes mellitus and in a small group with poor glycemic control.

#### Methods

Twenty obese male with type 2 diabetes mellitus (group A) and twenty obese male without type 2 diabetes mellitus (group B) were enrolled in the study. Patients having HbA1c greater than 8.0% were accepted as poorly controlled diabetes. The height (m), weight (kg) and BMI (kg/m2) were recorded. All subjects had a BMI equal to or greater than 30 for participating in the study as the obese subject. Before collecting venous blood samples using standard venipuncture, subjects were asked to have a fasting period of 12 h. In both groups, HbA1c and serum leptin levels were assessed at Microbiological laboratory, Chennai,India. HbA1c levels were measured using Nycocard reader. Serum leptin levels were measured using an enzyme immunoassay method (ALPCO,USA). The limit of detection for leptin is 0.50 ng/ml.

The results are expressed as Mean  $\pm$  SD for all the parameters and the statistical significance of differences among groups was examined by using t-test. For all

statistical assessments a value of p <0.05 was accepted to be statistically significant.

#### Results

The characteristics and biochemical parameters of obese diabetic and obese non-diabetic subjects are summarized in Table 1. Serum leptin concentration was significantly lower in group A than group B (34.38 $\pm$ 15.56 ng/ml versus 46.29  $\pm$  13.51 ng/ml, respectively; p< 0.01). Of the twenty diabetic subjects, leptin was also significantly lower (Table 2) with 9 poorly controlled diabetes mellitus individuals than 11 well-controlled diabetics (29.49  $\pm$  11.82 ng/ml versus 37.89  $\pm$  10.54 ng/ml, respectively; p < 0.05).

#### Discussion

Serum leptin levels are found higher in women than in men<sup>17</sup> and this is probably owing to adipose tissue in women being higher than in the opposite sex, the existence of negative correlation between leptin and testosterone levels<sup>18</sup>. Leptin has the ability of regulation of insulin secretion from the pancreatic islet cells.<sup>19</sup> After leptin was given to mice who had leptin deficiency, it has been demonstrated that there had been a decrease in hyperglycemia and hyperinsulinemia, inhibition in hepatic gluconeogenesis and insulin secretion via direct effects on beta cells.<sup>20</sup>

Some investigators have found that in more obese patients with type 2 diabetes mellitus, the leptin levels were less in patients with not well controlled diabetes than in well-controlled diabetic subjects.<sup>21</sup> This was related to the insulin deficiency. In our study also, leptin levels were significantly lower in patients who have HbA1c above 8.0%. It has been found that untreated diabetes gave rise to a reduction in

leptin levels owing to an ineffective release of insulin by the monodrug therapy<sup>22</sup>.

In this study, We found low serum leptin level in obese male with type 2 diabetes mellitus than non diabetic obese and also leptin is lower in poorly controlled diabetes than well controlled. We suggest that further studies are required to make clear the issue for lower leptin level and it's role in the development of insulin resistance.

### References

- 1. Rosenbaum M, Leibel RL. The role of leptin in human physiology. N Engl J Med 1999;341: 913-5.
- Considine RV, Sinha MK, Heinman ML, Kriauciunas A, Stephens TW, Nyce MR, et al. Serum immunoreactive leptin concentrations in normal-weight and obese humans. N Engl J Med 1996;334:292

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- 3. Sivitz WL, Walsh SA, Morgan DA, Thomas MJ, Haynes WG. Effects of leptin on insulin sensitivity in normal rats. Endocrinol 1997;138:3395–401.
- 4. Kamohara S, Burcelin R, Halaas JL, Friedman JM, Charron MJ. Acute stimulation of glucose metabolism in mice by leptin treatment. Nature 1997;389:374–7.
- 5. Kieffer TJ, Habener JF. The adipoinsular axis: effects of leptin on pancreatic β-cells. Am J Physiol Endocrinol Metab 2000;278(1):E1–E14.
- 6. Al-Shoumer KA, Vasanthy BK, Makhlouf HA, Al-Zaid MM.Leptin levels in Arabs with primary hyperthyroidism. Ann Saudi Med 2000;20(2):113–8.
- 7. Baig M, Kasira KA, Ahmad A, Zaidi P, Niaz K, Kamal S. Serum leptin level in hyperthyroid female patients. *J Pak Med Assoc* 2003; 53: 176-80.
- 8. Baig M. Role of serum leptin in primary infertility in females. *Ph.D Thesis, University of Karachi, Karachi,* 2008.

	Obese diabetic (group A)	Obese non-diabetic (group B)	p-value
BMI (kg/m2)	$31.24 \pm 3.60$	$33.09 \pm 2.19$	0.516
Leptin (ng/ml)	34.38±15.56	46.29 ±/13.51	< 0.01
HbA1c (%)	$8.86 \pm 2.01$	$5.8 \pm 0.12$	< 0.001

**Table 2:** Leptin levels in subjects who have poorly and well controlled diabetes mellitus.

	Poorly controlled diabetes	Well controlled diabetes	p - value
	( n = 9)	( n = 11)	
Leptin (ng/ml)	$29.49 \pm 11.82$	$37.89 \pm 10.54$	< 0.05

- 9. Mumtaz F, Memon AR, Yousfani S, Tahir SM, Khushk I, Memon M, et al. Role of serum leptin level as a marker of severity of pre eclampsia. *J Ayub Med Coll Abbottabad* 2008; 20: 13-5.
- Siddiqui AR, Abbas Z. Leptin and liver disease: facts and presumptions. J Coll Physicians Surg Pak 2004; 14: 122-4
- 11. Clement K, Lahlou N, Ruiz J, Hager J, Bougnères P, Basdevant A, *et al.* Association of poorly controlled diabetes with low serum leptin level in morbid obesity. Int J Obes 1997;21:556–61.
- 12. Roden M, Ludwig C, Nowotny P, Schneider B, Clodi M, Vierhapper H, *et al.* Relative hypoleptinemia in patients with type 1 and type 2 diabetes mellitus. Int J Obesity Relat Metab Disoord 2000; 24:976–81.
- 13. Widjaja A, Stratton IM, Horn R, Holman RR, Turner R, Brabant G. UKPD 20: Plasma leptin, obesity, and plasma insulin in type 2 diabetes subjects. J Clin Endocrinol Metab 1997;82:654–7.
- 14. Haffner SM, Stern MP, Miettinen H, Wei M, Gingerich RL.Leptin concentrations in diabetic and non-diabetic Mexican-Americans. Diabetes 1996;45:822–4.
- 15. Guler S, Cakir B, Demirbas B, Gursony G, Serter R, Araf Y.Leptin concentrations are related to glycemic control, but do not change with short-term oral antidiabetic therapy in female patients with type 2 diabetes. Diabetes Obes Metab 2000;2:313–6.

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- Schwartz MW, Prigeon RL, Kahn SE, Nicolson M, Moore J, Morawiecki A, *et al.* Evidence that plasma leptin and insulin levels are associated body adiposity via different mechanisms. Diabetes Care 1997;20:1476

  –81.
- 17. 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 1997; 7:79 80.
- 18. Vettor R, De Pergola G, et al. Gender differences in serum leptin in obese people: relationship with testosterone, body fat distribution and insulin sensitivity. Eur J Clin Invest 1997; 27: 1016 1024.
- 19. Ceddia RB, William WN Jr, Carpinelli AR, Curi R. Modulation of insulin secretion by leptin. Gen Pharmacol 1999; 32: 233 237.
- Pelleymounter MA, Cullen MJ, Baker MB, et al. Effects of the obese gene product on body weight regulation in ob/ob mice. Science 1995; 269:540
  543.
- Clement K, Lahlou N, Ruiz J, et al. Association of poorly controlled diabetes with low serum leptin in morbid obesity. Int J Obes Relat Disord 1997; 21: 556 561.
- 22. Sivitz WI, Wayson SM, Bayless ML, et al .Leptin and body fat in type 2 diabetes and monodrug therapy. J Clin Endocrinol Metab 2003; 88:1543 1553.