ORIGINAL ARTICLE

EFFECT OF BODY MASS INDEX ON SERUM LEPTIN LEVELS

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Background: Leptin is product of *ob* gene, an adipose tissue derived hormone that plays a key role in the regulation of body fat mass by regulating appetite and metabolism while balancing energy intake and energy expenditure. The objective of the study was to evaluate possible association between serum leptin levels and Body Mass Index (BMI) of gender in adult age group. **Methods**: Two-hundred-seventy subjects aged 20–50 years were randomly selected from general population of Abbottabad. The subjects were grouped on the basis on BMI (89 normal, 92 overweight, and 89 obese). After complete evaluation, demographic data was recorded and BMI. Non-fasting venous blood samples were drawn to measure serum leptin and serum glucose levels. The data were analysed using SPSS-15 calculating mean, percentage, independent *t*-test and chi-square test. Correlation and regression curve analysis were obtained, and *p* and *r* values were calculated. **Results**: Serum leptin levels and differences between genders were significant in all body mass indices. For normal BMI group the mean values for leptin were 2.6±1.5 ηg/ml in men, and 17.3±10.2 ηg/ml for women. For Group-2 mean leptin levels in men were 9.9±6.8 ηg/ml and in women were 34.8±13.6 ηg/ml. For Group-3 BMI comprising obese subjects mean values for men were 21.3±14.2 ηg/ml and for women were 48.21±21.2 ηg/ml ($p<0.001$). **Conclusion:** A progressive increase in serum leptin concentration was observed with an increase in BMI. Significant difference between leptin concentrations in either gender was found in normal, overweight and obese subjects.

Keywords: Serum leptin levels, weight gain, BMI

INTRODUCTION

Leptin is one of the most important adipose derived hormones. Leptin (from Greek word *leptos,* meaning thin) is a 16 KDa protein hormone that plays a key role in regulating energy intake and energy expenditure, including the regulation (decrease) of appetite and (increase) of metabolism.[1]

Leptin binds to ventromedial nucleus of hypothalamus, known as the 'appetite center'.[1] Binding of Leptin to this nucleus signals to the brain that the body has had enough to eat, a sensation of satiety. A very small group of humans possess homozygous mutations for Leptin gene which lead to a constant demand for food, resulting in severe obesity. The body mass index (BMI), or Quetelet index, is a statistical measure which compares a person's weight and height. Recent studies with obese and non-obese humans demonstrated a strong positive correlation of serum Leptin concentration with percentage of body fat, and also that there was a higher concentration of *ob* mRNA in fat from obese compared to thin subjects. It appears that as adipocytes increase in size due to accumulation of triglyceride, they produce more Leptin.[2]

Levels of Leptin in human blood correlate with body mass index (BMI) and fat mass. This hypothesis was confirmed by experiments with Leptin injections to Leptin-deficient *ob/ob* mice, which led to weight loss by decreased food intake and increased energy expenditure.[3]

From the first reports of Leptin measurements in human, it was already evident that a clear gender difference in Leptin levels existed: Leptin levels were found 2–3 fold higher in women than in men for the same BMI.[4] These differences reflect the difference in body composition between men and women. Women in general have a higher percentage of body fat and higher ratios of subcutaneous to visceral fat. Serum Leptin is strongly related to fat mass, and even stronger to subcutaneous fat[5,6], which has been shown to secrete more Leptin.[7,8]

Serum Leptin concentrations were significantly higher in normal weight women than in normal-weight men and in obese women than in obese men when the groups were defined by BMI.

However, when women and men with equivalent percentages of body fat were compared there was no difference between the sexes. In previous studies obese subjects have higher serum Leptin concentration than normal-weight subjects. Although several factors may contribute to the elevation of serum Leptin concentrations in obesity, the values were most closely related with the percentage of body fat.[9]

MATERIAL AND METHODS

This prospective analytical study was conducted in Department of Pathology, Ayub Medical Institute from Mar 2008–Mar 2009. For the present study altogether 270 subjects were selected randomly from the general population of Abbottabad of age groups 20–50 years.

After taking informed consent, demographic data was taken and detailed physical examination of all subjects was done. Subjects with any evidence of disease, illness, addictions or taking any medications were excluded from the study. Non-fasting venous blood samples were drawn and checked for serum leptin and serum glucose. All the data were recorded and analysed using SPSS-15. Subjects were divided into three groups according to their BMI:

- Control group (BMI 20–25 Kg/m^2) consisted of 89 subjects
- Overweight subjects (BMI 25.1–30 Kg/m^2) consisted of 92 subjects.
- Obese subjects (BMI ≥30.1 Kg/m^2) consisted of 89 subjects.

All *p*-values were two sided and $p \leq 0.05$ was considered statistically significant. Correlations, regression curves and partial correlation were also drawn among groups.

RESULTS

Frequency distribution of socio-demographic and biochemical data of all subjects including variables like age, weight, height, BMI, serum Leptin and serum glucose in gender groups are calculated. Then mean values for quantitative variables of all subjects and for gender in each BMI groups also calculated (Table-1).

Weight, height, BMI and serum leptin in both gender groups are highly significant ($p<0.001$ in Group-1 and Group-2 of BMI). Weight, height, BMI and serum leptin are significant ($p<0.001$) in women of Group-3 of BMI. Weight, height and serum leptin were significant ($p<0.001$) in men of group 3 of BMI. Weight, height and serum leptin are also significant ($p<0.001$) in two groups of gender in all subjects (Table-1).

The correlation and regression analysis of the curves related to all variables was done using linear, cubic, quadratic, logarithmic and exponential relationship. Curve estimation and significant correlation for all variables of interest for all women and men in BMI Groups are shown in Table-2. Correlation of BMI with Serum leptin is shown in Figure-1 and 2.

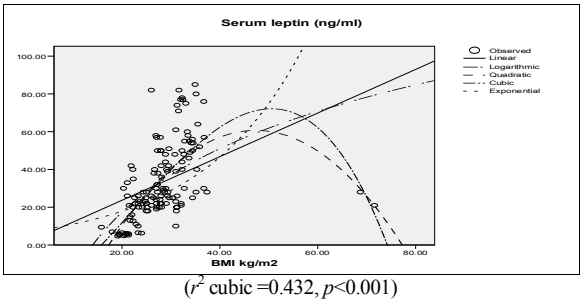
Table-1: Demographic and biochemical data and Mean±SD for gender groups in three groups of BMI

Gender groups	Variables	BMI Groups			
		Group-1 (89)	Group-2 (92)	Group-3 (89)	Total (270)
Women (n=135)	Age (Yr)	34.58±8.83	34.53±8.6	34.82±8.4	34.64±8.54
	Weight (Kg)	57.96±7.9*	74.1±8.4*	91±13.8*	74.36±17.0*
	Height (m)	1.61±0.05*	1.63±0.08*	1.64±0.07*	1.63±0.07*
	BMI (Kg/m^2)	22.2±2.2*	28.0±1.2*	34.93±7.9*	28.4±7.1
	Serum Leptin (ηg/ml)	17.3±10.2*	34.8±13.6*	48.21±21.1*	33.3±20.14*
	Serum glucose (mmol/l)	5.8±0.9	6.5±0.9	8.7±1.5	6.98±1.6
Male (n=135)	Age (Yr)	34.77±8.66	33.47±8.52	34.41±8.523	34.20±8.599
	Weight (Kg)	68.6±6.6*	83±9.0*	102.7±12.4*	84.80±16.9*
	Height (m)	1.7±0.07*	1.7±0.08*	1.69±0.06*	1.69±0.072*
	BMI (Kg/m^2)	23.6±2.1	28.6±1.2	36.4±5.5	29.5±6.2
	Serum Leptin (ηg/ml)	2.6±1.5*	9.9±6.8*	21.3±14.2*	11.24±11.9*
	Serum glucose (mmol/l)	5.82±1.1	6.56±1.0	8.4±1.1	6.92±1.51

*$p<0.001$

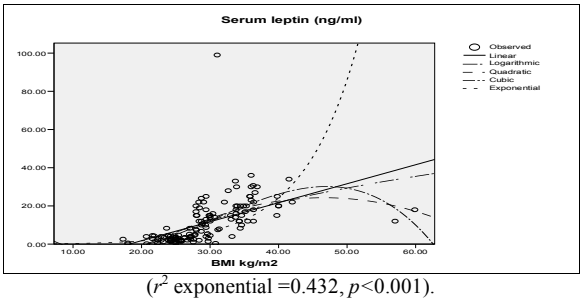
Table-2: Curve estimation for all variable with serum leptin (only most significant are shown)

Correlations of various variables		Curve Estimation (r^2, p)				
		Linear	Quadratic	Cubic	Logarithmic	Exponential
Women (135)	With weight	0.199, $p<0.001$	0.294, $p<0.001$	0.294, $p<0.001$	0.241, $p<0.001$	0.267, $p<0.001$
	With BMI	0.166, $p<0.001$	0.428, $p<0.001$	0.432, $p<0.001$	0.272, $p<0.001$	0.220, $p<0.001$
	With serum glucose	0.180, $p<0.001$	0.240, $p<0.001$	0.255, $p<0.001$	0.209, $p<0.001$	0.159, $p<0.001$
Men (135)	With weight	0.314, $p<0.001$	0.358, $p<0.001$	0.389, $p<0.001$	*0.334*, $p<0.001$	0.486, $p<0.001$
	With BMI	0.273, $p<0.001$	0.357, $p<0.001$	0.377, $p<0.001$	0.312, $p<0.001$	0.432, $p<0.001$
	With serum glucose	0.181, $p<0.001$	0.181, $p<0.001$	0.185, $p<0.001$	0.175, $p<0.001$	0.271, $p<0.001$
Women in BMI Group-1	With BMI	0.183, $p=0.003$	0.186, $p=0.013$	0.187, $p=0.013$	0.184, $p=0.003$	0.279, $p<0.001$
Women in BMI Group-2	With weight	0.168, $p<0.001$	0.188, $p<0.001$	0.190, $p<0.001$	0.182, $p<0.001$	0.168, $p<0.001$
Men in BMI Group-2	With weight	0.155, $p=0.006$	0.156, $p=0.024$	0.156, $p=0.024$	0.156, $p=0.006$	0.198, $p=0.002$
	With BMI	0.105, $p=.026$	0.228, $p=0.003$	0.229, $p=0.003$	0.110, $p=0.023$	0.057, $p=0.105$



(r^2 cubic =0.432, $p<0.001$)

Figure-1: Correlation of BMI with serum Leptin in women



(r^2 exponential =0.432, $p<0.001$).

Figure-2: Correlation of BMI with serum Leptin in men

DISCUSSION

Leptin belongs to a family of hormones that regulate body weight. It is released from the fat cells, and its level in blood is maintained in proportion to body fat. It acts as an auto-regulator of energy intake by acting on the hypothalamus to inhibit the biosynthesis of neuropeptide Y causing decrease in appetite.

The rise in serum Leptin levels between BMI Group-1 and 2 was 4 times higher compared to nearly 2 times rise between BMI Group-2 and 3. There was 2 times increase in overweight women compared to normal-weight women followed by a much smaller increase in the obese women group. These results were compatible with the study of Chow PT and Phtoon MC[10], Hickey MS *et al*[11], and Considine *et al*[12].

The serum Leptin level increased as BMI increases irrespective of gender; however, men showed a greater reactive response of increasing leptin secretion as their fat mass increased, while women having already higher basal levels showed a much smaller reactive response. The initial increase was marked in overweight groups in both genders as compared to the normal group. Serum Leptin did not increase to the same extent between overweight and obese groups. This indicates that most of the time serum Leptin increases during transition from normal to overweight and there after slowing down while approaching to obesity. This finding is also supported by a previous study of Fried *et al*[13], that on average leptin release per gram of adipose tissue is 2–3 times greater in obese than in lean subjects, because fat cells are usually enlarged 2–4 times in the obese. When expressed per fat cell, Leptin secretion can be up to 7 times higher in obese than in lean subjects. At certain level this increase of serum leptin becomes constant, that is why the increase of serum Leptin for overweight to obese was not as high as for normal to overweight. This is explained by the fact that significant transport saturation for Leptin occurs between 10–15 ηg/ml and 20–25 ηg/ml respectively, almost full saturation exists.[14]

In present study a significant positive correlation of serum Leptin and BMI was found. As BMI increased serum Leptin also increased in all subjects among BMI groups and in gender groups. Difference among the genders is perhaps reflective of the earlier noted observation that men respond with greater percent increase of Leptin secretion per fat mass compared to women, resulting in a greater value of *r*. It may be that men are required to maintain a leaner body mass in keeping with their occupational challenges compared to women who require more adipose tissue for their physiological and reproductive needs; this necessitates different basal and reactive secretory responses of leptin from the genders.

From the first reports of Leptin measurements in human, it was already evident that a clear gender difference in leptin level existed. Leptin levels were found to be 2–3 fold higher in women than in men for the same BMI.[12,15] This difference reflects the difference in body composition between men and women, women in general having higher percentage of body fat and higher ratio of subcutaneous to visceral fat. Although the present study has not taken up fat mass as measure of obesity but the findings with BMI closely reflects the finding of all the above mentioned researchers. *In vitro* data show that Leptin secretion by adipose tissue from men and women is different with a significantly higher spontaneous secretion by adipocytes from women than men.[16]

A study carried out in German/Nordic by Wisner *et al*[17] states that plasma Leptin concentration increased in obese male compared to lean men. Lean women also displayed elevated plasma levels compared to lean men. Similar results were found in present study.

CONCLUSION

A progressive increase in serum Leptin concentration was observed with an increase in BMI. Significant difference between Leptin concentrations in either gender was found in normal, overweight, and obese subjects. This indicates the important role of Leptin in human metabolism and obesity.

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