Original Research Article

Relation between Plasma Leptin, Anthropometric and Metabolic Covariates in Hypertensive Patients

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ABSTRACT

Background: Leptin is an adipose tissue-derived hormone revealed to be related to metabolic, inflammatory, and haemostatic factors concerned with hypertension progress. Higher leptin levels may trigger the sympathetic nervous system and cause rise in blood pressure (BP).

Material and methods: we examined the relationship between plasma leptin levels and hypertension in a respective of obese and non-obese adults. Hypertension was defined as BP-reducing medication use or having systolic BP ≥140 mm Hg and/or diastolic BP ≥90 mm Hg.

Results: We found that the leptin level is higher in obese hypertensive in comparison to obese non-hypertensive subjects which is statistically significant (P,<0.05). The leptin level is higher in obese hypertensive in comparison to lean hypertensive subjects which is statistically significant (P,<0.05). The leptin level is higher in lean hypertensive in comparison to lean non-hypertensive subjects but this is statistically insignificant. (P,>0.05) The leptin level is higher in obese in comparison with non-obese subjects which is statistically significant. (P <0.05)

Conclusion: Leptin is strongly correlated with hypertension and body mass index. Leptin level is directly proportional to body mass index.

Key Words: leptin, hypertension, adipokines, insulin

INTRODUCTION

Systemic hypertension remains the most common, readily identifiable and reversible risk factor for Stroke, Myocardial infarction, heart failure, atrial fibrillation, aortic dissection and peripheral arterial disease, affecting 1 billion people worldwide.

Because of increasing obesity and population aging in developed and developing countries, the worldwide burden of hypertension is intensifying and projected to affect 1.5 billion persons, one third of the world's population by the year 2025. Thus hypertension remains the foremost cause of death globally and one of the world's great public health problems. [1]

Most likely, high blood pressure is an important public health problem in developed and developing countries as well because it causes a significant morbidity and mortality. It is common, asymptomatic,
readily detectable, usually easily treatable and if untreated often leads to lethal complications. [2] Blood pressure is considered to be a continuously distributed variable and essential hypertension is one extreme of this distribution. [3] Hypertension is defined as either SBP> 140 mmHg and DBP> 90 mmHg and/or anti-hypertensive medication. [4] Hypertension is a major public health problem in developed as well as in developing countries. [5] In the initial stage of hypertension, most of the patients do not suffer any symptoms. Commonly, high blood pressure does not presents with symptoms like buzzing, headache, palpitation or vertigo. Therefore, most patients do not know that they have high blood pressure or hypertension, and in a while this is diagnosed, it is difficult to ascertain an exact duration of hypertensive conditions. [6]

Leptin (Greek Lepto meaning "Thin") is an adiposity derived hormone described by Friedman and colleagues in 1994. [7] LEPTIN, the obese (ob) gene product is a 16-K Da (containing 167 amino acid proteins) peptide hormone, secreted by adipocytes. [7] Leptin is thought to be lipostatic signal to brain centre controlling energy homeostasis. It could have an effect to body weight regulation through regulating feeding behavior and/or energy expenditure. [8] Leptin levels are higher in the obese, reflecting leptin resistance, possibility caused by reduced transport into the cerebrospinal fluid or defective post receptor signaling. [9]

Leptin implicated in the regulation of food intake and satiety, as well as in the control of fat accumulation. [10]

Human obesity is explained by elevated plasma leptin levels and "resistance" to the metabolic effect of the hormone to the extent that high plasma leptin levels are ineffective in reducing fat accumulation. [11]

Overweight, obesity and abdominal fat increase the risk of both cardiovascular and cerebrovascular diseases.

Some experimental animal studies advocate that higher leptin levels may stimulate the sympathetic nervous system and further rise in blood pressure (BP). [12]

The study has designed to investigate the relationship of serum leptin with essential hypertensive and non-hypertensive subjects.

MATERIAL AND METHODS

In the present study total 60 patients, were randomly selected from the out-door and indoor in the Department of Medicine of Jawahar Lal Nehru Hospital attached to Jawahar Lal Nehru Medical College and Associated Group of Hospitals, Ajmer and were divided into different groups.

The healthy subjects are recruited by advertisement informed and consent was taken from all the subjects (Hypertensive and Nonhypertensive) during the study.

The following four groups was studied in the present study –

- A- Lean Non-hypertensive (n = 15)
- B- Lean Hypertensive (n = 15)
- C- Obese Non-hypertensive (n = 15)
- D- Obese Hypertensive (n = 15)

In total 4 groups 15 patients in each, total 60 different patients were included in our present study. In this we observed the leptin levels. The body mass index (BMI) was calculated by body weight/height² (kg/m²). The WHR calculated by dividing the waist circumference by the hip circumference

Metabolic Measurements:

All the groups were screened according to guide line of Joint National committee (JNC-VII).
Base line sample was taken for plasma leptin after a 12 hour over night fast. Overnight fasting serum with stored at – 20°C for the analysis of leptin levels.

**Principle of the DRG leptin ELISA:**

The DRG Leptin ELISA kit is a solid phase enzyme – linked immunosorbent assay (ELISA) based on the sandwich principle.

The Microtiter wells are coated with a monoclonal antibody directed towards a unique antigenic site on a Leptin molecule.

An aliquot of patient sample containing endogenous leptin is incubated in the coated well with a specific rabbit anti leptin antibody. A sandwich complex is formed. After incubation the unbound material is washed off and an anti rabbit peroxidase conjugate is added for detection of the bound Leptin. Having added the substrate solution, the intensity of color developed is proportional to the concentration of Leptin in patient sample.

**Blood pressure measurement:**

The blood pressure measurement of participants was measured in the supine position in right upper arm after taking rest for 5 minutes. Two readings of blood pressure measurement were taken at 5 minute interval. If there is a variation of more than 10 mmHg in two reading then third reading was taken. A mercury column – sphygmomanometer was used one of two cuff size (adult or large) was chosen on the sorts of the arm circumference of the participants.

**Diagnosis of hypertension:**

Hypertension was defined as either as SBP> 140 mmHg and DBP> 90 mmHg and/or anti-hypertensive medication.

The guidelines of Joint National Committee on prevention, detection, evaluation and treatment of High blood pressure (JNC-VII) was taken which are as follows –

<table>
<thead>
<tr>
<th>BP Classification</th>
<th>SBP mmHg</th>
<th>DBP mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt; 120</td>
<td>&lt; 80</td>
</tr>
<tr>
<td>Pre hypertension</td>
<td>120 – 139</td>
<td>80 – 89</td>
</tr>
<tr>
<td>Stage I hypertension</td>
<td>140 – 159</td>
<td>90 – 99</td>
</tr>
<tr>
<td>Stage II hypertension</td>
<td>160 or above</td>
<td>100 or above</td>
</tr>
</tbody>
</table>

**Inclusive criteria for non-hypertensive subjects:**

BP < 140/90, and not diagnosed previously for hypertension.

**Definition:**

Obesity define as person having BMI>25kg/m². Hypertension diagnosed according to the JNC-VII criteria.

**Exclusion criteria:**

- Patients on Steroid
- Patient on Insulin
- Patient on Thyroxin
- Pregnancy
- Diabetic

**STATISTICAL ANALYSIS**

In the above study the following analytic statistical formulae were incorporated for various calculations.

i. **TESTS OF SIGNIFICANCE:** In order to calculate the tests of significance between two variable proportions "Unpaired t-Test" was applied.

ii. Karl Pearson Coefficient of Correlation "r".

**RESULTS**

Total 60 patients were included in the present study.

The maximum number of patients present between the groups of 41 – 60 i.e. 31. There were no patients in age group of 0 – 20.

The Leptin level in male and female is 6.614 ± 5.80 and 17.50 ± 16.66(Values in Mean ± S.D). Leptin level is statistically significant (t value = 3.13, P value = <0.05) higher in females in comparison to males.

On comparison of values of serum leptin level in hypertensive 15.3 ± 15.13 and non-
hypertensive (7.0 ± 8.04) we found that leptin level is higher in hypertensive in comparison to non-hypertensive subjects which is statistically significant (t value = 2.65, P value = <0.05).

**Table 1** Shows leptin level in different subjects

<table>
<thead>
<tr>
<th>Subject</th>
<th>Leptin Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lean Non-Hypertensive</td>
<td>5.02 ± 3.0</td>
</tr>
<tr>
<td>Lean Hypertensive</td>
<td>9.81 ± 9.2</td>
</tr>
<tr>
<td>Obese Non-Hypertensive</td>
<td>9.03 ± 11.0</td>
</tr>
<tr>
<td>Obese Hypertensive</td>
<td>20.73 ± 18.08</td>
</tr>
</tbody>
</table>

All values in Mean ± S.D.

- The leptin level is higher in obese hypertensive in comparison to obese non-hypertensive subjects which is statistically significant (t value = 2.37, P value = <0.05).
- The leptin level is higher in obese hypertensive in comparison to lean hypertensive subjects which is statistically significant (t value = 2.08, P value = <0.05).
- The leptin level is higher in lean hypertensive in comparison to lean non-hypertensive subjects but this is statistically insignificant. (t value = 1.92, P value = >0.05)
- The leptin level is higher in obese in comparison with non-obese subjects which is statistically significant. (t value = 2.37, P value = <0.05)

**Fig.1** Leptin levels in hypertensive and non-hypertensive

**Table 2. Co-relation between leptin level with waist hip ratio, waist circumference, body mass index, HDL-C**

<table>
<thead>
<tr>
<th>Covariates</th>
<th>Lean Non-Hypertensive</th>
<th>Lean Hypertensive</th>
<th>Obese Non-Hypertensive</th>
<th>Obese Hypertensive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leptin Level</td>
<td>5.02 ± 3.0</td>
<td>9.81 ± 9.2</td>
<td>9.03 ± 11.0</td>
<td>20.73 ± 18.08</td>
</tr>
<tr>
<td>Waist Hip Ratio</td>
<td>0.828±0.10</td>
<td>0.854±0.112</td>
<td>0.917±0.087</td>
<td>0.989±0.088</td>
</tr>
<tr>
<td>Correlation Coefficient (r)</td>
<td>0.862</td>
<td>0.846</td>
<td>0.789</td>
<td>0.767</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;0.05 (significant)</td>
<td>&lt;0.05 (significant)</td>
<td>&lt;0.05 (significant)</td>
<td>&lt;0.05 (significant)</td>
</tr>
<tr>
<td>Waist Circumference</td>
<td>76.95±11.80</td>
<td>81.29±12.70</td>
<td>103.98±10.99</td>
<td>109.59±16.49</td>
</tr>
<tr>
<td>Correlation Coefficient (r)</td>
<td>0.817</td>
<td>0.739</td>
<td>0.693</td>
<td>0.749</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;0.05 (significant)</td>
<td>&lt;0.05 (significant)</td>
<td>&lt;0.05 (significant)</td>
<td>&lt;0.05 (significant)</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>21.40±2.32</td>
<td>20.11±3.28</td>
<td>30.55±3.71</td>
<td>31.28±4.18</td>
</tr>
<tr>
<td>Correlation Coefficient (r)</td>
<td>0.658</td>
<td>0.816</td>
<td>0.750</td>
<td>0.827</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;0.05 (significant)</td>
<td>&lt;0.05 (significant)</td>
<td>&lt;0.05 (significant)</td>
<td>&lt;0.05 (significant)</td>
</tr>
<tr>
<td>HDL-C</td>
<td>48.06 ± 7.06</td>
<td>41.86 ± 7.41</td>
<td>36.66 ± 1.95</td>
<td>36.26 ± 2.63</td>
</tr>
<tr>
<td>Correlation Coefficient (r)</td>
<td>0.278</td>
<td>0.0291</td>
<td>0.472</td>
<td>0.224</td>
</tr>
<tr>
<td>P value</td>
<td>&gt;0.05 (insignificant)</td>
<td>&gt;0.05 (insignificant)</td>
<td>&gt;0.05 (insignificant)</td>
<td>&gt;0.05 (insignificant)</td>
</tr>
</tbody>
</table>

The co-relation between leptin level with waist hip ratio and there is positive co-relation between leptin level and WHR which is statistically significant. A positive
co-relation between leptin levels with waist circumference were found, which is statistically significant.
A positive co-relation between leptin levels with BMI was found which is statistically significant.
Table 2 shows inverse co-relation between leptin levels with S. HDL-C which is statistically insignificant.

DISCUSSION
The present study was conducted at J.L.N. Hospital attached to J.L.N. Medical College, Ajmer. A total number of 60 patients divided into different 4 groups consist of 15 patients in each group were studied and closely observed through different observation tables.
Anoop Shankar, Jie Xiao et al in year 2009 observed Positive Relationship between Plasma Leptin Level and Hypertension which also match with our study. They studied the third National Health and Nutrition Examination Survey participants >20 years of age (n=5599; 54.7% women). Plasma leptin levels were categorized into quartiles (women: <7.68, 7.68 to 13.18, 13.19 to 21.70, ≥21.70 fg/L; men: <2.64, 2.64 to 4.36, 4.37 to 7.12, ≥7.12 fg/L). Hypertension was defined as BP-reducing medication use or having systolic BP ≥140 mm Hg, or diastolic blood pressure (DBP) ≥ 90 mm Hg, or use of antihypertensive medication. Using logistic regression analysis, adjusting for age, sex, estimated glomerular filtration rate, triglycerides, high-density lipoprotein cholesterol (HDL-C), fibrinogen, and glucose, and with leptin and adiponectin included in the same model, leptin was significantly associated with new-onset hypertension with an odds ratio (95% confidence interval) of 1.28 (1.08-1.53; P < 0.005) for 1 s.d. higher level of log-transformed leptin, whereas adiponectin was not significantly associated with new-onset hypertension having an odds ratio of 1.02 (0.84-1.24; P = 0.83) for 1 s.d. higher level of log-transformed adiponectin.
In Present study we observed that leptin level is higher in obese group than lean group. The leptin level is highest in obese hypertensive group and least in lean non-hypertensive group.
A Mishra and N. Arora et al studied in 2001, the relationship of plasma leptin level with obesity, which showed that leptin level was higher in obese group in compare with lean group which match with our study.
This study investigated the relationship of plasma leptin to obesity, diabetes and hyperlipidaemia in Asian Northern Indian subjects, considered to have a predisposition...
to abdominal obesity and metabolic syndrome. A total of 72 subjects, subcategorised into lean and obese healthy subjects, lean and obese Type 2 diabetic and lean and obese non-diabetic hyperlipidaemic subjects were recruited. High leptin values were observed in all obese groups. When all lean and all obese subjects were analyzed in two separate groups, body mass index (BMI), percent total body fat, and body density significantly correlated with the plasma leptin levels (p<0.05). Leptin values, when correlated to all variables in all patients taken together, showed the greatest magnitude of correlation with BMI (r=0.64), percent total body fat (r=0.67), and waist circumference (r=0.51). The study suggested that plasma leptin has a strong positive correlation with percent total body fat in Asian Northern Indian subjects. Among other components of metabolic syndrome, only abdominal obesity is weakly correlated to serum leptin levels.

Haque Z and Rahaman et al in years 2003 observed and conclude the same results in their study. [16]

Mohammed F. Saed et al [17] 1998 studied that plasma leptin profiles were higher in obese than lean subjects and higher in females than males regardless of fat mass and similar finding observed in our study. Twenty-four-hour leptin profiles were evaluated in 31 subjects [17 male, 14 female; age: 36 ± 2 yr (mean ± SEM); body mass index: 27.5 ± 1.0 kg/m²]. Plasma leptin profiles were higher in obese (body mass index > 27 kg/m²) than in lean subjects and higher in women than in men, regardless of fat mass.

Masoud Y Al Maskari, Adel A Alnaqdy et al [18] in year 2006 also found that plasma leptin higher in obese than lean subjects and higher in females than males which support our study. Leptin levels were assessed in serum samples from 35 obese Omanis and 20 non-obese healthy subjects.

There was a significant difference (p<0.001) in serum leptin between the obese group (34.78 ± 13.96 ng/ml) and the control non-obese subjects (10.6± 4.2 ng/ml). Leptin levels were higher in females compared to males. There was a significantly positive correlation between leptin levels in obese subjects with weight (p=0.002), body fat percentage (p=0.0001) and BMI (p=0.001). They concluded that serum leptin levels are higher in the Omani obese group and correlate positively with body fatness and obesity.

CONCLUSION
In our present study we observed that the level of leptin is strongly correlated with hypertension and body mass index. Leptin level is directly proportional to body mass index. It is highest in obese hypertensive that have highest body mass index in their group. Leptin level is least in lean non hypertensive who have lowest body mass index.

Hence, our study is having strong correlation with hypertension and obesity. Although this study was done on small number of patients, a large double blind randomized study further required to validate this correlation.

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