



Original Research Article

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

Sandeep Vaishnav^{1*}, Rajesh Khoiwal¹

¹Dept. of Medicine, Geetanjali Medical College and Hospital, Udaipur (Rajasthan)

*Correspondence Email: drsvaishnav@ymail.com

Received: 26/09/2012

Revised: 11/10/2012

Accepted: 17/10/2012

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 –

BP Classification	SBP mmHg	DBP mmHg
Normal	< 120	< 80
Pre hypertension	120 – 139	80 – 89
Stage I hypertension	140 – 159	90 – 99
Stage II hypertension	160 or above	100 or above

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

Subject	Leptin Level
Lean Non-Hypertensive	5.02 ± 3.0
Lean Hypertensive	9.81 ± 9.2
Obese Non-Hypertensive	9.03 ± 11.0
Obese Hypertensive	20.73 ± 18.08

All values in Mean \pm S.D.

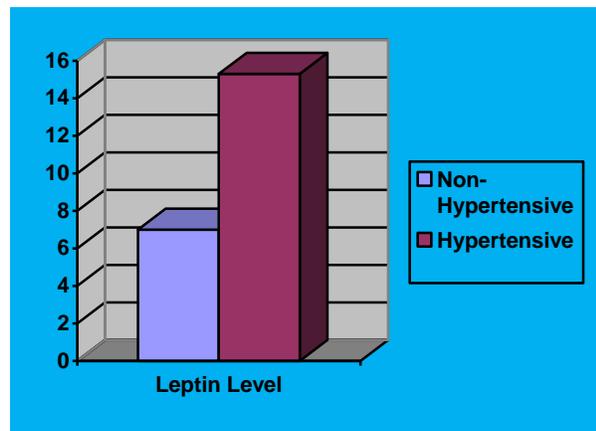


Fig.1 Leptin levels in hypertensive and non-hypertensive

- 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)

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

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

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. [13] 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 \geq 140 mm Hg and/or diastolic BP \geq 90 mm Hg. They found that higher plasma leptin levels were positively associated with hypertension. Compared with quartile 1 of leptin (referent), the odds ratio (95% CI) of hypertension associated with quartile 4 was 1.89 (1.24 to 2.09; *P* for trend=0.0036). The relation between leptin and hypertension by sex and body mass index categories also showed a consistent positive association. They finally conclude that higher plasma leptin levels were associated with hypertension both among women as well as men in a representative sample of US adults.

Asperg et al. [14] 2003, reported that plasma leptin level predicted the risk of developing hypertension in both men and women in the Copenhagen city Heart study. In a prospective study design, they examined new-onset hypertension in 620 women and 300 men who were normotensive in the third CCHS examination, which was performed in 1991-1994.

Between the third and the fourth CCHS examination, which was performed in 2001-2003, 254 had developed hypertension, defined as systolic blood pressure (SBP) $>$ or $=$ 140 mm Hg, or diastolic blood pressure (DBP) $>$ or $=$ 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 [15] 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. [15] 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, subcategorized 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 \pm 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.

REFERENCES

1. Compamini B: The world health Report: Reducing Risks, Promoting Healthy Life, Geneva, WHO, 2002.
2. Naomi D L, Gorden H. W. Hypertensive vascular disease. In: Dennis L.K. Principal of Internal medicine. Vol. 2, 16th Ed. New York : Mc-Graw Hill 2005 1463-81.
3. Kannel W B, elevated systolic blood pressure as a cardiovascular risk factor. Am J Cardiol 2000; 85 : 251-54.
4. The Seventh Report of the Joint National Committee on prevention, detection, evaluation and treatment of

- high blood pressure. JAMA 2003; 289: 2560-72.
5. MacMohan S, Peto R, Cutler J. Blood pressure, stroke and coronary heart disease I prolonged difference in blood pressure : prospective observational studies correlated for the regression dilution bias. Lancet 1990; 335 : 765-74.
 6. Hyman DJ, Pavlic VN. Characteristics of patient with uncontrolled hypertension in the United State. N Eng J Med 2002; 345 : 479-83.
 7. Zhang Y, Proenca R, Maffei M, Barone M, Leopold L, Friedman JM (December 1994) "Positional cloning of the mouse obese gene and its human homologue" Nature 372 (6505) : 425 – 32.
 8. Maffei M, Fei H, Lee G-H, et al 1995 Increased expression in adipocytes of ob RNA in mice with lesion of the hypothalamus and with mutation at the ob locus Proc Natl Acad Sci, USA 92 : 6957-6960.
 9. Considine RV, Sinha MK, Heiman ML et al 1996 serum immunoreactive – leptin concentration in (N) wt and obese humans N. Engl J. Med. 334:292 – 295.
 10. Friedman JM (2000) obesity in the new millennium Nature 404: 632 – 634.
 11. Narkiewicz K., Somers, V.K. Mos, L. et al (1999) An independent relationship between plasma leptin and heart rate in untreated patient with essential hypertension. J Hypertens 17 : 245 – 249.
 12. Carlyce M, Jones OB, Kuo JJ, Hall JE, Chronic cardiovascular and renal action of leptin : role of adrenergic activity. Hypertension 2002; 39 : 496 – 501.
 13. Anoop Shankar and Jie Xiao et al. Positive Relationship Between Plasma Leptin Level and Hypertension *Hypertension* 2010, 56:623-628: originally published online August 16, 2010
 14. Asferg C, Mogelvang R, Flyvbjerg A, Frystyle J, Jensen JS, Marolt JL, Appleyard M, Jensen GB, Jeppesen J. Leptin, not adiponectin, predicts Hypertension in the Copenhagen city heart study. AM J Hypertens. 2010; 23 : 327 – 333.
 15. A. Mishra, M. Arora, S. Mondal, R. Mohan Pandey, B. Jaikhani, S. Persin, D. Chaudhary, T. Saliya, P. Singh et al : Relation between plasma leptin and anthropometric and metabolic covariates in lean and obese diabetes and hyperlipidemic Asian Northern Indian subjects : Diab. Nutr Meta : 14; 18-26, 2001.
 16. Haque Z, Rahman MA "Serum leptin levels in female patients with NIDDM". J Coll physicians Surg Pak. 2003 Mar; 13(3):130-4.
 17. Mohammed F. Saed, Maggy G. Riad-Gabriel, Arshad Khah, Alok Sharma, Ragui Michael, Sujata D, Jinagouda, Rima Boyadjian and Garry M. Steil : Diurnal and ultradian rhythmicity of plasma leptin : The effects of gender and adiposity. Jour of clin. End. and Meta. 83/2/453.
 18. Masoud Y Al Maskari1, Adel A Alnaqdy et al. Correlation between Serum Leptin Levels, Body Mass Index and Obesity in Omanis. Sultan Qaboos University Medical Journal December 2006 VOL 6, NO. 2

How to cite this article: Vaishnav S, Khoiwal R. Relation between plasma leptin, anthropometric and metabolic covariates in Hypertensive patients. Int J Health Sci Res. 2012;2(7):63-69.
