# Leptin in obesity and hypertension

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## Abstract

**Background:** Obesity along with hypertension is the common risk factor for the development of cardiovascular disease. Leptin, an anti-obesity hormone, is currently considered to play a vital role in the development of hypertension in obesity. We aim to determine the leptin levels in hypertensive and normotensive participants and to find the correlation between leptin and hypertension in obese and non-obese hypertensive subjects.

**Material and methods:** A total of 94 participants aged > 18 years of either gender were included in the study. The participants were divided into obese (n = 55) and non-obese (n = 39) groups with further subgroups based on presence or absence of hypertension. Height, weight and blood pressure were taken with standard methods. Leptin was determined using ELISA method and intra and inter-group comparisons were made.

**Results:** The leptin levels were significantly higher in obese (p = 0.000), hypertensive (p = 0.048) and females (p = 0.001) compared to non-obese, normotensive and male participants. Furthermore, obese hypertensive participants were having higher leptin levels compared to obese normotensive participants but with no statistical significance (p = 0.14). Serum leptin levels positively correlated with serum LDL (p = 0.003), body mass index (BMI) (p = 0.000), serum uric acid (p = 0.034) and fasting plasma glucose (FPG) (p = 0.001). However, on correction for factors like BMI, and obesity, positive correlation persisted only for female gender (p = 0.048) and FPG (p = 0.029). Furthermore, BMI (p = 0.021) and FPG (p = 0.027) were found to be the independent risk factors for elevated leptin levels on multiple regression analysis.

**Conclusions:** Our study concluded that serum leptin levels are higher in obesity and have a direct correlation with degree of obesity. However, our study does not support any direct correlation between serum leptin and hypertension.

**Key words:** leptin; obesity; hypertension

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## Introduction

Obesity is a global epidemic and is thought to be one of the most neglected public health problems threatening the goal of achieving a healthy society as a result of its association with group of chronic diseases and along with hypertension, is the common risk factor for the development of cardiovascular disease. The two are intimately associated in individual patients with metabolic syndrome in addition to cluster of adverse health factors like insulin resistance, hyperinsulinemia and hyperlipidemia [1].

Excessive adiposity, characteristic feature of obesity is now considered an endocrinologicaly active organ [2] secreting large number of metabolically active peptides including angiotensin II, resistin,

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adiponectin and leptin. These metabolites act locally to have an effect on growth and differentiation of adipocytes in addition to participate in possible regulation of blood pressure and the development of obesity-related elevated blood pressure on being released into the blood circulation. Of all these factors, the role of leptin has generated lot of enthusiasm as an important hormone with significantly diverse actions on several organ systems [3, 4].

Leptin, an anti-obesity hormone owing to its action on increasing the satiety and decreasing the adipose tissue mass, is also involved in the promotion of increased arterial pressure via multiple physiological processes like sympathetic nervous system activation leading to increased fluid retention and vasoconstriction, activation of the renin-angiotensin system, renal hemodynamics (natriuresis and nitric oxide production), insulin resistance and hyperinsulinemia [5].

However, the concept of selective leptin resistance in obese individuals in particular to the central actions on the satiety and weight decreasing effect of the leptin hormone [6], with preserved leptin-mediated sympathetic activation possibly contribute to the pathogenesis of obesity related hypertension [7].

Understanding the role of leptin in hypertension and its correlation with obesity- related hypertension might provide a more rational basis for management especially drug treatment of obesity-related hypertension [8–10]. Therefore, the present study was undertaken to determine the level of leptin hormone in hypertensive and normotensive Kashmiri subjects and to find the correlation between leptin & hypertension in obese and non-obese subjects.

## Material and methods

The study was a hospital based, cross sectional, observational and case- control study carried in the Department of Medicine at Sher-i-Kashmir Institute of Medical sciences over a period of two years in accordance with the Declaration of Helsinki statement for medical research involving human subjects. The study was approved by the Institutional Ethical Committee. A well informed consent was obtained from all participants. A total of 94 participants aged > 18 years of either gender (45 men and 49 women) were included in the study and were divided into obese (n = 55) and non-obese (n = 39) groups. They were further categorized in subgroups as obese normotensive (n = 27), obese hypertensive (n = 28), non-obese normotensive (n = 23), and non-obese hypertensive (n = 16).

### Anthropometry and blood pressure measurement

Anthropometric measurements like height, and weight were taken with standard methods (11). BMI was calculated as per criteria given by International Obesity Task Force (IOTF) and World Health Organization (WHO). Participants with BMI ≥ 25 kg/m$^2$, 23–24.9 kg/m$^2$ and 18.5–22.9 kg/m$^2$ were considered as obese, overweight and as normal respectively [12]. Blood pressure (BP) measurement was done with mercury sphygmomanometer using auscultatory technique as in standard clinical practice [13]. The status of hypertension of the participants was classified according the standard criteria formulated by Joint National Committee (JNC)-VIII [14]. Systolic BP (SBP) level of ≥ 140 mm Hg and diastolic BP (DBP) ≥ 90 mm Hg were considered hypertensive. All patients with confirmed hypertension were investigated according to the standard protocol.

### Biochemical and leptin evaluation

Biochemical investigations like complete blood count, renal and liver function, fasting blood glucose and lipid profile were carried out on venous blood collected after an overnight fast. Serum was separated and stored at –70°C. Leptin ELISA kit manufactured by Ray Biotech USA was used to estimate Leptin level by sandwich ELISA [15–17]. We assayed levels of serum leptin in both obese and non-obese hypertensive and normotensive participants and intra- and inter-group comparisons were made. The impact of BP and BMI on leptin levels was also evaluated.

### Statistical analysis

The obtained data were first entered into Microsoft Excel datasheets. All statistical analyses were performed using the SPSS version 20 Armonk, NY: IBM Corporation, United States. The normality of the distribution of each variable was checked. The data were analyzed using the independent student's t-test and one-way ANOVA, along with multiple range tests and was expressed in the form of mean ± standard deviation. The comparison of categorical data parameters was performed by using the $\chi^2$ test. A p value < 0.05 was considered statistically significant.Multiple logistic regression analysis was carried out using serum leptin level as the dependent variable while age, gender, BMI, hypertension, FPG, HDL-cholesterol, serum cholesterol, serum triglycerides and LDL-cholesterol were taken as the independent variables.

## Results

Ninety-four participants (45 men and 49 women) with no concomitant disease like diabetes mellitus, hypothyroidisms were included in this study. These participants were further subdivided into obese (n = 55) and non-obese (n = 39) based on the BMI. They were further categorized in subgroups as obese normotensive (n = 27), obese hypertensive (n = 28), non-obese normotensive (n = 23), and non-obese hypertensive (n = 16). Comparison of normotensive and hypertensive individuals revealed that hypertensive participants were significantly older and had significantly higher levels of creatinine, serum uric acid and serum leptin levels (Tab. 1). Similarly on comparing obese with non-obese individuals, obese individuals were found to have significantly higher levels of serum cholesterol, serum triglycerides, serum LDL-cholesterol and serum leptin levels (Tab. 1). Hypertensive obese individuals were significantly older and had higher serum creatinine and serum uric acid levels when compared to normotensive non-obese. Serum leptin levels were higher among obese hypertensive cohort compared to non-obese hypertensives but didn't reach the statistical significance (Tab. 2). Furthermore serum leptin levels were significantly higher in females compared to males (39.55 ± 18.34 *vs.* 14.27 ± 8.16; p = 0.001). Serum leptin levels in the studied participants are depicted in Figure 1.

Serum leptin levels positively correlated with weight (r = 0.338, p = 0.003), BMI (r = 0.523, p = 0.000), serum LDL (r = 0.339, P = 0.003), serum uric acids (r = 0.247, p = 0.034) and FPG (r = 0.376, p = 0.001). On correction for factors like weight, BMI and obesity, positive correlation persisted only for female gender (r = 0.235, p = 0.048) and FPG (r = 0.260, p = 0.029).

Multiple logistic regression analysis revealed BMI (OR = 2.67, p = 0.021) and FPG (OR = 1.66, p = 0.027) as the risk factors for leptin levels.

## Discussion

The present study was carried out to determine whether there is significant difference between the serum leptin levels in obese and non-obese patients on one hand and hypertensive and normotensive obese patients on the other hand. Leptin has been found to have strong correlation with degree of adiposity, but whether this high leptin levels contribute independently to elevated blood pressure is not known [18]. A good number of studies have observed a strong correlation between leptin and hypertension in animals as well as humans implicating leptin to have a significant contribution in the pathophysiology of obesity induced hypertension [19–25], however, some studies were not able to demonstrate the same

**Table 1.** Comparative analysis of anthropometric, clinical and biochemical parameters among hypertensive vs normotensive and obese and non-obese subjects

| Variables | Hypertensive (n = 44) | Normotensive (n = 50) | p value | Obese (n = 55) | Non-obese (n = 39) | p value |
|---|---|---|---|---|---|---|
| Male (n) | 19 | 26 | | 20 | 25 | |
| Female (n) | 25 | 24 | | 35 | 14 | |
| Age [years] | 50.5 ± 11.4 | 43.3 ± 10.1 | 0.002* | 46.2 ± 11.6 | 47.4 ± 11.1 | 0.605 |
| Weight [kg] | 71.9 ± 13.1 | 71.3 ± 14.7 | 0.815 | 80.9 ± 9.2 | 58.41 ± 6.58 | 0.000* |
| Height [cm] | 159.7 ± 7.2 | 160.4 ± 8.2 | 0.687 | 158.8 ± 7.8 | 161.8 ± 7.3 | 0.059 |
| BMI [kg/m$^2$] | 28.4 ± 5.7 | 27.8± 5.9 | 0.648 | 22.3 ± 1.9 | 32.2 ± 3.8 | 0.000* |
| SBP [mm Hg] | 160.3 ± 6.5 | 117.6 ± 5.5 | 0.000* | 140.5±21.9 | 133.5 ± 22.2 | 0.132 |
| DBP [mm Hg] | 92.6 ± 3.2 | 76.2 ± 4.6 | 0.000* | 85.2 ± 8.5 | 82.0 ± 9.8 | 0.092 |
| Cholesterol [mg/dL] | 171.8 ± 49.8 | 174 .0 ± 43.7 | 0.818 | 194.3 ±45.1 | 143.0 ± 28.31 | 0.000* |
| Triglyceride [mg/dL] | 194.3± 87.1 | 167.9 ± 61.9 | 0.091 | 207.2 ± 79.7 | 142.4 ± 49.5 | 0.000* |
| HDL [mg/dL] | 40.1 ± 8.7 | 39.1 ± 6.49 | 0.527 | 38.8 ± 7.9 | 40.9 ± 7.02 | 0.200 |
| LDL [mg/dL] | 116.3 ± 72.9 | 100.1 ± 40.9 | 0.181 | 133.6 ± 60.2 | 71.3 ± 29.3 | 0.000* |
| Creatinine [mg/dL] | 0.85± 0.28 | 0.66 ± 0.27 | 0.002* | 0.83± 0.28 | 0.62 ± 0.26 | 0.001* |
| SUA [mg/dL] | 5.22 ± 1.5 | 4.51 ± 0.99 | 0.007* | 4.99 ± 1.6 | 4.65 ± 1.42 | 0.210 |
| Serum leptin [mg/dL] | 35.8 ± 20.2 | 21.1 ± 14.8 | 0.048* | 39.30±17.55 | 11.13 ± 8.65 | 0.000* |

Categorical data are shown as %; continuous variables are shown as mean ± standard deviation. BMI — body mass index; SBP — systolic blood pressure; DBP — diastolic blood pressure; HDL — high density lipoproteins; LDL — low density lipoproteins; SUA — serum uric acid; *significant

**Table 2.** Intergroup comparative analysis of anthropometric, clinical and biochemical details among obese (normotensive and hypertensive) and non-obese (normotensive and hypertensive)

| Variables | Non-obese (n = 39) | | | Obese (n = 55) | | | Intergroup p value |
|---|---|---|---|---|---|---|---|
| | Normotensive (n = 23) | Hypertensive (n = 16) | P value | Normotensive (n = 27) | Hypertensive (n = 28) | p value | |
| Age [years] | 44.3 ± 8.5 | 51.9 ± 13.1 | 0.03* | 40.5 ± 11.3 | 49.8 ± 10.6 | 0.017* | c* d* e f* F* |
| Weight [kg] | 58.2 ± 6.8 | 58.7 ± 6.4 | 0.83 | 82.4 ± 9.3 | 79.6 ± 9.2 | 0.25 | c* d* e* f F* |
| Height [cm] | 161.7 ± 8.4 | 162.1 ± 5.5 | 0.86 | 159.2 ± 7.9 | 158.4 ± 7.7 | 0.67 | c d e f F |
| BMI [kg/m$^2$] | 22.3 ± 1.8 | 22.3 ± 2.0 | 0.91 | 32.6 ± 3.7 | 31.8 ± 4.0 | 0.48 | c* d* e* f F* |
| SBP [mm Hg] | 115.9 ± 5.8 | 158.8 ±6.9 | 0.00* | 119.0 ± 4.8 | 161.2 ± 6.1 | 0.00 | c* d* e f* F* |
| DBP [mm Hg] | 74.7 ± 5.2 | 92.5 ± 2.9 | 0.00* | 77.5 ± 3.7 | 92.7 ± 3.4 | 0.00 | c* d* e f F* |
| Cholesterol [mg/dL] | 140.1± 23.0 | 147.1± 35.0 | 0.45 | 202.9 35.6 | 185.9 52.0 | 0.16 | c* d* e* f F* |
| Triglyceride [mg/dL] | 135.4 ± 33.2 | 152.5 ± 66.3 | 0.29 | 195.7 67.6 | 218.2 89.6 | 0.29 | c* d e* f F* |
| HDL [mg/dL] | 39.5 ± 5.8 | 42.8 ± 8.3 | 0.16 | 38.9 7.1 | 38.7 8.8 | 0.93 | c d e f F |
| LDL [mg/dL] | 68.0 ± 25.91 | 76.0 ± 34.0 | 0.41 | 127.5 30.0 | 139.4 79.5 | 0.46 | c* d* e* f F* |
| Creatinine [mg/dL] | 0.55 ± 0.21 | 0.73± 0.30 | 0.03* | 0.75 0.3 | 0.91 0.3 | 0.03* | c* d e* f* F* |
| SUA [mg/dL] | 4.20 ± 1.0 | 5.30 ± 1.72 | 0.01* | 4.8 0.9 | 5.2 1.3 | 0.20 | c* d e f F* |
| Serum leptin [ng/mL] | 8.6 ± 5.1 | 15.1 ± 10.5 | 0.41 | 31.6 ± 17.9 | 47.0 ± 19.1 | 0.14 | c* d e* f F* |

Categorical data are shown as %; continuous variables are shown as mean ± standard deviation. BMI — body mass index; SBP — systolic blood pressure; DBP — diastolic blood pressure; HDL — high density lipoproteins; LDL — low density lipoproteins; SUA — serum uric acid; *significant; c — comparison between non-obese normotensive and obese hypertensive patients; d — comparison between non-obese hypertensive and obese normotensive patients; e — comparison between non-obese hypertensive and obese hypertensive; f — comparison between obese hypertensive and obese normotensive; F — analysis of variance (ANOVA)

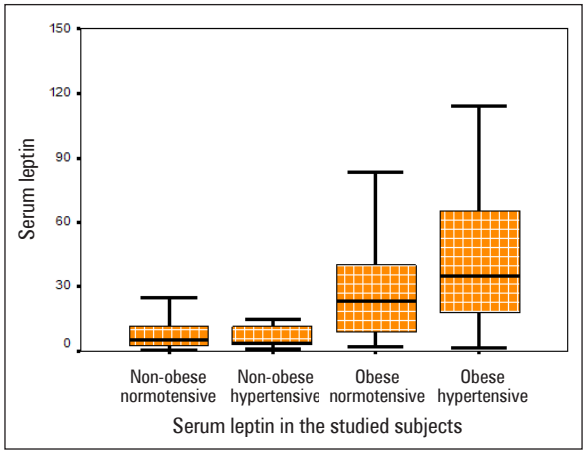


**Figure 1.** Serum leptin in the studied subjects

results to provide an irrefutable evidence of this association [26].

Our study was conceived to provide further insight into this relationship that may help to understand the contribution of leptin in pathogenesis of obesity induced hypertension. The present study revealed that serum leptin level was significantly higher in obese than non-obese participants which was consistent with the fact that leptin is related to the degree of adiposity. Thus, a close relationship between leptin and body adiposity was established. However, direct estimation of body fat content would have provided more credible evidence to our findings. This observation is consistent with the findings reported in the literature by other investigators [6, 27–29]. Similarly our results demonstrated that leptin levels are significantly higher in hypertensive patients than non-hypertensive patients with comparable BMI which is consistent with the observations from earlier studies [29–31].

There is a close relationship between leptin levels and body adiposity, but whether this high leptin levels contribute independently to elevated blood pressure is not known [18]. Our study revealed a direct and significantly positive relationship of plasma Leptin with hypertension and BMI; however after adjusting for BMI, there was no evidence for an independent contribution of leptin to blood pressure thus BMI was the variable that largely explained the positive association between leptin and blood pressure. The variable response associated with leptin-induced susceptibility to obesity-associated hypertension may be explained on the basis of genotypic differences in humans [32]. Thus our study demonstrated a positive relationship between leptin and obesity; however relationship between leptin and hypertension didn't persist after adjusting for BMI status.

The present study investigated indirectly the possible impact of adiposity via leptin, principally secreted from the subcutaneous fat on the occurrence of hypertension. The absence of an independent

association of leptin with blood pressure after adjusting for obesity in the current study, negate the possible contribution of leptin in the pathogenesis of hypertension which is in agreement with the results documented in literature [33, 34]. In an earlier study involving African women with obesity and hypertension, it was observed that the correlation between leptin and blood pressure disappeared after adjustments for other components of the insulin resistance syndrome is in agreement with results observed in our study [33]. Similarly in another study it was observed that a significant association between leptin and blood pressure disappeared after adjusting for BMI, whereas the association between blood pressure and BMI persisted after adjusting for leptin levels [34].

One of the observations of our study was the presence in a good number of normal weight individuals, of the increased leptin concentration. However, the fact that normal weight does not always rule out excess adiposity could explain the presence of higher leptin concentration in such individuals. This higher leptin concentration in individuals without excess adiposity could also be explained by the fact that leptin production occurs in several other sites other than the adipose tissue [35]. The impaired renal function can also explain the presence of elevated leptin levels [36]. However, this is not clearly apparent in "normal" renal function [37]. The possible differences in the pleiotropic effects for similarly raised leptin concentrations in the presence of hyperleptinemia, generally an expression of leptin resistance, may be the result of differential resistance to the leptin. In order to further understand why non-obese subjects have hyperleptinemia not associated with the unfavorable effects observed in overweight-obese persons requires further evaluation on more number of subjects in each group. Limitation of our study was lack of direct estimation of body fat content that would have provided more direct evidence to refute or accept the role of degree of obesity (adiposity) in leptin mediated influence on blood pressure status and small sample size that limits the generalizability of our findings.

To conclude, our study provides the direct demonstration in a case control study of leptin *vs*. blood pressure and BMI:

- serum leptin levels are significantly high in obese persons as well as in hypertensive patients irrespective of BMI;
- obese hypertensive persons have higher levels of serum leptin as compared to obese normotensive persons but with no statistical significance;
- serum leptin levels were not significantly raised in non-obese hypertensive when compared to non-obese normotensive persons.

Our study showed that serum leptin levels didn't have any direct correlation with hypertension when adjusted for BMI.

## Conclusion

Our study demonstrated that serum leptin levels are significantly elevated in obesity and have a direct correlation with the degree of obesity. However, our study does not support any direct correlation between serum leptin and blood pressure.

## References


1. Modan M, Halkin H, Almog S, et al. Hyperinsulinemia. A link between hypertension obesity and glucose intolerance. J Clin Invest. 1985; 75(3): 809–817, doi: 10.1172/JCI111776, indexed in Pubmed: 3884667.
2. Bradley RL, Cleveland KA, Cheatham B. The adipocyte as a secretory organ: mechanisms of vesicle transport and secretory pathways. Recent Prog Horm Res. 2001; 56: 329–358, doi: 10.1210/rp.56.1.329, indexed in Pubmed: 11237220.
3. Guha PK, Villarreal D, Reams GP, et al. Role of leptin in the regulation of body fluid volume and pressures. Am J Ther. 2003; 10(3): 211–218, doi: 10.1097/00045391-200305000-00008, indexed in Pubmed: 12756428.
4. Sharma V, McNeill JH. The emerging roles of leptin and ghrelin in cardiovascular physiology and pathophysiology. Curr Vasc Pharmacol. 2005; 3(2): 169–180, doi: 10.2174/1570161053586868, indexed in Pubmed: 15853636.
5. Hall JE, do Carmo JM, da Silva AA, et al. Obesity-induced hypertension: interaction of neurohumoral and renal mechanisms. Circ Res. 2015; 116(6): 991–1006, doi: 10.1161/CIRCRESAHA.116.305697, indexed in Pubmed: 25767285.
6. Considine RV, Sinha MK, Heiman ML, et al. Serum immunoreactive-leptin concentrations in normal-weight and obese humans. N Engl J Med. 1996; 334(5): 292–295, doi: 10.1056/NEJM199602013340503, indexed in Pubmed: 8532024.
7. Shan J, Nguyen TB, Totary-Jain H, et al. Leptin-enhanced neointimal hyperplasia is reduced by mTOR and PI3K inhibitors. Proc Natl Acad Sci U S A. 2008; 105(48): 19006–19011, doi: 10.1073/pnas.0809743105, indexed in Pubmed: 19020099.
8. Skurk T, van Harmelen V, Blum WF, et al. Angiotensin II promotes leptin production in cultured human fat cells by an ERK1/2-dependent pathway. Obes Res. 2005; 13(6): 969–973, doi: 10.1038/oby.2005.113, indexed in Pubmed: 15976138.
9. Fogari R, Derosa G, Zoppi A, et al. Comparison of the effects of valsartan and felodipine on plasma leptin and insulin sensitivity in hypertensive obese patients. Hypertens Res. 2005; 28(3): 209–214, doi: 10.1291/hypres.28.209, indexed in Pubmed: 16097363.
10. Masuo K, Mikami H, Ogihara T, et al. Weight reduction and pharmacologic treatment in obese hypertensives. Am J Hypertens. 2001; 14(6 Pt 1): 530–538, doi: 10.1016/s0895-7061(00)01279-6, indexed in Pubmed: 11411732.
11. Weiner JS, Lourie JA. Practical human biology. Academic Press, London–New York 1981: 439.
12. Pacific WHORO for the W. The Asia-Pacific perspective : redefining obesity and its treatment. Health Communications Australia. Sydney 2000. . https://apps.who.int/iris/handle/10665/206936 (2020 Mar 7).

13. Rose GA, Blackburn H, Rose GA, et al. Cardiovascular survey methods. Monogr Ser World Health Organ. 1968; 56(5): 1–188, indexed in Pubmed: 4972212.
14. Page MR. The JNC 8 hypertension guidelines: an in-depth guide. Am J Manag Care. 2014; 20(1 Spec No.): E8, indexed in Pubmed: 25618230.
15. Maffei M, Halaas J, Ravussin E, et al. Leptin levels in human and rodent: measurement of plasma leptin and ob RNA in obese and weight-reduced subjects. Nat Med. 1995; 1(11): 1155–1161, doi: 10.1038/nm1195-1155, indexed in Pubmed: 7584987.
16. Zhou YT, Shimabukuro M, Koyama K, et al. Induction by leptin of uncoupling protein-2 and enzymes of fatty acid oxidation. Proc Natl Acad Sci U S A. 1997; 94(12): 6386–6390, doi: 10.1073/pnas.94.12.6386, indexed in Pubmed: 9177227.
17. Way JM, Görgün CZ, Tong Q, et al. Adipose tissue resistin expression is severely suppressed in obesity and stimulated by peroxisome proliferator-activated receptor gamma agonists. J Biol Chem. 2001; 276(28): 25651–25653, doi: 10.1074/jbc.C100189200, indexed in Pubmed: 11373275.
18. Courten Mde, Zimmet P, Hodge A, et al. Hyperleptinaemia: the Missing Link in the Metabolic Syndrome? Diabet Med. 1997; 14(3): 200–208, doi: 10.1002/(sici)1096-9136(199703)14:3<200::aid-dia336>3.0.co;2-v, indexed in Pubmed: 9088768.
19. Kunz I, Schorr U, Klaus S, et al. Resting metabolic rate and substrate use in obesity hypertension. Hypertension. 2000; 36(1): 26–32, doi: 10.1161/01.hyp.36.1.26, indexed in Pubmed: 10904008.
20. Golan E, Tal B, Dror Y, et al. Reduction in resting metabolic rate and ratio of plasma leptin to urinary nitric oxide: influence on obesity-related hypertension. Isr Med Assoc J. 2002; 4(6): 426–430, indexed in Pubmed: 12073415.
21. Itoh K, Imai K, Masuda T, et al. Relationship between changes in serum leptin levels and blood pressure after weight loss. Hypertens Res. 2002; 25(6): 881–886, doi: 10.1291/hypres.25.881, indexed in Pubmed: 12484512.
22. Canatan H, Bakan I, Akbulut M, et al. Comparative analysis of plasma leptin levels in both genders of patients with essential hypertension and healthy subjects. Endocr Res. 2004; 30(1): 95–105, doi: 10.1081/erc-120029889, indexed in Pubmed: 15098923.
23. Schutte R, Huisman HW, Schutte AE, et al. Leptin is independently associated with systolic blood pressure, pulse pressure and arterial compliance in hypertensive African women with increased adiposity: the POWIRS study. J Hum Hypertens. 2005; 19(7): 535–541, doi: 10.1038/sj.jhh.1001856, indexed in Pubmed: 15759020.
24. Xie D, Bollag WB. Obesity, hypertension and aldosterone: is leptin the link? J Endocrinol. 2016; 230(1): F7–FF11, doi: 10.1530/JOE-16-0160, indexed in Pubmed: 27252389.
25. Kumar V, Evans LC, Kurth T, et al. Therapeutic Suppression of mTOR (Mammalian Target of Rapamycin) Signaling Prevents and Reverses Salt-Induced Hypertension and Kidney Injury in Dahl Salt-Sensitive Rats. Hypertension. 2019; 73(3): 630–639, doi: 10.1161/HYPERTENSIONAHA.118.12378, indexed in Pubmed: 30595123.
26. Almeida-Pititto B, Gimeno SGA, Freire RD, et al. Japanese-Brazilian Diabetes Study Group. Leptin is not associated independently with hypertension in Japanese-Brazilian women. Braz J Med Biol Res. 2006; 39(1): 99–105, doi: 10.1590/s0100-879x2006000100012, indexed in Pubmed: 16400470.
27. Harigaya A, Nagashima K, Nako Y, et al. Relationship between concentration of serum leptin and fetal growth. J Clin Endocrinol Metab. 1997; 82(10): 3281–3284, doi: 10.1210/jcem.82.10.4321, indexed in Pubmed: 9329354.
28. Saad MF, Riad-Gabriel MG, Khan A, et al. Diurnal and ultradian rhythmicity of plasma leptin: effects of gender and adiposity. J Clin Endocrinol Metab. 1998; 83(2): 453–459, doi: 10.1210/jcem.83.2.4532, indexed in Pubmed: 9467557.
29. Kennedy A, Gettys TW, Watson P, et al. The metabolic significance of leptin in humans: gender-based differences in relationship to adiposity, insulin sensitivity, and energy expenditure. J Clin Endocrinol Metab. 1997; 82(4): 1293–1300, doi: 10.1210/jcem.82.4.3859, indexed in Pubmed: 9100610.
30. Shankar A, Xiao J. Positive relationship between plasma leptin level and hypertension. Hypertension. 2010; 56(4): 623–628, doi: 10.1161/HYPERTENSIONAHA.109.148213, indexed in Pubmed: 20713919.
31. Henriksen J, Holst J, Moller S, et al. Elevated circulating leptin levels in arterial hypertension: relationship to arteriovenous overflow and extraction of leptin. Clin Sci (Lond). 2000; 99(6): 527, doi: 10.1042/cs20000062, indexed in Pubmed: 11099396.
32. Farias DR, Franco-Sena AB, Rebelo F, et al. Polymorphisms of Leptin (G2548A) and Leptin Receptor (Q223R and K109R) Genes and Blood Pressure During Pregnancy and the Postpartum Period: A Cohort. Am J Hypertens. 2017; 30(2): 130–140, doi: 10.1093/ajh/hpw147, indexed in Pubmed: 28077420.
33. El-Gharbawy AH, Kotchen JM, Grim CE, et al. Gender-specific correlates of leptin with hypertension-related phenotypes in African Americans. Am J Hypertens. 2002; 15(11): 989–993, doi: 10.1016/s0895-7061(02)03089-3, indexed in Pubmed: 12441220.
34. Hu FB, Chen C, Wang B, et al. Leptin concentrations in relation to overall adiposity, fat distribution, and blood pressure in a rural Chinese population. Int J Obes Relat Metab Disord. 2001; 25(1): 121–125, doi: 10.1038/sj.ijo.0801480, indexed in Pubmed: 11244467.
35. Eikelis N, Lambert G, Wiesner G, et al. Extra-adipocyte leptin release in human obesity and its relation to sympathoadrenal function. Am J Physiol Endocrinol Metab. 2004; 286(5): E744–E752, doi: 10.1152/ajpendo.00489.2003, indexed in Pubmed: 14722031.
36. Pecoits-Filho R, Nordfors L, Heimbürger O, et al. Soluble leptin receptors and serum leptin in end-stage renal disease: relationship with inflammation and body composition. Eur J Clin Invest. 2002; 32(11): 811–817, doi: 10.1046/j.1365-2362.2002.01063.x, indexed in Pubmed: 12423321.
37. Risch L, Saely C, Hoefle G, et al. Relationship between glomerular filtration rate and the adipokines adiponectin, resistin and leptin in coronary patients with predominantly normal or mildly impaired renal function. Clin Chim Acta. 2007; 376(1-2): 108–113, doi: 10.1016/j.cca.2006.07.026, indexed in Pubmed: 16956602.