

## Original Article

## CIRCULATING LEPTIN LEVELS IN OBESE AND NON OBESE MENOPAUSAL WOMEN: A POSSIBLE ASSOCIATION WITH HYPERTENSION

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**Objective:** To find out the role of serum leptin levels in obese menopausal women: a possible association with hypertension.

**Methods:** Study included 92 postmenopausal women with age > 50 years. Women were categorized as group A (Normotensive), group B (obese normotensive), group C (non obese hypertensive) and group D (obese hypertensive). Detailed history was recorded in proforma. Systolic /diastolic blood pressure was taken three times in sitting position using random-zero sphygmomanometry, and the mean of the 2nd and the 3rd measurements was considered. Level of serum leptin was estimated by the technique of ELISA.

**Results:** Mean values of serum leptin in normotensive obese menopausal women were significantly increased ( $P < 0.001$ ) as compared to control and non obese hypertensive menopausal women. On the other hand, mean values of serum leptin in obese hypertensive was significantly high ( $P < 0.001$ ) as compared to non obese normotensive and hypertensive menopausal women. Correlation of systolic blood pressure & diastolic blood pressure with serum leptin was significantly positive in obese hypertensive and non obese hypertensive menopausal women.

**Conclusions:** It is concluded that leptin may contribute to increase in blood pressure in obese menopausal women who may have a resistance to satiety effect of leptin.

**Keywords:** leptin, obesity, hypertension, menopause.

### Introduction

Menopause is an era during which women have a tendency to gain weight due to reduced level of estrogen hormone.<sup>1</sup> Women enters in the menopausal state with obesity and altered lipid and glucose metabolism may be due to the loss of function of ovary.<sup>2,3</sup> The prevalence of hypertension in post menopausal women is 35 % compared with 20% in pre menopausal state. Role of sex hormones in the pathogenesis of hypertension is not well understood as it is linked with effects of aging on the cardiovascular system and its relation with increased level of serum cholesterol and body weight.<sup>4</sup> Other factors are environmental factors, genetic factors and changes in the level of sex hormones.<sup>5</sup> Changes in the level of hormone and hypertension following menopause may results in cardiovascular disease such as coronary diseases, increased stiffness of arteries and stroke<sup>6</sup>. With the decrease of synthesis of oestrogen after the age of 40 years, women slowly develop atherosclerotic lesions with the formation of fibrous cap.<sup>7</sup> Leptin is a cytokine secreted by adipocytes in proportion to body fat

mass. It regulates energy balance via its role on appetite and expenditure of energy.<sup>8</sup> The level of leptin is changed from the stage of premenopause to the postmenopause in women with normal body weight.<sup>9</sup> Obese- women both in pre menopausal and post menopausal women showed increased level of serum leptin to women with normal body weight. comparison between the two the stages of menopause in normal and obese women showed that the level of leptin decreased in both stages. A significant association is observed between BMI, secretion of leptin and menopause. This association is mainly due to altered lipid metabolism and insulin resistance.<sup>10</sup> Leptin may have an effect on blood pressure and develop hypertension via activation of sympathetic system either at the level of kidney or in the vasculature.<sup>11</sup> The relationship between obesity and hypertension shows that there may be an important role of adipose tissue in maintenance of blood pressure.<sup>12</sup> It is reported that leptin stimulates sympathetic system and reninangiotensin system,<sup>13</sup> which may affect the level of blood pressure. Leptin also encourages natriuresis which shows the effect of leptin to hypertension.<sup>14</sup> A comparative/case control

women: a possible association with hypertension.

## Methods

Study included 92 postmenopausal women with age > 50 years. Women were selected from Medical Outdoor of Lahore General Hospital, Lahore. Duration of study was 26.12.2012 to 20.12.2013. Women were comprised as group A (Non obese normotensive), group B (obese normotensive), group C (Non obese hypertensive) and group D (obese hypertensive). Inclusion criteria include, women who reported that they did not have menstruation for at least one year were considered as post menopausal. Women with BMI > 25 Kg/m<sup>2</sup> were considered as obese and women with BMI < 25 Kg/m<sup>2</sup> were taken as nonobese. Women with blood pressure 140/90 mmHg or above were considered as hypertensive and rest were grouped under normotensive. Women taking hormone replacement therapy, any cardiovascular problem, hypertriglyceridemia, diabetes mellitus and renal failure were excluded from the study. Detailed history of each subject was recorded in proforma. Letter of consent was taken from each subject/patient. Study was approved by Post Graduate Medical Institute Ethical Committee, Lahore. Systolic/diastolic blood pressure was taken in sitting position using random-zero sphygmomanometer. Both Systolic and diastolic blood pressure were taken 3 times, and the mean of the 2nd and the 3rd measurements was considered. Level of serum leptin was estimated by the technique of ELISA in Pathological Laboratory of Lahore General Hospital Lahore. Data was entered in SPSS 20. Variables were expressed as mean±SD. Variables were compared by student 't' test. Correlation of variables was carried by Pearson correlation coefficient. P<0.05 is taken as significant.

## Results

It was observed that mean values of serum leptin in control (non obese normotensive) was 11.00 ng/ml with minimum and maximum values of 7.99 and 12.26 ng/ml respectively. Mean values of serum leptin in obese normotensive subjects was significantly increased (P<0.001) as compared to control with minimum and maximum level 20.56 and 43.87 ng/ml respectively. Mean values of serum leptin in non obese hypertensive women was 13.06 ng/ml with minimum and maximum level 10.98 and 15.43 ng/ml respectively. On the other

hand, mean values of serum leptin in obese hypertensive women was significantly high (P<0.001) with minimum and maximum level 47.22 and 58.23 ng/ml respectively as compared to non obese normotensive and hypertensive menopausal women (Table 1).

Correlation of systolic blood pressure diastolic blood pressure with serum leptin was significantly positive in obese hypertensive and non obese hypertensive menopausal women (Table 2). No of cases in parenthesis Variables are expressed as mean±SD.

Groups	Mean±SD	Min Level	Max Level
Non Obese Normotensive (23)	11.00±1.72	7.99	12.26
Obese Normotensive (23)	34.27±7.67**	20.56	43.87
Non obese Hypertensive (23)	13.06±1.28	10.98	15.43
Obese hypertensive (23)	52.62±2.77**	47.22	58.23

\*\*P <0.001 = Highly significant difference

Table-2: Correlation of blood pressure with serum leptin levels in obese hypertensive and non obese hypertensive menopausal women.

	Blood pressure (mmHg)	Obese hypertensive (46)	Non obese hypertensive (46)
Correlation coefficient @ value	Systolic blood pressure (mmHg)	0.85*	0.51*
Correlation coefficient @ value	diastolic blood pressure (mmHg)	0.826*	0.52*

\*P < 0.05 = Significant difference

## Discussion

Menopause is related with decreased level of estradiol and the ratio of estrogen to testosterone. This results in increased BMI and dysfunction of endothelium, which may increase sympathetic activation. Increased sympathetic activation may increase secretion of rennin and angiotensin II. On the other hand endothelial dysfunction related with decreased nitric oxide and raised endothelin results in an increased vasoconstriction of renal system and develop hypertension.<sup>15,16</sup> We have found that the levels of serum leptin in non obese hypertensive subject were mildly increased compared to controls. Increased level of serum leptin was also observed in hypertensive women by some studies. It is suggested that there is positive correlation between the level of serum leptin and hypertension in both pre and post menopausal women.<sup>17</sup> A study proposed that serum leptin may bring vasoconstriction in thoracic aorta and pulmonary artery in experimental hypertensive rat.<sup>18</sup>

We have observed that the level of serum leptin was

may bring vasoconstriction in thoracic aorta and pulmonary artery in experimental hypertensive rat.<sup>18</sup>

We have observed that the level of serum leptin was significantly increased in obese hypertensive subjects compared to control. A study found that Leptin may increase natriuresis, and also activation of sympathetic system particularly to the kidney, results in vasoconstriction, retention of sodium and increased blood pressure. It is therefore believed that leptin may play a significant role in increasing the risk of hypertension in obese person.<sup>19</sup>

According to our study the levels of serum leptin in obese normotensive was significantly increased as compared to control. However, a study is reported that the level of serum leptin was significantly increased in obese menopausal women compare to non obese menopausal women but insignificantly differ between post and premenopausal women.<sup>20</sup>

A study has proposed that leptin have a direct action on the cell of ovarian granulosa, which may

reduce the synthesis of estradiol.<sup>21</sup> Another study found that the alteration in the level of serum leptin and its receptor in adipose tissue and hypothalamus by estrogen show a cross-talk among peripheral tissues and central tissue in the maintenance of fat content and body weight.<sup>22</sup> Correlation of systolic/diastolic blood pressure with serum leptin was significantly positive in obese subjects and non obese hypertensive subjects. It is reported that hypertension is common in patients in the age of 50-60 years. Study suggested that increased blood pressure is mainly due to stiffening of arteries which may result due to vascular changes with increase in age. This may increase the risk of cardiovascular problems and decrease renal function.<sup>23</sup>

## Conclusion

It is concluded that leptin may contribute to increased blood pressure in obese menopausal women who may have a resistance to satiety effect of leptin.

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