INT. J. BIOL. BIOTECH., 21 (2): 169-173, 2024.

SERUM LEPTIN LEVELS IN NORMAL WEIGHT HYPERTENSIVE WOMEN DURING REPRODUCTIVE AGE

Shalan Alaamri

Department of Medicine, College of Medicine, University of Jeddah, Jeddah 21589, Saudi Arabia

ABSTRACT

Change and correlation of serum leptin (Lep) at lower normal weight (LNW) and higher/ upper normal weight (HNW) body mass index (BMI) in hypertensive women during reproductive age are not clearly known. Hence, it was planned to carry out the present study by dividing the hypertensive subjects with normal body weight into two groups having LNW-BMI (group-1) and HNW-BMI (group-2) that respectively showed the mean ± SD values of serum Lep (ng/mL) as 8.20 ± 3.43 and 10.15 ± 3.08 that revealed P value: 0.1130. The BMI was plotted against serum Lep in hypertensive women of LNW that gave highly significant positive linear correlation between BMI and serum Lep (R^2: 0.4351, P: 0.0075). High significant correlation was manifested due to increased rate of change from initial BMI levels to later or higher BMI levels. Association between BMI and serum Lep in hypertensive women with HNW showed a significant positive linear correlation (R2: 0.3861, P: 0.0130). The present investigation provides the insight of the involvement of serum Lep in progressively increasing BMI in LNW and HNW hypertensive women. Hence, the current study uncovers significant role of leptin in normal weight hypertensive women during reproductive age.

Key words: Hypertension, normal weight BMI, women during reproductive age, serum leptin

INTRODUCTION

The hypertension is quite a common manifestation in a number of diseases (Kearney *et al*., 2005) and it may occur with the increase in body weight or BMI even in normal healthy individuals having a tendency of increasing body weight (Jaacks *et al*., 2019) leading to various cardiovascular diseases (CVD). A significant correlation exits between body weight and hypertension (Grassi *et al*., 2014; Fantin *et al*., 2019). There are various diseases including hypertension, diabetes mellitus and other CVD problems wherein body weight or BMI increases (Wilson *et al*., 2002). Studies reveal that normal weight associates as well with the blood pressure (BP) (Ma *et al*., 2012; Linhart *et al*., 2016). It was found that BMI elevates in response to hypertension (Cutler *et al*., 2008)**.**

Furthermore, gradual increase in BP with the increase in body weight or BMI was investigated (NCD Risk Factor Collaboration, 2017) during the life course (Shihab *et al*., 2012)**.** Generally, the investigations were carried out considering the grades (1, 2 or 3) of the hypertension. The management, however, depends on the level of suitable lifestyle and medication usage irrespective of any grade. To make it more well controlled study, we selected the hypertension subjects suffering only from grade-1 (systolic/ diastolic BP: 140-159/ 90-99).

The BP in non-obese or normal weight subjects is generally less, and involvement of strategies for lifestyle changes further decreases the BP level (Higashino *et al*., 2013)**.** Since change of body weight influences the BP, it is considered to manage both of these variables not only in hypertensives but also in non-hypertensive subjects (Ho *et al*., 2016)**,** although both of these factors require change of lifestyle and other management approaches. Reducing the body weight causes reduction in BP and is efficacious for the risk of having hypertension even in those subjects that were never overweight or obese.

Serum Lep in most of the studies was determined in normal weight, overweight and obese subjects or subjects with various medical disorders (Jołda-Mydłowska *et al*., 2006; Sohail *et al*., 2013; Sohail and Hussain, 2013; Seven *et al*., 2014; Seven 2015; Serafi *et al*., 2016; Alaamri *et al*., 2023). However, change and correlation of serum Lep level at lower normal and higher/ upper normal body weight/ BMI in hypertensive women during reproductive age is not precisely known. To understand this, we planned to carry out the present study by dividing the hypertensive subjects with normal body weight into two groups- lower normal body weight hypertensive women and upper or higher normal body weight hypertensive women.

MATERIALS AND METHODS

The present study comprised hypertensive women in reproductive age. Age range in these subjects was 30-35 years. Total number of subjects studied in the present work was 30. The subjects were informed about the purpose of

Correspondence: Dr. Shalan Alaamri, Assistant Professor, Department of Medicine, College of Medicine, University of Jeddah, Jeddah 21589, Saudi Arabia, E.mail: shalaamri@uj.edu.sa

study. They participated voluntarily. Detailed history of the patients was recorded including the details of previous discomforts and medication and family history.

The present cross-sectional study contained two groups of subjects: Group 1 comprised the hypertensive women in reproductive age having lower normal weight BMI (LNW-BMI) levels; and group 2 of hypertensive women in reproductive age having higher normal weight BMI (HNW-BMI) levels. The group-1 subjects had BMI range of 23-23.9 kg/m^2 and group-2 subjects as 24-24.9 kg/m^2. The subjects having BMI of lower than 23 and higher than 24.9 were not included in the present study.

Subjects in both groups had the hypertension of grade-1 (140-159/ 90-99 mmHg). Those subjects having lower or higher blood pressure (BP) than the mentioned levels were not included. The patients suffering from grade-2 and grade-3 were not taken for the present study.

Dividing the body weight (kilograms) with the square of body height (meters) gave the BMI values. The systolic BP and diastolic BP were obtained using the routine procedures employing a mercury sphygmomanometer (MS-S1500 Mercury Sphygmomanometer, Medical Sources Co., Limited, Nanjing, Jiangsu). Blood samples were taken from subjects in both groups for the determination of serum Lep levels corresponding to various BMI levels using ELISA (enzyme-linked immunosorbent assay) kits.

The Statistical Package for Social Sciences (version 24.0) for Windows (SPSS Inc., Chicago, IL, USA) was incorporated for the analysis of present data. The GraphPad Prism (version 6.0) software, San Diego, CA, USA, was also employed mainly for drawing the figures. The mean ± standard deviation (SD) for both groups was obtained. The independent student t-test was analyzed for obtaining the value of t and p the probability of significance. The values of BMI and serum Lep were drawn against each other for the determination of correlation for linear regression lines. Coefficient of determination (R^2) was obtained to get the significance level. The value of significance (P) was obtained considering the previous published study (Zahir *et al*., 2014). The significance level of $p<0.05$ was considered as statistically significant.

RESULTS

The hypertensive women (n: 30; age range: 30-35 years) in reproductive age were studied for the serum Lep at LNW-BMI (group-1) and HNW-BMI (group-2). The results for BMI and Lep variation and their association were analyzed.

The LNW-BMI group-1 and HNW-BMI group-2 respectively had the mean ± SD values of BMI (kg/m^2) as 23.46 ± 0.26 and 24.48 ± 0.30. The unpaired t-test was employed and two-tailed P value analysis ($t = 10.0459$, $df = 28$, $p<0.0001$) gave highly significant difference.

The LNW-BMI group-1 and HNW-BMI group-2 respectively showed the mean ± SD values of serum Lep (ng/ml) as 8.20 ± 3.43 and 10.15 ± 3.08 that revealed $t = 1.6361$ ($df = 28$) and P value as non-significant ($p=0.1130$).

The BMI was plotted against serum Lep in hypertensive women at LNW (Fig.1) that gave highly significant positive linear correlation between BMI and serum Lep (df: 13, R^2: 0.4351, P: 0.0075). The high significant correlation is manifested due to increased rate of change from initial BMI levels to later BMI levels.

The association between BMI and serum Lep in hypertensive women with HNW was obtained diagrammatically by plotting BMI and Lep against each other (Fig. 2). A significant positive linear correlation (df: 13, R2: 0.3861, P: 0.0130) was obtained. Significant correlation in HNW group but lesser level of correlation as compared to that in LNW did not mean the less level of correlation (Fig. 2) since it demonstrates the correlation for ending levels of LNW group to later HNW levels. In view of this, the value of significance for correlation appears to be lesser.

DISCUSSION

We planned to investigate the association of lower and upper levels of body weight associated BMI in hypertensive women during reproductive age. One previous study of the data from similar population (Alaamri *et al*., 2023) showed significant changes and positive linear correlation among BMI, BP and serum Lep while studying the overweight 12-20 years age male university students and wherein low, medium and high levels of BMI of the subjects without hypertension was studied.

In view of the mentioned finding (Alaamri *et al*., 2023), it was planned to see how serum Lep changes occur in grade-1 hypertensive subjects having normal low and normal high BMI levels. It was found that though both groups (having normal lower weight BMI and normal higher weight BMI) of grade-1 hypertensive women in reproductive age did not manifest any significant variation in serum Lep levels, the correlation between BMI and serum Lep was positive linear with significant level. Such type of division of the data of normal hypertensive

subjects is scarce in literature. However, there are studies in overweight subjects that showed positive linear correlation of BMI and serum Lep (Jołda-Mydłowska *et al*., 2006; Seven *et al*., 2014; Seven, 2015), and it was found that serum lep levels have significant role in the pathophysiology of overweight related hypertension (Seven, 2015).

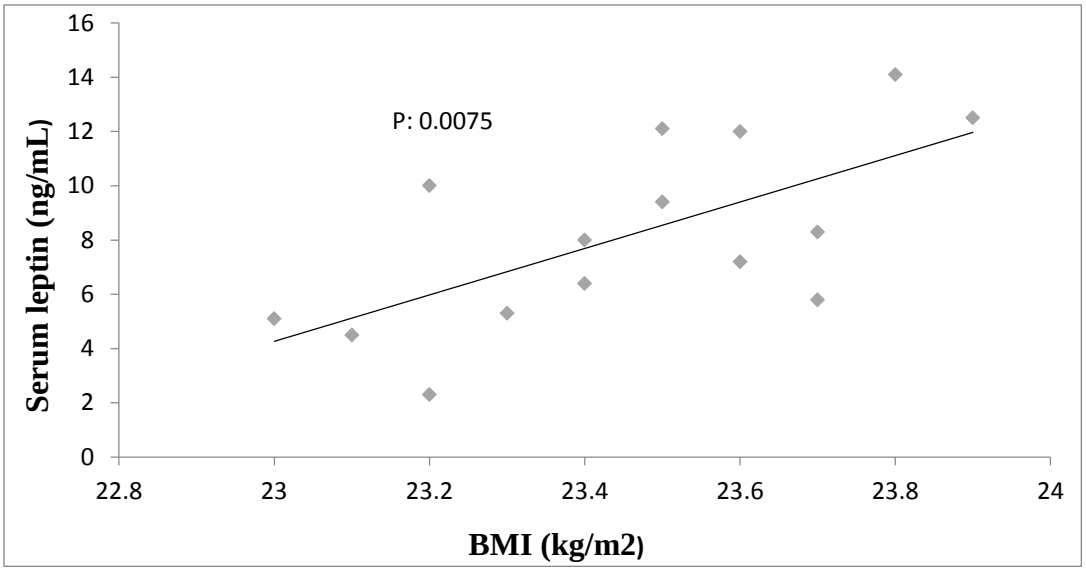

Fig.1. Association of Serum leptin and BMI in hypertensive women with lower normal weight.

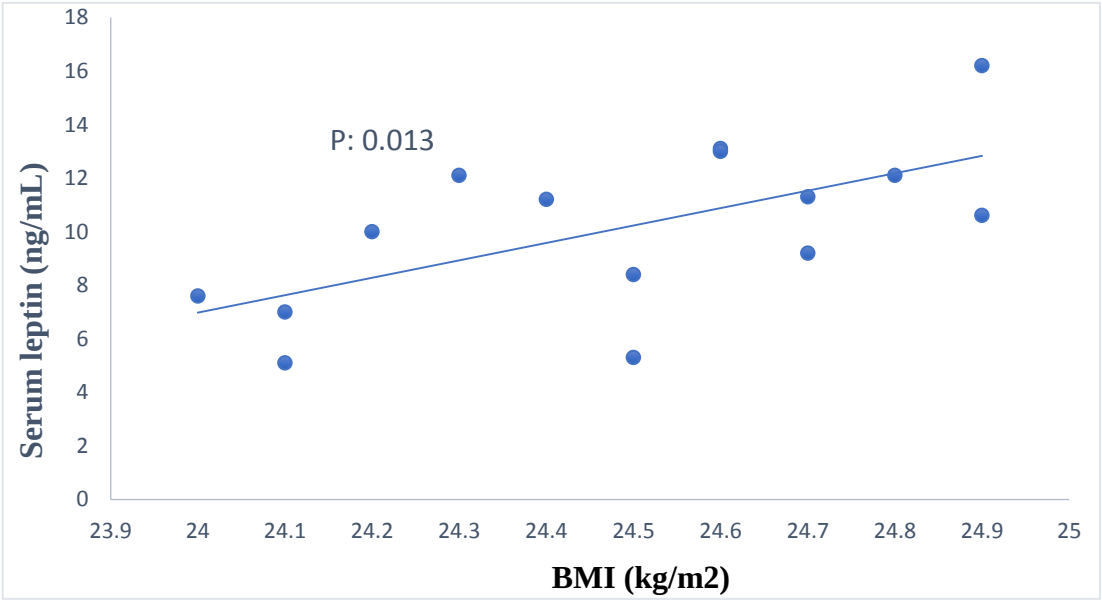

Fig. 2. Association of Serum leptin and BMI in hypertensive women with higher normal weight.

Iit is known that serum Lep relates partly to the endothelial dysfunction (Kofler *et al*., 2005; Zachariah *et al*., 2016). Furthermore, the inflammation caused by Lep and other pro-inflammatory cytokines may depend upon aortic stiffening leading to ventricular stiffness (Zanoli *et al*., 2018), and it seems possible that progressive increase in BMI may elevate BP and that may manifest hypertension of low grade (grade-1, as in the present study.

There are other indirect approaches to interpret the present investigations. Dysfunction in the tissues releasing Lep to the vascular wall (Szasz and Webb, 2012; Fernández-Alfonso *et al*., 2013; Szasz *et al*., 2013; Almabrouk *et al*., 2014; Xia and Li, 2017) influencing the endothelial dysfunction and inflammation (Fernández-Alfonso *et al*., 2013) may appear with the increasing BMI in subjects with lower and higher normal body weight BMIs.

Moreover, progressive increase in BMI elevates the production of contractile factors involving heightened arterial vasoconstriction and more vessel tone (Fernández-Alfonso *et al*.,2013; Van Dam *et al*., 2017). The association of Lep with the contractile activity is highly involved in hypertension that may explain the increased levels of Lep in patients with hypertension.

Increased activity of sympathetic nervous system with progressive increase in body weight (Grassi *et al*., 2014, 2015, 2018; Schütten *et al*., 2017; Fonkoue *et al*., 2019) associates with the development of hypertension with the increase in serum Lep and other proinflammatory markers (Grassi *et al*., 2014, 2015, 2018).

The Lep receptors present in aorta, arterial adventitia, tunica media and atherosclerotic plaques are involved in causing arterial stiffness by promoting the proliferation of vascular smooth muscle cells and migration (Parhami *et al*., 2001; Purdham *et al*., 2004). Other mechanisms verifying the present findings relate to the role of Lep causing endothelial oxidative stress/ ROS (reactive oxidative species) in experimental human cell models (Yamagishi *et al*., 2001), promoting the angiogenesis activating the immune processes, enhancing the platelet aggregation, and producing ROS (Werner and Nickenig, 2004).

The present investigations provide the insight of the involvement of serum Lep in progressively increasing BMI in lower normal body weight or higher normal body weight. Hence, the current study uncovers the role of leptin in normal weight hypertensive women in reproductive age.

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(*Accepted for publication March 2024*)