INTRODUCTION

Hypertension is a chronic non-communicable medical condition in which blood pressure (B.P) is elevated above the normal values. According to The Joint National Committee (JNC) on prevention, detection, evaluation and treatment of hypertension guidelines, normal blood pressure is defined as a systolic blood pressure of 120 mmHg and a diastolic blood pressure of 80 mmHg.1 The prevalence of hypertension in Pakistan as reported by National Health Survey of Pakistan (NHSP) is 17.9% in adults >15 years of age and 33% in patients >45 years of age.2 Primary or essential hypertension constitutes almost 90% of the cases of hypertension. This type of hypertension shows genetic predisposition and is often aggravated by certain contributing factors such as obesity, smoking, dietary factors and stressful life style.3 An increase in the sympathetic activity of the nerves in autonomic nervous system (ANS) that innervate the kidneys results in hypertension.4 Complications of Hypertension include coronary heart disease, cerebrovascular disease, heart failure and renal failure.5 Obesity is defined as abnormal or excessive fat accumulation. A person with a body mass index (BMI) equal to or more than 30 Kg/m² is regarded as obese.6 A BMI of 40 kg/m² is linked to seven times greater risk of developing hypertension.7 Increased sympathetic activity of kidney in obese people leads to sodium retention and impairment in pressure natriuresis leading to development of hypertension.8 However, Compared to BMI, waist hip ratio (WHR) is regarded as the more reliable indicator for mortality and morbidity due to cardiovascular diseases.9 Visfatin is an adipocytokine which was identified in 2005. Its production from visceral fat led to its name Visfatin.10 The organs with the highest production of visfatin include liver and bone marrow. The normal serum level of visfatin, in both males and females, is 15.8 ng/ml ±16.7 ng/ml.11 It is known to cause adipocyte proliferation and its levels are raised in obesity.12 The role of visfatin in the pathogenesis of hypertension is not clear. Many studies have pointed towards a direct role of visfatin in the pathogenesis of hypertension.13,14 It may act on immune cells to promote vascular smooth muscle inflammation which accounts for its potential role in vascular dysfunction and inflammatory changes associated with some metabolic disorders.15 Visfatin can cause oxidative stress leading to Nitric oxide breakdown and increase in Endothelin factor 1 (ET-1) levels leading to vasoconstriction and atherosclerosis.16,17 In contrast to the above view, Rezk et al., have suggested that
visfatin has a protective role against hypertension and is released from visceral adipose tissue as a compensatory mechanism to reduce raised blood pressure. Some studies have also reported direct cardioprotective effects of visfatin in improving reperfusion of myocardium and reduction of infarct size. The exact role of visfatin in hypertension is still unclear and needs further exploration.

This study was done to probe the possible link between serum visfatin levels and hypertension in obese and non-obese subjects. The control of hypertension and obesity is not possible without unraveling the complex mechanisms underlying their pathogenesis and the proposed link between the development of these conditions and the newly discovered adipokines such as visfatin. The study was conducted to compare the serum levels of visfatin in non-obese normotensives, non-obese hypertensive and obese hypertensive.

**METHODOLOGY**

This comparative cross sectional study was approved by the ethical committee of Postgraduate Medical Institute, Lahore, and was conducted in the Physiology Department of Postgraduate Medical Institute from November 01\(^{st}\), 2013 to October 30\(^{th}\), 2014 in collaboration with Services Institute of Medical Sciences, Lahore. The study was completed in twelve months. It was approved by the Advanced Science and Research Board of the University of Health Sciences (UHS), Lahore. Eighty one male and female subjects between 30 and 55 years of age, divided equally into three groups were included in the study. First group (controls) consisted of twenty seven non-obese normotensive subjects. Second group included twenty seven non-obese hypertensive subjects. Third group comprised of twenty seven obese hypertensive subjects.

Inclusion criteria for controls consisted of normotensive non-obese male and female subjects between 30 and 55 years of age. For cases inclusion criteria consisted of hypertensive male and female subjects, both non-obese and obese, diagnosed within last 6 months and their ages were between 30 and 55 years.

Obese or non-obese subjects with diagnosed hypertension for more than six months, any acute or chronic illness (except hypertension), patients of diabetes mellitus, patients taking anti-obesity drugs and pregnant females were excluded from the study. Study subjects were included in the study after taking informed consent. Special data collection forms were used to collect information, like physical and demographic characteristics, and general physical examination features such as height in meters and weight in kilograms.

Blood pressure readings were recorded with the help of mercury sphygmomanometer according to the guidelines laid down by the Joint National Committee (JNC) on prevention, detection, evaluation and treatment of hypertension. The readings were recorded at the time of inclusion of subjects using standard measurement techniques. Body Mass Index (BMI) was calculated using the formula: BMI = body weight (kg) / height (m)\(^2\). Waist Hip Ratio (WHR) was used as a measure of obesity. WHR > 0.9 for females and > 1 for males were labeled as obese. It was calculated using the following formula: WHR = Gw/Gh (girth of waist/girth of hip). The units used were in centimeters (cm). For estimation of visfatin 5 ml of fasting blood sample was drawn using aseptic technique. Serum was obtained for visfatin levels estimation and stored at -40\(^{\circ}\)C till further analysis. Sandwich ELISA technique was used for the quantitative estimation of serum visfatin by using ELISA kit for human soluble PBEF1/visfatin/NAMPT by Aviscera Bioscience.

**Data Analysis:** The collected data was entered into SPSS version 17 and was statistically analyzed. The quantitative variables of the cases and controls such as age, serum visfatin, level, BMI and WHR were expressed as mean ±SD. Qualitative variables such as gender were expressed in frequency and percentages. One way analysis of variance (ANOVA) was applied to compare these serum values in the three subject categories. Post-hoc Tukey test was used to see the difference between pair of means of the three groups. A \(p\)-value of <0.05 was considered statistically significant.

**RESULTS**

A total of 81 subjects between 30-50 years of age were included in the study. Subjects were divided equally into three study groups i.e. control, non-obese hypertensive and obese hypertensive.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control mean ±SD (n = 27)</th>
<th>Non-Obese hypertensive mean ± SD (n = 27)</th>
<th>Obese hypertensive mean ± SD (n = 27)</th>
<th>(p)-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m(^2))</td>
<td>23.11±1.16</td>
<td>23.07±1.14</td>
<td>32.59±1.55</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>WHR (cm)</td>
<td>0.73±0.11</td>
<td>0.69±0.11</td>
<td>1.12±0.26</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>111.85±7.36</td>
<td>146.67±7.85</td>
<td>151.30±10.71</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>73.52±4.12</td>
<td>97.78±5.43</td>
<td>97.59±4.68</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Serum Visfatin (ng/ml)</td>
<td>5.21±3.57</td>
<td>33.71±10.66</td>
<td>70.97±50.30</td>
<td>&lt;0.001***</td>
</tr>
</tbody>
</table>
The results show that the difference of BMI between controls and non-obese was non significant ($p > 0.05$) and controls and obese was significant ($p < 0.001$). The difference between non-obese and obese hypertensive was significant ($p < 0.001$). The difference of WHR between controls and non-obese hypertensives was nonsignificant ($p > 0.05$). A significant difference ($p < 0.001$) was observed between controls and obese hypertensives. Between non-obese and obese hypertensives the difference was also significant ($p < 0.001$).

A significant difference of diastolic blood pressure was seen between controls and non-obese hypertensives ($p < 0.001$) and obese hypertensives ($p < 0.001$). However, between non-obese hypertensives and obese hypertensives the difference was nonsignificant ($p > 0.05$).

The diastolic pressure difference between the controls and non-obese hypertensives ($p < 0.001$) and obese hypertensives was significant. The difference between non-obese hypertensives and obese hypertensives was nonsignificant ($p > 0.05$).

Serum visfatin level of obese hypertensive and non obese hypertensive were significantly higher compared to controls ($p < 0.05$). There was also a significant difference in the serum visfatin level of obese and non obese hypertensives ($p < 0.05$). A highly significant difference was observed between controls and obese hypertensives ($p < 0.001$) and between non-obese and obese hypertensives ($p < 0.001$).

**DISCUSSION**

Hypertension and obesity are one of the most common non-communicable diseases in the world. Research has led to the discovery of the role of some of the relatively newer compounds, such as visfatin, which are believed to play an important role in development of hypertension. A detailed understanding of these mechanisms involving visfatin and renin-angiotensin system is essential to unravel the pathways that predispose an individual to developing hypertension and obesity.

The current study was done to probe the possible link between serum visfatin levels and hypertension assuming that raised serum visfatin levels are one of the possible culprits for increased systolic and diastolic pressure in obese or non-obese primary hypertensive subjects. The study involves finding out the relationship between primary hypertension and physical and biochemical factors that are thought to contribute towards hypertension. Physical factors include WHR and BMI, while biochemical factors include serum visfatin levels. The relationship of each of these factors with primary hypertension and obesity was compared in the three study groups i.e. controls, non-obese hypertensives and obese hypertensives. Serum visfatin levels showed marked variations in the three study groups. The non-obese hypertensive and the obese hypertensive subjects both showed higher serum visfatin levels. The mean value of serum visfatin was highest in the obese hypertensive group. These mean values from the three study groups show a statistically significant difference ($p < 0.001$). These findings point towards a possible role of visfatin in the development of primary hypertension. The results from the current study are in agreement with the results from most of the
studies conducted earlier. The study by Gunes et al. also showed strong positive correlation between visfatin levels and systolic and diastolic blood pressures. In another study by Ozal et al. serum visfatin levels were found to be significantly higher in hypertensive patients. However, the study included only younger age group and non-obese subjects (BMI <25 kg/m2) in whom hypertension is less frequent. Rotkegel et al. stated that the interaction between visfatin and hypertension is complex. In order to find out the role of visfatin in the pathogenesis of hypertension various metabolic and endocrine factors must also be taken into consideration.

Visfatin is released from adipocytes in the visceral fat. Therefore, visfatin levels are believed to be related to the amount of visceral fat present in the body. The two parameters for assessing total body fat and central obesity i.e. BMI and WHR were measured for the three study groups and then compared with visfatin levels. In the current study, a highly significant (p < 0.001) positive correlation was observed between BMI and WHR with visfatin levels. Several studies have been directed towards finding a correlation between visfatin levels and obesity. A study in China in 2013 on eighty six children concluded that serum visfatin levels were significantly higher in obese children. Study on morbidly obese subjects undergoing gastric bypass surgeries showed that omental tissue expresses the highest levels of visfatin suggesting a variable expression of visfatin in generalized and central obesity.

Gastric banding surgeries have shown to result in a significant fall in visfatin levels as the patients begin to lose weight. Results from a study in Turkey showed a positive correlation of obesity indicators, such as BMI and WHR, with serum visfatin levels, not only in the obese subjects but also in the non-obese controls. In contradiction to the studies mentioned above Gunes et al. did not find any correlation between visfatin and obesity parameters such as BMI and WHR. Visfatin is a myokine secreted from skeletal muscles and not from visceral fat cells. That may be the reason that no relationship was observed between visfatin and body fat. Haider et al. also reported that there is no correlation between BMI and visfatin levels. Additionally it is still not clear if visfatin is directly related to obesity or is indirectly related by obesity related mechanisms such as hyperleptinemia and hyperinsulinemia. Dogru et al. also did not find any correlation between visfatin and obesity and concluded that visfatin levels may be influenced by multiple factors and adiposity alone may not be the determining factor.

The current study is an attempt to explore the complex mechanisms involving the pathogenesis of primary hypertension and obesity. The results show higher serum visfatin levels in obese and hypertensives as compared to non-obese hypertensives and controls and strong positive correlation of serum visfatin with hypertension, BMI and WHR. Although many studies have pointed out towards the role of physical and biochemical factors particularly the newly discovered adipokines such as visfatin in the development of hypertension and obesity, these results are however inconsistent and need further exploration. The incidence of hypertension and other cardiovascular diseases is constantly on the rise in Pakistan and other south Asian countries and it has become a leading cause of mortality in this part of the world. With a thorough understanding of these mechanisms we can work toward the prevention and cure of hypertension and obesity.

CONCLUSION

Serum Visfatin levels can be used as biomarker for the evaluation of hypertension in obese and non-obese patients.

REFERENCES


