Comparison of Serum Creatinine and Oxidative Stress in Normotensive and Hypertensive Obese Adults

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Abstract

Objective: To compare serum creatinine levels and oxidative stress in normotensive and hypertensive obese subjects.

Material and methods: This case control study was conducted at Physiology Department of Army Medical College Rawalpindi, in which 100 adult males were recruited and divided into two groups. Each group comprised of 50 normotensive and 50 hypertensive obese adults with BMI ≥ 25 kg/m² and age between 20-45 years. History and demographic data were also included. Serum creatinine levels and arterial stiffness indices were measured and compared in both groups.

Results: No significant difference (p-value = 0.621) in age, BMI (p-value = 0.265) and pulse pressure (p value 0.260) between obese controls and obese hypertensive patients was recorded. Systolic and diastolic blood pressures and mean arterial pressure were significantly elevated in hypertensive obese group as compared to normotensive obese (control) group. Data revealed significantly higher levels (p = 0.000) of serum creatinine in hypertensive obese subjects as compared to normotensive obese subjects. The measure of oxidative stress (8-isoprostane PGF₂α) revealed that it was significantly raised in hypertensive obese subjects in comparison with normotensive obese subjects.

Conclusion: Our study documented that there were no differences in BMI levels of normotensive and hypertensive obese subjects. Conversely, serum creatinine levels were significantly elevated in hypertensive obese patients.8-isoprostane PGF₂α, a marker of oxidative stress was increased in both groups with noticeable elevation in hypertensive group.

Keywords: Arterial pressure, Body mass index, Creatinine, Hypertension, Oxidative stress.

Introduction

Obesity has been designated by the World Health Organization (WHO) Consultation, as a chronic disease that has become a major threat to the health.¹ Sympathetic Body mass index is a universally accepted simple index of weight to height. Therefore it is used to define overweight and obesity in all age groups including children and adults. There is profound activation of sympathetic nervous system by adipose tissues in obese individuals. Along with sympathetic over drive there is activation of renin angiotensin system that leads to development of oxidative stress and endothelial dysfunction resulting in the development of hypertension.³,⁴,⁵

Oxidative stress is defined as an inequity between free radicals production and the capability of the body to detoxify their destructive and potentially lethal effects through deactivation by antioxidants. Major contribution of reactive oxygen species is provided by mitochondria during normal oxygen metabolism via electron transport chain.⁶,⁷,⁸ Many clinical studies have established the major role contributed by oxidative stress in renal dysfunction. Hypertension has been advocated among one of the major causes of development of renal failure. Obesity induced oxidative stress bridges the link between hypertension and renal impairment.⁹

The increasing prevalence of obesity worldwide is predisposing the population to many health issues like hypertension diabetes and kidney diseases. In obese individuals adipose tissue leads to suppression of renal function by changing intra-renal pressures and re-absorption by the tubules. Moreover chronic effects of obesity on kidney are more devastating leading to structural changes with loss of nephron function and augmentation in arterial pressure leading to severe renal disease in some cases.¹⁰ In fact prevalence of hypertension among overweight and obese persons is higher than normal weight individuals.¹¹ Oxidative stress has a prominent role in the pathophysiology of several kidney diseases, and complications of these diseases. Renal oxidative stress can be induced by many
Factors including hypertension, diabetes mellitus, dyslipidemias, smoking, alcohol, drugs, occupational and environmental toxins, chemicals and radiation. Kidneys of obese individuals are highly vulnerable to damage caused by reactive oxygen species. This can be attributed to abundance of long chain polyunsaturated fatty acids in the structure of renal lipids. In recent years, not much work has been focused on obesity induced oxidative stress and renal impairment in Pakistan. The present study was conducted to compare serum creatinine levels and oxidative stress in normotensive and hypertensive obese subjects.

Material and Methods
This case control study was conducted on 100 obese participants who were divided into two groups; 50 normotensive controls and 50 hypertensive obese cases. The study was conducted at Physiology Department, Army Medical College, Rawalpindi from January 2012 to January 2013. Approval of the study was taken from Ethical Review Committee, Army Medical College, and written and informed consent was obtained from all participants. These participants were selected by non-probability convenient sampling, with age range of 20-45 years and obese males with BMI $\geq$ 25 kg/m$^2$. The criteria for normotensive subjects was defined as participants with diastolic blood pressure (DBP) $< 80$ mmHg and systolic blood pressure (SBP) $< 120$ mmHg. The hypertensive subjects had DBP $>$ 90 mmHg and SBP of $> 130$ mmHg. The exclusion criteria for the participants included smoking huqqa or naswar addiction, intake of lipid lowering drugs, diabetes mellitus, acute infections and chronic inflammatory diseases.

Demographic information regarding age, weight, height, BMI, blood pressure was recorded. Blood pressure was measured by auscultatory method with the help of mercury sphygmomanometer. First reading was taken at the time of filling of proforma, second just before drawing of blood for biochemical analysis and third during recording of pulse wave contour for recording the stiffness of the vessel. Appearance of first phase Korotkoff sound was taken as systolic blood pressure while fifth phase was taken as diastolic blood pressure. The first measurement was discarded while the second and third measurements (mmHg) were averaged. For biochemical parameters fasting blood samples were collected from the subjects and processed for separation of serum. Serum isoprostane and serum creatinine were measured. The data were entered and analyzed by using SPSS (version 15). Mean with standard deviations were used to present quantitative data. Independent sample t-test was used to compare means of different parameters between normotensive and hypertensive obese subjects.

Results
In this case control study comparison of 50 control subjects (obese normotensive) and 50 obese hypertensive subjects demographic characteristics showed that there was no significant (p = 0.621) difference in age of obese controls and obese hypertensive group. BMI status of both groups was also comparable. There was no significant (p = 0.265) divergence in BMI of obese controls and obese hypertensive patients. The measure of oxidative stress (8-isoprostane) revealed that it was significantly raised in hypertensive obese subjects in comparison with that of normotensive obese subjects (table 1).

Table 1: Comparison of Age and BMI and F2-isoprostane in normotensive and hypertensive obese groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (yrs)</th>
<th>BMI (kg/m$^2$)</th>
<th>F2-isoprostane (pg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal controls</td>
<td>33.26±6.55</td>
<td>27.30±3.96</td>
<td>293.56±38.19</td>
</tr>
<tr>
<td>Hypertensive obese patients</td>
<td>34.00±8.27</td>
<td>26.40±4.09</td>
<td>322.43±49.82</td>
</tr>
<tr>
<td>P value</td>
<td>0.621</td>
<td>0.265</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Table 2: Comparison of parameters of blood pressure and creatinine in normotensive and hypertensive obese group

<table>
<thead>
<tr>
<th>Group</th>
<th>SBP(mmHg)</th>
<th>DBP(mmHg)</th>
<th>PP(mmHg)</th>
<th>MAP</th>
<th>Serum creatinine (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normotensive controls</td>
<td>105.90±7.73</td>
<td>67.66±7.58</td>
<td>38.24±7.11</td>
<td>80.40±6.85</td>
<td>1.01±0.24</td>
</tr>
<tr>
<td>Hypertensive obese</td>
<td>137.90±3.79</td>
<td>98.26±3.43</td>
<td>39.64±5.10</td>
<td>111.47±2.61</td>
<td>2.46±0.860</td>
</tr>
<tr>
<td>p value</td>
<td>0.000</td>
<td>0.000</td>
<td>0.261</td>
<td>0.000</td>
<td>0.000</td>
</tr>
</tbody>
</table>

SBP=Systolic blood pressure, DBP=Diastolic blood pressure, PP=Pulse pressure, MAP= Mean arterial pressure

The systolic and diastolic blood pressures were significantly elevated in hypertensive obese group as compared with the normotensive obese (control) group. Furthermore, it was found that there was no significant difference (p = 0.26) of pulse pressure between normotensive and hypertensive obese groups. The mean arterial pressure was found significantly higher in obese hypertensive subjects as compared with that of normotensive obese. The mean serum creatinine level was found higher in hypertensive obese subjects when compared to that of normotensive obese subjects. Data analysis of this study revealed that hypertensive obese subjects had significantly higher levels of serum creatinine as compared to that of normotensive obese subjects with p value of $< 0.05$.

Discussion
In this case control study, we attempted to investigate the relationship of oxidative stress and renal disease in obese...
hypertensive and normotensive patients. Demographic characteristics revealed significant (p=0.042) difference of age between the two groups; mean age of hypertensive subjects being higher 934.20±8.19 years) than that of normotensive subjects (31.22± 6.10 years). This indicated that prevalence of hypertension increased with increasing age. This finding is similar to the study in which it was reported that mean systolic and diastolic blood pressure in untreated male subjects increased to 138/91 mmHg and 159/91 mmHg at the age of 50 and 70 years respectively.12

BMI showed no significant difference amongst the two groups because the same criteria of BMI (≥ 25 kg/m²) was used to induct obese subjects in normotensive and hypertensive groups. Another study was conducted on the relationship of hypertension with body mass index and age in male and female population of Peshawar, Pakistan.13 The study was of one year duration in which 1006 individuals of both sexes were studied which revealed consistent relationship between hypertension and BMI. There was 19% increased incidence of hypertension in obese individuals when compared with non-obese. In present study, all individuals were obese and their BMI was 26.83±0.85 kg/m² in normotensive subjects and 27.004 ±0.95 kg/m² in hypertensive subjects. The female subjects were not included in the study and group size was also smaller, however, the results are comparable with the aforementioned study. Arterial hemodynamics such as SBP, wave reflection and pressure wave propagation are affected by the gender related differences in body size.14

Hypertension and dyslipidemia are risk factors for atherosclerotic disease and accelerated decline in normal renal function.15 Results of our study revealed high creatinine levels in obese hypertensive subjects (2.46±0.86 mg/dl) compared to normotensive subjects (1.01±0.23 mg/dl) which provided the evidence of deterioration of renal function in hypertension. Study from Asia Pacific Region on assessment of blood pressure as a major risk factor for renal damage revealed that both SBP and DBP were positively associated with the risk of renal damage and blood pressure was among the strongest predictors of renal damage.16 A population of 1829 white hypertensive patients (mean age 51 ± 12 years) were included in a study which revealed higher than normal serum creatinine levels in hypertensive subjects.17 Present study revealed 0.76 mg/dl higher than normal serum creatinine levels in hypertensive obese subjects compared to the normotensive obese. This difference of serum creatinine levels in two studies could be attributed to greater muscle mass in present study group. Increased muscle mass is associated with increased serum and urinary creatinine levels.18

Oxidative stress has been linked to the development of hypertension with an enhanced production of reactive oxygen species like O₂⁻, NADPH oxidase causing endothelial dysfunction and vascular hypertrophy leading ultimately to the development of hypertension.20 Increased levels of serum and urinary F₂ isoprostane have been found associated with hypertension. In the present study, there were increased F₂ isoprostane levels in both hypertensive and normotensive groups (463.80 pg/ml vs. 300.32 pg/ml respectively), however there occurred significant (p=0.002) rise in the levels of F₂ isoprostane in hypertensive as compared with that of normotensive obese subjects.

Another study measured the serum levels of F₂ isoprostane in 14 obese and 17 non-obese men and evaluated their relationship with body mass index.21 Obese men had significantly higher plasma concentration of F₂ isoprostane than non-obese men (p < 0.05). This finding is comparable to the present study and reveals that obesity is associated with increased oxidative stress, manifested by higher F₂ isoprostane levels in hypertensive obese subjects. It could be due to the increased ratio of oxidative damage to lipids, proteins, and amino acids in obese subjects.22

**Conclusion**

Our study signifies that obesity predisposes to oxidative stress which leads to deterioration in renal functions.

**Conflict of interest**

This study has no conflict of interest to declare by any author.

**References**