Original Research Article

Association of high-sensitivity C-reactive protein level with central obesity of the children in a tertiary care hospital of Bangladesh

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ABSTRACT

Background: Obesity is an exaggeration of normal adiposity. Central obesity in children has increased than general adiposity now a days, which is not routinely measured in clinical practice. Adipose tissue contributes to the secretion of a number of inflammatory cytokines which stimulate the production of high-sensitive C-reactive protein (hs-CRP) by the liver. The study was done to see the association of hs-CRP level with central obesity in Bangladeshi children.

Methods: A total of 110 obese children aged between 10 to 18 years with BMI≥95th centile and age and sex matched 55 non-obese children with BMI≥5th to <85th centile according to centers for disease control and prevention (CDC) growth chart were selected. A structured questionnaire was prepared taking into account demographic and clinical parameters. The hs-CRP were estimated in study subjects and then correlated to central obesity by waist height ratio (WHtR).

Results: The prevalence central obesity was 45.5% by WHtR and raised hs-CRP levels was 46.4% in obese children. About 62% of obese children had central obesity who had raised hs-CRP level ≥2 mg/l (high risk), which showed significant positive correlation with WHtR and was significantly raised in obese children.

Conclusions: A high proportion of central obesity was observed in obese children who had raised hs-CRP level, suggesting that it might be useful to assess future metabolic and cardiovascular complication.

Keywords: Central obesity, Physical activity, High-sensitive C-reactive protein, Body mass index

INTRODUCTION

Obesity in children is a major global health problem now a days. An excess of the abdominal fat is also known as central obesity. A number of studies have shown that central obesity is an independent risk factor for systemic arterial hypertension and a number of coronary artery diseases. In a systemic review published on 2015, the authors concluded that central body fat deposition in children increases the risk of cardio-metabolic risk. Therefore, more concentration should be paid to central obesity of children in both clinical practice and epidemiological studies. Body mass index (BMI) is widely used as an index of relative adiposity among children and adults. However, BMI does not always relate to central obesity. BMI cannot differentiate between fat and fat free mass. Waist height ratio (WHtR) has come into view as a good predictor for central obesity and cardiovascular risk factors. The rationale underlying this index is that, for a given height, there is an acceptable degree of fat stored on the upper body. In addition, it has been shown to be a simple, non-invasive and practical tool that correlates well with the visceral fat and is easier to use. Adipose tissue contributes to the secretion of inflammatory cytokines. These cytokines include interleukin-6 (IL-6), interleukin-1 (IL-1) and
tumor necrosis factor alpha (TNF-a), which stimulate hs-CRP production by the liver.11 The detection of hs-CRP level in the blood is regarded as the presence of subclinical inflammation. hs-CRP level ≥2 mg/l indicates low grade inflammation. Therefore, the early detection of low-grade inflammation in individuals with central obesity by doing a simple test hs-CRP is particularly important. This study aimed to observe the association of hs-CRP levels with the central obesity in children.

METHODS

This cross-sectional study was conducted in the department of paediatrics (paediatric endocrinology clinic, paediatric outpatient and inpatient department), Bangabandhu Sheikh Mujib medical university (BSMMU) and was approved by the institutional review board (IRB) of this institute. The study was carried out over a period of 12 months from September 2018 to August 2019. A total of 165 children were recruited from those who came for screening in the department of paediatrics. After taking informed written consent, the study subjects were allocated in the following two groups:

Group A (obese group): Total 110 newly diagnosed case of obese children (≥95th centile) and group B (non-obese group): Age and sex matched 55 normal weight healthy children (BMI ≥5th to <85th centile) according to CDC age and sex specific BMI criteria. Obese group were further subdivided into grade I and grade II obese group. In grade I obese group there was 64 obese children with BMI ≥95th centile and <120% of 95th centile and in grade II obese group newly diagnosed 46 obese children with BMI ≥120% of 95th centile according to CDC age and sex specific BMI criteria. Subjects suffering from any liver or renal diseases, infections, inflammation, taking any steroid and were in dietary restriction were excluded from the study. A detailed history was taken and then physical examination and measurements of anthropometric indices were taken. The weight was measured with using electronic weighing machine (Tanita, Japan) placed on a flat surface to a nearest 100 gm with barefoot and light clothing. Standing height was measured with a stadiometer and measurement was done to the nearest 0.1 cm. BMI was calculated as the ratio between weight (in kilograms) and the square of the height (in meters). Waist-to-height ratio (WHR) was calculated by dividing waist circumference by height in cm. A WHtR ≥0.5 is an indicator of abdominal obesity in both adults and children at any age.2,12-15

Blood sample was collected from the study subjects by venepuncture in clean and dry test tube containing no anticoagulant. Under all aseptic precautions 2 ml of venous blood was collected from the study subjects by using a disposable syringe from the ante-cubital vein. The needle was detached from the nozzle and blood was transferred immediately into a dry clean test tube with a gentle push to avoid hemolysis and was kept in standing position till clot formation. Serum was separated by centrifugation (5 min at 3000 rpm) within 30-120 min of collection. Then 1 ml clear serum was collected in Eppendorf tube and then hs-CRP was measured by nephelometric system (BN ProSpec, SIEMENS, USA). After measuring, hs-CRP was categorized according to American college of cardiology (ACC) and American heart association and centers for disease control and prevention (AHA/CDC) in 2013. Categorization of the hs-CRP level was-high risk ≥2 mg/l, Low risk <2 mg/l.

Data were expressed as mean±standard deviation (SD) and frequency and percentage. Data were analysed by Chi-square test, Fisher’s exact test and unpaired student t-test for quantitative data. Pearson correlation coefficient test and scatter diagram were applied to evaluate the correlation between the variables. P value <0.05 was considered as statistically significant.

RESULTS

Study population in this study were children aged between 10-18 years and clinically healthy. Comparison of demographic characteristics and anthropometric parameters between obese and non-obese groups (n=165) are shown in (Table 1). Majority of children in both obese and non-obese group were aged between 10 to 13 years (69.1%). The mean age of obese and non-obese children was 12.16±1.77 and 12.33±1.84 years respectively. Female were more in frequency in both groups (54.5%) in comparison to male (45.5%). However, the study population were similar in terms of gender.

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hs-CRP Level was raised (≥2 mg/l) in 46.4% of children in obese group than non-obese group (10.9%). It was statistically significant (p<0.001). Mean hs-CRP Level was significantly higher in obese group than in non-obese group (2.81±2.62 vs 0.922±0.852). It was statistically significant (p<0.001) are shown in (Table 2).

However, in grade II obese group hs-CRP level ≥2 mg/l (high risk group) was significantly elevated than hs-CRP level <2 mg/l (low risk group) (58.8% vs 25.4%; p<0.001). Mean WHtR was significantly elevated in who had raised hs-CRP level (0.55±0.11 vs 0.52±0.09; p<0.001). WHtR was significantly higher in high-risk group (hs-CRP level ≥2 mg/l) in comparison to low-risk group (60.8% vs 32.2%; p<0.002) (Table 3).

In the obese group, about 62% had central obesity who had ≥2 mg/l hs-CRP level and in the low-risk group 38% had central obesity who had <2 mg/l hs-CRP level (Table 4).

In terms of hs-CRP level, grade II obese group had significantly elevated mean hs-CRP level as compared to grade I obese group (4.33±2.83 vs 1.71±1.79). About 67% of grade II obese had hs-CRP level ≥2 mg/l in comparison to grade I obese group (31.3%). It was statistically significant (p<0.001) are shown in (Table 5).

To explore the relationship between hs-CRP level and the central obesity in the obese group, scatter diagram was prepared with the use of Pearson’s correlation coefficient (r) test. As shown in (Figure 2), hs-CRP level showed significant positive correlation with the WHtR (r=0.309, p=0.001).

### Table 1: Comparison of demographic and anthropometric parameters between obese and non-obese groups (n=165).

<table>
<thead>
<tr>
<th>Demographic and anthropometric parameters</th>
<th>Obese (n=110)</th>
<th>Non-obese (n=55)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) Mean±SD</td>
<td>12.16±1.77</td>
<td>12.33±1.84</td>
<td>0.582</td>
</tr>
<tr>
<td>10-13</td>
<td>76 (69.1)</td>
<td>38 (69.1)</td>
<td></td>
</tr>
<tr>
<td>14-18</td>
<td>34 (30.9)</td>
<td>17 (30.9)</td>
<td></td>
</tr>
<tr>
<td>Sex (%) Male</td>
<td>50 (45.5)</td>
<td>25 (45.5)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>60 (54.5)</td>
<td>30 (54.5)</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²) Mean±SD</td>
<td>28.97±3.98</td>
<td>18.08±1.99</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Waist-height ratio (%) Mean±SD</td>
<td>0.53±0.09</td>
<td>0.43±0.03</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥0.5</td>
<td>50 (45.5)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>&lt;0.5</td>
<td>60 (54.5)</td>
<td>55 (100)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

### Table 2: Compare the obese and non-obese groups according to category of hs-CRP level (n=165).

<table>
<thead>
<tr>
<th>Hs-CRP level</th>
<th>Obese (n=110)</th>
<th>Non-obese (n=55)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk group (hs-CRP level &lt;2 mg/l) N (%)</td>
<td>59 (53.6)</td>
<td>49 (89.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>High risk group (hs-CRP level ≥2 mg/l) N (%)</td>
<td>51 (46.4)</td>
<td>6 (10.9)</td>
<td></td>
</tr>
<tr>
<td>Mean±SD (mg/l)</td>
<td>2.81±2.62</td>
<td>0.92±0.85</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

### Table 3: Comparison of anthropometric parameters between low-risk group (hs-CRP level <2 mg/l) to high-risk group (hs-CRP level ≥2 mg/l) in obese children.

<table>
<thead>
<tr>
<th>Anthropometric parameters</th>
<th>Low risk group (hs-CRP level &lt;2 mg/l) (n=59)</th>
<th>High risk group (hs-CRP level ≥2 mg/l) (n=51)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td>Mean±SD 28.37±4.01</td>
<td>29.67±3.89</td>
<td>0.087</td>
</tr>
<tr>
<td>Grade I (%)</td>
<td>44 (74.6)</td>
<td>21 (41.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Grade II (%)</td>
<td>15 (25.4)</td>
<td>30 (58.8)</td>
<td></td>
</tr>
<tr>
<td>Waist-height ratio</td>
<td>Mean±SD 0.52±0.09</td>
<td>0.55±0.11</td>
<td>0.048</td>
</tr>
</tbody>
</table>

Continued.
DISCUSSION

The study was aimed to assess the relation between the hs-CRP level and central obesity. Obesity is increasing to an epidemic proportion in Bangladesh. In parallel, there is also an increase in the coronary events in young children. It has recently been found that that atherosclerosis, a cause for coronary vascular events, is an inflammatory condition. Moreover, many inflammatory cytokines are released from the adipose tissues. Among all the inflammatory cytokines, IL-6 plays a major role, most of which is produced from the adipose tissues. This cytokine and other proinflammatory mediators released from the adipose tissues stimulate the release of hs-CRP—a novel inflammatory marker released from the liver. Therefore, the early diagnosis of low-grade inflammation by doing hs-CRP has become a research priority in the context of central obesity and related co-morbidities.

In some recent studies, WHtR has appeared as a good predictor for abdominal obesity and cardiovascular diseases. In the present study, the mean WHtR was significantly higher in obese group (0.53±0.099) than in the non-obese group (0.439±0.031). In the obese group, 45.5% of children had high WHtR (central obesity). This finding reinforces the hypothesis that, it is at the limelight of the obesity epidemic. Although genetics play an necessary role in the obesity epidemic, other factors also play an important role too, including nutritional shift from healthy to junk foods as a result of urbanization, which the neglect of traditional healthy diets, less physical activity and consumption of energy dense foods and sugar-sweetened beverages. The prevalence of central obesity was found to be 16.7% in 1500 Egyptian males and females aged 11-19 years according to WHtR. Rodrigues et al. observed 21.9% had abdominal obesity aged between 6-10 years measured by WHtR. A study conducted in the Bangladesh institute of research and rehabilitation of diabetes, endocrine and metabolic disorders, Dhaka, Bangladesh, found that the prevalence of central obesity was 26%. In a large cohort among 985 girls (14-17 years old) in Iran, 18.2% were centrally obese. In the present study, we found higher WHtR in obese children but it was different from other studies. Several epidemiologic studies in Asian population have showed higher amounts of body fat at lower BMIs and waist circumference than do Western populations. In the obese group, mean WHtR was significantly higher in hs-CRP level ≥2 mg/l than hs-CRP level <2 mg/l (0.55±0.11 vs 0.439±0.031). In the obese group, 62% of children had central obesity according to WHtR in high-risk group (hs-CRP level ≥2 mg/l) than low risk group (38%). Sooye et al found almost similar finding to present study in high-risk group (69.4%). Rodrigues et al. said central obesity in children had increased to a higher degree than do the general adiposity. In another study in children aged between 8 to 18 years old found that WHtR was better than waist circumference (WC) and BMI at predicting adiposity in this paediatric population. WHtR can explained 80% of percent body fat variance, accounting for age and gender, as compared with 72% for WC and 68% for BMI. Central obesity stimulates the development of mediating factors such as insulin resistance, glucose intolerance, endothelial dysfunction and systematic inflammation, which contribute to the development of chronic diseases.

In this current study, mean BMI in obese group (28.97±3.987 kg/m²) was significantly higher than non-

<table>
<thead>
<tr>
<th>Anthropometric parameters</th>
<th>Low risk group (hs-CRP level &lt;2 mg/l) (n=59)</th>
<th>High risk group (hs-CRP level ≥2 mg/l) (n=51)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.50 (%)</td>
<td>40 (67.8)</td>
<td>20 (39.2)</td>
<td>0.002</td>
</tr>
<tr>
<td>≥0.50 (%)</td>
<td>19 (32.2)</td>
<td>31 (60.8)</td>
<td></td>
</tr>
</tbody>
</table>

| Table 4: Comparison of central obesity and non-central obesity according to waist-height ratio between low risk group (hs-CRP level <2 mg/l) and high-risk group (hs-CRP level ≥2 mg/l) in obese children (n=110). |

<table>
<thead>
<tr>
<th>Hs-CRP level</th>
<th>Central obesity (%)</th>
<th>Non central obesity (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk group (hs-CRP level &lt;2 mg/l)</td>
<td>19 (38)</td>
<td>36 (60)</td>
<td>0.021</td>
</tr>
<tr>
<td>High risk group (hs-CRP level ≥2 mg/l)</td>
<td>31 (62)</td>
<td>24 (40)</td>
<td></td>
</tr>
</tbody>
</table>

| Table 5: Comparison of grade I obese and grade II obese according to category of hs-CRP level in obese children (n=110). |

<table>
<thead>
<tr>
<th>hs-CRP level</th>
<th>Grade I obese</th>
<th>Grade II (severe obese)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>hs-CRP level in obese group Mean±SD (mg/l)</td>
<td>1.71±1.79</td>
<td>4.33±2.83</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Low risk group (hs-CRP level &lt;2 mg/l)</td>
<td>N (%)</td>
<td>44 (68.7)</td>
<td>15 (32.6)</td>
</tr>
<tr>
<td>High risk group (hs-CRP level ≥2 mg/l)</td>
<td>N (%)</td>
<td>20 (31.3)</td>
<td>31 (67.4)</td>
</tr>
</tbody>
</table>
obese group (18.08±1.993 kg/m²). A population based Korean study showed almost similar findings. As in case of mean BMI, Shilpa and Pires et al found similar finding of mean BMI among the obese group. Among the obese group, 58% were grade I obese and 42% were grade II obese (severe obese). In a research conducted in Spanish population found that 41.6% had severe obesity among the obese children. In the present study 60% of the obese children had grade II obesity (Severe obese) in high-risk group in comparison to lowrisk group. It was statistically significant (p<0.001). Paepageti et al showed almost similar finding (51.6 vs 48.8%) to present study but it was observed in adult population.

There is no study regarding hs-CRP level in obese children in our country. Dayal et al. found hs-CRP level raised in 55% of children in the obese group than in 10% in non-obese group. This finding almost similar to the present study (46.4 vs 10.9%). Mirhoseini and Rehnuma et al observed almost similar finding to present study. In another study conducted in adults, found that 31.5% had high hs-CRP level. Bennett et al observed a different finding from the present study (15% had high hs-CRP level in the obese children).

In our study, mean hs-CRP level was significantly higher in obese group (2.81±2.62 mg/l) in comparison to non-obese group (0.92±0.852 mg/l). Dayal and Shilpa et al found significantly higher mean hs-CRP level in obese children to non-obese group.

Mean hs-CRP level was significantly higher in grade II obese (severe obese) in comparison to grade I obese group (4.33±2.83 vs 1.71±1.79). About 67% grade II obese (severe obese) had raised hs-CRP level ≥2 mg/l in comparison to grade I obese group (31.3%). Elevated hs-CRP levels may be associated with the development of cardiovascular diseases and diabetes by means of a variety of mechanisms such as altered sensitivity to insulin, increased secretion of adhesion molecules by endothelium, increase production of fibrinogen and platelet coagulation factor by liver.

In the present study, the WHR showed the positive correlation with the hs-CRP level.

In this study, mean age of obese and non-obese children were (12.16±1.77 vs 12.33±1.84). In both the obese and non-obese groups, 54.5% were female and 45.5% were male. In a study done in Indonesia among the obese children and on that study, mean age of children were similar to present study and no significant sex difference was observed. Pires et al showed similar results to our study.

The present study has several limitations. Most important limitations are relatively small size and cross-sectional nature of the study.

We suggest routine screening of hs-CRP level in obese children especially who had grade II obesity and central obesity.

CONCLUSION

A high proportion of central obesity was observed in obese children who had raised hs-CRP level, suggesting that it might be useful to assess future metabolic and cardiovascular complication.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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