Serum Magnesium and High Sensitive C-Reactive Proteins in Hypertensive, Obese Female School Learners

AM Sekokotla¹, BN Nkeh-Chungag¹, JE Iputo¹, CR Sewani-Rusike¹, IM Malema², OV Adeniyi³, DT Goon⁴

ABSTRACT

Objective: To examine the relationship between serum magnesium and high sensitive C-reactive proteins (hsCRP) and overweight/obesity and its association with hypertension in lean versus overweight/obese, female, adolescent school learners living in Mthatha, Eastern Cape, South Africa.

Methods: A case-control study was conducted involving age-matched, non-pregnant and non-lactating lean and overweight/obese females, aged 13–17 years. Relevant data on demography, anthropometry (height, weight, waist and hip circumferences), blood pressure and venous blood samples were collected.

Results: A significant inverse correlation was observed between serum magnesium and waist circumference (r = -0.3153, 95% CI = -3.843 to -0.8681, p = 0.0022). Serum hsCRP levels were significantly higher in overweight/obese participants. Participants with waist circumference (WC) > 80 cm had significantly higher mean systolic blood pressure and mean diastole blood pressure (MDBP). Hip circumference (HC) >94 cm was associated with higher mean systole blood pressure (MSBP) and MDBP (120 ± 2 vs 113 ± 2, p = 0.009 and 73±2 vs 68±1, p=0.003). Both WC and HC correlated positively with both MSBP (r=0.2691, 95% CI = 0.042 – 0.457, p = 0.018; r = 0.2758, 95% CI = 0.03184 – 0.3001, p = 0.0159) and MDBP (r=0.2686, 95%CI = 0.0286 – 0.320, p = 0.19; r = 0.2836, 95% CI = 0.05382 – 0.4455, p = 0.013), respectively.

Conclusion: Findings of low grade inflammation and early-onset hypertension in overweight/obese adolescent females in our study were consistent with evidences supporting the beneficial effect of maintaining lean body habitus. There is urgent need to prevent overweight/obesity among adolescents.

Keywords: Adolescent, anthropometry, cardiovascular diseases, high sensitivity C-reactive protein, magnesium, obesity, South Africa

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INTRODUCTION

The increasing prevalence of obesity has become a public health issue (1–2). A recent analysis of trends in global, regional and national prevalence of overweight and obesity in children during 1980-2013, using data from surveys, reports and scientific literature (3), indicated that the proportion of children with a body mass index (BMI) of 25 kg/m² or greater have increased substantially, with no national success stories reported in the past 33 years. Worldwide, the prevalence of overweight and obesity among children has risen to 47.1% between 1980 and 2013. Genderwise, 23.8% of boys and 22.6% of girls were overweight or obese in 2013, compared with 16.9% of boys and 16.2% of girls in 1980 in developed countries. The prevalence of overweight and obesity has also increased in children and adolescents in developing countries from 8.1% to 12.9% in 2013 for boys and from 8.4% to 13.4% in girls (3).

Obesity is associated with increased risk factors for hypertension, hypercholesterolemia, insulin resistance and diabetes mellitus (4). Until recently, type 2 diabetes was considered an adult-onset, chronic disease. However, reports show an alarming increase in the prevalence of type 2 diabetes in obese children and adolescents (5, 6). Both childhood overweight and obesity are predictors of adult obesity and early-onset hypertension (2, 7, 8).

Evidence shows that C-reactive proteins (CRP) play a direct role in chronic, low-grade, vascular inflammation and is an independent marker of cardiovascular diseases (CVDs), such as hypertension (9). Elevated CRP levels have been shown to inhibit nitric oxide synthetase resulting in endothelial dysfunction (10), thus showing a relationship between CRP levels and CVDs. Due to the fact that overweight/obesity is associated with subclinical inflammation as reflected by increased CRP levels in the blood as well as increased oxidative stress, it increases the risk of atherosclerosis.
A recent World Health Organization (WHO) report underscored the fact that in countries undergoing an economic transition, over-nutrition and under-nutrition always co-exist (11). The ready availability of energy-dense, low-nutrient foods in rapidly growing urban areas provide excess calories, though being deficient in micronutrients. This causes children to store excess calories in the form of fats, thus becoming either overweight or obese, though suffering from micronutrient deficiency. Under-nutrition in obese children includes micronutrient deficiencies in substances such as magnesium and zinc, and has been associated with stunted growth in children (12).

Many studies have shown that magnesium deficiencies are linked to raised blood pressure, while magnesium supplementation prevents hypertension and suppresses atherosclerosis (13, 14). King et al (2006) showed that magnesium supplementation prevented elevation of CRP levels (15). Elevated levels of CRP were also found to be consistently associated with hypomagnesaemia in children (16). Hypomagnesaemia would therefore seem to be associated with chronic inflammation as suggested by high CRP levels and consequently contribute to increasing the risk for CVDs.

Several studies have reported on the various risk factors of CVDs (hypertension included) in children and adolescents in urban areas (17-19). However, there is a dearth of information on hypertension and other CVDs among adolescents in the peri-urban South African towns like Mthatha, and the relationship of hsCRP and serum magnesium with cardiovascular risk factors in overweight/obese adolescents has remained understudied in this region. This study examined the relationship of anthropometric measurements, serum magnesium and hsCRP as predictors of CVD (using hypertension as surrogate) among female adolescent school learners in Mthatha, Eastern Cape, South Africa.
SUBJECTS AND METHODS

An observational, case control-study was conducted at Umtata High School and Vela High School in Mthatha, South Africa from May to June 2012. Ethical approval was obtained from the Walter Sisulu University Ethics Committee (Ref No: 014/009). Also, the school authorities granted authorization to carry out the study.

The study population included 50 overweight/obese female, adolescent learners from Grade 9 – 12 as the “case group”. Fifty age-matched, lean, female adolescent learners from the same class were selected as the “control group”. Participants were classified as lean if their BMI was \( \leq 75^{\text{th}} \) percentile for age and overweight/obesity (SOMETHING SEEMS MISSING) if BMI \( \geq 85^{\text{th}} \) percentile for age (20); modified from Cornier et al, 2011. The purpose of the study was explained to all of the volunteers, and they were provided with participant information sheets, assent forms for their voluntary participation and consent forms for their parents/guardians to provide written consent. Participants were excluded if pregnant, breastfeeding, ill or handicapped in any way that would make anthropometric measurement difficult.

The height of the participants was taken without shoes, using a stadiometer. The mobile part of the stadiometer was adjusted to touch the participants’ heads and the height was measured in centimeters (cm).

A validated Omron Body Composition Monitor (BF511), designed to measure body composition in persons aged 8 – 80 years old, was used to measure BMI. The equipment was calibrated to each participant’s specific information such as height, age and gender. The equipment displayed the BMI, percentage abdominal fat, percentage lean muscle mass and resting metabolic rate of the participants.
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Waist circumference (WC) was measured around the smallest circumference of the waist for all participants, with the tape horizontal across the back and front. Hip circumference (HC) was measured around the maximum circumference of the buttocks, ensuring that the tape was horizontal across the back and front. Measurements were recorded to the nearest centimetre.

Participants were allowed to rest in the seated position for 5 minutes after which blood pressure was measured using a Microlife BP A100 Plus model. This instrument is equipped with a single and repeated measure function, which measures blood pressure three times and displays a calculated average value. Appropriate cuff sizes were used, depending on the size of participant’s arm. The cuff was wrapped around the upper arm and maintained in place with Velcro on the cuff. Blood pressure and heart rates were determined automatically.

Fasting venous blood was collected from the brachial vein into gel separator tubes and left at room temperature for 2 hours before centrifuging for 5 minutes at 3000 rpm to separate serum from cellular elements. Serum was collected into microeppendorff tubes and stored at 80 °C until processed. The fully automated Cobas® C501/502 (Roche) system was used for determining serum magnesium titers. High-sensitive C-reactive protein was quantified using the high-sensitive C-reactive protein ELISA kit from DRG ® International Inc, USA EIA – 3954.

Data were analysed by SPSS version 21 (SPSS Inc., Chicago, IL, USA). Data were expressed as the mean ± standard deviation. Data were checked for outliers, skewness and normality. Chi square test was conducted to evaluate the difference in the correlations among continuous variables. Fisher’s exact test was used to determine the difference between groups. A p-value < 0.05 was considered to be statistically significant and results were calculated within 95% confidence intervals. P-value < 0.05 was considered to be statistically significant.
RESULTS

Complete data were obtained for 38 ‘case’ participants; hence 38 matched controls were utilized. Table 1 shows the anthropometric distribution and blood pressure of the participants. In the absence of reference WC and HC cutoff points for African adolescents, we utilized WHO cut-off points of 80 cm for WC and 94 cm for HC (21).

Participants whose WC was > 80 cm or HC > 94 cm were significantly taller (160.8±1.1 vs 157.9 ± 0.8 cm, p = 0.046; 160.7 ± 0.8 cm vs 156.6 ± 1.1 cm, p = 0.003) than participants with a WC ≤ 80 cm. Participants who had higher WCs also had a significantly higher waist to height ratio (0.56 ± 0.01 vs 0.44 ± 0.01, p = 6.7E-15) and WHR (0.82±0.01 vs 0.76 ± 0.01, p = 4.2E-0.05). Similarly, higher HC was associated with higher WC-to-height ratio (0.54±0.01 vs 0.44±0.01, p = 6.7E-15) though hip to WHR was not different between the two groups.

Higher WC was associated with significantly higher MSBP (122 ± 2 vs 114±1 mm Hg, p = 0.009) and MDBP (73±1 vs 69 mm Hg±1, p = 0.03). Conversely, HC >94 cm was associated with both higher MSBP and MDBP (120±2 vs 113±2, p=0.009 and 73±2 vs 68±1, p = 0.003). Both WC and HC correlated positively with both MSBP (r=0.2691, 95% CI = 0.042 – 0.457, p = 0.018; 0.2758, 95% CI = 0.03184 – 0.3001, p = 0.0159) and MDBP (r=0.2686, 95% CI = 0.0286 – 0.320, p = 0.019; r=0.2836, 95% CI = 0.05382 – 0.4455, p = 0.013), respectively.

Mean systolic blood pressure was significantly (p < 0.05) higher in O/O females compared to lean females, though MDBP was not significantly different (Table 1). The overall prevalence of hypertension (MBDP > 95th percentile) and pre-hypertension (MSBP ≥90th <95th percentile or BP > 120/80 mm Hg) was 31.6% (19.7% and 11.8% in O/O and lean participants, respectively). 7 lean and 8 O/O participants had hypertension while 9 O/O participants were pre-hypertensive.
Serum magnesium levels were higher in lean participants compared to the O/O females (Table 2). However, the difference was not significant. A significant inverse correlation was observed between serum magnesium and WC ($r=-0.3153$, 95% CI = -3.843 to –0.8681, $p = 0.0022$). Although lean participants whose serum magnesium titers > 0.80 mg/l also had significantly lower WC (0.67 ± 0.61 mmol/l vs 0.72 ± 0.78 mmol/l; $p=0.031$) and weight (50.2 ± 0.64 mmol/l vs 54.1±0.59 mmol/l; $p= 0.39$), separating O/O participants by serum magnesium levels did not affect distribution of WC nor blood pressure.

Serum hs-CRP levels were significantly higher in O/O participants (1.55±0.17 mg/l vs 0.99 ± 0.13 mg/l; $p < 0.05$). The majority of the participants had hs-CRP levels > 3 mg/l (Table 2). When both cases and controls were grouped together, higher hs-CRP levels were significantly (p<0.05) associated with higher BMI (28.7 ± 2.2 mg/l vs 24.7 ± 0.6 mg/l, $p = 0.04$) and WC (85±5 vs 76±1, $p = 0.05$), respectively. There was a strong correlation between MSBP and BMI, while a non-significant correlation existed between magnesium, hs-CRP and MSBP (Table 3).

**DISCUSSION**

The present study examined the relationship between various anthropometric measurements, serum magnesium and serum hs-CRP levels with blood pressure measurements as a surrogate for increased CVD risks in obese versus lean female, adolescent school learners in Mthatha, Eastern Cape, South Africa. The findings of this study indicated that overweight and obesity were associated with higher MSBP, but not MDBP. Yipu *et al* (2012) also reported higher MSBP, but not MDBP in obese girls, though obese boys had higher MSBP and MDBP (22). The importance of BMI in the determination of blood pressure was further confirmed since this study showed
that overweight/obese participants had a higher proportion of pre-hypertensive and hypertensive adolescents compared to the lean group. Previous studies have reported the association of higher BMI with high blood pressures (23, 24) which is the most common risk factor.

BMI is generally used to diagnose obesity, overweight and underweight. However, BMI does not give insight into body fat distribution, even when it does indicate that an individual is obese. The waist circumference and the waist-to-hip ratio are better tools for determining body fat distribution and risk for CVDs (25, 26). The current study found higher MSBP and MDBP among adolescents with higher WC and HC. This result is at variance with previous reports (27, 28) that confirmed the cardio-protective effect of peripheral adiposity. The paradox of the relationship of hip circumference and the cardiovascular risks in this study require further investigations with a larger sample size.

Serum magnesium level is maintained within a narrow range for proper homeostatic function by the kidneys and the digestive tract. Serum magnesium levels were not significantly different between the groups, though lean participants tended to have higher levels compared to overweight/obese participants. The relationship between serum magnesium levels and CVD needs clarification. The present study showed that participants with relatively higher serum magnesium titers also had significantly lower WC. Importantly, since WC is positively associated with blood pressure, low serum magnesium may be a risk factor for increased WC, which in turn increases the risk for CVDs. Low magnesium levels have been associated with high levels of low-grade inflammation and high hs-CRP (15,29), both of which are risk factors for CVDs.

The results in this study failed to show higher levels of magnesium in lean, compared to obese adolescents. Jose et al study has shown an absence of an independent association between
low serum magnesium levels and CVD risk (30). These authors, however, indicated that a negative correlation exists between serum magnesium levels and WC. The association of magnesium with hypertension is plausible, considering the fact that magnesium is a co-factor for many enzymes involved with carbohydrate metabolism (31). Functional failure of these enzymes promotes fat deposition and increased WC which may result in obesity.

In the present study, there was strong correlation of elevated hs-CRP and waist circumference with higher BMI. This is similar to previous reports indicating strong association between obesity and elevated levels of CRP while others have demonstrated the effects of exercise and weight reduction on serum CRP levels (32-34). Importantly, besides being a marker of inflammation, CRP is an independent predictor of CVDs.

The sample size was small because some parents did not give consent for their children/wards to be recruited in the study as it involved the drawing of blood. Also, blood had to be collected after an overnight fast; some children whose parents had given written consent did not fast and were excluded. Again, given the small sample size, the results cannot be generalized to all female adolescents in the region or to the entire South Africa. Notwithstanding the limitations of the study, our findings provide useful information regarding the relationship between various anthropometric measurements, serum magnesium, and hs-CRP levels with blood pressure measurements as a surrogate for increased CVD risk in overweight/obese versus lean, female adolescent school learners in an understudied region. A similar study in male participants will be necessary to confirm the existence of similar trends and to determine if current findings are gender-related.
CONCLUSION

Obese/overweight female adolescents tended to have higher systolic and diastolic blood pressures, and a higher prevalence of pre-hypertension and hypertension - thus suggesting that obese adolescent school girls in this setting have substantially increased risk of CVDs compared to their lean counterparts. The high prevalence of pre-hypertension and hypertension in these female adolescents is a predictor of the great burden of chronic lifestyle diseases on the health care system if early intervention strategies are not instituted.
REFERENCES


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34. Yang SP, Gong CX, Cao BY, Yan C. Relationship between serum high-sensitive c-reactive protein and obesity and impaired glucose metabolism in children and adolescents. Zhonghua Er Za Zhi 2006; 44: 933–6.
Table 1: Characteristics of participants

<table>
<thead>
<tr>
<th>Variables</th>
<th>Whole Group (n=76)</th>
<th>Lean Participants (n=38) (BMI ≤ 75th percentile)</th>
<th>O/O Participants (n=38) (BMI &gt; 85th percentile)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>14.9±0.1</td>
<td>14.9±0.2</td>
<td>15.0±0.2</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>159.1±0.6</td>
<td>158.7±0.7</td>
<td>159.5±0.7</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>63.9±1.5</td>
<td>52.1±0.6</td>
<td>75.8±1.2**</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.2±0.6</td>
<td>20.7±0.2</td>
<td>29.8±0.5**</td>
</tr>
<tr>
<td>BMI percentile</td>
<td>70.5±2.1</td>
<td>58.5±1.8</td>
<td>91.4±0.28</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>77.7±1.2</td>
<td>69.4±0.7</td>
<td>86.0±1.1**</td>
</tr>
<tr>
<td>≤80 cm</td>
<td>46 }</td>
<td>36 }</td>
<td>10 }</td>
</tr>
<tr>
<td>&gt;80 &lt;88 cm</td>
<td>16 } 39.5%</td>
<td>1 } 5.3%</td>
<td>15 } 73.3%</td>
</tr>
<tr>
<td>≥88 cm</td>
<td>14 }</td>
<td>1 }</td>
<td>13 }</td>
</tr>
<tr>
<td>Waist-to-height-ratio</td>
<td>0.49±0.01</td>
<td>0.44±0.01</td>
<td>0.54±0.01**</td>
</tr>
<tr>
<td>Hip circumference (cm)</td>
<td>98.9±1.3</td>
<td>89.2±0.6</td>
<td>108±1.1**</td>
</tr>
<tr>
<td>Waist-hip-ratio</td>
<td>0.78±0.01</td>
<td>0.77±0.01</td>
<td>0.79±0.01</td>
</tr>
<tr>
<td>≤0.8</td>
<td>48 (63.2%)</td>
<td>27 (71.1%)</td>
<td>21 (55.3%)</td>
</tr>
<tr>
<td>&gt;0.8</td>
<td>28 (36.8%)</td>
<td>11 (28.9%)</td>
<td>17 (44.7%)</td>
</tr>
<tr>
<td>Mean SBP (mm Hg)</td>
<td>117±1.0</td>
<td>114±1.0</td>
<td>120±1.0*</td>
</tr>
<tr>
<td>Mean DBP (mmHg)</td>
<td>71±1.0</td>
<td>69±1.0</td>
<td>72±1.0</td>
</tr>
</tbody>
</table>

BMI = body mass index; O/O = overweight/obese; SBP = systolic blood pressure; DBP = diastolic blood pressure
*p < 0.05; **p < 0.01

Table 2: Clinical characteristics of lean and overweight/obese participants

<table>
<thead>
<tr>
<th>Variables</th>
<th>Whole Group (n=76)</th>
<th>Lean Participants (n=38)</th>
<th>Overweight/obese Participants (n=38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Magnesium (mmol/l)</td>
<td>0.76±0.04</td>
<td>0.81±0.06</td>
<td>0.73±0.02</td>
</tr>
<tr>
<td>Serum hs-CRP (mg/l)</td>
<td>1.22±0.15</td>
<td>0.90±0.13</td>
<td>1.55±0.17*</td>
</tr>
<tr>
<td>≤1</td>
<td>47</td>
<td>28</td>
<td>19</td>
</tr>
<tr>
<td>1-3</td>
<td>19</td>
<td>6</td>
<td>13</td>
</tr>
<tr>
<td>&gt;3</td>
<td>10</td>
<td>4</td>
<td>6</td>
</tr>
</tbody>
</table>

Hs-CRP = high sensitive C-reactive protein. Results are expressed as mean ± SD. *p< 0.05.
Table 3: Pearson’s correlations between measured risk factors for CVDs (hypertension)

<table>
<thead>
<tr>
<th>Relationship</th>
<th>Correlation coefficient (r)</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hs-CRP/MSBP</td>
<td>0.1715</td>
<td>-0.05619-0.3822</td>
<td>0.1385</td>
</tr>
<tr>
<td>BMI/MSBP</td>
<td>0.4131</td>
<td>0.2068-0.5842</td>
<td>0.0001**</td>
</tr>
<tr>
<td>WC/MSBP</td>
<td>0.05702</td>
<td>-0.2676-0.3700</td>
<td>0.7338</td>
</tr>
<tr>
<td>Magnesium/MSBP</td>
<td>-0.1457</td>
<td>-0.3622-0.8574</td>
<td>0.2156</td>
</tr>
</tbody>
</table>

Hs-CRP= high sensitive C-reactive protein, BMI=body mass index, MSBP= mean systolic blood pressure, WC= waist circumference