

Serum Magnesium and High-sensitive C-reactive Proteins in Hypertensive, Obese Female School Learners

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

ABSTRACT

Objective: To examine the relationship of serum magnesium and high-sensitive C-reactive proteins (hsCRPs) with overweight/obesity, and its association with hypertension in lean versus overweight/obese (O/O), 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 O/O females aged 13–17 years. Relevant data on demography, anthropometry (height, weight, and 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 (WC) ($r = -0.3153$; 95% CI = $-3.843, -0.8681$; $p = 0.0022$). Serum hsCRP levels were significantly higher in O/O participants. Participants with a WC > 80 cm had significantly higher mean systolic blood pressure and mean diastolic blood pressure (MDBP). A hip circumference (HC) > 94 cm was associated with higher mean systolic 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 were found to be positively correlated with both MSBP ($r = 0.2691$; 95% CI = $0.042, 0.457$; $p = 0.018$ and $r = 0.2758$; 95% CI = $0.03184, 0.3001$; $p = 0.0159$) and MDBP ($r = 0.2686$; 95% CI = $0.0286, 0.320$; $p = 0.19$ and $r = 0.2836$; 95% CI = $0.05382, 0.4455$; $p = 0.013$), respectively.

Conclusion: In our study, low-grade inflammation and early-onset hypertension in O/O adolescent females were consistent with evidence that support the beneficial effect of maintaining lean body habitus. There is an urgent need to prevent overweight/obesity among adolescents.

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

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/m^2 or greater had increased substantially, with no national success stories reported over

the past 33 years. Worldwide, the prevalence of overweight and obesity among children has risen to 47.1% between 1980 and 2013. In developed countries, 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. 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% for girls (3).

From: ¹Department of Physiology, Faculty of Health Sciences, Walter Sisulu University, Mthatha, South Africa, ²Department of Community Medicine, Faculty of Health Sciences, Walter Sisulu University, Mthatha, South Africa, ³Department of Family Medicine, Faculty of Health Sciences, Walter Sisulu University, East London Hospital Complex, East London, South Africa and ⁴School of Health Sciences, University of Venda, Thohoyandou, South Africa.

Correspondence: Professor BN Nkeh-Chungag, Department of Physiology, Faculty of Health Sciences, Walter Sisulu University, Mthatha, South Africa. Email: bnkehchungag@wsu.ac.za

Obesity is associated with increased risk 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 (CRPs) 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 which results 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 readily available energy-dense, low-nutrient foods in rapidly growing urban areas provide excess calories, though they are deficient in micronutrients. This causes children to store excess calories in the form of fats, thus becoming either overweight or obese but 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* 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). Therefore, hypomagnesaemia would seem to be associated with chronic inflammation as suggested by high CRP levels and would consequently contribute to increasing the risk for CVDs.

Several studies have reported on 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. Moreover, the relationship of high-sensitive C-reactive protein (hsCRP) and serum magnesium with

cardiovascular risk factors in overweight/obese (O/O) 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 O/O female adolescent learners from Grades 9–12 as the ‘case group’. A total of 50 age-matched, lean, female adolescent learners from the same class were selected as the ‘control group’. As modified from Cornier *et al* (2011), participants were classified as lean if their BMI was $\leq 75^{\text{th}}$ percentile and O/O if their BMI was $\geq 85^{\text{th}}$ percentile (20). The purpose of the study was explained to all of the volunteers, and they were provided with participant information sheets and assent forms for their voluntary participation and consent forms for their parents/guardians to provide written informed consent. Participants were excluded if pregnant, breastfeeding, ill or differently abled in any way that would make anthropometric measurement difficult.

Using a stadiometer, the heights of the participants (in centimeters) were taken without shoes. The mobile part of the stadiometer was adjusted to touch the participants’ heads.

A validated Omron Body Composition Monitor (BF511, Germany) designed to measure body composition in persons aged 8–80 years 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 the resting metabolic rates of the participants.

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 five minutes after which blood pressure was measured using a Microlife BP A100 Plus (Taiwan) monitor. 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 the participants' arms. 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 two hours before centrifuging for five 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, Canada) system was used for determining serum magnesium titers. High-sensitive C-reactive protein was quantified using the hsCRP ELISA kit EIA-3954 (DRG[®] International Inc., Springfield, NJ, USA).

Data were analysed by SPSS version 21 (SPSS Inc., Chicago, IL, USA) and expressed as the mean \pm standard deviation. They were checked for outliers, skewness and normality. The 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 of < 0.05 was considered to be statistically significant, and results were calculated within 95% confidence intervals.

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 cut-off points for African adolescents, we utilized WHO cut-off points of 80 cm for WC and 94 cm for HC (21).

Participants with WC > 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 those with WCs of ≤ 80 cm. Participants who had larger WCs also had a significantly higher waist-to-height ratio (0.56 ± 0.01 vs 0.44 ± 0.01 , $p = 6.7 \times 10^{-15}$) and waist-to-hip ratio (WHR) (0.82 ± 0.01 vs 0.76 ± 0.01 , $p < 0.001$). Similarly, a higher HC was associated with a higher WC-to-height ratio (0.54 ± 0.01 vs 0.44 ± 0.01 , $p < 0.001$), though the WHR was not different between the two groups.

Table 1: Characteristics of participants

Variables	Whole group (n = 76)	Lean participants (n = 38) (BMI $\leq 75^{\text{th}}$ percentile)	O/O participants (n = 38) (BMI $> 85^{\text{th}}$ percentile)
Age (years)	14.9 \pm 0.1	14.9 \pm 0.2	15.0 \pm 0.2
Height (cm)	159.1 \pm 0.6	158.7 \pm 0.7	159.5 \pm 0.7
Weight (kg)	63.9 \pm 1.5	52.1 \pm 0.6	75.8 \pm 1.2**
BMI (kg/m ²)	25.2 \pm 0.6	20.7 \pm 0.2	29.8 \pm 0.5**
BMI percentile	70.5 \pm 2.1	58.5 \pm 1.8	91.4 \pm 0.28
WC (cm)	77.7 \pm 1.2	69.4 \pm 0.7	86.0 \pm 1.1**
≤ 80 cm	46 }	36 }	10 }
> 80 – < 88 cm	16 } 39.5%	1 } 5.3%	15 } 73.3%
≥ 88 cm	14 }	1 }	13 }
Waist-to-height ratio	0.49 \pm 0.01	0.44 \pm 0.01	0.54 \pm 0.01**
Hip circumference (cm)	98.9 \pm 1.3	89.2 \pm 0.6	108 \pm 1.1**
Waist-to-hip ratio	0.78 \pm 0.01	0.77 \pm 0.01	0.79 \pm 0.01
≤ 0.8	48 (63.2%)	27 (71.1%)	21 (55.3%)
> 0.8	28 (36.8%)	11 (28.9%)	17 (44.7%)
Mean SBP (mmHg)	117 \pm 1.0	114 \pm 1.0	120 \pm 1.0*
Mean DBP (mmHg)	71 \pm 1.0	69 \pm 1.0	72 \pm 1.0

BMI = body mass index; O/O = overweight/obese; WC; waist circumference; SBP = systolic blood pressure; DBP = diastolic blood pressure.

* $p < 0.05$; ** $p < 0.01$.

A higher WC was associated with a significantly higher mean systolic blood pressure (MSBP) (122 ± 2 vs 114 ± 1 mmHg, $p = 0.009$) and mean diastolic blood pressure (MDBP) (73 ± 1 vs 69 ± 1 mmHg, $p = 0.03$). Conversely, a > 94 cm HC 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 were correlated positively with both MSBP ($r = 0.2691$; 95% CI = 0.042, 0.457; $p = 0.018$ and $r = 0.2758$; 95% CI = 0.03184, 0.3001; $p = 0.0159$) and MDBP ($r = 0.2686$; 95% CI = 0.0286, 0.320; $p = 0.19$ and $r = 0.2836$; 95% CI = 0.05382, 0.4455; $p = 0.013$), respectively.

Mean systolic blood pressure was significantly higher ($p < 0.05$) in O/O females than in lean females, though MDBP was not significantly different (Table 1). The overall prevalence of hypertension (MDBP $> 95^{\text{th}}$ percentile) and pre-hypertension (MSBP $\geq 90^{\text{th}}$ $\leq 95^{\text{th}}$ percentile or BP $> 120/80$ mmHg) was 31.6% (19.7% and 11.8% in O/O and lean participants, respectively). A total of seven lean and eight O/O participants had hypertension, whereas nine O/O participants had pre-hypertension.

Serum magnesium levels were higher in lean participants than those in 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 = $-3.843, -0.8681$; $p = 0.0022$). Although lean participants whose serum magnesium titers were > 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 neither affected the distribution of WC nor blood pressure.

Serum hsCRP 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 hsCRP levels of > 3 mg/L (Table 2). When both cases and controls were grouped together, higher hsCRP 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, hsCRP and MSBP (Table 3).

DISCUSSION

The present study examined the relationship of various anthropometric measurements, serum magnesium and serum hsCRP 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* 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 O/O participants had a higher proportion of pre-hypertensive and hypertensive adolescents than those in the lean group. Previous studies (23, 24) have reported the association of higher BMI with high blood pressures which is the most common risk factors for CVDs.

The body mass index is generally used to diagnose obesity, overweight and underweight. However, BMI does not give an insight into body fat distribution, even when it does indicate that an individual is obese. The WC and the WHR are better ways of determining body fat distribution and risk for CVDs (25, 26). The current study found higher MSBP and MDBP among adolescents with higher WCs and HCs. 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 requires further investigations with a larger sample size.

The 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 than O/O 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 hsCRP (15, 29), both of which are risk factors for CVDs.

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

Variables	Whole group (n = 76)	Lean participants (n = 38)	Overweight/obese participants (n = 38)
Serum magnesium (mmol/L)	0.76 ± 0.04	0.81 ± 0.06	0.73 ± 0.02
Serum hsCRP (mg/L)	1.22 ± 0.15	0.90 ± 0.13	1.55 ± 0.17*
< 1	47	28	19
1–3	19	6	13
> 3	10	4	6

HsCRP = high-sensitive C-reactive protein. Results are expressed as mean ± SD.

* $p < 0.05$.

Table 3: Pearson’s correlations between measured risk factors for cardiovascular diseases (hypertension)

Relationship	Correlation coefficient (r)	95% CI	p value
HsCRP/MSBP	0.1715	-0.05619, 0.3822	0.1385
BMI/MSBP	0.4131	0.2068, 0.5842	0.0001**
WC/MSBP	0.05702	-0.2676, 0.3700	0.7338
Magnesium/MSBP	-0.1457	-0.3622, 0.8574	0.2156

HsCRP = high-sensitive C-reactive protein; BMI = body mass index; MSBP = mean systolic blood pressure; WC = waist circumference.

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

In the present study, there was a strong correlation of elevated hsCRP and WC with higher BMI. This is similar to previous reports that indicated a strong association between obesity and elevated levels of CRP, whereas 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 extraction 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 of various anthropometric measurements, serum magnesium and hsCRP levels with blood pressure measurements as a surrogate for increased CVD risk in O/O *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 a 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 greater burden of chronic lifestyle diseases on the healthcare system if early intervention strategies are not instituted.

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