Assessment of Carotid Intima- Media Thickness and LV Structure and Function in Obese Adolescents

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Abstract

**Background:** obesity is becoming a global epidemic and there is increased prevalence of obesity among children and adolescents, which associated with increased cardiovascular risk comorbidities during childhood as hypertension, dyslipidemia, metabolic syndrome and left ventricular hypertrophy (LVH).

**Aim of the study:** assessment of the impact of obesity on carotid intima/media thickness and LV mass and function in obese adolescents.

**Methods:** the study included 52 obese adolescents (mean age 14.16± 2.64 year) and 52 control group (mean age 12± 2.3 years), who were attended the outpatient clinic of Suez Canal university hospital. The study population was submitted to medical history, clinical examination, laboratory investigations (Fasting blood sugar and lipid profile), echocardiographic examination of LV mass, dimensions and functions, and assessment of carotid intima- media thickness by using carotid duplex.

**Results:** Obese adolescents had a significant increase in total cholesterol, triglyceride, LDL-C, and low HDL-C compared to the control group; also there is significant increase in blood pressure, carotid intima/media thickness, LV mass and LV mass index. There was a significant correlation between BMI and Dyslipidemia, blood pressure, carotid intima/ media thickness, LV mass and posterior wall thickness. Carotid intima-media thickness had significant correlation with increased LDL-C and low HDL-C, blood pressure, LV mass and posterior wall thickness.

**Conclusion:** Obesity in childhood and adolescents is associated with increased risk of atherosclerosis and cardiovascular risk factors such as increased carotid intima/media thickness (as a marker of preclinical atherosclerosis), hypertension, dyslipidemia, left ventricular hypertrophy and metabolic syndrome.

**Keywords:** obesity, carotid intima/media thickness, LV mass, body mass index.
Introduction

Obesity is becoming a global epidemic; a dramatic increase on overweight among children and adolescents during the past two decades has been documented. Using the international definitions, at least 10% of the school age children are overweight or obese worldwide (1).

Martinez et al 2006 reported that the overall prevalence of overweight and obesity was 12.1 and 6.2%, respectively, among the Egyptian adolescents. (2).

Hafez et al 2000 reported the higher prevalence of obesity was among boys (21% in private school children versus 12.8% in public health schools) than girls (18.8% in private school children versus 10.8% in public health schools) (3).

Recent study was done in Ismailia city by the 1st year students of the faculty of medicine in Suez Canal University up on 2535 student. It was reported that the prevalence of obesity among school children between 7-14 years was 13.8% (4)

Increasing prevalence of obesity among children and adolescents has serious implications for their health because it is associated with comorbidities during childhood, as well as increased risk of chronic diseases as hypertension, dyslipidemia, metabolic syndrome, insulin resistance, diabetes, polycystic ovary syndrome, sleep apnea, endocrine abnormalities, orthopedic disorders and psychological problems), and decreased life expectancy (5).

Childhood obesity predispose to increased left ventricular mass (6), endothelial dysfunction, carotid intima-media thickening as a marker of early preclinical atherosclerosis, and the development of early aortic and coronary arterial fatty streaks and fibrous plaques (7).

Aim of the work

The purpose of this study is to assess of the impact of obesity on carotid intima-media thickness and LV mass and function in obese adolescents.

Materials and methods
This study was a case-control study to assess the impact of obesity on carotid intima/media thickness and LV mass and function in obese adolescents

**Study population**

The study population included 52 obese adolescents aged from 10-19 years, males and females with BMI > 95th percentile for age and sex (8) and a control group of 52 healthy adolescents age- and sex-matched were recruited from the relatives of the patients who attended the outpatients clinics of the Suez canal university hospital.

**Exclusion criteria**

1- Patients with type I diabetes mellitus

2- Patients with cardiac diseases (congenital heart disease, rheumatic heart disease ...etc),
   or secondary hypertension

3- Patients with syndromes including obesity (Turner syndrome, Stein-Leventhal syndrome and Prader Willi syndrome).

**Methods**

All the study population was subjected to through history taking (regarding the demographic data and the especial habits of medial importance as:

a- regular exercise: playing sports three times weekly

b- over watching TV: more than 4h hours/ day

c- computer user; more than 4 hours/ day

d- carbohydrate eating: such as rice, macaroni over eating), and meticulous clinical examination with emphasis on:

**Anthropometric measurements**

Biometric and anthropometric measurements of blood pressure (BP), height, and weight were made. Height was measured in meters. Body mass index (BMI) values were calculated as weight (in kilograms) divided by height squared (in square meters) and were compared with
age standards \(^9\), waist circumference is defined as the minimal circumference measured at the navel, and hip circumference is the widest circumference measured at the hips and buttocks \(^{10}\). Fat \%= 1.2 \times \text{BMI} + 0.23 \times \text{(age years)} - 1.62 \(^{11}\)

**Blood pressure measurements**

Blood pressure was measured by mercury sphygmomanometers on three separate occasions. Systolic and diastolic blood pressures (SBP&DBP) were measured with appropriate size cuff in the right arm with the subject seated, his or her back supported, feet on the floor and right arm supported, and cubital fossa at heart level. The right arm is preferred in repeated measures of BP for consistency and comparison with standard tables. SBP is determined by the onset of the "tapping" Korotkoff sounds (K1) and the fifth Korotkoff sound (K5), or the disappearance of Korotkoff sounds, as the definition of DBP \(^{12}\)

**Transthoracic echocardiographic (TTE)** Transthoracic echocardiographic measurements were performed with Hewlett Packard Sonos 1800 phased array system using a 3.0-mHz transducer for two-dimensional M-mode measurements of the left ventricular mass according to the recommendations of the American Society of Echocardiography \(^{13}\). M-mode echocardiography was used to measure left ventricular dimensions and left ventricular wall thickness, allowing for the calculation of left ventricular mass after correction for BSA; left ventricular mass was calculated by the following formula \(^{14}\):

\[
\text{LV mass (gm)} = 1.04 \times [(LVID + PWT + IVST)^3 - LVID^3] \times 0.8 + 0.6 \text{ g}
\]

Where LVID is the internal dimension, PWT is the posterior wall thickness, IVST is the interventricular septal thickness, 1.04 is the specific gravity of the myocardium, and 0.8 is the correction factor. All measurements are made at end-diastole (at the onset of the R wave) in centimeters (figure 1). Left ventricular mass index was calculated as Left ventricular mass (grams) divided by height (meters).
High resolution carotid ultrasound  High resolution carotid ultrasonographic studies were performed with a Hewlett Packard Sonos 1800, with a 7.5-MHz transducer (Hewlett-Packard, Seattle) with the subject in supine position. The study protocol involved scanning of the far wall of the right and left common carotid arteries in the distal 1·0 cm. The crest at the origin of the bifurcation was used as an anatomical landmark to identify the segment to be visualized (Figure 2) and three measurements of the intima–media thickness were averaged, in order to give the mean common carotid intima–media thickness for each side.

There are the far and near wall of the common carotid artery, which are displayed as two bright lines separated by a hypoechogenic space. The distance between the leading edge of the first bright line on the far wall (lumen –intima interface), and the leading age of the second bright line (media-adventitia interface) indicates the IMT of the far wall (Figure 2). For the near wall the distance between the lower edges of the first bright line to the lower edges of the second bright line at the near wall provides the best estimate of the near wall IMT\(^{15}\).
Laboratory investigations

Blood samples were drawn after an overnight fast from both groups of adolescents. Fasting total cholesterol, HDL-cholesterol, and triglyceride concentrations were analyzed using enzymatic methods with the use of Boehringer Manheim reagents with a fully automated analyzer (Hitachgi 917; Hitachi, Tokyo, Japan). LDL-cholesterol was calculated using the Freidewald equation (16), and fasting blood glucose (FBG) was analyzed using an enzymatic method.

Data analysis

All the data were collected and were statistically analyzed using SPSS 14 program. Numerical data were expressed as mean ± SD. Non-numerical data were expressed as percentage. The mean was compared using the unpaired Student’s t test. A value of P < 0.05 was considered statistically significant. Between-group comparisons were made using ANOVA to analyze differences between cases and controls. Correlations were performed by linear regression analysis.

Ethical consideration

This study was performed with parental consent and with the approval of the faculty’s ethics committee.
**Results**

The study included 52 obese adolescents (mean age 14.16± 2.64 year) and 52 control group (mean age 12± 2.3 years). There was increased over watching television (TV), net user for hours and decreased physical activities in obese adolescents compared to the control group and also they were different in food habits. Family history of obesity and chronic diseases were more common in obese adolescents (table 1).

Body mass index (BMI), fat % and systolic and diastolic blood pressure were significantly higher in the obese group. Although fasting blood sugar was in the normal range in both groups, it was higher in the obese adolescents (table 1) also they had a significant increase in total cholesterol, triglyceride, LDL-C, and low HDL-C compared to the control group.

Table 2 shows that carotid intima/media thickness, LV mass and LV mass index were increased in the obese adolescents. LV dimensions were greater in the obese group and ejection fraction although it was in the normal range on both groups; it was lower in the obese one. There was a significant correlation between BMI and dyslipidemia, blood pressure, carotid intima/media thickness, LV mass and posterior wall thickness (figure3, 4). Carotid intima/media thickness had significant correlation with increased LDL-C and low HDL-C, blood pressure, LV mass and posterior wall thickness (figure5, 6).

**Discussion**

Obesity is becoming a global epidemic for both adult and children and the prevalence of obesity continuing to rise. It is associated with a significant burden of ill health for obese children and for adults who were obese as children. Pediatric obesity is the leading cause of hypertension, insulin resistance, and dyslipidemia, type 2 diabetes mellitus and left ventricular hypertrophy and predisposes to endothelial dysfunction, carotid intimal -medial thickness and increased arterial stiffness.
In this study, the lifestyle was different between the obese adolescents and the control group. Physical activity was lower as they spent more watching TV and using computer and internet. Food habits as eating carbohydrates and junk food were more in obese group. Marshall et al reported that the time spent viewing television has been widely associated with greater adiposity in children. TV viewing could potentially influence adiposity by displacement of physical activity or increased energy intake through snacking promoted by advertising of energy dense food (17).

The family history of obesity, diabetes mellitus and hypertension was more in obese group; this finding is in accordance with the results of Burk 2006. (1)

The obese participants had higher blood pressure than normal weight adolescents; there results were supported by (18, 19)

Obesity is strongly associated with higher- than-optimal blood pressure this is due to the direct effects of obesity on homodynamics and the mechanisms linking obesity and an increase in peripheral vascular resistance: endothelial dysfunction, insulin resistance, sympathetic nervous system, substances released from adipocytes (IL-6, TNF-α, and so forth), and sleep apnea (20).

In the present study obese adolescents had a significant increase in total cholesterol, triglyceride, LDL-C, and low HDL-C compared to the control group. Chinali et al 2006 (21) found in their study that obese adolescents had significantly higher values of fasting glucose, lipid profile (higher triglyceride (TG) and lower HDL-c). Iannuzzi and Maria 2004 (18) showed that obese adolescents had significantly higher plasma concentrations of cholesterol and glucose. Pinhas et al 2007 (22) found that the most striking findings in their study were in the 5- to 17- year –old obese population, the combination of elevated TG and LDL-c and low HDL-c levels place hem at greater cardiovascular risk than their non-obese peers.
Carotid intima/ media thickness was increased significantly in the obese adolescents. This finding is in accordance with the results of Atabek et al 2007 (23) and Wunsch et al 2006 (19). Obesity is associated with abnormal endothelial function due to decrease in nitric oxide this may be related to an increase in oxidative stress, or may result from pro-inflammatory cytokines. In the Framingham heart study, BMI was highly associated with systemic oxidative stress, as determined by creatinine-indexed urinary 8-epi-PGF$_2$_a levels (24).

In this study there is a significant increase in LV mass and LV mass index, LV dimensions were greater in the obese group and ejection fraction although it was in the normal range on both groups; it was lower in the obese one. The same result was demonstrated by Chinali et al 2006 (21) and Friberg et al 2004 (25).

Obesity produces an increment in total blood volume and cardiac output that caused partly by the increased metabolic demand induced by excess body fat. Also, in obesity, the Frank-Starling curve is shifted to the left because if incremental increases in LV filling pressure and volume, which over time may produce chamber dilatation. Ventricular chamber dilatation may then lead to increased wall stress, which predisposes to an increase in myocardial mass and LV hypertrophy of eccentric type (26).

The present study demonstrated a relationship between BMI and cardiovascular risk factors; this suggests that these young obese individuals have a silent risk factor profile. Friberg et al 2004 (25) reported in their study that BMI correlated mainly with LV mass and systolic blood pressure, Yang et al 2007 (27) reported that BMI correlated with carotid intima/media thickness and blood pressure, also Teixeira et al 2001 (28) found in their study that BMI correlated significantly positive with triglycerides and LDL- cholesterol and negatively with HDL- cholesterol.
Carotid intima/media thickness had significant correlation with increased LDL-C and low HDL-C, blood pressure, LV mass and posterior wall thickness, thaws in agreement with the results of Yang et al 2007 (27) and Iannuzzi and Mraia 2004(18).

Clinical implications

Obesity in childhood and adolescents is associated with increased risk of atherosclerosis and cardiovascular risk factors such as increased carotid intima/media thickness (as a marker of preclinical atherosclerosis), hypertension, dyslipidemia, metabolic syndrome, insulin resistance, diabetes... etc) and decreased life expectancy.

Carotid artery duplex scanning is a simple technique to measure carotid intima/media thickness and to diagnose early atherosclerotic changes in obese adolescents.

Educational programs are mandatory in improving awareness of the parents about the pediatric obesity and its associated comorbidities during childhood, as well as increased risk of chronic diseases and decreased life expectancy in adult life

Avoidance of the factors that lead to obesity in children and adolescents principally by control of body weight, this achieved by sustainable life style changes: permanent changes to diet, sedentary behavior, and increased physical activity.

Study limitations

Some limitations exist in the present study. These limitations include the limited number of patients recruited within the study. There is a wide range of intima/media thickness normal values in adults (0.36- 0.9 mm) (29), and there is no intima/media thickness normal values in children and adolescents which need a study of a large number of this age group to detect the normal values.

Conclusion
Obese adolescents had a significant increase in total cholesterol, triglyceride, LDL-C, and low HDL-C compared to the control group; also there is significant increase in blood pressure, carotid intima/media thickness, LV mass and LV mass index.

There was a significant correlation between BMI and dyslipidemia, blood pressure, carotid intima/ media thickness, LV mass and posterior wall thickness.

Carotid intima/media thickness had significant correlation with increased LDL-C and low HDL-C, blood pressure, LV mass and posterior wall thickness.

References


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Table 1: Clinical characteristic of the obese and control adolescents.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Obese (n= 52) (Mean ±SD or %)</th>
<th>Control (n= 52) (Mean ±SD or %)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>14.16± 2.6</td>
<td>12 ± 2.3</td>
<td>0.01</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>30/22</td>
<td>25/27</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Physical activity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regular exercise</td>
<td>3</td>
<td>20</td>
<td>0.001</td>
</tr>
<tr>
<td>Overwatching television</td>
<td>46</td>
<td>22</td>
<td>0.01</td>
</tr>
<tr>
<td>Computer user for hours</td>
<td>27</td>
<td>19</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Food habits</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbohydrateover eating</td>
<td>47</td>
<td>32</td>
<td>0.01</td>
</tr>
<tr>
<td>Junk food</td>
<td>45</td>
<td>25</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>Family history</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td>17</td>
<td>9</td>
<td>0.01</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>9</td>
<td>5</td>
<td>0.03</td>
</tr>
<tr>
<td>Hypertension</td>
<td>18</td>
<td>8</td>
<td>0.01</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>39.98 ±39.36</td>
<td>17.90 ± 1.01</td>
<td>0.001</td>
</tr>
<tr>
<td>Fat %</td>
<td>26.26 ± 4.35</td>
<td>7.99 ± 1.73</td>
<td>0.001</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>118.80 ± 9.17</td>
<td>109.80 ± 8.68</td>
<td>0.001</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>75.60±6.11</td>
<td>66.40± 6.31</td>
<td>0.001</td>
</tr>
<tr>
<td>FBG</td>
<td>87.56 ± 14.62</td>
<td>82.43 ± 2.39</td>
<td>0.017</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>172.06 ± 16.75</td>
<td>160.10 ± 6.78</td>
<td>0.008</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>90.30 ± 35.28</td>
<td>61.86 ± 5.20</td>
<td>0.007</td>
</tr>
<tr>
<td>LDL-C</td>
<td>113.41 ± 15.47</td>
<td>92.05 ± 8.91</td>
<td>0.009</td>
</tr>
<tr>
<td>HDL-C</td>
<td>52.58 ±2.71</td>
<td>57.23 ± 1.60</td>
<td>0.005</td>
</tr>
</tbody>
</table>

BMI=body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, HDL: high density lipoprotein, FBS: fasting blood glucose, LDL=low density lipoprotein. NS: non-significant.
Table 2: Echocardiographic findings and Carotid intima/ media thickness (IMT) of the obese and control adolescents.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Obese (n=52) (mean ±SD)</th>
<th>Control (n=52) (mean ±SD)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV IDd (cm)</td>
<td>50.08 ± 0.38</td>
<td>44.7 ± 0.20</td>
<td>0.004</td>
</tr>
<tr>
<td>LV IDs (cm)</td>
<td>32.1 ± 0.33</td>
<td>24.4 ± 0.20</td>
<td>0.002</td>
</tr>
<tr>
<td>IVSd (cm)</td>
<td>8.90 ± 0.12</td>
<td>7.4 ± 0.3</td>
<td>0.008</td>
</tr>
<tr>
<td>LV PWd (cm)</td>
<td>8.40 ± 0.20</td>
<td>5.4 ± 0.3</td>
<td>0.006</td>
</tr>
<tr>
<td>EF%</td>
<td>64.17 ± 4.13</td>
<td>72.52 ± 1.15</td>
<td>0.003</td>
</tr>
<tr>
<td>LVMI (gm/m²)</td>
<td>62.71 ± 7.24</td>
<td>42.29 ± 5.75</td>
<td>0.003</td>
</tr>
<tr>
<td>Right carotid IMT (cm)</td>
<td>0.51 ± 0.10</td>
<td>0.40 ± 0.02</td>
<td>0.001</td>
</tr>
<tr>
<td>Left carotid IMT (cm)</td>
<td>0.50 ± 0.02</td>
<td>0.40 ± 0.02</td>
<td>0.001</td>
</tr>
</tbody>
</table>

LV IDd: left ventricular internal dimension in diastole, LV IDs: left ventricular internal dimension in systole, IVSd: interventricular septum in diastole, LV PWd: left ventricular posterior wall in diastole, EF: ejection fraction, LVMI: left ventricular mass index
Figure 3: Correlation between body mass index (BMI) and carotid intima-media thickness (CIMT).

Figure 4: Correlation between body mass index (BMI) and left vent. Mass index (LVMI)
Figure 5: Correlation between carotid intima-media thickness (CIMT) and left ventricle mass (LVM)

Figure 6: Correlation between carotid intima-media thickness (CIMT) and LDL-Cholesterol level.