Left Ventricular Hypertrophy in Obese Children

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Abstract

Childhood obesity is one of the most troubling health conditions worldwide, and it is associated with many diseases that eventually lead to serious morbidities and mortality in adulthood, such as insulin resistance, type 2 diabetes mellitus, high blood pressure, dyslipidemia, obstructive sleep apnea and subsequent renal, liver and cardiovascular diseases.

Cardiovascular disease carries the most risk of all of the long-term outcomes of obesity because it is associated with serious complications in adult life, such as heart failure, acute coronary syndrome, and premature sudden death.

This review aims to address childhood obesity as a worldwide health concern and focuses on the cardiovascular risk and adverse outcomes associated with this condition. This review presents details of obesity-related cardiac structural and functional changes, such as left ventricular hypertrophy (LVH) and dysfunction, respectively. A search of multiple medical databases was performed, and the results yielded many studies related to pediatric left ventricular hypertrophy; seventeen studies were found on left ventricular hypertrophy in obese children from 1980 to 2015.

Most of these studies demonstrated that obesity and its comorbidities are important predictors for left ventricular hypertrophy in the pediatric age group. Furthermore, weight reduction is an important measure to reverse these structural changes and reduce the associated risks.

Keywords: Obesity; Left ventricular hypertrophy; Obesity; Children

Introduction

Childhood obesity is one of the most troubling health conditions worldwide [1]. The association of this condition with many diseases that eventually lead to serious morbidities and mortality in adulthood makes it a challenging public health concern. Morbidities include insulin resistance, type 2 diabetes mellitus, high blood pressure, dyslipidemia, obstructive sleep apnea and subsequent renal, liver and cardiovascular diseases. Obesity is also a risk factor for multiple cancers in adults [2-4].

The prevalence of childhood obesity has increased significantly in recent years, and it has become an epidemic in certain areas. The recent WHO Global Database on Child Growth and Malnutrition report states “in the year 2013, an estimate of 42 million children under the age of five around the world are either overweight or obese” [5]. In addition to that, the prevalence of obesity is increasing in all childhood ages, including both males and females of different ethnicities, [6]. Obesity is most often caused by a disturbance in energy balance, which occurs when a child embraces a sedentary life style with decreased physical activity, increased caloric intake, or both. Other factors, such as hormonal, psychosocial, medical and genetic factors, also contribute to the development of obesity but to a much lesser extent.

Classification of childhood obesity as "overweight" or "obese" is determined using the body mass index (BMI) of the child compared to the average BMI for children of the same sex and age rather than the fixed parameters used in the adult index. These measurements are plotted on the growth charts displayed in Figures 1 and 2.

The Center of Disease Control and Prevention defines ‘overweight’ as “a BMI at or above the 85th percentile and below the 95th percentile for children and teens of the same age and sex”. Obesity is defined as “a BMI at or above the 95th percentile for children and teens of the same age and sex”.

Body mass index is calculated as the child’s weight in kilograms divided by the square of his/her height in meters. Many studies reported that obese children are more likely to turn into obese adults [7]. This observation emphasizes the importance of addressing this problem at an early stage.

Cardiovascular complications carry the greatest risk of all of the long-term complications of obesity because they are associated with serious consequences in adult life, such as heart failure, acute coronary syndrome and premature sudden death [8]. This review addresses childhood obesity and short-term changes related to obesity, including hormonal, metabolic, structural and functional changes, and it focuses on cardiovascular changes and risk. Details address cardiac structural...
Dyslipidemia

Children with increased body weight tend to exhibit an abnormal lipid profile. Increased body fat directly elevates lipid parameters [11]. Abnormalities that are classically observed in these populations are elevated triglyceride and decreased high-density lipoprotein (HDL) levels [12]. Low-density lipoprotein (LDL) levels may be normal or high.

Insulin resistance and the metabolic syndrome

Weiss et al. [13] defined childhood metabolic syndrome as a cluster of potent risk factors that present during childhood and significantly increase the likelihood of developing type 2 diabetes mellitus, atherosclerosis and subsequent cardiovascular disease in adults. This cluster of risk factors includes hypertension, hyperlipidemia, insulin resistance and obesity. The most significant impact of these factors is shown to be on the adult population, but the sequence of events that lead to the development of the cardiovascular disease begins during childhood.

Many studies demonstrated that obesity is the cornerstone of the development of childhood metabolic syndrome [14,15]. Weiss et al. also reported that the prevalence of metabolic syndrome was directly proportional to the severity of obesity. Metabolic syndrome is observed in up to 50 % of severely obese children and adolescents. The International Diabetes Federation provided more comprehensive criteria to define childhood metabolic syndrome based on the age of the child (table 3).

A local hospital-based study was conducted in Saudi Arabia at King Abdulaziz University hospital [16] to determine the prevalence of metabolic syndrome in overweight and obese Saudi children from 2 to 18 years of age. A total of 173 of the 387 participants exhibited hyperinsulinism (44.7 %), 55 children exhibited metabolic syndrome (14.29 %) and 35 children had type 2 diabetes mellitus (9.04 %). This study concluded that metabolic syndrome and type 2 diabetes mellitus were prevalent in overweight and obese children. Early management of obesity, with a hope of prevention, is vital to maintain optimal health and prevent unnecessary complications.

Childhood obesity and blood pressure

Recent studies reported that childhood hypertension was prevalent in overweight and obese children. Some studies stated that childhood obesity was the most relevant risk factor to essential high blood pressure in children [17-19] other risk factors included family history of hypertension and ethnicity. Hypertension in children is categorized based on the normal distribution of blood pressure in children of the same age and sex. Normal blood pressure is defined as "systolic and diastolic blood pressure that is less than the 90th percentile for sex, age, and height on at least three separate occasions". Stage 1 hypertension is "systolic and or diastolic BP between the 95th percentile and 5 mmHg above the 99th percentile or if in adolescents the BP exceeds 140/90 mmHg even <95th percentile". Stage 2 hypertension is "systolic and or diastolic BP ≥ 99th percentile plus 5 mmHg" [20]. High blood pressure is a serious condition that leads to dreadful adverse outcomes, such as cardiovascular accidents, heart failure, renal failure, seizures, and encephalopathy, if left unmanaged.

Weight is strongly associated with blood pressure, which supports the importance of weight loss on reducing elevated blood pressure. Weight loss is one of the most effective measures in the management and prevention of hypertension and its complications. Clarke et al.
Ref. Sample Date Outcome
Dušan et al. [36] 103 obese subjects aged 9 to 19 years 2015 LVH was found in 10 % of subjects
Pieruzzi et al. [44] 526 obese children aged 6 to 15 years 2015 Obesity was significantly associated with diastolic dysfunction and correlated with concentric hypertrophy of the left ventricles (P<0.001)
Bonito et al. [58] 281 obese children aged 6 to 16 years 2014 47 % had abnormal LV geometry, 18.5 % had eccentric LVH, 15.5 % had concentric LVH, and 13 % had concentric LV remodeling.
Alp et al. [37] 430 obese children aged 6 to 17 years 2014 BMI and total fat mass were predictors for abnormal left ventricular geometry.
Falkner et al. [51] 301 African -American adolescents aged 11 to 18 years 2013 High left ventricular mass index was found in 24 % obese children compared to 12 % non-obese children.
Dhuper et al. [45] 343 children, 213 obese, 130 non-obese 2011 The obese subjects had significantly higher LV mass index (LVMI; 49.6 ± 0.9 vs. 46.0 ± 1.0 g/m².7, (P = 0.01). Concentric remodeling (CR) was the most prevalent pattern noted in the obese group.
Chinali et al. [34] 460 adolescent participants aged 14 to 20 years Categorized as overweight, obese, or normal BMI 2006 Left ventricular hypertrophy was more prevalent in obese (33.5 %) and overweight (12.4 %), compared with normal weight participants (3.5 %), P < (0.001).
Khositseth et al. [32] 49 obese children aged 3.4 to 15.4 years 2010 47% had LVH, 6% had concentric remodeling, 12% had concentric hypertrophy, and 30% had eccentric hypertrophy.
Movahed et al. [33] 1,500 adolescents between the ages of 12 and 20 years who are actively involved in school sport programs 2009 10.32 % of obese athletes had left ventricular hypertrophy (LVM >215 g) in contrast to 0.2 % of controls. 41.4 % of obese students had relative wall thickness >0.43 vs. 15.7 % of controls.
Chinali et al. [34] 460 adolescent participants aged 14 to 20 years Categorized as overweight, obese, or normal BMI 2006 Left ventricular hypertrophy was more prevalent in obese (33.5 %) and overweight (12.4 %), compared with normal weight participants (3.5 %), P < (0.001).
Kinik et al. [48] 30 obese children who were matched to a control group 2006 Left ventricular hypertrophy was associated with children who had elevated BMI, insulin resistance, and dyslipidemia.
Friberg et al. [59] 19 obese and 20 lean adolescents were recruited. 2004 Left ventricular mass index was 16 % greater in obese compared to lean adolescents.
Urbina et al. [60] 160 healthy children and young adults, 9 to 22 years old 1995 Weight excess is an important predictor for elevated left ventricular mass.
Stephen et al. [41] 201 children and adolescents from 6 to 17 years old 1995 Lean body mass is a significant predictor for left ventricular mass.

Table 1: Summary of published studies of LVH in obese children.

<table>
<thead>
<tr>
<th>Ref.</th>
<th>Sample</th>
<th>Date</th>
<th>Outcome</th>
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<tbody>
<tr>
<td><strong>Hypertension</strong></td>
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<tr>
<td>Pieruzzi et al. [44]</td>
<td>526 obese children aged 6 to 15 years</td>
<td>2015</td>
<td>Blood pressure values and hypertension are independently associated with an increase in cardiac mass and the presence of cardiac hypertrophy (P&lt;0.001 and P&lt;0.05, respectively).</td>
</tr>
<tr>
<td>Falkner et al. [51]</td>
<td>301 African-American adolescents aged 13 to 18 years</td>
<td>2013</td>
<td>LVMI was high in hypertensive children (19 %) compared to children with normal blood pressure (12 %), and it was the highest in obese hypertensive children (17 %).</td>
</tr>
<tr>
<td>Pruette et al. [61]</td>
<td>141 hypertensive children</td>
<td>2013</td>
<td>The prevalence of LVH was 35 % overall, and it is more prevalent in obese African Americans than non-obese non-African-Americans</td>
</tr>
<tr>
<td>Karen et al [50]</td>
<td>163 adolescents, 44 with normal blood pressure, 116 hypertensive</td>
<td>2004</td>
<td>The prevalence of LVH in hypertensive children was higher (44.5 %) compared to children with normal blood pressure (9.1 %).</td>
</tr>
<tr>
<td>Stephen et al. [39]</td>
<td>201 children and adolescents from 6 to 17 years old</td>
<td>1995</td>
<td>The variance of left ventricular mass explained by the model was 77 %. Systolic blood pressure explained only 0.5 % of the variance.</td>
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<td><strong>Fat mass and distribution</strong></td>
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<tr>
<td>Pieruzzi et al. [44]</td>
<td>526 obese children aged 6 to 15 years</td>
<td>2015</td>
<td>Waist circumference z-scores were significantly associated diastolic dysfunction.</td>
</tr>
<tr>
<td>Daniels et al. [49]</td>
<td>123 children and adolescent aged 9 to 17 years</td>
<td>1999</td>
<td>There was a significant correlation between fat percentage and fat distribution with left ventricular mass (r=0.37).</td>
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<td><strong>Lipid profile</strong></td>
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Obesity-related hypertrophy or severe obesity in children and adolescents affects blood pressure and obesity together, with an additive effect on the risk of developing cardiovascular disease. This adds to the need for early intervention to prevent progression to more severe obesity-related cardiomyopathy.

**Childhood obesity and cardiovascular risk**

The presence of obesity in children increases the risk of developing cardiovascular disease during adulthood because of the association between obesity and the development of atherosclerosis (which is the main element of the pathogenesis of this disease). Excess adipose tissue in children often leads to physiological, inflammatory, and metabolic disturbances. These dysregulations increase the probability of children exhibiting signs of premature cardiac dysfunction and structural abnormalities in subsequent events. Therefore, obese children may exhibit cardiometabolic patterns that are similar to obese adults.

Wong et al. [25] defined obesity-related cardiomyopathy as “myocardial disease in obese individuals that cannot be explained by diabetes mellitus, hypertension, coronary artery disease or other etiologies.”

Recent studies identified obesity as an independent predictor for heart [26,27]. Furthermore, the duration of Obesity is another important predictor for the development of cardiac dysfunction and structural abnormalities, which predisposes children to heart failure in early adulthood [28,29]. Since obese children tend to grow into obese adults, early identification of these cardiovascular changes and weight reduction are important to ensure the reversibility of these changes.

**Obesity-related left ventricular hypertrophy (LVH) and cardiac dysfunction**

Left ventricular geometry is assessed using echocardiographic measurements. It is classified into the following four groups based on left ventricular mass (LVM) and relative wall thickness (RWT): concentric hypertrophy “increased mass and increased relative wall thickness”, eccentric hypertrophy “increased mass and normal relative wall thickness”; concentric remodeling “normal mass and increased relative wall thickness”, and normal geometry “normal mass and normal relative wall thickness” [30] (Figure 3). Left ventricular mass index (LVMI) is calculated by indexing the echocardiographic measurement to height to a 2.7 power. One study of more than 2000 children revealed that “for children above 9 years LVMI/height 2.7 values > 40 g/m 2.7 in girls and >45 g/m 2.7 in boys can be considered abnormal because it falls beyond the 95th percentile of the normal LVMI distribution for age and sex.” [31]. Cardiac diastolic function is evaluated using a Doppler echocardiography by measuring the mitral E/A ratio.

Obese children, especially children with severe obesity, exhibit a tendency to develop abnormal left ventricular geometry (left ventricular hypertrophy or relative wall thickness) and cardiac dysfunction [32-34]. The underlying pathogenesis is that obese children have increased metabolic activity due to the presence of excess adipose tissue, which leads to increased heart output and total blood volume to meet the metabolic demands. This compensatory process causes the structural changes and cardiac dysfunction that are occasionally observed in obese children [35].

One study of the relative effect of elevated blood pressure and obesity on left ventricular mass demonstrated statistically significant results, which supports the roles of obesity and elevated blood pressure as independent factors that increase the probability of the occurrence of LVH. Data analysis revealed that “obesity OR = 3.36, p<0.001. In addition, high blood pressure showed an OR = 2.92, p<0.001.” High blood pressure and obesity together exert an additive effect on the
dyslipidemia is a “comorbidity of obesity”. A recent study in Indonesia [47] examined the relationship between lipid profile and LVM in obese adolescents, and the results demonstrated no significant association with cardiovascular accidents, and plays a role in the pathogenesis of developing atherosclerosis. However, it is not well known whether caused by obesity and elevated fat mass. Moreover, it is associated with obesity is an independent risk factor for the development of LVH and hypertension. LVH correlates with the severity of hypertension, and it generally indicates a worse prognosis [50]. Falkner et al. [51] investigated 301 African-American adolescents and reported that “adolescents with higher blood pressure had higher left ventricular mass index (33.2 vs. 38.7 gm/m².7; p<0.001) and greater left ventricular hypertrophy”. The effect of blood pressure was independent of obesity. Obesity and high blood pressure promote concentric LV remolding, but this change is more highly associated with high blood pressure than obesity [52,53].

Obstructive sleep apnea and LVH

Obstructive sleep apnea is defined as a complete cessation of airflow for >10s during sleep. The decrease in airflow leads to a fall in oxygen saturation (i.e., nocturnal hypoxemia). Obstructive sleep apnea is associated with obesity. A strong association between obstructive sleep apnea and LVH was reported previously [54]. LVH was observed in 78-88% of adults [55,56] as well as 40% of children with obstructive sleep apnea. “Low nocturnal oxygen saturation” was the strongest independent predictor for LVH compared to other factors, such as systolic BP and BMI (P<0.001) [57,58].

Conclusion

Obesity is one of the most prevalent public health problems worldwide, and it affects nearly one in five children. Obesity is associated with many short- and long-term complications, and it predisposes children to adult onset obesity, cardiovascular-associated morbidities and premature death. The process of developing this risk begins during childhood because obesity is an independent risk factor for the development of LVH and cardiac dysfunction. Other factors that are generally associated with obesity, such as dyslipidemia, insulin resistance, fat mass distribution, high blood pressure, and nocturnal hypoxemia, are also related to LVH. These factors, especially high blood pressure and nocturnal hypoxemia, exert a synergistic effect with obesity for the development of LVH, which is more common and prevalent when these two conditions coexist.

Obesity prevention and early management using weight reduction (conventional or surgical) are important nonpharmacological measures to ameliorate left ventricular mass and reverse most cardiac abnormalities that are associated with obesity in children. One study [46] has evaluated morbidity obese adolescents before and after bariatric surgery and demonstrated that the prevalence of concentric LVH improved from 28% pre-operatively to only 3% at follow up. Furthermore, normal LV geometry was more frequently observed from 36% to 79% at follow up, and diastolic function also improved.

Fat mass and distribution and LVH

In addition to abnormal lipid profile, the percentage of fat and its distribution are also related to LVH. One study demonstrated significant (P<0.05) univariate correlations between fat distribution (central deposition of fat-android pattern) and fat mass with LVM. The correlation coefficient between the android pattern and LVH was equal (r=0.37) [49].

High blood pressure and LVH

Hypertension is an independent predictor for the development of LVH, and LVH is the most prevalent end organ damage in children with hypertension. LVH correlates with the severity of hypertension, and it generally indicates a worse prognosis [50]. Falkner et al. [51] investigated 301 African-American adolescents and reported that “adolescents with higher blood pressure had higher left ventricular mass index (33.2 vs. 38.7 gm/m².7; p<0.001) and greater left ventricular hypertrophy”. The effect of blood pressure was independent of obesity.

Lipid profile and LVH

An abnormal lipid profile is one of the metabolic disturbances caused by obesity and elevated fat mass. Moreover, it is associated with cardiovascular accidents, and plays a role in the pathogenesis of developing atherosclerosis. However, it is not well known whether a significant relationship between dyslipidemia and LVH exists or the relationship is not more than an indirect association because dyslipidemia is a “comorbidity of obesity”. A recent study in Indonesia [47] examined the relationship between lipid profile and LVM in obese adolescents, and the results demonstrated no significant association between lipid profile disturbances with LVM. Another study [48] demonstrated that relative left ventricular wall thickness (intraventricular septum and left ventricular posterior wall thickness) correlated with insulin, very low-density lipoprotein, and triglyceride levels. Data in this area are inconsistent, and further research is needed.
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References


