

Introduction

Pediatric obesity is an increasing phenomenon (**Ebbeling et al., 2002**). Childhood obesity has a wide range of serious complications and increases the risk of early illness and death in later life. As in adulthood, obesity in childhood contributes to an increased prevalence of cardiovascular risk factors, such as hypertension, hypertriglyceridemia, low high-density lipoprotein (**HDL**) cholesterol, and impaired glucose metabolism (**Ebbeling et al., 2002; Reinhar et al., 2005; Reinhar et al., 2004; Wabitsch et al., 2004**). Exposure to these cardiovascular risk factors in early life may induce changes in the arteries contributing to the development of atherosclerosis in adulthood (**Raitakari et al., 2003**).

Metabolic and cardiovascular diseases are well known to be more prevalent in obese individuals than non-obese individuals (**Despres, 2006**). More specifically, increased visceral adipose tissue (**VAT**), the fat that surrounds the internal organs (e.g., heart, intestines) in the cavities of the body, predicts an unfavorable cardiovascular and metabolic risk profile (**Despres, 2006; Miller et al., 2005; Chan et al., 2002; Ross et al., 2002; Tagushi et al., 2001**).

Echocardiographic epicardial adipose tissue could be applied as an easy and reliable imaging indicator of VAT and cardiovascular risk. Epicardial adipose tissue (**EAT**) is a particular form of visceral adipose tissue deposited around the heart and found in considerable quantities around subepicardial coronary arteries. EAT shares a common embryological origin

with abdominal adipose tissue. Apart from the anatomical description, there is growing evidence about the physiological and metabolic importance of EAT, especially in the association of cardiovascular risk profiles and the pathogenesis of atherosclerotic coronary artery disease (**CAD**) (**Prati et al., 2003**).

Increases in epicardial adipose tissue seem to be associated with abnormal cardiac morphology. Studies show that epicardial adipose tissue is associated with increased ventricular mass (**Corradi et al., 2010**). A recent study also demonstrates that atria enlargement and impairment in diastolic filling is associated with epicardial adipose tissue in morbidly obese subjects (**Iacobellis et al., 2006**). Recent research has found that left ventricular hypertrophy is related to other risk factors, including obesity and insulin resistance in children and adolescents. (**Urbina et al., 1999**)

Echocardiography is non-invasive and safe. It is also relatively cost and time efficient since it may be part of the routine assessment that patients suspected to be at risk for cardiovascular or metabolic illness (**Iacobellis et al., 2003**).

In 1998, the World Health Organization (**WHO**) designated obesity as a global epidemic affecting adults and children. Within the scientific community, the discovery of leptin and the elucidation of disorders affecting various neuroendocrine pathways and the genetic linkages of obesity have promulgated the notion that obesity is a disease.

The circumference of the waist relates closely to body mass index (**BMI**) and is also the dominant measure in the waist-to hip ratio, which reflects the proportion of the body fat located intra-abdominally, as opposed to subcutaneously (**Bjorntop, 1987**).

The waist circumference is a better index of android (abdominal) obesity than waist-to-hip ratio and is the best indicator of changes in the intraabdominal fat during weight loss (**Kurpad et al., 2004**). Waist circumference independently contributes to the prediction of non-abdominal, abdominal subcutaneous and visceral fat in both sexes. It has the ability to act as a surrogate for abdominal fat (**National Institute of Health, 2008**). These observations reinforce the importance of using waist circumference in clinical practice (**Janssen et al., 2002**).

Aim of the Work

Since there are established studies revealing the increased risk of cardiovascular and metabolic diseases in obese children with visceral obesity, this study aims to identify obese children with epicardial adipose tissue and abnormal cardiac morphology via echocardiography as a reliable indicator of visceral obesity and its relation to the degree of obesity, lipid profile, arterial blood pressure and insulin resistance.

Childhood Obesity

Introduction:

Childhood obesity continues to be a major focus of public health efforts. Obese children may be at risk for both short term health consequences and long term tracking of obesity to adulthood. Some have suggested that the prevalence of obesity among children will reach 30% by 2030 (*Ogden et al., 2012*).

In (2010), *World Health Organization (WHO)* statistics revealed that at least 300 million adults are obese and at least a billion are overweight.

The *Centers for Disease Control* (CDC) reports that obesity in children begins at the 97th percentile. The 95th percentile roughly corresponds to the obesity point for adults, which is a BMI of 30(*CDC, 2009*).

Definition of obesity using BMI:

For children between 2 and 19 years, BMI is plotted on the CDC growth chart to check for the corresponding age and sex related percentile. Childhood obesity is defined as a BMI at or above 97th percentile for children of same age and sex (*CDC, 2009*). A child's weight status is determined based on an age- and sex-specific percentile for BMI rather than by the BMI cutoff points used for adults (*CDC, 2009*).

The World Health Organization (WHO) recommends weight-for-height Z-scores to be used as definition for obesity in children aged 10 years or less. In adolescents (aged 10-19 years), WHO defines at risk of overweight as an age- sex-specific BMI greater than the 85th percentile of the reference population (**WHO, 2013**), overweight as BMI between 85th and 95th percentile and obesity as age and sex specific BMI above 95th percentile (**WHO, 2013**).

International Obesity Task Force (IOTF) recommends the definition established by the use of *age- and gender-specific BMI cutoff points rather than percentiles* to determine overweight (**Cole et al., 2000**). Obesity was defined according to the BMI more than 97th percentile (**Kromeyer-Hauschild, 2002**).

Epidemiology of childhood obesity:

More than 30 million overweight children are living in developing countries and 10 million in developed countries (**WHO, 2013**).

In 2010, World Health Organization (WHO) statistics revealed that childhood obesity is on the rise all over the world, which reduces life expectancies, as well as significantly increasing the risk of early onset of obesity related morbidities, such as cancers and cardiovascular illnesses (**WHO, 2010**).

The worldwide prevalence of childhood overweight and obesity increased from 4.2% in 1990 to 6.7% in 2010. This trend is expected to reach 9.1% or ≈60 million, in 2020. The

estimated prevalence of childhood overweight and obesity in Africa in 2010 was 8.5% and is expected to reach 12.7% in 2020. The prevalence is lower in Asia than in Africa (4.9% in 2010), but the number of affected children (18 million) is higher in Asia (*de Onis et al., 2010*).

Based on CDC growth charts, *Salazar-Martinez et al (2006)* found that 7% of Egyptian boys and 18% of Egyptian girls were overweight and 6% of boys and 8% of girls were obese. The factors correlated with increased BMI among Egyptian adolescents in their study were age and rural residence.

The International Obesity Task Force, Egypt, has said that more than 25% of children aged 4 years are overweight. Not only obesity, but also diabetes is a growing concern in Egypt (*IOTF, 2009*).

Egypt, a lower middle income country, has exhibited an increase in obesity prevalence. Despite its poverty it was in 2010 the fattest nation in Africa and among the top three fattest Middle Eastern countries in terms of adult overweight/obesity (*Shaltout, 2010*).

Obesity rates in Egypt have reached 66%, being the fifth worldwide after American Samoa 93.5%, Kiribati 81.5%, USA 66.7%, and Germany 66.5%. (*Even, 2011*)

More than 30 per cent of school students in **Dubai** are either obese or overweight, according to a latest survey conducted by the Beat Obesity campaign (*CDC, 2011*).

Approximately 70 percent of **Saudis** are obese, announced by the head of Saudi Arabia's obesity research unit. 36 percent of Saudis are morbidly obese. In addition, 3 million children in the Kingdom are obese. (*Al-Qathany, 2011*)

In developing countries, the prevalence of overweight/obesity in older children is reported to be much higher than in preschoolers. Among developing countries, the prevalence of childhood obesity is highest in the Middle East and in Central and Eastern Europe (*James et al., 2011*).

Childhood-adult obesity linkage:

Given the morbidity and mortality associated with adult obesity, the link between childhood obesity and adult obesity is a major concern. A number of studies have found an association between childhood weight status and adult weight status (*Freedman et al., 2005; Togashi et al., 2002; Wright et al., 2001*).

Genome-wide association study for early-onset and morbid adult obesity identified three new risk loci in European populations; in *NPC1* (endosomal/lysosomal Niemann-Pick C1 gene), near *MAF* (encoding the transcription factor c-MAF) and near *PTER* (phosphotriesterase-related gene) (*Meyre et al., 2009*). The combined obesity allele risk score is associated with higher rates of weight gain and adult obesity, and weight gain and growth even in the first few weeks after birth may be the beginning of a pathway of greater adult obesity risk (*Elks et al., 2010*).

Jounala et al. (2011) reported that childhood BMI, CRP, family income (inversely), mother's BMI, and polymorphisms near genes *FLJ35779*, *TFAP2B*, and *LRRN6C* are independently related to adulthood obesity and cardiovascular diseases risk.

Classification of obesity:

Obesity is a disease whose pathology lies in the increased size and number of fat cells. The number of fat cells can be estimated from the total amount of body fat and the average size of a fat cell. The number of fat cells can increase three-to-fivefold when obesity occurs in childhood or adolescence (*Janesick and Blumberg, 2011*).

- ***Classification of obesity according to fat cell size and number (hypertrophic and hypercellular obesity):***

a. Hypertrophic Obesity

Enlarged fat cells tend to correlate with an android or truncal fat distribution and are often associated with metabolic disorders such as glucose intolerance, dyslipidemia, hypertension, and coronary artery disease (*Janesick and Blumberg, 2011*).

b. Hyper cellular Obesity

Increased numbers of fat cells usually occur when obesity develops in childhood. Whether it begins in early or middle childhood, this type of obesity tends to be severe. Increased

numbers of fat cells may also occur in adult life when the body mass index (BMI) is $>40\text{kg/m}^2$ (*Janesick and Blumberg, 2011*).

- ***Classification of obesity according to fat distribution (central and peripheral obesity):***

Measuring fat distribution in subcutaneous versus visceral compartments is important because visceral fat predicts development of health risks more than total body fat (*Mokha et al., 2010*). Recent studies in children showed that increased central fat correlates with less favorable patterns of serum lipoprotein concentrations, increased blood pressure (*Daniels, 2009*), adverse levels of cardiovascular risk (*Mokha et al., 2010*) and increased risk of metabolic complications (*McCarthy et al., 2008*).

Abdominal obesity is commonly associated with hyperinsulinemia, impaired glucose tolerance, hyperglycemia, as well as increase in plasma triglycerides, small LDL cholesterol particles and apolipoprotein B and a decrease in HDL-C. Also, abdominal obesity is a major component of the metabolic syndrome (*Karnik and Kanekar, 2012*).

The only truly reliable estimates of visceral fat are made by computed tomography (CT) or magnetic resonance imaging (MRI) (*Sjostrom et al., (1997). Pouliot et al., (1994) and Lean et al., (1995)* showed that waist circumference was as good as or better than WHR or subscapular fat assessment in estimating visceral fat. *Broning et al., (2010)* demonstrated that the bioelectrical impedance (BIA) is a precise and useful measure of both abdominal fat and WC. Although BIA measurements

show no closer correlation with MRI total abdominal adipose tissue than manual WC, the BIA may overcome the observer error associated with manual WC.

Assessment of obesity in pediatrics:

Various measures are used to estimate the degree of obesity in large-scale epidemiological settings, smaller-scale studies and clinical settings.

Anthropometric Measures

Anthropometric measures are the most commonly used method for defining overweight and obesity in children and adolescents and includes the following:

I- Weight

The standard weight is usually determined as the mean or median determined from a reference distribution for the population with obesity defined in different ways (***Gorber et al., 2007***):

- Classification systems use certain ***percentiles in the reference growth curves*** to define weight status with the 95th percentile commonly used as the cut-off point for overweight and 97th percentile for obesity.

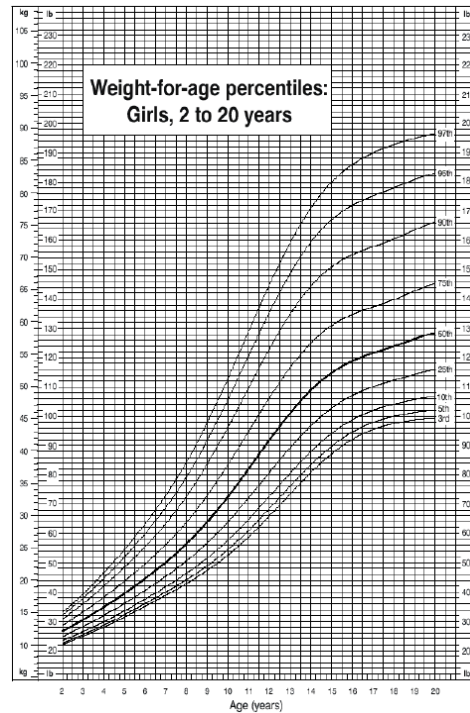


Figure (1): Weight for age percentile growth chart (NCHS, 2000).

- A more sophisticated and precise measure of weight status involves calculating **the Z (or standard deviation) score** by subtracting the reference value from the measured weight and dividing by the standard deviation of the reference population. A Z score of 2 or more (i.e. 2 SD above the median) is usually taken to indicate obesity.

II- Body Mass index

In large-scale population surveys and clinical public health screening, an index of body weight adjusted for stature is commonly used as a surrogate for body fat content (**Gorber et al., 2007**).

The most widely used is *Quetelet's index, better known as body mass index (BMI)*. This index has been estimated as body weight (kg) divided by height squared (m^2) to correlate weakly with height and strongly with body fatness in adults. It has been shown to be a good indicator of adiposity in adults and there is a wide body of evidence which links increasing BMI to increased risk of morbidity and mortality in adults (*Garabed, 2007*).

In general, Body Mass Index is the standard measurement used to describe a child's (age 2 years or older) or adolescent's weight status (*WHO, 2007*). Duplicate assessment of both weight and height is recommended, with a third taken if the first two significantly differ (*WHO, 2007*).

BMI for age is determined using gender-specific growth charts that place a child in a percentile relative to weight and height. Weight categories are determined based on these percentiles and are defined as:

< 5th percentile » underweight, 5th to 85th » normal, 85th to 95th » at risk for overweight, 95th » overweight and 97th » obese (*WHO, 2007*).

Several expert and advisory groups have recommended BMI as the preferred measure for evaluating obesity among children and adolescents 2 to 19 years of age (*Stommel and Schoenborn, 2009; WHO, 2007; Koplan et al., 2005*).

BMI charts characteristic:

Adiposity rebound:

The normal pattern is for BMI to decrease from 2 years of age until 5 or 6 years of age and to increase thereafter through the remainder of childhood and into young adulthood. The resulting V-shaped pattern in early childhood has been termed the “*adiposity rebound*” (Tylor *et al.*, 2011).

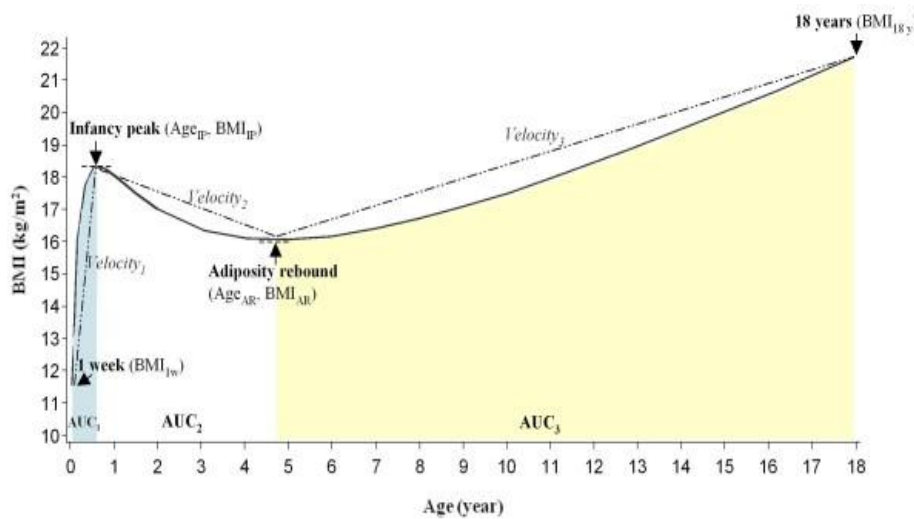


Figure (2): Adiposity rebound curve (Wen, 2012).

The age of adiposity rebound, the point of the BMI nadir before body fatness begins to increase (between 5 and 6 years of age) is an important predictor for adult obesity. Children with early adiposity rebound have a fivefold greater chance of becoming obese as adults, compared to those with late adiposity rebound. At the age of adiposity rebound, children who are already overweight have a six-fold greater risk for adult obesity compared to lean children (Taylor *et al.*, 2011).

Growth spurt velocity:

BMI developmental curve lacks the marked increase in growth velocity during the adolescent spurt that is characteristic of height and weight growth curves. Although BMI increases during the adolescent spurt, the slope with age is dampened by the nature of the BMI ratio and the difference in timing of the growth spurts of height and weight (**Malina et al., 2004**).

III- Skin fold Thickness

Skin fold thickness is double, compressed thicknesses of subcutaneous fat and skin measured with standardized calipers at selected sites (e.g., triceps, sub scapular and supra iliac sites).

Triceps skin fold thickness should be measured on a child's right upper arm with the child standing upright (**Addo and Himes, 2010**). Skin fold measurements taken at triceps by trained operators were shown to correlate well with estimates of total adiposity from DEXA in children and measurements of abdominal skin folds also correlated highly with estimates of intra-abdominal adiposity obtained from CT or MRI scans (**Addo and Himes, 2010**).

The skin fold measurements perform as well as BMI or waist circumference values (**Addo and Himes, 2010**). However, accuracy is greatly dependent upon the skills of the examiner, and there is a high degree of variability between assessors. It is a challenge to assess triceps skin fold in children who are heavier (**Addo and Himes, 2010**).