Clinical Biochemistry 48 (2015) 370–376

Contents lists available at ScienceDirect

Clinical Biochemistry

journal homepage: www.elsevier.com/locate/clinbiochem

Review

Laboratory assessment of cardiometabolic risk in overweight and obese children

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ARTICLE INFO

Article history:
Received 28 August 2014
Received in revised form 23 December 2014
Accepted 24 December 2014
Available online 10 January 2015

Keywords:
Childhood obesity
Cardiovascular diseases
Cardiometabolic risk factors
Adipocytokines
Familial hypercholesterolemia
Dyslipidemia
Non-alcoholic fatty liver disease

ABSTRACT

Childhood obesity has been identified as one of the most important risk factors of developing cardiovascular diseases. The global prevalence of overweight and obesity among children shows an increasing tendency. Many of overweight or obese children will become obese adults with enhanced risk for cardiovascular diseases. Childhood obesity is often accompanied by serious consequences such as dyslipidemia, hypertension, diabetes, pro-inflammatory state and non-alcoholic fatty liver disease. Hypertension, high LDL-cholesterol and triglyceride concentrations, insulin resistance, inflammation and disturbances in adipocytokines secretion are associated with endothelial dysfunction which precedes the development of atherosclerosis. Obese children and adolescents with a clinically-proven non-alcoholic fatty liver disease, which is currently recognized as the hepatic component of metabolic syndrome, are at more severe cardiovascular risk compared with normal-weight. Obesity-related insulin resistance is highly prevalent in children and adolescents, and is associated with the increased lifetime risk of type 2 diabetes and cardiovascular disease. Adipokines contribute to obesity-atherosclerosis relationships yet among several recently discovered adipokines only few (adiponectin, resistin, chemerin, fibroblast growth factor 21, apelin) have been partly studied in obese pediatric population. The aim of this review was to describe the spectrum of cardiovascular abnormalities observed in children with overweight and obesity and the role of laboratory in the assessment of cardiometabolic risk in order to differentiate between healthy obese and those at risk to most effectively prevent progression of cardiovascular disease in childhood.

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Introduction

Childhood obesity has been identified as one of the most important risk factors of developing cardiovascular diseases. Earlier estimates of global prevalence of childhood overweight and obesity came true in most countries of different regions in the world [1]. A report from the United States (US) showed that between 2007 and 2008 among 2–19-year-olds 16.9% were obese and 31.6% were overweight [2]. Recent UNICEF report from 2013 indicated Canada, Greece and US as the countries with the highest prevalence of obesity (over 20%) among children of 11, 13 and 15 years of age, and US and Canada with the highest

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http://dx.doi.org/10.1016/j.clinbiochem.2014.12.024
0009-9120/

prevalence of overweight (30% and 20%, respectively), as classified by body mass index (BMI). Interestingly, within the last 10 years in US, the number of obese among children 2–5 year-olds remained stable, at about 17%, but the number of extremely obese is growing. Nearly 6% of all US children age 18 or younger are severely obese and present with higher blood pressure, elevated triglyceride concentrations, proinflammatory state, and greater oxidative stress than their overweight or obese peers [3]. Severely obese children and adolescents also show more signs of subclinical atherosclerosis, impaired glucose tolerance, and prediabetes.

According to World Health Organisation (WHO), overweight in children is defined as a BMI within the 85th–95th percentile and obesity as a BMI at or above the 95th percentile for age and sex [4]. In Europe, the prevalence of overweight in the age categories 11, 13 and 15 years, in most countries, ranges from 10 to 19% and only in three countries does not reach 10%, including the Netherlands with the lowest prevalence of 8%. The results of Polish "OLAF study 2007–2010" have shown that higher prevalence of overweight and obesity occurs in children aged 11 to 12 years and accounts for 13.8% and 14.7% than in adolescents 17–18-years-old (7.8% and 5%, respectively) [5]. Findings from this study indicated that overweight and obesity occurs more often in boys than in girls. Table 1 presents some of the UNICEF data, reported in 2013 on the changes, between 2001/2002 and 2009/2010 in the percentage of young children aged 11, 13 and 15 years who were overweight [6].

To rely solely on BMI to define obesity in children has been questioned for a long time and there are data showing that up to 25% of children with normal BMIs will have an excessive amount of fat when measured by other means [7]. Excess adiposity increases the fat-to-muscle content in the body, particularly in children, that poses later risk for cardiovascular diseases, diabetes, metabolic syndrome and non-alcoholic fatty liver disease (NAFLD). Normal-BMI children may have increased risk for cardiovascular disease.

Obesity in children is an early phenomenon. Cunningham et al performed a long-term observation on 7738 children who entered kindergarten in 1998 and were followed up through 2007 [8]. Among these children at average age of 5.6 years, 12.4% were obese and 14.9% were overweight. By the age of 14.1 years, the frequency of obese children increased almost two-fold, up to 20.8% whereas the frequency of overweight increased only up to 17%. The authors concluded that children with high birth weight and overweight before age of 5 years were at the highest risk of obesity. Many of these children/adolescents will become obese adults with enhanced risk for cardiovascular diseases (CVD). The US predictions are that the number of additional cardiovascular events in adulthood, attributable to excess weight in adolescence, is expected to be >100,000 by 2035 [9].

The aim of this review is to describe the spectrum of cardiometabolic abnormalities observed in children with overweight and obesity and the role of laboratory in the assessment of cardiovascular risk in order to predict those at highest risk to most effectively prevent progression of cardiovascular disease in childhood.

Table 1
Changes between 2001/2002 and 2009/2010 in the percentage of young children aged 11, 13 and 15 years who were overweight in selected countries (author's modification).

Country	% of overweight 2001/2002	% of overweight 2009/2010
Decreased		
France	12.0	11.0
United Kingdom	16.5	12.0
Leveled-off		
Denmark	9.0	9.1
Increased		
Netherlands	6.5	8.5
Sweden	10.0	11.5
Czech Republic	9.5	14.2
Poland	8.0	15.1
Canada	18.5	19.7
Greece	16.5	20.7
United States	24.0	29.0

Cardiometabolic risk factors related to childhood obesity

The etiology of childhood obesity may differ however, endocrine disturbances (hypothyroidism, growth hormone deficiency or resistance, excess of cortisol) and defects of the hypothalamus or genetic syndromes are rare. Development of obesity in children and adolescents has a harmful effect on the levels of several cardiovascular risk factors. The pattern of fat distribution has a profound influence on cardiometabolic risk and the increase in abdominal adipose tissue confers an independent risk. Childhood obesity is often accompanied by serious consequences such as dyslipidemia, hypertension, diabetes and non-alcoholic fatty liver disease [Fig. 1]. Increased body fat in children was also associated with vitamin D insufficiency and iron-deficiency, instead bone mass in obese children was shown to be greater [1]. The studies performed between 2001 and 2008 on large populations of children, reported that in 52% of overweight children at least one cardiovascular and metabolic risk factor was seen, with the highest frequency of hypertension (35%) with increased left ventricular mass or arterial stiffness [10]. Dyslipidemia was found in up to 32% and hyperglycemia or glucose intolerance in 3%. Hypertension, insulin resistance and dyslipidemia were better correlated to waist circumference than BMI and body fat.

Evidently, early in life cardiovascular disease has not yet progressed to the same endpoint as in adults. Besides, some abnormalities such as alterations in glucose metabolism are age-, gender- and pubertal stage-dependent [11]. Nevertheless, obesity in childhood at ages 9 to 12 years, was associated with increased cardiovascular risk factors in 15 to 16 year-olds, although the risk can be decreased in obese children by achieving normal weight by adolescence [12]. It was found that the association between body fat mass measured in childhood and cardiovascular risk factors in adolescence was gender-dependent and stronger in boys. In addition, boys who lost weight by ages 15–16 years had higher systolic blood pressure, higher triglycerides and lower HDL-cholesterol levels than those who were normal weight at both ages [13].

In obese children changes in cardiac structure and function, similar to that of middle-age adults, are observed. BMI in childhood is a good predictor of left ventricular mass in early or mid adulthood [12]. Very recently, assessing geometric and functional changes of the heart in obese compared with nonobese children and adolescents, with the use of 2-dimensional echography (2D) and 2D speckle-tracking analysis, Mangner et al have found that childhood obesity is associated with significant changes in myocardial geometry and function [14]. These observations confirm an early onset of unfavorable alterations in the myocardium. Interestingly, obese children with diagnosed non-alcoholic fatty liver disease (NAFLD) were shown to exhibit subclinical left ventricular dysfunction independent of cardiovascular and metabolic alterations other than liver damage [15,16].

Increasing prevalence of obesity in children leads to a greater occurrence of NAFLD which comprises several conditions: fatty liver, nonalcoholic steatohepatitis accompanied by inflammation and fibrosis (NASH) and cirrhosis with increased risk of hepatocellular carcinoma [17]. NAFLD development is influenced by multiple genetic and environmental factors. Currently NAFLD is recognized as the hepatic component of metabolic syndrome due to the strong association with obesity, insulin resistance index (HOMA-IR), dyslipidemia and hypertension. The relationship among adiposity and metabolic abnormalities such as insulin resistance, dyslipidemia, hypertension and NAFLD was assessed in children aged 2–5.8 years at the onset of overweight or obesity [18]. NAFLD was the most prevalent metabolic abnormality diagnosed in overweight and obese children followed by dyslipidemia and hypertension. Impaired glucose metabolism was the less prevalent metabolic