

# Metabolic Syndrome in Children

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## Abstract

There is no widely used international definition of Metabolic Syndrome (MetS) in children and adolescents, but all definitions include obesity as a prerequisite for the development of MetS, even in children. Obesity is one of the most important cardiometabolic risk factors and is strongly associated with a group of metabolic diseases associated with hyperlipidemia, hypertension and insulin resistance that are driven by underlying factors such as visceral obesity, systemic inflammation and cellular dysfunction. These risks increasingly begin in childhood and adolescence and are associated with a higher probability of future chronic disease in adulthood. Efforts should be made to recognize this metabolic risk screen for potentially associated Type 2 diabetes and primarily target affected individuals for appropriate treatment with lifestyle modification.

**Keywords:** Cardiovascular diseases • Metabolic syndrome • Obesity • Type 2 diabetes

## Introduction

Cardiovascular disease, the most common cause of death among adults worldwide, has its roots in childhood, underscoring the need to identify and intervene in children at risk [1,2]. This is even more important in the reality of the global obesity epidemic, where more than 100 million children worldwide are obese, including in developing regions [3].

Many children affected by the MetS already present with one or more cardiovascular risk factors or metabolic disorders such as dyslipidemia, impaired glucose tolerance and even type 2 diabetes, hyperuricemia, arterial hypertension and others [4]. As disease-related comorbidities increase with the severity of obesity at a young age, many obese children and adolescents already have elevated transaminases and Non-Alcoholic Fatty Liver Disease (NAFLD), orthopaedic problems, psychological comorbidities such as depression or attention deficit disorders and sleep disorders. In addition, the risk of malignancy increases significantly later in life.

This review aims to provide a brief and critical overview of our current understanding of metabolic syndrome in childhood and adolescence and to highlight the seriousness of the condition.

## Literature Review

There is no accepted international consensus on how to define MetS in children, so far. According to the most widely used MetS definitions for the pediatric population, by the International Diabetes Federation (IDF) and Cook, et al. As described, MetS can be diagnosed by the presence of abdominal obesity and two or more other clinical features [5,6]. Abdominal obesity is defined as increased waist circumference (WC) based on age- and sex-specific percentile curves. **Table 1** shows the diagnostic criteria for metabolic syndrome [7-10].

The pathophysiology of MetS (Metabolic Syndrome) is not yet

fully understood. The World Health Organization assumes that insulin resistance (IR) is the most important factor in the development of MetS. It is widely accepted that obesity and secondary inflammation are major components of IR.

A thorough clinical examination is essential to identify cardiometabolic risk in obese children. Anthropometric measurements should include standard determination of body weight, height, hip and waist circumferences by applying age and sex-specific percentages. Clinical examination should also include a pubertal assessment according to Tanner, clinical signs of cardiometabolic risk factors such as acanthosis nigricans, striae distensae, and hirsutism. By investigating symptoms such as dysmorphia, mental retardation and growth retardation, syndromes associated with obesity can be excluded [11]. If the presence of cardiometabolic complications is suspected, a fasting blood sample should be obtained and a basal check should be performed, including fasting glucose and insulin, transaminases, lipids, uric acid. In addition to fasting glucose and fasting insulin,

HOMA-IR (Homeostatic Model Assessment Of Insulin Resistance) should be evaluated [4]. It should be emphasized that HOMA-IR cannot be evaluated in adolescents as in adults. The reduced insulin sensitivity associated with the onset of puberty should be kept in mind [12]. According to the recommendation of the American Diabetes Association (ADA), an oral glucose tolerance test should be performed in children older than 10 years of age who are obese and have a relative with type 2 diabetes (first or second degree), provided that a maximum of 75 g glucose is used at a dose of 1.75 g/kg [13].

Uric acid is a product of purine metabolism due to protein catabolism. Its increased levels are associated with a high intake of purines (animal protein, meat and seafood) and fructose (processed food). Uric acid plays an important role in the pathophysiology of arterial hypertension, kidney function, congestive heart failure and the development of type 2 diabetes. [14]. Non-Alcoholic Fatty Liver Disease (NAFLD) has been recognized as hepatic involvement of MetS. It is the most common form of chronic liver

**Table 1:** Diagnostic criteria for metabolic syndrome in children adapted from flemming et al. [10].

Authors (Ref.), year	Criteria for metabolic syndrome (three or more criteria fulfilled?)
Cook et al. (6), 2003	WC: Waist Circumference TG: Triglycerides SBP: Systolic Blood Pressure pct.: Percentile HDL-C: High-Density Lipoprotein Cholesterol WC ≥ 90 th pct., SBP or DBP ≥ 90th pct., TG ≥ 1.24 mmol/L or HDL-C ≤ 1.03 mmol/L, fasting glucose ≥ 6.11 mmol/L
De Ferranti et al. (7), 2004	WC > 75 th pct., BP > 90 th pct., TG ≥ 1.1 mmol/L, HDL-C < 1.17 mmol/L (girls), HDLC < 1.3 mmol/L (boys), fasting glucose ≥ 6.1 mmol/L BP: Blood Pressure
Viner et al. (8), 2005	BMI ≥ 95 th pct., SBP ≥ 95th pct., TG ≥ 11.6 mmol/L or HDL-C ≤ 0.91 mmol/L or total cholesterol ≥ 95th pct., insulin ≥ 104.2 pmol/L or fasting glucose ≥ 5.55 mmol/L
Zimmer et al. (IDF) (4), 2007	WC ≥ 90 th pct., SBP ≥ 130 mm Hg or DBP ≥ 85 mm Hg, TG ≥ 1.69 mmol/L or HDL-C ≤ 1.03 mmol/L, fasting glucose ≥ 5.55 mmol/L DBP: Diastolic Blood Pressure
Ahrens et al. (9), 2014	WC ≥ 90 th (95 th) pct., SBP/DBP ≥ 90th (95th) pct., TG ≥ 90 th (95th) pct. or HDL-C ≤ 10th (5th) pct., HOMAIR ≥ 90th (95th) pct. or fasting glucose ≥ 90 (95th) pct. HOMA-IR: Homeostatic Model Assessment of Insulin Resistance

disease in childhood, and it is estimated that 20% of obese children already suffer from NAFLD. High levels of Alanine-Aminotransferase (ALAT) and Gammaglutamyl Transferase (GGT) may give us a clue about the disease. In addition, these two parameters are strongly associated with BMI or high waist circumference [15].

Arterial blood pressure, one of the cardiometabolic risk factors, should be measured at rest and in the lying position, and the mean value of the three measurements should be documented. If systolic or diastolic blood pressures are greater than the 95th percentile on the curves calculated for children, arterial hypertension should be suspected and confirmed by 24-hour blood pressure measurement [16]. Adipose tissue is considered an endocrine organ that secretes a variety of different factors such as adipokines (eg, adiponectin, chemerin, leptin) and proinflammatory cytokines (eg, TNF- $\alpha$ , IL-6). These factors are associated with metabolic and cardiovascular risk factors [17].

Adipocyte dysfunction includes decreased adiponectin production (which appears to be in the causal pathway of insulin resistance) and a higher release of free fatty acids [7,18]. In peripheral tissues, these high levels of free fatty acids and triglycerides alter mitochondrial function and increase the degree of oxidative stress through the effect of a general decrease in insulin's ability to stimulate glucose transporters to the cell surface.

Obese adolescent girls should be evaluated for PCOS, even though there is still controversy about the underlying etiopathogenesis, diagnostic criteria, and recommendations for PCOS in adolescents. Diagnostic criteria for PCOS in adolescents include an abnormal uterine bleeding pattern (abnormal for age or gynaecological age, persistent symptoms for 1 year-2 years) and evidence of hyperandrogenism (persistent elevation of testosterone above adult norms, moderate-to-severe hirsutism, and moderate-to-severe inflammatory acne) [19].

Early diagnosis and successful treatment are known to be the basis for reducing morbidity and mortality associated with MetS [20]. We recommend screening children for overweight and obesity and their comorbidities, using the WHO definition of overweight (one standard deviation BMI for age and sex) and obesity (two standard deviations BMI for age and sex) (last accessed 11.11.2019). Lifestyle intervention forms the basis of obesity treatment. It is the "gold standard" or major treatment option for the majority of adolescents and pediatric patients to date. Lifestyle change should include a balanced diet with energy-dense, reduced sugar and fat-rich products, an increase in daily physical activity, and behavioural therapy [11].

## Conclusion

The best way to reduce the prevalence of MetS in the future is to prevent obesity in children and adolescents. This includes efforts to promote an active lifestyle from a young age and maintain physical activity levels among younger children. In addition, families should be encouraged to consume fresh food and stay away from energy-intensive prepared foods. The availability of safe spaces for physical activity and healthy eating options in schools should be ensured.

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