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METABOLIC SYNDROME IN CHILDREN AND ADOLESCENTS

Introduction: The metabolic syndrome in adults has been defined as a cluster of the most dangerous risk factors for cardiovascular disease and type 2 diabetes mellitus which include abdominal obesity, high cholesterol, high blood pressure, diabetes and raised fasting blood glucose. (1). People with the metabolic syndrome are two to three times as likely to have a heart attack or stroke and five times as likely to develop type 2 diabetes compared with people without the syndrome. Almost, four million deaths every year are a consequence of diabetes-related causes (1).

A quarter of the adult population has metabolic syndrome. The prevalence of this condition is rising in children and adolescents due to the growing prevalence of obesity (2, 3).

The aim to rationalize the existing multiple definitions of the metabolic syndrome and establish a single, universally accepted diagnostic method easy to use in clinical practice, not only founded upon measurements mostly available in research setting, in 2005, the International Diabetes Federation (IDF) published its definition of the metabolic syndrome in adults (1). The use of a single unified definition makes it possible to estimate the world prevalence of metabolic syndrome and make valid comparisons between countries.

In similar to the definition in adults, the consensus definition of metabolic syndrome in children and adolescents was established and obtained a universally accepted tool easy to use for the early diagnosis of syndrome (1).

Global burden of children and adolescents with obesity

In 2004, the World Health Organization estimated that approximately 22 million children under the age of five years were overweight or obese (4). According to a report from the International Obesity Task Force (IOTF), at least 10% of school-aged

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children between five and 17 years are overweight or obese representing a total of 155 million children. Approximately 30 - 45 million of these children are obese, accounting for 2-3% of the world's children aged 5-17.

The situation in almost all countries of the world is getting worse. For example, in the United States the rate of overweight and obesity in children and adolescents aged 6 to 18 years increased to more than 25% in the 1990s from 15% in the 1970s. (6). The increase of prevalence of obesity is not restricted to developed countries; it has been registered in many low- and middle-income countries. It is estimated that 17 of 22 million obese children under five live in developing countries (7).

Obesity in early life is of particular concern due to its associated health consequences and its influence on young people's psychosocial development. Treatment of obesity is complex related with significant material expenses and often unsuccessful. Almost one half of overweight adolescents and more one third of overweight children remain obese as adults (7).

Each of these children is at increased risk of developing metabolic syndrome and progressing to type 2 diabetes and cardiovascular disease in later life. Early identification of children at risk and preventive action are therefore very important. Unless action is taken, diabetes experts agree that this is the first generation where children may live shorter than their parents (2).

Definition and prevalence of metabolic syndrome in children and adolescents

Obesity is the main phenotypic characteristic of metabolic syndrome in adults and has been determined as a key precipitating factor of the syndrome (1). The data of increasing prevalence of obesity in children and adolescents raise a question about the prevalence of metabolic syndrome in these age groups. The findings of the Bogalusa Heart Study from United States show that almost 50 per cent of obese adolescents have one or more components of metabolic syndrome (8). In children and adolescents with BMI higher than 85. percentile for age and sex, probability of findings of high cholesterol level were 2,4 times, high LDL-cholesterol 3,0 times, low HDL-cholesterol 3,4 times, high triglycerides 7,1 times, and hypertension 4,5 times more than in children with normal body weight (8).

The total prevalence of metabolic syndrome, and prevalence of each single components of syndrome, increase directly with the body weight independently of the age, gender and pubertal stage. The new epidemiological studies show that 4 per cent of all adolescents and 30 per cent of obese adolescents from United States have metabolic syndrome (3). In obese children and adolescents prevalence of metabolic syndrome reach 30-50 per cent (9, 10, 11).

In spite of the mentioned, it is necessary to point out that metabolic syndrome is not a universal phenomenon even in the children who are overweight at early age

(12). Namely, in some children with extreme type of obesity there is not even one sign of metabolic syndrome nor signs indicating direct risk of development of type 2 diabetes. The risk of insulin resistance increases in puberty when sex and ethnic differences regarding insulin-sensitivity of tissues became more manifested. It is assumed that the risk rate of development of metabolic syndrome is also significantly influenced by differences in prenatal and postnatal growth velocity, or weight gain which particularly increased in children born with low or high body mass (13, 14).

The people with higher level of central obesity develop this syndrome more frequently than people with peripheral type of obesity (15). In children the total amount of body fat and amount of visceral fat influences to the level of insuline resistance. The visceral fat has prevalent influence to fasting insuline levels (16). In addition to peripheral insuline resistance, obese children have elevated levels of metabolic and inflamatory factors from adipose cells (17).

The rationale for the new definition of metabolic syndrome

The new definition is simple and easy to apply in clinical practice. Similarly to the adult criteria, waist measurement is the main component because it is an independent predictor of insulin resistance, lipid levels, and blood pressure (20). In young people who are obese and have similar body-mass index (BMI), insulin sensitivity is lower in those with high amounts of visceral adipose tissue than in those with low amounts (21, 22).

Blood pressure, lipid levels as well as body size and proportiona change with age and development. Puberty has an impact on fat distribution and on both insulin sensitivity and secretion (23). Although, single cut-off points can not be used to define abnormalities in children. Percentiles, rather than absolute values of waist circumferencs have been used to compensate for variation in child development and ethnic origin. So for example, values above 90th, 95th or 97th percentile for gender and age are used. Although there has not been universal agreement as to which level to use for the criteria for metabolic syndrome, several studies, have used the 90th percentile as a cut-off for waist circumference. (1, 2, 24). Children with a waist circumferenec higher than 90th percentile are more likely to have multiple cardiovascular disease risk factors thane are those with a waist circumference below this level (25). IDF has chosen cut-off for waist circumference, which will be reassessed when more outcome data become available.

Diagnosis of metabolic syndrome in children and adolescents

For the dignosis of metabolic syndrome in children and adolescents the same criteria for the diganosis in adults can be used with adaptations of criteria according to age and gender of patients (17). Clinical definition of metabolic syndrome includes the findings of three or more characteristic clinical or laboratory findings:

- obesity defined as BMI higher than 97. percentile (standard deviation score or z-score $\geq 2,0$),
- triglyceride higher than 95. percentile,
- HDL-cholesterol below 5. percentile
- systolic or diastolic blood pressure higher than 95. percentile
- disorder of glucose tolerance.

The new IDF definition is divided according to age-groups because of age-related differences in children and adolescents: age 6 years to younger than 10 years; age 10 years to younger than 16 years; and 16 years or older (1, 24, 25). IDF suggests that the metabolic syndrome should not be diagnosed in children younger than 10 years, but a strong message for weight reduction should be delivered for those with abdominal obesity. For children age 10 years or older, metabolic syndrome can be diagnosed with abdominal obesity and the presence of two or more other clinical features (elevated triglycerides, low HDL-cholesterol, high blood pressure, increased plasma glucose). For adolescents older than 16 years, the IDF adult criteria can be used. The IDF consensus definition of metabolic syndrome in children and adolescents are presented in Table 1. Further research is needed to identify optimum criteria for definition of the syndrome.

Table 1. *The IDF consensus definition of metabolic syndrome in children and adolescents (24).*

Age 6 – 10 years
- Obesity defined as waist circumference ≥ 90 th percentile
- Further measurement should be made if there is a family history of metabolic syndrome, type 2 diabetes mellitus, dyslipidemia, cardiovascular disease, hypertension and/or obesity
Age 10 – 16 years
- Obesity defined as waist circumference ≥ 90 th percentile
- Triglycerides $\geq 1,7$ mmol/l
- HDL-cholesterol $\geq 1,03$ mmol/l
- Systolic blood pressure ≥ 130 or diastolic ≥ 85 mmHg
- Glucose $\geq 5,6$ mmol/l or type 2 diabetes mellitus
Age >16 years
- Use criteria for adults

Recommendation for prevention and treatment

IDF recommends that prevention and management for the metabolic syndrome is a healthy lifestyle that include: moderate calorie restriction to achieve a 5-10 per cent loss of body weight in the first year, moderate increase in physical activity and change in dietary composition. Pharmacotherapy can be included if its safety has been clearly demonstrated.

Early detection and treatment is likely to reduce morbidity and mortality in adulthood and help keep to a minimum burden of cardiovascular disease and type 2 diabetes mellitus.

References

- Alberti KGMM, Zimmet PZ, Shaw JE. The metabolic syndrome – a new world-wide definition from the International Diabetes Federation Consensus. *Lancet* 2005; 366:1059–62.
- Weiss R, Dziura J, Burgert TS, Tamborlane WV, Taksali SE, Yeckel CW, et al. Obesity and metabolic syndrome in children and adolescents. *N Engl J Med* 2004; 350:2362–74.
- Cook S, Weltzman M, Auinger P, Nguyen M, Dietz WH. Prevalence of metabolic syndrome phenotype in adolescents: findings from the third National Health and Nutrition Examination Survey, 1988–1994. *Arch Pediatr Adolesc Med* 2003; 157:821–7.
- World Health Organization. Global strategy on diet, physical activity and health: Obesity and overweight, 2004. Available from: <http://www.who.int/dietphysicalactivity/publications/facts/obesity/en/> Accessed on 20/11/2009.
- Lobstein T, Baur I, Uauy R; IASO International Obesity Task Force. Obesity in children and young people: a crisis in public health. *Obes Rev* 2004; 5 Suppl 1, 4–104.
- Wang Y, Lobstein. Worldwide trends in childhood overweight and obesity. *Intern J Pediatr Obesity* 2006; 1:11–25.
- World Health Organization, Fight Childhood Obesity to prevent diabetes, say WHO and IDF. Available from: <http://www.who.int/mediacentre/news/releases/2004/pr81/en/index.html>. Accessed on 01/12/2009.
- Freedman DS, Khan LK, Dietz WH, Srinivasan SR, Berenson GS. Relationship of childhood obesity to coronary heart disease risk factors in adulthood: the Bogalusa Heart Study. *Pediatrics* 2001; 108:712–8.
- Weiss R, Dziura J, Burgert T, Tamborlane W, Taksali S, Yeckel CW, et al. Obesity and the metabolic syndrome in children and adolescents. *N Engl J Med* 2004; 350:2362–74.
- Viner RM, Segal TY, Lichtarovitz-Krynska E, Hindmarsh P. Prevalence of the insulin resistance syndrome in obesity. *Arch Dis Child* 2005; 90:10–4.
- Bokor S, Frelut ML, Vania A, Hadjiathanasiou CG, Anastasakou M, Malecka-Tendera E, et al. Prevalence of metabolic syndrome in European obese children. *Int J Pediatr Obes* 2008; 3 Suppl 2:3–8.
- Weill J, Vanderbecken S, Froguel P. Understanding the rising incidence of type 2 diabetes in adolescence. *Arch Dis Child* 2004; 89:502–5.

- Ong KKL, Dunger DB. Thrifty genotypes and phenotypes of type 2 diabetes mellitus. *J Paediatr Endocrinol Metab* 2000; 13:1419–24.
- Li C, Johnson MS, Goran MI. Effects of low birth weight on insulin resistance syndrome in Caucasians and African-American children. *Diabetes Care* 2001; 24:2035–42.
- Kissebah AH, Krakower GR. Regional adiposity and morbidity. *Physiol Rev* 1994; 74:761–71.
- Goran MI, Gower BA. Longitudinal study on pubertal insulin resistance. *Diabetes* 2001; 50:2444–50.
- Weiss R, Dziura J, Burgert T, Tamborlane W, Taksali S, Yeckel CW, et al. Obesity and the metabolic syndrome in children and adolescents. *N Engl J Med* 2004; 350:2362–74.
- Hirschler V, Aranda C, Calcagno Mde L, Maccalini G, Jadzinsky M. Can waist circumference identify children with the metabolic syndrome? *Arch Pediatr Adolesc Med* 2005; 159:740–4.
- Lee S, Bacha F, Arslanian SA. Waist circumference, blood pressure, and lipid components of the metabolic syndrome. *J Pediatr* 2006; 149:809–16.
- Bacha F, Saad R, Gungor N, Arslanian SA. Are obesity-related metabolic risk factors modulated by the degree of insulin resistance in adolescents? *Diabetes Care* 2006; 29:1599–604.
- Bloch CA, Clemons P, Sperling MA. Puberty decreases insulin sensitivity. *J Pediatr* 1987; 110:481–7.
- Singh R, Shaw J, Zimmet P. Epidemiology of childhood type 2 diabetes in the developing world. *Pediatric Diabetes* 2004; 5:154–68.
- Maffeis C, Pietrobelli A, Grezzani A, Provera S, Tato L. Waist circumference risk factors in prepubertal children. *Obes Res* 2001; 9:179–87.
- Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. *Lancet* 2005; 365:1415–28.
- Zimmet P, Alberti KGMM, Kaufman F, Tajima N, Silink M, Arslanian S, et al. IDF Consensus Group. The metabolic syndrome in children and adolescents – an IDF consensus report. *Pediatric Diabetes* 2007; 8:299–306.