Archives of Medical Research 47 (2016) 40–48

ORIGINAL ARTICLE

Models Predictive of Metabolic Syndrome Components in Obese Pediatric Patients

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Received for publication May 25, 2015; accepted January 14, 2016 (ARCMED-D-15-00370).

Background and Aims. Components of metabolic syndrome (MetS) are complications caused by abdominal obesity and insulin resistance (IR). Diagnosis of MetS by clinical indicators could help to identify patients at risk of cardiovascular disease and type 2 diabetes. We undertook this study to propose predictive indicators of MetS in obese children and adolescents.

Methods. A cross-sectional study was carried out. After obtaining informed consent and the registration of the study with an institutional research committee, 172 obese patients from an Obesity Clinic, aged 6–15 years, were included. Variables included were waist circumference (WC), glucose, high-density lipoprotein (HDL), triglycerides (TGL), blood pressure, insulin resistance (by homeostatic model assessment HOMA-index), acanthosis nigricans (AN), uric acid, serum glutamic oxaloacetic transaminase (GOT) and alanine transaminase, and hepatic sonogram. International standards for age and sex variables were used. Multivariate analysis was applied.

Results. Variables predicted components of MetS in children: HOMA-IR (insulin resistance by HOMA index) was increased by 2.4 in hepatic steatosis, by 0.6 for each unit of SUA (serum uric acid), and by 0.009 for every mg/dL of triglycerides. In adolescents, every cm of waist circumference increased systolic blood pressure by 0.6 mmHg, and each unit of SUA increased it by 2.9 mmHg.

Conclusions. Serum uric acid and waist circumference are useful and accessible variables that can predict an increased risk of cardiovascular disease in obese pediatric patients.

Key Words: Insulin resistance, Obesity, Uric acid, Waist circumference.

Introduction

In pediatrics, metabolic syndrome (MetS) is defined as a set of metabolic, vascular, inflammatory, profibrinolytic, and coagulation disturbances and is associated with an increased risk of developing type 2 diabetes mellitus (DM2) and cardiovascular diseases (CVD) (1). MetS is manifested primarily in overweight or obese children, with alterations in lipid metabolism particularly low concentrations of high-density cholesterol (HDL ≤40 mg/dL) and high levels of triglycerides (TGL ≥150 mg/dL), hypertension (≥130/85 mm/Hg), and alterations in the glucose metabolism (fasting hyperglycemia ≥100 mg/dL by glucose intolerance, prediabetes, or DM2) (2,3).

In addition to these established components of MetS, other common disorders are included. These are classified as nontraditional components of MetS such as microalbuminuria (albumin-creatinine ratio 30–300 mg/g), high

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0188-4409/$ - see front matter.
http://dx.doi.org/10.1016/j.arcmed.2016.01.003

HOMA-IR (insulin resistance by HOMA index ≥3 μU/mL), acanthosis nigricans (AN = pigmented and rough areas of skin especially in folds), nonalcoholic fatty liver disease (NAFLD), high SUA (≥5.2 mg/dL), polycystic ovaries, hypercoagulability, fibrinolysis, gallstones, osteoporosis and, finally, a high risk of developing CVD in adulthood (4). However, these components have not been added to the definitions of MetS because their measurement is not routinely performed (5).

Early diagnosis of MetS in adults is important because it allows us to identify individuals with an increased risk of CVD and diabetes mellitus (DM); however, for pediatric patients, the diagnosis has not been standardized. Studies in children and adolescents indicate that the process of atherosclerosis begins in childhood and is associated with obesity and other components of MetS (6).

For example, waist circumference (WC) as a predictor of cardiovascular risk has been considered to be controversial in children. However, some studies define it as a good indicator of IR, likewise the HOMA-IR index as a predictor of MetS. IR in obese children is closely associated with components of MetS. If MetS is already present in children, early individual diagnosis of its components can identify children at risk of future cardiovascular disease as previously described in adults (7,8).

Several population studies indicate that biological markers of inflammation predict CVD. Thus, elevation of serum levels of C-reactive protein (CRP), uric acid, interleukin 6 (IL-6), tumor necrosis factor alpha (TNF-α), leptin, and decreased levels of adiponectin and interleukin-10 (IL-10) are variables that are correlated with alterations of MetS (1,9).

Increased insulin levels are a predictor of atherogenic changes, even in the earlier stages of hyperglycemia, considering it to be among the markers of subclinical atherosclerosis in asymptomatic patients (10).

Obesity in childhood is predictive of MetS in adults, and this prediction is strengthened if the obesity is in concert with comorbidities. It is important to consider that this condition has a long period of evolution until adulthood, causing an extended exposure to conditions that cause cardiovascular disease or diabetes in early stages of adult life, which has severe consequences for the quality and expectation of life of every individual affected. Hence the importance of identifying the components of MetS in children and adolescents, seeking to intervene in order to prevent comorbidities (11).

Therefore, the pediatrician should actively look for components of MetS in overweight or obese children and adolescents, seeking to treat them in a timely manner to prevent or delay the onset of additional comorbidities (hypertension, dyslipidemia, impaired glucose tolerance, or DM2), which cause a high level of damage to the health of persons at all ages (12).

The prediction models could perform as early indicators of the most frequent and future complications. In other words, the individual detection of MetS components can predict a higher risk of future complications and comorbidities.

The aim of our study was to propose models predictive of MetS components to improve our opportunity for identifying obese youth at the highest metabolic and cardiovascular risk.

Methods

After approval of the study by the Local Committee for Research of the Pediatric Hospital #R-2012-1302-38 and after the children's parents had signed informed consent, 172 patients aged from 6 to 15 years were included in our study. All were obese outpatients attending the Obesity Clinic of the UMAE Hospital de Pediatria, Western National Medical Center of IMSS in Jalisco, Mexico; a third level reference facility localized on the Western coast of Mexico treating an average of 20 new overweight and obese children per month. All invited participants agree to be included in the study, without any refusals. Clinical and biochemical evaluations included belong to a standardized screening protocol of care in the clinic. Only those who fulfilled the clinical and biochemical evaluation were included in the study. Patients were classified into two groups: children 6−10 years and adolescents aged 11−15 years according to the classification of the World Health Organization. We excluded patients with endocrine and genetic pathologies as well as those receiving glucocorticoids.

Measurements

For each participant, the following measurements were taken including weight, height, WC, and waist-to-height ratio (WHtR) to determine percentiles of body mass index (BMI) according to the CDC (Centers for Disease Control and Prevention) (13). Based on tables for age and sex, WC was considered as abdominal obesity when the measurement was at or above the 90th percentile for age and sex according to the tables of Fernández et al. (14).

The patient's medical history was obtained by questioning the family member who accompanied the patient at the outpatient appointment. All patients were requested to undergo laboratory tests to determine glucose, total cholesterol, HDL, total TGL, fasting insulin, liver transaminases, SUA, and HOMA-IR, which were calculated to assess insulin resistance and considered to be abnormal when the value was ≥3 μU/mL and to be hyperinsulinemia when the value was ≥15 μU/mL, corresponding to the 95th percentile (15).

Clinical and Biochemical Examination

For the lipid profile, we considered the standardized values for age and sex of the ESC/EAS (European Society of Cardiology/European Society of Atherosclerosis) (16), and