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Prevalence of the Metabolic Syndrome in Overweight Children and Adolescents

Kobra Shiasi Arani

Research Center for Biochemistry and Nutrition in metabolic diseases, Kashan University of Medical Sciences, Kashan, I.R. Iran

Correspondence to:

Kobra Shiasi Arani, MD

Department of Pediatric Endocrinology

Kashan University of Medical Sciences Iran

Tel: +98-31-55580190

Fax: +98-31-55548900

Email: kobra.shiasi@yahoo.com

ABSTRACT:

Background— the prevalence of overweight and obesity among children and adolescents is increasing worldwide. Concordantly with the increase in obesity the prevalence of the metabolic syndrome is raising in children and youth. The metabolic syndrome imposes a substantial risk for type 2 diabetes mellitus and premature coronary heart disease.

Methods— Metabolic syndrome is defined by the Third Report of the Adult Treatment Panel (ATP III) using criteria easily applied by clinicians and researchers for adults. There is no standard pediatric definition. We defined pediatric metabolic syndrome using criteria analogous to ATP III as 3 of the following: (1) fasting triglycerides over 95 th percentile for age and gender; (2) high density lipoprotein (HDL) cholesterol level below 5 th percentile for age and gender; (3) fasting glucose ≥6.1 mmol/L (110 mg/dL); (4) body mass index (BMI) ≥ 95 th percentile for age and gender; and (5) systolic blood pressure over 95 th percentile for age and gender. We used the Homoeostasis model assessment score (HOMA score) to detect the degree of insulin resistance.

Results —The study included 484 children and adolescents aged 4 to 18 years (290 girls and 194 boys; mean age10.58 years; mean BMI: 11.11). Metabolic syndrome was present in 30.7% of overweight adolescents (BMI ≥95 th percentile) compared with 3.7% of at-risk adolescents (85 th to 95 th BMI percentile) and none of those with a BMI below the 85 th percentile (P<.001). About 36.4% of normal weight subjects, 54.5% of at risk of overweight subjects and 55.7% of overweight had at least 1 metabolic abnormality (fasting glucose≥110 mg/dl, high triglyceride, low HDL). Mean HOMA index is 2.16 in normal weight subjects, 2.60 in at risk of overweight subjects and 3.85 in overweight subjects. HOMA score =3.18 had 67**%** sensitivity and 60.8**%** specificity for predict of metabolic syndrome in overweight subjects.

Conclusions—Metabolic syndrome is common in overweight Iranian children and adolescents and they have similar prevalence of metabolic derangements associated with obesity. Because childhood metabolic syndrome likely tracks into adulthood, early identification may help target interventions to improve future cardiovascular health.

Key Words: metabolic syndrome _ pediatrics _ overweight _ HOMA index

INTRODUCTION

The prevalence of the overweight and obesity is rising in children and youth worldwide (1) concordantly with the increase in obesity the prevalence of the metabolic syndrome is raising in children and adolescents (2). Studies among Iranian school children indicate a similar trend (3, 4).The syndrome is characterized by several metabolic abnormalities, including insulin resistance, glucose intolerance, dyslipidemia and hypertension (2) .South Asian children living in the United Kingdom have a relative risk for type 2 diabetes that is 14 times greater than in white European children(5) , and Whincup et al found that British children of South Asian ethnicity have higher levels of glucose and insulin compared to their British counterpart(6). Ethnic differences in the prevalence of the metabolic syndrome were partly explained by various degrees of obesity. The prevalence of the overweight and obesity in Iranian children and adolescents is estimated to be 21% but there is a lack of sufficient data about the prevalence of metabolic syndrome in overweight Iranian children and adolescent(7). The aim of this study is to determine the prevalence of metabolic syndrome in overweight Iranian children and adolescent.

METHODS

The individuals were evaluated in a clinic interview to determine current medical conditions, medication use, and family medical history. Height was measured in an standing position with a stadiometer, and weight (kilograms) was obtained with a digital scale. BMI was calculated by dividing body weight (in kilograms) by height (in meters square). To describe the proportion of children with increased body weight, the CDC's BMI-for-age and gender-specific growth charts were used to classify children as "normal weight" if their calculated z-score placed them below the 85^{th} percentile, "at risk for overweight" between the 85^{th} and 95^{th} percentile, or "overweight" if it was above the 95^{th} percentile. The Tanner stage of pubertal development was determined for both sexes as described by Tanner. Girls were staged according to breast development and pubic hair growth and boys were staged according to pubic hair growth and male genital stages .Blood pressure measurements were obtained by using repeated standard medical procedures, in that systolic and diastolic blood pressure measurements were taken twice. One average value for the systolic as well as the diastolic measurement was calculated and provided as systolic and diastolic blood pressure in millimeters of mercury (mmHg). The first and fifth Korotkoff sounds were used to represent

the systolic and diastolic values. Fasting blood samples were collected from Children and adolescents 4–18 years old (n = 484) after 12 hour fasting. Total triglycerides, high density lipoprotein (HDL), and fasting blood glucose levels were provided in milligrams per deciliter (mg/dL). The details of determination and analysis of the triglyceride levels, HDL cholesterol levels and glucose values previously have been described (8). We used the Homoeostasis model assessment score (HOMA score) to detect the degree of insulin resistance, with higher levels representing greater degrees of insulin resistance. HOMA score is assessed from the fasting glucose and insulin concentrations according to the formula: HOMA score = insulin [mU/L] × glucose [mmol/L]/22.5 (9). The sample consisted of 484 subjects aged 4 to 18 years, to whom the following exclusion criteria were applied:(1) had not fasted for 8 hours, (2) was currently pregnant, or (3) was taking medication classified as a blood glucose regulator, such as insulin, androgens or anabolic steroids, or adrenal corticosteroids.

DEFINITIONS

Although there is agreement on the diagnostic criteria for metabolic syndrome in adults, there is no consensus on the appropriate cut points for diagnosis in children(10, 11) .However, there is agreement that a measured fasting blood glucose value of ≥ 100 mg/dL reflects hyperglycemia(12).According to the National Cholesterol Education Program (NCEP, or Adult Treatment Panel III [ATP III]), persons meeting at least 3 of the following 5 criteria qualify as having the metabolic syndrome: elevated blood pressure, a low high density lipoprotein (HDL) cholesterol level, a high triglyceride level, a high fasting glucose level, and abdominal obesity. There is no general agreement for criteria of the metabolic syndrome in children or adolescents. Cook et al used modified the adult criteria for metabolic syndrome: (1) fasting triglycerides ≥110 (2) HDL ≤40 mg/dL; (3) fasting glucose ≥6.1 mmol/L (110 mg/dL); (4) Abdominal obesity, waist circumference ≥90 th Percentile for age and gender ; and (5) systolic blood pressure over 90 th percentile for age and gender(13). Magnhild L. et al also used these criteria for his study(14).

For more adaptation with age and gender we use from percentiles of triglycerides and high density lipoprotein (HDL) levels for definitions of hypertriglyceridemia and low HDL (15). Since there are no international standards for WC we used from body mass index (BMI) as a marker of obesity. Elevated systolic or diastolic blood pressure was defined as a value at or above the 95 th percentile for age, sex, and height. The reference value for elevated fasting

glucose was taken from the American Diabetes Association guideline of 110 mg/dL or higher (≥6.1 mmol/L) (16). To obtain overall prevalence estimates of metabolic syndrome, the children were classified as having metabolic syndrome when they met any three of the five possible diagnostic criteria.

STATISTICAL ANALYSIS

Metabolic syndrome prevalence was estimated in the study subgroups .Prevalence values were compared using the x^2 test for proportions for those children with and without the metabolic syndrome. Comparisons of means of continuous variables were done with the *t* test. To compare the means of age, BMI, Triglyceride, LDL, HDL, fasting glucose, fasting insulin and HOMA score the independent sample *t*-test was used for continuous normally distributed data and the Mann–Whitney *U*-test for not normally distributed data. The Chi-square test was obtained for compare qualitative independent variables in children's with and without the metabolic syndrome. All P-values are two-sided and a 5% level of significance was used . All statistical analyses were performed with SPSS 14.0.S

RESULTS

Characteristics of the subjects are shown in Table 1. The study included 484 children and adolescents aged 4 to 18 years (290 girls and 194 boys; mean age10.58 years; mean BMI 11.11kg/m^2).

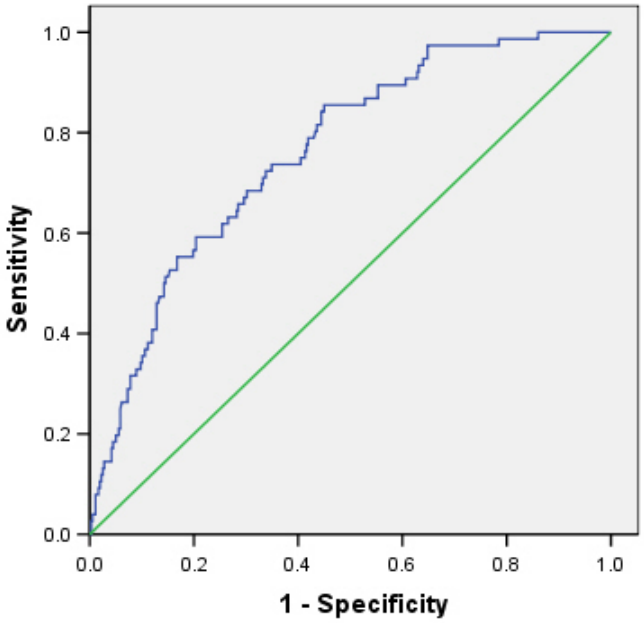
Table1:Demographic characteristics and prevalence of the metabolic syndrome in different weight groups.

Variables	Normal Weight	At Risk Of Overweight	Overweight
Mean age(yr)	10.42	11.73	10.21
Mean BMI(kg/m2)	16.46	22.85	27.83
High Triglyceride (%)	25	35.8	47.8
Low HDL (%)	12.5	31.3	24.4
High Total Cholesterol (%)	16.7	14.4	25.9
High LDL (%)	16.7	14.3	19.3

Variables	Normal Weight	At Risk Of Overweight	Overweight
Hypertension(%)	12.8	16.1	22.3
Impaired Fasting Glucose(%)	1.3	7.5	6
Mean Fasting Glucose(mg/dl)	94.60	94.08	95.35
Mean Fasting Insulin(micu/ml)	9.24	11.21	16.24
Mean HOMA score	2.16	2.60	3.85
Metabolic Syndrome(%)	0	3.7	30.1

The groups consisted of 75 subjects with normal wheight;107 subjects at risk of overweight and 302 overweight subjects (with CDC definition) and 233 subjects had BMI greater than 2SDS The overall prevalence of the metabolic syndrome was 19.6%(20.6% of males and 19% of females were affected(*P*=.35).The syndrome was present in 30.7% of overweight adolescents (BMI ≥95 th percentile) compared with 3.7% of at-risk adolescents (85 th to 95 th BMI percentile) and none of those with a BMI below the 85 th percentile (*P*=.001). Therefore is a strong association between weight status and prevalence of metabolic syndrome. About 36.4% of normal weight subjects, 54.5% of at risk of overweight subjects and 55.7% of overweight had at least 1 metabolic abnormality (fasting glucose≥ 110 mg/dL, high triglyceride, low HDL). Only 3 people of overweight subjects have all 5 of these risk factors. There were no significant differences in prevalence of metabolic syndrome in regard to pubertal stage (*P*=.55). Mean HOMA score is 2.16 in normal weight subjects, 2.60 in at risk of overweight subjects and 3.85 in overweight subjects. There is significant differences in mean HOMA score between the three groups (*P*=.0001) and the differences remained significant after adjustment for age and gender. HOMA score =3.18 had 67% sensitivity and 60.8% specificity for prediction of metabolic syndrome in overweight subjects. ROC curve for of HOMA score in overweight group is shown in the Figure1.

Figure1. ROC curve for HOMA score in overweight children and adolescents.



The study included 302 overweight subjects {168 girls (55.6%) and 134 boys (44.4%); mean age10.22 years; mean BMI 27.80 kg/m2). Prevalence of individual metabolic syndrome risk factors in overweight children with and without the metabolic syndrome are shown in Table 2.Overall, high triglyceride levels (91.2%)and low HDL (62.5%)cholesterol levels were most common, whereas high fasting glucose levels(14.2%) was the least common. Difference in the means of the age, BMI, pubertal stage and LDL cholesterol levels were not significant between two groups.

Table 2. Prevalence of individual metabolic syndrome risk factors in overweight children with and without metabolic syndrome.

Variables	NMS	MS	P value
Total (no)	211	91	
Male	94	39	0.78
Female	711	52	
Total (no)	901	73	
Prepubertal*	47.9	41.1	0.32
Pubertal*	52.1	58.9	
Mean age(yr)	0.151	0.331	0.60
Mean BMI(kg/m2)	27.57	28.44	0.019
Mean Triglyceride (mg/dl)	01.571	85.861	0.0001

Variables	NMS	MS	P value
High Triglyceride*	26.7	91.2	0.0001
Mean HDL (mg/dl)	47.46	38	0.0001
Low HDL*	7.9	62.5	0.0001
Mean LDL(mg/dl)	09.72**1**	5.11**11**	0.086
High LDL*	6.3**1**	26.1	0.052
Hypertention*	9.9	51.1	0.0001
Mean Fasting Glucose(mg/dl)	94.52	97.26	0.048
Mean Fasting Insulin(micu/ml)	4.32**1**	21.26	0.0001
Impaired Fasting Glucose*	2.4	4.3**1**	0.0001
Diabetes Mellitus*	**1**	2.3	0.54
Mean HOMA score	3.37	5.11	0.0001

MS: metabolic syndrome**; NMS**: no metabolic syndrome

*Described as percent.

DISCUSSION

Childhood and adolescent obesity may tracks into adulthood and predicts the development of metabolic syndrome in adulthood, although this is controversial (17, 18). In addition, Adults with metabolic syndrome frequently progress to type 2 diabetes with increased risk of morbidity and mortality from cardiovascular disease (19). Overweight and obesity in childhren and adolescent are associated with higher prevalence of physical morbidity and premature mortality in adulthood.(20)

Obesity alone increases the risk of hypertension, cholecystitis, and slipped capital femoral epiphysis and is associated with psychosocial symptoms in children (21).The metabolic syndrome affects an estimated 47 million American adults (8). An estimated 7% of men and 6% of women aged 20 to 29 years are affected with the metabolic syndrome (8). According report of *Cook et al* perhaps 4% of adolescents overall and nearly 30% of overweight adolescents meet the criteria for metabolic syndrome (13). Similarly our study demonstrates that a metabolic syndrome phenotype may exist in 3.7% of at-risk children and adolescents (85 th to 95 th BMI percentile) and 30.7% of overweight children and adolescents. Also our findings is similar with research in US children , in whom the prevalence of metabolic syndrome in US overweight/obese children aged 12 to 19 years was approximately 1 in 3

(Among children with BMI≥ 85th percentile for age and gender, the prevalence of metabolic syndrome was 31.2%) (22).The metabolic syndrome in adults is largely confined to the overweight population(8), similar with our findings and other researches in children and adolescents(13).Our study should be interpreted in light of its limitations. The primary limitation is that study outcomes depend on our definition of metabolic syndrome, a problem inherent to any of the adult definition to a pediatric population. The first our limitation was to consider how to define the metabolic syndrome for pediatric patients. Multiple definitions of pediatric metabolic syndrome have been used in various studies. The Quebec family cohort studies used skinfold measurement and mean blood pressure, criteria more cumbersome for the primary pediatrician(23). In a high-risk US population of obese children, 39% had metabolic syndrome when defined by body mass index instead of waist circumference, lipid levels >95 th percentile (or< 5 th percentile for HDL), and oral glucose tolerance testing (24).We use from BMI as a index of obesity (instead of waist circumference as a marker of abdominal obesity) as a criteria of metabolic syndrome. Similarity of our results with other studies suggests that BMI can be used as criteria of metabolic syndrome instead of waist circumference. Second limitation is definition of low HDL, in adults it considered as HDL<40mg/dl, however we consider HDL below 5th percentile for age and gender. For hypertriglyceridemia we consider fasting triglycerides over 95th percentile for age and gender instead of triglycerides ≥150 mg/dl in Adult Treatment Panel III [ATP III]) definition, and triglycerides ≥110 in one pediatric definition (13). Similarly for elevated blood pressure we consider systolic blood pressure over 95th percentile for age and gender, instead of systolic blood pressure ≥ 130/85 mmHg in Adult Treatment Panel III [ATP III]) definition. In contrast, in the case of glucose, we consider fasting glucose ≥6.1 mmol/L (110 mg/dL) as a definition of high fasting glucose similar to Adult Treatment Panel III [ATP III]) definition. Results of the Bogalusa Heart Study show that when insulin concentrations are increased in childhood they tend to remain elevated in adulthood, and those adults with consistently elevated insulin levels tend also to have increased rates of obesity, hypertension, and dyslipidemia(25).In the present study, children and adolescents with the metabolic syndrome had a HOMA index and mean fasting insulin levels meaningfully above that children and adolescents without the metabolic syndrome. These data confirm the relation of metabolic syndrome and insulin resistance.

CONCLUSION

This study demonstrates that a metabolic syndrome phenotype may exist in perhaps 30% of overweight Iranian children and adolescents. These data indicate that a substantial percentage of overweight Iranian children and adolescents may be at significantly high risk for the metabolic syndrome in adulthood and the subsequent risks for diabetes type 2 and premature coronary artery disease. Diet and life style changes might help prevent the development of the disease not only by preventing the onset of childhood obesity but also by improving diet quality to lower the risk for dyslipidemia in children independent of their weight status.

ABBREVIEATIONS

BMI, body mass index; CDC, Centers for Disease Control and Prevention HOMA score, homoeostasis model assessment score; ATP III ,Adult Treatment Panel III ; HDL, High Density Lipoproteins; LDL; low Density Lipoproteins; NHANES , National Health and Nutrition Examination Survey

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