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An Index for the Differential Diagnosis of Morbid Obese Children with and without Metabolic Syndrome

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***Abstract*—**Metabolic syndrome (MetS) is a severe health problem caused by morbid obesity, the severest form of obesity. The components of MetS are rather stable in adults. However, the diagnosis of MetS in morbid obese (MO) children still constitutes a matter of discussion. The aim of this study was to develop a formula, which facilitated the diagnosis of MetS in MO children and was capable of discriminating MO children with and without MetS findings. The study population comprised MO children. Age and sex-dependent body mass index (BMI) percentiles of the children were above 99. Increased blood pressure, elevated fasting blood glucose (FBG), elevated triglycerides (TRG) and/or decreased high density lipoprotein cholesterol (HDL-C) in addition to central obesity were listed as MetS components for each child. Two groups were constituted. In the first group, there were 42 MO children without MetS components. Second group was composed of 44 MO children with at least two MetS components. Anthropometric measurements including weight, height, waist and hip circumferences were performed during physical examination. BMI and homeostatic model assessment of insulin resistance (HOMA-IR) values were calculated. Informed consent forms were obtained from the parents of the children. Institutional Non-Interventional Clinical Studies Ethics Committee approved the study design. Routine biochemical analyses including FBG, insulin (INS), TRG, HDL-C were performed. The performance and the clinical utility of Diagnostic Obesity Notation Model Assessment Metabolic Syndrome Index (DONMA MetS index) [(INS/FBG)/(HDL-C/TRG)*100] was tested. Appropriate statistical tests were applied to the study data. p value smaller than 0.05 was defined as significant. MetS index values were 41.6 ± 5.1 in MO group and 104.4 ± 12.8 in MetS group. Corresponding values for HDL-C values were 54.5 ± 13.2 mg/dl and 44.2 ± 11.5 mg/dl. There was a statistically significant difference between the groups ($p < 0.001$). Upon evaluation of the correlations between MetS index and HDL-C values, a much stronger negative correlation was found in MetS group ($r = -0.515$; $p = 0.001$) in comparison with the correlation detected in MO group ($r = -0.371$; $p = 0.016$). From these findings, it was concluded that the statistical significance degree of the difference between MO and MetS groups was highly acceptable for this recently introduced MetS index. This was due to the involvement of all of the biochemically defined MetS components into the index. This is particularly important because each of these four parameters used in the formula is a cardiac risk factor. Aside from discriminating MO children with and without MetS findings, MetS index introduced in this study is important from the cardiovascular risk point of view in MetS group of children.

***Keywords*—**Fasting blood glucose, high density lipoprotein cholesterol, insulin, metabolic syndrome, morbid obesity, triglycerides.

I. Introduction

METABOLIC syndrome (MetS) may increase the risk of some chronic diseases. Obesity, as the major determinant, and insulin resistance are associated with most cases. As its name implies, metabolic derangements including various aspects of metabolism such as some physiological changes as well as biochemical alterations occur during the course of this syndrome. The most striking impaired physiology can be observed with elevated blood pressure values in systolic blood pressure and diastolic blood pressure. In addition to central obesity, elevated FBG, elevated TRG and/or decreased HDL-C are the biochemical abnormalities expected in MetS. Aside from obesity, the presence of at least two of these findings will lead to the diagnosis of MetS [1]-[4].

For the purpose of diagnosing MetS, some equations were introduced to be used in clinical practice and research by specifying the scores of the patients suffering from this disorder in adults. In one of such reports, in equations introduced for the calculation of these scores, waist circumference, height, FBG, TRG, SBP, HDL-C, age, gender and family history of cardio/cerebrovascular events were required [5].

The detection of the cases with MetS is well-established in adults, however, there are still some ambiguities concerning the MetS diagnosis in pediatric population, particularly among children other than adolescents. In some reports performed on pediatric population, researchers used INS instead of FBG [6], [7]. Our team also published an article reporting the preponderance of INS over FBG to represent MetS in children [8].

Classic cardiovascular risk factors tend to cluster into MetS among children [7], [9]-[14]. Whether the clustering of MetS components is attributable to only one or to multiple determinants is a matter of debate [15]. In adults, confirmatory factor analysis studies have suggested that there are four factors (obesity, blood pressure, insulin resistance, lipids) underlying MetS [16]-[18].

This study was designed to propose a formula to represent MetS cases among children. The aim was to develop a simple equation for the purpose. Biochemical parameters, which were known both as cardiovascular risk factors and also MetS

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components were used during the derivation of the equation. This index was evaluated in MO children with and without MetS.

II. Patients and Methods

A. Patients

In this study, two groups of morbidly obese children were formed. MO children, whose anthropometric, physiological and biochemical profiles did not exhibit characteristic features of specified parameters confined to MetS findings were included in the first group. These parameters were waist circumference (WC), systolic blood pressure (SBP), diastolic blood pressure (DBP), FBG, TRG, HDL-C. In the second group, there were MO children with MetS findings. Each child in this group had at least two of the previously specified MetS components. These abnormalities set were listed as follows: Central obesity, FBG levels above 100 mg/dl, SBP higher than 130 mm Hg and/or DBP higher than 85 mm Hg, TRG values higher than 150 mg/dl and/or HDL-C values lower than 40 mg/dl. Morbid obesity criteria were set based upon the World Health Organization recommendations [19]. Determinants of MetS were investigated for each participant [20]. In this study, children whose age and sex-adjusted BMI percentile values above 99 were defined as MO. The first group was composed of 42, and the second group comprised 44 MO children. Informed consent forms were filled out and signed by the parents of the participants. The study protocol summary was accepted by the Institutional Ethics Review Committee.

B. Anthropometric Measurements and Laboratory Tests

Anthropometric measurements e.g. height, weight, waist, hip, head, neck circumference values were recorded. Blood pressure values were determined. FBG, insulin, TRG, HDL-C analyses were performed.

C. Ratios, Obesity Indices Based on Body Weight and Body Fat, Cardiometabolic Index

Values for two previously reported ratios; (waist circumference + hip circumference)/2 and (trunk fat + leg fat)/2, were determined. Total body fat mass, total body fat percent, trunk fat mass, trunk fat percent, leg fat mass, leg fat percent as parameters related to body fat composition were determined using TANITA Bioelectrical Impedance Analysis. BMI, fat mass index (FMI), cardiometabolic index (CMI), HOMA-IR index, diagnostic obesity notation model assessment-II index (D2I) were calculated.

Values for D2I and FMI values as obesity indices based on body fat were calculated using the following formulas:

$$[\text{FMI} = \text{total body fat (kg)} / \text{height (m)}^2] \quad (1)$$

$$[\text{D2I} = \text{total body fat (kg)} * 100 / \text{height (cm)}] \quad (2)$$

$$[\text{CMI} = (\text{TRG-to-HDL-C ratio}) * (\text{waist circumference-to-height ratio})] \quad (3)$$

$$[\text{MetSI} = (\text{insulin-to-FBG ratio}) / (\text{HDL-C–to-TRG ratio})] \quad (4)$$

Equation (4) was developed in this study for the calculation of MetSI.

D. Statistical Analysis

Descriptive statistics, t-test, correlation analyses were performed and linear regression plots were drawn using the statistical package program SPSS.

III. Results

Mean ± standard deviation values of parameters and ratios related to anthropometry, fat distribution, biochemical parameters, obesity indices, insulin resistance index, CMI and MetSI calculated for MO children with and without MetS findings are listed in Table I.

TABLE I
Anthropometric Measurements, Biochemical Parameters, Fat Distribution Ratios and Obesity Indices of the Groups (mean ± SD)

Parameter	MO Group 1	MetS Group 2
WC*	83.0 ± 13.4	96.2 ± 17.1
FBG ^{NS}	89.8 ± 5.7	90.1 ± 5.3
INS ^{NS}	18.9 ± 15.5	24.8 ± 12.9
HDL-C *	54.5 ± 13.2	44.2 ± 11.5
TRG *	90.6 ± 33.7	150.4 ± 71.3
HOMA-IR ^{NS}	4.2 ± 3.6	5.6 ± 3.1
(WC+HC)/2*	88.0 ± 14.1	101.0 ± 17.1
(TF+LF)/2*	8.2 ± 4.8	14.5 ± 10.0
BMI*	25.8 ± 4.2	31.5 ± 8.3
FMI*	18.9 ± 11.1	30.7 ± 15.6
D2I*	12.6 ± 5.8	19.4 ± 9.1
MetSI *	41.6 ± 5.1	104.4 ± 12.8
CMI *	1.04 ± 0.51	2.38 ± 1.76

Ht = Height, INS = insulin, TF = trunk fat, LF = leg fat, D2I = diagnostic obesity notation model assessment-II index, MetSI = metabolic syndrome index, ^{NS} = not significant, [$^{*} < 0.001$]

WC values were significantly increased in Group 2 due to MetS findings. Similar patterns were observed for anthropometric ratios (WC+HC)/2, ratio using body fat compartments (TF+LF)/2, weight-based indices (BMI), fat-based indices (FMI, D2I) as well as CMI and the recently introduced MetSI.

Compared with FMI, the difference between the groups were much more striking for D2I. In a similar manner, compared with CMI, the difference between the groups were much more striking for MetSI.

Upon examination of correlations between HDL-C and MetSI, significant correlation coefficients and significance degrees were calculated. The plots concerning related regression lines are shown in Figs. 1 and 2.

Significant correlations between HDL-C and MetSI were obtained. In the first group, these values were r = -0.371, p = 0.016. The corresponding values were r = -0.515, p = 0.001 in MO children with MetS components. A much stronger correlation was detected in MetS group.

Partial correlations between CMI and MetSI obtained in both groups have pointed out interesting relations. Correlation between these two parameters were r = 0.624 and r = 0.679 in MO MetS- and MO MetS+ groups, respectively, when controlled by (WC+HC)/2.

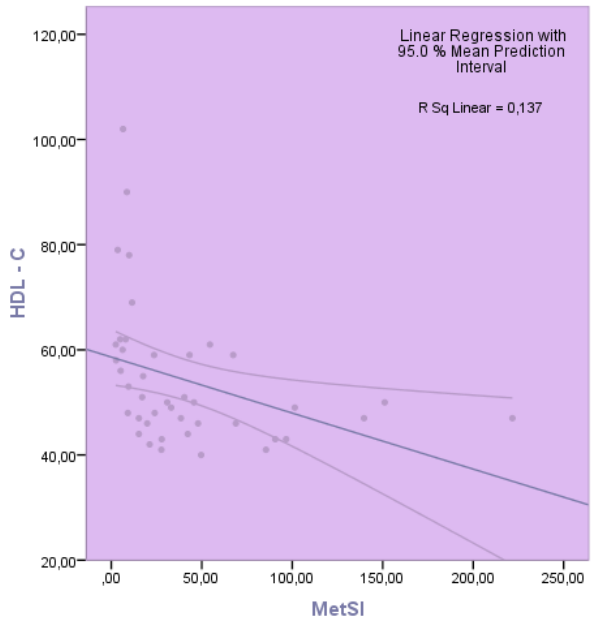

Fig. 1 Correlation between MetSI and HDL-C in MO group

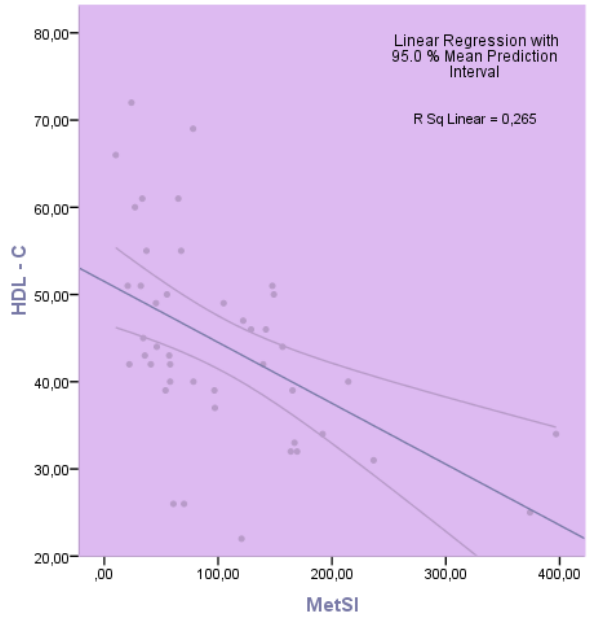

Fig. 2 Correlation between MetSI and HDL-C in MetS group

The correlation coefficients were found to be as r = 0.472, p = 0.013 and r = 0.676, p = 0.001 upon controlling for WC and D2I.

IV. Discussion

Associations between surrogate insulin resistance indices and the risk of MetS in both adults and children were being investigated for years and the best index, which is capable of making discrimination between MO individuals with and without MetS was searched [21]-[29].

In a previous study performed on children, a much stronger correlation between HOMA-IR and INS was reported than the correlation between this well-accepted and commonly used IR index and FBG. Also, INS was pointed out as the only parameter discriminating between MO children and those with MetS2 as well as MetS3, and between MetS2 and MetS3 [8].

In this study, the relation of MetS index with cardiometabolic risk was investigated to confirm the clinical utility of the suggested index to predict possible future cardiovascular problems. Actually all of four parameters used in (4) were known as cardiac risk factors.

Metabolic syndrome index was also checked from its association with CMI point of view. First bivariate correlations were calculated. These figures were almost the same in MO and MetS groups. When these associations were checked by partial correlation, upon controlling by WC and D2I, these correlations were resulted in r = 0.472; p = 0.013 and r = 0.676; p = 0.001 for MO and MetS groups, respectively.

Correlation between MetSI and CMI was much stronger in MO group with MetS components than that observed in MO group without MetS findings. This finding has shown that WC to some extent, can be accepted as the indicator of abdominal obesity should also be included into the matter. Besides, the most important contributor was D2I.

A striking difference between MO and MetS comes into the stage when the essential component of MetS (WC) and D2I parameter, which is derived from total body fat mass and height parameters were also considered during the calculation of partial correlations between MetSI and CMI when adjusted by WC and D2I.

In conclusion, MetSI was shown to be clinically available to differ MO children with and without MetS. Also, it confirmed that MO children with MetS had more tendency towards developing cardiovascular diseases than MO children without MetS findings.

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