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Coalescence of Insulin and Triglyceride/High Density Lipoprotein Cholesterol Ratio for the Derivation of a Laboratory Index to Predict Metabolic Syndrome in Morbid Obese Children

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Abstract**—**Morbid obesity is a health threatening condition particularly in children. Generally, it leads to the development of metabolic syndrome (MetS) characterized by central obesity, elevated fasting blood glucose (FBG), triglyceride (TRG), blood pressure values and suppressed high density lipoprotein cholesterol (HDL-C) levels. However, some ambiguities exist during the diagnosis of MetS in children below 10 years of age. Therefore, clinicians are in the need of some surrogate markers for the laboratory assessment of pediatric MetS. In this study, the aim is to develop an index, which will be more helpful during the evaluation of further risks detected in morbid obese (MO) children. A total of 235 children with normal body mass index (N-BMI), with varying degrees of obesity; overweight (OW), obese (OB), MO as well as MetS participated in this study. The study was approved by the Institutional Ethical Committee. Informed consent forms were obtained from the parents of the children. Obesity states of the children were classified using BMI percentiles adjusted for age and sex. For the purpose, tabulated data prepared by WHO were used. MetS criteria were defined. Systolic and diastolic blood pressure values were measured. Parameters related to glucose and lipid metabolisms were determined. FBG, insulin (INS), HDL-C, TRG concentrations were determined. Diagnostic Obesity Notation Model Assessment Laboratory ($DONMA_{LAB}$) Index [ln TRG/HDL-C*INS] was introduced. Commonly used insulin resistance (IR) indices such as Homeostatic Model Assessment for IR (HOMA-IR) as well as ratios such as TRG/HDL-C, TRG/HDL-C*INS, HDL-C/TRG*INS, TRG/HDL-C*INS/FBG, log, and ln versions of these ratios were calculated. Results were interpreted using statistical package program (SPSS Version 16.0) for Windows. The data were evaluated using appropriate statistical tests. The degree for statistical significance was defined as 0.05. 35 N, 20 OW, 47 OB, 97 MO children and 36 with MetS were investigated. Mean ± SD values of TRG/HDL-C were 1.27 ± 0.69, 1.86 ± 1.08, 2.15 ± 1.22, 2.48 ± 2.35 and 4.61 ± 3.92 for N, OW, OB, MO and MetS children, respectively. Corresponding values for the $DONMA_{LAB}$ index were 2.17 ± 1.07, 3.01 ± 0.94, 3.41 ± 0.93, 3.43 ± 1.08 and 4.32 ± 1.00. TRG/HDL-C ratio significantly differed between N and MetS groups. On the other hand, $DONMA_{LAB}$ index exhibited statistically significant differences between N and all the other groups except the OW group. This index was capable of discriminating MO children from those with MetS. Statistically significant elevations were detected in MO children with MetS ($p < 0.05$). Multiple parameters are commonly used during the assessment of MetS. Upon evaluation of the values obtained for N, OW, OB, MO groups and for MO children with MetS, the [ln TRG/HDL-C*INS] value was unique in discriminating children with MetS.

Keywords**—**Children, index, laboratory, metabolic syndrome, obesity.

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I. Introduction

MORBID obesity is associated with a cluster of abnormalities, particularly in the pediatric population. Since it is the first step in the way towards cardiovascular disease, diabetes mellitus, various types of cancers, and MetS in the future lives of MO children, it deserves great care and attention.

IR is one of the hallmarks of morbid obesity. MetS diagnosis in children is quite problematic [1]-[5]. There are controversies on the matter. Aside from morbid obesity, some physiological measurements as well as certain laboratory tests are being used for the purpose. Cut-off points for blood pressure, TRG, HDL-C and FBG are in current use to separate MO children with MetS from MO children who do not exhibit MetS findings.

For the moment, there is an immense need for some other parameters and/or indices for the more detailed and clear-cut evaluation of such children. Some indices introduced more than 30 years ago, are still being used widely [6]. Some other indices have already been suggested and comparisons are being performed with the previously reported surrogate indices [7]-[9].

IR-related lipid and lipoprotein derived indices, indices derived from FBG as well as INS, indices, which combine both lipid and carbohydrate-related parameters, [8], [10]-[14] each, constitutes important milestones of this complicated network. Recently, a completely different index derived from the ratio of aminotransferases has been reported as one of the best markers of IR [7].

The performances of these indices have generally been tested mostly on adult populations [7], [8], [11], [14], [15]. The reports on the pediatric population are scarce [9]. Particularly, testing new indices on varying obesity groups including also children with MetS is extremely rare.

In this study, the aim is to introduce a new laboratory index to predict MetS in MO children by compiling and comparing

the data from children with N-BMI, as well as OW, OB, MO and MetS groups.

II. Patients and Methods

A. Patients

The study was performed on 235 children. Five groups were constituted; 35 N-BMI, 20 OW, 47 OB, 97 MO and 36 MetS. Written informed consent forms were filled and the institutional ethics committee approved the study.

B. Measurements

Anthropometric measurements including waist circumference values were taken. Aside from the weights and heights of the children, systolic and diastolic blood pressure readings were also recorded.

C. Obesity Classification

Children were classified based on World Health Organization BMI percentiles adjusted for age and sex [16].

D. MetS Diagnosis

MO children were evaluated for their waist circumference, blood pressure, FBG, TRG, and HDL-cholesterol values. MetS criteria previously defined by [17] were used for MetS diagnosis.

E. Laboratory Analyses

FBG, INS, TRG, HDL-cholesterol (HDL-C) analyses were performed.

F. Ratio Calculations

BMI values were calculated from the weight and height values of the children. HOMA-IR values, TRG/HDL-C, TRG/ HDL-C*INS, HDL-C/TRG*INS, TRG/HDL-C*INS/FBG values, *log*, and *ln* versions of these ratios were calculated. *ln* TRG/HDL-C*INS was introduced as the DONMA$_{LAB}$ index.

G. Statistical Analyses

Statistical package program SPSS for Windows Version 16.0 was used to calculate descriptive statistics as well as correlations between the parameters, and to draw scatter plot linear regression lines. As well, $p \leq 0.05$ was accepted as statistically significance degree.

III. Results

Mean ± SD values of TRG/HDL-C as well as DONMA$_{LAB}$ index were shown in Table I.

For this set of data, HOMA-IR values did not exhibit any difference among the groups. There was a significant difference between TRG/HDL-C ratios of N and MetS groups. The DONMA$_{LAB}$ index of N group differed significantly from the values of the other groups except OW group. The important point was the significant difference between MO and MetS groups ($p \leq 0.001$).

Correlation analyses have also confirmed the superiority of the DONMA$_{LAB}$ index values over TRG/ HDL-C values. Figs. 1 and 2 show correlations between the BMI and DONMA$_{LAB}$ index as well as TRG/HDL-C, respectively.

TABLE I
TRG/HDL-C and Donma $_{LAB}$ Index Values in Children

Groups	TRG/HDL-C	DONMA$_{LAB}$ Index
N	1.27 ± 0.69	2.17 ± 1.07
OW	1.86 ± 1.08	3.01 ± 0.94
OB	2.15 ± 1.22	3.41 ± 0.93
MO	2.48 ± 2.35	3.43 ± 1.08
MetS	4.61 ± 3.92	4.32 ± 1.00

DONMA-diagnostic obesity notation model assessment, lab-laboratory.

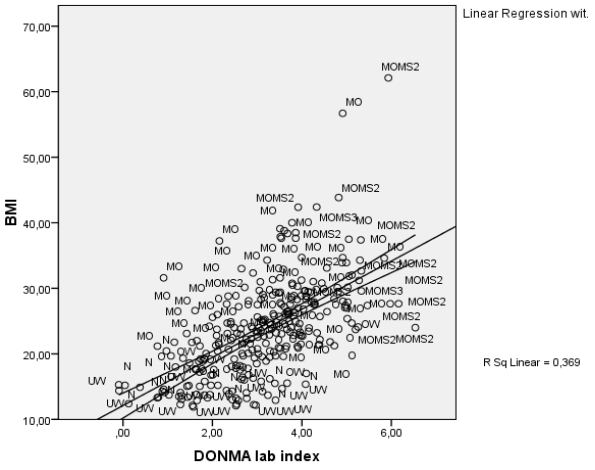

Fig. 1 Association between BMI and DONMA$_{LAB}$ index

The correlation between BMI and TRG/HDL-C was r = 0.289, while this value for BMI and DONMA$_{LAB}$ index was r = 0608.

In a similar manner, correlations between waist circumference and TRG/HDL-C as well as DONMA$_{LAB}$ index were calculated as 0.279 and 0.650, respectively.

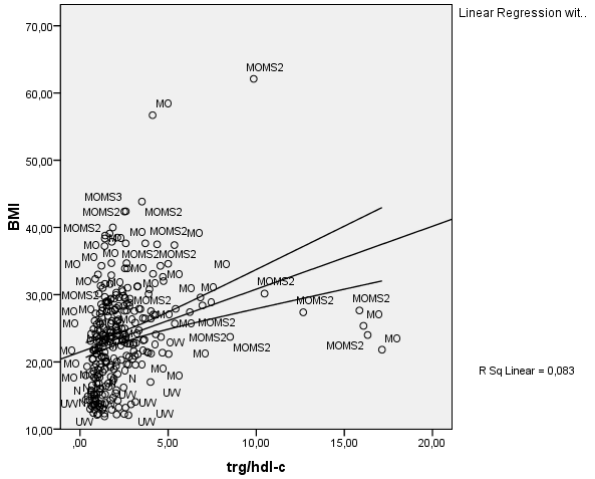

Fig. 2 Association between BMI and TRG/HDL-C

In Figs. 3 and 4, another widely used obesity parameter, waist circumference values were evaluated. In the first and

latter figures, its correlations with $DONMA_{LAB}$ index and TRG/HDL-C were displayed, respectively.

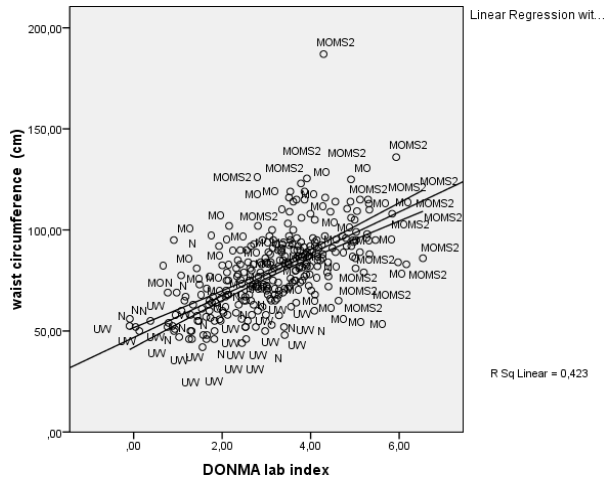

Fig. 3 Association between waist circumference and $DONMA_{LAB}$ index

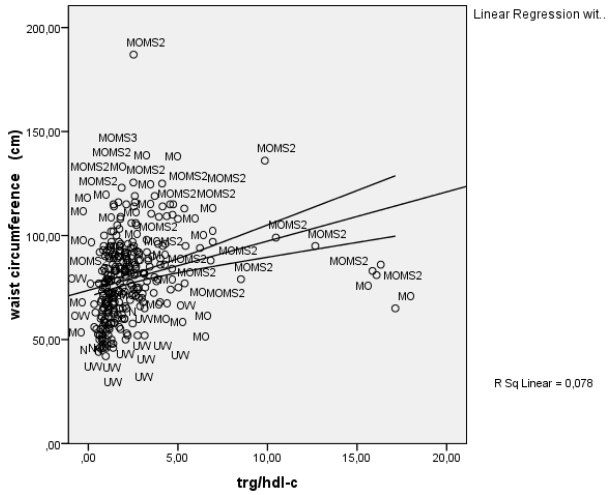

Fig. 4 Association between waist circumference and TRG/HDL-C

IV. Discussion

So far, many studies have been organized for the determination of IR for the early prediction of some diseases such as MetS and diabetes mellitus (DM) [10], [13], [17]. Obesity is in close contact with such diseases. Among the parameters, which are commonly used during this stage, waist circumference values as well as FBG, INS, TRG, HDL-C concentrations are the most commonly used values. Therefore, many simple ratios or indices derived from the combinations of these parameters have recently emerged. Of them, TRG-FBG was not found as a useful tool for predicting DM [10]. It was also less effective at predicting cardiovascular diseases [14]. In another report [8], it was introduced as a more independently associated index with coronary artery atherosclerosis than is HOMA-IR. However, alanine aminotransferase/aspartate aminotransferase ratio was suggested as one of the best markers for IR [7]. Lipid or lipoprotein-derived indices were also being investigated widely. These ratios (TRG/HDL-C, TC/HDL-C, LDL-C/HDL-C) seem comparable in their association with cardiometabolic risk [11].

In a recent study [18], FBG was reported as a stronger predictor of diabetes than TRG – FBG index, TRG/HDL-C, and HOMA-IR. However, although FBG is one of the diagnostic components of MetS, it did not differ between the groups in this study. INS exhibited much more striking differences. In our study, a frequently used ratio; TRG/HDL-C has given weaker correlations with BMI as well as waist circumference compared to the correlations calculated for the $DONMA_{LAB}$ index. In our opinion, addition of INS to TRG/HDL-C strengthens the power of this index.

In conclusion, this index was capable of discriminating MO children from those with MetS upon evaluation of the values obtained for the study groups.

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