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An Indispensable Parameter in Lipid Ratios to Discriminate between Morbid Obesity and Metabolic Syndrome in Children: High Density Lipoprotein Cholesterol

Orkide Donma, Mustafa M. Donma

***Abstract*—**Obesity is a low-grade inflammatory disease and may lead to health problems such as hypertension, dyslipidemia, diabetes. It is also associated with important risk factors for cardiovascular diseases. This requires the detailed evaluation of obesity, particularly in children. The aim of this study is to enlighten the potential associations between lipid ratios and obesity indices and to introduce those with discriminating features among children with obesity and metabolic syndrome (MetS). A total of 408 children (aged between six and eighteen years) participated in the scope of the study. Informed consent forms were taken from the participants and their parents. Ethical Committee approval was obtained. Anthropometric measurements such as weight, height as well as waist, hip, head, neck circumferences and body fat mass were taken. Systolic and diastolic blood pressure values were recorded. Body mass index (BMI), diagnostic obesity notation model assessment index-II (D2 index), waist-to-hip, head-to-neck ratios were calculated. Total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDLChol), low-density lipoprotein cholesterol (LDLChol) analyses were performed in blood samples drawn from 110 children with normal body weight, 164 morbid obese (MO) children and 134 children with MetS. Age- and sex-adjusted BMI percentiles tabulated by World Health Organization were used to classify groups; normal body weight, MO and MetS. 15^{th}-to-85^{th} percentiles were used to define normal body weight children. Children, whose values were above the 99th percentile, were described as MO. MetS criteria were defined. Data were evaluated statistically by SPSS Version 20. The degree of statistical significance was accepted as $p \leq 0.05$. Mean±standard deviation values of BMI for normal body weight children, MO children and those with MetS were 15.7±1.1, 27.1±3.8 and 29.1±5.3 kg/m^2, respectively. Corresponding values for the D2 index were calculated as 3.4±0.9, 14.3±4.9 and 16.4±6.7. Both BMI and D2 index were capable of discriminating the groups from one another ($p \leq 0.01$). As far as other obesity indices were considered, waist-to hip and head-to-neck ratios did not exhibit any statistically significant difference between MO and MetS groups ($p \geq 0.05$). Diagnostic obesity notation model assessment index-II was correlated with the triglycerides-to-HDL-C ratio in normal body weight and MO ($r=0.413$, $p \leq 0.01$ and $r=0.261$, ($p \leq 0.05$, respectively). Total cholesterol-to-HDL-C and LDL-C-to-HDL-C showed statistically significant differences between normal body weight and MO as well as MO and MetS ($p \leq 0.05$). The only group in which these two ratios were significantly correlated with waist-to-hip ratio was MetS group ($r=0.332$ and $r=0.334$, $p \leq 0.01$, respectively). Lack of correlation between the D2 index and the triglycerides-to-HDL-C ratio was another important finding in MetS group. In this study, parameters and ratios, whose associations were defined previously with increased cardiovascular risk or cardiac death have been evaluated along with obesity indices in children with morbid obesity and MetS. Their profiles during childhood have been investigated. Aside from the nature of the correlation between the D2 index and triglycerides-to-HDL-C ratio, total cholesterol-to-HDL-C as well as LDL-C-to-HDL-C ratios along with their correlations with waist-to-hip ratio showed that the combination of obesity-related parameters predicts better than one parameter and appears to be helpful for discriminating MO children from MetS group.

***Keywords*—**Children, lipid ratios, metabolic syndrome, obesity indices.

O. D., Prof. Dr., is with the Istanbul University, Cerrahpasa Medical Faculty, Department of Medical Biochemistry, Istanbul, Turkey (corresponding author to provide phone: 00-90-532-371-72-07; fax: 00-90-212-632-00-50; e-mail:odonma@gmail.com).

M. M. D., Prof. Dr., is with the Namik Kemal University, Faculty of Medicine, Department of Pediatrics, Tekirdag, Turkey (e-mail: mdonma@gmail.com).

I. Introduction

OBESITY is being increased in prevalence and a nominee for becoming the disease of the age. It is well-known that plasma lipid fractions are frequently determined parameters in obesity and obesity associated health problems such as hypertension, dyslipidemia, diabetes, MetS.

Since obesity is also associated with inflammation, it is an important risk factor also for cardiovascular diseases (CVDs). Therefore, a detailed evaluation of obesity particularly in children is needed.

LDLChol and high density HDLChol are components of total cholesterol (TChol) and they are suggested to be linked to the risk of sudden cardiac death [1]. However, their ratios are not used as commonly as TChol, triglycerides (TRG), HDLChol and LDLChol.

Very recent studies have included some lipid ratios into the lipid panel for the investigation of type 2 diabetes mellitus (T2D), even in ankylosing spondylitis to find out their preponderance over individual lipid parameters if there is any [2], [3]. Ratios also gained importance among children particularly in T1D as atherogenic indices or for their relation to hypertension [4], [5].

The relationships between lipid ratios and arterial stiffness were also reported. Most studies evaluating the associations between arterial stiffness and single lipid parameters such as TChol or LDLChol, found weak or no significant relationships [6]. Plasma TRG and HDLChol concentrations are independently related to insulin-mediated glucose disposal and, many studies suggest that the TRG/HDLChol ratio provides a simple way to identify individuals who are insulin resistant and at increased cardiometabolic risk[7]-[9]. This ratio is also regarded as the strongest correlate of small dense LDL particles, which-compared with larger LDL particles-exhibit a greater negative impact on endothelial function and this may potentially impair arterial distensibility [6].

A recent study [10] reported that lipoprotein ratios, especially the TRG/HDLChol ratio, are better than conventional lipid parameters in predicting arterial stiffness in young men. This correlation may partly mediate the enhanced cardiovascular risk associated with an increased TRG/HDLChol ratio [6].

The aim of this study is to interpret the clinical utility of lipid ratios as well as their potential in making the discrimination between obesity and MetS in pediatric population.

II. Patients and Methods

A. Patients

Children aged six to eighteen years old were included into the scope of the study. The study population was composed of 110 children with normal BMI (NW), 164 MO children and 134 children with MetS. Written informed consent forms were given by the participants or their parents. The study was approved by the Ethics Committee.

B. Anthropometric Measurements

Weight, height as well as waist, hip, head, neck circumferences (Cs) and body fat mass were measured.

C. Obesity and MetS Criteria

For the classification of the groups (NW, MO and MetS), age and sex-adjusted BMI percentile tables prepared by World Health Organization were used [11]. Children, whose percentiles were between 15^{th} and 85^{th}were included in the group with normal BMI. Those possessing the values above 99th percentile were described as MO. The components of MetS were specified [12].

D. Laboratory Methods

TChol, TRG, HDLChol, LDLChol analyses were performed in blood samples.

E. Ratio Calculations

The calculations of BMI, diagnostic obesity notation model assessment index-II (D2 index) [13], waist-to-hip and head-to-neck ratios were performed.

F. Statistical Evaluations

The statistics program SPSS Version 20 was used for the statistical analysis of the data. The degree for statistical significance was a p value greater than 0.05.

III. Results

BMI values (mean±SD) were calculated as 15.7±1.1 kg/m^2, 27.1±3.8 kg/$m^2$and 29.1±5.3 kg/$m^2$for the group with normal BMI, MO group and MetS group, respectively. Values obtained for D2 index were 3.4±0.9, 14.3±4.9 and 16.4±6.7, successively. Fig. 1 shows that both BMI and D2 indices can be used to discriminate the groups (p≤0.01). However, waist-to-hip and head-to-neck ratios did not differ between the groups (p≥0.05).

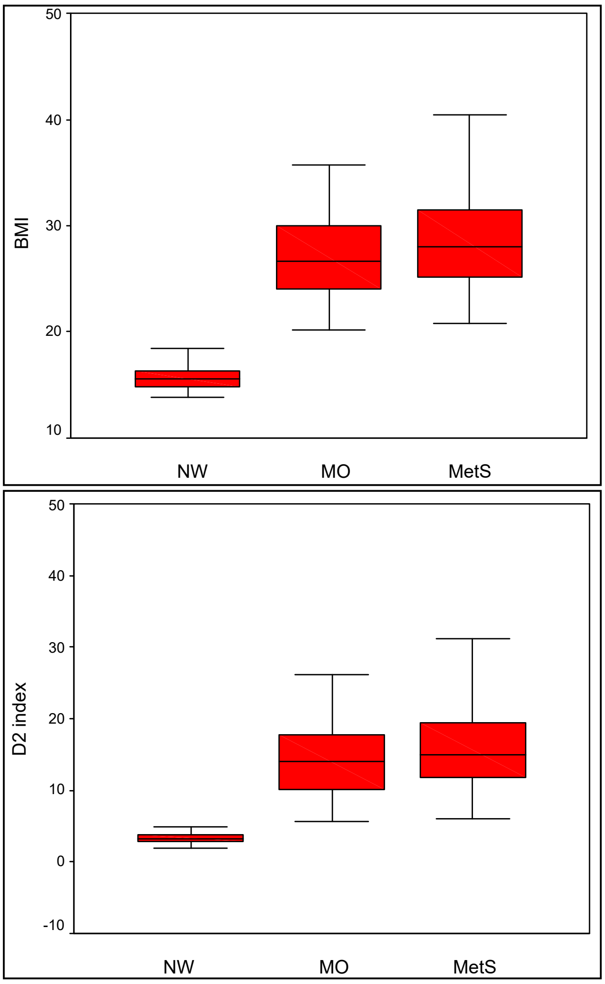

Fig. 1 Box plots for BMI and D2 indices in groups

D2 index was correlated with TRG/HDLChol ratio in NW and MO (r=0.413, p≤0.01 and r=0.261, (p≤0.05, respectively) (Fig. 2).

TChol/HDLChol and LDLChol/HDLChol were able to discriminate between NW and MO groups as well as MO and MetS groups (p≤0.05) (Fig. 3).

Only in MetS group, waist-to-hip ratio was significantly correlated with both TChol /HDL cholesterol and LDL cholesterol/HDL cholesterol. (r=0.332 and r=0.334, p≤0.01, respectively) (Fig. 4).

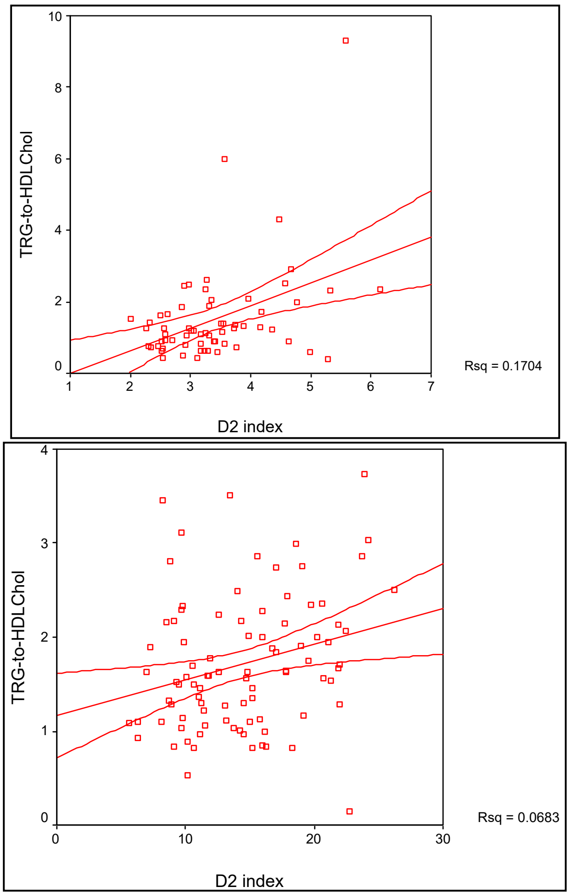

Fig. 2 Correlations between TRG/HDLChol and D2 index in NW and MO groups

Lack of correlation between D2 index and TRG/HDLChol ratio was another important finding in MetS group.

IV. Discussion

Circulating lipids are considered predictors of CVDs, diabetes and MetS. Recently the ratios of circulating lipids have gained importance and they are involved even in genome studies. Usefulness of lipid ratios is being investigated. They remain useful tools also for the diagnosis or prognosis of CVDs by their associations with lipid parameters and their high predictive values [14], [15].

In a very recent study, lipid ratios; TRG/HDLChol, TChol/HDLChol and LDLChol/HDLChol were found to be correlated with prevalent diabetes among hypertensives. TRG/HDLChol showed the optimal discriminating power for diabetes in hypertensive adults [16].

Lipid ratios were also suggested as the suitable tools to identify individuals with MetS risk. Of them TRG/HDLChol ratio is the best clinical marker for the diagnosis of MetS compared with other lipid ratios. It was reported that for any unit of increases in TRG/HDLChol, the risk of developing MetS will increase by 2.12 times. Therefore, it is recommended to be used as a feasible tool to identify individuals with MetS risk [17].

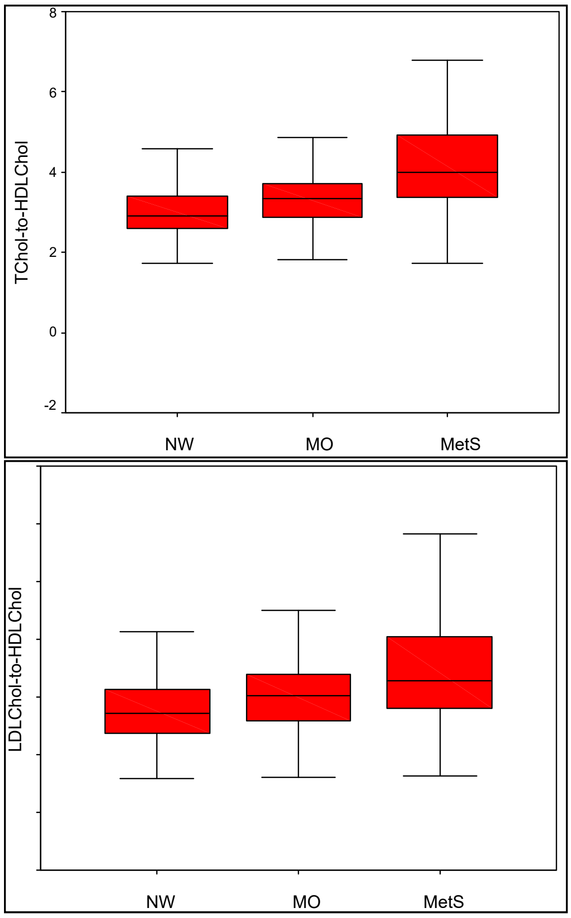

Fig. 3 Box plots of TChol/HDLChol and LDLChol/HDLChol in groups

Lipid ratios make a sensation on their association with IR. It was concluded that TRG/HDLChol, TChol/HDLChol and TRG are associated with IR in overweight/obese adults. LDLChol/HDLChol is the only ratio associated with IR in NW women. TRG/HDLChol and TRG might be used as surrogate markers for assessing IR [18].

In another study, TRG/HDLChol had the strongest associations with IR. This ratio is suggested as a useful index for predicting the concomitant presence of MetS, IR and dyslipidemia [19].

Ina similar study performed in Canada, clinical usefulness of lipid ratios to identify individuals with MetS was discussed. As a result of this study TRG/HDLChol is a superior marker to identify men and women with MetS compared to TChol/HDLChol, LDLChol/HDLChol [20].

Lipid ratios; TRG/HDLChol, TChol/HDLChol and LDLChol/HDLChol were compared for their strength and independence as risk factors for IR [21].

Insulin resistance is the underlying mechanism for MetS and associated dyslipidemia that theoretically implies a practical tool for identifying individuals at risk for CVDs and T2D. Another screening tool is the hypertryglyceridemic waist phenotype [19].

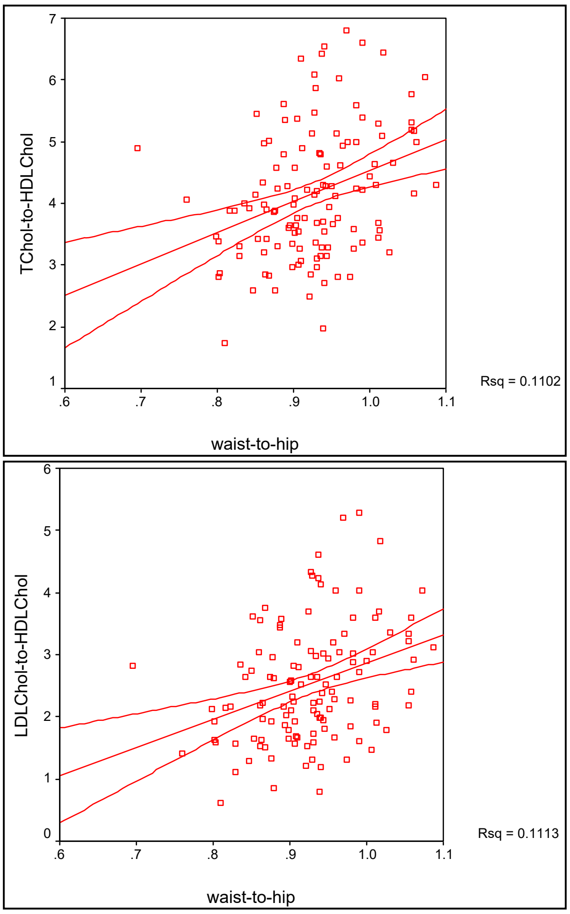

Fig. 4 Correlations between waist-to-hip ratios and TChol/HDLChol as well as LDLChol/HDLChol in MetS group

Coronary heart disease risk is known to be increased in diabetic as well as obese patients due to their atherogenic lipid profile. Significant associations were noted between glycemic status and dyslipidemia [2].

Lipid ratios were largely involved also in the investigations performed on patients with CVDs. A study reported that serum lipid ratios may be used in addition to lipid parameters in clinical practice to assess cardiovascular risks even when lipid profiles are apparently normal [22]. Besides, in patients with rheumatoid arthritis, the effects of inflammation on individual lipid levels may underestimate lipid-associated CVD risk, thus lipid ratios may be more appropriate for CVDs risk stratification in this disease [23].

Lipid ratios were also investigated in patients with myocardial infarction [24]. In a study performed on men, although LDLChol or HDLChol was not found to be associated with an increased risk of sudden cardiac death, elevated serum LDLChol/HDLChol ratio was found to be independently associated with this critical condition [1].

TRG/HDLChol is a good marker for early identification of IR. A study suggested using lipid ratios as a screening test in females with acne vulgaris to diagnose dyslipidemia at an early stage [25].

In a study performed on the elderly aged 80 years and older [26], LDLChol/HDLChol, TRG/HDLChol were negatively associated with all-cause mortality among this population.

Lipid parameters as well as their ratios are included also in studies performed on children and adolescents. In a study reported from Poland, LDLChol/HDLChol ratio was related to higher waist-to-hip ratio and poorer glycemic control [4].

In another study reported from Mexico, TRG/HDLChol ratio was found to be associated with prehypertension in children [5].

It has also been stated that a high TRG/HDLChol ratio may be useful in clinical practice to detect children with an unfavorable cardiometabolic profile who need early intervention to promote healthier lifestyles and to prevent CVDs in adulthood [7], [27].

In our study, TRG/HDLChol ratio in NW and MO was correlated with D2 index ($r=0.413$, $p\leq0.01$ and $r=0.261$, ($p\leq0.05$, respectively), but not with BMI. Lack of correlation between D2 index and TRG/HDLChol ratio in MetS group was an important finding.

Two lipid ratios; TChol/HDLChol and LDLChol/HDLChol were the ratios capable of discriminating MO children from children with MetS, because they were correlated with waist-to-hip ratio only in MetS group.

V. Conclusion

In this study, parameters and ratios, previously reported to be associated with increased cardiovascular risk were evaluated along with obesity indices in three groups of pediatric population. The characteristic features of the correlations among anthropometric ratios, obesity indices and lipid ratios showed that the use of more than one obesity-related parameter might be helpful for discriminating MO children from MetS group.

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