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The Evaluation of a Cardiac Index Derived from Anthropometric and Biochemical Parameters in Pediatric Morbid Obesity and Metabolic Syndrome

Mustafa M. Donma

Abstract**—**Metabolic syndrome (MetS) components are noteworthy among children with obesity and morbid obesity, because they point out the cases with MetS, which have the great tendency to severe health problems such as cardiovascular diseases both in childhood and adulthood. In clinical practice, considerable efforts are being observed to bring into the open the striking differences between morbid obese cases and those with MetS findings. The most privileged aspect is concerning cardiometabolic features. The aim of this study was to derive an index, which behaves different in children with and without MetS from the cardiac point of view. For the purpose, aspartate transaminase (AST), a cardiac enzyme still being used independently to predict cardiac-related problems was used. 124 children were recruited from the outpatient clinic of Department of Pediatrics in Tekirdag Namik Kemal University, Faculty of Medicine. 43 children with normal body mass index, 41 and 40 morbid obese (MO) children with MetS and without the characteristic features of MetS, respectively, were included in the study. Weight, height, waist circumference (WC), hip circumference (HC), head circumference (HdC), neck circumference (NC), systolic and diastolic blood pressure values were measured and recorded. Body mass index and anthropometric ratios were calculated. Fasting blood glucose (FBG), insulin (INS), triglycerides (TRG), high density lipoprotein cholesterol (HDL-C) analyses were performed. The values for AST, alanine transaminase (ALT) and AST/ALT were obtained. Advanced Donma cardiac index (ADCI) values were calculated. Statistical evaluations including correlation analysis were done by a statistical package program. The statistical significance degree was accepted as $p < 0.05$. The index, ADCI, was developed from both anthropometric and biochemical parameters. All anthropometric measurements except weight were included in the equation. Besides all biochemical parameters concerning MetS components were also added. This index was tested in each of three groups. Its performance was compared with the performance of cardiometabolic index (CMI). It was also checked whether it was compatible with AST activity. The performance of ADCI was better than that of CMI. Instead of double increase, the increase of three times was observed in children with MetS compared to MO children. The index was correlated with AST in MO group and with AST/ALT in MetS group. In conclusion, this index was superior in discovering cardiac problems in MO and in diagnosing MetS in MetS groups. It was also arbiter to point out cardiovascular and MetS aspects among the groups.

Keywords**—**Aspartate transaminase, cardiac index, metabolic syndrome, obesity.

M. M. D. is with the Tekirdag Namik Kemal University, Faculty of Medicine, Department of Pediatrics, Tekirdag, Turkey (phone: 00-90-532-371-72-07; fax: 00-90-282-250-99-28; e-mail: mdonma@gmail.com).

I. Introduction

MORBID obesity is an important milestone in the way going towards cardiovascular diseases (CVDs). Morbid obesity may also lead to MetS, which is a cluster of symptoms. Alterations in distinct biochemical and anthropometric parameters point out the life-threatening points in this triangle [1]-[3].

Aside from central obesity, which was often indicated by increased WC associated with increased hip and neck circumferences; two biochemical parameters from fat metabolism and the other two from glucose metabolism are the major players of the game. Height is another dimension in this discussion. Its close association with physiological parameters, e.g. blood pressure values, makes this parameter arbiter within the scope of anthropometric parameters [4], [5]. Ratios are also important as the predictors of CVDs [6], [7].

High TRG values are detrimental for cardiovascular system. Reducing the values is helpful for the protection from CVDs. HDL-C is of a protective nature against heart diseases. FBG and INS behavior are key factors to be considered for the definition of insulin resistance (IR), an indispensable associate of morbid obesity. IR is one of the earliest constellations of cardiometabolic diseases. All together they contribute to the risk of multiple cardiometabolic diseases, including type 2 diabetes (T2D) and CVDs [8], [9]. These biochemical parameters are clinically being used as also MetS components during the diagnosis of the disease [10]. It is known that cardiovascular problems as well as the development of MetS are severe ultimate conclusions, which can be evaluated as adverse side effects of morbid obesity.

A new generation of cardiovascular risk markers is currently being evaluated [11]. However, in recent years, some cardiac enzymes also regained importance for the diagnosis of cardiac problems. Aspartate transaminase (AST), the most important member of liver transaminases, is a rather old enzyme in this context. However, it still is being used independently to predict cardiac-related morbidity and mortality [12]. Aspartate aminotransferase to alanine aminotransferase ratio (AST/ALT) was widely investigated and reports concluded that this ratio is of an importance during MetS and cardiometabolic diseases [13]-[16].

There are investigations that develop and introduce cardiometabolic or MetS indices performed among obese individuals [17]-[20]. However, it is almost impossible to distinguish between cardiovascular system and MetS-related alterations. So far, to the best of our knowledge, an index,

which was confined to cardiac alterations that occur during the development of MetS, has yet to be introduced. The aim of this study was to develop a functional cardiac index also in cases developing MetS.

II. Patient and Methods

A. The Study Population

43 children with normal body mass index (N-BMI) and 81 MO children, who admitted to the pediatric outpatient clinic of Faculty of Medicine Hospital were included into the study. 41 MO children were observed to possess MetS criteria.

All parents gave informed consent according to the Declaration of Helsinki. The study protocol was approved by the institutional non-interventional Ethical Committee.

B. Definition of Morbid Obesity

Children with normal-BMI and morbid obesity were selected based on the age and gender-adjusted BMI percentile tables prepared by World Health Organization [21]. Children with percentiles between 15 and 85 were in N-BMI group. Those above 99th percentile were included in MO groups with and without MetS.

C. Selection Criteria for MetS

MO children exhibiting MetS criteria were in MetS group. Aside from central obesity, elevated systolic (above 120 mm Hg) and/or diastolic (above 80 mm Hg) blood pressure, elevated FBG (above 100 mg/dl) and elevated TRG (above 100 mg/dl) and/or low HDL-C concentrations (below 40 mg/dl) constitute the list of MetS components [10]. In addition to central obesity, the presence of at least two criteria from this list was sufficient for a participant to be included into the MetS group.

D. Anthropometric Parameters and Indices

Weight, height, WC, HC, HdC and NC measurements were performed and recorded. BMI, waist-to-hip, waist-to-height and waist-to-hip-to-height ratios were calculated.

E. Blood Pressure Measurements and Biochemical Tests

Systolic and diastolic blood pressure values were obtained. Concentrations of FBG, INS, TRG, HDL-C were determined.

F. Calculation of Indices

The formula for ADCI was: [(TRG / HDL-C) * (INS / FBG)] * [(WC+HC)/Height] * [(HdC+NC)/Height]

G. Statistical Evaluation

A statistical package program was used for the statistical analysis. Data were examined in terms of descriptive parameters. Correlation analysis was performed. p value smaller than 0.05 was accepted as statistically significant.

III. Results

Mean age ± standard deviation of three groups were 10.9 ± 4.2 years for N-BMI group, 10.6 ± 3.5 years for MO group and 12.1 ± 2.6 years for MO group with MetS findings. There was no statistically significant difference between groups ($p > 0.05$).

Weight, height, WC, HC, HdC and NC values were tabulated in Table I.

TABLE I
ANTHROPOMETRIC MEASUREMENTS

Parameter/Groups	N-BMI	MO	MetS
Weight	39.3 ± 17.9	63.7 ± 26.5	75.0 ± 20.4
Height	144.8 ± 23.2	148.2 ± 18.9	155.8 ± 12.4
WC	64.9 ± 11.8	88.2 ± 14.2	97.1 ± 10.4
HC	77.4 ± 14.7	97.0 ± 16.2	104.7 ± 14.3
HdC	53.1 ± 2.7	55.1 ± 2.3	55.3 ± 2.2
NC	29.3 ± 3.8	33.6 ± 3.8	35.0 ± 5.6

Statistically significant increases were observed in weight, WC, HC and NC values from N-BMI to MO, MO to MetS groups. BMI, waist-to-hip, waist-to-height, waist-to-hip-to-height ratios were listed in Table II.

TABLE II
ANTHROPOMETRIC RATIOS

Parameter/Groups	N-BMI	MO	MetS
BMI	17.6 ± 2.9	27.6 ± 5.3	30.3 ± 4.7
Waist-to-hip	0.84 ± 0.07	0.91 ± 0.06	0.94 ± 0.11
Waist-to-height	0.45 ± 0.05	0.60 ± 0.05	0.62 ± 0.05
Waist-to-hip-to-height	0.60 ± 0.12	0.63 ± 0.10	0.61 ± 0.10

For BMI values, statistically significant increase was observed in MO group when compared with N-BMI group. Although increases were obtained, any significant difference could not be noted for anthropometric ratios between MO and MetS groups.

Blood pressure values, TRG, HDL-C, FBG, INS values were shown in Table III.

TABLE III
METABOLIC SYNDROME RELATED PARAMETERS

Parameter/Groups	N-BMI	MO	MetS
SBP	102.4 ± 10.1	113.2 ± 12.2	126.2 ± 16.3
DBP	69.3 ± 7.8	71.9 ± 10.2	84.5 ± 11.3
TRG	84.6 ± 43.1	90.8 ± 40.8	165.9 ± 89.0
HDL-C	56.2 ± 12,9	51.5 ± 8.5	46.8 ± 9.9
FBG	92.5 ± 5.9	90.6 ± 5.5	98.0 ± 8.3
INS	11.8 ± 6.9	20.9 ± 16.9	36.1 ± 17.4

SBP = systolic blood pressure, DBP = diastolic blood pressure.

Statistically significant increases were noted when MetS group compared to the values observed in MO group for MetS related parameters.

AST, alanine transaminase, AST-to-ALT ratio, CMI and ADCI values were shown in Table IV.

TABLE IV
TRANSAMINASES AND INDICES

Parameter/Groups	N-BMI	MO	MetS
AST	22.3 ± 6.2	45.7 ± 51.8	50.1 ± 55.4
ALT	14.0 ± 4.9	31.8 ± 23.7	42.1 ± 36.5
AST/ALT	1.72 ± 0.70	1.33 ± 0.63	1.16 ± 0.62
CMI	0.78 ± 0.67	1.01 ± 0.55	2.24 ± 1.33
ADCI	0.14 ± 0.17	0.31 ± 0.51	1.04 ± 0.88

CMI and ADCI values increased in MO and MetS groups compared to N-BMI group. However, increases in ADCI were more striking than increases in CMI.

Values for CMI were slightly increased in MO group. However, for ADCI, the increase in MO group was twice the values obtained in N-BMI group. CMI values observed in MetS group were almost twice that of MO group. On the other hand, ADCI values in MetS group were three times higher than values obtained in MO group.

Correlation analysis was performed. ADCI values were given in Table IV. Correlations between ADCI and AST as well as AST/ALT in three groups were given in Table V. p values for significance check of correlation were also shown.

TABLE V
SIGNIFICANCE CHECK OF CORRELATIONS

Parameter/Groups	N-BMI	MO	MetS
ADCI			
AST	0.096	0.021	0.910
AST/ALT	0.952	0.064	0.034

Statistically significant correlations were calculated between ADCI and AST in MO group, between ADCI and AST/ALT in MetS group. The correlations between CMI and AST as well as AST/ALT were not statistically significant.

IV. DISCUSSION

AST was the first cardiac biomarker to be used [22], [23]. Positive association was observed between AST and CVD in epidemiological studies [24]. However, it is still being accepted as one of cardiac enzymes [12], [25] and is still being used for the evaluation of cardiotoxicity [26], [27]. It is also used as one of the cardiac damage markers [28] or cardiac injury markers [29]. In a similar manner, in a study [30], an association between AST activity and the risk of cardiac mortality in patients with ischemic heart disease was reported.

In this study, any correlation was not observed between ADCI and neither AST nor AST/ALT in the N-BMI group ($p = 0.096$ and $p = 0.952$). This was an expected result for a cardiac index. In MO group, there was a correlation of ADCI at limit ($p = 0.064$) with AST/ALT. Significant correlation was observed between ADCI and AST ($p = 0.021$). This finding highlights that AST acts as a cardiac marker in this group. These results highlight both the MetS aspect as well as the cardiac problems related aspect of this index. In this group, the index emphasizes the cardiovascular risk as well as a tendency towards MetS.

These inferences are confirmed by the results obtained in the group with MetS. In this group, the correlation of ADCI with AST, which is an absolute cardiac marker, was lost. In contrary, a statistically significant correlation ($p = 0.034$) was detected between ADCI and AST/ALT. Accordingly, the index emphasizes MetS in the group with MetS. Here, the relationship with MetS comes to the fore.

A study confirmed the association of AST/ALT ratio with MetS. The ratio but not AST was found to be significantly correlated with components of MetS (negatively with WC, SBP, DBP, FBG, TRG and positively with HDL-C; $p < 0.01$) [13].

When the performance of CMI was evaluated, it was associated with the risk of metabolic associated fatty liver disease [18]. It was reported to exhibit a good performance in detecting MetS in women [31]. In another study, a positive association between CMI levels and the risk of new-onset CVD in patients with hypertension and obstructive sleep apnea was reported [32].

In the present study, CMI was associated with neither AST nor AST/ALT parameters in any of the groups.

V. CONCLUSION

The ADCI index presented in this study makes a difference because of its relationship, confirmed by AST and AST/ALT, with both CVDs and MetS, respectively.

REFERENCES

[1] S. M. Grundy, "Obesity, metabolic syndrome and cardiovascular disease," *J. Clin. Endocrinol. Metabol.*, vol.89, no.6, pp.2595-2600, Jun 2004.

[2] C. D. Bendor, A. Bardugo, O. Pinhas-Hamiel, A Afek and G. Twig, "Cardiovascular morbidity, diabetes and cancer risk among children and adolescents with severe obesity," *Cardiovasc. Diabetol.,* vol.19, no.1 pp. 79, Jun 2020.

[3] B. A. Aulinger, T. To Viet, E. Waldmann and K. G. Parhofer, "Prevalence of the metabolic syndrome in severely obese patients presenting for bariatric surgery," *Dig. Dis.,* vol.39, no.4, pp. 334-340, 2021.

[4] P. Piqueras, A. Ballester, J. V. Durá-Gil, S. Martinez-Hervas, J. Redón and J. T. Real, "Anthropometric indicators as a tool for diagnosis of obesity and other health risk factors: A literature review," *Front. Psychol.,* vol.12, pp.631179, Jul. 2021.

[5] B. Bourgeois, K. Watts, D. M. Thomas, O. Carmichael, F. B. Hu, M. Heo, J. E. Hall and S. B. Heymsfield, "Associations between height and blood pressure in the United States population," *Medicine (Baltimore),* vol.96, no.50, pp.e9233, Dec. 2017.

[6] J. H. Page, K. M. Rexrode, F. Hu, C. M. Albert, C. U. Chae, and J. E. Manson, "Waist-height ratio as a predictor of coronary heart disease among women," *Epidemiology,* vol.20, no.3, pp.361-366, May 2009.

[7] M. Mahdavi-Roshan, A. Rezazadeh, F. Joukar, M. Naghipour, S. Hassanipour, and F. Mansour-Ghanaei, "Comparison of anthropometric indices as predictors of the risk factors for cardiovascular disease in Iran: The PERSIAN Guilan Cohort Study," *Anatol. J. Cardiol.,* vol.25, no.2, pp.120-128, Feb. 2021.

[8] S. E. Kahn, R. L. Hull and K. M. Utzschneider, "Mechanisms linking obesity to insulin resistance and type 2 diabetes," *Nature,* vol.444, no.7121, pp.840-846, Dec. 2006.

[9] M. Laakso and J. Kuusisto, "Insulin resistance and hyperglycaemia in cardiovascular disease development," *Nat. Rev. Endocrinol.,* vol.10, no.5, pp.293-302, May 2014.

[10] P. Zimmet, K. G. AlbertiG, F. Kaufman, N. Tajima, M. Silink, S. Arslanian, G. Wong, P. Bennet, J. Shaw, S. Caprio, and IDF consensus group, "The metabolic syndrome in children and adolescents-an IDF consensus report," *Pediatr. Diabetes,* vol.8, no.5, pp. 299-306, 2007.

[11] M. Donma, S. Kacmaz, A. Yilmaz, S. Guzel, and O. Donma, "The evaluation of new generation cardiovascular risk markers in childhood obesity," *Int. J. Med. Health Sci.,* vol.15, no.12, pp.308–314, 2021.

[12] S. Thupakula, S. S. R. Nimmala, H. Ravula, S. Chekuri, and R. Padiya, "Emerging biomarkers for the detection of cardiovascular diseases," *Egypt Heart J.*, vol.74, no.1, pp. 77, 2022.

[13] P. Deepa and N. Sasivathanam, "A study of AST/ ALT ratio in metabolic syndrome," *Int. J. Contemp. Med. Res.,* vol.4, no.1, pp.28-30, 2017.

[14] S. Lin, L. Tang, R. Jiang, Y. Chen, S. Yang, L. Li and Li P, "The relationship between aspartate aminotransferase to alanine aminotransferase ratio and metabolic syndrome in adolescents in Northeast China," *Diabetes Metab. Syndr. Obes.,* vol.12, pp.2387-2394,

Nov. 2019.
[15] F. Yan, G. Nie, N. Zhou, M. Zhang, and W. Peng, "Combining fat-to-muscle ratio and alanine aminotransferase/aspartate aminotransferase ratio in the prediction of cardiometabolic risk: A cross-sectional study," *Diabetes Metab. Syndr. Obes.*, vol.16, pp.795–806, 2023.
[16] H. Liu, C. Ding, L. Hu, M. Li, W. Zhou, T. Wang, L. Zhu, H. Bao and X. Cheng, "The association between AST/ALT ratio and all-cause and cardiovascular mortality in patients with hypertension," *Medicine (Baltimore),* vol.100, no.31, pp.e26693, Aug. 2021.
[17] I. Wakabayashi and T. Daimon, "The "cardiometabolic index" as a new marker determined by adiposity and blood lipids for discrimination of diabetes mellitus," *Clin. Chim. Acta,* vol.438, pp.274-278, Jan 2015.
[18] S. Duan, D. Yang, H. Xia, Z. Ren, J. Chen and S. Yao, "Cardiometabolic index: A new predictor for metabolic associated fatty liver disease in Chinese adults," *Front. Endocrinol. (Lausanne),* vol.13, pp.1004855, Sep. 2022.
[19] I. Soldatovic, R. Vukovic, D. Culafic, M. Gajic, and V. Dimitrijevic-Sreckovic, "siMS score: Simple method for quantifying metabolic syndrome," *PLoS One*, vol.11, no.1, pp. e0146143, Jan. 2016.
[20] M. M. Donma and O. Donma, "A new index for the differential diagnosis of morbid obese children with and without metabolic syndrome," *Int. J. Med. Health Sci.,* vol.17, no.2, pp.1, 2023.
[21] WHO World Health Organization. The WHO Child Growth Standards. Available at: http://www.who.int/childgrowth/en/ Accessed on June 10, 2016.
[22] S. Patibandla, K. Gupta and K. Alsayouri, "Cardiac Enzymes," Aug. 2022. In: StatPearls (Internet). Treasure Island (FL): StatPearls Publishing; 2023 Jan–.
[23] J. S. Ladue, F. Wroblewski and A. Karmen, "Serum glutamic oxaloacetic transaminase activity in human acute transmural myocardial infarction," *Science,* vol.120, no.3117, pp.497-499, Sep. 1954.
[24] G. Ndrepepa, "Aspartate aminotransferase and cardiovascular disease—a narrative review," *J. Lab. Precis. Med.,* vol.6, pp.6, 2021.
[25] W. Liu, C. Chen, X. Gu, L. Zhang, X. Mao, Z. Chen and L. Tao, "AM1241 alleviates myocardial myocardial ischemia-reperfusion injury in rats by enhancing Pink1/Parkin- mediated autophagy," *Life Sci.,* vol.272, pp.119228, May 2021.
[26] A. Sikandar, K. Farhat, A. Afzal, K. Ajmal, M. Laeeq and A. Khokhar, "Protective effects of Trimetazidine against Doxorubicin-induced cardiotoxicity and hepatotoxicity in mice," *J. Ayub. Med. Coll. Abbottabad,* vol.32, no.3, pp.304-309, Jul-Sep. 2020.
[27] K. A. Olofinsan, R. A. Ajala-Lawal and T. O. Ajiboye, "Loperamide-induced cardiotoxicity in rats: Evidence from cardiac and oxidative stress biomarkers," *J. Biochem. Mol. Toxicol.,* vol.33, no.4, pp.e22278, Apr. 2019.
[28] A. S. Mandour, R. F. Elsayed, A. O. Ali, A. E. Mahmoud, H. Samir, A. A. Dessouki, K. Matsuura, I. Watanabe, K. Sasaki, S. Al-Rejaie, T. Yoshida, K. Shimada, R. Tanaka and G. Watanabe, "The utility of electrocardiography and echocardiography in copper deficiency- induced cardiac damage in goats," *Environ. Sci. Pollut. Res. Int.,* vol.28, no.7, pp.7815-7827, Feb. 2021.
[29] P. Liu and Q. Pan, "Butein inhibits oxidative stress injury in rats with chronic heart failure via ERK/Nrf2 signaling," *Cardiovasc. Ther.,* vol.2022, pp.8684014, Jan. 2022.
[30] G. Ndrepepa, S. Holdenrieder, S. Cassese, E. Xhepa, M. Fusaro, K. L. Laugwitz, H. Schunkert and A. Kastrati, "Aspartate aminotransferase and mortality in patients with ischemic heart disease," *Nutr. Metab. Cardiovasc. Dis.,* vol.30, no.12, pp. 2335-2342, Nov. 2020.
[31] S. Lazzer, M. D'Alleva, M. Isola, M. De Martino, D. Caroli, A. Bondesan, A. Marra and A. Sartorio, "Cardiometabolic index (CMI) and visceral adiposity index (VAI) highlight a higher risk of metabolic syndrome in women with severe obesity," *J. Clin. Med.,* vol.12, no.9, pp.3055, 2023.
[32] X. Cai, J. Hu, W. Wen, J. Wang, M. Wang, S. Liu, Q. Zhu, J. Hong, Y. Dang, X. Yao, L. Sun, D. Zhang, Q Luo and N. Li, "Associations of the cardiometabolic index with the risk of cardiovascular disease in patients with hypertension and obstructive sleep apnea: Results of a longitudinal cohort study," *Oxid. Med. Cell Longev.,* vol.2022, pp.4914791, Jun. 2022.