

Understanding the Nature of Blood Pressure as Metabolic Syndrome Component in Children

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Abstract—Pediatric overweight and obesity need attention because they may cause morbid obesity, which may develop metabolic syndrome (MetS). Criteria used for the definition of adult MetS cannot be applied for pediatric MetS. Dynamic physiological changes that occur during childhood and adolescence require the evaluation of each parameter based upon age intervals. The aim of this study is to investigate the distribution of blood pressure (BP) values within diverse pediatric age intervals and the possible use and clinical utility of a recently introduced Diagnostic Obesity Notation Model Assessment Tension (DONMA tense) Index derived from systolic BP (SBP) and diastolic BP (DBP) [SBP+DBP/200]. Such a formula may enable a more integrative picture for the assessment of pediatric obesity and MetS due to the use of both SBP and DBP. 554 children, whose ages were between 6-16 years participated in the study; the study population was divided into two groups based upon their ages. The first group comprises 280 cases aged 6-10 years (72-120 months), while those aged 10-16 years (121-192 months) constituted the second group. The values of SBP, DBP and the formula (SBP+DBP/200) covering both were evaluated. Each group was divided into seven subgroups with varying degrees of obesity and MetS criteria. Two clinical definitions of MetS have been described. These groups were MetS3 (children with three major components), and MetS2 (children with two major components). The other groups were morbid obese (MO), obese (OB), overweight (OW), normal (N) and underweight (UW). The children were included into the groups according to the age- and sex-based body mass index (BMI) percentile values tabulated by WHO. Data were evaluated by SPSS version 16 with $p < 0.05$ as the statistical significance degree. Tension index was evaluated in the groups above and below 10 years of age. This index differed significantly between N and MetS as well as OW and MetS groups ($p = 0.001$) above 120 months. However, below 120 months, significant differences existed between MetS3 and MetS2 ($p = 0.003$) as well as MetS3 and MO ($p = 0.001$). In comparison with the SBP and DBP values, tension index values have enabled more clear-cut separation between the groups. It has been detected that the tension index was capable of discriminating MetS3 from MetS2 in the group, which was composed of children aged 6-10 years. This was not possible in the older group of children. This index was more informative for the first group. This study also confirmed that 130 mm Hg and 85 mm Hg cut-off points for SBP and DBP, respectively, are too high for serving as MetS criteria in children because the mean value for tension index was calculated as 1.00 among MetS children. This finding has shown that much lower cut-off points must be set for SBP and DBP for the diagnosis of pediatric MetS, especially for children under-10 years of age. This index may be recommended to discriminate MO, MetS2 and MetS3 among the 6-10 years of age group, whose MetS diagnosis is problematic.

Keywords—Blood pressure, children, index, metabolic syndrome, obesity.

I. INTRODUCTION

MetS is associated with several systemic alterations and also variations in physiological and biochemical parameters. These add to the difficulties during the diagnosis of MetS [1]-[4].

To some extent, adult criteria is well-defined by considering central obesity, reduced high density lipoprotein cholesterol (HDL-C) (≤ 40 mg/dl in men and ≤ 50 mg/dl in women), elevated triglycerides (TRG) (≥ 150 mg/dl), and elevated fasting blood glucose (FBG) (≥ 100 mg/dl). Aside from these components, BP values must also be considered. Systolic pressure (SP) (≥ 130 mm Hg), as well as diastolic pressure (DP) (≥ 85 mm Hg) are indispensable parameters contributing to the consensus definition of MetS [1], [5], [6]. However, using these criteria for growing and developing organisms such as children may not be appropriate. For the evaluation and interpretation of the pediatric population, diverse values should be considered due to various age intervals. This gains importance particularly during the laboratory assessment and for setting pediatric MetS diagnosis [1].

Definitions given for the diagnosis of MetS in adults are not the same as the criteria set for the diagnosis of pediatric MetS. Changes in body size and proportion concomitant with the increasing age as well as puberty, which is associated with drastic alterations, are some of the causes. Therefore, each parameter must be evaluated with great care for children and adolescents [1], [2].

The International Diabetes Federation (IDF) consensus definition of MetS in pediatric population excludes children younger than 6 years. For adolescents older than 16 years, the use of IDF adult criteria is recommended. It is stated that for children aged 6-10 years, MetS cannot be diagnosed. For children aged $10 < \text{years}$ and <16 years, some recommendations have been given. Actually, the IDF definition of pediatric MetS does not provide criteria to diagnose children under the age of 10 years. Besides, BP values are the same as in the list given for adults. It is reported that they are too high (SP ≥ 130 mm Hg and DP ≥ 85 mm Hg) [1], [6].

Pediatric obesity and hypertension are major health problems throughout the world. Therefore, screening for obesity as well as hypertension is recommended. Development of obesity in childhood may be linked to the increased risk of hypertension. By ambulatory BP monitoring, abnormal BP

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was observed in about half of OB children and MetS was diagnosed in nearly one-third of children with obesity [7]-[9].

The aim of this study was to determine BP values in children aged $6 \leq$ year and ≤ 10 years, as well as $10 <$ years and < 16 years and to propose a simple, practical and diagnostic index to differentiate MO children and children with MetS.

II. PATIENTS AND METHODS

A. Patients and Protocols

This study was performed on 554 children between ages six and 16 years. Informed consent forms were obtained from the parents. Two groups were constituted: Children aged 72-120 months and those aged 121-192 months. Namik Kemal University Non-interventional Ethical Committee approved the study design.

B. Anthropometric and BP Measurements

Anthropometric measurements including weight, height, waist circumference (C), hip C, head C and neck C were performed. A flexible, non-elastic tape was used for measurements. Body weight and height were measured using portable digital scale and portable stadiometer, respectively.

Blood P values of the children were determined by manual BP auscultation method, with an upper arm BP device (sphygmomanometer; ERKA BP monitoring) using adequate cuff and pediatric stethoscope. The child should be seated in a chair prior to and during the measurement, with feet on the floor and arm supported so child's elbow is at about heart level. Talking should be prevented. The cuff should completely cover about 80% of the upper arm. It should be placed on bare skin and on the arm with the arrow on the cuff over the brachial artery. During deflation of the cuff, SP and DP were recorded at the Phase 1 and Phase 5 Korotkoff sounds, respectively [10], [11].

C. Ratio Calculations

BMI values were determined by calculation using weight and height of the individuals. Tense index values were obtained from SP and DP.

D. Obesity Classification

OB children were grouped according to World Health Organization criteria [12]. For the purpose, age and sex-adjusted BMI percentile tables were used. Children with 15th to 85th, 85th to 95th, 95th to 99th percentiles were included in the healthy with normal BMI (N), OW, OB groups, respectively. Children above the 99th percentile were described as MO.

E. Criteria for MetS

The components of MetS were specified [6]. Two MetS groups were constituted based upon the presence of two or three major components. If a partial combination of the elements constitutes only two, this group was called MetS2. The MetS3 group was composed of cases having three elements.

F. Biochemical Analyses

Blood samples were obtained after an overnight fasting.

Glucose, TRG, HDL-C concentrations were determined.

G. Statistical Evaluations

SPSS Version 16 was used to perform statistical analyses. Mean \pm SD values were calculated. Correlation analyses were performed. Linear regression lines were drawn. A degree for statistical significance was accepted as $p < 0.05$.

III. RESULTS

Data collected for 554 children distributed into healthy N, OW, OB, MO and MetS groups were examined both for cases aged 72-120 months and for cases aged 121-192 months.

In children aged 72-120 months, mean age \pm SD values were 95.6 ± 14.5 , 94.7 ± 14.3 , 107.5 ± 9.1 , 96.6 ± 12.9 and 98.2 ± 13.8 years for N, OW, OB, MO and MetS groups, respectively.

The corresponding values in children aged 121-192 months were 139.5 ± 19.5 , 151.7 ± 20.9 , 153.7 ± 19.3 , 148.1 ± 17.4 , and 149.9 ± 18.6 years.

In Table I, values for waist C and tension index in the group, which includes children aged $6 \leq$ years and ≤ 10 years, were shown.

TABLE I
WAIST CIRCUMFERENCE AND TENSION INDEX VALUES IN 6-10 YEAR-OLD CHILDREN

Groups	Waist Circumference (cm)	Tension Index
N	55.3 ± 5.9	0.85 ± 0.06
OW	62.4 ± 7.6	0.88 ± 0.09
OB	72.8 ± 6.7	0.87 ± 0.07
MO	79.6 ± 8.8	0.90 ± 0.09
MetS2	78.2 ± 9.4	0.90 ± 0.08
MetS3	82.6 ± 10.9	1.03 ± 0.12

N- normal BMI.

As WC values increase going from healthy individuals to MetS3, the similar pattern was observed for tension index values.

Upon evaluation of tension index values, significant differences were noted between MO and MetS groups ($p = 0.001$ for MO vs. MetS3 and $p = 0.003$ for MetS2 vs. MetS3).

The values obtained for MetS components other than WC and BP were tabulated in Table II.

TABLE II
FBG, TRG AND HDL-CHOLESTEROL VALUES IN 6-10 YEAR-OLD CHILDREN

Groups	FBG (mg/dl)	TRG (mg/dl)	HDL-C (mg/dl)
N	86.9 ± 11.9	77.7 ± 49.2	54.2 ± 15.1
OW	89.1 ± 14.1	88.1 ± 44.2	48.5 ± 15.9
OB	88.4 ± 6.6	78.5 ± 39.8	53.4 ± 23.9
MO	88.1 ± 6.2	79.9 ± 36.2	51.2 ± 8.9
MetS2	87.6 ± 7.4	133.5 ± 69.7	40.0 ± 10.7
MetS3	96.9 ± 10.9	144.7 ± 90.5	36.3 ± 7.8

N- normal BMI.

Values of WC and tension index as well as FBG, TRG and HDL-C concentrations in children aged 121-192 months found for healthy N, OW, OB, MO, and MetS groups were listed in Tables III and IV, respectively.

Similar increasing pattern existed for WC as well as tension index values. The tension index between the MO and MetS

groups did not differ statistically.

TABLE III
WAIST CIRCUMFERENCE AND TENSION INDEX VALUES IN 11-16 YEAR-OLD CHILDREN

Groups	Waist Circumference (cm)	Tension Index
N	61.0 ± 5.7	0.89 ± 0.08
OW	78.4 ± 6.2	0.88 ± 0.12
OB	84.5 ± 7.8	0.94 ± 0.08
MO	94.3 ± 9.9	0.96 ± 0.09
MetS2	96.8 ± 12.8	0.98 ± 0.11
MetS3	100.0 ± 12.3	1.02 ± 0.14

N- normal BMI.

TABLE IV
FBG, TRG AND HDL-CHOLESTEROL VALUES IN 11-16 YEAR-OLD CHILDREN

Groups	FBG (mg/dl)	TRG (mg/dl)	HDL-C (mg/dl)
N	89.2 ± 8.7	91.1 ± 71.0	52.4 ± 14.6
OW	89.4 ± 8.2	99.0 ± 58.0	50.4 ± 13.6
OB	88.5 ± 7.8	112.3 ± 64.8	45.8 ± 11.1
MO	88.7 ± 6.2	92.9 ± 30.9	52.6 ± 26.4
MetS2	89.6 ± 14.7	139.1 ± 59.0	40.8 ± 8.9
MetS3	101.3 ± 6.8	136.8 ± 55.0	42.9 ± 7.8

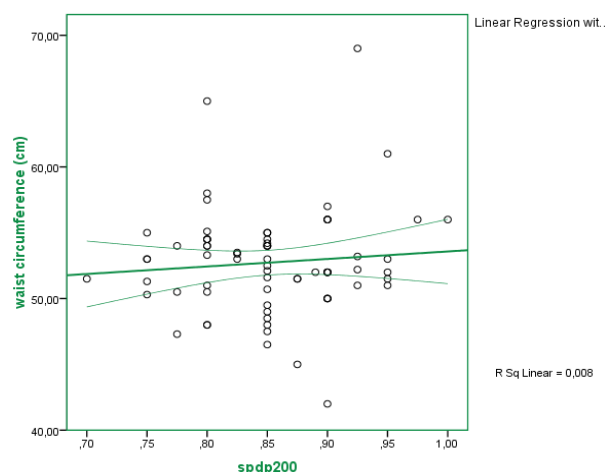
N- normal BMI.

In MO children aged 6 ≤ years and ≤10 years, a strong correlation was detected between WC and tense index ($r=0.384$, $p=0.001$) (Fig. 1 (B)).

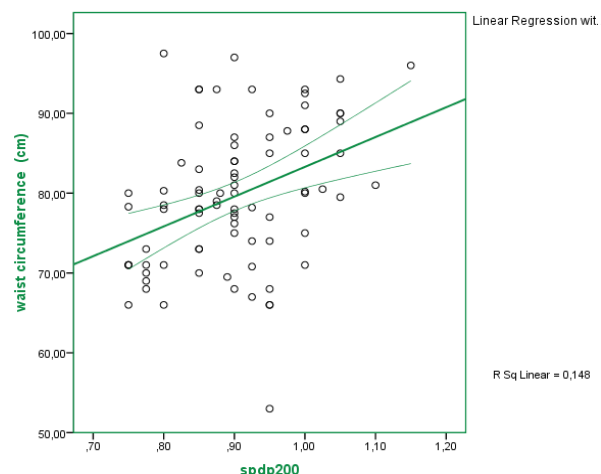
Significant correlations were calculated between WC and TRG ($r=0.451$, $p=0.031$) in the OB group as well as WC and HDL-C ($r=-0.304$, $p=0.042$) in the MetS group.

Significant differences noted between MO and MetS groups and the strong correlation detected between WC and tense index in MO group, in children aged 72-120 months could not be observed in children aged 121-192 months.

Significant correlations were found between the BMI and tension index values of the MO and MetS groups in the 72-120 month group. Much less stronger correlations existed in the 121-192 months group.



(A) Children with normal BMI



(B) MO children

Fig. 1 Association between waist circumference and tension index in children (aged 6-10 years) with normal BMI and morbid obesity

IV. DISCUSSION

Some controversies exist concerning the diagnosis of hypertension and the evaluation of BP values. Attempts related to the matter are being introduced in recent years. The impact of two guidelines on hypertension screening in OW/OB youth was evaluated. As a result of the comparison of European Society of Hypertension Guidelines 2016 (ESHG 2016) and the American Academy of Pediatrics Guidelines 2017 (AAPG2017), it was reported that prevalence of youth at a high risk of hypertension was 13% higher using AAPG2017 than ESHG2016 [13]-[15].

It is suggested that anthropometric indices must be considered in pediatric BP evaluation. Associations of anthropometric indices with obesity and MetS were investigated. Relations between adiposity indicators and BP as well as hypertension were suggested. High BP values were more frequent in OB children. Adiposity was confirmed to be a determinant of high BP. Anthropometric indices showed positive correlations with arterial pressure, WC and MetS. Higher anthropometric indices were associated with higher MetS risk score in children and adolescents. It was reported that high BMI values were associated significantly with elevated SP and DP values, particularly among OB children, whose ages were higher than 11 years. It has also been reported that risk factors covering also OW/OB, dyslipidemia, impaired glucose regulation, which, altogether, are components of MetS, were associated with the risk of new-onset hypertension [16]-[21].

The findings of this study were in agreement with the results of the other studies. Significant associations between tense index -derived from BP values- and WC as well as BMI values were found in MO and MetS groups, which are composed of, particularly, 6-10-year-old children

This study introduced a simple, practical tense index, which is shown to be diagnostic among MO children with and without MetS. It is also suggested that 130 mm Hg and 85 mm

Hg cut-off points for SBP and DBP, respectively, are too high as a MetS component in children because the tension index value calculated for MetS children was 1.00. This suggested that values lower than the above may be used for SBP and DBP for the MetS diagnosis in children, especially those below 10 years of age. This index may be helpful for the differential diagnosis of MO, MetS2 and MetS3 among 6-10-year-old children, for which, MetS cannot currently be diagnosed.

REFERENCES

- [1] V. Higgins, and K. Adeli, "Pediatric metabolic syndrome: pathophysiology and laboratory assessment," *J. Int. Fed. Clin. Chem. Lab. Med.*, vol. 28, pp. 25-42, March 2017.
- [2] T. T. K. Huang, S. S. Sun, and S. R. Daniels, "Understanding the nature of metabolic syndrome components in children and what they can and cannot do to predict adult disease," *J. Pediatr.*, vol.155, pp. e13-e14, Sept. 2009.
- [3] T. T. K. Huang, "Finding thresholds of risk for components of the pediatric metabolic syndrome," *J. Pediatr.*, vol.152, pp.158-159, Feb. 2008.
- [4] E. S. Ford, and C. Li, "Defining the metabolic syndrome in children and adolescents: Will the real definition please stand up?," *J. Pediatr.*, vol.152, pp. 160-164, Feb. 2008.
- [5] R. Weiss, A. A. Bremer, R. H. Lustig, "What is metabolic syndrome, and why are children getting it?," *Ann. N. Y. Acad. Sci.*, vol.1281, pp.123-140, Apr. 2013.
- [6] P. Zimmet, K. G. Alberti, F. Kaufman, N. Tajima, M. Silink, S. Arslanian, G. Wong, P. Bennett, 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, Oct. 2007.
- [7] C. Koebnick, M. H. Black, J. Wu, M. P. Martinez, N. Smith, B. Kuizon, D. Cuan, D. R. Young, J. M. Lawrence, and S. J. Jacobsen, "High blood pressure in overweight and obese youth: Implications for screening," *J. Clin. Hypertens.*, vol. 15, pp. 793-805, Nov. 2013.
- [8] A. A. Oduwole, T. A. Ladapo, I. B. Fajolu, E. N. Ekure, and O. F. Adeniyi, "Obesity and elevated blood pressure among adolescents in Lagos, Nigeria: A cross-sectional study," *BMC Public Health*, vol. 12, pp. 616: 1-6, Aug. 2012.
- [9] W. Strojny, D. Drozd, K. Fijorek, M. Korostynski, M. Piechota, W. Balwierz, J. A. Pietrzyk, P. Kwinta, M. Siedlar, and S. Skoczen, "Looking for a new diagnostic tools and biomarkers of hypertension in obese pediatric patients," *Blood Press. Monit.*, vol.22, pp.122-130, Jun. 2017.
- [10] Harvard Health Publishing, Harvard Medical School, Tips to measure your blood pressure correctly. Available at: <https://www.health.harvard.edu>, 2010-2019 Harvard University.
- [11] Great Ormond Street Hospital for Children, NHS Foundation Trust, Blood pressure monitoring. Available at: <https://www.gosh.nhs.uk>, 2019.
- [12] World Health Organization (WHO). The WHO Child Growth Standards. Available at: <http://www.who.int/childgrowth/en/> Accessed on June 10, 2016.
- [13] P. Di Bonito, G. Valerio, L. Pacifico, C. Chiesa, C. Invitti, A. Morandi, M. R. Licenziati, M. Manco, E. M. D. Giudice, M. G. Baroni, S. Loche, G. Tornese, F. Franco, C. Maffei, G. de Simone, CARITALY Study Group; on the behalf of the Childhood Obesity Study Group of the Italian Society of Pediatric Endocrinology, Diabetology, "Impact of the 2017 Blood Pressure Guidelines by the American Academy of Pediatrics in overweight/obese youth," *J. Hypertens.*, vol.37, pp. 732-738, Apr. 2019.
- [14] P. Di Bonito, G. Valerio, L. Pacifico, C. Chiesa, C. Invitti, A. Morandi, C. Maffei, M. R. Licenziati, M. Manco, E. M. D. Giudice, M. G. Baroni, S. Loche, G. Tornese, M. Tomat, G. de Simone, CARITALY Study Group, "A new index to simplify the screening of hypertension in overweight or obese youth," *Nutr. Metab. Cardiovasc. Dis.*, vol.27, pp.830-835, Sept. 2017.
- [15] R. Kelishadi, M. Bahreynian, R. Heslimat, M. E. Motlagh, S. Djalalinia, F. Naji, G. Ardalan, H. Asayesh, and M. Qorbani, "Accuracy of blood pressure-to-height ratio to define elevated blood pressure in children and adolescents: The CASPIAN-IV Study," *Pediatr. Cardiol.*, vol.37, pp. 378-385, Feb.2016.
- [16] K. Rimarova, E. Dorko, J. Diabelkova, Z. Sulanova, K. Frank, J. Bakova, T. Uhrin, P. Makovicky, N. Pelechova, and N. Konradova, "Anthropometric predictors of systolic and diastolic blood pressure considering intersexual differences in a group of selected schoolchildren," *Cent. Eur. J. Public Health*, vol. 26, pp. S4-S11, Dec. 2018.
- [17] M. L. Marcovecchio, A. Mohn, G. Diddi, N. Polidori, F. Chiarelli, and N. Fuiano, "Longitudinal assessment of blood pressure in school-aged children: A 3-year follow-up study," *Pediatr. Cardiol.*, vol.37, pp.255-261, Feb. 2016.
- [18] A. O. Fowokan, Z. Punthakee, C. Waddell, M. Rosin, K. M. Morrison, M. Gupta, K. Teo, S. Rangarajan, and S. A. Lear, "Adiposity measures and their validity in estimating risk of hypertension in South Asian children: a cross-sectional study," *BMJ Open*, vol.9, pp.e024087, Feb. 2019.
- [19] H. S. Ejtahed, M. Qorbani, M. E. Motlagh, P. Angoorani, S. Hasani-Ranjbar, H. Ziaodini, M. Taheri, Z. Ahadi, S. Beshtar, T. Aminae, R. Heshmat, and R. Kelishadi, "Association of anthropometric indices with continuous metabolic syndrome in children and adolescents: the CASPIAN-V study," *Eat. Weight Disord.*, vol.23, p. 597-604, Oct. 2018.
- [20] A. E. Al-Agha, and A. O. Mahjoub, "Impact of body mass index on high blood pressure among obese children in the western region of Saudi Arabia," *Saudi Med. J.*, vol.39, pp.45-51, Jan. 2018.
- [21] Y. Huang, Z. Deng, Z. Se, Y. Bai, C. Yan, Q. Zhan, Q. Zeng, P. Ouyang, M. Dai, and D. Xu, "Combined impact of risk factors on the subsequent development of hypertension," *J. Hypertens.*, vol.37, pp. 696-701, Apr. 2019.