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Evaluation of Neck Circumference as Potential Marker for Metabolic Syndrome in Children

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Abstract

Background: Metabolic syndrome (MetS) is complicated condition especially in pediatrics. For better MetS definition, marker discovery are interested. More accurate simple indices may be of value, such as neck circumference (NC). We investigated accuracy of NC for the diagnosis of MetS in adolescent girls.

Materials and Methods: This cross-sectional study was conducted on schoolgirl who live in Mashhad and Sabzevar cities, Razavi Khorasan, Iran at 2018. The study sample comprised 988 girls with mean age 14.56 ±1.53 years old. The NC measured in site between mid-cervical spine and mid-anterior neck and enzymatic commercial kits measured biochemical analysis. The definitions of MetS included: IDF, NCEP-ATP III, and two modified NCEPs.

Results: Often subjects are non-smoker, menstruated, and reside in Mashhad. The age, living location, and dwelling type showed the very weak association with NC. NC was significantly associated with WC and elevated TG. The highest (r= 0.275 (P= 0.0001), and lowest (r= 0.155 (P< 0.001) association were between NC and the DeFerranti's and IDF definitions, respectively. The odd ratios (CI 95%) estimated for the different definitions were as follows: IDF: 1.41 (1.18- 1.69), NCEP: 1.54 (1.31- 1.79), Cook's: 1.68 (1.37- 2.07), and DeFerranti's: 1.59 (1.40- 1.80). ROC analysis showed that the specificity ranged between 78.57 – 100.00% and sensitivity ranged between 62.10 – 78.22% of NC for the different definitions of MetS definitions. A NC of >31 cm estimated as cutoff for all studied definitions except Cook's definition.

Conclusion: Besed on the results, NC should be considered as marker for central obesity and fat distribution in the diagnosis of MetS.

Key Words: Children, Anthropometric index, Metabolic Syndrome, Obesity.

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1- INTRODUCTION

Metabolic syndrome (MetS) is a clustering of metabolic abnormalities that are associated with an increased risk of CVD and diabetes. The cardio-metabolic risk related to MetS is thought to be mediated in part by the impact of visceral adiposity (1). The MetS prevalence in children and adolescents have only recently been assessed, because there is no established definition for MetS in this group, and investigators have attempted to identify new markers for better definition in this age group. Visceral adiposity and upper body fat have a key influence on CVD risk, and neck circumference (NC) has been used as a marker for these risk factors (2-4). There is a lack of epidemiological data for the applicability of NC in defining MetS. The accuracy in determining of central obesity and fat distribution patterns using anthropometric measures is challenging in defining MetS in children (5). Many studies have shown a relationship between NC and the risk of CVD and metabolic syndrome (6-11). NC may also be used for the prediction of hyperinsulinemia and the identification of insulin resistance (9, 12). In this study, we aimed to investigate the association between NC and different criteria including International Diabetes Federation (IDF), National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATPIII), modified NCEP such as Cook et al. and DeFerranti et al.'s definitions (1, 8, 14, 15), to introduce potential marker for definition of MetS in pediatrics.

2- MATERIALS AND METHODS

2-1. Study design and population

This cross-sectional study was conducted in 2018. It performed as secondary studies on population compromised 988 schoolgirl children ranged in 12 to 18 years old (14.56 ± 1.53), who resided in Mashhad and Sabzevar cities in Razavi Khorasan province, Iran, which participated in vitamin D supplementation RCT program at 2015 to 2018. The subjects were selected by random cluster sampling.

2-2. demographic and anthropometric assessments

Some demographic data including age, smoking status, menstruation, parental education, dwelling type, and location were collected by using researcher-made questionnaire. The anthropometrics measured by well-trained staff in health centers. An aneroid sphygmomanometer with pediatric cuff was used for measurement of blood pressure on right arm of participants, who were in sitting position. The level midway between the lower rib margin and the iliac crest at the end of expiration was measured as waist circumference, while individuals were standing and wearing only underwear. NC was measured in the midway of the neck between mid-cervical spine and mid-anterior neck to 0.5 cm, if palpable, just below the laryngeal prominence while the subjects hold erect their heads in the horizontal Frankfort plane positioning. All anthropometric indices were measured twice by non-stretchable metric tape. The hip circumference (HiC) measures performed at the sites of suggested by WHO. Some anthropometrics such as body mass index (BMI), waist to height ratio (WHtR), and waist to hip ratio (WHR) used for better description of obesity (13).

2-3. Biochemical measurements

Blood samples were taken after 12-14 hours fasting, using standard protocols. Collected blood samples were analyzed at the laboratory immediately in ice-box. Serum was separated by centrifugation at room temperature (Behdad, Tehran, Iran). Biochemical analysis including serum concentrations of total cholesterol, fasting triglycerides, glucose, and HDL-cholesterol were determined via enzymatic methods by using commercial kits (Pars Azmoon Teb Co., Tehran, Iran) using a Cobas 2000 autoanalyzer (Roche Diagnostics International Ltd, US).

2-4. the MetS definitions

In present study four criteria which adopted for MetS in adolescents was used. The IDF, NCEP-ATPIII, Cook et al and De Ferranti et al definition criteria were used for the diagnosis of metabolic syndrome (1, 8, 14, 15).

2-5. Ethical consideration

The Ethics Committee of the Medical Faculty, Mashhad University of Medical Sciences, approved the study (ID-code: IR.MUMS.fm.REC.1395.12). Written informed consent for participation was obtained from their parents on behalf of all individuals.

2-6. Inclusion and exclusion criteria

The subjects with some diseases such as autoimmune diseases, cancer, metabolic bone disease, hepatic or renal failure, cardiovascular disorders, malabsorption or thyroid, parathyroid or adrenal disease have been excluded from study. As well, the participants excluded who were taking medication including anti-inflammatory, anti-depressant, anti-diabetic, or anti-obesity drugs and hormone therapy within the last six months. In final, the subjects with neck masses and deformity excluded.

2-7. Data Analyses

The normality of data was tested using the Kormogrov-Smirnov test for all variables that use in determining the presence of the MetS. Descriptive parameters are shown as age-adjusted estimated mean ± standard error, or as percentages. Two-sided t-tests and Pearson's chi-square tests were used to analyze the differences between means and proportions of groups. Pearson correlation coefficients were analyzed to study the relationship between variables. The correlation between quantitative values of NC and dichotomous measures calculated by point-biserial correlation test. A binary logistic regression analysis was applied to drive the odd ratio (95% CI), likelihood ratio and R-square statistics to identification of prediction ability of NC for pediatric MetS. Binary logistic regression provides a probability of pediatric MetS estimation based on maximum likelihood approach. All data were analysis, using SPSS version 16.0 (SPSS Inc., Chicago, IL, US). A p-value of <0.05 was considered as significant. The receiver operating characteristic (ROC) curves were plotted for estimation of efficacy of NC for screening of individuals with MetS. ROC analysis and computing of sensitivity and specificity of NC were performed using the MedCalc version 15.8 (MedCalc software, Osted, Belgium).

3- RESULTS

The demographic information and its association with NC showed in **Table.1**. Our findings are shown in **Table.2**, with NC values in different MetS definitions and its components. For most of the MetS criteria, NC was associated with WC and lipid profile and its difference was shown to be statistically significant between individuals with and without MetS. NC was significantly higher in subjects who met the hypertriglyceridemia criterion of MetS, and the point-biserial correlation coefficient between them was r= 0.076, P=0.024). IDF defined MetS and NC showed a significant correlation (r= 0.155, P<0.001). For the NCEP-ATPIII definition, NC was associated with WC, diastolic blood pressure (DBP), and triglyceride (TG) with r= 0.462, P< 0.001), r= 0.104, P=0.002), and r= 0.096, P=0.004), respectively. Point- biserial correlation analysis revealed that there is significant positive association between MetS definition based on NCEP-ATPIII definition and NC (r= 0.220, P< 0.001). As for the IDF definition, among the criteria of Cook's definition only WC (r= 0.462, P< 0.001), and TG (r= 0.096, 0.004) were observed to correlate with NC. In contrast with the other definitions of MetS, the criteria for the De Ferranti's definition were significantly associated with NC apart from fasting blood glucose (FBG) (r= 0.049, P=0.152). In spite of statistically significant correlation between NC and some MetS parameters, these relationships often are weak. NC showed a positive association with several anthropometric measures of obesity or central obesity. The greatest correlation was observed for WHtR (r= 0.734, P= 0.0001), a measure of the distribution of body fat. In addition, NC was associated with weight (r= 0.733, P= 0.0001), BMI (r= 0.714, P= 0.001), WC (r= 0.705, P= 0.0001), HiC (r= 0.677, P= 0.0001), and WHR (r= 0.262, P= 0.0001). Binary logistic regression was performed to derive the likelihood statistics, R- square statistic, to identify a prediction model of MetS using NC measure and computed odd ratios (95% CI) of high NC values for pediatric MetS in this population (**Table.3**). Among different pediatric MetS definitions, NC appeared to be the best predictor of MetS using the DeFerranti's definition and was a good predictor for NCEP and Cook's definitions (**Table.3**).

Table-1: The demographic information and its correlation with NC measures.

Demographic information	Measures	Correlation with NC	P-value
Age	14.56 ± 1.53	0.167	0.0001
Smoking status		-0.04	0.211
No smoke exposure	67.6 (650)		
Passive smoker			
Less than 1 h	11.8 (113)		
1 to 3 h	3.6 (35)		
More than 3 h	4.7 (45)		
No idea	12.3 (118)		
Menstruation		-0.240	0.0001
Yes	88.1 (869)		
No	11.9 (119)		
Parental education		0.038	0.254
Illiterate	4.4 (41)		
Educated	95.6 (879)		
Academic degree	15.5 (141)		
dwelling type		0.069	0.028
Apartment	39.6 (368)		
Independent home	60.4 (620)		
Living location, city		0.070	0.027
Mashhad	70.2 (720)		
Sabzevar	29.8 (268)		

* Data shown as number (%). SD: Standard deviation. NC: Neck circumference.

** Point-biserial correlation used for described the correlation between NC and demographic information (dichotomous variables).

Table-2: Mean differences and correlation coefficients between neck circumference and MetS risk factors based four definitions.

Definition	Criteria	Neck circumference (cm), mean± SD		P-value	Correlation coefficient (P-value)
		Non-MetS	MetS		
IDF (15)	WC	30.74±2.035	34.57 ± 2.722	0.0001	0.462 (0.0001)
	FBG	31.18±2.350	31.08 ± 2.692	0.689	-0.014 (0.689)
	SBP	31.09±2.365	32.16 ± 2.588	0.051	0.063 (0.051)
	DBP	31.09±2.385	31.70 ± 1.932	0.168	0.045 (0.168)
	TG	31.10±2.367	31.85 ± 2.527	0.024	0.076 (0.024)
	HDL	31.07±2.301	31.47 ± 2.689	0.051	0.067 (0.051)
	MetS *	31.07±2.347	34.42 ± 1.929	0.0001	0.155 (0.0001)
NCEP-ATPIII, (1)	WC	30.74 ± 2.035	34.57 ± 2.722	0.0001	0.462 (0.0001)
	FBG	31.15 ± 2.384	31.79 ± 2.440	0.152	0.049 (0.152)
	SBP	31.09 ± 2.370	31.62 ± 2.316	0.268	0.037 (0.268)
	DBP	31.02 ± 2.365	31.77 ± 2.313	0.002	0.104 (0.002)
	TG	31.03 ± 2.229	31.60 ± 2.881	0.004	0.096 (0.004)
	HDL	31.06 ± 2.287	31.44 ± 2.674	0.054	0.066 (0.054)
	MetS *	31.03 ± 2.247	34.42 ± 4.242	0.0001	0.220 (0.0001)
Cook et al., 2003, (14)	WC	30.76 ± 2.035	34.57 ± 2.722	0.0001	0.462 (0.0001)
	FBG	31.15 ± 2.384	31.79 ± 2.440	0.152	0.049 (0.152)
	BP	31.09 ± 2.370	31.62 ± 2.316	0.268	0.037 (0.268)
	TG	31.03 ± 2.229	31.60 ± 2.881	0.004	0.096 (0.004)
	HDL	31.06 ± 2.287	31.44 ± 2.674	0.054	0.066 (0.054)
	MetS *	31.05 ± 2.259	35.57 ± 4.783	0.000	0.226 (0.000)
DeFerranti et al., 2004, (8)	WC	30.65 ± 2.008	33.89 ± 2.532	0.0001	0.475 (0.0001)
	FBG	31.15 ± 2.384	31.79 ± 2.440	0.152	0.049 (0.152)
	BP	30.65 ± 2.204	30.65 ± 2.204	0.008	0.125 (0.008)
	TG	30.97 ± 2.207	31.65 ± 2.777	0.0001	0.125 (0.0001)
	HDL	30.79 ± 2.310	31.37 ± 2.410	0.001	0.118 (0.001)
	MetS *	30.98 ± 2.221	34.16 ± 3.345	0.0001	0.275 (0.0001)

WC: Waist circumference; FBG: Fasting blood glucose; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; TG: Triglyceride; HDL: High-density lipoprotein. MetS: Metabolic syndrome, NC: Neck circumference, SD: Standard deviation, *Association between MetS as dichotomous variable and NC (quantitative variable) was computed by point- biserial correlation test.

Table-3: ROC analysis of NC for all different pediatric MetS definitions.

Definition, (1, 8, 14, 15)	Neck Circumference (cm)			
	Specificity (%)	Sensitivity (%)	AUC (95% CI)	Cut-off value (cm)
IDF	100.00	62.10	.878 (.856-.897)	>31
NCEP-ATP III	83.33	62.46	.801 (.703-.899)	>31
Cook et al., 2003	78.57	78.22	.860 (.762-.957)	>32
DeFerranti et al., 2004	83.72	63.40	.815 (.753-.877)	>31

IDF: International Diabetes Federation, NC: Neck circumference, CI: Confidence interval, ROC: Receiver operating characteristic, AUC: Area under the curve.

The ROC analysis shown specificity and sensitivity of NC for MetS definitions ranged from 78.57–100.00% and 62.10–78.22%, respectively. The highest specificity observed in adopted IDF definition and lowest contributed to Cook et al. definition. In contrast with these findings, NC have highest (78.22%), and lowest (62.10%) sensitivity for Cook's and IDF definitions, respectively. Area under curve (AUC) of NC in IDF definition showed the largest (0.878 (.856-.897) amount and this area in NCEP- ATPIII definition was smallest [(0.801 (.703-.899)] area among all four studied definitions. In general, IDF and Cook's definitions illustrated larger AUC than other used definitions. NC more than 31 cm estimated as cutoff for all studied definitions except Cook's definition (**Table.4 and Figure.1**).

Table-4: ROC analysis of NC for all different pediatric MetS definitions.

Definition, (1, 8, 14, 15)	Neck Circumference (cm)			
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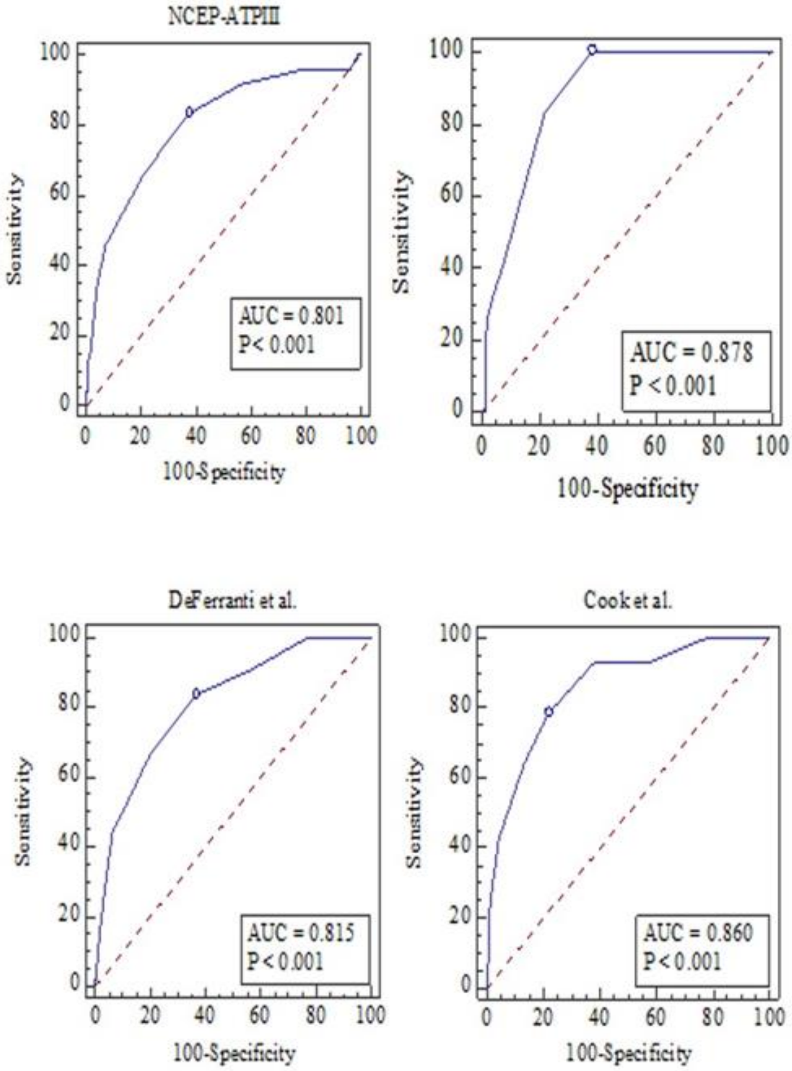

Fig. 1: ROC for NC in four different MetS definitions. These definitions adopted for pediatrics, as showed in charts, larger AUC belongs to NC for IDF and Cook et al. definitions, respectively.

NC: Neck circumference, IDF: International diabetes federation, NCEP-ATPIII: National Cholesterol Education Program-Adult Treatment Panel III.

4- DISCUSSION

We have investigated the relationship between NC and the components of MetS in children, using four different and most frequently used criteria for MetS in children and adolescents. The NC measures were associated with WC, which is recently proposed as a possible marker for central obesity and a marker of MetS. Overweight and obesity are major risk factors for some chronic diseases such as metabolic syndrome, diabetes, CVDs and cancer. general and central obesity were estimated by means of BMI and WC indices, respectively and these indices are important to assessment of the level and distribution of obesity (7). In the definition of MetS especially in adolescents, WC has received more attention than BMI; nevertheless cutoff values of WC for overweight and obesity maybe influenced by geographic conditions, ethnicity, gender, and age. Therefore, various techniques are used for assessing central obesity including NC. Furthermore such anthropometric indices can be useful for determining body fat distribution (16).

An investigation of adults in China has shown that the NC is an acceptable marker for assessing obesity and, the MetS factors were also correlated positively with a higher NC (17). NC can be used as potential index for distribution of upper-body subcutaneous fat, as well as this measure is inexpensive, simple, fast and reliable method for assessment of obesity (16, 18); in present study, we seen good association between NC and WHtR even more than body weight and BMI, which may be represent NC as fat distribution measure. On the other hand, observations revealed that in women association of increased neck circumference with disproportionate increase in adipose tissue, are more than man (7, 16). NC was associated with conventional obesity indexes including weight, BMI, waist and hip circumferences and waist/hip ratio in both genders (9), in similar to Saka et al., association of NC with such obesity indices have been observed in this study. Combination of NC with other anthropometric measures can be useful for partitioning of influences of visceral and subcutaneous fat and its distribution on metabolic indicators. Many researchers shown positive correlation between NC and insulin resistance and MetS components (4, 6, 11, 19); Yang et al concluded that in Chinese subjects with type 2 diabetes, NC has positive relation with BMI, WC, and MetS (20). Our results were proved these findings, positive correlation between NC and BMI, WC and MetS and some its components have seen in this population. The observations shown that individuals in the highest quintile of NC had lipid or glucose metabolism disorders and fasting hyperinsulinemia (12, 21). According to the results of the Framingham study, NC was positively associated with triglycerides, fasting plasma glucose in women (22). The NC was associated with BMI, WC, waist/hip, total cholesterol, LDL- cholesterol, TG and, glucose (7).

In our study NC was correlated with obesity indexes and TG as component of MetS; but there is no association between NC and FBG in this population that may be arose age, sex, ethnicity even health status of studied population. In children, Androutsos et al., showed that NC have had correlated with most CVD risk factors including SBP, HDL, insulin-related indices and TG, similar to these findings have been observed in association of NC with components of MetS based on De Ferranti's definition (23). Some investigators stated that the NC and neck fat have association with insulin resistance, glucose impairment, hyperlipidemia and hypertension (21, 24). As well as association between NC and insulin resistant, hypertension, and dyslipidemia has been determined in Framingham Heart study (22); in our study, only in De Ferranti's association between NC and BP has been significant, but in all studied definitions, significant association of NC and elevated TG have been observed. The NC may be a novel index of upper-body obesity; moreover this anthropometric measure has been related to cardiovascular risk factors, insulin resistance and some MetS components and also Stabe et al., found only in women the relationship between elevated NC measurements and the chance to developing MetS (6, 18, 21, 25). So NC could be good excess marker for MetS evaluation especially in girls in combination with other criteria. The NC is associated with visceral fat, MetS components and insulin resistance; these hallmarks made it suitable method to ascertain specially body fat distribution in women.

4-1. Study Limitations

The main limitation in this study was female study population and lack of data from both genders, and another limitation arose from low prevalence of MetS in our studied population.

5- CONCLUSION

The assessment of MetS in children is difficult, because there are no appreciate and as enough as comprehensive definition for MetS in pediatrics, and investigators have attempted to identify new markers for better definition. Determining of obesity was most challenging problem, because adipose tissue function influenced by growth and pubertal changes, therefore some studies focused on finding marker for obesity in this age group for better measuring of obesity. The neck circumference introduced as potential marker for obesity. In present study, we attempt to investigate the suitability and functionality of NC as measure for pediatric MetS. In final, we concluded that NC can be measured as potential marker for MetS in pediatrics; but further studied needed to prove this results especially on both genders and other ethnic groups of pediatric population.

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7- CONFLICT OF INTEREST: None.

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