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Comparison of Components of Metabolic Syndrome among Metabolically Obese Normal Weight, Metabolically Benign Normal Weight, and Metabolically Abnormal Obese Iranian Children and Adolescents in Ahvaz

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ABSTRACT

Background: Metabolically obese normal-weight (MONW) children and adolescents are characterized by body mass index (BMI) lower than +1SD with metabolic disorders such as hyperglycemia, hypertriglyceridemia, and/or hypertension. This study wants to determineprevalence of MONW, metabolically benign normal weight (MBNW), metabolically abnormality obese (MAO) and comparethe components of metabolic syndrome (MetS) in some Iranian normal-weight children and adolescents in Ahvaz, Iran. **Methods:** This cross-sectional study was conducted on 1124 boys and 1128 girls, aged 10–18 y, Ahvaz, Khuzestan.Participants were selected from 6 health centers in Ahvaz by a multistage cluster random sampling method. The Mets was defined according to the modified Adult Treatment Panel III (ATP III). Anthropometric measurements and blood pressure were measured according to standard protocols. Fasting blood samples were collected for biochemical assessment. **Results:** MetS prevalence in normal weight group was 5.4% and 1.45% in boys and girls, respectively (P = 0.001) showing a significant difference. Triglyceride abnormality percentages (MBNW = 23.9%, MAO = 88.8%, MONW = 91%) and high density lipoprotein (MBNW = 19.2%, MAO = 73.8% and MONW = 67.2%) were higher than other MetS components in these groups. **Conclusions:** Since BMI in children and adolescents with metabolically obese-normal weight is normal, the continuous measurements and treatment of MetS components especially in boys are important from public health view. The components mean of MetS was higher in MONW and MAO individuals compared with MBNW.

Keywords: *Metabolic syndrome; Metabolically obese-normal weight; Children.*

Introduction

Obesity is characterized by excessive fat accumulation whichis associated with a greater risk of many chronic diseases (World Health Organization, 2015). The global prevalence of overweight and obesity in 5-15 years old

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children is 10%. This prevalence is dramatically different in developing countries, from 5.7% to over 40% in Pakistan and Mexico, respectively (Gupta *et al.*, 2012). Although one of the major obesity-related phenotypes is metabolic syndrome (MetS) (Kwon et al., 2013) and itenhances with increasing degree of obesity (the prevalence may reach 50% in severely obese children and adolescents) (Weiss et al., 2004), there is not any absolutelinear association between metabolic abnormalities and body weight. Therefore, we can say that there is dysmetabolic status in normal weight subjects (Kwon et al., 2013). The specific type of obesity defined as metabolically obese normal weight subjects (MONW) was first introduced by Ruderman, in the early 80s (Ruderman et al., 1981a, Ruderman et al., 1981b). These individuals were characterized by normal body weight with elevated seruminsulin levels and metabolic disorders such as hyperglycemia, hypertriglyceridemia, or hypertension. The presence of this phenotype in children increases the risk of developing atherosclerosis, cardiovascular diseases, type 2 diabetes mellitus, and stroke later in life (Ruderman et al., 1981a, Ruderman et al., 1981b). In some studies visceral fat is used as the cut-off point to diagnose MONW subjects (Anastasiou et al., 2010). Waist circumference (WC) is applied as an appropriate screening tool for predicting the presence of excessive abdominal fat content and the MetS for children and adolescents. It is estimated that5–30% of population with normal-weight are considered MONW (St-Onge et al., 2004). It has been estimated that individuals with MONW phenotype are around 9.9% and 11.0%, of urban Iranian males and females, respectively (Hadaegh et al., 2007). The etiology of the MONW phenotype is multifactorial as well as genetic and metabolic and environmental factors have some contributions in it. There are some publications suggesting these contributing factors, such as gender, ethnicity/race, physical activity, smoking (St-Onge et al., 2004) high sensitivity CRP (Kwon et al., 2013), the distribution of fat mass and lean body mass (De Lorenzo et al., 2006), high carbohydrates diet (Ruderman *et al.*, 1981b), reduction in VO2max (Ruderman *et al.*, 1998), abdominal and visceral fat accumulation (Bednarek-Tupikowska et al., 2012), and the differences in muscle tissues(Marques-Vidal et al., 2010).

Non-obese children with metabolic abnormality are predisposed to the development of MetS despite having a normal weight.Since some obese individuals are phenotypically obese but metabolically normal, therefore primary prevention of chronic disease should not be limited to obese children.

To the best of our knowledge, most studies about MONW have been conducted on adults and there are few studies reporting such anassociation among NWO, MONW, and components of the MetS in children and adolescents especially in developing countries. Studies in this field are potentially important because the process of atherosclerosis, which is linked to components of MetS begins in early ages.This study was applied to compare each components of MetS in metabolically obese- normal weight, metabolic syndrome-obese, and no metabolic syndrome-normal weight subjects in a representative sample of children and adolescents from a non-Western population.

Materials and Methods

Participants and study design: This cross-sectional study was carried out on 1128 girls and 1124 boys aged < 18 y from 6 health centers in Ahvaz, Iran. In each selected center, a representative sample (23 households) was selected by a multistage cluster random sampling method. Written informed consent was obtained from all parents of children.

Measurements: Weight was measured while participants were wearing light clothing without shoes using a Seca scale (Seca Company, Hamburg, Germany) with an accuracy of 100 g. Height was measured applying a tape while subjects were standing without shoes, in the normal position of shoulders. Height recorded to the nearest 0.1 cm. WC was measured in the narrowest level at the midway

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point between the lowest rib and the right iliac crest. In order to calculate body mass index (BMI) we divided weight in kilograms by height in squared meters. Blood pressure was measured twice using a standard mercury sphygmomanometer (model ALPK2; Tycosw, Arden, NC, USA), with an appropriate cuff size. Participants were in a comfortable seated position for 15 minutes before blood pressure measurement. Two blood pressure measurements were calculated with 5 minutes interval. The mean of the two measured systolic and diastolic blood pressures was used for the analysis. To reduce the measurement error, all measurements were performed by a trained nutritionist. Fasting blood samples were taken after a 12-hour overnight fast. One of their parents was present at the time of blood sampling. The blood samples were centrifuged and their serums were stored in the refrigerator. Fasting blood glucose (FBG), triglyceride (TG), high density lipoprotein (HDL), and total cholesterol (TC) were measured by enzymatic colorimetric technique with Pars Azmoon kits in (Biotechnical tools model BT-3000, Germany).

Definitions: According to modified Adult Treatment Panel III (ATP III) criteria for the diagnosis of MetS in children and adolescents three or more of the following conditions were used for diagnosis: 1. Abdominal obesity (waist circumference ≥ 90th percentile for age and sex of the study population) 2. Hypertension (systolic blood pressure and diastolic pressure ≥ 90th percentile for sex and age, with the exception of 18 and 19, which are ≥ 130 mmHg systolic blood pressure and ≥ 85 mmHg diastolic blood pressure are considered) 3. Low HDL levels (≤ 40 mg/dl) 4. High levels of TG (≥ 110 mg/dl) 5. High levels of FBG (≥ 100 mg/dl) (Kelishadi et al., 2008).

The participants were divided into three groups: 1.Metabolically benign normal weight (MBNW), with a BMI is lower than +1SD in the population under study with ≤ 2 components of MetS. 2. Metabolically abnormal obese (MAO) with a BMI above +1 SD and 3 or more of the five MetS. 3. Metabolically obese- normal weight (MONW) is defined as the presence of 3 or more of the five MetS components and BMI lower than + 1SD.

Data analysis: Chi-square test and independent sample *t*-test were performed for correlation assessment using SPSS version 19 (SPSS Inc., Chicago). In order to provide figures, chart builder was considered and P-value < 0.05 was set as the statistically significant level.

Results

General characteristics of participant are shown in **Table 1**. Boys had a higher WC and a lower BMI than girls (P < 0.001). Boys had a higher FBG and TG levels, but lower HDL concentration compared with girls. No statistically significant differences were found between girls and boys in systolic and diastolic blood pressures.

Table 1. Comparing the mean of study variable between boys and girls

Variables/Sex	Boys (n = 1124)	Girls (n = 1128)	P-value[a]	Total
Age (year)	14.2 ± 2.6[b]	14.8 ± 2. 8	0.001	14.50 ± 2.72
Waist circumference (cm)	70.7 ± 11.2	68.1 ± 9.8	0.001	69.41 ± 10.58
Body mass index (kg/m^2)	19.8 ± 4.4	20.8 ± 4.2	0.001	20.29 ± 4.34
Fasting blood sugar (mg/dl)	91.0 ± 19.0	89.2 ± 12.5	0.006	90.09 ± 16.05
Triglyceride (mg/dl)	111.6 ± 67.0	100.4 ± 57.6	0.001	105.94 ± 62.67
Systolic blood pressure (mmHg)	106.0 ± 11.3	106.0 ± 10.2	0.852	106.54 ± 10.72
Diastolic blood pressure (mmHg)	64.7 ± 10.1	65.0 ± 9.3	0.515	64.82 ± 9.70
High density lipoprotein (mg/dl)	53.8 ± 12.2	55.6 ± 11. 8	0.001	54.71 ± 12.01

[a]: Student *t*-test ; [b]: Mean ± SD

The prevalence of MetS in 886 boys and 863 girls with normal weight was 8% and 2.9% (*P* = 0.001), respectively. Subjects were classified into three groups: MBNW (n = 1572, 71.4 % of total subjects and 89.98% of normal weight subjects), MAO (n = 80, 3.6% of total subjects and 15.77% of obese subjects) and MONW (n = 122, 5.5% of total subjects and 6.98% of non-obese subjects). The differences of mean of WC, TG and FBG were significant among groups but no statistically significant differences were observed in HDL and blood pressure. Percent of abnormality of TG than normality of TG compared to other components of MetS was higher in three groups (**Table 2)**. As it is shown in **Table 3**, the difference of TG in boys and girls was significant among 3 groups. In the differences of means of waist were significant in girls among the studied groups too.

Table 2. Frequency distribution of study population in terms of obesity type and components of metabolic syndrome status in children and adolescents, Ahvaz, Iran

	HDL		TG		BP		WC		FBG	
	Normal	Abnormal	normal	abnormal	normal	abnormal	Normal	abnormal	normal	Abnormal
MBNW (n = 1572)	1270(81)*	302(19)	1196(76)	376(24)	1288(82)	284(18)	1513(96)	59(4)	1367(87)	205(13)
MAO (n = 80)	21(26)	59(74)	9(11)	71(89)	31(39)	49(61)	38(47.5)	42(52.5)	51(64)	29(36)
MONW (n = 122)	40(33)	82(67)	11(9)	111(91)	50(41)	72(59)	60(49)	62(51)	54(44)	68(56)
P-value	0.188		<0.001		0.200		0.001		0.049	

*: n (%), WC: waist circumference (less than 90th percentile), HDL: high-density lipoprotein, TG: triglyceride, FBG: fasting blood glucose, BP: blood pressure, MBNW: Metabolically benign normal weight, MAO: Metabolically abnormal obese, MONW: Metabolically obese- normal weight

Table 3. Frequency distribution of study population in terms of obesity type, components of metabolic syndrome status, and sex in children and adolescents, Ahvaz, Iran

Variables		Boys				Girls			
		MBNW	MAO	MONW	P-value	MBNW	MAO	MONW	P-value
HDL	Normal	612(79)*	6(18)	35(39)	0.93	658(83)	15(32)	5(15)	0.07
	abnormal	165(21)	27(82)	54(61)		137(17)	32(68)	28(85)	
TG	Normal	577(74)	1(3)	11(33)	0.01	619(78)	8(17)	4(12.1)	.001
	abnormal	200(26)	32(97)	22(67)		176(22)	39(83)	29(88)	
BP	Normal	623(80)	11(33)	36(40)	0.37	665(84)	20(43)	14(42)	0.44
	abnormal	154(19)	22(67)	53(60)		130(16)	27(57)	19(58)	
WC	Normal	742(96)	23(70)	41(46)	0.75	771(97)	15(32)	19(58)	0.001
	abnormal	35(5)	10(30)	48(54)		24(3)	32(68)	141(42)	
FBG	Normal	658(85)	19(58)	41(46)	0.07	709(89)	32(68)	13(39)	0.45
	abnormal	119(15)	14(43)	48(54)		86(11)	15(32)	20(61)	

*: n (%),WC: waist circumference (less than 90thpercentile),HDL: high-density lipoprotein,TG: triglyceride,FBG: fasting blood sugar,SBP: systolic blood pressure,DBP: Diastolic Blood Pressure, MBNW: Metabolically benign normal weight, MAO: Metabolically abnormal obese, MONW: Metabolically obese- normal weight

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The percent of abnormal of metabolic syndrome was higher in MONW and MAO groups compared with MBNW group (**Table 4**).

Table 4. The percent of abnormal components of metabolic syndrome in children and adolescents

Groups	HDL	TG	SBP	DBP	WC	FBG
MBNW (n = 1572)	56.1	93.7	105.5	63.9	66.3	89.4
MAO (n = 80)	46.3	166.6	112.8	68.7	81.2	92.5
MONW (n = 122)	45.5	179.0	112.0	88.9	80.8	99.9

WC: waist circumference (less than 90th percentile),HDL: high-density lipoprotein, TG: triglyceride, FBG: fasting blood glucose, SBP: systolic blood pressure, DBP: Diastolic Blood Pressure, MBNW: Metabolically benign normal weight, MAO: Metabolically abnormal obese, MONW: Metabolically obese- normal weight.

Discussion

In this cross sectional study, the prevalence of MONW among children and adolescents aged 10–19 y was 5.4% based on the modified ATPIII 2005 criteria which was significantly higher in boys than girls.To our knowledge, this is the first study which compares different components of MetS in MBNW, MAO, and MONW in Iranian children and adolescents. The results of this study showed that there are children and adolescents with MetS who are not obese according to BMI percentile.As early as 1981, Rudermanand colleagues, proposed that MONW adult population might be characterized by the increase in fat cell size and hyper insulinemia compared to patients of similar height, weight, and age or to themselves at an earlier time (Ruderman et al., 1981b). The prevalence of low HDL and high TG levels was high in this study which is similar to Tenhola(Tenhola et al., 2000), Qorbani (Qorbani *et al.*, 2013)and Kelishadi (Kelishadi et al., 2008)studies, and it seems that these components are predominant featuresofdyslipidemiaamong the normal weght children in our survey.Differences in prevalence of components of MetS lead to differences in prevalence of MetS in societies (Shahbazian et al., 2013). The relationship between metabolic risk factors and obesity has been confirmed for many years. Obese children had higher prevalence of metabolic disordersthan non-obese children. Inthis research, the percentage of overweight and obesity was 15.8% among children and adolescents with MetS. These results were in line with the data reported from children in other countries such as China (Ma et al., 2006), Mexico (Perichart-Perera et al., 2007), Iran (Hamidi et al., 2006), Germany (Reinehr et al., 2005)and The United States (Pan and Pratt, 2008). The concept of MONW is not limited to. In recent years, several studies have investigated childhood obesity as a problem inlater years of life. Although obese adolescents are moresusceptible to have disturbed metabolism than their normal-weight peers, but this relationship does not mean that children and adolescents with normal-weight are not at risk. Cook et al. (Cook et al., 2003) reported the prevalence of MONW in children and adolescents in the United States to be 0.1% from 1988 to 1994. Another study, which was carried out from 1999 to 2002, showed a prevalence of 1% for children and adolescents (Messiah et al., 2008).Comparing the relative risks of Metabolic syndrom in obese and overweight samples with their normal-weight peers, Li et al., reported the prevalence of MONW as 15.5% and 18.8% among boys and girls, respectively (Li et al., 2005). In our study, the prevalence of MONW in children and adolescents is close to Lim's study (5.7%) (Lim et al., 2014).The difference in the prevalence of this syndrome is associated with multiple definitions related to the percentage of body fat. A current challenge inevaluating body fat is that there is no consensusabout the best cut off for the body fat percentage to define excess fatness. The different

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proposed cut off points of body fat vary between 20 to 25% for men and 30 to 37% for women (Marques-Vidal et al., 2010). Hypertriglyceridemia and low HDL are the predominant patterns observed in Asian Indians (Zhang et al., 2010) and South Asians in British cities (France et al., 2003). In French children (Botton et al., 2007), the percentages of high levels of TC, LDL, TG, and HDL are 10, 5.9, 3.7, and 0.5% in MONW children, respectively. But the most common forms of dyslipidemia in school children in Eastern countries werelow HDL level and hypertriglyceridemia (Fesharakinia et al., 2008). Diets that are high in terms of unsaturated fatty acids may increase TG levels, decrease HDL levels, and interfere with fatty acid metabolism (Kelishadi et al., 2008). A study based on an urban population of Iran with a relatively large sample size that provided a condition to identify the metabolic risk factors in children and adolescents with normal-weight and extensive information of confounding factors are strengths of this study. The cross-sectional nature of this study is a limitation that makes it impossible to analyse causative relationships. Thesignificant prevalence of low HDL and high TG in normal-weight childrenmay be due to ethnicdifferences in MetS and lifestyle factors.

Conclusions

Since BMI is normal in metabolically obese-normal weight children and adolescents, continuous measurements of components of MetS especially in boys are essential.

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Author contributions

Karandish M participated to conception and design of study, managing the project and drafting the manuscript. Hosseinpour M and Latifi SM participated to acquisition of data, data analysis and drafting the manuscript. Rashidi R and Moravej Aleali A participated to laboratory evaluation and drafting the manuscript. All authors read manuscript and they finally verified it.

Conflicts of Interest

There is not conflict of interest.

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