# **Original Article**

# Prevalence of Metabolic Syndrome and Insulin Resistance in Children and Adolescent of Qazvin, Iran

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# Abstract -

Background: The prevalence of metabolic syndrome (MetSyn) is increasing worldwide. The aim of this study was to determine the prevalence of MetSyn and insulin resistance (IR) in children and adolescents in Qazvin, Iran.

Methods: A cross-sectional study was conducted in 338 children and adolescents aged 10–18 years old who were selected by a multistage cluster random sampling method. We performed standardised measurements of variables including waist circumference (WC), blood pressure, plasma glucose level, total cholesterol, high-density lipoprotein cholesterol (HDL), triglycerides, and insulin. MetSyn was defined according to the International Diabetes Federation criteria. IR was estimated by the homeostatic model assessment.

Results: Of the 338 total subjects, 172 were female. The overall prevalence of MetSyn and IR were 3.4% and 18.2%, respectively. There was no sex difference for the prevalence of MetSyn. A total of 185 subjects (56.4%) had one or two components of MetSyn. The most common component was low HDL levels in both sexes, which was followed by high WC in females and high fasting plasma glucose levels in males.

Conclusion: The lack of a standard definition of MetSyn in children and adolescents combined with the geographical and socioeconomic differences make it difficult to compare the results from different studies. Modification of lifestyle habits is an important strategy in preventing MetSyn and IR.

**Keywords:** adolescent, body mass index, insulin resistance, Metabolic Syndrome X

# Introduction

According to the World Health Organization (WHO), 75% of all deaths in developing countries will be due to non-communicable diseases by the year 2020 (1). Metabolic syndrome (MetSyn), a well-recognised risk factor of cardiovascular disorders and diabetes mellitus (2), is a cluster of metabolic abnormalities that includes impaired glucose metabolism, atherogenic dyslipidaemia, abdominal obesity and hypertension.

The worldwide prevalence of MetSyn has increased in the last few decades. In a study among 1 844 Chinese children (7 to 14 years old), the prevalence of overweight, obesity, and MetSyn was 11%, 7.2% and 6.6%, respectively (3). In Iran, Kelishadi et al. reported an increase in obesity and a 14% prevalence of MetSyn (4).

MetSyn is not a disease by itself, rather it is a set of undesirable characteristics that are associated with habits, unhealthy lifestyle, and obesity. Recent evidence suggests that modern lifestyles and lack of activities are the main causes of the increasing obesity trend. Childhood obesity is a key component of MetSyn and insulin resistance (IR) (5). Furthermore, MetSyn and IR are major predisposing factors for type 2 diabetes mellitus (6).

Although adulthood is the main window for the onset of atherosclerotic cardiovascular symptoms, it has been shown that the processes resulting in these symptoms begin in childhood. Early diagnosis of MetSyn and IR with appropriate interventions can lead to better prevention and control of type 2 diabetes mellitus and cardiovascular diseases (7).

The reported prevalence of MetSyn provides inconsistent estimates that cannot be generalised. Additionally, limited reports are available on the prevalence of IR in children and adolescents in Iran. To address this problem, the aim of this study was to determine the prevalence of these two conditions in children and adolescents (10 to 18 years old) in Qazvin, Iran.

#### **Methods**

#### **Subjects**

This cross-sectional study was carried out in children and adolescents (10 to 18 years old) from the Mindoodar district of Qazvin, Iran, from September to November 2011. Qazvin is located in the northwest of Iran. The methods were in agreement with the Declaration of Helsinki and were approved by the ethics committee of Qazvin University of Medical Sciences. All households of the Mindoodar district had health files at the Mindoodar Health Center and thesampling unit was the household. The Mindoodar district was divided into four geographical divisions that were similar and homogeneous in terms of population size. Each division was considered a cluster. Therefore, four main clusters were identified in this district. The subjects were selected by multistage cluster random sampling method. Owning an apartment and residence for at least the next 5 years in the area were inclusion criteria. Children and adolescents (10 to 18 years old) and their parents were invited to the study. Children and adolescents with an inflammatory disease and those who were taking anti-inflammatory medicines were excluded. The sample size was calculated using this formula:

$$n = \frac{Z_{(1-\alpha/2)}^2 P (1-P)}{d^2}$$

Considering Z as the statistic corresponding to the level of confidence,  $\alpha$ : 0.05, precision (d): 5%, and prevalence of MetSyn (P): 14% (4), the calculated sample size (n) was 186. However, 338 subjects were selected to increase the study power. Written informed consent was obtained from both parents and participants.

#### Data collection

Demographic information was collected by a general practitioner using a self-reported questionnaire. Adolescents (12 to 18 years old) completed the questionnaire by themselves and

parents completed it for children (< 12 years old). All anthropometric and laboratory measurements were performed after 12 hours of fasting. Weight was measured by a Seca scale (Germany) with a sensitivity as low as 0.1 kg. A tape measure with an accuracy of 0.5 cm was used to measure the height in a barefoot standing position. The waist circumference (WC) was measured halfway between the costal margin and the iliac crest and at the end of a normal expiration. Body mass index (BMI) was estimated as weight (kg) divided by the height (m) squared. On a single occasion, blood pressure (BP) was measured twice following a 10 minutes rest. A mercury sphygmomanometer was used to measure BP in a seated position. The BP measurement was performed twice with at least a 10 minutes interval between measures and the mean value was used as their BP in the analysis. All physical examinations were performed by a paediatrician.

A venous blood sample was taken from all subjects. The samples were analysed in a regional certified medical laboratory. Fasting plasma glucose (FPG), insulin, triglycerides (TGs), total cholesterol, low density lipoprotein (LDL) cholesterol, high density lipoprotein (HDL) cholesterol and C-reactive protein (CRP) were measured. Insulin levels were measured by the ELISA method using a reagent (Monobind Company, USA) with a within-run precision coefficient of variation (CV) of 4.9 and a total precision CV of 4.9. An oral glucose tolerance test (OGTT) with 75 g of glucose was performed on subjects without a previous diagnosis of diabetes.

FPG levels were measured by a Hitachi 704 auto-analyzer using the GOD-PAP method and reagent (Parsazmun Company, Tehran, Iran); mean intra- and interassay CVs were 1.28 and 0.84, respectively. Insulin levels were measured by the ELISA method using a reagent (Monobind Company, USA) with a within-run precision CV of 4.9 and a total precision CV of 4.9. TGs were measured with a Hitachi 704 auto-analyzer using GPO-PAP and reagent (Parsazmun Company); mean intra- and interassay CVs were 1.82 and 1.04, respectively. Cholesterol was measured by a Hitachi 704 auto-analyzer using CHOD-PAP and reagent (Parsazmun Company); mean intra- and interassay CVs were 0.61 and 1.22, respectively. To measure LDL and HDL levels, a Hitachi 704 auto-analyzer with immunoturbidimetric and reagent (Parsazmun Company) was used; mean intra- and interassay CVs for LDL were 0.63 and 1.29, respectively, and for HDL they were 0.73 and 1.8, respectively.

## **Definitions**

Overweight was defined as having a BMI between the 85th and the 95th percentiles for age and sex. BMI levels over the 95th percentile for age and sex were considered as obesity (8). MetSyn was defined according to the International Diabetes Federation (IDF) criteria (9). Specifically, from the ages of 10 to 16 years, a subject was considered to have MetSyn when at least three of the following five components were present: 1) WC > 90th percentile; 2) TGs > 150 mg/dL; 3) HDL < 40 mg/dL; 4) systolic BP > 130 mmHg or diastolic BP > 85 mmHg; and 5) FPG > 100 mg/dL or previously diagnosed with type 2 diabetes mellitus. For a MetSyn determination in ages older than 16 years, subjects needed to have central obesity (WC > 94 cm in boys and WC > 80 cm in girls) with any two of the following four components: 1) TGs: > 150 mg/dL or treatment for hypertriglyceridemia; 2) HDL < 40 mg/dL in males and < 50 mg/dL in females, or treatment for this condition; 3) systolic BP > 130 mmHg or diastolic BP > 85 mmHg, or treatment for hypertension; and 4) FPG > 100 mg/dL, or previously diagnosed with type 2 diabetes. IR was determined by the homeostatic model assessment (HOMA-IR). HOMA-IR was calculated as fasting serum insulin (μIU/mL) × fasting plasma glucose (mmol/L)/22.5 (10). The HOMA-IR cut-off point for the diagnosis of IR was 2.5 (10).

#### Data analysis

The Kolmogorov-Smirnov test was used to examine the normality of each variable. Data are described as mean (standard deviation (SD)), median (minimum – maximum), or frequency (percent). Anthropometric and biochemical measurements were compared between males and females using t tests or Mann-Whitney U tests, where appropriate. The prevalence of MetSyn components (high WC, high TGs, low HDL, high BP, and high FPG) was compared between males and females using the chi square test. IR was considered as the gold standard. Sensitivity and specificity of MetSyn for IR diagnoses were also calculated as shown below.

Sensitivity = true positive/(true positive + false negative)

Specificity = true negative/(true negative + false positive)

P values of less than 0.05 were considered statistically significant. All of the analyses were performed using SPSS software version 22 (SPSS, Inc., Chicago, IL, USA).

#### Results

In terms of sexes, from a total of 338 subjects, females accounted for 50.1% of all participants. Anthropometric and biochemical characteristics of the subjects are shown in Table 1. Systolic and diastolic BP and FPG were significantly different between males and females. A total of 287 subjects (84.9%) had normal weights, 35 (10.4%) were overweight and 16 (4.7%) were obese.

The overall prevalence of MetSyn was 3.4%. There was no sex difference for the prevalence of MetSyn (6 [3.8%] in males vs 5 [3%] in females; P = 0.081). The prevalence of IR was 18.2% overall. The sex difference for the prevalence of IR was not statistically significant (23 [14.4%] in males vs 37 [21.9%] in females; P = 0.087). The sensitivity and specificity of MetSyn for the diagnosis of IR was 10.34% and 98.13%, respectively.

The frequencies of the various MetSyn components are shown in Table 2. A total of 185 subjects (56.4%) had 1 to 2 MetSyn components, however, none of the subjects had all of the components.

The prevalences of MetSyn risk factors are shown in Table 3. The most common component in both sexes was low HDL. The second most common component was high WC in females and high FPG in males. The prevalence of high WC and low HDL was significantly different with regard to the sexes.

# **Discussion**

MetSyn is mainly related to the development of cardiovascular disease and diabetes mellitus, and has been turned into a modern worldwide epidemic (11). The presence of each component of MetSyn during childhood is an important predictive tool for adulthood diseases. It is important to continually monitor the trends of cardiovascular risk factors, MetSyn and IR. In the present study, the prevalence of MetSyn was 3.4% according to IDF criteria, however, the prevalence of IR was about five times more than MetSyn.

The reported prevalence of MetSyn has been inconsistent in previous studies. In Iran, Salem and Vazirinejad (12) reported a prevalence of 3.9% for MetSyn among 4,246 girls aged 11–18 years in Rafsanjan, which was similar to the results observed in the present study; however, the prevalence of MetSyn was 14% in a study by Isfahan (4). Cook et al. (13) reported the MetSyn prevalence as 4.2% among 12 to 19 years old in the U.S. population, while de Ferranti et al. (14) reported a prevalence of 9.2% among American

Table 1: Anthropometric and biochemical characteristics of the study subjects by gender

	Total	Male	Female	<i>P</i> -value
Agea	15.10 (2.43)	15.00 (2.43)	15.18 (2.42)	$0.233^{\circ}$
Body mass index (kg/m²)	19.86 (4.08)	19.72 (3.96)	19.91 (4.10)	0.400°
Waist circumference (Cm)	72.76 (9.87)	73.56 (10.07)	72.08 (9.63)	0.241 <sup>c</sup>
Systolic blood pressure (mmHg)	103.05 (14.99)	105.05 (16.18)	101.13 (13.52)	0.020 <sup>c</sup>
Diastolic blood pressure (mmHg)	63.74 (9.87)	65.18 (9.94)	62.36 (9.62)	0.003°
Fasting plasma glucose (mg/dl)	86.69 (11.05)	88.06 (12.08)	84.77 (9.93)	$0.028^{c}$
Blood glucose after 2 h (mg/dl)	93.04 (17.12)	92.01 (15.26)	92.5 (17.74)	0.774 <sup>c</sup>
Insulin (μIU/ml) <sup>b</sup>	0.7 (0.1-126.1)	0.5 (0.1-85.7)	0.7 (0.1-126.1)	$0.228^{d}$
$HOMAIR^b$	0.148 (0.02-26.93)	0.138 (0.02-23.15)	0.156 (0.02-26.93)	$0.381^{\rm d}$
Triglycerides (mg/dl) <sup>b</sup>	85 (34.5-753)	86 (35-288)	83 (34.5-753)	0.768 <sup>d</sup>
Cholesterol (mg/dl)	152.07 (29.62)	150.75 (28.36)	152.36 (30.57)	$0.128^{c}$
LDL (mg/dl)	88.57 (21.35)	87.65 (21.51)	89.94 (21.7)	$0.227^{c}$
HDL (mg/dl)	41.45 (8.33)	40.55 (8.00)	41.83 (8.64)	0.096°
C-reactive protein (mg/dl) <sup>b</sup>	0.25 (0-8.85)	0.27 (0-8.85)	0.25 (0.01-5.2)	$0.819^{d}$

 $<sup>^{\</sup>rm a}$ Mean (SD);  $^{\rm b}$ Median (minimum-maximum);  $^{\rm c}$ t test;  $^{\rm d}$ Mann Whitney U test.

 $\textbf{Table 2:} \ \textbf{Frequency of Metabolic Syndrome components in the study subjects}$ 

Number of components	Frequency (%)			
_	Total	Male	Female	
0	132 (40.20)	72 (45.30)	60 (35.50)	
1	144 (43.90)	68 (42.80)	76 (45.00)	
2	41 (12.50)	13 (8.20)	28 (16.60)	
3	10 (3.00)	5 (3.10)	5 (3.00)	
4	1 (0.30)	1 (0.60)	0	
5	0	0	0	

Table 3: Prevalence of metabolic syndrome components in the study subjects by gender

	Frequency (percent)			Dyvolusoa	
	Total	Male	Female	<i>P</i> value <sup>a</sup>	
High waist circumference	32 (9.50)	8 (4.90)	24 (14.00)	0.005	
High triglycerides	36 (10.90)	17 (10.50)	19 (11.20)	0.861	
Low HDL	154 (46.70)	65 (40.40)	89 (52.70)	0.028	
High blood pressure	10 (3.00)	6 (3.60)	4 (2.30)	0.536	
High fasting plasma glucose	29 (8.80)	18 (11.10)	11 (6.50)	0.174	

<sup>&</sup>lt;sup>a</sup>Chi square test.

teenagers. Furthermore, according to 2005 report, the prevalence of MetSyn was 10–15% in China, Taiwan, Hong Kong, and Thailand (15).

The lack of a standard MetSyn definition and non-uniform cut-off points for anthropometric measurements, lipid levels, blood pressure and glucose, in various definitions have resulted in differing reported prevalence rates for this syndrome. Therefore, it is difficult to compare the prevalence of MetSyn between studies. In a systematic review by Friend et al. in the paediatric population, the MetSyn prevalence was 3–10% based on ATP criteria and 1–7% based on IDF criteria (16). The lowest MetSyn prevalence was related to studies in Europe and Asia (3.3–4.2%), while the highest prevalence rates were for the Middle East and North America (4.2%–10%) (16).

The MetSyn prevalence was not significantly different with regards to sex in the present study. Likewise, in the Daratha and Bindler (17) and Santos et al. (18) studies, the difference in MetSyn prevalence was not significant with regard to sex, however, in the Mar Bibiloni et al. (19) study, the MetSyn prevalence in adolescent boys was more than that observed in girls.

MetSyn is associated with obesity and being overweight. Obesity is a risk factor for IR, hyperinsulinemia, type 2 diabetes, cardiovascular disease, hypertension and dyslipidaemia (20). In a study by Guzmán-Guzmán et al., the MetSyn prevalence was 44.3% in the obese group and 0.84% in normal-weight children (21). In the Saffari et al. study, MetSyn was present in 50% of the overweight and 66.2% of the obese subjects based on NCEP ATP III criteria (22). The low MetSyn prevalence in the present study may be the result of the low prevalence of obesity. It seems that the best way to reduce the risk of MetSyn is to prevent obesity.

In the present study, despite the low prevalence of MetSyn, 56.4% of the subjects had one or two components of MetSyn. In the Esmaillzadeh et al. study, 58.8% of adolescents had one or two components of MetSyn, which was similar to the present study (23). Guzmán-Guzmán et al. showed that one third of children with normal weight had one component of MetSyn (21). The presence of as few as three components may serve as a warning signal about the future risk of MetSyn.

The most common component of MetSyn was low HDL levels, regardless of the sex; this was followed by high WC in females in the present study. In Mexican children, impaired glucose and low HDL were the most frequent abnormalities in the normal-weight group (21). In China, the most

frequent component was also low HDL levels (24). Park et al. conducted a study in both Korean and American adolescents (25). They found that the most common metabolic disorders in U.S. adolescents are abdominal obesity and low HDL, while the most common in Korean adolescents are low HDL and abdominal obesity. Kelishadi performed a review among children and adults and concluded that high TGs and low HDL were the most common components of MetSyn in Iran and Turkey (26). It has been shown that diets rich in saturated fats and trans-fatty acids are correlated with a high prevalence of dyslipidaemia among Iranian adolescents (26).

IR is a predisposing factor of type 2 diabetes that begins in childhood and it is not benign. IR does not always lead to diabetes; however, it is a main risk factor of other complications including atherosclerosis, high blood pressure, obesity, acanthosis nigricans, dyslipidaemia, polycystic ovarian syndrome, fatty liver, and higher cancer rates (7).

IR prevalence was 18.2% in the present study. In a study by Goodman et al., hyperinsulinemia was defined as the top quartile of insulin among non-diabetic subjects (27). This cross-sectional study was conducted in 1 513 black, white, and Hispanic 12-18 year-old teens, and the prevalence of hyperinsulinemia was 25% (27). In another study from Quebec, Canada, the estimated prevalence of IR syndrome was as high as 11.5% (95% CI: 10.2-12.9) in children and adolescents (28). Genetic and environmental factors may be associated with ethnic differences in IR. IR increases during puberty and its levels remain higher in adulthood than pre-pubertal levels (27). Part of the IR prevalence in the present study is attributable to the transient physiological IR of puberty. However, the association of pubertal IR and the development of MetSyn is unknown (27).

IR and MetSyn are closely linked. Although IR may have a central role in the pathogenesis of MetSyn, it is not sufficient for the development of the syndrome. Other factors are involved in the pathophysiology underlying MetSyn (29). Dyslipidaemia, especially hypertriglyceridemia, and low HDL, are strongly associated with IR and are also components of MetSyn. It is unclear whether IR develops lipid abnormalities or whether IR and lipid abnormalities are associated through other factors (29). However, puberty may be the main contributing factor for the IR prevalence observed in the present study, and the role of IR as a main underlying cause of MetSyn should also be considered.

The prevalence of MetSyn and IR is related to

a sedentary lifestyle in the modern world. Lifestyle modifications for sleep habits (30, 31) nutritional habits and physical activity could considerably reduce the risk of cardiovascular disease and diabetes. It has been shown that increased consumption of whole grain foods improves insulin sensitivity in adults (32). Exercise also influences improvements in insulin sensitivity, HDL levels, glucose levels and blood pressure (32).

One of the strengths of this study is the availability of a homogenous population in Qazvin province. A potential limitation of the present study is its cross-sectional design. There is also no consensus about which criteria of MetSyn to use. Other criteria may be more appropriate than the IDF criteria for the diagnosis of MetSyn in children and adolescents.

#### Conclusion

The prevalence of MetSyn was 3.4% in the 10–18 yearsold population in Qazvin. The lack of a standard definition of MetSyn in children and adolescents, as well as the geographical and socioeconomic differences, make it difficult to compare different results. While part of the IR prevalence in the present study is attributable to the transient physiological IR of puberty, it also shows the future burden of type 2 diabetes and MetSyn. Therefore, screening of children susceptible to IR is necessary. Lifestyle modifications are important strategies for preventing MetSyn and IR. Further studies are needed to investigate the risk factors of IR.

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# **Conflict of interest**

None.

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None.

## **Authors' Contributions**

Conception and design, administrative, technical or logistic support: SJ, MJ

Analysis and interpretation of the data: SJ, AJ

Drafting of the article: SJ

Critical revision of the article for the important

intellectual content: MM, MJ

Final approval of the article: SJ, AJ, MM, MF, MJ Provision of study materials or patient: SJ, MM,

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