



Metabolic Syndrome: Findings from 20 Years of the Tehran Lipid and Glucose Study

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Abstract

Context: In recent decades, investigations have been focused on the definition, incidence and predictors of metabolic syndrome (MetS) in Iranians. This study aimed to review systematically investigations on MetS, conducted among the Tehran lipid and glucose study (TLGS) participants.

Evidence Acquisition: Literature on MetS documented by TLGS studies published from 2000 to 2017 were searched using Pubmed and Scopus database in English language with a combination of following keywords: Metabolic syndrome, TLGS.

Results: The harmonized definition of MetS was confirmed, based on the estimated cut point of waist circumference (WC) \geq 95 cm for both genders in Iran. The incidence rate was 550.9/10000 person/years, lower among women (433.5/10000) than men (749.2/10000). The prevalence of abdominal obesity, high triglycerides (TG), low high density lipoprotein cholesterol (HDL-C), high blood pressure (BP), and high fasting blood glucose (FBG) was 30, 46, 69, 34, and 12%, respectively. The prevalence of MetS in adolescents was 10.1% with no significant difference between boys and girls (10.3% in boys and 9.9% in girls). A strong association of WC (OR: 2.32, CI: 2.06 - 2.59) and TGs (OR: 1.95, CI: 1.65 - 2.11) with development of MetS was found. In adolescent boys, WC had the highest OR for MetS risk. WHO-defined MetS was a significant predictor of total and cardiovascular mortality both in men (HR: 1.66, CI: 1.23 - 2.24; HR: 1.93, CI: 1.26 - 2.94) and women (HR: 2.01, CI: 1.39 - 2.88; HR: 2.71, CI: 1.44 - 5.09).

Conclusions: Our results indicate high incidence of MetS in Tehranian adults and adolescents; high WC also appears to be a strong predictor of MetS. All definitions of MetS predicted cardiovascular disease.

Keywords: Metabolic Syndrome, Obesity, Hypertension, Hyperlipidemia, HDL-C, LDL-C, Tehran Lipid and Glucose Study

1. Context

Metabolic syndrome (MetS) is characterized as having 3 or more risk factors including abdominal obesity, hypertension, hyperglycemia, and dyslipidemia, is a pathological condition which increases risk of various non-communicable diseases (NCDs) (1). There is limited global data for prevalence of MetS but over a billion people around the world were estimated to have MetS. Its prevalence varies worldwide and it is highly associated with urbanization and life style (2). A nationally representative study of Iranians living in both urban and rural area of 30 provinces of Iran, aged 25 - 64 years, showed a high prevalence for MetS in 2007 (3). In 1999 - 2001, it has been estimated that 30.1% adults living in Tehran have MetS (4). In addition to the variation in prevalence, the predictors of

MetS also differ across populations (5).

The rate of MetS is also high among overweight/obese children and adolescent, and is simultaneously increasing with the prevalence of obesity. At least one criteria of MetS can be seen in 90% of obese children and adolescent (6). MetS in childhood is associated with higher risk of diabetes and coronary heart diseases in adulthood (7).

Tehran lipid and glucose study (TLGS) is an ongoing study started in 1999 with a representative sample of 15005 individuals aged \geq 3 years, recruited from residence of district no.13 of Tehran, the capital of Iran (8). This prospective study provides an opportunity to study different aspects of NCDs in this Middle-Eastern population. This study aimed to review all findings of studies conducted in framework of TLGS regarding the prevalence and incidence of MetS and its predictors in different age groups, providing a deeper

insight into this syndrome in this population in order to design better preventive strategies for high risk individuals.

2. Evidence Acquisition

2.1. Methods

All English-language studies focused on the prevalence and incidence of MetS, and its potential predictors in different age groups in the framework of the TLGS, were searched using PubMed, Scopus, and Embase databases. A structured search strategy with using combination of keywords “metabolic syndrome AND Tehran lipid and glucose study” was conducted to identify records in each database. Eventually, 35 relevant papers were included in this review. Seven papers described different definition of MetS in the TLGS population; its prevalence and incidence were described in 10 papers. Prevalence, incidence and risk factors of MetS in children and adolescents were clarified in 8 articles. Ten studies focused on the potential usefulness of MetS in prediction of cardiovascular (CVD) events, all-cause and CVD mortality and type 2 diabetes in different age groups.

2.2. Metabolic Syndrome Definitions

MetS is a complex accumulation of risk factors containing hypertension, central obesity, high fasting blood glucose (FBG) and dyslipidemia. The World Health Organization (WHO), Adult Treatment Panel (ATP) III, International Diabetes Federation (IDF), American Heart Association (AHA), and the National Health Lung and Blood Institute (NHLBI) have presented various definitions for MetS (Table 1). Considering the sharp rising trend in the prevalence of obesity and MetS in Iran, having a uniform and harmonized definition for waist circumference (WC) and MetS would facilitate the comparison of clinical and epidemiological investigations for trend studies; the Iranian national committee of obesity hence designated a cut point of WC \geq 95 cm for both genders in Iranian adults (9).

3. Results

3.1. Prevalence and Incidence of Metabolic Syndrome in Adults

The prevalence of MetS in a study population of 10368 adults (4397 men and 5971 women), aged \geq 20 years recruited at the initiation of TLGS (1999 - 2001), was 30.1% and age-standardized prevalence was 33.7% based on the ATP III definition; the prevalence was higher in women (42%) than in men (24%), and increased with aging in both genders. The most prevalent metabolic abnormality was low-HDL, followed by high TG, hypertension, abdominal obesity, and high FPG (4). Another study conducted on 10368 adults,

aged \geq 20 years suggested a prevalence ranging between 17.5 - 31.7%, depending different definition for MetS; highest and lowest estimations was based on the ATP III and the WHO definitions, respectively (10). The prevalence of MetS in elderly participants, aged \geq 65 years, ranged between 42 and 52.5% based on different definitions. High BP was the most prevalent component based on the ATP and the IDF definitions, whereas obesity was the most prevalent, based on the WHO definition. The prevalence of MetS in the elderly was lower in men than in women (11).

Another study conducted among 1737 men and 1707 women with normal weight (BMI = 18.5 - 24.5) also reported high prevalences of 9.9% in men and 11% in women based on the ATP III definition (12). The prevalence of MetS rose 4-fold during 6.6 years in a normal weight adult population from 2.3% at initiation of the TLGS study to 9.6% in the third examination (2005 - 2008), an incremental trend significant only among men accompanied by an increasing trend in abdominal obesity, seen only in men (13).

The age-adjusted incident rate of MetS during a 3-year follow-up was estimated to be 20.4 (95% CI: 19.6 - 21.2) in 2217 Iranian participants, aged \geq 20 years (14). The incidence rate of MetS during 9.3 years of follow-up was 550.9/10000 person/years, and risk of developing MetS was 50% lower in women, compared with men (749.2/10000 person/years in men and 433.5/10000 person/years in women) based on the Joint Interim Statement (JIS) definition (15).

The prevalence of MetS is high among Tehranian populations in all adult age groups, and is even higher among normal weight adults, and the increasing trend in prevalence of MetS and abdominal obesity especially, especially among men with normal weight, should be considered in future public health programs. The incidence of MetS was higher among men which may be due to the rising trend of abdominal obesity observed more among men than women.

Nationally representative study of prevalence of MetS also showed a high burden for MetS with age-adjusted prevalence of 34.7% (95% CI = 33.1 - 36.2%) based on the ATP III definition in 2007 on 3024 living in 30 provinces of Iran. Consistent with our findings, the prevalence reported for women in this study was higher than in men, and an increase in prevalence of MetS was observed by increasing age in both sexes. Low-HDL was the most prevalent of metabolic abnormalities as was seen in TLGS (3) (Table 2).

3.2. Predictors of Metabolic Syndrome

A 6.5-year cohort study on subjects aged 20 - 87 years aimed to resolve which constituent of the MetS is the best predictor of its progress; WC, HDL-C and TG predicted the development of MetS better than blood pressure (BP) or FBG; a model that comprised WC and TG or WC and HDL-C

Table 1. Important Definitions of Metabolic Syndrome in Adults

	IDF	ATP III	EGIR	WHO
Definitions	Abdominal obesity + two or more of these components	Presence of three or more of these components	Elevated plasma insulin (> 75th percentile) plus two other factors from among the following:	Glucose intolerance, impaired glucose tolerance (IGT) or diabetes mellitus (DM), and/or insulin resistance, together with two or more of the components listed below:
BMI, kg/m²	BMI is > 30	-		Body mass index (BMI) > 30
WHR or WC, cm	Dependent to population If BMI is > 30kg/m ² , central obesity can be assumed and waist circumference does not need to be measured	Dependent to population	Waist circumference (WC) ≥ 94 cm in men and ≥ 80 cm in women	Waist/hip ratio (WHR) > 0.9 in men and > 0.85 in women
TG, mg/dL	≥ 150 (1.7 mmol/L) or specific treatment for this lipid abnormality	> 150 or drug treatment for elevated triglycerides	≥ 150	≥ 150
HDL, mg/dL	< 40 (1.03 mmol/L) in males < 50 (1.29 mmol/L) in females or specific treatment for this lipid abnormality	Men: < 40 Women: < 50	< 39 for both men and women	< 35 in men and < 39 in women
BP, mm Hg	Systolic BP ≥ 130 or diastolic BP ≥ 85 or treatment of previously diagnosed hypertension	> 130/85 or drug treatment for elevated blood pressure	≥ 140/90 or on antihypertensive treatment	≥ 140/90
FBG, mg/dL	(FPG) ≥ 100 (5.6 mmol/L), or previously diagnosed type 2 diabetes If above 5.6 mmol/L or 100, OGTT is strongly recommended but is not necessary to define presence of the syndrome	> 100 or drug treatment for elevated glucose	Impaired fasting glucose (IFG) or IGT, but no diabetes	
Albuminuria, μg/min	-	-	-	Urinary albumin excretion rate ≥ 20 μg/minute or albumin/creatinine ratio ≥ 30 μg/mg.

Abbreviations: AACE, American Association of Clinical Endocrinologists; AHA/NHLBI, American Heart Association/National Heart, Lung and Blood Institute; BMI, body mass index; BP, blood pressure; EGIR, European Group for Study of Insulin Resistance; FBG, fasting blood glucose; HDL, high density lipoprotein-cholesterol; IDF, International Diabetes Federation; INCO, Iranians National Committee of Obesity; NCEP ATP III, National Cholesterol Education Program Adult Treatment Panel III; TG, triglyceride; WC, waist circumference; WHO, World Health Organization; WHR, waist to hip ratio.

predicted MetS, like a model that constituted all five MetS components (19).

A 6.6 year-cohort study investigating the effect of changes in WC on MetS status and its parameters in adults concluded that waist gain, although mild, was a risk factor of the development of MetS and its components (20). During a three year follow-up, weight gain > 1.3% initial weight in women and > 4% in men were related to increased risk of MetS (14). A population-based cohort study confirmed the importance of BP, WC and lipid measurements in risk stratification of MetS in adulthood (21).

These findings are in agreement with previous study conducted among Iranian populations (22). Obesity, especially central obesity, increased risk of developing MetS 19-fold among 15 - 65 years participants (23), which could be due to WC being strongly associated with chronic systemic low-grade inflammation (24), which is considered to be the underlying cause of MetS (25), indicating that greater de-

creases in WC with medical weight loss are related to significant improvement in components of MetS, independent of sex (26).

The independent predictors of MetS include all components of MetS, obesity, family history of diabetes and age. Moreover individuals in the 4th quartile of HOMA-IR had significant risk for MetS in both genders (15). The independent association of family history of diabetes with MetS indicates that genetic susceptibility plays a role in the risk of MetS (27).

The incidence of MetS among 433 healthy obese individuals was 44.0% (36.8 - 55.0) over 10 years of follow-up; predictors of MetS in healthy obese subjects included hypertension, high TG, low HDL-C and insulin resistance; WC was also a weak predictor of MetS in these subjects (5). In spite of short-term follow-up studies reporting no relation between metabolically healthy obesity and cardiovascular disease, long-term follow-up studies showed an increased

Table 2. Prevalence and Incidence of Metabolic Syndrome in the Tehran Lipid and Glucose Study

Year	Reference No.	Number of Participants	Age, y	BMI Group, kg/m ²	Criteria of Diagnosis	Prevalence, %	Incidence, %	Incidence Rate
1999 - 2001	(4)	10368	≥ 20	-	ATP	33.7	-	-
1999 - 2001	(10)	10368	≥ 20	-	ATP	32.1	-	-
1999 - 2001	(10)	10368	≥ 20	-	IDF	33.2	-	-
1999 - 2001	(10)	10368	≥ 20	-	WHO	18.4	-	-
1999 - 2001	(11)	720	≥ 65	-	ATP	50.8	-	-
1999 - 2001	(11)	720	≥ 65	-	IDF	41.9	-	-
1999 - 2001	(11)	720	≥ 65	-	WHO	41.8	-	-
1999 - 2001	(12)	3444	≥ 20	18.5-24.9	ATP	9.9 (men) 11 (women)	-	-
1999 - 2001	(13)	5269	≥ 20	18.5-24.9	IDF	2.3	-	-
2002 - 2005	(13)	5269	≥ 20	18.5-24.9	IDF	4.0	-	-
2005 - 2008	(13)	5269	≥ 20	18.5-24.9	IDF	9.6	-	-
From 1999 - 2001 to 2002 - 2005	(14)	2217	≥ 20	> 18.5	ATP	-	20.4	-
From 1999 - 2001 to 2008 - 2011	(15)	2858	≥ 20	-	JIS	-	-	550.9/10000
1999 - 2001	(16)	3036	10 - 19	-	ATP	10.1	-	-
From 1999 - 2001 to 2003 - 2005	(17)	932	10 - 19	-	ATP	-	5.2	-
From 1999 - 2001 to 2003 - 2005	(17)	932	10 - 19	-	IDF	-	6.8	-
From 1999 - 2001 to 2003 - 2005	(17)	932	10 - 19	-	AHA	-	8.3	-
From 1999 - 2001 to 2003 - 2005	(17)	932	10 - 19	-	NHANES	-	8.8	-
1999 - 2001	(18)	1424	11 - 18	-	Cook	13.1	-	-
1999 - 2001	(18)	1424	11 - 18	-	de Ferranti	26.4	-	-
1999 - 2001	(18)	1424	11 - 18	-	Pediatric NCEP	11.7	-	-
1999 - 2001	(18)	1424	11 - 18	-	Pediatric IDF	8.4	-	-

Abbreviations: AHA: American Heart Association; ATP III: adult treatment panel III; IDF: International Diabetes Federation; JIS: joint interim statement; NHANES: National Health and Nutrition Examination Survey; WHO: World Health Organization.

risk, since metabolic abnormalities occurred over longer follow-up periods (28).

A cross sectional study conducted on 5720 women and 4040 men, reported that hip circumference is independently and inversely associated with high LDL-C, diabetes, hypertension, low HDL-C and abnormal glucose homeostasis (29, 30). This finding confirms the importance of hip circumference measurements in epidemiological studies which are in line with previous studies in Australian (31) and Canadian (32) populations. It seems this association is independent of race.

3.3. Metabolic Syndrome Studies in Children and Adolescents

Although MetS has been extensively studied in adults (33), limited attention has been focused on children and adolescents. To investigate the prevalence of MetS in Iranian adolescents based on the ATP definition, a cross-sectional study (1999 - 2001) was conducted among adolescents, aged 10 - 19 years. The prevalence of MetS was 10.1% with no significant difference between boys and girls (10.3% in boys and 9.9% in girls), although those with a family history of diabetes and overweight had higher prevalence of MetS. Odds of MetS was higher in girls than boys [1.34 (1.03 -

1.76)] and in overweight than normal weight ones [17.8 (13.2 - 24)]. Of MetS components, low HDL-C (42.8%) and high TGs (37.5%) were the most prevalent, and high FBS (0.6%) was the least prevalent component (16). The incidence of MetS between the 1999 - 2001 and 2003 - 2005 surveys was 5.2% (95% CI: 3 - 6) based on ATPIII, 6.8% (95% CI: 5 - 8) based on IDF, 8.3% (95% CI: 6 - 10) based on AHA, and 8.8% (95% CI: 6 - 10) based on NHANES definitions (17). Furthermore, based on different definitions, the prevalence of MetS according to the Cook, de Ferranti, pediatric ATPIII and pediatric IDF was 13.1, 26.4, 11.7, and 8.4, respectively. Findings showed that the pubertal group (11 - 14 years) had higher prevalent MetS than those in late-pubertal groups (15 - 18 years). Most frequent MetS constituents found in two groups were low HDL-C and high TGs (18). The prevalence and incidence of MetS among adolescents of TLGS are comparable to those of other study in Iran (34). According to a 2013 systematic review, median prevalence were 5.2% in boys and 3.1% in girls (35). It seems that prevalence of MetS among adolescents varies by different study years with recent studies indicating a decreasing trend of MetS; however, studies periods in TLGS were 1991 - 2005 and no other study has reported recent trends of MetS data from the TLGS. Observations from two systematic reviews prior to 2013 suggest increasing prevalence of the MetS in youth, particularly in regions, such as the Far East and the Indian Subcontinent indicate that potential gender and regional differences in prevalence and that it may prove difficult to estimate the likely prevalence of MetS. More data is also needed to the two components of high TGs and low HDL-C which are determining factors of MetS worldwide (36, 37).

Another important explanation for the varying prevalence of MetS between TLGS and other studies is the use of different definitions. There is no general concern on the cut-off rates and its parameters (38). Different definitions of MetS in adolescents including Cook, Duncan, Boney, Cruz, and de Ferranti, showed that the highest correlation and prediction of adult MetS after 6.6 years of follow-up, using ATPIII criteria, was attained by de Ferranti's definition (39). Furthermore, in a longer follow-up study of 10.4 years with the joint interim statement (JIS) definition for adult MetS, the accordance of childhood MetS definitions and JIS was weak ($\kappa = 0.094 - 0.255$); however, the best accordance was found between JIS and Cook's definition in the late-pubertal group ($\kappa = 0.255$), in which group, the predictive power of each childhood definition was slightly higher for adulthood MetS. Among the Cook, de Ferranti, pediatric ATPIII and pediatric IDF definitions, Cook's and deFerranti's had better predictive powers (18). Besides the classic definition of MetS as having three of the five components including central obesity, hypertension, high fasting blood glucose, low HDL-C, and high TGs, factor analysis has been used to identify cardio-metabolic risk factor

models in adolescents. Using exploratory factor analysis to extract factor structure of MetS components, six measured variables were reduced to two sets of inter-correlated factors, BP and adiposity/lipids. The goodness of fit of the two-factor model was appropriate for boys and girls (40).

Except the MetS entity in adolescents, different metabolic phenotypes have recently been investigated in this age group. Adolescents with the hypertriglyceridemic waist (HW) phenotype had higher prevalence of all metabolic risk factors including high LDL-C, low HDL-C, and hypercholesterolemia than did those without this phenotype (41).

Prospective studies have reported that risk factors cluster together from childhood into adulthood and are strongly associated with obesity and insulin resistance. To find out the predictive value of WC and BMI, their best cut-off points for the incidence of MetS, a 6.6 year, follow up study was conducted on children; conclusions convey that both BMI and WC have the same power to predict MetS, therefore, children with higher BMI or WC are more exposed to MetS (42). However, when adolescents were followed to explore the best anthropometric parameter to predict early adulthood MetS, in boys, WC had the highest OR for the MetS risk, followed by waist-to-height ratio (WHtR). Adjusting BMI in addition to WC did not change the results in the 11 - 14-year age group, suggesting that WC may predict MetS risk above BMI. None of the anthropometric parameters were observed to have significant relationships with subsequent MetS risk in girls (43). In addition to anthropometric indices, several metabolic factors including high TGs/low HDL-C, high TG/high WC, high WC/low HDL, and high BP/low HDL-C phenotypes in adolescents predicted early adult MetS, independent of baseline BMI Z-Score and BMI change (44). An important finding was that adolescent MetS or higher weight gain were not able to predict early adult MetS, after controlling for adult BMI. In addition, the risk of developing MetS in early adulthood was higher among participants who were constantly obese or who became obese in adulthood than those who were overweight or obese during adolescence but non-obese in adulthood (45) (Table 2).

3.4. MetS Prediction for CVD and Diabetes

In a study conducted on 7932 subjects, aged ≥ 30 years who were followed for 9.0 ± 2.3 years, WHO-defined MetS was a significant predictor of total and cardiovascular mortality in men (HR=1.66, 95% CI=1.23 - 2.24, and HR=1.93, 95% CI = 1.26 - 2.94) and women (HR = 2.01, 95% CI = 1.39 - 2.88 and HR = 2.71, 95% CI = 1.44 - 5.09) (46). WHO-defined MetS could also predict 10-year risk of CVD and all-cause mortality events (HR=1.55, 95% CI=1.15 - 2.09, and HR=2.08 95% CI = 1.23 - 3.51, respectively) in 922 adults, aged ≥ 65 years (47); JIS-defined MetS showed a risk for CVD mortality (HR=1.65

(95% CI = 1.03 - 2.65) (47). In a 9.3 year follow-up of 5198 non-diabetic individuals, aged ≥ 30 years (mean age 45.6 years, 45% men), the HRs of CVD events according to the NCEP-ATP III, AHA/NHLBI, IDF and JIS definitions of MetS were 1.55 (1.21 - 2.00), 1.73 (1.35 - 2.20), 1.54 (1.22 - 1.94) and 1.70 (1.34 - 2.17), respectively (48). Evaluation of agreement between different definitions of MetS and insulin resistance in 347 non-diabetic individuals (aged ≥ 20 years) also showed poor agreement between ATP III or JIS and HOMA-IR (Kappa = 0.14 and 0.16, respectively); both criteria had also low sensitivities and specificities for detecting insulin resistance (49). Moreover, findings of a principal component analysis, of data of a 10-year follow-up performed to extract standardized factors from MetS components, identified three factors including BP, lipids and glycemia; WC was shared in three all factors (50); their results showed that BP, lipids and glycemia were related to the incidence of diabetes (OR = 2.23, 95% CI = 1.31 - 3.78, OR = 1.89, 95% CI = 1.27 - 3.67, and OR = 7.54, 95% CI = 4.09 - 13.91, respectively), in men and (OR = 2.13, 95% CI = 1.34 - 3.40, OR = 2.06, 95% CI = 1.35 - 3.15, and OR = 13.91, 95% CI = 7.29 - 26.51, respectively), in women, for the third versus the first tertile of these standardized factors (50).

All definitions of MetS were associated with cardiovascular disease (CVD). In a cross-sectional study, all definitions of MetS were related to CHD after adjustment for controlling factors in both genders (51). During 9.3 years of follow-up, the hazard ratios (HR) of MetS defined by JIS were 2.71 (1.57 - 4.68) and 2.07 (1.63 - 2.64) respectively for incident cardiovascular events and CHD; However, after controlling for MetS components, these relationship were no longer significant. In all definitions, high BP predicted both CVD and CHD events, and high FBS was also an independent predictor for CHD (52, 53). In subjects with diabetes, adding MetS did not change the CVD risk compared to individuals without MetS; however, the risk of CVD in IFG/IGT subjects increased 2.5 fold after addition of MetS, compared to IFG/IGT individuals without MetS (54).

Moreover, although all definitions of MetS seem to be predict type 2 diabetes, IGT had the highest predictive power for diabetes, compared to other definitions (55).

Previous studies confirmed the potential role and clinical usefulness of MetS for predicting CVD events and type 2 diabetes. A 18-year follow-up of Finnish males and females indicated that subjects with MetS had a 2.01-fold (95% CI = 1.46 - 2.77) higher risk for cardiovascular events, compared with subjects without MetS; compared with those without any components of MetS, having five components of MetS was related to hazards of 7.89 (2.26 - 27.60) for cardiovascular events (56). Having MetS was also related to incident diabetes, regardless of whether the MetS was defined according to NCEP ATP III (OR = 2.03, 95% CI = 1.10 - 3.75) or the IDF criteria (OR = 2.14, 95% CI = 1.29 - 3.55) (57). In a 20-year

follow-up of adult men, baseline MetS was a predictor of developing CHD (RR = 1.64, 95% CI = 1.41 - 1.90), stroke (RR = 1.61, 95% CI = 1.26 - 2.06), and type 2 diabetes (RR = 3.57, 95% CI = 2.83 - 4.50); however MetS could not predict CHD as well as the Framingham risk score (58). Overall, current evidence indicates that MetS can be used as a simple and useful predictor of future risk of CVD and type 2 diabetes; however MetS seems to be a more accurate tool for identifying individuals at risk of type 2 diabetes.

4. Conclusions

This review indicates high incidence of MetS in Tehranian adults and adolescents, in which related factors like age and gender play a pivotal role. Increased WC was a strong predictor of MetS both in adults and adolescents. All definitions of MetS predicted cardiovascular disease and diabetes.

More information about time trends of MetS is needed, in addition to a comprehensive understanding of the genetic determinants of MetS.

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Footnotes

Authors' Contribution: Firoozeh Hosseini-Esfahani, Zahra Bahadoran, Nazanin Moslehi, Golaleh Asghari, Emad Yuzbashian, Somaye Hosseinipour designed the study and interpreted the data, and drafting the manuscript; Fereidoun Azizi and Parvin Mirmiran supervised the study, Fereidoun Azizi critically revised the manuscript for important intellectual content and final approval of the version to be published.

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