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Familial Aggregation of Metabolic Syndrome With Different Socio-Behavioral Characteristics: The Fourth Phase of Tehran Lipid and Glucose Study

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Abstract

Background: Since genetic and most environmental factors shape the context of families, some studies have been initiated to investigate the role of familial relationships in metabolic syndrome (MetS).
Objectives: To estimate the familial aggregation of MetS and its components by identifying both case and control probands among Tehranian adults with different socio-behavioral and reproductive characteristics.
Patients and Methods: This case-controlled/family-based study was conducted on 1,777 families (635 case probands) who participated in the Tehran Lipid and Glucose Study (TLGS). Socio-demographic and reproductive information including levels of education, marital status, occupation status, age at menarche, number of abortions, number of children, and lifestyle habits such as smoking, physical activity and regular diet were obtained from the TLGS data bank. Metabolic syndrome was defined according to the joint interim statement (JIS) criteria. To estimate the regression co-efficient for familial aggregation and environmental factors, the generalized estimation equation method was used.
Results: The risk of having MetS among family members for case versus control probands was 2.19 (95% CI: 1.68 - 2.84), which, after adjusting for potential confounders including age, sex, educational level, marital status, occupation, age at menarche and energy, soft drink and starchy vegetable intake, increased to 2.31 (95% CI: 1.81 - 2.94; $P < 0.05$). Compared to control probands, the risk of having MetS components increased significantly from OR = 1.28 for both high waist circumference (WC) and blood pressure (BP) to OR = 1.72 for high triglycerides in cases. Familial aggregation inherited from the father was significantly observed in all MetS components, from adjusted OR = 1.63 for hyperglycemia to adjusted OR = 2.69 for high WC, except for low HDL, after controlling for potential confounders.
Conclusions: Considering spouses and siblings, there was a higher risk for MetS components among families whose fathers and offspring had MetS components, implying the pivotal role of genetic inheritance in the incidence of the syndrome and its components.

Keywords: Metabolic Syndrome, Familial Aggregation, Socio-Behavior

1. Background

Metabolic syndrome (MetS), a cluster of medical disorders including central obesity, glucose intolerance, dyslipidemia, hypertension and hyperglycemia, is known to increase the risk of developing cardiovascular diseases (CVD) and type 2 diabetes (T2D) (1). The alarming prevalence of MetS worldwide varies based on populations, lifestyle status and socioeconomic factors. Evidence reveals that about 24 and 42% of Iranian males and females have MetS, respectively (2).

Previous studies have shown the role of genetics and socio-behavioral factors on educational levels, smoking, physical inactivity and inappropriate dietary habits in the incidence of MetS (3). Genetic studies on MetS, including classical twin studies (4), family-based studies using a modeling technique (5) and genome-wide linkage scans (6) coincide with a great challenge, due to the complex traits and association with these socio-behavioral factors. These studies found the occurrence of MetS to be positively associated with low educational levels (7), low levels of physical activity (PA) (8), the "western diet" (9) and also inversely associated with dairy consumption. Furthermore, the negative effect of some nutritional habits like frequent coffee consumption, the absence of vegetables in daily meals and the desire for high-calorie dishes on the occurrence of MetS has been documented (10). Since genetic and most environmental factors shape the context of families, some studies have been initiated to investigate the role of familial relationships in MetS. For instance, first-degree relatives of persons with diabetes are more prone to have the syndrome (11); likewise, persons with the syndrome are more likely to have members with similar cardio-metabolic risk factors (12).

While several studies have assessed genetic and environmental factors related to the development of MetS, there is a paucity of population-based family studies to elucidate these contributions, particularly in an Iranian population. Limited investigations in this field have been conducted in East and South Asia but there is no survey available from the Middle East region concerning familial aggregation and the impact of socio-behavioral factors on MetS.

2. Objectives

This study is the first attempt to explore the possibility of a relationship between familial aggregation and the development of MetS in Tehranian families.

3. Patients and Methods

3.1. Study Population

This case-control/family-based study was conducted on all 3,958 families of the Tehran Lipid and Glucose Study (TLGS). The design of the TLGS included two major components: a cross-sectional study to investigate the prevalence of cardiovascular disease and its risk factors, and a prospective 20-year follow-up with approximately 3.5 year intervals. Details of the TLGS design and its preliminary results have been described elsewhere (1) . All data for the TLGS was collected through face-to-face interviews administered by trained research staff. For the present study, 1,776 families that have at least one member with MetS in the fourth phase (2009 - 2012) of the TLGS were recruited.

Participants provided written informed consent and the study was approved by the ethics committee of the research institute for endocrine sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran (ethics code 750EC, 2012). The authors are committed to protecting and ensuring the privacy and confidentiality of the personal health information of their participants.

3.2. Study Design

This was a case-controlled, family-based study. Of 12,823 subjects participating in the fourth phase of the TLGS, those aged < 19 years (n = 1,758), family members other than first and second degree (n = 30), and those with missing data (n = 175) were excluded, with 10,860 subjects remaining. Metabolic syndrome, diagnosed by the joint interim statement (JIS) criteria, led to 4,422 and 6,438 subjects with and without MetS, respectively. Using random sampling, 635 case-probands and 1,142 control-probands were selected from subjects with and without MetS, respectively. Finally, family members of probands were recruited, yielding 635 families of case probands (1,175 subjects with MetS and 1,423 subjects without MetS) and 1,142 families of the control probands (1,350 subjects with MetS and 3,187 subjects without MetS; Figure 1).

Data on MetS, its components, and the socio-behavioral and reproductive characteristics of participants were obtained from the TLGS data bank.

3.3. Measurements

All variables including body mass index (BMI), waist circumference (WC) and systolic and diastolic blood pressure (SBP and DBP) were measured according to standardized protocols (13). Furthermore, blood samples were taken after 12 - 14 hours of overnight fasting for biochemical analysis of triglycerides (TGs), high-density lipoprotein cholesterol (HDL-C), and fasting blood sugar (FBS). All assays, including those of FBS, TG and HDL-C levels were performed on the day of sampling. FBS levels were measured using the glucose oxidase method (Glucose kit; Pars Azmun, Tehran, Iran). TG levels of the samples were determined using the enzymatic colorimetric method (TG kit; Pars Azmun, Tehran, Iran). HDL-C levels of the samples were determined using the precipitation and enzymatic colorimetric method (HDL-C kit; Pars Azmun, Tehran, Iran). Coefficients of variation (CV) for HDL-C and TG measurements were < 5%.

Levels of education were categorized as primary (< 6 years), secondary (6 - 12 years), and higher ($\geq$ 12 years). Marital status was defined at three levels as single, married and divorced. In addition, based on the occupation status, participants were placed in three groups of unemployed, employed, and unemployed but having income.

The TLGS questionnaire included information on three major sections regarding lifestyle habits: smoking, PA and regular diet. Smoking status was classified as never, current and ex-smoking. Information about PA was collected using the modifiable activity questionnaire (MAQ) (14) to calculate the metabolic equivalent (MET) based on min/wk.

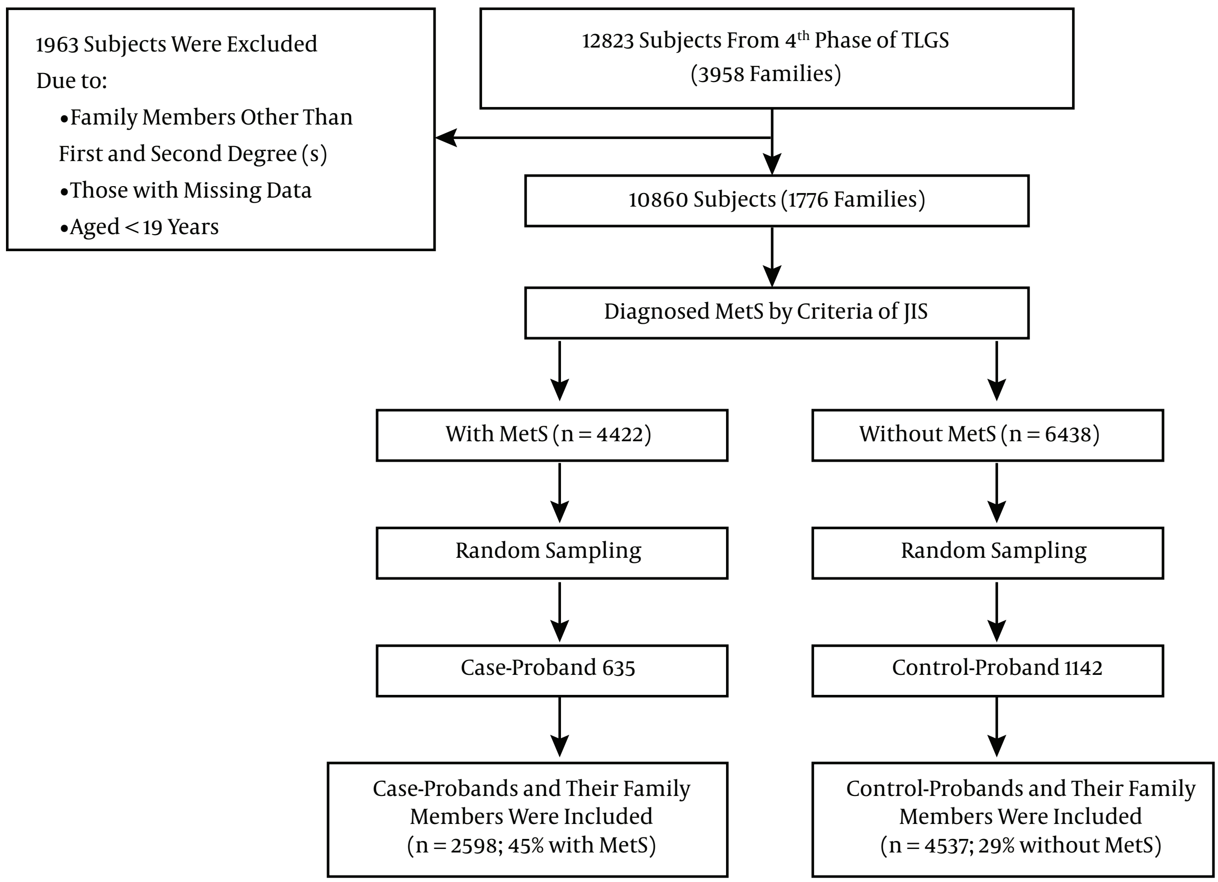

Figure 1. Sampling Frame of the Current Study

High reliability (98%) and moderate validity (47%) were reported for the Persian version of MAQ (14, 15). Physical activity levels were categorized as low (MET < 600 min/wk), moderate (MET 600 - 1499 min/wk), and high (MET $\geq$ 1500 min/wk) (16).

3.4. Dietary Assessments

Dietary data were collected using a valid and reliable 147-item semi-quantitative food frequency questionnaire (FFQ) (17), which asked the participants to provide their regular intakes over last year on a daily, weekly or monthly basis. The daily intakes were calculated and the portion sizes of foods converted to grams using household measures. Each food and beverage was analyzed for energy and nutrient intake using the United States department of agriculture (USDA) food composition table (FCT). In the current study, dietary factors including energy, leafy vegetables, red vegetables, orange vegetables, starchy vegetables, coffee, soft drinks, tea, fruits, dairy products and synthetic fruit juice were measured and categorized into quartiles of intake. The first and the last quartiles of dietary factors have been considered as the least and the most consumption, respectively. Reproductive variables considered were age at menarche, number of abortions and number of children.

3.5. Definitions

Metabolic syndrome was defined based on the JIS criteria (18) as having three or more of the following components: TGs $\geq$ 150 mg/dl or drug treatment, HDL-C < 40 mg/dl in men and < 50 mg/dl in women or drug treatment, SBP $\geq$ 130 mmHg and/or DBP $\geq$ 85 mmHg or drug treatment, FBS $\geq$ 100 mg/dl or drug treatment, and WC $\geq$ 89 cm for men and $\geq$ 91 cm for women (19).

3.6. Statistical Analysis

Normal distribution of continuous data was assessed by the Kolmogorov-Smirnov test and non-normal variables were transformed to logarithms. Continuous and categorical variables were expressed as mean ± SD and percentage, respectively. The Liang and Pulver method was used as a statistical model (20), enabling the assessment of familial aggregation, environmental risk factors and relevant interactions allowing for correlation. A detailed description of the mathematical model was given by Chiu et al. (10). The generalized estimation equation (GEE) method was used to estimate the regression coefficients for familial aggregation and environmental factors using SPSS software (Version 20; SPSS, Chicago, IL, USA). Adjusted odds ratios (OR) and their respective 95% CIs for environmental risk factors were also reported.

4. Results

The mean for cardio-metabolic risk factors was higher in cases than controls except for HDL, which was lower in cases ($P < 0.001$) (data not shown). A comparison of socio-demographic, behavioral, reproductive characteristics and dietary factors among the 7,135 participants between case and control groups is shown in Table 1.

The frequency of males in the case and control groups was 46.1 and 59.2 %, respectively. Subjects in the case group were older (52.0 ± 14.7 vs. 36.6 ± 14.4 years), with more females (53.9%), married (83.2%), current smokers (13.2%), unemployed but having income (19.8%), less high educated (16.8 vs. 32.0%), higher mean of abortion (0.56 ± 0.96 vs. 0.22 ± 0.59) and children (3.76 ± 2.51 vs. 1.34 ± 1.74) ($P < 0.001$). Mean intake of dietary factors including leafy, red and orange vegetables and tea were higher in cases, while intakes of coffee and synthetic fruit juice were higher in controls ($P < 0.05$). The difference of PA levels was nearly significant between the case and control groups ($P = 0.067$) (Table 1).

As shown in Table 2, the odds ratio for having MetS among family members for case versus control probands was 2.19 (95% CI: 1.68 - 2.84), which, after adjusting for potential confounders including age, sex, educational level, marital status, occupation, age at menarche, and energy, soft drink and starchy vegetable intake, increased to 2.31 (95% CI: 1.81 - 2.94; $P < 0.05$).

In the final model, after excluding non-significant variables, the odds ratios (95%CI) were 1.62 (1.02 - 2.59), 2.35 (1.40 - 3.96), 1.51 (1.00 - 2.27), 0.90 (0.83 - 0.97), 0.70 (0.50 - 0.98), and 1.72 (1.18 - 2.49), for lower education (R: higher education), married status (R: single), unemployment with having income (R: employed), age at menarche, starchy vegetables (R: the fourth quartile) and higher intakes of soft drinks (R: the fourth quartile), respectively (Table 2).

Compared to control probands, the risk of high WC, high BP, hyperglycemia, high TG, and low HDL increased significantly to 1.28 (1.10 - 1.48), 1.28 (1.09 - 1.49), 1.49 (1.28 - 1.75), 1.72 (1.50 - 1.98), and 1.49 (1.31 - 1.69), respectively in cases. Familial aggregation inherited from the father was significantly observed in all MetS components (from OR = 1.63 for hyperglycemia to OR = 2.69 for high WC) except for low HDL, after controlling for potential confounders. Familial aggregation resulting in offspring was significantly found for high WC (OR = 1.58) and hyperglycemia (OR = 1.64). Familial aggregation attributed from mothers and spouses were significantly predictive for high TG (OR = 0.29 and OR = 0.57, respectively) in both and high WC (OR = 0.33) just for mothers (Table 3).

5. Discussion

The present study reveals the familial aggregation of MetS, even after adjusting for potential socio-demographic and behavioral confounders. Compared to the control group, case-proband families had approximately a > two-fold risk of having MetS. In cases, among socio-demographic and reproductive factors, level of education, marital status, occupation, age at menarche, and some dietary factors were significantly associated with an elevated risk of MetS compared to the control group. The risk of all MetS components significantly increased from 1.28-fold for both high WC and BP to 1.72-fold for high TG among the case-proband group. Considering spouses and siblings, higher risk for MetS components among families whose fathers and offspring had MetS components implies the pivotal role of genetic inheritance in the incidence of this syndrome and its components. However, lack of the same association among families whose mothers had MetS components could emphasize the probable role of the other socio-behavioral factors. Our results are consistent with a previous TLGS study, which showed that children of parents with MetS had a > four-fold risk of having this syndrome (21). In addition, more findings from the TLGS show a high recurrence risk ratio (five-fold) of MetS among siblings and a higher significantly higher risk of MetS aggregation among probands' families affected, even after adjustment for age, gender and smoking (22).

The recurrence risk of sibling and familial aggregation of MetS and its components has been previously studied (23). A strong tendency to familial aggregation of MetS has been reported among Taiwanese people, even after controlling for potential confounders (10). Another study among the Chinese population revealed familial similarity regarding body fat, lipid profiles, FBS, insulin levels and blood pressure (24). Similar results from the Framingham Heart and Offspring Cohort have also shown family pair correlations for some of cardio-metabolic risk factors, specifically for BMI and lipid levels (25). Although

Table 1. Comparison of Demographics and Anthropometric Factors Between Case and Control Groups

Variables	Case, n = 2525	Control, n = 4610	P Value
Gender			< 0.001
Female	1163 (53.9)	2728 (40.8)	
Male	1362 (46.1)	1882 (59.2)	
Age, y	52.0 ± 14.7	36.6 ± 14.4	< 0.001
Education			< 0.001
Primary, (< 6 y)	889 (35.3)	507 (11.0)	
Secondary, (6 - 12 y)	1207 (47.9)	2619 (57.0)	
Higher, (≥ 12 y)	424 (16.8)	1469 (32.0)	
Marriage			< 0.001
Single	201 (8.0)	1562 (33.9)	
Married	2100 (83.2)	2908 (63.1)	
Divorced	223 (8.8)	136 (3.0)	
Smoking			< 0.001
Never	1871 (74.3)	3775 (82.0)	
Ex-smoker	314 (12.5)	317 (6.9)	
Current	333 (13.2)	512 (11.1)	
Physical activity			0.067
Low	1723 (77.1)	2842 (74.8)	
Moderate	342 (15.3)	613 (16.1)	
High	170 (7.6)	347 (9.1)	
Occupation			< 0.001
Unemployed	1026 (40.7)	2271 (49.7)	
Employed	995 (39.5)	1944 (42.5)	
Unemployed but having income	500 (19.8)	357 (7.8)	
Reproductive status			
Age at menarche	13.46 ± 1.57	13.45 ± 1.56	0.661
Number of abortions	0.56 ± 0.96	0.22 ± 0.59	< 0.001
Number of children	3.76 ± 2.51	1.34 ± 1.74	< 0.001
Dietary factors			
Leafy vegetables, g	37.6 (19.6, 66.4)	33.9 (17.5, 60.6)	0.001
Red vegetables, g	72.7 (31.7, 122.7)	54.4 (21.7, 112.2)	< 0.001
Orange vegetables, g	4.1 (0, 16.2)	2.9 (0, 13.5)	0.026
Starchy vegetables, g	15.7 (7.3, 27.4)	15.7 (7.6, 28.5)	0.245
Coffee, g	0.38 (0, 4.67)	1.15 (0, 9.33)	< 0.001
Soft drinks, g	13.33 (3.29, 36.66)	13.33 (3.29, 42.85)	0.254
Tea, g	439 (194, 729)	374 (175, 683)	< 0.001
Fruits, g	244 (117, 437)	231 (99, 421)	0.055
Dairy products, g	347 (211, 487)	336 (213, 497)	0.888
Synthetic fruit juices, g	4.4 (0, 26.4)	6.7 (0, 33)	0.002

these studies discuss genetic influences on the MetS and its components, the spousal correlations observed for this syndrome, as a whole or some of its components, in some of participants imply the role of environmental factors in shaping this familial aggregation (26, 27).

In the current study, compared to higher-educated subjects, familial aggregation of MetS was significantly higher in less-educated case probands. Despite considering education as a socio-demographic indicator in most previous studies, only a few discussed educational level as a determinant factor for incidence of MetS and its components (10, 28, 29). In line with our findings, another study showed that the familial aggregation of MetS was more likely among those with lower educational levels (10). In addition, there is more evidence showing that the incidence risk of MetS decreases with an increase in the years of education among Norwegian men and women (29). However, Ngo et al. emphasized the role of area-level of education in shaping the distribution and development of MetS rather than individual-level of education (30).

Table 2. Adjusted Odds Ratios for Familial Aggregation and Environmental Risk Factors Associated with MetS

Variables	OR (95% CI)[a]	P	OR (95% CI)[b]	P Value
Familial aggregation	2.19 (1.68 - 2.84)	< 0.001	2.31 (1.81 - 2.94)	< 0.001
Age	-		1.10 (1.08 - 1.11)	< 0.001
Sex	-		2.71 (2.21 - 3.33)	< 0.001
Socioeconomic status				
Education (secondary/ higher)	1.47 (1.00 - 2.15)	0.046	1.54 (1.08 - 2.20)	0.018
Education (primary/higher)	1.48 (0.90 - 2.45)	0.122	1.62 (1.02 - 2.59)	0.041
Marriage (married/single)	2.08 (1.19 - 3.61)	0.009	2.35 (1.40 - 3.96)	0.001
Marriage (divorced/single)	1.99 (0.88 - 4.51)	0.097	2.03 (0.91 - 4.50)	0.082
Occupation (unemployed/employed)	1.61 (0.41 - 0.95)	0.029	1.51 (1.00 - 2.27)	0.046
Occupation (unemployed but having income/employed)	1.44 (0.50 - 1.76)	0.322	1.33 (0.68 - 2.59)	0.641
Lifestyle factors				
Smoking (ex-smoker/never)	0.91 (0.31 - 2.70)	0.867		
Smoking (daily/never)	1.25 (0.61 - 2.56)	0.547		
Physical activity (times of per week) × (minutes of per time)				
Exercise intensity (low/high)	1.36 (0.83 - 2.22)	0.221		
Exercise intensity (moderate /high)	1.33 (0.75 - 2.35)	0.318		
Reproductive status				
Age at menarche	0.92 (0.83 - 0.99)	0.037	0.90 (0.83 - 0.97)	0.010
Number of abortions	1.01 (0.87 - 1.18)	0.867		
Number of children	1.05 (0.94 - 1.16)	0.381		
Dietary factors, Quartile 4/Quartile 1				
Leafy vegetables (Q4/Q1)	0.78 (0.52 - 1.16)	0.223		
Red vegetables (Q4/Q1)	1.36 (0.92 - 2.00)	0.121		
Orange vegetables (Q4/Q1)	1.18 (0.78 - 1.79)	0.439		
Starchy vegetables (Q4/Q1)	0.69 (0.48 - 0.99)	0.046	0.70 (0.50 - 0.98)	0.038
Coffee (Q4/Q1)	1.25 (0.80 - 1.94)	0.325		
Soft drinks (Q4/Q1)	1.46 (0.97 - 2.19)	0.067	1.72 (1.18 - 2.49)	0.004
Tea (Q4/Q1)	0.91 (0.63 - 1.33)	0.641		
Fruits (Q4/Q1)	0.89 (0.61 - 1.30)	0.532		
Dairy products (Q4/Q1)	0.95 (0.66 - 1.37)	0.785		
Synthetic fruit juices (Q4/Q1)	1.24 (0.84 - 1.82)	0.279		

[a]OR: adjusted odds ratio for each variable by including factors (age and gender of case and control proband and Kcal) and age and gender of family members from each case or control proband in the model.
[b]OR, adjusted for familial aggregation and significant factors.

In addition to educational level, in the current study, marital status and occupation was significantly associated with familial aggregation of MetS. Growing literature has documented the relationship between socioeconomic position and a wide range of health outcomes, including cardio-metabolic diseases (30). For example, associations between state-level income inequality and cardio-metabolic risk factors such as BMI, hypertension and sedentarism have been found to be stronger in low-income individuals (31).

Based on our findings, lower age at menarche was associated with higher risk of MetS among families, whereas, in contrast, another study showed no significant association between age at menarche and the familial aggrega-

Table 3. Adjusted Odds Ratios for Familial Aggregation Associated with Individual Components of MetS[a]

Components of metabolic syndrome	Case Proband/Control Probands[b]	Adjusted Odds Ratio				
		Father	Mother	Offspring	Siblings	Spouse
High WC	1.28 (1.10 - 1.48)	2.69 (1.84 - 3.93)	0.33 (0.18 - 0.63)	1.58 (1.22 - 2.05)	0.61 (0.26 - 1.44)	0.79 (0.59 - 1.07)
High BP	1.28 (1.09 - 1.49)	2.25 (1.55 - 3.25)	0.58 (0.31 - 1.10)	1.18 (0.86 - 1.62)	1.25 (0.51 - 3.05)	0.72 (0.50 - 1.03)
Hyperglycemia	1.49 (1.28 - 1.75)	1.63 (1.13 - 2.38)	0.73 (0.39 - 1.38)	1.64 (1.19 - 2.24)	0.79 (0.35 - 1.79)	0.87 (0.61 - 1.23)
High TG	1.72 (1.50 - 1.98)	1.96 (1.40 - 2.75)	0.29 (0.16 - 0.54)	1.18 (0.90 - 1.55)	0.67 (0.31 - 1.45)	0.57 (0.42 - 0.78)
Low HDL	1.49 (1.31 - 1.69)	1.31 (0.96 - 1.78)	0.83 (0.49 - 1.44)	1.20 (0.96 - 1.51)	1.43 (0.69 - 3.00)	1.14 (0.87 - 1.49)

[a] $P < 0.05$.
[b] Other independent variables controlled in the model included age, sex, level of education, marital status, occupation, starchy vegetables and soft drinks for central obesity, high blood pressure, hyperglycemia, triglycerides and HDL.

tion of MetS (10). Our study findings are in agreement with those of the Bogalusa heart study conducted among 1,479 adult women, which reported that early menarche is characterized by a higher prevalence of clustered risk variables as MetS components (32). This effect could be a combination of lifestyle risk factors and/or biological changes associated with age at menarche.

In the current study, higher consumption of soft drinks was associated with greater risk of MetS. Similarly, among middle-aged adults of the Framingham Heart Study, a significant association was reported between a higher prevalence of MetS and consumption of more than one serving of soft drink per day. In a prospective analysis, a 44% increase of incidence of MetS was seen among adults who consumed at least one serving of soft drink per day and daily consumption of soft drinks was also associated with a higher incidence of each MetS component (33). Nettleton et al. showed that among participants of the Multi-Ethnic Study of Atherosclerosis, sugar-sweetened beverages were directly related to a 36% higher risk of incidence of MetS along with a greater risk of high FBS and enlarged WC, but not with other MetS components (34). It may be explained that higher consumption of added synthetic sugar such as fructose corn syrup can lead to weight gain, increased insulin resistance, lower HDL-C, and increased TGs (35-37). The increased sweetness of diet foods may lead to conditioning for a greater preference of sweetened items. The caramel content of both regular and dietary drinks may be a potential source of advanced glycation end products, promoting insulin resistance and inflammation (38, 39).

In the current study, the proband parents, offspring, siblings, spouses and other second-degree relatives were studied and the impact of each family member was assessed separately. The higher risk found in parents compared with the offspring, siblings and spouses suggest that genetic inheritance plays a key role, although the contribution of lifestyle habits conferred by parents cannot ruled out. When considering individual components of MetS after adjusting for environmental factors, paternal influence was shown to play major role in the incidence of abdominal obesity, hypertension, hyperglycemia and high TGs.

5.1. Strength and Limitations

The strength of the current study is its representation of Tehranians, because results were based on a large general population of Tehran. Furthermore, data on lifestyle, reproductive history and multiple cardiovascular risk factors were available and measured according to a standardized protocol. Nevertheless, some limitations should be mentioned. First of all, this study was conducted in an urban community, which could be different from rural areas in some aspects. Second, adjustment for family size was not used in this study. In addition, missing data on behavioral factors such as PA and smoking could affect the results associated with these variables. However, to the authors' knowledge, this is the first report to use a genetic epidemiology approach to dissect the genetic, socio-behavior components and odds ratio of MetS in an Iranian population.

In conclusion, the risk of all MetS components were significantly raised from 1.28 fold for both high WC and BP to 1.72 fold for high TG among case probands. Considering spouses and siblings, the higher risk for MetS components among families whose fathers and offspring had MetS components implies a pivotal role of genetic inheritance in incidence of the syndrome and its components. However, lack of the same association among families in which the mothers had MetS components could emphasize the probable role of the other socio-behavioral factors.

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Footnotes

Authors' Contribution: Study concept and design, Maryam Zarkesh and Parisa Amiri; acquisition of data, Maryam Zarkesh, Golaleh Asghari, Mehdi Hedayati and Arash Ghanbarian; analysis and interpretation of data, Maryam Zarkesh, Nima Hosseinzadeh and Golaleh Asghari; drafting of the manuscript, all authors; critical revision of the manuscript for important intellectual content, Parisa Amiri and Fereidoun Azizi; statistical analysis, Maryam Zarkesh, Nima Hosseinzadeh and Golaleh Asghari; administrative, technical and material support, Parisa Amiri and Fereidoun Azizi; study supervision, Parisa Amiri.

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