The Prevalence of Cardiovascular Risk Factors in Patients with and Without Metabolic Syndrome in Diabetes Mellitus: A Study Based on Rafsanjan Cohort Study

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Abstract

Background

Cardiovascular disease (CVD) is the leading causes of death and disability in diabetes. This study aimed to determine the prevalence of cardiovascular risk factors in people with and without metabolic syndrome (MtS) in diabetes mellitus (DM).

Methods

This cross-sectional study was part of Rafsanjan Cohort Study (RCS).as part of the comprehensive PERSIAN (Prospective Epidemiological Research Studies in IrAN) on adults with and without MtS in DM. CVD risk factors, including gender, age, blood pressure, dyslipidemia, smoking, alcohol consumption, fasting blood sugar, creatinine, blood urea, waist circumference, body mass index, family history, physical inactivity, fruit and vegetable consumption were collected in the PERSIAN Cohort Questionnaire. The data were analyzed by SPSS software version 22.

Results

The prevalence of MtS in 1933 participants was estimated to be 80% (95% confidence interval 81.8% -78.1%). In the logistic regression model, smoking, alcohol consumption, triglyceride to HDL (High Density Lipoprotein) ratio, abdominal obesity, and hypertension were identified as the factors associated with MtS.

Conclusions

Our results show that Based on our study, the prevalence of cardiovascular risk factors in DM was high. Reducing smoking and alcohol consumption and controlling hypertension, hyperlipidemia, and overweight are the suggested solutions in this field.

Introduction

The International Diabetes Federation (IDF) estimates that diabetes accounts for 8.8% of the world's population and is projected to increase to 642 million by 2040. The prevalence of diabetes mellitus (DM) is constantly increasing over time (1). In Iran, the prevalence of DM in adults aged 25 to 70 years is reported to be 11.9%. It is estimated that by 2030, about 9.2 million Iranians are likely to have DM. Cardiovascular disease (CVD) is one of the leading causes of death and disability in people with DM (2). The risk of CVD is constantly increasing by increasing fasting plasma glucose levels, even before reaching a sufficient level to diagnose DM (3). DM reduces life expectancy by up to 10 years and more

than 50% of patients die of a cardiovascular event (4). People with DM are more likely to be affected by CVD than non-diabetic people (2, 5).

Diabetic patients had a 10% higher risk of CVD, a 53% higher risk of MI, a 58% higher risk of stroke, and a 12% higher risk of heart failure than the non-diabetic population. Thus, DM is a major risk factor for CVD and its consequences (6). The literature review shows that in New York, patients with DM are almost three times more likely to develop heart disease than their non-diabetic counterparts (7). This ratio has been studied in some areas in Iran. For instance, the risk of CVD in DM patients in a study in Yazd was about 2-4 times (8). and in another study in Ahvaz was 2-8 times that of the general population (9).

The risk of CVD in DM follows a slope, and the severity of this slope depends on a combination of multiple risk factors (10). Most of these additional risks of CVD in DM are associated with an increased prevalence of known risk factors, such as hypertension, dyslipidemia, and obesity (11). Over the last decade, studies have shown that treating known risk factors for patients with DM is extremely important in reducing the risks of CVD (12). Poor control of most cardiovascular risk factors has been observed in the diabetic population. However, the additional risks of CVD in DM patients cannot be attributed solely to the higher prevalence of known risk factors (13). Therefore, other risk factors may be important in people with DM (14). A set of interrelated risk factors characterize metabolic syndrome (MtS), including hypertension, hyperglycemia, abdominal obesity, and dyslipidemia (15). The disease is associated with an increased risk of cardio-vascular events, DM, and deaths (16).

NCEP-ATPIII (the National Cholesterol Education Program-Adult Treatment Panel) Criteria, IDF, and WHO (World Health Organization) definitions reported that the prevalence of MtS in DM were 45.8%, 57.7%, and 28%, respectively in India (17). According to a study conducted in Nepal, the total age adjusted prevalence rates of MtS according to Harmonized, NCEP ATP III, WHO and IDF definitions were 80.3%, 73.9%, 69.9%, and 66.8%, respectively. The lowest agreement was observed between WHO and IDF definitions and the highest overall agreement was between Harmonized and NCEP ATP III definitions (18).

The extent of these risk factors has been widely examined in studies; since finding the correlation between DM risk factors and CVD can be effective in preventing the incidence of morbidity and mortality in patients (19). Endocrinologists and cardiologists suggest that more efforts should be made to improve the risk factors for heart disease in diabetic patients due to their higher risk of heart attack and the higher mortality rate (20). Therefore, this study aimed to determine the prevalence of cardiovascular risk factors in people with and without MtS in DM in Rafsanjan adult cohort study.

Materials And Methods

This cross-sectional study was performed based on Rafsanjan Cohort Study (RCS) (21) as part of the comprehensive PERSIAN (Prospective Epidemiological Research Studies in IrAN) (22). The cohort study included 10,000 people aged 35-70 years who were randomly invited to the study from urban and rural areas covered by the health centers of this city. The inclusion criteria of cohort study were 1- Iranian citizenship 2- having an age range of 35-70 years, 3- living at least 9 months a year in the studied area in

Rafsanjan city. The exclusion criteria included lack of understanding the Persian language and the existence of severe physical and mental disorders. PERSIAN Cohort standard questionnaires consisting of 482 questions in 3 major sections of general, medical, and nutrition were asked from the participants by a trained interviewer. The validity and reliability of all questionnaires were confirmed. The face to face interview was conducted by trained interviewers and the participants' answers were collected electronically and confidentially after obtaining their consent (21).

In this study, all the DM patients in the cohort population were included based on the past medical history and their self-expression. The presence of MtS in each individual was assessed and they divided to two groups with and without MtS. The diagnostic criteria for this syndrome were defined in such a way that the patient met at least three of the five MtS criteria at the same time as described by American Heart Association. (23), including: (a) central obesity determined by waist circumference equal to or greater than 88 cm (35 inches) in women and equal to or greater than 102 cm (40 inches) in men; (b) fasting serum triglyceride level equal to or greater than 150 mg/dL or on drug therapy for hypertriglyceridemia (e.g., fibrates, nicotinic acid); (c) High Density Lipoprotein (HDL) level less than 50 mg/dL in women and less than 40 mg/dL in men or on drug therapy for low high-density lipoprotein level (fibrates, nicotinic acid); (d) elevated diastolic blood pressure equal to or greater than 85 or elevated systolic blood pressure equal to or greater than 130 or on drug therapy for hypertension; (e) elevated fasting glucose level equal to or greater than 100 mg/dL or on drug therapy for hyperglycemia/diabetes.

Demographic and clinical characteristics of individuals were extracted from the cohort center database, including gender, age, education level, residence, race, hypertension, dyslipidemia, smoking, alcohol consumption, systolic and diastolic blood pressure, heart rate, fasting blood sugar, triglycerides, LDL (low-density lipoprotein), HDL (High Density Lipoprotein), creatinine, blood urea nitrogen (BUN), alkaline phosphatase (ALP), waist circumference, body mass index ($BMI = \text{weight (kg)} / \text{height}^2 \text{ (m)}$), height and weight, family history of cardiovascular disease, physical inactivity, and insufficient consumption of fruits and vegetables.

In this study, the ratio of triglyceride to high-density lipoprotein cholesterol (TG/HDL-C) was less than 2, 2 to 3.8, and more than 3.8, indicating favorable, moderate risk, and high risk of insulin resistance, respectively (24). The participants were classified in three different groups in terms of physical activity based on the Scoring the International Physical Activity Questionnaire (IPAQ) recommendations for scoring protocol. The groups included low active (<600 MET-minutes/week); moderate active (≥ 600 MET-minutes/week) and high active (≥ 3000 MET-minutes/week) (25), considering the MET-min/wk of the sum of walking, moderate-intensity physical activities, and vigorous-intensity physical activities. In terms of fruit and vegetable consumption, the subjects were divided into two groups according to the WHO recommendation, including high consumption (more than 400 grams of fruits and vegetables per day) and low consumption (less than 400 grams of fruits and vegetables per day) (26). BMI categories were defined as follows: normal, BMI 20 to 24.9; overweight, BMI 25 to 29.9; obese I, BMI 30 to 34.9; obese II, BMI 35 to 39.9; morbid obesity, $BMI \geq 40$ (27).

Statistical analysis:

All the data were entered in SPSS software version 22 and for descriptive analysis of data, mean and standard deviation or frequency and percentage were used. In order to investigate the relationships due to abnormality, Mann-Whitney U test and Chi-square test (for classification variables) were used. Multiple logistic regression model was used to determine the factors associated with MtS. The significance level (P value) was considered less than 0.05.

Results

Out of 1933 patients with DM in this study, 1213 (62.8%) were female and 720 (37.2%) were male. The mean age of the participants was 55.92 ± 8.17 years. The prevalence of MtS in this study was estimated to be 80% with a 95% confidence interval 81.8% -78.1%, so that 1546 patients had at least three of the 5 diagnostic factors of MtS. The prevalence of MtS was significantly higher in women (66.9%) compared to men (33.1%) (P-value<0.001). Moreover, the mean age of the subjects in the MtS group was significantly higher than the group without MtS (56.31 ± 7.98 years compared to 54.37 ± 8.74 years, P-value <0.001). The frequency distribution comparison of demographic and clinical characteristics of the patients in the two groups with and without MtS is given in Table 1 and Figure 1. As can be seen, education level, marital status, smoking, alcohol consumption, history of hypertension, history of ischemic heart disease, family history of stroke, and consumption of fruits and vegetables were significantly different between the two groups (P-value <0.05). All the participants were low active and most of the subjects (84.7%) were in the group of low consumption of fruits and vegetables.

Table 1

Comparison of demographic and clinical characteristics in the two groups with and without MtS in type 2 diabetes mellitus

Variables		Total (1933=n)	Without metabolic syndrome (387=n)	With metabolic syndrome (1546=n)	P- value
Age		(62-50) 57	(61-47) 5/55	(63-51) 57	001/0>
Gender	Male	(2/37) 720	(54) 209	(1/33) 511	001/0>
	Female	(8/62) 1213	(46) 178	(9/66) 1035	
Marital status	Single	(2/11) 217	(9/5) 23	(5/12) 194	001/0>
	Married	(8/88) 1716	(1/94) 364	(5/87) 1352	
Education level	Illiterate	(3/18) 353	(4/12) 48	(7/19) 305	001/0>
	Diploma and lower	(0/71) 1373	(7/67) 262	(9/71) 1111	
	Academic degree	(7/10) 207	(9/19) 77	(4/8) 130	
Family history of ischemic heart disease	Yes	(3/14) 276	(3/16) 63	(8/13) 213	208/0
	No	(7/85) 1657	(7/83) 324	(2/86) 1333	
family history of heart attack	Yes	(5/11) 223	(6/11) 45	(5/11) 178	950/0
	No	(5/88) 1710	(4/88) 342	(5/88) 1368	
Family history of high blood pressure	Yes	(7/19) 380	(2/21) 82	(3/19) 298	397/0
	No	(3/80) 1553	(8/78) 305	(7/80) 1248	
Family history of diabetes mellitus	Yes	(0/22) 426	(5/24) 95	(4/21) 331	183/0
	No	(0/78) 1507	(5/75) 292	(6/78) 1215	

Variables		Total (1933=n)	Without metabolic syndrome (387=n)	With metabolic syndrome (1546=n)	P- value
family history of stroke	Yes	(3/8) 161	(1/11) 43	(6/7) 118	027/0
	No	(7/91) 1772	(9/88) 344	(4/92) 1428	
consumption of fruits and vegetables	Low	(7/84) 888	(2/90) 194	(2/83) 694	011/0
	Normal	(3/15) 161	(8/9) 21	(8/16) 140	

Medium (first quarter-third quarter) for age and frequency (%) is reported for qualitative variables. In order to compare age in the two groups, Mann-Whitney test and to perform other comparisons Chi-square test were used.

The prevalence of risk factors in the group without MtS included 33.9% abdominal obesity (95% confidence interval: 29.18-38.62), 19.7% obesity (95% confidence interval: 17.72-21.68), 27.1% hypertriglyceridemia (95% confidence interval: 22.67-31.53), 15.8% hypertension (95% confidence interval: 12.17-19.43), 15.8% smoking (95% confidence interval: 12.17- 19.43), 12.7% the history of ischemic heart disease (95% confidence interval: 9.39-16.01), 5.9% alcohol consumption (95% confidence interval: 3.55-8.25), and low HDL 1.3% (95% confidence interval: 0.18-2.42), respectively. The prevalence of risk factors in the MtS group was reported 80.5% hypertriglyceridemia (95% confidence interval: 78.54-82.46), 75.9% abdominal obesity (95% confidence interval: 73.76-78.04), 64% hypertension (95% confidence interval: 61.66-66.39), 48% low HDL (95% confidence interval: 45.51-50.49), 43.8% obesity (95% confidence interval: 41.33-46.27), 22.3% smoking (95% confidence interval: 20.22-24.38), 19% history of ischemic heart disease in (95% confidence interval: 18.80-19.20), and 9.4% alcohol consumption (95% confidence interval: 7.95-10.85), respectively. Figure 1 reveals that the prevalence of the above factors in the two groups were statistically significant (P-value <0.05).

Given the studied subjects were all patients with DM, all of them had at least one of the 5 factors of MtS. Therefore, the frequency distribution of the number of MtS factors included 4.4% only one factor (n=85), 15.6% two factors (n=302), 37.1% three factors (n=716), 31.1% four factors (n=601), and 11.7% five factors (n=226).

Given the abnormal distribution of anthropometric indices and biochemical and laboratory indices, the Mann-Whitney non-parametric test was used for comparing the two groups, which is shown in Table 2. The median of BMI, systolic blood pressure, diastolic blood pressure, heart rate, triglyceride, ALP, and TG

to HDL ratio were significantly higher in the MtS group and HDL was significantly lower than the group without MtS.

Table 2
Comparison of the median of anthropometric and laboratory indices of patients with type 2 diabetes mellitus in the two groups with and without MtS

Variables	Total (1933=n)	Without metabolic syndrome (387=n)	With metabolic syndrome (1546=n)	P- value
Waist circumference	(6/106-6/92) 5/99	(53/99-08/87) 05/94	(9/107-5/94) 2/101	001/0>
BMI	(93/31-84/25) 66/28	(01/29-12/24) 45/26	(49/32-40/26) 30/29	001/0>
Systolic blood pressure	(125-100) 115	(5/118-100) 108	(125-100) 115	001/0>
Diastolic blood pressure	(80-65) 70	(80-65)70	(80-65) 75	001/0>
Heart rate	(82-70) 76	(80-68) 74	(83-70) 76	001/0
Fasting blood sugar	(188-114) 144	(25/182-111) 143	(189-115) 145	3/0
Triglyceride	(229-121) 165	(160-100) 126	(240-5/132) 179	001/0>
Cholesterol	(223-167) 193	(218-164) 5/191	(225-167) 194	098/0
HDL	(64-49) 56	(66-52) 59	(63-48) 56	001/0>
LDL	(124-78) 100	(125-80) 99	(124-78) 100	430/0
Creatinine	(2/1-9/0) 1	(2/1-9/0) 1	(2/1-9/0) 1	143/0
BUN	(17-12) 14	(17-12) 14	(17-12) 14	261/0
ALP	(277-192) 232	(259-75/186) 219	(281-194) 235	001/0>
TG to HDL ratio	(29/4-07/2) 96/2	(84/2-60/1) 15/2	(49/4-25/2) 22/3	001/0>
Median (first quarter-third quarter) is reported for the variables. Mann-Whitney test was used to compare the two groups. Low-Density Lipoproteins (LDL), High-Density Lipoproteins (HDL), Alkaline Phosphatase (ALP), Blood Urea Nitrogen (BUN)				

In order to investigate the relationship between demographic characteristics, disease history, anthropometric indices, and biochemical factors with MtS, univariate logistic regression was performed for all the studied variables. Then, significant variables at the level of 0.1 were entered into the multiple logistic regression model using Backward LR method. According to the results of logistic regression

model (Table 3), smoking, alcohol consumption, TG to HDL ratio, abdominal obesity, and hypertension were identified as factors associated with MtS in this study. So the risk of MtS was increased by smoking 5.60% (95% confidence interval: 3.67-8.55), alcohol consumption 4.1% (95% confidence interval: 2.32-7.23), TG to HDL ratio 1.42% (95% confidence interval: 1.30-1.55), abdominal obesity 13.73% (95% confidence interval: 9.77-19.29), and hypertension 13.54% (95% confidence interval: 9.55-19.19), respectively. Considering that hypertension and abdominal obesity are the 5 causes of MtS, it is associated with a high risk of developing MtS.

Table 3
Multivariate logistic regression results

Variables		OR (95% CI)	P-value
TG to HDL ratio		(55/1-30/1) 42/1	001/0>
Abdominal obesity	No	ref	–
	Yes	(29/19-77/9) 73/13	001/0>
Smoking	No	ref	–
	Yes	(55/8-67/3) 60/5	001/0>
Alcohol consumption	No	ref	–
	Yes	(23/7-32/2) 098/4	001/0>
Hypertension	No	ref	–
	Yes	(19/19-55/9) 54/13	011/0
Multiple logistic regression model using Backward LR method. High-Density Lipoproteins (HDL), Triglyceride (TG)			

Discussion

Cardiovascular diseases are the leading cause of death and disability in diabetic patients (28). high blood pressure, hyperlipidemia, MtS, and smoking are important risk factors for cardiovascular disease (29), and the association of these factors with cardiovascular disease is completely identified (30, 31). The results of the present study revealed that in patients with DM smoking, alcohol consumption, triglyceride to HDL ratio, abdominal obesity, and hypertension were identified as the factors associated with MtS.

MtS is a set of multiple risk factors for atherosclerotic cardiovascular disease and DM (32). MtS is strongly associated with DM. In this type of diabetes, there is insulin resistance with secondary hyperinsulinemia and it is often associated with high blood pressure, dyslipidemia, atherosclerosis, and most importantly obesity, especially central obesity. Etiology of MtS consists of separate components of the MtS (such as hypertension, DM, dyslipidemia) causing complex conditions (33). The prevalence of MtS in this study was estimated to be 80%. Its prevalence according to IDF criteria in people with Type 2

Diabetes Mellitus in the study by Moreira et al. was reported to be 74.3% *. It was also 69.5% in the study by AlSaraj et al. (34). Different prevalence of MtS in populations, in addition to methodological differences, could be due to various nutritional, epidemiological, and demographic transitions (35), as well as ethnic (36), social, and environmental (37) disparities.

In this study, the prevalence of hypertension in the group without MtS was 15.8% and in the MtS group was 64%. However, the prevalence of hypertension with diabetes varied in different ethnic, racial, and social groups (33). In previous studies, the prevalence of hypertension in patients with diabetes, covering more than 30,000 people in different areas, 70% of diabetic patients have been reported to have hypertension (38). This rate is more consistent with the blood pressure statistics in diabetic patients with MtS in this study.

In the current study, smoking, alcohol consumption, and TG to HDL ratio were also identified as factors associated with MtS in patients with DM. These results were confirmed by Lindsay et al. and Mottillo et al. (39, 40). Slagter et al. reported that alcohol and cigarette consumption increase the risk of MtS and some of its components in a dose-dependent manner (41). It has been found that high levels of LDL, high blood pressure, and smoking are the most important risk factors for cardiovascular disease in DM and low HDL cholesterol, insulin resistance, hyperglycemia, and inflammation are also predictors of cardiovascular complications (42).

Previous studies have reported that obesity, especially central obesity, is the main underlying cause of MtS, causing a genetic predisposition for other risk factors, such as dyslipidemia and hypertension (43). In the present study, the prevalence of abdominal obesity in diabetic patients without MtS was 33.9%, which reached 75.9% in DM patients with MtS. In the study by Cheng et al., abdominal obesity was reported in 91.6% of people with DM (44), which is higher than the results of the present study. Central obesity is a major risk factor for MtS and diabetes (45), also increases the risk of dyslipidemia and coronary artery disease (46).

Lack of access to complete information in the files and the defects in the files were among the most important limitations of this study, which were controlled as much as possible by removing incomplete files and replacement.

Conclusion

The high prevalence of MtS in patients with DM in Rafsanjan adult cohort study indicates the importance of this issue. Therefore, high risk patients can be identified using MtS screening in primary health centers, and they can benefit from timely multifactorial interventions. Reducing smoking and alcohol consumption, and controlling hypertension, hyperlipidemia, and overweight are some of the suggested solutions in this regard.

Abbreviations

CVD, Cardiovascular disease; MtS, metabolic syndrome; DM, diabetes mellitus; RCS, Rafsanjan Cohort Study; PERSIAN, Prospective Epidemiological Research Studies in IrAN; IDF, International Diabetes Federation; NCEP-ATPIII, the National Cholesterol Education Program-Adult Treatment Panel; WHO, World Health Organization; LDL, low-density lipoprotein; HDL, High Density Lipoprotein; BUN, blood urea nitrogen; ALP, alkaline phosphatase; BMI, body mass index.

Declarations

Ethics approval and consent to participate

Study was carried out in accordance with ethical guidelines of prospective epidemiological studies of the population in Iran (PERSIAN cohort) and ethical Committee for Rafsanjan University of Medical Sciences, Rafsanjan, Iran (IR.RUMS.REC.1399.050). All patients provided written informed consent. Our present medical research was conducted according to the principles expressed in the 1975 Declaration of Helsinki.

Consent for publication

Not applicable

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due to PERSIAN cohort policy on availability of health care registers, but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

ZK and GhB initiated the study and were responsible for elaborating the concept of it, and critically revised the manuscript. ZK and MA contributed to the extraction, analysis and interpretation of the data. ZK, GhB, HAand AEN contributed to the quality assessment of data, data analysis and interpretation, and drafted the manuscript. All authors read and approved the final manuscript.

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Figures

Figure 1

Prevalence (95% confidence interval) of risk factors in the two groups with and without MtS