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Several Risk Factors Associated with Cardiovascular Disease Event: Results from The Population-based MASHAD Cohort Study

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ABSTRACT

Introduction: Cardiovascular disease (CVD) is the leading cause of mortality and one of the main challenges for health systems worldwide. In this study, we aimed to evaluate the association of socio-demographic, lifestyle, psychological and anthropometric factors and underlying diseases such as hypertension (HTN), diabetes mellitus (DM) and metabolic syndrome (MS) with CVD risk among a subpopulation of Iranian adults.

Methods: In this prospective study, a total of 235 CVD patients along with 8405 healthy and non-symptomatic individuals who participated in MASHAD cohort study were enrolled. CVD diagnosis was performed by taking electrocardiogram (ECG) and medical history and performing physical examination for each participant. Health and lifestyle questionnaires, the Beck's anxiety inventory (BAI), Beck's depression inventory (BDI) and the James and Schofield human energy requirements equations were completed for all participants. Anthropometric measurements were also recorded for all subjects. All statistical analyses including chi-square and student independent T-test were performed using SPSS 16.0 software (SPSS Inc., Chicago, IL, USA) at a significant level of 0.05.

Results: We found that there were significant associations between CVD risk and age, body mass index (BMI), waist circumference (WC), waist-to-height ratio (WHtR), diabetes mellitus (DM) and family history (FH) of CVD in both genders; though, there was a significant negative correlation between physical activity level (PAL) and risk of CVD among men and women. Also hypertension (HTN), metabolic syndrome (MS), depression and anxiety were positively and higher education level was negatively associated with CVD events only in females. While, waist-to-hip ratio (WHR) was an independent predictor of CVD among males (P-value< 0.05).

Conclusion: There are several modifiable and non-modifiable risk factors that are independently considered as CVD predictors among the MASHAD study population. It is recommended to prioritize the lifestyle modification, development of local risk calculators and gender-related stratified strategies in order to prevent and manage CVD among the Iranian population.

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Introduction

Cardiovascular disease (CVD) is the leading cause of mortality and morbidity worldwide (1, 2). CVD accounts for 17.3 million deaths per year in 2015 (3) which is more deaths than caused by all nutritional, communicable, neonatal and maternal disorders combined (4, 5). It is estimated that the mortality rate from CVD grows to more than 23.6 million by 2030 with a total direct medical cost of $749 billion in 2035 (3, 6). Although the incidence rate of CVD has been shown to have a declining pattern in developed countries, it is still a growing concern among developing countries such as Iran (7, 8). CVD is responsible for about 50% of total deaths in Iranian population annually (9); including ischemic heart disease (26% in both genders), stroke (10% in men, 13% in women), hypertensive heart disease (5% in both genders) and other CVDs (5% in men and 6% in women) (10). CVD prevention is the most important step to eliminate and minimize the disease impact and its related disabilities (11, 12). Risk assessment and identification of high-risk populations and individuals, as a screening program for high-risk individuals and with CVD treating them, allow early preventive strategies and should be considered by health politicians (11, 13). Nevertheless, risk estimation methods that are clinically utilized in a particular country or ethnicity may not be useful for the other populations (11,14).

CVD is known to have many bio-psycho-social and genetic factors with complex interactions. However Age, diabetes mellitus (DM), total cholesterol (TC), low and high-density lipoprotein cholesterol (LDL-C and HDL-C), high blood pressure (BP), metabolic syndrome (MS) and smoking are well-known risk factors for CVD (15-21). There are different patterns of these risk factors and their interactions among different populations (22). The incidence rate of stroke and its related risk factors are higher among the Iranian population compared to the western countries (23). One study in Sweden showed that the immigrant Iranian women had higher body mass index (BMI), abdominal obesity, risky lipid profile and lower physical activity level (PAL) and therefore higher incidence of CVD compared to the Swedish women (24). These variations can be explained by the role of genetic and ethnicity, socio-demographic status, lifestyle and psychological differences, which have been emphasized in previous studies (25-31). This raises the priority of local population-based studies on CVD risk factors in order to develop regional risk assessment methods and population-based policies.

Low and middle income countries (LMICs) such as Iran are mostly affected by CVD (almost 80% of CVD burden) (32), but the majority of high-quality studies on CVD risk factors have been conducted in high income countries (HICs); Moreover, there are some inconsistencies among previous studies and they had some limitations such as small sample sizes and short-term follow-ups (33, 34). While findings from HICs may not be generalizable to LMICs, and previous studies mostly evaluated the association of just one or two parameters with CVD, it is necessary to carry out large and comprehensive longitudinal studies in order to have a better overview of which risk factors is CVD associated with in LMICs to establish efficient health policies in these countries.

This study aimed to investigate the association of socio-demographic, lifestyle, psychological and anthropometric factors and underlying diseases such as hypertension (HTN), DM and MS with CVD risk in a large population of Iranian adults after six years of follow-up.

Materials and Methods

Study Population

The Mashhad stroke and heart atherosclerotic disorder (MASHAD) study (2010-2020) was a large longitudinal prospective cohort study with the aim of determining the prevalence of CVD and its biological, environmental, social, and behavior-related risk factors in Mashhad, north-eastern Iran. Using a stratified cluster random sampling method, 9704 healthy individuals who were free of CVD and the other chronic diseases with the age between 35 to 65 years were recruited from three regions in Mashhad. Informed consent was obtained from all participants. Comprehensive information on design and baseline characteristics of the MASHAD study population was published in 2015 (35). The subjects were followed up in 2011, 2014 and 2016. In the third follow-up, the study participants were followed up from April 2015 to May 2016 and 235 (2.42%) patients were diagnosed with CVD. The individuals with incomplete data (n=88) and those who did not take part in different stages of follow-up (n=1152) were excluded from the present analysis. Eventually, a total of 8640 participants were enrolled in the current study including 235 patients who developed CVD (120 patients with UA, 75 patients with SA, and 40 patients with MI), and 8405 individuals did not have any CVD events. The study was approved by the Ethics Committee of Mashhad University of Medical Sciences.

Blood Sampling

According to a standard protocol, all the blood samples were taken from the antecubital vein and mid-stream urine was collected from all the participants. Further details on laboratory measurement are explained in the baseline report of the MASHAD cohort study; biochemical factors were analyzed by auto-analyzer BT-3000 (36).

Data Collection

All necessary information including the patient socio-demographic characteristics and lifestyle factors (PAL and tobacco use) were collected according to a comprehensive questionnaire (37). The presence of anxiety and depression was evaluated by using Beck's anxiety inventory (BAI) and Beck's depression inventory (BDI) (38). The PAL and anthropometric assessments (includes weight, height, body mass index (BMI), waist-to-hip ratio (WHR), waist to height ratio (WhtR), waist circumference (WC), hip circumference (HC) and mid-upper arm circumference (MAC)) were explained in detail previously (35). BP measurements were also done three times with a 30 minutes interval by two certified health care professionals and a certified nurse using a sphygmomanometer. The averaged of the two closest measurements was reported as the final blood pressure. SBP and DBP were determined from the left arm (after 15 minutes of resting) (39). Family history (FH) of CVDs was diagnosed by premature CVD events among first or second relatives.

CVD Diagnosis

CVD diagnosis in the MASHAD cohort study has been explained in detail previously (35, 37). Participants with suspected CVD were examined by echocardiography, stress echocardiography, radioisotope, angiography, Computed Tomography angiography and Exercise Tolerance Test. The CVD diagnosis was done by taking electrocardiogram (ECG) and medical history and performing physical examination for each participant. The presence of CVD was corroborated by a history of MI or angina pectoris or presence of a definite Q wave in ECG in the third follow-up (40, 41). The Framingham cardiovascular examination questionnaire was also completed for the entire population (42).

Disease Criteria

Disease criteria for DM, HTN, dyslipidemia and MS were explained previously in the MASHAD study reports (35). MS was defined based on IDF recommendation as having at least three or more components of its criteria (43): Increased waist circumference; Triglycerides ≥ 150 mg/dl or treatment for elevated TG; HDL < 40 mg/dl in men or < 50 mg/dl in women or low HDL treatment; Systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 mmHg or anti-hypertensive treatment; and Fasting plasma glucose ≥ 100 mg/dl or previously diagnosed type 2 DM.

Smoking habits were classified as current smoker (daily smoking of at least one cigarette), ex-smoker (formerly a daily smoker, but does not smoke currently) and non-cigarette smoker .

Statistical Analysis

Descriptive statistics including mean ± standard deviation (SD) and frequency (percentage) were reported for continuous and categorical variables, respectively. Moreover, the chi-square and Student Independent T-test were used to compare the frequency distribution between two qualitative variables and the mean of quantitative variables between two groups, respectively. All statistical analyses were performed using SPSS 16.0 software (SPSS Inc., Chicago, IL, USA) at a significant level of 0.05.

Results

The basic characteristics of the participants are shown in Table.1. The participants with developed CVD were significantly older, with higher frequency of smoking and lower PAL compared to those with no CVD event (P= 0.001 for PAL and <0.001 for others). According to the anthropometric measurements, parameters such as weight, BMI, WC, WHR and WHtR were significantly higher among patients with CVD compared to patients without CVD (P was 0.01 for weight, 0.001 for BMI and <0.001 for others). As expected, the prevalence of chronic disorders such as DM, HTN, dyslipidemia, MS, depression and anxiety scores and also prevalence of FH of CVD were significantly higher among CVD patients (P<0.01).

Association of various risk factors with CVD event among men and women of the study

Table 2 summarizes the association of different risk factors evaluated in this study with CVD

Table 1. Comparing baseline characteristics of study participants after follow up.

	Variables	CVD Event		P-value
		No (n=8405)	Yes (n=235)	
Socio-demographics	Age (year)	47.88 ± 8.11	54.26 ± 6.96	<0.001
	Marital status% (N) Married Single/divorced/widow	 93.80% (8774) 6.20% (521)	 92.30% (217) 7.70 %(18)	0.361
Lifestyle factors	Smoking status%(N) Non smoker Ex-smoker Current smoker	 69.60% (5846) 9.80 (820) 20.70 (1739)	 61.30 (144) 17.40 (41) 21.30 (50)	<0.001
	PAL	1.59 ± 0.28	1.53 ± 0.28	0.001
Anthropometric measurements	Height (m)	1.60 ± 0.09	1.60 ± 0.09	0.407
	Weight (kg)	71.88 ± 12.84	74.07 ± 12.50	0.010
	BMI (kg/m2)	27.84 ± 4.70	28.87 ± 4.56	0.001
	WC (cm)	95.11 ± 12.01	98.97 ± 10.68	<0.001
	HC (cm)	103.66 ± 9.26	104.20 ± 9.50	0.378
	WHR	0.92 ± 0.08	0.95 ± 0.07	<0.001
	WhtR	0.59 ± 8.23	0.62 ± 7.75	<0.001
	MAC (cm)	30.58 ± 3.94	30.59 ± 3.61	0.960
	Demispan (cm)	76.94 ± 5.59	76.82 ± 6.32	0.758
Disease characteristics	Family history of CVD	34.90 (2912)	44.60 (103)	0.002
	DM, %(N)	8.30 (698)	27.90 (65)	<0.001
	HTN, %(N)	22.60 (1900)	44.40 (104)	<0.001
	Dyslipidemia, %(N)	85.20 (7164)	91.40 (212)	0.009
	MS, %(N)	14.90 (1251)	39.10 (91)	<0.001
Psychological factors	Depression score	12.28 ± 9.53	14.06 ± 9.41	0.005
	Anxiety score	10.39 ± 9.72	12.78 ± 10.98	<0.001

Abbreviations: PAL: physical activity level; **BMI:** body mass index; **WC:** waist circumference; **HC:** hip circumference; **WHR:** waist-to-hip ratio; **WHtR:** waist-to-height ratio; **MAC:** mid-upper arm circumference; **CVD:** cardiovascular disease; **DM:** diabetes mellitus; **HTN:** hypertension; **MS:** metabolic syndrome.
Data presented as mean±SD or median (IQR). Independent sample t-test was used where appropriate.
The data of WC (n=7), WHR (n=7), MAC (n=4), demispan (n=19), BFP (n=486), SBP (n=1), DBP (n=1), FBG (n=4), TC (n=2), TG (n=2), LDL-C (n=3), HDL-C (n=3), uric asid (n=3), WBC (n=113), RBC (n=112), HGB (n=112), HCT (n=112), MCV (n=112) MCH (n=171), MCHC (n=112), PLT (n=179), FH of CVD (n=71), DM (n=4), HTN (n=1), dyslipidemia (n=4), and MS (n=3) were missed for study participants.

Table 2. Adjusted HRs of developing cardiovascular disease according to different risk factors.

Variable	Mean ± SD or % (N)	Male (n= 3560)			Mean ± SD or %	Female (n=5080)		
		HR	95% CI	P-value		HR	95% CI	P-value
Socio-demographics								
Age (year)	48.88 ± 8.36	1.08	1.05 – 1.11	**<0.001**	47.47 ± 7.94	1.11	1.08 – 1.14	**<0.001**
Marital status								
Married %(N)	98.7 (3515)	Ref.		0.901	90.3 (4586)	Ref.	0.73 – 2.15	
Not Married % (N)	1.3 (45)	0.88	0.12 – 6.33		9.7 (494)	1.26		0.403
Lifestyle factors								
Smoking status								
Non smoker	58.6 (2086)	Ref.			76.9 (3904)	Ref.	0.80 – 2.50	
Ex-smoker	15.3 (544)	1.59	0.99 – 2.55	0.055	6.2 (317)	1.42	0.67 – 1.73	0.230
Current smoker	26.1 (930)	1.35	0.85 – 2.15	0.208	16.9 (859)	1.07	0.11 – 0.70	0.772
PAL	1.43 ± 0.29	0.40	0.18 – 0.85	**0.018**	1.69 ± 0.22	0.28		**0.006**
Anthropometric measurements								
Height (m)	1.68 ± 0.06	0.18	0.01 – 3.06	0.237	1.55 ± 0.06	1.75	0.08 – 37.52	0.722
Weight (kg)	75.16 ± 12.86	1.01	1 – 1.03	0.102	69.67 ± 12.32	1.01	1 – 1.03	0.056
BMI (kg/m^2)	26.41 ± 4.11	1.06	1.01 – 1.11	**0.015**	28.87 ± 4.81	1.04	1 – 1.07	**0.046**
WC (cm)	93.81 ± 10.93	1.02	1 – 1.04	**0.028**	96.19 ± 12.59	1.02	1 – 1.03	**0.032**
HC (cm)	101.14 ± 7.93	1.01	0.99 – 1.04	0.219	105.44 ± 9.71	1.01	0.99 – 1.03	0.205
WHR	0.92 ± 0.07	8.17	1.22 – 54.96	**0.031**	0.91 ± 0.08	7.13	0.81 – 62.50	0.076
WhtR	55.69 ± 6.60	1.04	1.01 – 1.07	**0.010**	61.99 ± 8.25	1.02	1 – 1.05	**0.033**
MAC (cm)	30.31 ± 3.92	1.01	0.96 – 1.05	0.816	30.77 ± 3.92	1.02	0.97 – 1.06	0.478
Demispan (cm)	81.21 ± 4.36	0.97	0.93 – 1.01	0.177	73.93 ± 4.29	1.01	0.98 – 1.05	0.475
Disease characteristics								
Family history of CVD	32.2 (1132)	1.59	1.08 – 2.34	**0.018**	37.3 (1883)	1.64	1.15 – 2.34	**0.006**
DM, %(N)	8.6 (307)	2.52	1.60 – 3.96	**<0.001**	9.0 (456)	3.46	2.35 – 5.08	**<0.001**
HTN, %(N)	24.4 (868)	1.24	0.83 – 1.86	0.300	22.4 (1136)	2.14	1.48 – 3.10	**<0.001**
Dyslipidemia, %(N)	80.4 (2861)	1.21	0.71 – 2.07	0.480	85.4 (7376)	2.56	0.94 – 6.96	0.066
MS, %(N)	13.6 (483)	1.58	0.89 – 2.81	0.115	16.9 (859)	2.05	1.24 – 3.41	**0.005**
Psychological factors								
Depression score	10.44 ± 8.68	1.01	0.99 – 1.03	0.419	13.65 ± 9.87	1.02	1 – 1.03	**0.029**
Anxiety score	8.25 ± 8.46	1.01	0.99 – 1.03	0.349	12.00 ± 10.29	1.03	1.01 – 1.04	**<0.001**

Abbreviations: **PAL:** Score of physical activity level; **BMI:** body mass index; **WC:** waist circumference; **HC:** hip circumference; **WHR:** waist-to-hip ratio; **WHtR:** waist-to-height ratio; **MAC:** mid-upper arm circumference; **CVD:** cardiovascular disease; **DM:** diabetes mellitus; **HTN:** hypertension; **MS:** metabolic syndrome; **Ex-smoker:** former smoker; **HR:** hazard ratio, **CI:** confidence interval.

† HR was adjusted for age and significant parameters in univariate (including DM and FH of CVD).

Socio-demographics and lifestyle characteristics

After adjustment of confounding factors (age, diabetes mellitus and family history of cardiovascular disease), age was positively associated with CVD risk in both genders (HR and 95% CI: 1.08, 1.05 – 1.11 in males; 1.11, 0.08 – 1.14 in females, P<0.001). Though, higher PAL was negatively associated with CVD risk in two sexes (HR and 95% CI: 0.40, 0.18 – 0.85 in males; 0.28, 0.11 – 0.70 in females, P<0.05).

Anthropometric Measurements

Among anthropometric criteria, BMI (HR and 95% CI: 1.06, 1.01 – 1.11 in males; 1.04, 1 – 1.07 in females, P<0.05), WC (HR and 95% CI: 1.02, 1 – 1.04 in males; 1.02, 1 – 1.03 in females, P<0.05) and WHtR (HR and 95% CI: 1.04, 1.01 – 1.07 in males; 1.02, 0.97 – 1.06 in females, P<0.05) were directly associated with CVD risk among two genders (P<0.05); although, WHR and CVD risk had positive association only in males (HR: 8.17, 95% CI: 1.22 – 54.96, P<0.05).

Disease Characteristics

The presence of the FH of CVD (HR and 95% CI: 1.59, 1.08 – 2.34 in males; 1.64, 1.15 – 2.34 in females, P<0.05) and DM (HR and 95% CI: 2.52, 1.60 – 3.96 in males; 3.46, 2.5 – 5.08 in females, P<0.001) were positively associated with CVD risk among both males and females. Even though, HTN (HR and 95% CI: 2.14, 1.48 – 3.10, P<0.001), and MS (HR and 95% CI: 2.05, 1.24 – 3.41, P= 0.005) had positive association with CVD risk only among women.

Psychological Factors

Both of the depression (HR and 95% CI: 1.02, 1 – 1.03, P<0.05) and anxiety (HR and 95% CI: 1.03, 1.01 – 1.04, P<0.001) scores were directly associated with CVD risk among women.

Discussion

In the current study, the association of several risk factors including socio-demographic, lifestyle, psychological, anthropometric factors and underlying diseases with CVD risk was evaluated in a large cohort-design study. We observed significant direct association of age, BMI, WC, WHtR, FH of CVD and DM and also negative association of PAL with the risk of CVD events among both genders. WHR increased the risk of CVD in males. In addition, higher CVD incidence was in a relationship with some other underlying disorders including HTN, MS, depression and anxiety in females. There are various reports about the different risk factors and their effects on CVD incidence (14). Cardiovascular risk factors can be categorized as unmodifiable and modifiable risk factors (44). In the present study, we defined the association of some risk factors with CVD incidence in a 6 years follow-up cohort study. All of these impressive risk factors are categorized as modifiable risk factors, except for age and positive FH, and should be concerned in the policy of the governments (44). As well, preventive medicine should be at attention for people with positive FH and ageing process (44).

Anthropometric Measurements

This study has shown that WHR is the best anthropometric index as far better as BMI, WC and WHtR to use in clinic to recognizing subjects with risk factors for CVD; also, it was the most effective risk factor for CVD by the greatest HR; since, increasing one unit of WHR increased CVD risk as 8.17 times. Filippatos et al. have shown that anthropometric indices (BMI, WHR, WC, WHR and WHtR) were autonomously associated with the 10-year CVD risk (45). Individuals with different ethnicities have different body characteristics (46) and it's so crucial to clarify easy and useful anthropometric measurements for screening and pre-screening of subjects particularly those with higher metabolic risk in different populations. As a result, Ethnicity should be integrated into CVD assessment and this area (Ethnic Specific) in the case of CVD prevention and treatment strategies need further studies and should be more developed (47). Few studies have investigated the relationships between anthropometric measurements and common cardiovascular risk factors in Iran (48-50) and we wanted to determine the best anthropometric measurements that predict

CVD in a cohort study. Although BMI analysis is simple and convenient to monitor, many clinical and metabolic studies have revealed that, when obesity is defined just based on BMI alone, it considers the heterogeneous condition, which patients with a close BMI may have distinct metabolic and CVD features (51, 52). Esmaillzadeh et al. in a cross-sectional survey has demonstrated that WHR is a better predictor for CVD risk factors rather than BMI, WHtR and WC in adult men of Tehran (a city of Iran) (50). In a cross-sectional study, they have represented that WC is the best screening measure for CVD risk factors, in the adult population of Tehrani women (49). Yan et al. have supported the WHR is useful for evaluating atherosclerotic burden in obesity screening and clinical researches. They showed that the elevated CVD risk associated with abdominal obesity may be mediated in part by the raised anatomic extent of atherosclerotic vascular disorder (53). In a Multi-Ethnic Study in 52 countries, the data have demonstrated that by redefinition of overweight and obesity criteria based on WHR instead of BMI, the number of people in the worldwide who categorized at risk of heart attack will be increased three folds (54) and it was a significant predictor of MI among both genders without an enlarged WC in adjusted analyses (55). Sehested et al. illustrated that in various forms of obesity and overweight measures, WHR was the only meaningful predictor of the incident of CVD, and the relationship between WHR and risk of CVD was refereed by noted CVD risk factors (56). Simpson et al. in a cohort study have revealed that WHR was positively related to all main causes of mortality including anthropometric factors for both genders (57). However, WC, not WHR in some communities (58, 59), and WHtR in others (60, 61) have been suggested as a better screening tool for CVD risk factors. Our findings showed that WHR is the best anthropometric index for identifying men with risk factors for CVD in Iranian males, in consent to Esmaillzadeh et al. study in Tehran (50).

Disease characteristics

DM

We also found that DM was associated with nearly 2 and 3 folds higher CVD risk in males and females of the study, respectively. DM is associated with micro- and macro-angiopathies, systemic inflammation and oxidative stress which predispose the patients for developing CVD events and exacerbating the atherogenesis process (62-65). Because of the elevation of inflammatory biomarkers like C-reactive protein and fibrinogen, which was reported in new-onset DM patients (66). As well, these biomarkers are enhanced in CVD patients (66, 67). Ho et al. showed in a cohort study in women with average of 8.3 years follow-up that DM patients had the similar risk for incidence of stroke (a type of CVD) compared to patients who had a history of previous stroke (68). Also, Wannamethee et al. showed in a cohort design study of men (60 – 79 years old) suffering from DM increased the incidence of coronary heart disease (69). These findings agree with our results about two genders.

MS and HTN

MS increases the risk of CVD (particularly coronary artery disease) or stroke by three folds (70). In a 2018 systematic review, the prevalence of MS was reported up to 42% in the Iranian population and 15.8% of CVD burden in the Middle-East was attributed to this risk factor (71). An analysis of people living in Tehran showed that MS increased the risk of CVD development only in women (72). Our results illustrated the same findings and showed that MS was considered as a major CVD risk factor only in women. Also, in our population HTN associated with higher CVD events only in women; though, WC and DM were risk factors in both genders and dyslipidemia did not enhance the risk of CVD in both sexes. Therefore, we can imply that probably HTN played a major role in the positive association of MS and CVD risk among females of the study. However, in other countries HTN was a CVD risk factor in males too; for instance, Sesso et al. demonstrated in a median follow-up of 10.8 years of United States males that the average of SBP, DBP and mean arterial pressure are strong predictors for CVD incidence in men, with higher relative risk (RR) in men <60 comparing to ≥60 years old (73). These differences might be related to the sociocultural, ethnic and genetic determinants of different regions (74-77). Also, in a research on the Iranian population of Tehran, it was found that female gender is a protective factor in developing HTN (78); this contrast finding in two regions of Iran (Mashhad and Tehran) may be related to lifestyle and diet habits (76).

FH of CVD

We mentioned to genetic predisposition as an impressive factor for occurrence of CVD (77). Genetic predisposition affects the incidence of CVD by multigenic pathways (79, 80); hence, pharmacogenetics have tried to treat CVD by affecting different genes which induce CVD (80). In this study, we did not evaluate the different genes that impress CVD incidence; though, we assessed the influence of presence of positive FH of CVD as a possible predictor of CVD. Glowinska et al. demonstrated that children and adolescents with positive FH of CVD had higher BMI and lipoprotein-A level than persons with negative FH (81). Also, Wright et al. showed the effect of positive FH of CVD on the body response to stressful situations (82). They showed that persons with positive FH had higher SBP and DBP and poorer BP recovery after stress (82). In addition, Scottish people with positive FH had higher ASSIGN score (a scoring system for CVD risk) (83). Thereby, the influence of positive FH on the CVD occurrence is explained by its effect on the presence of other CVD risk factors like high BMI, lipoprotein-A level and BP.

Lifestyle Factors

PAL

We found the major protective effect of PAL against CVD incidence. This finding was expected according to previous studies (84, 85). In a 5-years cohort study in Denmark, it was shown that as the PAL increased, weight, WC and DBP were decreased in both sexes; while, HDL-C was increased in men (84). Recently, in a meta-analysis it was demonstrated that sedentary behaviors like sitting time (ST) and television time (TT) per day had a dose-dependent association with CVD mortality in inactive persons (9 – 32% higher risk for ST and 3 – 59% higher risk for TT) (85). Therefore, enhancing the PAL, as an item of lifestyle factors, can strongly reduce the CVD risk and mortality (85-87).

Psychological factors

In our study depression and anxiety scores were positively related to CVD risk, but they only increased the CVD risk as 2 and 3 percents, respectively. Actually, relationship between depression and anxiety with CVDs is bidirectional; since, people who suffer from CVDs experience lower quality of life and sequentially they become isolated and thereafter depressed (88). At the other side, people who suffer from behavioral factors like depression, have tendency towards smoking and inactivity; which are two important CVD risk factors (88). Additionally, Stetope et al. showed that loneliness and social isolation increased as 50% in CVD risk (89). In our study, both of the depression and anxiety could enhance a little in CVD risk only in women. It might to be related to higher prevalence of these two behavioral issues in women in Iran; as Khalighi et al. showed in a meta-analysis study in Iranians, that depression prevalence was higher in females to males (63.9% vs. 46.3%) (90).

Strengths and limitations

The strength of the present study was documenting and following up the traditional risk factors for CVD in detail in a large population for the first time in Mashhad. The large sample size and type of this study make our results useful as baseline data for future research, especially focusing on WHR as a screening method for abdominal obesity. Since, World Health Organization (WHO) advocates the use of some anthropometric measurements as a screening resource for individuals under cardiometabolic risk (91). Nevertheless, there are several potential limitations that need to be addressed; although we considered all the possible risk factors in our analysis, residual unknown confounders may be still present. It is possible that genetic and environmental factors including lifestyle characteristics and certain dietary habits influence the relationships between the cardiovascular event and its risk factors.

According to the findings of this study, there are several modifiable and non-modifiable risk factors of CVD among Iranian urban population including socio-demographic (high age, lower education level, family history of CVD), lifestyle (low physical activity), psychological (depression and anxiety) and anthropometric factors (high BMI, waist circumference, waist-to-height ratio and waist-to-hip ratio) and also comorbidities such as diabetes, hypertension and metabolic syndrome; So it is of great importance to establish preventive health policies such as disease screening and periodic clinical evaluations for adults to reduce the burden of CVD. Also, because of bio-psycho-social nature of CVD development, an inter-disciplinary approach is needed to overcome its underlying causes.

Conflict of interests

The authors have no conflicts of interest to declare.

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