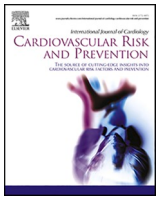
International Journal of Cardiology Cardiovascular Risk and Prevention 23 (2024) 200332

Contents lists available at ScienceDirect

International Journal of Cardiology Cardiovascular Risk and Prevention

journal homepage: www.journals.elsevier.com/international-journal-of-cardiology-cardiovascular-risk-and-prevention



Association of classic cardiovascular risk factors with myocardial infarction and ischemic stroke: A cross sectional analysis of the Shiraz Heart Study

Haleh Ghaem [a], Mohammad Javad Zibaeenezhad [b], Mehrab Sayadi [b], Sheida Khosravaniardakani [c], Nader Parsa [b], Iman Razeghian-Jahromi [b,*]

[a] Non-Communicable Diseases Research Center, Epidemiology Department, School of Health, Shiraz University of Medical Sciences, Shiraz, Iran
[b] Cardiovascular Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
[c] Student research committee, Shiraz University of Medical Sciences, Shiraz, Iran

ARTICLE INFO

Handling editor: D Levy

Keywords:
Cardiovascular risk factors
Myocardial infarction
Stroke

ABSTRACT

Background: Myocardial infarction (MI) and ischemic stroke are the leading deadly clinical outcomes globally. This study aimed to investigate the association of classic cardiovascular risk factors with MI and ischemic stroke in a general population.

Methods: This cross-sectional study used the baseline data of the Shiraz Heart Study, a prospective cohort that investigate risk factors of coronary heart disease in a general population of Iran. Middle-aged citizens of 40–70 years old were included. Univariable and multivariable logistic regression analysis was performed to explore the association between sociodemographic, clinical, and metabolic factors and prevalent MI and stroke.

Results: Out of 7225 adults, 1.9 % (n = 135) had prior MI or stroke. Multiple logistic regression revealed that age≥60 years (aOR: 2.22, 95 % CI 1.45–3.20; $P < 0.001$), male sex (aOR: 3.82, 95 % CI 2.56–5.71; $P < 0.001$), history of hypertension (aOR: 1.71, 95 % CI 1.18–2.50; $P < 0.005$), history of hyperlipidemia (aOR: 2.42, 95 % CI 1.68–3.48; $P < 0.001$), having four 1st degree family members with sudden cardiac death (aOR: 26.28, 95 % CI 0.59–432.09; $P < 0.022$), and having a 1st degree family member with history of cardiovascular disease (aOR: 1.69, 95 % CI 1.13–2.54; $P < 0.001$) were associated with prior MI and stroke. Unlike high-density lipoprotein ($P = 0.723$) and triglyceride ($P = 0.643$), there were significant differences in the levels of fasting blood sugar ($P < 0.001$), total cholesterol ($P < 0.001$), and low-density lipoprotein ($P < 0.001$) between those with and without history of MI/stroke.

Conclusions: Being aged ≥60 years, history of hypertension and hyperlipidemia along with familial history of CVD and sudden cardiac death were in association with MI and stroke.

1. Introduction

Cardiovascular disease (CVD) is the leading cause of mortality and disability globally [1]. In 2010 and 2015, the Global Burden of Disease study showed that CVD accounted for 46 % of all deaths and an approximate of 20–23 % of disease burden in Iran [2–4]. Previous studies reported considerable prevalence of cardiovascular risk factors including hypertension (42.2 %), diabetes mellitus (18.7 %), high-LDL-C (58.9 %), low HDL-C (52.3 %), hypertriglyceridemia (52.7 %), hypercholesterolemia (65.4 %), obesity (26.4 %) and current smoking (13 %) among adults (>40 years age) in Iran [5,6]. Fortunately, controlling these modifiable risk factors may reduce the risk of CVD up to 80 % [7].

Determining risk factors pertinent to cardiovascular events such as myocardial infarction (MI) and stroke, which totally constitute the most part of disease burden, has long been the subject of many previous investigations [8]. The occurrence of about 80 % of the cardiovascular events in low- and middle-income countries [9–11] shows that availability of health resources and infrastructure facilities necessitates unique therapeutic and preventive approaches in each region [12]. This study aimed to clarify the extent of classic risk factors association to the risk of MI and stroke in an urban general population.

* Corresponding author.
E-mail address: razejahromi@yahoo.com (I. Razeghian-Jahromi).

https://doi.org/10.1016/j.ijcrp.2024.200332
Received 5 June 2024; Received in revised form 31 August 2024; Accepted 10 September 2024
Available online 11 September 2024

2. Methods

2.1. Study design and setting

This is a cross-sectional analysis of the baseline data of the Shiraz Heart Study (SHS). Data were collected between 2016 and 2019. Methodological details are presented elsewhere [13].

2.2. Study population

Participants were Iranian aged 40–70 years old and living in Shiraz city, the capital of Fars province of Iran. We excluded individuals with psychological disorders, or existence of acute disease that were under treatment, those who did not provide informed consent or did not adhere to periodic visits.

2.3. Data collection

Participants underwent an interview with a trained nurse for obtaining required data including sociodemographic parameters, smoking status, history of hypertension, history of diabetes, history of hyperlipidemia, and history of renal disease through different questionnaires. History of CVD and sudden cardiac death in 1st degree relatives were also collected. It should be noted that history of diseases was only considered in the case of presenting valid medical documents or being under treatment with relevant medications. Anthropometric indices (body mass index and waist circumference) were measured by a trained nurse according to clinical guideline [14]. A 12-lead computer-based digital electrocardiography was used for recording electrocardiogram. Blood pressure was measured by a digital sphygmomanometer three times with a 10-min interval between each measurement, and finally, the mean was considered. Moreover, blood sample was collected for measuring fasting plasma glucose (FBS), total cholesterol, HDL-C, LDL-C, and triglycerides. Myocardial infarction and stroke were only considered based on medical documents issued by a cardiologist/neurologist.

2.4. Definitions of variables

Sociodemographic parameters include name/sure name, date of birth, date of enrollment, number of childes, telephone number, address, sex, marital status, educational level, income, and occupation. Body mass index was calculated as weight (Kg) divided by the square of height (m^2). Waist circumference is the measurement of the abdomen at the level of the umbilicus and above the hipbones with the breath out and without compressing the skin. Abnormal waist circumference was considered $\geq$88 cm for females and $\geq$102 cm for males. Current use of any amount/kind was considered as smoking. Regarding history of hypertension, some questions were asked about measuring blood pressure during the last year, any advice from a physician/health expert about the possible existence of hypertension, and using any related medical interventions like antihypertensive drugs. Abnormal systolic and diastolic blood pressure were regarded as $\geq$140 mmHg and $\geq$90 mmHg, respectively. Also, abnormal FBS as $\geq$126 mg/dL, abnormal total cholesterol as $\geq$200 mg/dL, abnormal HDL-C as $<$50 mg/dL in male and $<$40 mg/dL in female, abnormal LDL-C $\geq$116 mg/dL, and abnormal TG as $\geq$200 mg/dL were considered. In the area of diabetes history, hyperlipidemia history, and history of renal disease, similar questions were sought. In the case of family history in the 1st degree relatives (father, mother, brothers, and sisters), participants were asked for history of CVD in terms of history of coronary-, carotid-, or vertebral atherosclerosis, abdominal aorta aneurysm, atherosclerosis in peripheral arteries, heart failure, vulvular heart disease, and heart arrhythmias. Sudden cardiac death was defined as a non-violent death related to cardiac reasons that occurs in less than 24 h following the onset of symptoms (based on a certificate issued by health authority).

2.5. Statistical analysis

Data was analyzed using IBM SPSS Statistics 16.0 for Windows (Chicago, Illinois, USA). Continuous variables were presented as mean with standard deviation, and categorical variables as frequency with percentages. Independent sample *t*-test and chi square were used as appropriate for seeking any relation between variables. Fisher's exact test was used whenever conditions for using Chi-square were not met. The role of independent variables on MI and stroke were determined by univariable logistic regression. To control the effect of confounders, multivariable logistic regression was used. Each of the variables was adjusted to the remaining variables within the model. Only variables with three conditions were included in multivariable logistic regression,: 1- *P* value of $\leq$0.2 in univariable logistic regression, 2- without collinearity with other variables [15], and 3- sufficient cases of MI/stroke for that variable in order to generate a stable model. Forward method was used in order to include and report only statistically significant variables. *P* value of less than 0.05 was considered as statistically significance.

3. Results

3.1. General characteristics of the study population

We included 7225 participants with the mean age of 52.14 $\pm$ 8.00 years and of whom 47.7 % were male (n = 3445). Most of them were married (90.7 %, n = 6588) were married, 72.7 % (n = 5251) had education (high school and more), and only about 5 % were illiterate. Regarding occupation, they were mostly (39.9 %, n = 2884) technician, manual worker, and office employee, and nearly four fifth of them (80.8 %, n = 5835) had low income (Table 1).

3.2. Prevalence of cardiovascular risk factors

19.8 % of the participants were current smokers. Body mass index and waist circumference were abnormal in 73.4 % and 57.0 %. Hypertension was diagnosed in 14.0 % and 25.8 % with regard to high systolic and diastolic blood pressure, respectively. About 12.1 % had hyperglycemia. Hyperlipidemia was found in 39.7 % for total cholesterol, 37.8 % for LDL-C, 21.5 % for TG, and 56.6 % showed low HDL-C. History of hyperlipidemia (28.5 %) and history of hypertension (22.5 %) were more prevalent compared with history of diabetes (15.7 %) and history of renal disease (5.2 %) (Table 2). Logically, most of the participants had no 1st degree family members with history of CVD and history of sudden cardiac death (Table 3).

3.3. Prevalence and factors associated with myocardial infarction and stroke

Prior MI/stroke was found in 1.9 % (n = 135) of participants, including 1.6 % (n = 118) who had prior MI and 0.4 % (n = 27) prior stroke. The prevalence of MI/stroke was significantly different among age categories ($P < 0.001$) with the lowest and the prevalence rates of prior MI/stroke observed in the age categories 40–44 (0.3 %) and 65–70 (7.1 %). Furthermore, males experienced significantly more MI/stroke than females (2.9 % versus 0.9 %, $P < 0.001$). Unlike marital status, the prevalence of MI/stroke was statistically different in subgroups of education ($P = 0.002$), occupation ($P < 0.001$), and income ($P = 0.002$) (Table 1).

Comparison of variables between subjects with and without MI/stroke (Table 2) reveled that younger adults experienced less MI/stoke ($P < 0.001$). The status of current smoking ($P = 0.786$), body mass index ($P = 0.253$), and abdominal circumference ($P = 0.071$) were not significantly different between two groups. However, both systolic and diastolic blood pressures were considerably impaired in those with MI/stroke ($P < 0.001$). Moreover, FBS, total cholesterol, and LDL-C were

Table 1
Demographic characteristics and prevalence of myocardial infarction/stroke in subgroups.

Variable	Number (percentage)	MI/stroke	*P* value
Age categories			<0.001
• 40-44	1548 (21.4 %)	4 (0.3 %)	
• 45-49	1495 (20.7 %)	10 (0.7 %)	
• 50-54	1411 (19.5 %)	20 (1.4 %)	
• 55-59	1247 (17.3 %)	42 (3.4 %)	
• 60-64	1066 (14.8 %)	27 (2.6 %)	
• 65-70	458 (6.3 %)	32 (7.1 %)	
Sex			<0.001
• Male	3445 (47.7 %)	100 (2.9 %)	
• Female	3780 (52.3 %)	35 (0.9 %)	
Marital status			0.115
• Married	6588 (52.3 %)	121 (1.8 %)	
• Single	217 (3.0 %)	2 (0.9 %)	
• Widower/widow	318 (4.4 %)	11 (3.5 %)	
• Divorced	102 (1.41 %)	1 (1.0 %)	
Education			0.002
• illiterate	398 (5.5 %)	13 (3.3 %)	
• High school/Associate's degree	5251 (72.7 %)	107(2 %)	
• Bachelor's/Master's/PhD degree	1576 (21.8 %)	15 (1 %)	
Occupation			<0.001
• Technician/Manual worker/Office employee	1396 (19.3 %)	19 (1.4 %)	
• Housekeeper	2884 (39.9 %)	34 (1.2 %)	
• Retired	1275 (17.6 %)	42 (3.3 %)	
• Self-employment	833 (11.5 %)	17 (2.0 %)	
• Other	837 (11.6 %)	23 (2.7 %)	
Income			0.002
• Low	5835 (80.8 %)	119 (2.0 %)	
• Middle	1237 (17.1 %)	10 (0.8 %)	
• High	148 (2.1 %)	6 (4.1 %)	

P values derived from comparison of myocardial infarction/stroke prevalence among subgroups for each variable.
MI: myocardial infarction. Possible differences between included participants (7225) and total number of individuals in certain categories are due to data loss or incompleteness.

Table 2
Prevalence of cardiovascular risk factors stratified by history of myocardial infarction/stroke.

Variable	Total (number, percentage) (N = 7225)	No history of MI/stroke (N = 7090)	History of MI/stroke (N = 135)	*P* value
Age categories				<0.001
• 40-59	5701 (78.9 %)	5625 (98.7 %)	76 (1.3 %)	
• 60-70	1524 (21.1 %)	1465 (96.1 %)	59 (3.9 %)	
Sex				<0.001
• Male	3445 (47.7 %)	3345 (97.1 %)	100 (2.9 %)	
• Female	3780 (52.3 %)	3745 (99.1 %)	35 (0.9 %)	
Current smoking				
• Yes	1432 (19.8 %)	1404 (98.0 %)	28 (2.0 %)	0.786
• No	5793 (80.2 %)	5686 (98.2 %)	107 (1.8 %)	
body mass index (Kg/m^2)				0.253
• <25	1895 (26.2 %)	1865 (98.4 %)	30 (1.6 %)	
• ≥25	5250 (73.4 %)	5145 (98.0 %)	105 (2.0 %)	
Waist circumference				0.071
• Normal	3106 (43.0 %)	3037 (97.8 %)	69 (2.2 %)	
• Abnormal	4039 (57.0 %)	3973 (98.4 %)	66 (1.6 %)	
Systolic blood pressure				<0.001
• Normal	6220 (86.0 %)	6117 (98.3 %)	103 (1.7 %)	
• Abnormal	952 (14.0 %)	920 (96.6 %)	32 (3.4 %)	
Diastolic blood pressure				0.023
• Normal	5364 (74.2 %)	5274 (98.3 %)	90 (1.7 %)	
• Abnormal	1808 (25.8 %)	1763 (97.5 %)	45 (2.5 %)	
FBS				<0.001
• Normal	6353 (87.9 %)	6245 (98.3 %)	108 (1.7 %)	
• Abnormal	824 (12.1 %)	698 (96.4 %)	26 (3.6 %)	
Total cholesterol				<0.001
• Normal	4357 (60.3 %)	4225 (97.7 %)	102 (2.3 %)	
• Abnormal	2723 (39.7 %)	2691 (98.8 %)	32 (1.2 %)	
HDL-C				0.723
• Normal	3065 (43.4 %)	3009 (98.2 %)	56 (1.8 %)	
• Abnormal	4015 (56.6 %)	3937 (98.1 %)	78 (1.9 %)	
LDL-C				<0.001
• Normal	4402 (62.2 %)	4299 (97.7 %)	103 (2.3 %)	
• Abnormal	2675 (37.8 %)	2644 (98.8 %)	31 (1.2 %)	
TG				0.643
• Normal	5555 (78.5 %)	5452 (98.1 %)	103 (1.9 %)	
• Abnormal	1522 (21.5 %)	1491 (21.5 %)	31 (2.0 %)	
History of hypertension				<0.001
• Yes	1646 (22.7 %)	1588 (96.5 %)	58 (3.5 %)	
• No	5579 (77.3 %)	5502 (98.6 %)	77 (1.4 %)	
History of diabetes				<0.001
• Yes	1143 (15.8 %)	1102 (96.4 %)	41 (3.6 %)	
• No	6018 (84.2 %)	5924 (98.4 %)	94 (1.6 %)	
History of hyperlipidemia				<0.001
• Yes	2081 (28.8 %)	2007 (96.4 %)	74 (3.6 %)	
• No	5091 (71.2 %)	5030 (98.8 %)	61 (1.2 %)	
History of renal disease				0.026
• Yes	382 (5.2 %)	369 (96.6 %)	13 (3.4 %)	
• No	3843 (94.8 %)	6721 (98.2 %)	122 (1.8 %)	

MI: myocardial infarction; Abnormal waist circumference: ≥88 cm for females; ≥102 cm for males, Abnormal systolic blood pressure: ≥140 mmHg. Abnormal diastolic blood pressure≥90 mmHg, Abnormal fasting blood sugar (FBS): ≥126 mg/dL, Abnormal total cholesterol: ≥200 mg/dL, Abnormal high-density lipoprotein cholesterol (HDL-C): <50 mg/dL in male; <40 mg/dL in female, Abnormal low-density lipoprotein cholesterol (LDL-C) ≥116 mg/dL, Abnormal triglyceride (TG): ≥200 mg/dL.

elevated in adults with history of MI/stroke. Those with MI/stroke was indeed characterized by history of hypertension ($P < 0.001$), history of diabetes ($P < 0.001$), history of hyperlipidemia ($P < 0.001$), and history of renal disease ($P = 0.026$). Trend test showed that history of MI/stroke was in a significant association with increasing number of family members with history of CVD (Trend test, $P < 0.001$) or sudden cardiac death (Trend test, $P < 0.001$) (Table 3).

In univariable logistic regression (Table 4), age of ≥60, male sex, history of hypertension, history of diabetes, history of hyperlipidemia, and history of renal disease reached statistical significance. Regarding history of CVD and sudden cardiac death in family members, nearly all situations showed statistically significant difference. Multivariable logistic regression revealed that history of MI/stroke was associated with age≥60 (aOR: 2.22, 95 % CI 1.45–3.20; P < 0.001), male sex (aOR: 3.82, 95 % CI 2.56–5.71; P < 0.001), history of hypertension (aOR: 1.71, 95 % CI 1.18–2.50; P < 0.005), history of hyperlipidemia (aOR: 2.42, 95 % CI 1.68–3.48; P < 0.001), and having four family members with sudden cardiac death (aOR: 26.28, 95 % CI 1.59–432.09; P < 0.022). Also, the prevalence of MI and stroke was in association with even one family member with history of CVD (aOR: 1.69, 95 % CI 1.13–2.54; P < 0.001). It should be noted that variables were entered in multivariable logistic regression if: 1- they have *P* values of <0.2 in univariable logistic

Table 3
Trend test of the prevalence of cardiovascular disease and sudden cardiac death in 1st degree family members stratified by history of myocardial infarction/stroke.

Variable				*P* Value
No. of 1st degree family members with history of CVD:	Total (number, percentage) (N = 7141)	No history of MI/stroke (N = 7006)	History of MI/stroke (N = 135)	<0.001
• 0	4332 (60.6 %)	4275 (98.7 %)	57 (1.3 %)	
• 1	2085 (29.1 %)	2040 (97.8 %)	45 (2.2 %)	
• 2	578 (8.09 %)	556 (96.2 %)	22 (3.8 %)	
• 3	114 (1.59 %)	107 (93.9 %)	7 (6.1 %)	
• 4	32 (0.44 %)	28 (87.5 %)	4 (12.5 %)	
No. of 1st degree family members with history of sudden cardiac death:	Total (number, percentage) (N = 7120)	No history of MI/stroke (N = 6985)	History of MI/stroke (N = 135)	<0.001
• 0	5796 (81.4 %)	5699 (98.3 %)	97 (1.7 %)	
• 1	1094 (15.3 %)	1063 (97.2 %)	31 (2.8 %)	
• 2	192 (2.6 %)	189 (98.4 %)	3 (1.6 %)	
• 3	35 (0.4 %)	32 (91.4 %)	3 (8.6 %)	
• 4	3 (0.04 %)	2 (66.7 %)	1 (33.3 %)	

CVD: cardiovascular disease; MI: myocardial infarction.

regression and, 2- they were not in collinearity with other variables, and 3- there were sufficient cases of MI/stoke in relevant subgroups in order to establish an stable model.

4. Discussion

One-third of global deaths was due to CVD in 2019, and nearly 33 % occurred in the ages of 30–70 years [1]. In Iran, it is projected that the burden of CVD will be in rise from 2005 to 2025 mainly because of population aging [16]. However, age-standardized CVD mortality in hotspot locations throughout the world shows that there are other important underlying risk factors responsible for this concerning challenge [1]. Of 7225 adults, most of them were in the age category of 40–59 years. The prevalence of current smoking (19.8 %), body mass index of>25 (73.4 %), high waist circumference (57.0 %), high systolic-(14.0 %), and diastolic blood pressure (25.8 %) were revealed. Also, 12.1 % of the adults had hyperglycemia, and 39.7 %, 56.6 %, 37.8 %, 21.5 % showed dyslipidemia in terms of high total cholesterol, low HDL-C, high LDL-C, and high triglyceride.

In one national study that sought determinants of CVD in an adult population, several risk factors were identified including age, diabetes, smoking, hypertension, triglycerides, waist circumference, total cholesterol, and HDL-C [17]. Other national studies introduced obesity, high LDL-C, and hypertriglyceridemia as three prevalent CVD risk factors [5,6]. There are considerable overlaps between risk factors discovered in our study and others, and seemingly, hypertension besides hyperlipidemia were the main culprits. GBD 2019 study reported that high systolic blood pressure, dietary risks, and high LDL-C, which are fundamentally contributed to atherosclerotic and hypertensive vascular diseases, are the global leading modifiable risk factors [1]. Worldwide prevalence of hypertension (high systolic blood pressure) was increased from 1990 to 2019. In fact, 9 out of 10 adults in the world is endangered. In 2019, hypertension-attributed DALYs were not similar for different age categories. While high systolic blood pressure was more prevalent in men from ages 15 to 19 through 70–74 years, it becomes higher in females of >80 [1]. Moreover, global trend of high LDL, as the prominent element in the incidence of MI/stroke, is rising, and men experienced higher burden of DALYs. Different regional patterns of LDL level may be originated from dissimilarities in physical activity, body mass index, dietary patterns, and tobacco use [1].

Table 4
Association of risk factors with history of myocardial infarction/stroke in univariable and multivariable logistic regression.

Variable	History of MI/stroke			
	Unadjusted odds ratio (95 % CI)	*P* value	Adjusted odds ratio (95 % CI)	*P* value
Age categories		<0.001		<0.001
• 40-59	Reference			
• ≥60	2.98 (2.11–4.20)		2.22 (1.45–3.20)	
Sex		<0.001		<0.001
• Male	3.19 (2.17–4.17)		3.82 (2.56–5.71)	
Waist circumference		0.072		–
• Abnormal	0.73 (0.52–1.02)			
Hypertension	2.59 (1.83–3.67)	<0.001	1.71 (1.18–2.50)	<0.005
Diabetes	2.34 (1.61–3.40)	<0.001		–
Hyperlipidemia	3.03 (2.15–4.28)	<0.001	2.42 (1.68–3.48)	<0.001
Chronic kidney disease	1.91 (1.07–3.42)	<0.028		–
No. of 1st degree family members with history of CVD				
• 0	Reference	<0.001		<0.001
• 1	1.64 (1.11–2.44)	0.013	1.69 (1.13–2.54)	<0.001
• 2	2.95 (1.79–4.86)	<0.001	2.80 (1.65–4.75)	<0.001
• 3	4.88 (2.17–10.95)	<0.001	3.45 (1.48–8.45)	0.005
• 4	10.66 (3.62–31.38)	<0.001	6.21 (1.75–21.98)	<0.001
No. of 1st degree family members with history of sudden cardiac death				
• 0	Reference	<0.001		0.036
• 1	1.71 (1.13–2.58)	0.010	1.17 (0.76–1.81)	0.461
• 2	0.93 (0.29–2.96)	0.906	0.44 (0.13–1.45)	0.178
• 3	5.50 (1.65–18.29)	0.005	2.98 (0.81–10.98)	0.100
• 4	29.37 (2.64–326.69)	0.006	26.28 (1.59–432.09)	0.022

CVD: cardiovascular disease; MI: myocardial infarction; Abnormal waist circumference: ≥88 cm for females; ≥102 cm for males. It should be noted that variables were entered in multivariable logistic regression if: 1- They have significant *P* values (<0.2) in univariable logistic regression and, 2- They were not in collinearity with other variables and, 3- There were sufficient cases of MI/stoke present in relevant subgroup in order to establish an stable model. 1st degree relatives include father, mother, sister, and brother. OR: odds ratio, CI: confidence interval.

In our study, the prevalence of MI and stroke was 1.9 %, which was increased with age (≥60 years), male sex, history of hypertension, history of hyperlipidemia along with history of CVD in family members. Although having four family members with history of sudden cardiac death seems to be statistically associated with higher prevalence of MI/stroke, its wide confidence interval makes it less important for clinical translation. At the national level, one study reported that acute MI, unstable angina pectoris, sudden cardiac death, and stroke were occurred in 427 out of 6504 adults, and incidence of these events was found to be independent of age except for sudden cardiac death and stroke [5]. Other study reported chronic kidney disease, hypertension, and diabetes as strongest predictors of stroke [18].

INTERHEART [19] and INTERSTROKE [20] are two international studies that sought the association of classic risk factors with the burden of ischemic events. The multicenter INTERHEART study reported that risk of MI was significantly associated with tobacco smoking, dyslipidemia, hypertension, diabetes, abdominal obesity, and psychological factors. Interestingly, INTERHEART study showed that the highest mean of risk score belongs to high-income countries that paradoxically possess lowest major CVD events and vice versa for low-income countries. This finding may be related to the availability of sufficient medical care in high-income countries. In the INTERSTROKE study [20], hypertension, cardiac causes, psychological factors, alcohol abuse, poor quality of diet, and dyslipidemia were found to be in close association with the incidence of stroke. In another study, glycated hemoglobin level, systolic blood pressure, and physical activity were considered as the strongest factors for acute MI and stroke [21]. Similarities and discrepancies in identification of principle risk factors involving in MI and stroke among studies may be related to differences in study design and population characteristics. Also, the underlying reasons for such discrepancy may be partly interpretable by different prevalence of risk factors at the scale of individuals and communities along with the effects of other competing risk factors [19,20,22]. In addition, coronary vessels and carotid artery are different with each other regarding the existence of perivascular fat as well as plaque characteristics substantiating in varying atherogenesis [23]. This may show the distinct biology of these two vascular beds. Different contribution of risk factors to coronary events versus stroke possibly means different etiologies of these two disorders [24], which should be considered in preventive and therapeutic strategies.

However, contradictory findings are existed like any other investigations. In a large cohort on people with more than 80 years old, no association was reported between classic cardiovascular risk factors and all-cause/cardiovascular mortality [25]. Another study claimed that classic risk factors are not able to identify patients who are at risk of cardiovascular death [26]. Moreover, classic risk markers were found to be poor predictors of recurrent cardiovascular events and related mortality [27], and history of CVD was proposed as the valuable prognosticator of CVD instead [28]. In the current study, some parameters of lipid profile like HDL-C and TG were not in statistically significant association with ischemic events. This observation is partly explained by the lack of statistical power to detect the real correlation between variables. Also, similar observations were reported in previous studies. For instance, Zheng et al. demonstrated that HDL was not associated with the risk of stroke [29]. Intriguingly, lack of significant association do not always translate into being safe. Park et al. showed that even mild abnormal lipid levels are associated with an increased future risk of atherosclerotic events, particularly MI [30]. Moreover, there are certain differences in inherent characteristics of populations such as genetic background that may cause disparities in association of risk factors with ischemic events. Judging from these findings, some researchers suggested that coronary events and ischemic stroke should be considered separately in research studies rather than composite CVD endpoints as a whole [24]. This strategy provides detailed insights into the underlying mechanisms in charge of different degrees of association between risk factors and each clinical event, and also helps to establish a more precise risk stratification platform [31].

One of the limitations of this study is its cross-sectional nature. Also, association of classic risk factors with ischemic events, as a whole, was sought and no borderline was considered between MI and stroke separately. Although we performed multivariable analysis to assess independent association of risk factors with MI and stroke, there might be hidden confounders that have been ignored. For instance, it was not feasible for us to consider the impact of medication use by the participants. One of the strengths of this study is its large sample size which was derived from a general urban population. Indeed, this is among the scarce studies in Eastern Mediterranean region that makes an update regarding the association of classic risk factors with two main reasons of disease burden.

5. Conclusion

Prevalence of MI/stroke was found to be 1.9 % in an adult urban population, which was significantly associated with age≥60 years, male sex, history of hypertension, history of hyperlipidemia, as well as history of CVD in family members.

Funding

This study was financially supported by Shiraz University of Medical Sciences [grant number: 22643].

CRediT authorship contribution statement

Haleh Ghaem: Writing – review & editing, Methodology, Formal analysis, Data curation, Conceptualization. **Mohammad Javad Zibaeenezhad:** Writing – review & editing, Methodology, Conceptualization. **Mehrab Sayadi:** Writing – review & editing, Methodology, Investigation, Formal analysis, Data curation. **Sheida Khosravaniardakani:** Writing – review & editing, Methodology, Investigation. **Nader Parsa:** Writing – review & editing, Methodology, Investigation. **Iman Razeghian-Jahromi:** Writing – review & editing, Writing – original draft, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

References

[1] G.A. Roth, G.A. Mensah, C.O. Johnson, G. Addolorato, E. Ammirati, L.M. Baddour, et al., Global burden of cardiovascular diseases and risk factors, 1990–2019: update from the GBD 2019 study, J. Am. Coll. Cardiol. 76 (25) (2020) 2982–3021.
[2] M. Naghavi, S. Shahraz, S.G. Sepanlou, D. Dicker, P. Naghavi, F. Pourmalek, et al., Health transition in Iran toward chronic diseases based on results of Global Burden of Disease 2010, Arch. Iran. Med. 17 (5) (2014).
[3] A.N. Shabestari, S.S. Moghaddam, F. Sharifi, R. Fadayevatan, F. Nabavizadeh, A. Delavari, et al., The most prevalent causes of death, DALYs, and geriatric syndromes in Iranian elderly people between 1990 and 2010: findings from the global burden of disease 2010 study, Arch. Iran. Med. 18 (8) (2015), 0-.
[4] English LDJIJoSe. STEM education K-12, Perspectives on integration 3 (1) (2016) 1–8.
[5] M. Talaei, N. Sarrafzadegan, M. Sadeghi, S. Oveisgharan, T. Marshall, G. N. Thomas, et al., Incidence of cardiovascular diseases in an Iranian population: the isfahan cohort study, Arch. Iran. Med. 16 (3) (2013), 0-.
[6] M. Sadeghi, M. Talaei, S. Oveisgharan, K. Rabiei, M. Dianatkhah, A. Bahonar, et al., The cumulative incidence of conventional risk factors of cardiovascular disease and their population attributable risk in an Iranian population: the Isfahan Cohort Study, Adv. Biomed. Res. 3 (2014).
[7] N. Sarrafzadegan, N. Mohammmadifard, Cardiovascular disease in Iran in the last 40 years: prevalence, mortality, morbidity, challenges and strategies for cardiovascular prevention, Arch. Iran. Med. 22 (4) (2019) 204–210.
[8] P.A. Sytkowski, W.B. Kannel, R.B. D'Agostino, Changes in risk factors and the decline in mortality from cardiovascular disease: the Framingham Heart Study, NEJM 322 (23) (1990) 1635–1641.
[9] K.M. Anderson, P.M. Odell, P.W. Wilson, W.B. Kannel, Cardiovascular disease risk profiles, Am. Heart J. 121 (1) (1991) 293–298.
[10] D.R.G.J. Diabetes, The Diabetes Control and Complications Trial (DCCT): design and methodologic considerations for the feasibility phase 35 (5) (1986) 530–545.
[11] Diabetologia UPDSGJ, UK prospective diabetes study (UKPDS) VIII, Study design, progress and performance 34 (12) (1991) 877–890.
[12] K.K. Teo, Rafiq TjcjoC, Cardiovascular risk factors and prevention: a perspective from developing countries, Can. J. Cardiol. 37 (5) (2021) 733–743.
[13] M.J. Zibaeenezhad, H. Ghaem, N. Parsa, M. Sayadi, M. Askarian, M. Kasaei, et al., Analysing cardiovascular risk factors and related outcomes in a middle-aged to older adults population in Iran: a cohort protocol of the shiraz heart study (SHS), BMJ Open 9 (4) (2019) e026317.
[14] R. Ness-Abramof, Apovian Cmjnicp, Waist circumference measurement in clinical practice, Nutr. Clin. Pract. 23 (4) (2008) 397–404.
[15] J.H. Kim, Multicollinearity and misleading statistical results, Korean journal of anesthesiology 72 (6) (2019) 558–569.
[16] M. Sadeghi, A.A. Haghdoost, A. Bahrampour, Dehghani Mjijoph, Modeling the burden of cardiovascular diseases in Iran from 2005 to 2025: the impact of demographic changes, International Journal of STEM Education 46 (4) (2017) 506.
[17] M.H. Emamian, H. Hashemi, A. Fotouhi, Predicted 10-year risk of cardiovascular disease in the Islamic Republic of Iran and the body mass index paradox, East. Mediterr. Health J. 26 (12) (2020).

[18] N. Fahimfar, D. Khalili, R. Mohebi, F. Azizi, FJBn Hadaegh, Risk factors for ischemic stroke; results from 9 years of follow-up in a population based cohort of Iran, BMC Neurol. 12 (1) (2012) 1–7.
[19] S. Yusuf, S. Hawken, S. Ôunpuu, T. Dans, A. Avezum, F. Lanas, et al., Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study, Lancet 364 (9438) (2004) 937–952.
[20] M.J. O'Donnell, S.L. Chin, S. Rangarajan, D. Xavier, L. Liu, H. Zhang, et al., Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study 388 (10046) (2016) 761–775.
[21] N.J. Kassebaum, M. Arora, R.M. Barber, Z.A. Bhutta, J. Brown, A. Carter, et al., Global, regional, and national disability-adjusted life-years (DALYs) for 315 diseases and injuries and healthy life expectancy (HALE), 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015, Lancet 388 (10053) (2016) 1603–1658.
[22] S. Yusuf, P. Joseph, S. Rangarajan, S. Islam, A. Mente, P. Hystad, et al., Modifiable risk factors, cardiovascular disease, and mortality in 155 722 individuals from 21 high-income, middle-income, and low-income countries (PURE): a prospective cohort study, Lancet 395 (10226) (2020) 795–808.
[23] F. Sigala, E. Oikonomou, A.S. Antonopoulos, G. Galyfos, Tousoulis Djcoip, Coronary versus carotid artery plaques. Similarities and differences regarding biomarkers morphology and prognosis, Curr. Opin. Pharmacol. 39 (2018) 9–18.
[24] I.F. Muhammad, Y. Borné, S. Zaigham, M. Söderholm, L. Johnson, M. Persson, et al., Comparison of risk factors for ischemic stroke and coronary events in a population-based cohort, BMC Cardiovasc. Disord. 21 (1) (2021) 1–10.
[25] B. Vaes, D. Depoortere, G. Van Pottelbergh, C. Matheï, J. Neto, Degryse Jjbg, Association between traditional cardiovascular risk factors and mortality in the oldest old: untangling the role of frailty, BMC Geriatr. 17 (1) (2017) 1–8.
[26] W. De Ruijter, R.G. Westendorp, W.J. Assendelft, W.P. den Elzen, A.J. de Craen, S. le Cessie, et al., Use of Framingham risk score and new biomarkers to predict cardiovascular mortality in older people: population based observational cohort study, Bmj 338 (2009).
[27] P.G. van Peet, Y.M. Drewes, A.J. de Craen, J. Gussekloo, W.J.P.O. de Ruijter, NT-proBNP best predictor of cardiovascular events and cardiovascular mortality in secondary prevention in very old age: the Leiden 85-plus Study, PLoS One 8 (11) (2013) e81400.
[28] P.G. van Peet, Y.M. Drewes, A.J. de Craen, R.G. Westendorp, J. Gussekloo, W.J. A. de Ruijter, Prognostic value of cardiovascular disease status: the Leiden 85-plus study, AGE 35 (4) (2013) 1433–1444.
[29] J. Zheng, Z. Sun, X. Zhang, Z. Li, X. Guo, Y. Xie, et al., Non-traditional lipid profiles associated with ischemic stroke not hemorrhagic stroke in hypertensive patients: results from an 8.4 years follow-up study 18 (2019) 1–9.
[30] J.-B. Park, D.H. Kim, H. Lee, I.-C. Hwang, Y.E. Yoon, H.E. Park, et al., Mildly abnormal lipid levels, but not high lipid variability, are associated with increased risk of myocardial infarction and stroke in "statin-naive" young population a nationwide cohort study 126 (7) (2020) 824–835.
[31] B.J. van Kempen, B.S. Ferket, M. Kavousi, M.J. Leening, E.W. Steyerberg, M. A. Ikram, et al., Validating, Updating, and Extending Long-Term Framingham Cardiovascular Disease Predictions: the Rotterdam Study, Am Heart Assoc, 2012.