Int J Public Health (2015) 60:561–572
DOI 10.1007/s00038-015-0679-6

ORIGINAL ARTICLE

Mashhad stroke and heart atherosclerotic disorder (MASHAD) study: design, baseline characteristics and 10-year cardiovascular risk estimation

Majid Ghayour-Mobarhan · Mohsen Moohebati · Habibollah Esmaily · Mahmoud Ebrahimi · Seyed Mohammad Reza Parizadeh · Ali Reza Heidari-Bakavoli · Mohammad Safarian · Naghmeh Mokhber · Mohsen Nematy · Hamidreza Saber · Maryam Mohammadi · Mohammad Sobhan Sheikh Andalibi · Gordon A. Ferns · Mahmoud Reza Azarpazhooh

Received: 20 July 2014 / Revised: 27 March 2015 / Accepted: 30 March 2015 / Published online: 6 May 2015

Abstract
Objective The Mashhad stroke and heart atherosclerotic disorder (MASHAD) study is a 10-year cohort study that aims to evaluate the impact of various genetic, environmental, nutritional and psychosocial risk factors on the incidence of cardiovascular events among an urban population in eastern Iran.
Methods The MASHAD study comprises a cohort of 9704 individuals aged 35–65 years using a stratified cluster random sampling design. This cohort will be followed up until 2020, with follow-up examinations being undertaken every 3 years. Ten-year cardiovascular disease (CVD) risk estimation was determined using NCEP ATP III criteria.
Results Overall, 88.4 % of women and 79.2 % of men ($P < 0.001$) had at least one lipid abnormality. The 10-year risk for CVD of <10, 10–20 and >20 % were observed to be 86.6, 11 and 2.5 %, respectively. Predicted risk of CVD > 10 % using the Framingham algorithm was considerably higher in men compared to women. Overall, 9.5 % [95 % confidence interval (CI) 8.9–10.1 %] of our subjects had prevalent CAD.
Conclusion The prevalence of CVD risk factors within our population is high compared to Western countries, indicating the necessity for interventional risk modifications.

Keywords Cardiovascular disease · Epidemiology · Risk factor · Metabolic syndrome · Iran

Introduction

Cardiovascular disease (CVD) is a major cause of morbidity and mortality globally (Husten et al. 1998; Dawber et al. 1957). The early identification of individuals at high risk of CVD allows timely intervention and is an important part of health policy in many countries. For example in the United Kingdom vascular risk screening has recently been introduced for individuals over 40 years of age (updated: The Handbook for Vascular Risk Assessment, Risk

Electronic supplementary material The online version of this article (doi:10.1007/s00038-015-0679-6) contains supplementary material, which is available to authorized users.

M. Ghayour-Mobarhan · M. Moohebati · H. Esmaily · S. M. R. Parizadeh · M. Safarian · M. Nematy · M. Mohammadi · M. S. S. Andalibi
Biochemistry of Nutrition Research Center, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

M. Ghayour-Mobarhan · M. Moohebati · M. Ebrahimi · A. R. Heidari-Bakavoli · M. R. Azarpazhooh (✉)
Cardiovascular Research Center, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
e-mail: azarpazhoohmr@mums.ac.ir

H. Esmaily
Department of Biostatistics and Epidemiology, School of Health, Mashhad University of Medical Sciences, Mashhad, Iran

N. Mokhber
Psychiatry and Behavioral Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

H. Saber
Department of Epidemiology, Boston University School of Public Health, Boston, USA
e-mail: hsaber@bu.edu

G. A. Ferns
Division of Medical Education, Brighton and Sussex Medical School, University of Brighton, Rm 342, Mayfield House, Brighton BN1 9PH, UK

Reduction and Risk Management, 2012). It is now well recognized that cardiovascular disease has a complex, multi-factorial basis (Kuulasmaa et al. 2000; Smith et al. 2010; Uthoff et al. 2010; Schweigman et al. 2006). In recent years the global prevalence of CVD has changed significantly. Although it has been well documented that the mortality attributable to stroke and ischemic or coronary heart disease has declined in Western countries (Sytkowski et al. 1996; Beaglehole et al. 1997; Lloyd 1994; Ornish et al. 1998), its prevalence in many developing countries has increased substantially over the same period (Azarpazhooh et al. 2010; Monge and Beita 2000; Beaglehole 1993; Najeeb 1993). CVD now accounts for 47.3 % of all-cause mortality in Iran (Sarraf-Zadegan et al. 1999). Whilst there has been a decline in mortality related to infectious diseases as a result of improvement in health services, as in many other Asian countries, there has been an increase in CVD burden in Iran (Esteghamati et al. 2008; Kelishadi et al. 2008; Delavari et al. 2009; Harati et al. 2009; Hajian-Tilaki and Heidari 2007; Sarrafzadegan et al. 2010).

Few well-designed prospective studies have investigated risk factors of cardiovascular diseases in populations of developing countries such as those of the Middle East. An analysis of the clinical impact of the traditional and emerging CVD risk factors in a developing country would have implications for the global management of this chronic disease, and may provide insights into the risk of CVD among ethnic minorities living in the West. Data from the Mashhad Stroke Incidence Study (MSIS), a 1-year community-based incidence stroke study conducted in Mashhad (2006–2007), provided evidence for a relatively high incidence of stroke, which was also found to occur at a younger age, in Iran compared to those reported in Western countries (Azarpazhooh et al. 2010). However, the reason for these patterns of variations in our population is unclear. Genetic, ethnic and social differences, differences in the pattern of prevalent cardiovascular risk factors, and the systems that exist for managing them, may account for these variations. Furthermore, there has been no systematic attempt to examine genetic susceptibility and gene–environment interaction in a cohort from the Middle East. On this basis, we planned to conduct a large longitudinal cohort study, the Mashhad stroke and heart atherosclerotic disorder (MASHAD) study, the aim of which was to investigate the determinants and other risk markers of CAD and stroke in our population. The clinical endpoints for follow-up are CAD and stroke and participants will be followed for a period of at least 10 years. The specific aims of the project were to: (1) determine the prevalence of stroke and coronary disease and their biological, environmental, social, and behavior-related risk factors in a defined geographic area in north-western Iran; (2) identify characteristics related to the development of clinically evident CAD and stroke; (3) identify the association between various genetic and environmental risk indicators and cardiovascular and cerebrovascular disease endpoints; and (4) track the changes in CAD and stroke risk indicators during a period of at least 10 years.

The objective of the present paper is to describe the rationale, design and cross-sectional baseline characteristics of the cohort, as well as providing an estimate of 10-year CVD risk in this population.

Methods

The MASHAD study started in 2010 and will continue until 2020. The total population in the city of Mashhad was estimated using the national Iranian census in 2006. Participants were drawn from three regions in Mashhad, located in the north-eastern Iran, using a stratified cluster random sampling technique. Each region was divided into nine sites centered upon Mashhad Healthcare Center divisions. Households with individuals of eligible age between 35 and 65 years were identified and the local population authorities provided families with an information brochure of the study. Community leaders who were familiar with the families in the community also assisted with the identification and recruitment of potential participants. After identifying eligible participants, they were contacted to arrange an appointment for the formal physical examination. Eighty-two percent of subjects responded and agreed to enroll in the study. The non-responders ($n = 2035$) were contacted and information was sought regarding their demographic and socioeconomic profile and self-reported diabetes and hypertension status. Our primary analysis showed no significant differences in age and gender distribution of responders and non-responders.

The demographic, anthropometric and lifestyle data were collected and recorded by two certified health care professionals and a nurse. Our health-related questionnaires included (a) demographic data, physical exercise, tobacco and alcohol use, food frequency questionnaire (FFQ) and 24-h food record (b) anthropometric measurements, cardiovascular risk-related questionnaire and (c) anxiety and depression tests.

Study phases

Results from this cohort will be reported in two phases. In the first phase, we will report the cross-sectional data for all participants recruited into the study including those with and without history of CVD. In the second phase, after exclusion of prevalent cases of CAD, stroke and peripheral arterial disease, subjects will be followed for 10 years to

determine the incidence rates of these disorders in our cohort of healthy individuals (Fig. 1). Individuals with medium and high risk will be given counseling about healthy diet, physical activity and smoking cessation. Those with elevated blood pressure, serum cholesterol, or other findings will be sent for medical follow-up. Any "alert" findings of conditions that should be medically evaluated on an urgent basis will be reported to the participant and his or her physician by telephone as soon as they were identified. In this present paper, we report the cross-sectional data for the prevalence of classic risk factors in our total participants based on a survey in 2010–2011.

Baseline examinations

Blood and mid-stream urine samples were collected from participants. Blood samples were taken between 8 and 10 a.m. by venepuncture of an antecubital vein after 14 h overnight fasting. The samples were collected in vacuum tubes (20 ml) from subjects in a sitting position, according to a standard protocol. All blood specimens were centrifuged at room temperature within 30–45 min of collection to separate the serum and plasma into six aliquots (0.5 ml), which were then sent to the Bu Ali Research Institute, Mashhad. Aliquots of serum were also kept frozen at −80 °C for future analysis. Low-density lipoprotein cholesterol (LDL-C) was calculated from the serum total cholesterol (TC), triglycerides (TGs), and high-density lipoprotein cholesterol (HDL-C) concentrations expressed in mg/dl using Friedewald formula (Castelli et al. 1986) if serum TGs concentrations were lower than 400 mg/dl. A baseline 12-lead electrocardiogram (ECG) was undertaken for each participant. All ECGs were scored blindly using the Minnesota codes, and were stored digitally for subsequent analysis. Dyslipidemia was defined as TC $\geq$ 200 mg/dl (5.18 mmol/l), LDL-C $\geq$ 130 mg/dl (3.36 mmol/l), or TG $\geq$ 150 mg/dl (1.69 mmol/l), or HDL-C $<$ 40 mg/dl (1.03 mmol/l) in men and $<$50 mg/dl (1.30 mmol/l) in women (2002).

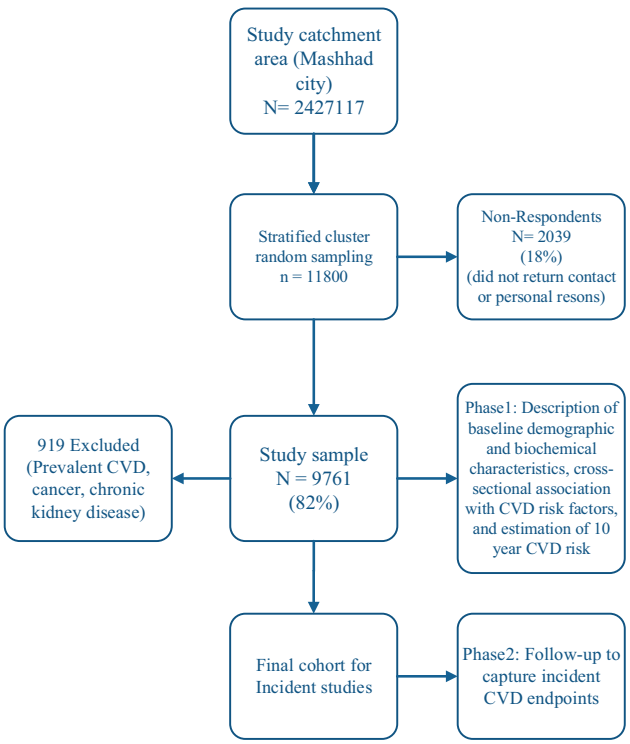

Fig. 1 Description of sample recruitment and study phases within the MASHAD study, Mashhad, Iran 2010

Diabetes mellitus was defined as a FBG $\geq$ 126 mg/dl or being treated with existing oral hypoglycemic agents or insulin treatment. According to the World Health Organization recommendations for obesity, (25 $\geq$ BMI $>$ 25 kg/m^2) was defined as overweight and (BMI $\geq$ 30 kg/m^2) was considered as obese. Truncal obesity was defined as a WHR $\geq$ 0.95 in men and a WHR $\geq$ 0.8 in women. Based on International Diabetes Federation (IDF) cut-off points, WC $\geq$ 94 cm in men and $\geq$80 cm in women were considered high. Hypertension was diagnosed in individuals with systolic blood pressure at or above 140 mmHg and/or diastolic blood pressure at or above 90 mmHg, and in persons who were on anti-hypertension medication.

According to the World Health Organization (WHO) definition, stroke is defined as "rapidly developing signs of focal or global disturbance of cerebral function lasting $>$24 h with no apparent cause other than of vascular origin (Hatano 1976). The presence of coronary heart disease was established by a history of myocardial infarction or angina pectoris or electrocardiographic evidence for a definite Q wave using the Minnesota Code. A current smoker was defined as smoking cigarettes at least once a day. An ex-smoker was formerly a daily smoker, but someone who currently did not smoke. Data for non-cigarette smoking were also obtained. Psychometric tests were performed using the Beck's anxiety inventory (BAI) to calculate an anxiety score that is explained as follows: a 0–7, minimal level of anxiety; 8–15, mild anxiety; 16–25, moderate anxiety and 26–63, severe anxiety. The Beck's depression inventory II (BDI-II) was also used to evaluate depression. The cut-offs used were as follows: 0–13, minimal depression; 14–19, mild depression; 20–28, moderate depression; and 29–63, severe depression.

Statistical analysis

Data collected at the field centers were transmitted to the data bank using Microsoft visual studio.NET software which is exclusively designed for data management in

Table 1 Age distribution of participants by gender in the MASHAD study, Mashhad, Iran, 2010

Age (years)	Men, *N* (%)	Women, *N* (%)	Total, *N* (%)
35–39	664 (17.1)	1141 (19.6)	1805 (18.5)
40–44	701 (18.1)	1150 (19.7)	1851 (19.1)
45–49	734 (18.8)	1213 (20.7)	1947 (20.0)
50–54	742 (19.1)	1103 (18.8)	1845 (18.9)
55–59	561 (14.4)	696 (11.9)	1257 (12.9)
60–64	501 (12.9)	556 (9.5)	1056 (10.8)
Total	3903	5859	9761

MASHAD study. Descriptive analysis was used to process the outcomes in tables and graphs. Values were expressed as mean ± SD for normally distributed variables. Baseline demographics and clinical characteristics were compared between groups using independent samples *t* test, Chi-square and/or Fisher's exact test, as appropriate. Prevalence rates are reported as the crude and age-standardized rates using WHO population data. Sex-specific estimates for determining the 10-year risk for developing CVD was carried out using a modified Framingham risk scoring according to the NCEP ATP III for participants without self-reported CVD or CVD equivalent (heart attack and angina pectoris, stroke, peripheral vascular disease and diabetes). Risk scores were calculated to determine the 10-year absolute risk. Three levels of risk were defined as <10, 10–20, and >20 %. Patients with CVD or a CVD risk equivalent were considered to be at very high risk for sustaining an acute cardiovascular event. SPSS software (version 15, Chicago, IL, USA) was used for statistical analysis. For all analyses, statistical significance was assessed at a level of 0.05 (two-tailed) and *P* value less than 0.05 was considered significant.

Follow-up

It is intended that the subjects recruited into the MASHAD study will be monitored for at least 10 years and will be contacted at 3-yearly intervals to reduce the risk of losing contact. They will be asked to complete the follow-up questionnaire to identify any changes in their state of health and lifestyle. A follow-up analysis will be performed every 3 years. However, certain data will be collected more frequently as required for the particular sub-projects. Morbidity and mortality data and myocardial infarction (MI) and stroke rates are being collected regularly from the reference community.

Ethics

Documents explaining the study were provided to the participants before enrollment. Moreover, a 10-min face-to-face explanation was provided for groups of individuals. Each item for agreement was explained individually to obtain a written consent for those who agreed to participate in the study. The study was approved by the Ethic Committee of Mashhad University of Medical Sciences.

Results

There were a total of 9761 participants, of whom approximately 40 % were males and 60 % females. Table 1 shows the age distribution of our participants by gender.

Sociodemographic findings

The mean age was 48.1 years in the total population, while men were slightly older than women (48.9 vs 47.6 years). Table 2 shows the socioeconomic status of the participants. Overall, 61 were single, 9083 were married, 135 were divorced and 474 were widowed.

Among participants, 305 (7.8 %) of men and 1027 (17.5 %) of women were illiterate.

Of the male population, 2866 (73.4 %) were employed and 700 (17.9 %) were retired. Among the female population, 706 (12 %) were employed and 252 (4.3 %) were retired. Smoking was more prevalent among males. Approximately, 28.5 % of men and 18 % of women were current smokers and 13.9 % of men and 6.3 % of women were ex-smokers. While 75.7 % of women were never-smokers, only 57.5 % of men had never been smokers in the past.

Blood biochemistry

Baseline biochemical values of participants are shown in Table 3. Overall, 23.7 % of our total population had elevated blood pressure (SBP $\geq$ 140 and/or DBP $\geq$ 90 mmHg). The prevalence of raised BP was higher among men compared to women (24.4 vs 23.3 %) (Table 4). The higher prevalence of HTN among men as compared to women was more pronounced for the two

Table 2 Sociodemographic characteristics of the MASHAD study population, Mashhad, Iran 2010

	Total		Male		Female	
	N	%	*N*	%	*N*	%
Members in each family						
1	145	1.5	23	0.6	122	2.1
2	674	6.9	163	4.2	511	8.7
3	1435	14.7	571	14.6	864	14.7
4	2919	29.9	1318	33.8	1601	27.3
5	2535	26.0	1028	26.3	1507	25.7
6	1239	12.7	480	12.3	759	13
7 or above	815	8.4	320	8.2	495	8.5
Types of properties						
Personal	7641	78.3	3013	77.2	4628	79
Organizational	24	0.2	8	0.4	16	0.5
Leased	1823	18.7	783	20.1	1040	17.8
Other	274	2.8	99	2.5	175	3
Having a car						
Yes	5418	55.5	2437	62.3	2981	50.9
No	4344	44.5	1466	37.7	2878	49.1
Last educational level						
Illiterate	1332	13.6	305	7.8	1027	17.5
Elementary school	4001	41.0	1311	33.6	2690	45.9
High school or equivalent	3370	34.6	1611	41.3	1759	29.9
Some college	363	3.7	220	5.6	143	2.4
Bachelor's degree	583	6.0	372	9.5	211	3.6
Master's degree	76	0.8	58	1.5	18	0.3
Doctoral degree or above	21	0.2	15	0.4	6	0.1
Seminary degree	14	0.1	10	0.3	4	0.1
Job status						
Student	22	0.3	10	0.3	12	0.2
Employed	3572	36.6	2866	73.4	706	12
Unemployed	5216	53.4	327	8.4	4889	83.4
Retired	951	9.7	700	17.9	252	4.3
Marriage status						
Single	61	0.6	21	0.6	40	0.7
Married	9083	93.1	3847	98.7	5236	89.4
Divorced	135	1.4	17	0.4	118	2
Widowed	474	4.9	14	0.4	460	7.9

extremes of age groups (35–39 and 60–65 age group) (Table 4). Fourteen point one percent of the total population sample were diabetics; the prevalence of DM was higher in women as compared to men (14.5 vs 13.5 %). We observed an increasing prevalence of DM across age groups and women 60–65 years old had the highest prevalence of DM (27.3 %). Lipid profile disturbances were also significantly higher in women. Overall, 88.4 % of women and 79.2 % of men ($P < 0.001$) had at least one lipid abnormality to be categorized as dyslipidemic. The mean level of serum TC was 186.4 ± 38.1 in men and 194 ± 40.3 mg/dl in women. At-risk values of serum TC (>200 mg/dl) were significantly more prevalent in women than in men (41.5 vs 34 %, $P < 0.001$). Serum TG levels were significantly higher in men than in women (124.03 vs 117 mg/dl, $P < 0.001$). A high serum TG level (>150 mg/dl) was present in 36.9 % of men and 31.8 % of women ($P < 0.001$). The mean level of serum LDL-C was 113.5 ± 35.5 mg/dl in men and 118.1 ± 36.1 mg/dl in women ($P < 0.001$). Ten point five percent of our total population sample had an elevated serum LDL-C (>160 mg/dl), whilst the prevalence of an elevated serum

Table 3 Baseline biochemical and anthropometric characteristics of individuals with and without CVD in MASHAD study, Mashhad, Iran, 2010

	Male (N = 3878)				Female (N = 5826)				Total (N = 9704)			
	Mean	SD/IQR	95 % CI		Mean	SD/IQR	95 % CI		Mean	SD/IQR	95 % CI	
			Upper bound	Lower bound			Upper bound	Lower bound			Upper bound	Lower bound
Age (year)	48.9	8.4	49.1	48.6	47.6	8.0	47.8	47.4	48.09	8.24	48.8	48.0
HDL-c (mg/dl)	39.9	9.2	39.6	40.1	44.88	9.99	45.1	44.6	42.9	10.02	43.1	42.7
LDL (mg/dl)	113.1	35.16	114.2	112.0	118.3	36.1	119.2	117.4	116.31	35.88	117.0	115.6
TC (mg/dl)	186.5	38.15	187.8	185	194.41	40.0	195.4	193.3	191.2	39.47	192.1	190.5
TG (mg/dl)[a]	124.0	86.5–179.0	152.6	146	117.0	83–167	140.4	135.8	120.0	85–172	144.5	140.7
FBG (mg/dl)	92	38.19	93.2	90.8	93.1	40.4	94.2	92.1	92.77	39.68	93.6	92.0
Uric acid (mg/dl)	5.2	4.3–6.1	5.4	5.2	4.1	3.4–5	4.5	4.2	4.5	3.7–5.5	4.9	4.6
hs-CRP (mg/L)[a]	1.4	0.9–3.0	4.7	3.9	1.8	1.1–4	5.3	4.7	1.6	1.0–3.6	5.1	4.6
WBC (cells/ml)	6.13	1.8	6.2	6.1	5.9	1.7	6.0	5.9	6.0	1.83	6.04	5.97
RBC ($\times 10^6$/ml)	5.07	0.7	5.09	5.07	4.6	0.6	4.62	4.58	4.8	1.03	4.81	4.79
Hgb (g/dl)	14.6	2.1	14.7	14.5	12.84	2	12.89	12.79	13.55	2.41	13.6	13.5
HCT (%)	43.3	6.1	43.5	43.1	38.9	5.5	39.1	38.7	40.7	6.81	40.8	40.5
Height (m)	1.68	0.1	1.68	1.68	1.55	0.1	1.55	1.54	1.60	0.12	1.61	1.60
Weight (kg)	75.0	13	75.4	74.6	69.8	14.6	70.2	69.4	71.9	12.9	72.2	71.6
WC (cm)	93.7	11	94.0	93.3	96.1	12.5	96.5	95.8	95.2	18.57	95.4	94.9
SBP (mmHg)	122.4	17.21	122.9	122	121.3	19.3	121.8	120.8	121.8	18.5	122.1	121.4
DBP (mmHg)	80.04	10.8	80.4	79.7	78.5	11.6	78.8	78.2	79.12	11.3	79.3	78.9
Depression score	10.6	8.95	10.9	10.4	13.8	9.9	14.1	13.5	12.6	9.7	12.8	12.4
Anxiety score	8.5	8.4	8.7	8.2	12.2	10.5	12.5	12.0	10.7	9.9	10.5	11.0

Becks anxiety and depression inventory scale were used for depression and anxiety scoring

CVD cardiovascular disease, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *TC* total cholesterol, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *TG* triglyceride, *BMI* body mass index, *WHR* waist hip ratio, *FBG* fasting blood glucose, *RBC* red blood cell, *WBC* white blood cell, *Hgb* hemoglobin, *WC* waist circumference, *IQR* inter-quartile range

[a] Parameters that considered non-normally distributed and used Mann–Whitney U test and expressed by median/IQR

LDL-C was significantly higher in women than in men (11.8 vs 8.6 %, $P < 0.001$). Women in 60–65 age group had the highest levels of serum LDL-C among the participants. Mean serum HDL-C concentrations was higher in women than in men (44.9 ± 10.1 vs 39.9 ± 9.3 mg/dl, $P < 0.001$). Overall, the prevalence of low serum HDL-C (<35 mg/dl) was 21.3 % in our total population and low serum HDL-C was found to be significantly more common in men than in women (32.1 vs 14 %, $P < 0.001$).

Age-standardized prevalence rates (using WHO population data) were 13.8 % for DM, 14.47 % for low serum HDL, 11.74 % for high cholesterol 11.34 % for high serum LDL and 22.06 % for HTN in our total population (Table 5).

Ten-year absolute CAD risk

Among participants without CVD or a CVD equivalent, the 10-year risk for CAD of <10, 10–20 and >20 % were estimated to be 86.6, 11 and 2.5 %, respectively (Table 6). Women constituted a larger proportion of individuals in <10 % risk category than men (98.9 vs 68.1 %), a greater percentage of men had 10–20 and >20 % risk for CAD development compared with women (25.7 and 6.1 vs 1.1 and 0 %, respectively). Based on these findings, approximately 300 men and 270 women without CVD or CVD risk equivalent are predicted to develop an event over 10 years, with approximately 57 new cases/year in these individuals.

Table 4 Distribution of conventional CAD risk factors (%) by gender in the MASHAD study, Mashhad, Iran, 2010

	Men			Women			Total population		
	N (%)	95 % CI		*N* (%)	95 % CI		*N* (%)	95 % CI	
		Upper bound (%)	Lower bound (%)		Upper bound (%)	Lower bound (%)		Upper bound (%)	Lower bound (%)
HDL cholesterol (mg/dl)									
<35	1250 (32.1)	33.6	30.6	815 (14.0)	14.9	13.1	2065 (21.3)	22.1	20.5
35–59	2515 (64.5)	65.0	63.0	4556 (78.4)	79.5	77.3	7071 (72.8)	73.7	71.9
≥60	133 (3.4)	3.7	3.1	444 (7.6)	8.3	6.9	577 (5.9)	6.4	5.4
Total	3898			5815			9713		
LDL cholesterol (mg/dl)									
<100	1338 (34.9)	36.4	33.4	1743 (29.9)	31.1	28.7	3081 (31.9)	32.8	31.0
100–160	2172 (56.6)	58.2	55.0	3390 (58.2)	59.5	56.9	5562 (57.6)	58.6	56.6
≥160	329 (8.6)	9.5	7.7	688 (11.8)	12.6	11.0	1017 (10.5)	11.1	9.9
Total	3839			5821			9660		
Total cholesterol (mg/dl)									
<200	2538 (65.8)	67.3	64.3	3403 (58.4)	59.7	57.1	5941 (61.4)	62.4	60.4
200–239	985 (25.3)	26.7	23.9	1704 (29.2)	30.4	28.0	2689 (27.8)	28.7	26.9
≥240	333 (8.6)	9.5	7.7	719 (12.3)	13.1	11.5	1052 (10.9)	11.2	10.6
Total	3856			5826			9682		
Triglycerides (mg/dl)									
<150	2437 (63.1)	64.70	61.5	3974 (68.2)	69.4	67.0	6411 (66.2)	67.1	65.3
150–199	668 (17.3)	18.50	16.1	949 (16.3)	17.2	15.4	1617 (16.7)	17.4	16.0
200–499	714 (18.5)	19.70	17.3	870 (14.9)	15.8	14.0	1584 (16.3)	17.0	15.6
≥500	41 (1.1)	1.20	1.0	36 (0.6)	0.8	0.4	77 (0.8)	0.9	0.7
Total	3860			5829			9689		
Diabetes status									
Non-diabetic	3376 (86.5)	87.5	85.5	5009 (85.5)	86.4	84.6	8385 (85.9)	86.6	85.2
Diabetic	527 (13.5)	12.5	14.5	850 (14.5)	13.4	15.6	1377 (14.1)	14.7	13.4
Blood pressure (mmHg)									
Normal (including optimal)[a]	2448 (62.7)	64.2	61.2	3857 (65.8)	67.0	64.6	6305 (64.6)	65.5	63.7
High normal	502 (12.9)	13.9	11.9	642 (11.0)	11.8	10.2	1144 (12)	12.3	11.1
Hypertension stage I	680 (17.4)	18.6	16.2	923 (15.8)	16.7	14.9	1603 (16.4)	17.1	15.7
Hypertension stage II–IV	273 (7. 0)	7.8	6.2	437 (7.5)	8.1	5.9	710 (7.3)	7.8	6.8
Total	3903			5859			9762		

Table 4 continued

	Men			Women			Total population		
	N (%)	95 % CI		*N* (%)	95 % CI		*N* (%)	95 % CI	
		Upper bound (%)	Lower bound (%)		Upper bound (%)	Lower bound (%)		Upper bound (%)	Lower bound (%)
Smoking habit									
No (never)	2240 (57.5)	59.0	56.0	4437 (75.7)	76.80	74.60	6677 (68.4)	69.3	67.5
Current smoker	1120 (28.7)	30.1	27.3	1054 (18.0)	19.0	17.0	2174 (22.3)	23.1	21.5
Past smoker	542 (13.9)	14.9	12.9	370 (6.3)	6.9	5.7	912 (9.3)	9.9	8.7
Total				5861			9763		
CAD status									
CAD−	3541 (90.7)	91.60	89.8	5293 (90.4)	91.10	89.70	8835 (90.5)	91.1	89.9
CAD+	362 (9.3)	10.20	8.4	565 (9.6)	10.30	8.90	927 (9.5)	10.1	8.9
Total	3903			5859			9762		

CAD coronary artery disease, *TC* total cholesterol, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *SBP* systolic blood pressure, *DBP* diastolic blood pressure

[a] Normal: SBP < 130 and DBP < 85. High normal: SBP: 130–139 and DBP: 85–89. Stage I: SBP: 140–159 and DBP: 90–99. Stage II–IV: SBP ≥ 160 and DBP ≥ 100

Discussion

Since the landmark studies on CVD risk, such as the Framingham Study (Dawber et al. 1957), considerable efforts have been made to investigate factors associated with the progression of CVD in a large number of geographically or ethnically diverse populations. Such efforts have provided important information, increased the awareness of cardiovascular risk factors, and helped to develop strategies for lipid, hypertension, and diabetes control, exercise, and smoking prevention (Luepker et al. 1994; Ornish et al. 1998; Smith et al. 2010; Wilson et al. 1980). Nevertheless, there is still scant population-based information for populations from developing countries (Ergör et al. 2012) and this is an important omission as the WHO has predicted that non-communicable diseases, and particularly cardiovascular disease will exert the greatest disease burden in this region.

A high prevalence of CVD risk factors among Iranian middle-aged adults is probably now associated with the current high levels of CVD mortality and morbidity observed in Iran (Azizi et al. 2002; Esteghamati et al. 2008; Hadaegh et al. 2010). At baseline, a considerable proportion of our adult population aged 35–65 had hypertension, DM and hyperlipidemia that is markedly higher than reports from Western countries (Geiss et al. 2006). For example, based on the latest heart disease and stroke statistics for 2013, 8.3 % of adults in the USA had DM while the prevalence of DM was 14 % in our cohort of middle-aged individuals. Mean serum HDL levels were also lower in our subjects compared to the mean USA HDL levels (40 vs 51 mg/dl). The high prevalence of CVD risk factors among the women is another interesting feature of this population compared to others derived from the Western world. For instance, the prevalence of DM and hyperlipidemia was considerably higher in women compared to men amongst the population of subjects we have sampled. This finding is in contrast with reports from Western population (Slavenka et al. 2014) and China. However, these studies have also reported a tendency for these risk factors to cluster among overweight/obese women. This requires more detailed follow-up and analysis. Will these risk factors impact on future cardiovascular events in this population? In a recent 1-year incidence study of stroke in Mashhad, we observed relatively low crude rates of stroke, but very high age-standardized incidence rates after adjustment to European or WHO population, higher than all previous ideal incidence stroke studies around the world that can be explained by the young structure of our population (Azarpazhooh et al. 2010). Hence a high rate of CVD may be anticipated during the aging transition of our population. In the present study, our estimated risk for future CAD was in line with

Table 5 Age-standardized distribution of CVD risk factors among participants in MASHAD study, Mashhad, Iran, 2010

	HDL < 35			LDL > 160 (%)			Hypertensive		
	n	Crude rate	Standardized rate	*n*	Crude rate	Standardized rate	*n*	Crude rate	Standardized rate
Men									
35–39	207	31.2		46	7.0		86	13.0	
40–49	471	32.9		115	8.2		253	17.6	
50–59	409	31.4		124	9.7		406	32.2	
60–64	163	32.7		24	8.9		208	41.6	
Total	1250	32.1	32.0	329	8.6	8.5	953	24.4	23.4
Women									
35–39	181	16.0		58	5.1		86	7.5	
40–49	343	14.7		217	9.2		421	17.8	
50–59	210	11.7		297	16.6		598	33.2	
60–64	80	14.6		115	21.2		250	45.5	
Total	814	14.0	14.0	687	11.8	11.9	1355	23.2	23.2
Total population									
35–39	388	21.5		104	5.8		172	9.5	
40–49	814	21.6		332	8.8		674	17.7	
50–59	619	20.0		421	13.7		1004	32.4	
60–64	243	23.2		159	15.3		458	43.6	
Total	2064	21.3	21.3	1016	10.5	10.4	2308	23.7	23.2

	Cholesterol > 240			Diabetes		
	n	Crude rate	Standardized rate	*n*	Crude rate	Standardized rate
Men						
35–39	40	6.1		34	5.1	
40–49	114	8.1		151	10.5	
50–59	131	10.2		244	18.7	
60–64	48	9.6		98	18.6	
Total	333	8.6	8.4	527	13.5	13.1
Women						
35–39	50	4.4		60	5.3	
40–49	203	8.6		279	11.8	
50–59	340	19.0		358	19.9	
60–64	125	23.1		150	27.3	
Total	718	12.3	12.5	847	14.5	14.5
Total population						
35–39	90	5.0		94	5.2	
40–49	317	8.4		430	11.3	
50–59	471	15.3		602	19.4	
60–64	173	16.6		248	23.6	
Total	1051	10.9	10.6	1374	14.1	13.8

CVD cardiovascular disease, *TC* total cholesterol, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *SBP* systolic blood pressure, *DBP* diastolic blood pressure

[a] Values are standardized to the WHO reference population

findings from the USA population. Data from the NHANES III in the USA have indicated that among participants without CVD, 81.7 % had a 10-year risk for CAD of <10 %, 15.5% of 10–20 % and 2.9 % of >20 %. Data from a previous cohort in Iran, the Tehran Lipid Glucose Study (TLGS), estimated the 10-year risk for CAD of <10 %, 10–20 % and >20 % to be 86.0, 12.0 and 2.0 % among participants with two or more risk factors and

Table 6 Age and gender-stratified distribution of CAD risk among Mashhad study participants, Mashhad, Iran, 2010

	10-year CAD risk prediction		
	<10 %	10–20 %	>20 %
Men			
<40	592 (92.64 %)	40 (6.26 %)	7 (1.1 %)
40–49	1131 (84.87 %)	143 (10.70 %)	59 (4.43 %)
50–59	635 (55.60 %)	411 (35.99 %)	96 (8.41 %)
>60	35 (8.66 %)	315 (77.98 %)	54 (13.37 %)
Total	2393 (68.02 %)	909 (25.84 %)	216 (6.14 %)
Women			
<40	1086 (99.72 %)	3 (0.28 %)	
40–49	2153 (99.09 %)	18 (0.82 %)	2 (0.09 %)
50–59	1549 (98.73 %)	20 (1.27 %)	0 (0 %)
>60	421 (96.56 %)	15 (3.44 %)	0 (0 %)
Total	5209 (98.90 %)	56 (1.06 %)	2 (0.04)
Total population			
<40	1678 (97.11 %)	43 (2.49 %)	7 (0.41 %)
40–49	3284 (93.66 %)	161 (4.59 %)	61 (1.75 %)
50–59	2184 (80.57 %)	431 (15.90 %)	96 (3.54 %)
>60	456 (52.29 %)	330 (39.29 %)	54 (6.43 %)
Total	7602 (86.53 %)	965 (10.98 %)	218 (2.49 %)

10-year risk calculation was done with NCEP ATPIII criteria

Percentage amounts are based on each specified age group in each column

CAD coronary artery disease

without CVD or a CVD risk equivalent, respectively. These comparisons indicate that along with rapid westernization in developing countries including Iran, the risk of CAD may increase to levels similar to, or indeed exceeding those within many developed countries.

The various aspects of socioeconomic status (SES) have a complex impact on cardiovascular health, and this may differ in men and women in various communities. In a previous cohort of an Iranian population from Isfahan, the authors found no independent association between the SES and incident CVD (Masoudkabir et al. 2012). It is anticipated that our cohort will provide additional data for exploring the association between SES and cardiovascular disease among men and women in our population.

Furthermore, the genetic susceptibility loci for CAD, stroke and atrial fibrillation are largely unknown in the Middle-Eastern populations. Our bank of blood and DNA samples will enable us to study the role and the contribution of genetic and environmental factors to CVDs in this population.

Our project also has the potential to influence the implementation of community interventions to target smoking, unhealthy diet, and physical inactivity. We will also have potential for other interventions throughout the course of the project targeting the community in general. The design of our study will enable us to reach individuals who would not normally seek medical help, and therefore has the potential to reduce the inequalities in utilization of services. This will enable us not only to determine CVD risks, but also to evaluate the impact of community interventions for disease prevention and risk reduction.

Whilst the participation rate was high in our study, there is still the possibility for non-participation bias and differential misclassification of CVD risk factors among different SES, gender or age groups. A random sample of non-respondents did not show significant difference regarding age and gender. Therefore, we can assume that non-respondent bias in the study was small and the respondents were generally representative of the target population. However, our data could result in spuriously high estimates of risk factor and disease prevalence if the non-response rate and/or the baseline differences had been considerably larger. This is mainly because individuals with known disease conditions are more likely to seek free medical evaluations. Also, our sample is mainly from urban population that may limit generalizability of our findings to rural populations.

Finally, it has been demonstrated that more locally based risk engines such as QRISK in the UK, may perform better in predicting clinical outcomes (Hippisley-Cox et al. 2007). In addition, most of these CVD risk algorithms are based on a limited set of variables that do not include

factors such as obesity, physical activity, psychosocial status, family history of CVD, genetic susceptibility, etc. Additional emerging risk factors for CVD, for example hs-CRP and inflammatory biomarkers and plasma fatty acid concentrations may also need to be considered for inclusion to improve these algorithms. We have also developed a comprehensive model for quality assurance and several validated instruments that will allow comparisons with the results of other epidemiological studies that provides a basis for international collaboration. In conclusion, our 10-year follow-up results would provide a useful resource to help address the above-mentioned epidemiologic and public health issues in anticipation of a significant increase of persons at risk for CAD and stroke in our young but aging population.

Conflict of interest Authors have no conflict of interest to disclose.

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