Trends of Major Cardiovascular Risk Factors in Iranian Population During Years 2001 - 2013: The Isfahan Cohort Study

Masoumeh Sadeghi [1], Kiyan Heshmat-Ghahdarijani [2, *], Nizal Sarrafzadegan [3], Mohammad Talaei [4], Minoo Dianatkhah [5], Mehrbod Vakhshoori [2] and Hamidreza Roohafza [3]

[1]Cardiac Rehabilitation Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran
[2]Heart Failure Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran
[3]Isfahan Cardiovascular Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran
[4]Saw Swee Hock School of Public Health, National University of Singapore, Singapore
[5]Interventional Cardiology Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran

*Corresponding author: Cardiology Department, Isfahan University of Medial Sciences, Isfahan, Iran. Tel: +98-9131133949, Email: kiyan_heshmat@yahoo.com

Abstract

Background: Trends of major cardiovascular risk factors are less investigated in Middle-Eastern countries.
Objectives: This study aimed to assess the trend of major cardiovascular risk factors among Iranian individuals.
Methods: This Longitudinal population-based study was performed by multistage random sampling on 6504 participants aged at least 35 years for 12 years initiating in 2001 until 2013 in three phases. Cardiovascular risk factors including systolic blood pressure (SBP), diastolic blood pressure (DBP), waist circumference (WC), waist to hip ratio (WHR), body mass index (BMI), fasting blood sugar (FBS) and lipid indices were measured for each subject in 2001, 2007 and 2013 and were analyzed using repeated measure analysis of variance using Bonferroni correction.
Results: Mean value of SBP, DBP, BMI and FBS increased significantly in both genders during follow-up (SBP: 119.3 ± 18.7 to 128.4 ± 17.5 mmHg, P value < 0.001, DBP: 76.7 ± 11.8 to 82.8 ± 12.5 mmHg, P value < 0.001, BMI: 27.4 ± 4.4 to 28 ± 4.6 kg/m^2, P value < 0.001, FBS: 86.7 ± 29.6 to 106.5 ± 38 mg/dL, P value < 0.001). Lipid profiles including total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C) and TG/ high-density lipoprotein cholesterol (HDL-C) showed favorable downward patterns in population (TC: 219.5 ± 51.3 to 200.1 ± 40.9 mg/dL, P value < 0.001, TG: 200.2 ± 110.3 to 155.1 ± 85 mg/dL, P value < 0.001, LDL-C: 132.6 ± 42.4 to 111.7 ± 27.8 mg/dL, P value < 0.001, TG/HDL-C: 4.5 ± 2.8 to 3.9 ± 2.8, P value < 0.001) with an exception of HDL-C showing less desirable results. In spite of controversial results in terms of WC and WHR changes relative to gender, total population changes of those variables were not significant.
Conclusions: Although favorable patterns were observed in most lipid indices, other risk factors showed an inverse or insignificant trend. Several health-promoting strategies are required in order to improve lifestyle in a way that those raising cardiovascular risk factor trends would decline.

Keywords: Blood Glucose, Blood Pressure, Body Mass Index, Cardiovascular Diseases, Cohort Study, Iran, Life Style, Lipids, Risk Factors, Waist Circumference, Waist-Hip Ratio

1. Background

Despite the improvement in health-care systems and increasing life expectancy, cardiovascular diseases (CVDs) are the leading cause of mortality in developing countries, especially in low and middle-income ones in a way that it has been predicted more than 23.6 million deaths will occur annually by the year 2030 (1-3). While a decline in CVDs' incidence in developed regions has been observed, which is far from optimal yet, cardiovascular events remain the leading cause of death globally (1, 2, 4). A great economic burden which is caused by this category of disease is in-

evitable. For example, annual attributable costs for CVDs in America and European countries were estimated to be $149 billion and €169 billion, respectively (5, 6). In China, 26.1 billion US dollars had been estimated to be spent each year as direct costs for these events (7). Several risk factors most of which are preventable have been demonstrated to play a role in CVD pathogenesis. The three most common causes which have been investigated in multiple studies and mostly resulted from western lifestyle patterns like sedentary lifestyle, stress, high caloric food intake and lack of exercise include tobacco usage, hypertension, and hyperlipidemia especially abnormal cholesterol levels (8-11).

In several Middle-Eastern developing countries, especially Iran, the transition period has initiated, and most of the behavioral and dietary habits are now becoming westernized. Multiple studies with their particular designs have been done investigating the trends of cardiovascular risk factors on different populations (12, 13). For instance, in a cohort study done by Liu and colleagues a total number of 6624 Chinese workers and farmers aged between 25 and 64 years were recruited in order to assess the trends of cardiovascular event risk factors in a follow-up duration of 10 years. The final outcomes revealed that despite the decreased smoking prevalence, body mass index (BMI) and blood pressure levels were heightened significantly plus unfavorable results in terms of lipid profiles (12). Also, the relations of other modifiable risk factors with mortality due to CVD were assessed in other studies during 12 years and showed that the increasing patterns of some variables including cholesterol, systolic blood pressure, BMI and diabetes were main contributors of raising death rates (13). Due to diversity in cultures and different dietary habits and limitations of relevant prospective cohort studies, a thorough survey is mandatory. To date, there are few studies done in Iran in order to assess these kinds of patterns. One of these studies was performed on elderly individuals in just one city of Iran with a follow-up duration of 8.7 years (14).

2. Objectives

This article aimed to define the trends of major cardiovascular risk factors among Iranian adults in a 12-year follow-up duration in three consecutive phases with 6-year intervals.

3. Methods

3.1. Study Population

This study was in the context of a cohort project called Isfahan cohort study (ICS). ICS is a longitudinal prospective population-based study initiated in the year 2001 in both urban and rural areas of three different cities in Iran (Isfahan, Arak, and Najafabad) the methodology of which had been discussed elsewhere (15). Isfahan healthy heart program (IHHP) had been determined as an original source for participant enrollment. This cohort study was performed in urban and rural individuals living in the aforementioned counties. Based on the population at that time, two-stage cluster random sampling method was utilized in order to recruit eligible participants. Poliomyelitis campaign conducted by Iranian Ministry of Health was used and random census blocks were selected from each county.

Isfahan, Arak, and Najafabad were divided to 93, 60 and 47 clusters, respectively. Each cluster was defined to be equal to 1000 households. By random sampling method 25, 23, and 15 clusters were selected from the aforementioned cities, respectively. With 90% of power for detection of relative risk of 0.75 at a significance level of 0.05 plus estimating the prevalence of cardiovascular risk factors would be 0.2, IHHP sample size was estimated to be 12600 in which 99.3% (n = 12514) of individuals of at least 19 years were eligible for recruitment from January 2nd until September 28th of 2001 in the baseline survey (16). By multistage random sampling, 6504 non-pregnant mentally competent individuals with Iranian nationality aged at least 35 years and without any apparent CVDs were eligible for enrollment in the study. All participants received and signed a written consent form. From that total number of recruited individuals, 3356 and 1735 subjects completed the first and second follow-ups, respectively. The response rate was 51.59% and 26.67% in each follow-up period. Data merging of other individuals could not be utilized due to the absence of participating in both follow-ups, death occurrence during study time and presence of data inaccuracy in each phase which caused a missing rate of 48.41% and 73.33%, respectively; mainly because of all aforementioned factors being defined as exclusion criteria. Finally, information of 20.98% of the total study population (n = 1365) participating in the entire follow-up was available for analysis. The flow diagram of the current study at the baseline and during follow-ups is represented in Figure 1. All procedures performed in the current research were completely compatible with ethical criteria and with Helsinki declaration in 1964. At any time during the entire follow-up all participants were completely free getting out of the project without any probable consequences. This study was approved by the Ethics Committee affiliated with Isfahan Cardiovascular Research Center, which is a World Health Organization (WHO) collaborating center.

3.2. Assessment of Variables

Blood pressure indices [systolic blood pressure (SBP) and diastolic blood pressure (DBP)] were measured twice using a calibrated sphygmomanometer and appropriate sized cuff in a sitting position and the mean value was computed and considered as blood pressure of each participant. Waist circumference (WC) was measured at the midpoint between costal region and iliac crest. Waist to hip ratio (WHR) was defined by dividing waist over hip circumference. After approximately 12 hours of fasting, blood sample was taken from each participant in order to assess laboratory variables. An autoanalyzer (Eppendorf, Hamburg, Germany) was used for determining to-
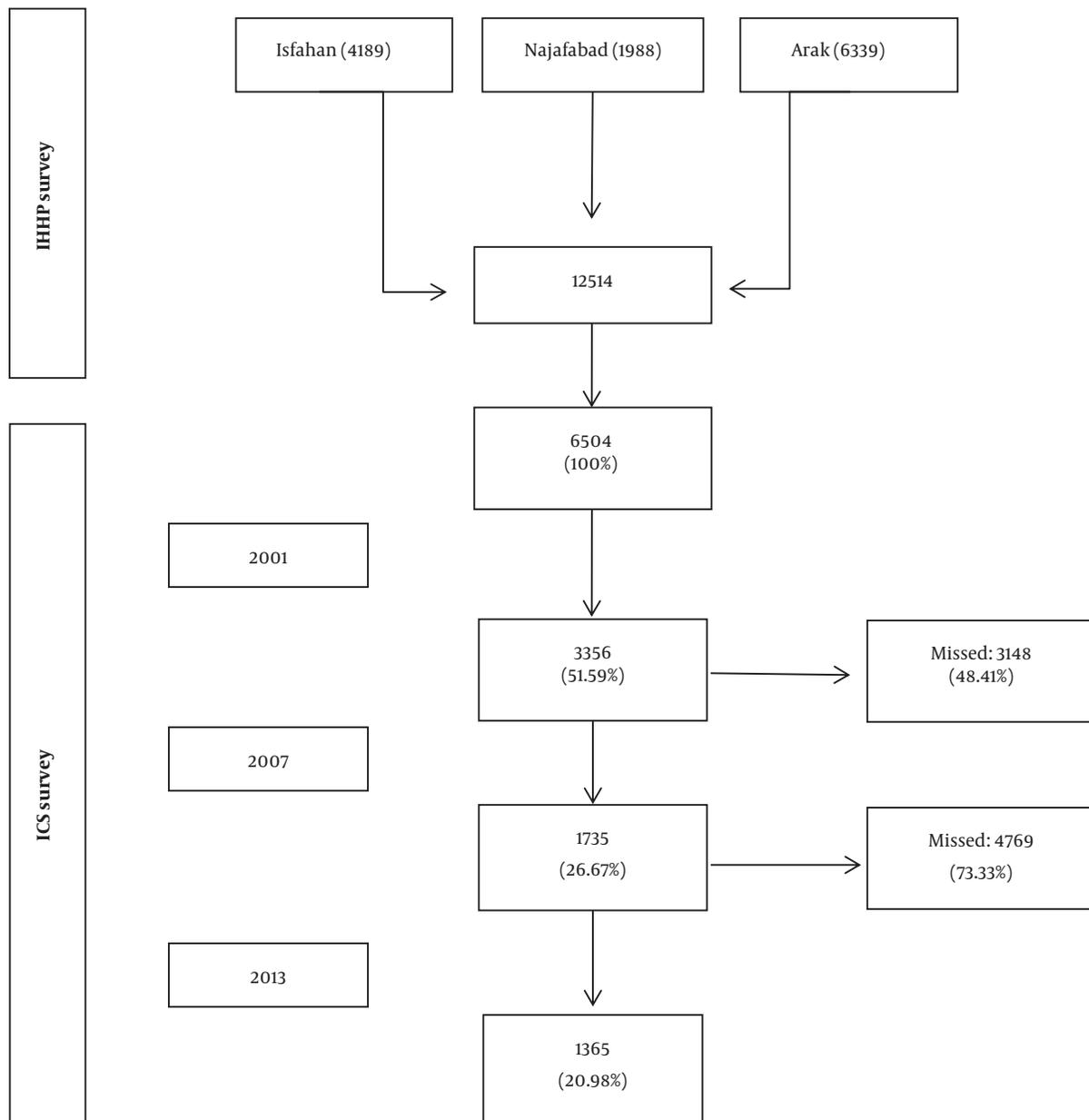
Figure 1. The flow diagram of study

tal cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and fasting blood sugar (FBS). TG/HDL-C ratio was assessed through the division of TG over HDL-C. All measurement tools including blood pressure sphygmomanometer, metal tape, weight scale and auto analyzer used for laboratory data assessment were utilized by fully trained personnel, and all aforementioned devices were calibrated by a standard method in pre-defined durations.

3.3. Follow-Up Surveys

Every two years, a telephone-based interview was done for each participant. Individuals were invited every five years to come to health care clinics for performing thorough medical interview, physical examinations, and laboratory tests like baseline survey. Data of baseline survey and two consecutive phases with a 6-year interval period (2001, 2007 and 2013) were used for analysis.

3.4. Statistical Analysis

Continuous and categorical data were reported as mean $\pm$ standard deviation (SD) and frequency (percentage), respectively. Repeated measure analysis of variance with Bonferroni as post hoc was used to evaluate differences between years. The Greenhouse-Geisser correction was used if Mauchly's test of sphericity was significant. All data were analyzed using IBM Statistical for Windows, version 22 (IBM Corp, Armonk, N.Y., USA), and P values less than 0.05 were considered statistically significant. Due to the presence of one observer, there was no need to use any agreement indexes like kappa coefficient.

4. Results

Mean age of individuals at baseline was 47.3 ± 9.11 years and females posed the dominant percentages of participants (51.6% vs. 48.4%). The general cardiovascular risk factor trends among all individuals were shown in Table 1. During the first follow-up, a significant rising trend was observed in terms of SBP, DBP, BMI, and FBS, but WC plus all lipid profiles except in terms of HDL showed a declining trend ($P < 0.001$). WHR changes were not statistically significant. Similar risk factors patterns were observed from 2007 to 2013 with an addition of declining trend in HDL ($P < 0.001$). Analysis of the entire follow-up period revealed that during 12 years, SBP, DBP, BMI, and FBS increased and TC, TG, HDL-C, LDL-C and TG/HDL-C decreased significantly ($P < 0.001$). There was no statistically significant relation with WC and WHR from 2001 through 2013.

Gender specified analyses were depicted in Figure 2. Both men and women showed significant increasing levels of SBP and DBP during follow-up, except females in terms of DBP trend from 2001 - 2007 ($P = 0.2$). Mean WC of male and female individuals showed a declining trend in the first follow-up, but a raising pattern was observed from 2007 to 2013 (92.5 ± 10 cm to 97.2 ± 10.3 cm for men, 95.1 ± 12.1 cm to 97.9 ± 12 cm, $P < 0.001$). In terms of WHR, increasing and decreasing patterns were observed among men and women, respectively, except in females' ratio during the first follow-up, which showed no significant relationship ($P = 0.08$). From 2001 to 2007, BMI trend was insignificant for men ($P = 0.06$), but overall raising patterns were observed among both genders. Laboratory parameters showed that during two follow-up periods, FBS and TC patterns were vice versa in which the former and latter had increasing and decreasing trends, respectively. Both sexes showed a dropping level of other lipid profiles like TG and LDL-C during 12 years of follow-up with an exception of females' TG in the second phase ($P = 0.2$). The mean males' HDL-C decreased significantly during these two follow-up surveys, but females showed an increasing and decreasing HDL-C level in the first and second follow-ups, respectively. Decreasing TG/HDL-C ratio was observed in both genders in which it was significant for men and women in the second and first survey, respectively.

5. Discussion

The aim of our study was investigating the trends of major CVDs risk factors among Iranian adults. The data revealed that through a 12-year period, lipid profiles including TC, TG, LDL-C, and TG/HDL-C ratio showed favorable changes, unlike blood pressure, BMI, FBS and HDL-C which displayed an increasing trend. We found no significant variation in terms of WC and WHR during the entire follow up survey. Due to leading causality of CVDs in mortality rate and developing great economic burden, monitoring and early management of major cardiovascular risk factors would be beneficial by declining the rising incidence trend of cardiovascular events.

Our data demonstrated that both SBP and DBP raised significantly among both genders during 12 years. In agreement with our findings, several studies showed similar results (14, 17). Huang et al.'s results based on two community-based cross-sectional studies were done, ten years apart, revealed that mean SBP and DBP increased

Table 1. Mean Cardiovascular Diseases Risk Factor Trends in the Study Population During 2001 - 2013

Parameters	2001	2007	2013
SBP, mmHg	119.3 ± 18.7	124.2 ± 18.3^a	$128.4 \pm 17.5^{b,c}$
DBP, mmHg	76.7 ± 11.8	78.3 ± 10.3^a	$82.8 \pm 12.5^{b,c}$
WC, cm	97.7 ± 11.2	93.9 ± 11.1^a	97.5 ± 11.2^c
WHR	0.94 ± 0.06	0.94 ± 0.07	0.94 ± 0.07
BMI, kg/m^2	27.4 ± 4.4	27.7 ± 4.3^a	$28 \pm 4.6^{b,c}$
FBS, mg/dL	86.7 ± 29.6	101.4 ± 38.7^a	$106.5 \pm 38^{b,c}$
TC, mg/dL	219.5 ± 51.3	210.1 ± 42.4^a	$200.1 \pm 40.9^{b,c}$
TG, mg/dL^d	$174 (121 - 245)$	$143 (93 - 214)^a$	$137 (102 - 182)^{b,c}$
HDL-C, mg/dL	47 ± 10.3	46.7 ± 11.3	$43.6 \pm 10.5^{b,c}$
LDL-C, mg/dL	132.6 ± 42.4	127.3 ± 30.2^a	$111.7 \pm 27.8^{b,c}$
TG/HDL-C	4.5 ± 2.8	4.1 ± 3.7^a	$3.9 \pm 2.8^{b,e}$

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; FBS, fasting blood sugar; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride; WC, waist circumference; WHR, waist to hip ratio.
[a] P value between 2001 and 2007 and < 0.01.
[b] P value between 2001 and 2013 and < 0.01.
[c] P value between 2007 and 2013 and < 0.01.
[d] Triglyceride was reported as median (IQR) because of non-normality distribution and tested with Mann-Whitney u-test.
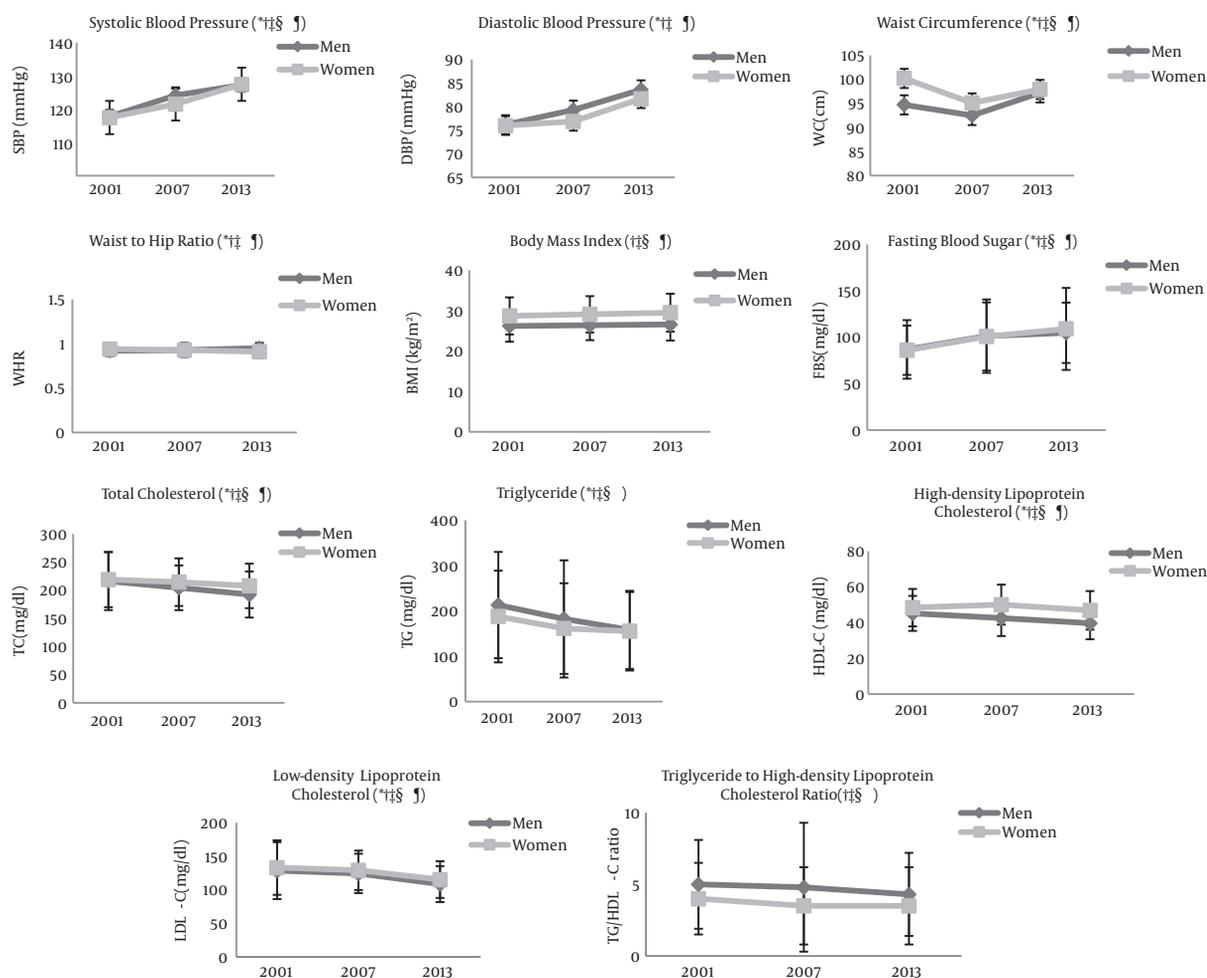[e] P value between 2007 and 2013 and < 0.05.

Figure 2. Mean cardiovascular diseases risk factor trends specified by gender from 2001 till 2013.*: P values < 0.05 for men from 2001 to 2007, †: P values < 0.05 for men from 2001 to 2013, ‡: P values < 0.05 for men from 2007 to 2013, §: P values < 0.05 for women from 2001 to 2007, ||: P values < 0.05 for women from 2001 to 2013, ¶: P values < 0.05 for women from 2007 to 2013.

from 117.8 ± 33.9 to 132 ± 21.2 mmHg and 75.3 ± 19.1 to 79.3 ± 11.2 mmHg, respectively (17). An Iranian cohort study done on 1490 participants aged at least 60 years demonstrated that during a median follow-up of 8.76 years, DBP increased significantly in both genders, but SBP remained steady throughout the phases (14). In contrast, a number of studies mostly performed in developed countries showed a reverse trend (4, 18). Six population-based surveys performed from 1986 to 2009 in Sweden revealed that on a total of 10586 participants aged 25 - 64 years, their blood pressure decreased by 1.8/1.5 and 4.9/3.9 mmHg in terms of systolic and diastolic pressures, respectively (4). A 4-year follow-up duration in Finland showed a decreasing pattern of both SBP and DBP in both genders (SBP: -4% in men, -3% in women, DBP: -3.3% in men, -3% in women) (18).

It seems that successful health-promoting programs and healthy dietary changes would play essential roles in decreasing blood pressure indices trend in developed countries. The present study showed an increasing trend in terms of blood pressure components during follow-up. There are several factors responsible for this possible association. Iran is a developing country, but industrialization has been initiated and this country is experiencing a transition situation. Due to urbanization, work-related stress becomes prominent, and could be an explanation for this growing pattern (17). Furthermore, several other factors like increasing BMI and obesity, dietary habits changing and sedentary lifestyle have some influences in this kind of relationship (4, 17, 19). One important element which has been demonstrated to be effective in increasing blood

pressure is salt intake. According to WHO, maximum daily salt intake should have to be 5 grams, but the mean salt consumption of Iranian individuals is 10 - 15 grams (14). Since blood pressure is one of the preventable CVDs risk factors, designing and performing health-promoting programs in order to reverse this pattern should be one of the most important priorities of health care managers.

In terms of anthropometric variables, our findings suggested that there was only an increasing pattern observed for BMI and the mean of WC and WHR remained constant during follow-up. Several studies confirmed the growing pattern of obesity and increasing BMI among individuals worldwide (14, 20, 21). In line with our findings, a comprehensive Iranian cohort study on older people revealed a rising trend of BMI in both sexes (14). Preis et al.'s study demonstrated that BMI increased by 0.39 kg/m² per every ten years (20). Furthermore, this growing pattern was observed among children and adolescents. Analysis of two cross-sectional studies on 72755 students aged 7 - 18 years demonstrated an increasing BMI pattern (21). BMI has direct positive effect on both SBP and DBP, and increasing these two variables concomitantly would cause a great raising of CVDs incidence and prevalence in which our findings were in agreement with elevation of both variables (4). Thus, it is mandatory for health care policy makers inventing projects declining these unfavorable trends. Although there was no statistically significant alteration observed with WC and WHR in total population during the whole follow-up, these variables showed an increasing and decreasing trend between males and females, respectively. Within two follow-ups, inconsistent results were found. This finding might be explained by the presence of greater awareness of females in conjunction with health issues in comparison with men (22). Multiple prospective studies are required investigating differences found between those aforementioned patterns among genders.

The present study showed an increasing pattern of FBS during two follow-ups in both genders. With respect to this finding, several studies demonstrated this growing pattern, ultimately leading to raised diabetes mellitus prevalence. A systematic analysis on 2.7 million individuals aged at least 25 years from 199 countries during 1980 to 2008 announced that age-standardized mean fasting plasma glucose (FPG) for males and females was 5.5 mmol/L (95% uncertainty interval: 5.37 - 5.63) and 5.42 mmol/L (95% uncertainty interval: 5.29 - 5.54), respectively at the end. For each ten year, mean FPG increased by 0.07 mmol/L in men, and 0.09 mmol/L in women (23). Furthermore, two cross-sectional studies done seven years apart on at least 6600 participants aged more than 35 years showed that from 2009 to 2016, the overall prevalence of impaired FPG raised from 8.4% to 19% (24). The imbalance between energy intake and expenditure, leading to disturbed BMI and obesity, plays pivotal role for this circumstance. Declining physical activity and increasing sedentary lifestyle plus diet quality and possible mental and social stress might explain a part of this growing pattern. Moreover, in spite of widespread usages of specific drugs designed for declining some major cardiovascular risk factors including hypercholesterolemia or HTN, medication specifically designed for primary prevention and management of glycemic indices are being investigated yet (23). Unless health care managers execute general health seeking strategies in order to decrease this rising trend, we would see a diabetes epidemic in the early future.

Although HDL-C trend was less desirable, other lipid indices showed a downward favorable pattern. A number of studies were consistent with our findings in this regard and confirmed decreasing indices among nations (4, 14, 25). Based on Eriksson et al.'s study performed on 10586 individuals resulting from six population-based surveys from 1986 till 2009, cholesterol levels decreased by 0.9 mmol/L (4). From 2002 to 2014, favorable lipid indices trends including TC, TG, HDL-C, and LDL-C were observed among at least 1400 older Iranian subjects (14). Moreover, these desirable patterns were also observed among Iranian children and adolescents. LDL-C levels decreased significantly in boys within all age groups and girls aged 7 - 17 years. In terms of TC decreasing pattern observed among all boys, but the only significant age group among Iranian girls was 7 - 12 years. TG just showed a considerable decreasing pattern among boys aged 7 to 12 years (25). Several possibilities might explain these favorable findings. This downward trend might be due to dietary habit changing and decreasing consumption of trans-fatty acids and carbohydrates. Furthermore, those patterns could be the outcome of more usage of lipid-lowering drugs due to increased level of diagnosing and treating of people suffering from disturbed lipid profiles. Also, successful general health education programs on media could be partly effective for these desirable trends (4, 14).

Further to a quite large sample size and worthiness of cohort studies in comparison to other ones, three-time assessments of all intended variables during 12 years in order to remove diversity effect was another strength of our study. Furthermore, this research was the first in the literature evaluating the trends of major cardiovascular risk factors in one of the countries passing the rapid era of industrialization with a reasonable period of follow-up duration in order to assess the precise trend of previously aforementioned contributing risk factors. All measurements were done using calibrated tools with standard methods. By the way, this present article was not free from limitations. The most primarily restriction was missing of par-

ticipants which is inevitable in cohort designed studies. Moreover, a less accurate method of obtaining medication data by the self-reported way, and absence of assessing psychiatric, smoking and physical activity information were some other limitations making caution for generalization of findings.

5.1. Conclusions

Although unfavorable trends were observed in terms of blood pressure components, BMI, FBS, and HDL-C levels, other lipid indices showed downward patterns. Due to high mortality and morbidity of CVDs, it is necessary for policy makers designing ideas and performing multiple health-promoting programs in order to terminate those inappropriate patterns.

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Footnotes

Authors' Contribution: Study concept and design: Masoumeh Sadeghi, Kiyan Heshmat-Ghahdarijani, and Nizal Sarrafzadegan. Analysis and interpretation of data: Masoumeh Sadeghi, Minoo Dianatkhah, and Mohammad Talaei. Drafting of the manuscript: Kiyan Heshmat-Ghahdarijani and Mehrbod Vakhshoori. Critical revision of the manuscript for important intellectual content: Masoumeh Sadeghi, Kiyan Heshmat-Ghahdarijani, Nizal Sarrafzadegan, and Roohafza. Statistical analysis: Minoo Dianatkhah and Mehrbod Vakhshoori. Study supervision: Masoumeh Sadeghi, Kiyan Heshmat-Ghahdarijani, and Nizal Sarrafzadegan.

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