

## Review Article

# Cardiovascular Disease in Iran in the Last 40 Years: Prevalence, Mortality, Morbidity, Challenges and Strategies for Cardiovascular Prevention

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Four decades ago, Iran encountered rapid sociodemographic and economic transitions. This review was carried out to investigate the trend of cardiovascular disease (CVD) prevalence, mortality and morbidity, relevant challenges and suggestions for prevention of CVD. In Iran, the most prevalent causes of death have transitioned from infectious and diarrheal diseases in 1960 to CVD few decades ago. CVD was the first leading cause of mortality and a million disability adjusted life years (DALYs) led to 46% of all deaths and 20%-23% of the burden of disease in Iran. Ischemic heart disease and stroke are considered the first and second cause of death and DALYs in Iran, respectively. CVD rising epidemic might be related to socioeconomic and cultural changes, nutrition transition, inadequate physical activity, industrialization and urbanization and increasing life expectancy, increasing metabolic and physical risk factors, low accessibility and affordability to primary care and treatment, and low compliance because of economic and psychological problems. Thus, planning and implementing strategies for prevention and control of the disease and its risk factors are on top of the ministry of health agenda in the recent years. Health promotion strategies to prevent and control CVD risk factors, early detection of the disease and treatment of acute and chronic CVD events are essential elements for reducing the burden of CVD in Iran.

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**Introduction**

Cardiovascular disease (CVD) are the global leading cause of premature death.<sup>1</sup> CVD led to about 17.9 million deaths in 2012 and 347.5 million disability adjusted life years (DALYs) were due to CVD in 2015 worldwide.<sup>1</sup> The majority of CVD deaths are due to ischemic heart disease (IHD) and stroke and one third occur in those aged less than 70 years. IHD induced 8.1 million deaths in 2013 which was the most frequent in developing countries with nearly 164 million DALYs in 2015.<sup>2,3</sup> It was predicted that CVD would be the cause of more than 23 million (about 30.5%) deaths by 2030 worldwide.<sup>4,5</sup> Although in the last decades, CVD mortality rates decreased in high income regions,<sup>6</sup> 50% of CVD mortality and 80% of the CVD global burden have occurred in low- and middle-income countries (LMIC) mostly in the Eastern Mediterranean Region (EMR). In which it is a growing epidemic problem in recent years.<sup>7</sup> Iran may have the highest burden of CVD in the EMR.<sup>8</sup> According to the global burden of diseases (GBD), the prevalence of hypertension was more than 25% in the adult population globally in 2000. It has been estimated to grow by 60% to a total of 1.56 billion in 2025. It is the second contributor to GBD and is a main

health challenge especially in the LMIC.<sup>9</sup>

In the last four decades, Iran has encountered rapid sociodemographic and economic transitions. The war with Iraq was very close to the Islamic revolution, several earthquakes and political sanctions have possibly affected the country's economic status. On the other hand, growing urbanization, significant reduction in fertility and communicable disease prevention and control by improved access to primary health care (PHC),<sup>10</sup> which subsequently led to increasing life expectancy,<sup>11</sup> shifted the public health problems in the society to non-communicable disease (NCD). The developing health system in rural areas, establishing more medical universities and improving health care services by increasing hospitals and physicians per capita around the country<sup>3</sup> are possibly other effective aspects in CVD progression and early detection.

As the health care system in Iran faced many transitions in the last few decades, we aimed to review the trend of CVD burden like prevalence, mortality and morbidity as well as relevant challenges and suggestions for prevention.

**Cardiovascular Disease in Iran**

In Iran, the most prevalent causes of death have transitioned

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from infectious and diarrheal diseases in 1960 to CVD a few decades ago.<sup>11</sup> CVD mortality increased from 26.6% in 1981 to 47.3% in 1995.<sup>13</sup> According to GBD's previous reports in 2010 and 2015, CVD was the first leading cause of mortality and DALYs that led to 46% of all deaths and 20-23% of the burden of diseases in Iran.<sup>3,14,15</sup> The GBD 2010 revealed that CVD mortality and DALY rates were higher in Iranian men than women. However, Isfahan Cohort Study (ICS) reported that the 10-years difference has decreased in occurrence of CVD between men and women.<sup>16</sup> In agreement with some prior studies,<sup>8</sup> among all CVD, IHD with about 26% of total deaths and 11% of total burden of disease in 2015 was the first while ischemic stroke was the second cause of death and DALY in Iran.<sup>14</sup> According to GBD 2015, Iran with more than 9000 cases of CVD per 100 000 persons was one of the countries with the highest CVD rate in the world.<sup>15</sup> ICS reported that age-adjusted incidence rates of total CVD was 1307 in 100 000 person-years and various types of CVD events including CVD mortality, total coronary heart disease (CHD) and stroke were 328, 1027 and 280 in 100 000 person-years, respectively. In comparison to previous studies, CVD risk was higher in young participants, particularly in women, and there was less difference between the occurrence of IHD among men and women and urban and rural areas compared to previous reports.<sup>17</sup>

### Ischemic Heart Disease

Consistent with the global decrease in age-standardized IHD mortality, years of life lost (YLL), years lived with disability (YLD) and DALY were decreased from 1990 to 2010 in Iran. However, by increasing life expectancy and population growth, the total burden of IHD was increased and IHD mortality remains as the most important contributor to disease burden.<sup>18</sup> In addition, death rate due to IHD in Iran was 174.9 per 100 000 and higher than global rate in 2010.<sup>3</sup> About four decades ago, Iran had the greatest increase in life expectancy by 21 years for men and 22 years for women among other countries in the world.<sup>19</sup>

CHD prevalence was 19.4% in Isfahan city which was more prevalent in women than men in 1999.<sup>20</sup> However, the GBD 2014 study indicated that the prevalence of IHD and relevant DALYs rate were higher in men than women and increased by age in Iran which was consistent with GBD results at global level.<sup>6</sup> Other studies<sup>6,18,21,22</sup> reported similar results. Besides the well-known hormonal effects in women, it might be due to higher adherence to lifestyle modification and more use of primary care in women than men.<sup>23</sup> In addition, the 50% and 33% of DALYs rate rise in men and women aged less than 60 years can lead to higher burden of IHD in productive years of life and ultimately to economic problems.<sup>24</sup> According to several studies in Tehran and 3 districts in central part of Iran, the incidence of CHD was around 12 and less than 9 per 1000

person-years in men and women, respectively (17,25). As a comparison, the incidence rate of CHD in different parts of Iran had the average rate of CHD among other countries in the world.<sup>25</sup>

Given the above reasons, primary prevention of CVD is necessary, especially in youth.<sup>26</sup> In spite of many developments in diagnostic and new treatment procedures for IHD that are available in many parts of the country nowadays, IHD burden is still high. This may be due to socioeconomic and cultural changes, unhealthy lifestyle including nutrition transition, inadequate physical activity because of industrialization and urbanization, increasing life expectancy, increasing metabolic and physical risk factors, low accessibility and affordability to primary care and treatment, low compliance because of economic and psychological problems.

MI is one of the most important health problems increasing in Iran and worldwide.<sup>17,27-29</sup> In-hospital MI mortality rate was 8.36 and 6.12 in 100 person-years in Iranian women and men in 2012, respectively.<sup>28</sup> The increasing death rate in MI patients was associated with being women, aged over 65 years, illiterate and having low socioeconomic status.<sup>30</sup> Even after 30 days, MI mortality rate was higher in Iran than some European countries.<sup>31</sup> However, the contributing factors were similar in Iran, USA and many European countries.<sup>32,33</sup> In addition, factors like chest pain before hospital admission, no thrombolytic therapy, smoking, right bundle branch block, ST elevation MI (STEMI), lateral MI, and ventricular tachycardia were other contributors for MI mortality in Iran.<sup>34</sup>

The prevalence of registered STEMI patients was about higher than non-STEMI in Iran.<sup>35</sup> It might be due to decreasing non-STEMI patients before hospital arrival.<sup>35</sup> Another study found that the frequency of STEMI was 13.6% of whole registered patients in four years.<sup>36</sup> However, around 25% of Iranian acute coronary syndrome (ACS) patients had STEMI, which was in line with the findings in high income countries (HIC) and higher than LMIC and Middle East countries. Although the time between start of chest pain and arrival to the hospital had some delay, reperfusion in-hospital was well-timed in Iranian STEMI patients.<sup>37</sup> One of the most important in-hospital death in MI patients was STEMI. It can be used for monitoring, planning prevention program in health system and improving treatment of patients.<sup>38</sup> Risk factors of STEMI are age, male gender, smoking, family history of CVD, hypertension, hypertriglyceridemia and previous coronary artery bypass grafting (CABG).<sup>39,40</sup>

### Atrial Fibrillation

The atrial fibrillation (AF) prevalence was 2.8% in adults aged over 50 in PHC setting in Iran<sup>41</sup> which was in agreement with its prevalence of about 2% in the general population in the world.<sup>42</sup> Owing to improving/increasing life expectancy and improving health care, the prevalence of

stroke and AF have increase, subsequently.<sup>22</sup> The prevalence of AF, as the most common persistent cardiac arrhythmia was about 2%. It is a severe indication in up to 50% of patients after CABG and in more than 60% of cases after CABG accompanying with valve replacements or repair. AF risk factors included oxidative stress, inflammation, prothrombotic state, and sympathetic/parasympathetic activation.<sup>43,44</sup> Hence, the assessment of inflammatory factors before cardiac surgery like CRP, IL-6, IL-8, and IL-10 can assist predicting the occurrence of post operating AF.<sup>45</sup> Some preoperative predictors of postoperative AF were weight, no use of preoperative digoxin use, age, preoperative less hematocrit, less pO<sub>2</sub>, left main coronary disease, high preoperative serum creatinine, diabetes, smoking, chronic obstructive pulmonary disease, heart failure (HF), no use of preoperative nifedipine. Intraoperative predictors are left internal mammary artery, higher clamp time, pump time and inotropic support while postoperative predictors are intra-aortic balloon pump, respiratory complication, reintubation, postoperative bleeding and MI and death.<sup>46</sup> Both low body mass index and obesity were associated with AF occurrence and long term events and hospital charges.<sup>47,48</sup> Using low-molecular-weight heparin vs. unfractionated heparin was more efficient and a cost benefit approach for AF in stroke patients in Iran. Atorvastatin use had beneficial effect on AF after CABG.<sup>49-51</sup> In addition, polyunsaturated fatty acid of fish oil and antioxidant such as vitamin could improve AF by reducing the risk of AF and shortening ICU and hospitalization period in Iranian CABG patients.<sup>48,52</sup> As AF has adverse effect in stroke and cardiac surgery patients by extending hospitalization time and hence increasing cost of treatment, it is necessary to plan for diagnosis, monitoring, prevention and treatment of AF.

### Heart Failure

HF is an advanced heart problem and one of the main causes of death and burden in many countries, particularly in LMICs.<sup>53-56</sup> HF prevalence is between 0.4% and 4.3% in the general population and between 2% and 20% in the elderly population over 75 years.<sup>57</sup> It has been estimated to increase by two times in two decades.<sup>58,59</sup> The 1-year mortality rate of HF was 32% in Iran which fell in the range of this rate in other countries.<sup>60-62</sup> HF mortality predictors are hypotension during hospitalization, anemia, hyponatremia, heart valve disease and renal disease, pulmonary hypertension, tachycardia and less use of medications including ACE inhibitor/angiotensin receptor blocker and beta blocker (BB) in the follow-up period.<sup>63</sup> Age, diabetes mellitus, hypertension, stroke, atrial fibrillation (AF), ventricular tachycardia (VT), left or right bundle branch block (LBBB, RBBB), percutaneous coronary intervention (PCI), CABG and chest pain were associated with increase in HF and decrease in use of medications including thrombolytic, ACE inhibitor and

diuretics with decreasing the recurrence of myocardial ischemia in Iran.<sup>64,65</sup> Self-care of HF patients in Iran were not suitable and need to be improved.<sup>66</sup>

### Hypertension

The highest risk of CVD events is attributed to hypertension in the Iranian population.<sup>16</sup> It's because hypertension has the highest prevalence among CVD which range between 17.3% to more than 20% in Iranian adults aged over 18 years old<sup>67</sup> and 26.9% in population aged 40-75 years.<sup>68</sup> About 6.6 million of Iranians aged 25-64 years were hypertensive in 2005.<sup>69</sup> When pre-hypertension is considered, half of the Iranian adult population are hypertensive or pre-hypertensive<sup>70</sup> According to a national study among 69 722 Iranian adults aged 25-65 years, the prevalence of hypertension was 19.8% in men and 26.9% in women and pre-hypertension was prevalent in 59.6% and 44.5% men and women, respectively. In addition the hypertension prevalence was a bit higher in urban vs. rural areas.<sup>10</sup> Similar to other CVD types, the increasing trend of hypertension prevalence might be related to socioeconomic and lifestyles changes, urbanization and rising life expectancy.<sup>71,72</sup> More important is the challenge of lack of awareness and uncontrolled high blood pressure in Iran and other LMIC. One of two Iranian hypertensive patients are aware of their hypertension.<sup>68</sup> Diverse studies reported a range of 17 to 50% of hypertension control in treated hypertensive patients in Iran based on different areas, age and sex. Hence, most published or unpublished reports, even the Ministry of health reports, refer to the high uncontrolled rate of hypertension in Iran.<sup>67-70</sup> It's important to consider hypertension awareness, treatment and control as priorities on the health agenda.

### Stroke

Stroke is the second most prevalent type of CVD in Iran, more prevalent than western countries. The incidence rate of stroke was between 23 and 103 per 100 000 persons in different age groups of the Iranian population.<sup>73</sup> Particularly, its morbidity and mortality are higher in young Iranian adults compared to the Western population.<sup>74,75</sup> Prevalence of Stroke is higher in Iranian women than men which might be due to the higher life expectancy in women.<sup>76</sup> The total mortality rate was 24.6% in central part of Iran and in-hospital death rate was 20% and both were comparable with Arab Middle-Eastern and North African, but higher than Western countries.<sup>11</sup> The high case fatality in stroke patients are possibly due to the lack of specialized stroke units and under diagnosis of stroke<sup>77,78</sup> which cause late referral. In addition, limited financial, nursing and rehabilitation care may lead to re-hospitalization and low survival rate in stroke patients.<sup>11</sup> Lack of social insurance, social and family support are among main challenges in stroke patients that lead to low quality of life and make distress for patients and their families.<sup>79</sup>

A longitudinal study in Isfahan found that although the incidence of stroke was high, its trend has decreased, especially the intracranial hemorrhagic type from 2003 to 2013 which may be related to better hypertension diagnosis and control. Ischemic stroke is increasing in Iran and worldwide due to the increase of same risk factors of IHD. Owing to the young population of Iran now, all types of stroke may increase in the future.<sup>80</sup>

#### Cardiovascular Risk Factors

The prevalence of CVD risk factors including hypertension, diabetes mellitus, high LDL-C, low HDL-C, hypertriglyceridemia, hypercholesterolemia, obesity and current smoking were 42.2%, 18.7%, 58.9%, 52.3%, 52.7%, 65.4%, 26.4% and 13% among Iranian population aged more than 40 years, respectively.<sup>17,81</sup> The risk of CVD attributed to diabetes mellitus, hypertension, smoking history, abdominal obesity and high LDL-C were 9.9%, 36%, 5.5%, 18.9% and 24.1% in Iranians.<sup>81</sup> According to the prevalence of CVD risk factors and the risk of CVD, it has been concluded that prevention and control of these modifiable risk factors can prevent the incidence of CVD by 80%.

#### Strategies for CVD Prevention

Based on the current status of CVD in Iran, health promotion strategies to prevent and control of CVD risk factors, early detection of the disease and treatment of acute and chronic CVD events are essential elements for reducing the burden of CVD.<sup>82</sup> Modification of CVD risk factors could prevent more than 90% of MI risk.<sup>83</sup> Isfahan Healthy Heart Program (IHHP), as a comprehensive population-based interventional program in Iran,<sup>8</sup> showed that implementing educational, environmental, legislation and intersectoral collaboration strategies could improve lifestyle behaviors, physical and metabolic risk factors and ultimately decrease the incidence of CVD.<sup>80,85</sup> Implementation research on Iranian programs for CVD prevention can be helpful to recognize what facilitators and barriers exist in order to build new strategies for prevention and control.<sup>85</sup> Generally, however, some opportunities exist that can be used as a platform to prevent the disease or promote healthy lifestyle. These include good PHC infrastructure in Iran to integrate CVD and risk factor prevention programs, the WHO HEARTS Package in which 6 necessary elements were introduced to integrate CVD management strategies within the PHC system, the existing national document of NCD prevention to achieve the WHO global target in 2025, existence of new diagnostic and treatment technology at nationwide scale, knowledge improvement of health care providers and policy makers in CVD prevention and control arena, progress in providing secondary prevention and rehabilitation services to cardiac patients in public and private sectors to reduce revascularization, rehospitalization and improvement of

quality of life. Presence of health networks and recent family physicians in urban areas by using the earlier experience of rural areas that was efficient in Iran may lead to a better implementation of CVD prevention strategies in the PHC system.<sup>86</sup> If the new strategy of family physicians works well in urban areas, it can provide another opportunity for early detection, monitoring and prevention of CVD events and its risk factors in Iran. Family physicians should follow the existing Iranian guidelines such as the hypertension guidelines.<sup>87</sup> However, it seems that we still need extensive public education activities for health promotion, risk factor awareness, prevention and control, adherence to treatment, and self-care education, all need to be on the health maker's agenda that should consider the social, economic and cultural situation in Iran. In addition, controlling other environmental factors like air pollution will have an extremely important role in primary or secondary prevention of CVD. Preventive actions coverage by health insurance, availability and affordability of healthy food, and appropriate circumstances for physical activity especially for women, stress control and social support are among other main components for CVD prevention and control.<sup>85,88</sup>

In conclusion, CVD is the first leading cause of mortality and DALYs in Iran. Therefore, planning and implementing strategies for prevention and control of the disease and its risk factors is on the top of the ministry of health agenda in recent years. Health promotion strategies to prevent and control CVD risk factors, early detection of disease and treatment of acute and chronic CVD events are essential elements for reducing the burden of CVD in Iran.

#### Conflict of Interest Disclosures

The authors have no conflicts of interest.

#### Ethical Statement

Not applicable.

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