



Gender and Age-Based Differences in Risk Factors and Symptoms of Acute Coronary Syndrome in a Sample of Iranian Patients

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Abstract

Background: Acute coronary syndrome (ACS) is one of the most serious diseases with high mortality. Concerning the influence of age and gender on ACS properties, this study aimed to determine gender and age-based differences in risk factors and symptoms of the ACS in a sample of Iranian patients.

Methods: This cross-sectional study was conducted on 450 patients with ACS in Kerman from 10 September, 2018 to 25 February, 2019. The data were collected through face-to-face interviews in the coronary care unit (CCU) after ACS diagnosis. A trained interviewer collected the data using a demographic and clinical information checklist. Statistical analyses were performed using chi-square, Fisher exact test, and Mann-Whitney U test and through SPSS software (version 23).

Results: In this study, more than half of the patients with ACS were males (n=240, 53.4%). In one-third of the patients, ACS symptoms were presented in the age range of 60-69 years (n=145, 32.2%). In the female patients compared to the male patients, there were more cases of underweight [58 (27.6%) versus 45 (18.8%), *P* value: 0.02], positive family history of coronary heart disease (CHD) [102 (48.6%) versus 92 (38.3%), *P* value: 0.02], and hypertension [119 (56.7%) versus 113 (47.1%), *P* value: 0.04]. In contrast, there were no differences in common symptoms and pain severity in patients in various age and sex groups.

Conclusion: Attention to the differences in the profile of risk factors and symptoms of ACS in males and females of different ages, would be helpful in choosing the best clinical approach.

Keywords: Acute coronary syndrome, Age, Gender, Iran, Risk factors, Symptoms

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Introduction

Cardiovascular diseases (CVDs) are considered a leading cause of mortality, morbidity, and disability in both men and women (1). CVDs cause a costly condition and have still remained a health challenge in the world (2) and are responsible for half of the cardiovascular deaths. The mortality rate of CVDs has been reduced in the developed countries due to the improved preventive and therapeutic interventions (3). However, half of the CVD mortalities and the majority of its global burden have occurred in low and middle-income countries, such as the Eastern Mediterranean Region (4).

Acute coronary syndrome (ACS) is a severe form of CVDs with high mortality in most countries. ACS comprises a spectrum of conditions caused by the interruption of blood flow to the heart due to plaque or thrombosis formation (5,6). The most important markers of ACS presentation in patients are unstable angina, non-ST-elevation myocardial (NSTEMI), and ST-elevation myocardial (STEMI).

According to the recent studies, risk factors, clinical symptoms, and outcomes of ACS differed by sex and age of patients. For example, the elderly patients constituted a remarkable part of ACS cases with different clinical profiles and outcomes (7) and more than half of the admission and hospital mortality cases due to ACS occurred among this age group (6). However, the findings of recent studies on sex differences are more controversial. Although, some related studies have shown that female patients with ACS had similar or better outcomes and lower mortality and lower risk of cardiac events in comparison to men (8), another study showed that short-term and long-term outcomes are worse in women than men (9).

ACS risk factors are mostly related to patients' lifestyle. For example, hypertension, diabetes mellitus, lipid disorder, obesity, and smoking habits which account for CVD are usually observed among patients with ACS (10,11). Recent studies have reported that women with ACS had more comorbidities such as hypertension,



diabetes mellitus, and hyperuricemia compared to men. In contrast, the prevalence of current smoking was higher in men than women (12,13). In addition, early detection of symptoms leads to early diagnosis of disease, reduces the treatment time, and decreases the fatal outcomes (14). In fact, early diagnosis and accurate interpretation of symptoms have a considerable influence on the outcome in ACS patients (15).

Studies in Iran revealed that cardiac risk factors are prevalent among Iranian adults (16), and CVD in Iran is responsible for half of the annual mortality rate (10). Considering differences in profiles, risk factors, and symptoms of ACS in different populations, as well as, among individuals within one population, this study was performed to determine the risk factors for ACS in terms of gender and age (younger than 60 years old vs. 60 years old and over) in a sample of Iranian patients.

Materials and Methods

Subject and setting

This cross-sectional study was conducted from September 10, 2018 to February 25, 2019 in Shafa and Afzalipour hospitals of Kerman University of Medical Sciences as heart referral centers of Kerman province. All patients with unstable angina and myocardial infarction who referred to the cardiac emergency ward or were hospitalized in the coronary care unit (CCU) and diagnosed as ACS were included in the study.

Sample size and sampling method

According to the sample size estimation formula for proportion, the sample size for the present study was estimated based on the ACS prevalence which was unknown in Kerman ($P: 0.50$). Taking the 95% confidence interval ($\alpha: 0.05$) and error level ($d=0.05$), the sample size was approximately calculated as 385 persons. To evaluate the power of the study and compensate for the dropout rate (10% to 15%), 450 patients with ACS were selected through convenience sampling. The sampling was not restricted to the sex and age of patients.

$$n = \frac{z1 - a / 2^2 * p * q}{d^2} = \frac{1.96^2 * 0.5 * 0.5}{0.05^2} = 384.16 \approx 385$$

Data collection

The data were collected prospectively through face-to-face interviews in the CCU after ACS diagnosis. For data collection, a checklist was designed and completed for all patients by a trained interviewer. The checklist consisted of four separate parts. The first part assessed the patients' demographic information such as age, sex, weight, height, cigarette smoking habits, and family history of CVD. For the analyses, age was categorized into the two groups of < 60 years, and ≥ 60 years. In the next part of the checklist, comorbidities were recorded (i.e., hypertension, diabetes mellitus, hypercholesterolemia, hypothyroidism,

renal disorders, asthma, or chronic obstructive pulmonary disease). Common symptoms of ACS such as chest pain, nausea, vomiting, dyspnea, sweating, and headache were assessed and recorded in the third part of the checklist. The last part of the checklist recorded the type and severity of any pain experienced by the patient during a heart attack. Pain was classified as typical and atypical pain. Retrosternal pain was considered as typical pain, and pains experienced in other sites of the body such as left hemithorax, right hemithorax, hemithorax radiated to the neck, shoulder, and arms, retrosternal radiated to left and right arm, between shoulders, neck, and arms were categorized as atypical pain.

Data analysis

The data were described using mean \pm standard deviation (SD) and frequency (%). Furthermore, the qualitative data such as sex, body mass index (BMI), family history of coronary heart disease (CHD), cigarette smoking status, comorbidities and common symptoms of ACS, and also pain severity of disease were compared using chi-square and Fisher exact test. The age of patients was compared through Mann-Whitney U test. Two-sided P -values of less than 0.05 were considered statistically significant. Data analysis was performed using SPSS software (version 23).

Results

Demographic and clinical characteristics of patients with ACS

A total of 450 patients with ACS participated in this study. The patients' mean age was 61.8 ± 12.8 years (age range: 25 to 98 years). Almost one-third of patients were 60-69 years old ($n=145$, 32.2%). The number of male patients ($n=240$, 53.4%) was slightly greater than the female patients. Figure 1 shows the ACS symptoms presented by the male patients at least 10 years earlier. In the present study, the patients had normal BMI ($n=345$, 76.7%). More than one-third of patients were cigarette smokers ($n=176$, 39.1%). Less than half of the subjects had a family history of CHD ($n=194$, 43.1%). Hypertension ($n=232$, 51.6%), hypercholesterolemia ($n=218$, 48.4%), and diabetes mellitus ($n=114$, 25.3%) were the most



Figure 1. Age distribution of patients with ACS according to sex.

prevalent comorbidities among the patients (Table 1).

Common symptoms of ACS among patients

Chest pain was the most common symptom among ACS patients (n=426, 94.7%). Digestive symptoms such as nausea and vomiting (n=379, 84.2%) and dyspnea (n=226, 50.2%) were other common symptoms of the disease (Table 1). The results revealed that severe and moderate pain was frequent among the patients (n=230, 51.1%, and n=150, 33.3%; respectively). Eleven patients did not report any pain (2.4%) and other patients suffered from mild pain (13.1%). Almost two-thirds of pains was reported as atypical (n=326, 74.2%) and others as typical pain (n=113, 25.8%).

Sex differences in ACS risk factors and symptoms

Analysis of the data on the patients' baseline and clinical characteristics indicated that the female patients significantly differed from the male patients in terms of

BMI, family history of CHD, smoking status, and some comorbidities. In fact, the female patients compared to males were more underweight (27.6% versus 18.8%; P value=0.02) and almost half of them had a positive family history of CHD in comparison to the males (48.6% versus 38.3%; P value=0.02). The results also suggested that compared to the male patients, the female patients were more frequently suffering from hypertension (56.7% versus 47.1%; P value=0.04), hypothyroidism (6.7% versus 1.3%; P value \leq 0.001), and hypercholesterolemia (54.8% versus 42.9%; P value=0.01). In contrast, the number of smokers was greater in the male patients than the females (54.6% versus 21.4%; P value \leq 0.001). However, both groups were similar in terms of symptoms of ACS and severity of pain (Table 2).

Age differences in ACS risk factors and common symptoms

According to the results, baseline characteristics such

Table 1. Demographic and clinical characteristics of patients with ACS

	Variables	Level of variables	No. (%)	
Demographic characteristics	BMI	Normal	345 (76.7)	
		Underweight	103 (22.9)	
		Over-weight and obese	2 (0.4)	
	Family history of CHD	Negative	256 (56.9)	
		Positive	194 (43.1)	
	Cigarette smoking	Non-smoker	274 (60.9)	
		Smoker	176 (39.1)	
	Comorbidities	Hypertension	Negative	218 (48.4)
			Positive	232 (51.6)
		Diabetes mellitus	Negative	336 (74.7)
Positive			114 (25.3)	
Hypercholesterolemia		Negative	232 (51.6)	
		Positive	218 (48.4)	
Hypothyroidism		Negative	433 (96.2)	
		Positive	17 (3.8)	
Renal disorders		Negative	432 (96)	
		Positive	18 (4)	
Asthma or chronic obstructive pulmonary disease	Negative	423 (94)		
	Positive	27 (6)		
Common symptoms	Chest pain	Negative	24 (5.3)	
		Positive	426 (94.7)	
	Nausea/ vomiting	Negative	71 (15.8)	
		Positive	379 (84.2)	
	Dyspnea	Negative	224 (49.8)	
		Positive	226 (50.2)	
	Sweating	Negative	273 (60.7)	
		Positive	177 (39.3)	
	Headache	Negative	434 (96.4)	
		Positive	16 (3.6)	

Table 2. Comparison of risk factors and common symptoms of ACS based on sex of patients

	Variables	Males (n=240)	Females (n=210)	P value
Demographic characteristics	Age (mean±SD)	61.2±13.4	62.5±12.0	0.30
	Normal BMI (%)	193 (80.4)	152 (72.4)	
	Underweight (%)	45 (18.8)	58 (27.6)	0.02
	Overweight and obese (%)	2 (0.8)	0	
	Positive Family history of CHD (%)	92 (38.3)	102 (48.6)	0.02
	Cigarette smoker (%)	131 (54.6)	45 (21.4)	≤0.001
Comorbidities	Hypertension (%)	113 (47.1)	119 (56.7)	0.04
	Diabetes mellitus (%)	54 (22.5)	60 (28.6)	0.14
	Hypercholesterolemia (%)	103 (42.9)	115 (54.8)	0.01
	Hypothyroidism (%)	3 (1.3)	14 (6.7)	≤0.001
	Renal disorders (%)	12 (5)	6 (2.9)	0.24
	Asthma or chronic obstructive pulmonary disease (%)	16 (6.7)	11 (5.2)	0.52
Common symptoms	Chest pain	224 (93.4)	202 (96.1)	0.17
	Nausea/ vomiting	209 (87.1)	170 (81)	0.07
	Dyspnea	111 (46.2)	115 (54.7)	0.07
	Sweating	103 (42.9)	74 (35.2)	0.09
	Headache	11 (4.6)	5 (2.4)	0.28
	Severity of pain	No pain	7 (2.9)	4 (1.9)
	Mild	30 (12.5)	29 (13.8)	
	Moderate	83 (34.6)	67 (31.9)	0.80
	Severe	120 (50)	110 (52.4)	

as BMI, history of CHD, and smoking status as well as comorbidities such as hypertension and hypothyroidism were statistically different based on the patients' age. For instance, the patients aged less than sixty-one were more underweight compared to older patients (27.8% versus 17.9%; P value=0.01), were more likely to have a positive family history of CHD (50.7% versus 34.5%; P value \leq 0.001), and smoked more frequently (43.6% versus 34.5%; P value=0.05). However, the patients older than 60 years old had more comorbidities compared to the younger patients. They were more hypertensive (60.5% versus 42.7%; P value \leq 0.001) and were more likely to have hypothyroidism (5.8% versus 1.8%; P value=0.02). Nevertheless, there was no statistically significant difference in terms of common ACS symptoms and the severity of pain between the two age groups (Table 3).

Discussion

CVDs are among the main public health challenges globally. Thus, analysis of epidemiological and clinical profiles of the risk factors and symptoms of these diseases can be very beneficial for public health practitioners. The current study showed that more than half of the patients with ACS were males. In one third of patients, ACS symptoms were reported in the patients aged 60-69 years, and in men these symptoms were present ten years earlier than females. The patients' demographic and clinical information such as BMI, the positive family

history of CHD, smoking status, and comorbidities like hypertension were significantly different in terms of sex and age, but there was no difference in common symptoms and pain severity of the patients in various age and sex groups.

Recent studies revealed that the age of CVD incidence has been decreasing over time (17). Nedkoff et al found that the age of ACS incidence was decreased dramatically among men and women from 1996 to 2007 (18). In another study, the age of women with myocardial infarctions statistically decreased during a decade in Iran (19). Moreover, one study in Iran revealed that more than half of male patients with ACS were 30 -64 years old and women were 65 to 84 years old (20). The results of the present study showed that the mode of age interval was 60-69 years among female and male patients followed by an age interval of 50-59 years in both sexes. On the other hand, our findings revealed a decrease in the age of onset of ACS, especially in men, which was in line with the mentioned studies. There are many factors involved in the early onset of ACS. The result of one study showed that ACS in young patients was related to some demographic and clinical factors such as the BMI score, hypertension, diabetes Mellitus, and hyperlipidemia as chronic diseases, and mental disorders like depression, and anxiety (21). According to the data in the present study, CVD occurred earlier in males than females. The lower incidence age for men has been confirmed in a similar study (22). The

Table 3. Comparison of risk factors and common symptoms of ACS based on age of patients

	Variables	< 60 (n=227)	≥ 60 (n= 223)	P value
Demographic characteristics	Female sex (%)	107 (47.1)	103 (46.2)	0.84
	Normal BMI (%)	164 (72.2)	181 (81.2)	
	Underweight (%)	63 (27.8)	40 (17.9)	0.01
	Overweight and obese (%)	0	2 (0.9)	
	Positive Family history of CHD (%)	115 (50.7)	79 (34.5)	0.001
	Cigarette smoker (%)	99 (43.6)	77 (34.5)	0.05
Clinical characteristics	Hypertension (%)	97 (42.7)	135 (60.5)	0.0001
	Diabetes mellitus (%)	51 (22.5)	63 (28.3)	0.15
	Hypercholesterolemia (%)	101 (44.5)	117 (52.6)	0.09
	Hypothyroidism (%)	4 (1.8)	13 (5.8)	0.02
	Renal disorders (%)	9 (4)	9 (4)	1
	Asthma or chronic obstructive pulmonary disease (%)	11 (4.8)	16 (7.2)	0.29
Common symptoms	Chest pain	217 (95.6)	209 (93.7)	0.37
	Nausea/ vomiting	187 (82.4)	192 (86.1)	0.27
	Dyspnea	116 (51.1)	110 (49.3)	0.70
	Sweating	83 (36.6)	94 (42.2)	0.22
	Headache	11 (4.8)	5 (2.2)	0.16
Severity of pain	No pain	3 (1.3)	8 (3.6)	
	Mild	33 (14.5)	26 (11.7)	
	Moderate	75 (33)	75 (33.6)	
	Severe	116 (51.1)	114 (55.1)	0.73

earlier incidence of CVD among men can be due to the higher prevalence of risk factors such as smoking in this group. Besides, the protective effects of estrogen in menarche age among women should be considered (23).

Family history is one of the main risk factors for ACS, and CHD in young individuals is usually assumed to have a genetic cause (1). Genetics plays a role in the onset of ACS in young people. The results of related studies revealed that family history of CAD was related to ACS among chest pain patients especially in young patients (24,25). The results of the present study showed that patients younger than 60 years and also females were significantly more likely to have a family history of CAD that has been reported by Labos et al and Hemal et al too (26,27). However, Haff et al. showed that the family history of CAD was statistically less frequent among female versus male patients with ACS (13). Another study showed that family history of CAD was similar between female patients of reproductive age and healthy controls (28). While, a higher frequency of family history in female patients with ACS may be related to the role of coding for the mitochondrial genome (29), more studies are needed to determine the role of family history of CAD for the onset of ACS among men and women.

The risk of CHDs among smokers is higher than that in non-smokers (30). The odds ratio of CVD for smokers has been reported between 6 to 32.8 in different studies (31,32). It means that the odds of CVD among smokers

is 6 to 32 times more than that in nonsmokers (33,34). According to the findings of the present study, more than one-third of patients were cigarette smokers and the prevalence of smoking among males was more than females. These findings were consistent with other studies (35,36). This difference between the two genders is due to social factors, especially in Iran, but this difference has diminished over time. The present study also revealed that the prevalence of smoking was higher among patients younger than 60 years. Some studies have shown smoking as an important risk factor for ACS among young patients. While smoking is a modifiable risk factor, it was highly prevalent among young patients with ACS (37,38). These findings were in line with the observations made in the present study.

The older patients (aged 60 years and more) in the present study had more comorbidity such as hypertension and hypothyroidism than younger patients. Overall, the risk of cardiovascular and other non-communicable diseases has a positive correlation with age especially among women, and an increase in age can increase the risk of the mentioned diseases (7,39-41). A population-based study showed that the prevalence of some risk factors such as total cholesterol among men until the fifth decade of life was more than females, but after this period, women had a higher prevalence of these risk factors (42). The higher prevalence of these risk factors in women over 50 years can be due to menopause changes and

decreased estrogen levels in the body. The increased risk factors among older males can be attributed to physical inactivity, an unhealthy diet, etc. The higher risk factors among females can also be due to an unhealthy lifestyle such as a sedentary lifestyle and lack of physical activity in this group. Moreover, the effect of menopause and the decreased level of estrogen hormone among women should be considered (23,43). According to another study, obesity occurs more frequently after menopause in women. This can increase the risk of diabetes mellitus, hypertension, and hypercholesterolemia in females (44). The decrease in estrogen levels after menopause age can increase risk factors for CHDs such as hypertension (45). An increase in blood pressure after menopause age can be due to increasing salt sensitivity and sympathetic activity in postmenopausal women (46). In addition to blood pressure, another study confirmed the increase level of LDL, triglycerides, and body mass index among postmenopausal women (47).

According to the data in the present study, the symptoms of ACS among males and females followed a similar pattern. The prevalence rates of chest pain, nausea/vomiting, dyspnea, sweating, and headache among the two genders were not statistically significant. Another study reported that symptoms such as abdominal pain, dyspnea, back pain, nausea or vomiting, neck pain, jaw pain, and chest pain were significantly more prevalent in women than men (48,49). Another study showed that the probability of reporting chest pain among men was more than females (50,51). In another study, chest pain was equally reported in both genders but the prevalence of jaw pain and nausea was higher among women (52). The conflicting results in different studies can be attributed to different populations or different age groups. In general, the cause of differences in symptoms between the two genders is unknown but according to some studies, women generally tend to experience MI in an older age than men, so old age can be considered as an effective factor on symptoms presentation among women (53).

Conclusion

According to the current study, most of the ACS cases were males. Factors such as BMI, a positive family history of CHD, smoking status, and comorbidities such as hypertension were significantly different between the two genders and different age groups. Thus, clarifying different patterns among different age groups and the two genders warrant more analytical epidemiological studies.

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Competing Interests

None.

Ethical Approval

The protocol of the present study was reviewed and approved by the Ethics Committee of Kerman University of Medical Sciences (ethic No. IR.KMU.AH.REC.1396.2204). Written informed consent was obtained from the pregnant women before the initiation of the study.

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