Seasonal pattern in admissions and mortality from acute myocardial infarction in elderly patients in Isfahan, Iran

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Original Article

Abstract

BACKGROUND: Seasonal variation in admissions and mortality due to acute myocardial infarction has been observed in different countries. Since there are scarce reports about this variation in Iran, this study was carried out to determine the existence of seasonal rhythms in hospital admissions for acute myocardial infarction, and in mortality due to acute myocardial infarction (AMI) in elderly patients in Isfahan city.

METHODS: This prospective hospital-based study included a total of 3990 consecutive patients with acute myocardial infarction admitted to 13 hospitals from January 2002 to December 2007. Seasonal variations were analyzed with the Kaplan-Meier table, log rank test, and Cox regression model.

RESULTS: There was a statistically significant relationship between the occurrence of heart disease based on season and type of acute myocardial infarction anatomical (P < 0.001). The relationship between the occurrence of death and season and type of AMI according to International Classification of Diseases code 10 (ICD) was also observed and it was statistically significant (P = 0.026). Hazard ratio for death from acute myocardial infarction were 0.96 [Confidence interval of 95% (95% CI) = 0.78-1.18], 0.9 (95%CI = 0.73-1.11), and 1.04 (95%CI = 0.85-1.26) during spring, summer, and winter, respectively.

CONCLUSION: There is seasonal variation in hospital admission and mortality due to AMI; however, after adjusting in the model only gender and age were significant predictor factors.

Keywords: Acute Myocardial Infarction, Season, Admission in Hospital, Mortality, Isfahan

Introduction

Cardiovascular disease (CVD) is the most common cause of death in Iran.[1] There has been an increasing trend in proportional mortality rate since 1981. In 1995, 47.3% of all deaths were due to CVD. According to the first national burden of disease study for the year 2003, the third highest disability-adjusted life years (DALYs) in all ages and both sexes (16% of total burden) attributed to this disease which included one billion years of life lost (YLL) due to premature mortality and 500 thousand years lived with disability (YLD).[2]

During recent years, admission rate for myocardial infarction (MI) has risen. According to the World Health Organization (WHO) Monitoring Trends and Determinants in Cardiovascular Disease (MONICA) project, 28-day case-fatality rates ranged from 37% to 81% for men (average, 48% to

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49%), and from 31% to 91% for women (average, 54%).[3] Studies in the UK showed similar results.[4,5] The figure is very diverse in Iran; from 16% to 65.5%.[4'5] In a study recently performed in Iran (Isfahan), 28-day case-fatality rate was 9.1%.[6]

However, seasonal variation in admissions and mortality due to acute myocardial infarction has been observed in different countries.[7-10] Therefore, most studies suggest that the highest occurrence of acute myocardial infarction, or admission to hospital and mortality has occurred during the winter[9-11] and the lowest during the summer.[10,11] However, one study concluded that the highest occurrence rate of disease is in spring.[12] Previous studies have reached diverse conclusions regarding the association of weather and weather change with the threat of having or dying from an acute myocardial infarction (AMI). Although AMI is the most serious coronary disease all around the world, background of its beginning and mortality are not wholly understood, particularly in Iran. The aim of this paper is to explain seasonal admissions to hospitals and AMI mortality pattern in elderly patients in Isfahan, Iran.

Materials and Methods

This study is a prospective hospital-based study that was implemented to appraise seasonal patterns of hospital admissions and mortality from AMI. The study population consisted of patients who had suffered their first AMI at the age of 65 or over during 2002-2007 in 13 private and academic hospitals in the city of Isfahan. In this study we used convenience sampling. However, given that all patients with acute myocardial infarction admitted to the hospital were included in the study, and given the fact that data were collected from 13 hospitals in Isfahan city, it can be inferred that the study population was a good representative of the population. The research team consisted of a cardiologist, a number of nurses trained in receiving and recording patient information, and biostatisticians and epidemiologists. Patients with AMI were diagnosed by cardiologists at hospitals based on the International Classification of Diseases code (ICD10). Basic information related to patients was collected by trained nurses, who used special forms to interview patients or obtained information from their hospital records, and then the data was collected in the Isfahan Cardiovascular Research Center (ICRC).

Patients were investigated after admission to hospitals, and patients with AMI related to different event locations were assigned a specific code according to ICD10, these codes were I21.0, I21.1,

I21.2, I21.3 I21.4, and I21.9, considering categorized acute myocardial infarction.

Monica and the World Health Organization protocol defined AMI as a 28-day repeated attack, not considered as separate attacks but in fact related to the first AMI; however, following the first night of the 27th day after the attack it is considered as a new attack. Patients who died during the first 28 days are considered as death due to first AMI. The first 28-day follow-up, considered incidence symptoms, abnormal electrocardiogram (EKG), or abnormal enzymes at first day of onset.[13]

After collecting basic information about patients, their survival or death during the 28 days after the AMI were evaluated. A 28-day follow-up was performed for each patient, their survival rate and death was also evaluated based on each case. The follow-up was started from hospital for the hospitalized patients. For discharged patients, follow-up was first executed by telephone, but when their survival rates were not determined after 3 telephone calls we went to the patients' homes. When previous efforts in terms of getting information about survival rate failed, using the organization's registration information and Rizwan Garden, we tried to find out if the patient had died; we found the cause of death, and exact date and location of the burial.

This study included only patients who were living in Isfahan with first AMI. If a patient died during the 28 days after the first attack due to accident, suicide, homicide, chronic obstructive pulmonary disease, cancer, liver cirrhosis, rheumatic heart disease, vascular disease, or atherosclerosis without mention of any cardiovascular disease they were excluded from the study. In addition, if the exact date of the occurrence or death from the disease was not specified, the patient was excluded from the study; because the 28-day duration after the attack could not be calculated in these cases.[13] This study was performed on patients aged 65 and over, because according to other studies on the occurrence of heart disease by season the greatest difference was visible in older patients.[3,11,12]

Statistical analysis

In this study, to compare average age between the two genders we used Student's independent t-test, and for comparison of the mean age at the time of the occurrence of disease and death according to different seasons ANOVA test was used. Furthermore, for the evaluation of the relationship between seasons and the occurrence of and mortality due to AMI according to the ICD10

(International Classification of Disease) chi-square test was used. In addition, in order to assess survival according to season the Kaplan-Meier analysis, and to compare survival rate the logrank test were used. To calculate the hazard ratio of death during the 28 days of onset acute myocardial infarction Cox regression was used, and the category with the lowest mortality rate was considered as reference group. SPSS for Windows (version 15; SPSS Inc., Chicago, IL, USA) was used for data analysis. All values of P < 0.05 were considered significant.

Results

Overall, 4497 patients with acute myocardial infarction were admitted to the hospitals of Isfahan during the study period. Among these, 241 patients (152 men and 89 women) were excluded because their acute myocardial infarction type was not determined according to the International Classification of Diseases ICD10. An additional 180 patients (108 men and 72 women) were excluded because outcome was unknown. Finally, 86 patients were eliminated because

of missing information on baseline clinical and demographical variables. Therefore, 3990 patients, 2469 (61.9%) men and 1521 (38.1%) women, remained in the study (Table 1).

In this study, the average age of patients at the time of disease occurrence (3990 patients) was 73.39 ± 6.10, in men (2469 patients) it was 72.98 ± 5.88 and in women (1521 patients) 74 ± 6.38; this difference was statically significant (P < 0.001). The average age of patients who died during the 28 days after the onset (724 deaths) was 75.29 ± 6.6, in men (386 patients) it was 74.58 ± 6.32 and in women (338 patients) 76.11 ± 6.82; this difference was not significant (P = 0.446). The average occurrence age of the disease at the time of admission to hospitals and mortality of disease during the first 28 days after the onset was compared based on season; their difference was no significant (P = 0.670, and P = 0.853, respectively) (Figure 1). The difference between average follow-up time for all patients and the death group according to season was not significant (P = 0.478, and P = 0.801, respectively) (Figure 1).

Table 1. Demographic and clinical data of hospitalized myocardial infarction patients

Variables		Alive	Death	Total
Sex	Male	2083	386	2469
	Female	1183	338	1521
Age	74-65	2054	336	2390
	84-75	1104	326	1430
	85 years and older	108	62	170
EKG	Abnormal	2606	565	3171
	Possible changes	41	7	48
	Ischemic changes	522	83	605
	Normal	10	1	11
	Arrhythmia	58	37	95
	Lost	29	31	60
Cardiac enzymes	Normal	268	44	312
	Atypical	409	65	474
	Typical	2523	495	3018
	Miss	66	120	186
Type of acute myocardial infarction, according to ICD10	Acute subendocardial myocardial infarction	388	15	403
	Acute transmural myocardial infarction of other sites	107	8	115
	Acute transmural myocardial infarction of inferior wall	946	138	1084
	Acute transmural myocardial infarction of anterior wall	1105	194	1299
	Acute myocardial infarction, unspecified	679	345	1024
	Acute transmural myocardial infarction of unspecified site	41	24	65
Hospital	Private hospitals	237	65	302
	Public-education hospitals	3029	659	3688
Occurrence season	Spring	875	199	1074
	Summer	749	162	911
	Autumn	793	157	950
	Winter	849	206	1055
Streptokinase	The group receiving Streptokinase	1517	302	1819
	Group not receiving Streptokinase	1749	422	2171

EKG: Electrocardiogram; ICD10: International Classification of Diseases code 10
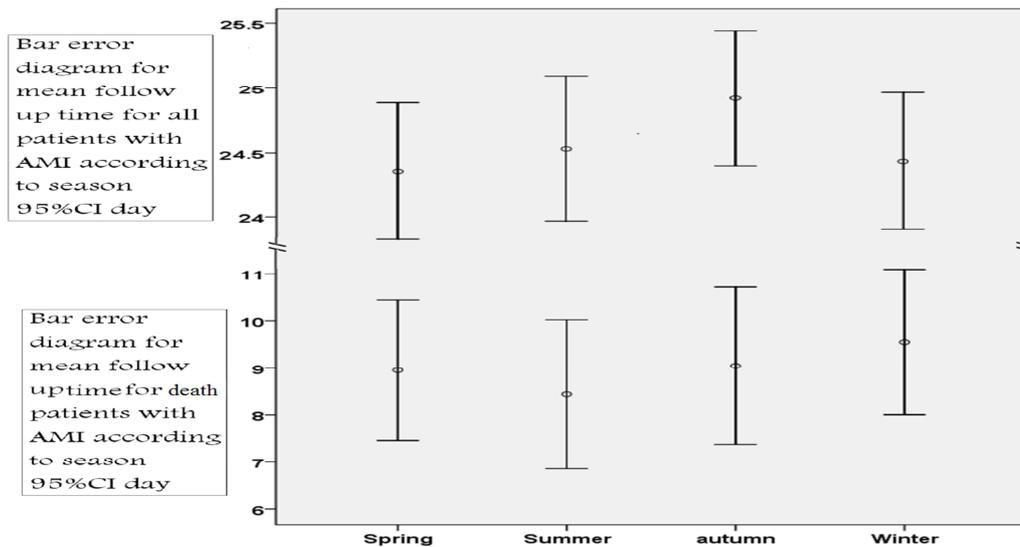
Figure 1. Bar error diagram for mean follow up time for death and all patients with AMI according to season
AMI: Acute myocardial infarction; CI: Confidence interval

In the Evaluation of patients admitted to the hospital, the lowest hospital admission for AMI was seen during the summer season and highest during the spring. They increased 17.8%, 15.8%, and 4.2% during the spring, winter, and autumn, respectively, more than the summer. Assessment of the occurrence of death according to season showed that the lowest mortality rates occurred during the autumn, the highest percentage was in winter; 30.5% in winter, 26% in spring, and 5.1% in summer increased compared with autumn. The highest survival rate was observed in patients who were suffering in autumn and the lowest survival was observed in patients who were suffering during the winter. However, significant differences in survival were not observed in different seasons (P = 0.358) (Figure 2 and Table 2).

A statistically significant relationship was observed between admission in hospital on the basis of season and type of AMI according to ICD10 (P < 0.001), and between the occurrence of death based on season and type of AMI according to ICD10 (P = 0.026) (Table 2).
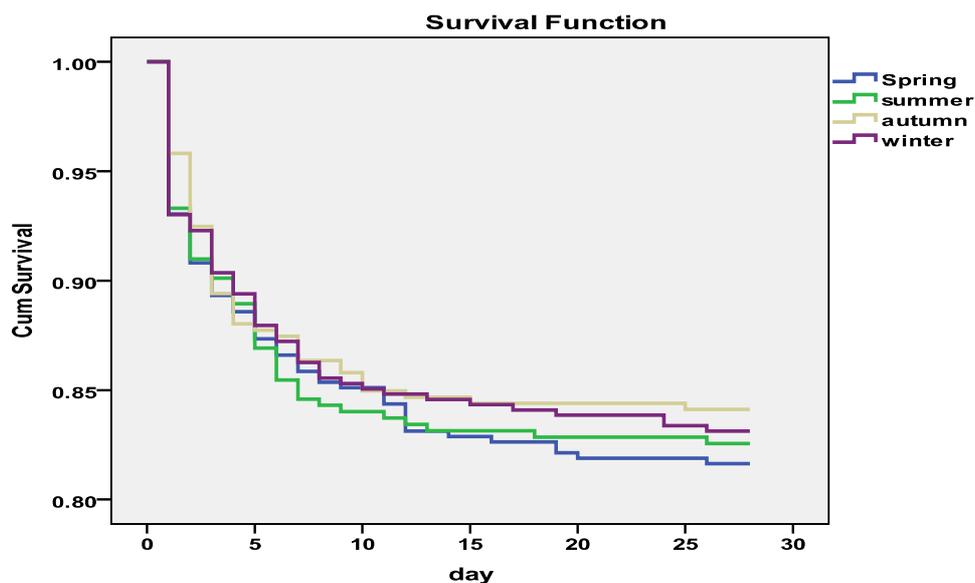
Figure 2. 28 day survival in patients with acute myocardial infarction according to season

Assessment of the hazard ratio of mortality resulting from acute myocardial infarction showed that the lowest mortality was in the autumn; to calculate the hazard ratio, this season was considered as a basis and the multiple regression Cox model was used. We observed that the hazard ratio for death from acute myocardial infarction were 0.96 CI95% 0.78-1.18 during spring, 0.9 CI95% 0.73-1.11 during summer, and 1.04 CI95% 0.85-1.26 during winter; however, for females it was 1.38 CI95% 1.19-1.6, and in the 70-74 years age group was 1.29 CI95% 1.04-1.6, in 75-79 years group 1.77 CI95% 1.43-2.2, in 80-84 years group 2.2 CI95% 1.73-2.8, and for 85 years and higher it was 3.08 CI95% 2.28-4.16 (Table 3).

Table 2. Survival, hospital admission, and death of acute myocardial infarction according to season

	Total	Spring	Summer	Autumn	Winter	P
Overall patients	3990	1074	911	950	1055	
Number of deaths	724	199	162	157	206	
Patients surviving	3266	875	749	793	849	0.358
Survival rate	81.9%	81.5 %	82.2%	83.5%	80.5%	
Survival time (mean ± SD)	24.57 ± 0.136	24.42 ± 0.268	24.53 ± 0.288	24.92 ± 0.266	24.45 ± 0.270	
Type of MI						
Acute transmural myocardial infarction of anterior wall	1299	369 (28.4%)	306 (23.6%)	280 (21.6%)	344 (26.5%)	
Acute transmural myocardial infarction of inferior wall	1084	285 (26.3%)	260 (24.0%)	258 (23.8%)	281 (25.9%)	
Acute transmural myocardial infarction of other sites	115	27 (23.5%)	27 (23.5%)	28 (23.8%)	33 (28.7%)	0.001
Acute transmural myocardial infarction of unspecified sites	65	18 (27.7%)	5 (7.7%)	6 (9.2%)	36 (55.4%)	
Acute subendocardial myocardial infarction	403	96 (23.8%)	91 (22.6%)	117 (29%)	99 (24.6%)	
Acute myocardial infarction, unspecified	1024	279 (27.2%)	222 (21.7%)	261 (25.5%)	262 (25.6%)	
Death during the 28 days						
Acute transmural myocardial infarction of anterior wall	197	55 (27.9%)	45 (22.8%)	42 (21.3%)	55 (27.9%)	
Acute transmural myocardial infarction of inferior wall	138	30 (21.7%)	30 (21.7%)	27 (19.6%)	51 (37.0%)	
Acute transmural myocardial infarction of other sites	8	1 (12.5%)	0	5 (62.5%)	2 (25.0%)	0.026
Acute transmural myocardial infarction of unspecified sites	24	6 (25.0%)	4 (16.7%)	3 (12.5%)	11 (45.8%)	
Acute subendocardial myocardial infarction	14	4 (28.6%)	6 (42.9%)	0	4 (28.6%)	
Acute myocardial infarction, unspecified	344	102 (29.7%)	80 (23.3%)	80 (23.3%)	82 (23.8%)	

MI: Myocardial infarction

Table 3. Hazard ratio of death from acute myocardial infarction according to age, sex, and season of occurrence

Variable	HR	95% CI for HR	P
Autumn	R	-	-
Spring	0.96	(0.78-1.18)	0.713
Summer	0.90	(0.73-1.11)	0.326
Winter	1.04	(0.85-1.26)	0.677
Male	R	-	-
Female	1.38	(1.19-1.60)	< 0.001
65-69	R	-	-
70-74	1.29	(1.04-1.60)	0.019
75-79	1.77	(1.43-2.20)	< 0.001
80-84	2.20	(1.73-2.80)	< 0.001
85 and higher	3.08	(2.28-4.16)	< 0.001

HR: Hazard ratio; CI: Confidence interval

Discussion

In this study, we observed that the highest rate of hospital admission occurred in spring and the second highest in winter, and the lowest was in summer. The lowest mortality rate was during autumn, the highest percentage was in winter. The difference between the occurrence of the disease, hospital admissions, and deaths in relevance with the seasons has been reported in different parts of the world.[7-10] However, in Iran a study on this topic has not been administered with a large sample size. In this study, we surveyed 3990 patients with acute myocardial infarction during 2002-2007 in private and public-education hospitals in the Isfahan city. They were included and categorized in accordance with the International Classification of Diseases ICD10. Identification of particular patterns at the time of the beginning of AMI has scientific value, because such patterns mean that there are triggers peripheral to the atherosclerotic plaque.

Age is a factor that has a large impact on mortality from heart attack; older people are at greater risk of mortality from acute myocardial infarction. In a study conducted in Japan by Isao Kubota et al., it was observed that the average age for patients who died 28 days after the occurrence of AMI was 76.1 ± 9.4 and for patients that survived was 67.6 ± 11.8, and this difference was statistically significant.[14] Moreover, in a study performed by Macintyre et al. on patients who had their first acute myocardial infarction and survived by hospital admission, the average age was compared with the cohort of patients who died before reaching hospital. The results maintained that dead patients were 7 years older than the surviving patients.[15] Based on these studies, it can be concluded that if the average age of patients admitted to hospital differs according to season, there if higher probability of death in the season in which the average age is higher, parallel mortality is higher and vice versa. Consequence probability differences in mortality between seasons are a result of differences in average age of patients based on season. to asses this assumption, the average age of patients was compared with season. There were no statistically significant differences between the average age of patients in the episode and death from the disease. In fact, the average age of patients at the time of occurrence of disease and death during the first 28 days of AMI on the basis of season was similar. Gender is one of the important factors that influence mortality from AMI; women are at a greater risk for mortality from this disease. In a study conducted by Herman et al., 28-day survival rates in men and women were compared with each other; the survival rate was 83.9% in men and 76.9% in women. This difference observed between the two sexes was statistically significant and women had a weaker prognosis than men.[16] Of course, the lower survival and higher mortality rates in women than men were observed in a number of other studies.[17-26] However, perhaps the difference in mortality between seasons is due to the difference in percentage of female patients in each season. For examination of this theory we identified the percentage of occurrence of AMI between seasons for each sex. We observed that this percentage for females is between 26.5%-27.7%, and in fact the almost constant percentage of patients belonged to women. On the basis of this result we can express that the seasonal variation in the mortality from the disease has not been influenced by gender.

In this study, we observed that the highest rate of hospital admission occurred in the spring and the second highest rate occurred in winter, and the

lowest in summer. Of course, in a number of studies the major event occurred in spring. In a study conducted by Kriszbacher et al. on 81,956 patients between 2000 and 2004, the highest incidence of disease was observed in spring and lowest in summer.[8] The results of our study are in accordance with this study and other studies conducted in different regions of the world.[8,27] However, in a number of studies, the highest rate of hospital admission or the occurrence of disease was considered to be during winter.[9,12] In many studies the lowest rate of hospital admission occurred during summer.[12,27,28]

The minimum and maximum rate of hospital admission for AMI, respectively, was in summer and spring. They increased 17.8%, 15.8%, and 4.2% during spring, winter, and autumn, respectively, in comparison to summer. However, in a study conducted by Stewart et al. it was observed that in winter hospital admissions, compared with average, increased about 15% to 18%. In fact, hospital admissions increased in winter compared with other seasons.[11]

The highest rate of mortality during the first 28 days in patients with AMI was in winter and spring, and the lowest in autumn. In a study conducted by Rumana et al., the highest mortality rate of AMI in the first 28 days after the occurrence of AMI was in winter and the second highest in spring.[9]

In the present study, the magnitude of seasonal variation was fairly modest. However, the reason for seasonal variation of AMI in ICRC is not clear. There are no administrative procedures (e.g., submission of reporting forms to meet a specific deadline at definite times of the year) that would create a misleading seasonal variation. We do not believe that a simulate, such as ICRC coordinator of summer or Nowruz holiday was effective on the observed seasonal pattern, because the examination was based on the date of AMI onset rather than on the dates that the case report forms were submitted to ICRC. We think that the most logical reason is that the seasonal variation in AMI cases of ICRC may, in fact, reveal an increased prevalence of AMI onset at certain times of the year.

Some studies found a statistically significant relationship between low temperature and mortality from acute myocardial infarction.[29] A study conduct by Larcan et al. in France compared the meteorological parameters of the day when the infarct occurred with that of the day preceding its occurrence. This study concluded that the occurrence of myocardium infarct was paralleled to a climatic tendency conforming to cold, bad, or deteriorating weather.[30] Peters et al., in a study, concluded that raised concentrations of fine particles in the air may transiently elevate the risk of MIs within a few hours and 1 day after exposure.[31] Vasconcelos et al., in a study conducted in portugal, observed the negative outcome of cold weather conditions on acute myocardial infarctions; for every degree decrease in PET in winter, there was an increase of up to 2.2% (95% CI = 0.9%; 3.3%) in day by day hospital admission.[32] In the study by Sarna et al. atmospheric pressure was found to be the meteorological variable with the highest correlation with the occurrence of myocardial infarction. Rapid decrease in atmospheric pressure was also related with increased incidence of acute myocardial infarction.[28] In a study by Foster et al., a significant relationship was found between influenza and acute myocardial infarction, whereas this correlation was not seen in stroke.[33]

Furthermore, Ulmer et al. found that cholesterol, blood pressure, and body mass index vary according to season and were also significantly higher during winter in comparison to other seasons, and this finding was observed in all age groups and both sexes.[34] However, different explanations exist for the observed variation in hospital admission and mortality from AMI in different parts of the world. Ornato et al., in their study concluding from other studies in this scope, explicated that numerous ideas have been offered to make clear an increased prevalence of AMI or its complications in the winter and cold season.[29] Weather or a quick conversion in the climate can increase arterial blood pressure, blood viscosity, arterial spasm, plasma fibrinogen and factor VII, and serum cholesterol levels (by 2% to 3%), platelet, and red blood cell counts. Exposure to cold weather has also important hemodynamic effects, including an increase in systemic vascular resistance, myocardial oxygen intake, and body metabolic rate. Contemporary infections, particularly those involving the respiratory band, during the winter months have also been claimed as a trigger for mortality due to acute cardiovascular. Other mechanisms that have been proposed to describe the increase in cardiovascular events during cold weather include seasonal variation in bodily activity, food, weight, and worry and stress during the holiday season and seasonal variety in the secretion of physiologically active substances similar to those that trigger seasonal depression. The other

possibility is that the seasonal pattern could be payable to a summer decline in events relative to other times of the year.[29]

This article was extracted from a research project with the title "Evaluation of 28-day survival and predictors of survival in patients with acute myocardial infarction in Isfahan" that was done with the cooperation and support of the Isfahan Cardiovascular Research Center with the approved code of 84130 in 2011.

Limitations

In this study, other groups of patients were not included in the study, such as MI cases that were managed at home or in health cores. This figure might be very small, because MI event is considered as an emergency in the health care system in Iran and all hospitals must admit such patients irrespective of their insurance status. In the Danish MONICA population this amount was measured to be less than 1% of the entire MI cases in a year. Another problem that can be expressed in this study is that patients who died before reaching the hospital or patients who failed to receive medical care due to their lack of access to information were not considered.

Conclusion

The results presented indicate that there is a classical seasonal pattern with increased admissions during spring and winter, and the lowest rate in summer. The highest mortality rate was observed in winter and the lowest in autumn, although these differences were not significant. There are seasonal variations in hospital admission and mortality due to AMI; however, after adjusting the model only gender and age were significant predictor factors.

This paper was extracted from the MSc theses of Abdolah Mohammadian Hafshejane in Epidemiology from Tehran Medical University that was conducted in the Isfahan Cardiovascular Research Center (ICRC) of the Isfahan Medical University.

Conflict of Interests

Authors have no conflict of interests.

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