

Original Article

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Daily, Monthly, and Seasonal Pattern of ST-Segment Elevation Myocardial Infarction (STEMI) Occurrence in Western Iran; a Cross-Sectional Study

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Abstract

Introduction: Acute myocardial infarction (AMI) is a leading cause of death and disability worldwide. Determining seasonal pattern of AMI may contribute to disease prevention and better treatment.

Objective: The present study was conducted to investigate daily, monthly, and seasonal pattern for symptoms onset in the patients with ST-segment elevation myocardial infarction (STEMI), and also other possible associated factors.

Methods: This cross-sectional study was conducted on 777 patients diagnosed with STEMI admitted at the Imam Ali Cardiovascular Hospital affiliated with Kermanshah University of Medical Sciences (KUMS), Kermanshah province, Iran from March 2018 to February 2019. Data were collected using a checklist developed based on the study's objectives. Differences between subgroups were assessed using one-way analysis of variance (ANOVA) followed by Tukey's post-hoc test and Chi-Square test (or Fisher's exact test).

Results: Out of 777 patients, 616 (79.3%) of them were male. Mean age of the patients was (mean±SD) equal to 60.93±12.86 years old. Occurrence of STEMI was most common in winter (38.4%), followed by autumn (27.8%), spring (22.9%), and summer (10.9%), respectively. Monthly occurrence of AMI was at the highest level in January (10.8%) and December (9.9%), and it was at the lowest level in July (4.9%). Most patients were admitted on Fridays (15.8%) and Wednesdays (15.6%). Hypercholesterolemia, prior congestive heart failure (CHF), prior MI, prior stroke, prior atrial fibrillation (AF), low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides, total cholesterol, creatine phosphokinase (CPK), and creatine kinase myocardial band (CK-MB) were significantly associated with seasonal pattern of STEMI (p-value<0.05).

Conclusions: Results of the present study on Iranian patients with STEMI revealed that AMI occurred more frequently on Wednesdays and Fridays and during winter from December to January compared to the other days of the week, months, and seasons.

Key words: Disease Attributes; Myocardial Infarction; Iran; Periodicity; Seasons

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INTRODUCTION

Acute myocardial infarction (AMI) is a leading cause of mortality and disability worldwide. ST-segment elevation myocardial infarction (STEMI), as the most deadly sub-class of AMI accounts for more than 35% of the cases (1). Chronobiological variation of AMI is an issue of interest in the epidemiological studies for diagnosis of biological mechanism that may trigger AMI. Most of the alive creatures have a chronobiological mechanism, which may automatically change their condition by temporal changes in daily, monthly, and seasonal pattern. This mechanism might be influenced by various factors, such as hormonal, neurological, chemical, genetic, and immunological factors (2, 3). Usually, epidemiological studies have reported

a winter peak for AMI onset, indicating that more infarcts occur on colder days. In fact, the increased mortality caused by AMI in winter was first reported in the 1930s (4). The role of temperature and weather patterns in seasonal rhythms of AMI occurrence has also been reported with different results. For instance, an increase in AMI occurrence in colder weather has been reported in different locations across the world (5, 6). In contrast, some studies have reported an increase in AMI occurrence in warmer weather (7). There is little information on seasonal variation in onset of AMI symptoms, and also data on the role of environmental temperature are conflicting. Given the conflicting data, it remains momentous to

determine whether there is seasonal variation in the occurrence of AMI. Therefore, the present study was conducted to investigate daily, monthly, and seasonal pattern of symptoms onset in the patients with STEMI, and also other associated factors.

Methods

Study design and setting

This cross-sectional study was done at Imam Ali Cardiovascular Hospital, affiliated with the Kermanshah University of Medical Sciences (KUMS), Kermanshah, Iran. This mega general hospital, as the main cardiovascular center in western Iran covers a population about 2,000,000 patients. This medical center, with 280 active beds, provides cardiovascular care services. The study protocol was approved by the Research Ethics Committee of KUMS (IR.KUMS.REC.1398.702). In addition, individuals' personal information was kept confidential.

Study population

For one-year assessment, from March 1, 2018 to February 30, 2019, all the patients with the diagnosis of STEMI referred to the mentioned center were evaluated. Actually, all the eligible patients were included based on inclusion criteria. Inclusion criteria were having ≥ 18 years of age and definite diagnosis of STEMI. Criteria for diagnosis of STEMI were according to the third universal definition of AMI introduced by the European society of cardiology (ESC) / American college of cardiology foundation (ACCF) / American heart association (AHA) / and world heart federation (WHF) Task Force for the Universal Definition of Myocardial Infarction (8). Diagnosis of STEMI was based on the following elements: 1) characteristic chest pain or discomfort 2) electrocardiographic changes in accordance with new ST-segment elevations or left bundle branch block (LBBB), and 3) the elevated levels of cardiac markers (CPK, troponins, etc.). The patients with incomplete personal or medical information were excluded.

Instruments and data collection

A trained nurse obtained the data using a checklist developed based on the study's objectives. Face validity of the questionnaire was assessed and approved, by obtaining experts' opinions including two cardiologists and a statistician. A pilot study was designed and performed on 30 patients with STEMI to complete and modify the questionnaire, as a result of which medications were added to the questionnaire. Finally, the checklist included five following parts:

demographic characteristics (e.g., gender), clinical histories (e.g., previous chest pain), medication (e.g., Statin), cardiac enzyme (e.g., CK-CPKMB), and the time for onset of AMI.

The data were obtained from both paper and electronic medical records to prevent any bias in data collection. Moreover, the results were evaluated through checking hospitals' managerial information.

Statistical analysis

Data analysis was performed using statistical package for social sciences (SPSS) statistical software (Version 23.0; IBM Corporation, Chicago, USA). Quantitative variables (e.g., BMI or age) were described using mean \pm standard deviation (SD) and qualitative/categorical variables were expressed as frequencies and percentages. Differences between subgroups were assessed using one-way analysis of variance (ANOVA) followed by Tukey's post-hoc test for continuous and normally distributed variables and Chi-Square test (or Fisher's exact test) for categorical variables. Chi-square goodness of fit test was performed to test uniformity in distribution of the patients between various seasons, months, and days. A probability value (p-value) of less than 0.05 was considered as statistically significant.

RESULTS

During 12 months, a total of 777 patients with STEMI including 616 (79.3%) men, and 161 (20.7%) women met the inclusion criteria to be included in the present study. Mean age of the patients was (mean \pm SD) equal to 60.93 \pm 12.86 years old. All the patients (100%) reported a history of chest pain, 48.9% of them were current smoker, 40.3% of them were hypertensive, 21.1% of them had hypercholesterolemia, 18.3% of them had diabetes mellitus (DM), 25.2% of them had a history of angina, about 15% of them had a history of MI, 27.7% of them used aspirin, and 21.2% of them took beta-blockers. Mean ejection fraction (EF) was equal to 37.18 \pm 10.65. Regarding the lipid profiles, mean level of LDL was equal to 108.61 \pm 35.90. Mean level total cholesterol was equal to 173.78 \pm 41.83 mg/dL. Mean level of triglycerides was equal to 142.62 \pm 83.30 mg/dL. All the patients' demographic and clinical characteristics are shown in table 1.

Three hundred and sixty-five days of the year were classified into four seasons: spring (March, April, May), summer (June, July, August), autumn (September, October, November), and winter (December, January, February). Seasonal variation of MI occurrence is shown in figure 1. Occurrence

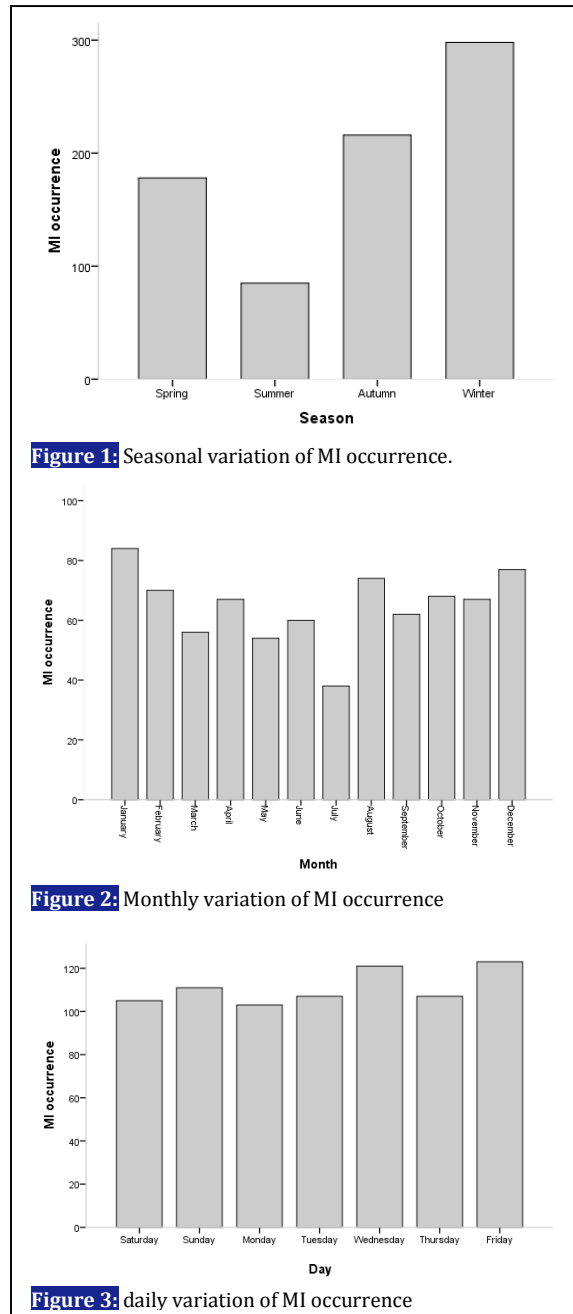
Table 1: Association of various characteristics and seasonal pattern of STEMI (N=777)

Characteristic	Total	Spring	Summer	Autumn	Winter	p-value
Age	60.93±12.86	59.28±11.89	60.80±13.82	60.62±12.57	62.22±13.28	0.118
BMI	25.95±3.87	25.95±3.70	25.74±3.39	26.40±3.90	25.68±4.09	0.207
Male sex	616 (79.3)	149 (83.7)	66 (77.6)	176 (81.5)	225 (75.5)	0.139
Current smoker	380 (48.9)	89 (50.0)	46 (54.1)	112 (51.9)	133 (44.6)	0.268
Past medical history						
Diabetes mellitus	142 (18.3)	42 (23.6)	14 (16.5)	36 (16.7)	50 (16.8)	0.242
Hypertension	313 (40.3)	69 (38.8)	34 (40.0)	93 (43.1)	117 (39.3)	0.617
Hypercholesterolemia	164 (21.1)	44 (24.7)	14 (16.5)	40 (18.5)	66 (22.1)	0.009
Cancer	7 (0.9)	0 (0.0)	3 (3.5)	0 (0)	4 (1.3)	0.064
Sleep apnea	9 (1.2)	2 (1.1)	0 (0.0)	4 (1.9)	3 (1.0)	0.799
CHF	28 (3.6)	2 (1.1)	3 (3.5)	20 (9.3)	3 (1.0)	0.001
MI	116 (14.9)	28 (15.7)	10 (11.8)	23 (10.6)	55 (18.5)	0.001
Angina	196 (25.2)	38 (21.3)	15 (17.6)	61 (28.2)	82 (27.5)	0.118
Stroke	47 (6.0)	9 (5.1)	11 (12.9)	9 (4.2)	18 (6.0)	0.033
Atrial fibrillation	16 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	16 (100)	0.001
PCI	67 (8.6)	13 (7.3)	4 (4.7)	20 (9.3)	30 (10.1)	0.617
CABG	31 (4.0)	7 (3.9)	1 (1.2)	12 (5.6)	11 (3.7)	0.360
Drug history						
Aspirin	215 (27.7)	49 (27.5)	23 (27.1)	61 (28.2)	82 (27.5)	0.997
Clopidogrel	34 (4.4)	6 (3.4)	2 (2.4)	9 (4.2)	17 (5.7)	0.468
Beta-Blocker	165 (21.2)	33 (18.5)	13 (15.3)	46 (21.3)	73 (24.5)	0.216
ARB	86 (11.1)	22 (12.4)	8 (9.4)	24 (11.1)	32 (10.7)	0.903
ACE inhibitor	149 (19.2)	34 (19.1)	20 (23.5)	40 (18.5)	55 (18.5)	0.753
Statin	106 (13.6)	22 (12.4)	11 (12.9)	25 (11.6)	48 (16.1)	0.334
Biochemical profile						
LDL (mg/dl)	108.61±35.90	112.26±39.38	120.56±38.50	101.29±27.99	108.21±36.95	0.001
HDL (mg/dl)	41.46±10.96	41.18±11.31	38.69±6.90	39.84±8.24	43.74±12.99	0.001
Triglycerides (mg/dl)	142.62±83.30	150.30±87.79	139.87±85.98	115.59±57.88	176.04±95.46	0.001
Total Chol (mg/dl)	173.78±41.83	173.32±42.90	175.17±43.16	167.16±36.95	178.53±43.67	0.027
CK-MB (units/L)	140.29± 116.58	116.73±90.70	186.67±140.80	135.12±110.33	144.57±123.0	0.001
CPK (units/L)	1656.87± 1215.35	1117.38±940.60	2190.57±1402.86	1810.22±1263.45	1707.85±1151.79	0.001
Troponin (ng/mL)	13.34± 63.50	15.97±92.96	11.09±8.44	11.90±54.48	13.56±61.77	0.922
Creatinine (mg/dl)	1.18±0.28	1.21±0.27	1.18±0.18	1.17±0.37	1.19±0.20	0.866
LDH (units/L)	337.69± 153.73	274.70±70.00	348.80±61.58	337.75±249.29	393.42±199.24	0.572
ESR (mm/hour)	9.18±11.62	12.81±26.13	10.26±7.83	8.09±7.77	8.49±6.34	0.139
EF (%)	37.18± 10.65	38.43±10.87	37.47±10.19	36.48±10.74	36.86±10.59	0.296

ACE: angiotensin converting enzyme; ARB: angiotensin receptor blockers; BMI: body mass index; CABG: coronary artery bypass grafting; CHF: congestive heart failure; Chol: cholesterol; CPK: creatine phosphokinase; CK-MB: creatine kinase-myocardial band; EF: ejection fraction; ESR: erythrocyte sedimentation rate; HDL: high-density lipoprotein; LDH: lactic acid dehydrogenase; LDL: low-density lipoprotein; MI: myocardial infarction; PCI: percutaneous coronary intervention

of STEMI was most common in winter (38.4%), followed by autumn (27.8%), spring (22.9%), and summer (10.9%), respectively ($p=0.001$). Regarding monthly variation, the results showed that most patients (10.8%) were admitted in January as a first peak of AMI, the second peak was in December (9.9%) and the third peak was in August (9.5%); and the least frequency of the patients (4.9%) was recorded in July ($p=0.149$) (Figure 2). The results demonstrated that most patients were admitted on Fridays (15.8%) and Wednesdays (15.6%) ($p=0.411$) (Figure 3). Hypercholesterolemia, prior congestive heart failure (CHF), prior MI, prior stroke, prior atrial fibrillation (AF), low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides, total cholesterol, creatine phosphokinase (CPK), and creatine kinase myocardial band (CK-MB) were significantly associated with seasonal pattern of STEMI ($p<0.05$). In winter, frequency of the patients who had prior AF at the time of presentation was significantly higher than the

other seasons (100% vs. 0% to 2.1; $p=0.001$). In winter, frequency of the patients who had prior MI was significantly higher than the other seasons (18.5% vs. 10.6 to 15.7%; $p=0.001$). A statistically significant seasonal pattern for onset of AMI symptoms with a peak in spring was observed in the patients with hypercholesterolemia (24.7% vs. 16.5 to 22.1%; $p=0.009$). A significant autumn peak in onset of MI symptoms was seen among the patients with prior CHF (9.3% vs. 1.0 to 3.5%; $p=0.001$). Patients who had prior stroke revealed a summer peak in terms of the onset of MI symptoms (12.9% vs. 4.2 to 6.0%; $p=0.033$). ANOVA was used followed by Tukey's post-hoc test to show the difference in the following variables: LDL, HDL, triglycerides, total cholesterol, CK-MB, CPK, troponin, lactate dehydrogenase (LDH), creatinine, erythrocyte sedimentation rate (ESR), and EF between the four seasons. According to the results of Tukey's post-hoc test, mean level of LDL in spring was significantly higher than autumn (112.26±39.38 vs. 101.29±27.99;



$p=0.013$), and also mean level of LDL in summer was significantly higher than autumn (120.56 ± 38.50 vs. 101.29 ± 27.99 ; $p=0.001$) and winter (120.56 ± 38.50 vs. 108.21 ± 36.95 ; $p=0.026$). Likewise, mean level of HDL in winter was significantly higher than summer (43.74 ± 12.99 vs. 38.69 ± 6.90 ; $p=0.001$) and autumn (43.74 ± 12.99 vs. 39.84 ± 8.24 ; $p=0.001$). Results of the Tukey's post-hoc test showed that mean level of triglycerides in winter was significantly higher than summer (176.04 ± 95.46 vs. 139.87 ± 85.98 ; $p=0.036$) and autumn (176.04 ± 95.46 vs.

115.59 ± 57.88 ; $p=0.001$). Also, mean level of total cholesterol in winter was significantly higher than autumn (178.53 ± 43.67 vs. 167.16 ± 36.95 ; $p=0.014$). Mean level of CPK in spring was significantly lower than the other three seasons (1117.38 ± 940.60 vs. 1707.85 ± 1151.79 to 2190.57 ± 1402.86 ; $p=0.001$), and also mean level of CPK in winter was significantly lower than summer (1707.85 ± 1151.79 vs. 2190.57 ± 1402.86 ; $p=0.008$). Mean level of CK-MB in summer was significantly higher than spring (186.67 ± 140.80 vs. 116.73 ± 90.70 ; $p=0.001$), autumn (186.67 ± 140.80 vs. 135.12 ± 110.33 ; $p=0.004$), and winter (186.67 ± 140.80 vs. 144.57 ± 123.0 ; $p=0.020$).

DISCUSSION

This cross-sectional study was performed to assess seasonal pattern of AMI occurrence in the patients with STEMI admitted at Imam Ali Cardiovascular Hospital affiliated with KUMS, Kermanshah province, Iran from March 2018 to February 2019. Seasonal patterns of AMI have been considered for many years and in different geographical areas. Although, the previous evidence shows conflicting findings based on geographical and climatic variations. In the regions with temperate and cold climate, such as Finland, occurrences of AMI have been found to be higher in winter. In subtropical regions, such as Egypt, although, daily hospital admissions of AMI have been reported to be more common in summer. Kermanshah province, located in Western Iran has a temperate and cold climate. The results of the present study illustrated that AMI occurred more frequently on Wednesdays and Fridays and during winter from December to January compared to the other days of the week, months, and seasons.

The results of this study demonstrated a greater occurrence of MI on Wednesdays and Fridays. In comparison with the previous studies, Vander-Palen et al., (1995) from New Zealand (9), Willich et al., (1994) from Germany (10), Spelberg et al., (1995) from Germany (11), and Genechi-Roscone et al., (1994) from Italy (12), reported an increasing trend of MI occurrence on Mondays. Jalali et al., in a study from Babol state (Mazandaran province) in Iran (2002) reported that AMI occurred more frequently on Saturdays compared to the other days (2). Our results are not consistent with those reported in the previous studies; since Monday in Christian calendar and Saturday in solar calendar are the starting working days of the week whereas Wednesday

and Friday in Iranian population are the weekend days.

Regarding monthly variation of MI onset, it was found that occurrence of MI was more from December to January. Our results are in line with the findings of the previous studies. Meal et al., in a study from England found that MI mostly occurred in January (13). Hopstock et al., found that occurrence of MI was higher from November to January (14). Lee et al., reported that occurrence of AMI was at the highest level in January (15). Results of a study from Germany revealed that the highest occurrence of AMI was in December and January (16). Nevertheless, some researchers have reported contradictory results. Jalali et al., reported that occurrence of MI was significantly increased in November (2). Spielberg et al., reported that the most occurrence of MI was in March (11). Loughnan et al., in a study (2008) reported July as peak month of MI occurrence (17).

Regarding seasonal variation of MI, it was found that occurrence of MI was more in winter. In accordance with our findings, Nagarajan et al., in a study from US in 2017 found that AMI admissions were higher in winter (6). Keller et al., in a study from Germany (2019) showed that seasonal incidence and in-hospital mortality caused by AMI were higher in winter (5). Conversely, Jalali et al., found that MI mostly occurred in autumn (2). Akioka et al., found that AMI onset was mostly in summer in 2019 (7).

Some situations related to an increased risk of AMI are more common during the coldest season (December- January), that may explain our findings. For instance, influenza and respiratory tract infections are well known as risk factors for AMI that usually occur in winter (18). Jeffrey et al., reported a 6-fold increase in the AMI occurrence 7 days after an influenza infection in 2018 (19). Furthermore, influenza vaccination reduces the risk of AMI and re-infarction. Season-related behavioral patterns, like seasonal depression, dietary changes, the decreased physical activity, and the reduced sunshine duration and vitamin D uptake may also contribute to the increase in the AMI occurrence in winter (20). Our findings, in accordance with the literature showed that cholesterol levels are lower during summer, probably contributing to lower related risk of AMI in summer (21, 22).

Some potentially interesting results were also found in the subgroup analyses. Winter predominance was pronounced in the patients who had a history of AF and MI, while

hyperlipidemic patients had more admissions in spring. Investigating the patients who had a history of stroke, a significant seasonal variation with summer predominance was found in AMI admissions. A significant difference was observed in the seasonal variation of AMI occurrence with autumn peak while investigating the patients who had a history of CHF.

Limitations of the Study

This study had well-known limitations of a cross-sectional design of study and our data were obtained from a single center. Hence, our participants may not be representative of the whole patients with STEMI. Thus, it is suggested to assess the effect of season on type of MI and mostly on MI in the future studies.

CONCLUSIONS

Results of the present study on Iranian patients with STEMI revealed that AMI occurred more frequently on Wednesdays and Fridays and during winter from December to January compared to the other days of the week, months, and seasons. Moreover, hypercholesterolemia, prior CHF, prior MI, prior stroke, prior AF, LDL, HDL, triglycerides, total cholesterol, CPK, and CK-MB were significantly associated with seasonal pattern of AMI.

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AUTHORS' CONTRIBUTION

NS and RHM developed the original idea, the protocol, and study design. AR, NM, JA collected and manage the data. PJ, MR participated in data analyses. NS and RHM participated in drafting and MR participated in editing manuscript. All authors provided comments, participated in writing manuscript, and approved the final manuscript.

CONFLICT OF INTEREST

The authors declare that there they have no conflicts of interest. In addition, the authors have no financial interest related to any aspect of the study.

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