Research Article

Modes of presentation of acute myocardial infarction and circadian, circaseptan, circannual rhythms

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Abstract

Background and Objectives: To study the Modes of presentation of MI along with Circadian, Circaseptan, Circannual pattern of onset in local population and the effect of time delay on mortality. **Methods:** Presentation of 316 patients (October 2006 to September 2009) of acute myocardial infarction (AMI) with typical chest pain and atypical symptoms were studied. The circadian, circaseptan and circannual rhythm of onset noted along with risk factors and delay in treatment and outcome. **Results:** 273 (86.39%) patients presented with chest pain, mean age (51.5) and 43(13.60%) with atypical symptoms, mean age (56.3) had proportionately more females. A larger (115 patients) morning peak (1st quarter) of onset of AMI and lesser (85patients) evening peak was noted. 12.97% mortality in patients presenting <6 hours and 24.75% in >6 hours. More onset of AMI on Friday and Sunday (circaseptan). 109 patients had onset of AMI in monsoon. **Conclusion:** 13.60% of individuals had atypical presentation of MI. Delay of arrival was associated with increased mortality rate and decreased thrombolysis there was significant morning peak in the onset of MI and seasonal peak onset in monsoon. But least onset in winter and no significant circaseptan pattern.

Keywords: Acute Myocardial Infarction, modes of onset, Circadian, Circaseptan, Circannual rhythm.

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INTRODUCTION

Cardiovascular diseases are major causes of mortality and disease in the Indian subcontinent, causing more than 25% of deaths. It has been predicted that these diseases will increase rapidly in India and this country will be host to more than half the cases of heart disease in the world within the next 15 years. The World Health Organization requires the presence of chest pain as one of the cornerstone features in its diagnosis of Myocardial Infarction (MI).[1] The absence of chest pain at hospital presentation was among the most significant factors predicting lower use of thrombolytic therapy among a subset of MI patients eligible for such treatments in the National Registry of Myocardial Infarction 2 (NRMI-2)[2]. Understanding the factors associated with atypical presentations (i.e., no chest pain) may help in the earlier identification and treatment of these patients with MI. Acute myocardial infarctions (AMI) are not random events. Incidence of AMI is influenced by variations in the seasonal (circannual), weekly (circaseptan), and circadian patterns, as well as by external trigger factors such as physical or mental stress. Peaks of incidence occur in the morning, on Mondays, and in winter. There is a difference in the pattern of incidence in different subgroups.[3] Recent advances in the study of endothelial function, cytokine biology, and adhesion molecules have led to new insights into the way that natural fluctuations in these systems may affect ACS incidence. It is hoped that understanding these developments will lead to therapeutic advances in ACS prevention[3]. We have undertaken to study the various modes of presentation of AMI in local population, its influence by various subgroups and its association with the circadian, circaseptan and circannual variation and factors influencing delay in approaching hospital for appropriate care by patients.

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SUBJECTS AND METHODS

All the Patients of acute myocardial infarction admitted in Bidar institute of medical sciences (BRIMS) hospital, Bidar over 3 years from October 2006 to September 2009 were studied. The diagnosis of AMI was done using the clinical features, ECG changes and or enzyme abnormalities. A total of 316 cases were studied. They were also followed up over the period of their hospital stay. The findings of the examination and the results of all the investigations were recorded, tabulated and compared using Chi Square test. The criteria of ECG changes are- a. Presence of pathological Q waves. b. Hyperacute tall T wave or inverted T wave. c. Persistent ST segment elevation > 2.5mm. The CIRCADIAN-time of the day(grouped into four quarterly periods of 00:00 to 6:00 hrs,6:01 to 12:00 hrs,12:01 to 18:00 hrs and 18:01 to 24:00 hrs) CIRCASEPTAN-day in a week(Monday to Sunday), and CIRCANNUAL-Prevailing season in a year in Bidar such as; Winter (December 1st to February 7th), Summer (February 8th to May 31st), Monsoon(June 1st to September 30th), Post Monsoon (October 1st to November 30th) at the onset of symptoms were recorded. Patients presenting symptom of typical chest pain or with atypical symptoms at onset of AMI, the delay in time to reach hospital for treatment from the time of onset of symptoms, receiving thrombolytic therapy, in-hospital mortality, age, gender, history of Ischemic heart disease, hypertension and diabetes mellitus were recorded, grouped and studied for their association, applying non parametric chi square test for statistical analysis.

RESULTS AND OBSERVATION

43 patients presented with chest pain and 273 patients presented with atypical symptom with dyspnoea (39.53%) as the most common symptom followed by vomiting (32.55%) and syncope(25.58%) along with others noted more frequently in inferior wall MI and anterior wall MI. With advancing age the proportion of acute MI with atypical presentations increased in the respective age group from <30 years to >80 years with maximum number of cases[11] in 61 to 70 yrs and least number in less than 30 years[2]. Only 3 patients out of 43 with atypical symptoms had previous history of angina (6.97 %) compared to the patients with typical symptoms, in that 6.59 % of patient gave past history of angina. 25.58% of atypical MI had hypertension compared to 18.68% of typical MI with hypertension which were statistically not significant. In this study there were only 31 diabetic patients, out of which 4 (9.30%) patients presented with atypical symptoms. When compared to 27 (9.89%) presenting with typical AMI. Which was statistically not significant. The in-hospital mortality of AMI patients who presented with typical and atypical symptoms were 19.41% and 30.23 %. Which was found statistically not significant. In this study, Anterior wall myocardial infarction (AWMI) was the commonest (50 %) followed by inferior wall myocardial infarction (IWMI) (34.17 %).Out of 43 cases of atypical MI, IWMI(53.48%) presented more often followed by AWMI(25.58%). This association was found statistically significant at P<0.01. Out 316 patients, 31 patients came to the hospital within one hour of onset of symptoms, 184 patients delayed between 1 to 6 hours and 101 took more than 6 hours to reach the hospital. Among the group of patients who delayed their arrival to hospital for more than 6 hours included proportionately more number of elderly >60 years (43.56% vs 33.49%), more females (27.72% vs 21.40%), more atypical MI (18.81% vs 11.16%), more diabetics (11.88% vs 8.84%), with lesser history of IHD (4.95% vs 7.44%), with similar hypertensives (18.81% vs 20.00%), more mortality(24.75% vs 19.07%). But however above findings were not statistically significant, except lesser number of delayed patients undergoing thrombolysis (35.64% vs 69.77%) which was found to be highly significant. P < 0.001 statistically. A single peak of onset (115 patients) of AMI symptoms was seen in second quarter of the day between 6:01 to 12:00 hrs with a trough between 18:00 to 24:00 hrs which was found to be highly significant P<0.001.The circadian peak was seen in various sub groups alike such as gender, diabetes and in cases with history of IHD, day, season, except in elderly (>60 yrs) who had an evening (12:00 to 18:00 hrs) peak with increased mortality for cases with onset in evening. Though more number of AMI onset was on Friday[63] followed by Sunday[50] almost equal distribution of cases was found throughout the week which was statistically insignificant. There was a peak onset of cases in monsoon[109], summer[89] followed by postmonsoon[69] and least cases in Winter[49].

Table 1: characteristics of patients presenting with and without chest pain

Variable	Without chest pain (Atypical)	With chest pain(Typical)	P Value
Mean age	56.3	51.5	
Total patients	**43**	**273**	
<60 Years	22(51.16%)	178(65.20%)	X^2= 3.151 P<0.05 Not Significant
≥60 Years	21(48.83%)	95(34.79%)	
Female	14(32.55%)	60(21.97%)	X^2= 2.319 P<0.05 Not Significant
Male	29(67.44%)	213(78.02%)	

Diabetics	4(9.30%)	27(9.89%)	X2= 0.0145 P<0.05 Not Significant
Hypertension	10(23.25%)	51(18.68%)	X^2= 1.121 P <0.05 Not Significant
I H D	3(6.97%)	18(6.59%)	X^2= 0.010 P <0.05 Not Significant
Thrombolysis	18(41.86%)	168(61.53%)	X^2= 14.426 P <0.001 Highly Significant
Mortality	13(30.23%)	53(19.41%)	X2= 2.63 P<0.05 Not Significant.

Table 2: Mode of presentation and prognosis according to site of infarction

Atypical symptom	Frequency of symptom	Site of infarction	Total Cases	Atypical	Mortality
Dyspnoea	17	Anterior wall	158	11(6.96%)	2
Vomiting	14	Inferior wall	108	23(21.29%)	8
Syncope	11	Inf+lat	4	1(25%)	1
Epigastric pain	6	Ant + Lat	2	0	0
Backache	5	Posterior wall	1	0	0
Bodyache/ Loose motion/ Sweating	3	Ant + Inf	2	0	0
Jaw pain / Pain in throat/ Cough / Wheeze	1	Ant + Septal	41	8(19.51%)	2

X2= 20.357 P<0.01 Significant

Table 3: Characteristics according to delay after the onset of acute symptom until hospital arrival

Character	≤ 1 Hr	1 to 6 Hrs	Total < 6Hrs	> 6Hrs	P Value
No of patients	**31**	**184**	**215**	**101**	
<60	21	122	143 (66.51%)	57 (56.44%)	X^2=3.003 P<0.05 Not Significant
≥ 60	10	62	72 (33.49%)	44 (43.56%)	
Male	27	142	169 (78.60%)	73 (72.28%)	X^2=1.534 P<0.05 Not Significant
Female	4	42	46 (21.40%)	28 (27.72%)	
Atypical symptoms	3	21	24 (11.16%)	19 (18.81%)	X^2=3.420 P<0.05 Not Significant
Typical Symptoms	28	163	191 (88.83%)	82 (81.18%)	
DM	4	15	19 (8.84%)	12 (11.88%)	X^2=0.720 P<0.05 Not Significant
IHD	3	13	16 (7.44%)	5 (4.95%)	X^2=1.12 P<0.05 Not Significant
HTN	12	31	43 (20.00%)	19 (18.81%)	X^2=0.062 P<0.05 Not Significant
Thrombolysis	23	127	150 (69.77%)	36 (35.64%)	X^2=33.045 P<0.001 Highly Significant
Mortality	6	35	41 (19.07%)	25 (24.75%)	X^2=1.343 P<0.05 Not Significant

Table 4:

CIRCADIAN	0.01 to 0.02 6:00 Hrs	6:01 to 12:00 Hrs	12:01 to 18:00 Hrs	18:01 to 24:00 Hrs	x^2/P Value/Significance
Number of Cases	58	115	85	58	Applied Goodness of Fit. X^2=28.025 P<0.001 Highly Significant

CIRCASEPTAN	Mon	Tue	Wed	Thu	Fri	Sat	Sun	x^2/P Value/Significance
Number of Cases	39	34	44	40	63	46	50	Applied Goodness of Fit. X^2=11.805 P<0.05 Not Significant

CIRCANNUAL	Winter	Summer	Monsoon	Post Monsoon	x^2/P Value/Significance
Number of Cases	49	89	109	69	Applied Goodness of Fit. X^2=25.316 P<0.001 Highly Significant

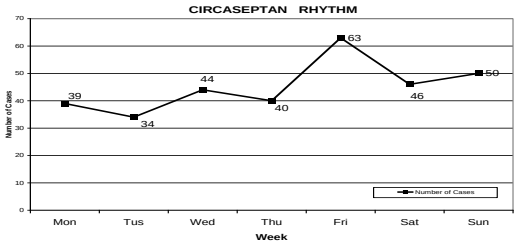

Figure 1:

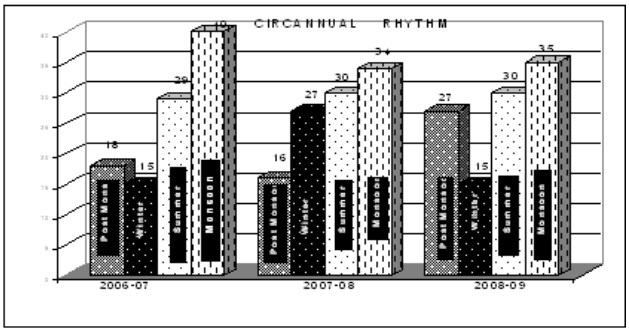

Figure 2:

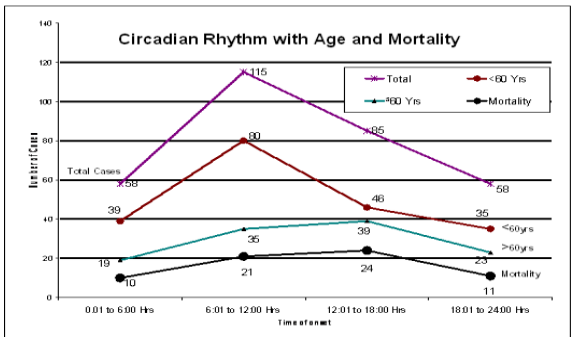

Figure 3:

DISCUSSION

In this study, the patients with atypical MI (13.60%), were older (mean age of 56.3 vs 51.5) and the proportion of females was higher (32.35% vs.21.9%) when compared to typical MI (86.39%) though statistically not significant. In the Reykjavik[4] study, about 30% of myocardial infarction presented with atypical symptoms. Results from other population studies have shown that between 20% and 60% of all MI are presented with atypical symptoms. According to study by John G .Canto[5] and others patients presenting with atypical symptoms were older (mean age 74.2 yrs vs 66.9 yrs) and females were 49% vs 38% males. In a hospital based study by chowta *et al*. 20% of cases were atypical AMI, with older age(mean age 61 vs 58 years) and were women(35% vs 12.5%)[6] Grouped according to age, there is a slight increase in incidence of painless infarction with increasing age. In the age group 51-60 years, 20.9% of patients and in 61-70% age group 30.23% presented with atypical symptoms out of total 43 patients. This is comparable with William B. Kennel *et al*[7] ,where the values were 27% and 31% respectively. But in contrast to earlier studies in which patients who were 70 years or older were more likely to present without chest pain. In this study only 10 patients above 70 yrs presented with atypical symptoms out of 43. The gender difference of females with males is proportionately higher in the incidence of atypical presentation. This is similar to the results found in the study conducted by Muller RT *et al*[8]. An increase in proportion of atypical MI with advancing age was not statistically significant although it is uncommonly seen before age 55 yrs. A much larger sample would be required to prove or disprove the possibility. In this study only 3 patients with previous history of angina presented with atypical symptoms of AMI, showing a lower prevalence of angina among those with atypical (unrecognized) MI group. This was statistically not significant in the present study. This is in comparison with Framingham study[9] and Honolulu heart program study[10] which also showed a low prevalence of angina pectoris among unrecognized MI. The lower frequency of prior history of angina in the atypical MI group suggested a reduced sensitivity to ischemic pain. In this study, 23.25% of hypertensives patients were among atypical MI compared to 18.68% with typical presentation. This supports partially the Honolulu Hawai Heart program study[10] in which the patients with atypical symptoms were more likely to be hypertensive, to have diabetes or impaired glucose tolerance but they were less likely to have angina pectoris. Whereas our study had proportionately similar number of diabetics in typical (9.89%) and atypical (9.30%) AMI. A greater prevalence of hypertension and diabetes in the atypical MI group was also noted in Framingham study[9] and study by John G Canto[5]. In this study a higher percentage of inferior wall MI patients presented with atypical symptoms (53.48%) which is statistically significant. Honolulu Hawai Heart program study[10] also supports the same thing, which demonstrated a pronounced increase in painless infarction with inferior wall MI patients (51%).That is, higher proportion of inferior wall MI tends to cause atypical symptoms, such as epigastric pain or abdominal distress which would fail to be recognized as MI. But study by William B. Kennel and others[11]showed that there was no difference in the elecrocardiographic location of infarct between those with atypical and typical symptoms of MI. In the Framingham study[9] the proportion of atypical MI did not vary with electrocardiographic location of the infarct. For patients presenting ≤1 hour,>1 to 2 hours, and >2 to 3 hours, >9 to 10 hours, >10 to 11 hours, and >11 to 12 hours after symptom onset, the use of any reperfusion therapy were 77%, 77%, 73%, 53%, 50%, and 46% respectively[12]; which is comparable to the present study where 69.77% of the group of patients presenting less than 6 hrs after onset of AMI symptoms were thrombolysed compared to 35.64% who presented later than 6 hrs was found statistically significant. Patients with atypical MI group showed a higher mortality than did the typical MI group (30.23% vs 19.41%) though statistically not significant. In the Framingham study[31] also, age adjusted long term mortality for all cases were slightly worse among unrecognized MI cases than among

recognized MI. But this is in contrast to Reykjavik study[1], where the prognosis for patients with atypical MI is no better than that for patients with recognized MI 9.8% of patients with AMI arrived at the hospital within 1 hour and 58.22% within 6 hours and 31.96% more than 6 hours. Increase in the delay was associated with a trend of proportionately increasing age, female sex and with atypical symptoms (statistically not significant). The Worchester heart attack study[13] findings showed Case fatality did not differ significantly with delay of arrival at the hospital. A slightly higher mortality for early arrivers may be due to the fact that the early arrivers are less likely to be hemodynamically stable and therefore more likely to be hypotensive or in cardiogenic shock, whereas late arrivers are more stable. In contrast, according to United Kingdom Heart attack study[14], case fatality did not differ significantly for delays upto 12 hours, but it was higher for patients who delayed for more than 12 hours. In this study in- hospital mortality for early arrivers (<6hrs) were 19.06% and that for late arrivers (>6hrs) 24.75% is comparable though statistically not significant. There is compelling evidence to show that there is an increased incidence of coronary events in the mornings, on Mondays, and in winter. There is strong evidence for the existence of a second peak later in the afternoon, but some controversy remains regarding the pattern seen in some subgroups. It is likely that an interaction of several factors is responsible for the patterns seen. The interactions between the sympathetic nervous system, blood coagulation, and coronary artery tone are likely to be especially important. Other factors such as the effects of genetic polymorphisms, endothelin, endothelial function, adhesion molecules, free radicals, and interleukins have still to be fully evaluated. There may be different balances in the influence exerted by individual factors, resulting in the differing subgroup patterns and in the difference between the morning and evening peak[3]. In this study, the circadian frequency of onset of MI as determined by onset of AMI symptoms over four quarterly periods of 6 hours each in a 24hrs day, for 316 patients confirmed circadian pattern with peak onset in second quarter of day (6:01 to 12:00 hrs.). The incidence of onset of MI was 36.39% in 2nd and 26.89% in 3rd and 4th quarters of the day (45.3% and 40%). This is comparable to the study by SR. Mehta *et al*[15].where a significant circadian pattern was evident with a peak in 2nd quarter (33.55%).The incidence of onset of events in this quarter was (1.71)times greater than the average incidence during the other three quarters. However the incidence was equally distributed over first and fourth quarter (18.35%) The various subgroups like modes of MI, age, sex, hypertension and diabetes had no influence on circadian rhythm contrary to other studies,[3]however an evening peak(12:00 hrs to 18:00 hrs) was noted in >60 yrs subgroup though statistically not significant. Many studies have shown an excess of cardiovascular events on Mondays. A relative trough has been seen on Saturdays and Sundays compared with the expected number of cases. A similar pattern was seen in most subgroups irrespective of age, gender, cardiac medication, and infarct characteristics (first or recurrent), Q or non-Q, site[3] .In this study 19.93% cases had onset of AMI on Friday followed by 15.82% on Sunday contrary to other studies. In Northern Europe a peak seasonal incidence of AMI and sudden cardiac death (SCD) has been seen between January and March. This is corroborated by data from the USA showing that 53% more cases of AMI were reported in the winter than in the summer. This was true for men and women of all ages and mirrored the in-hospital case fatality rates. In England and Wales, over the winter of 1999/2000, 8% of deaths (9,000 persons) were attributable to the winter excess. Various other factors have been suggested as the cause of increased mortality in the winter months. These include hours of sunlight, higher fibrinolytic activity in the summer, and higher plasma cortisol levels, hematocrit, and granulocyte levels in the winter. Blood catecholamine levels rise in exposure to cold, and increased sympathetic activity in the winter may be the culprit for the seasonal variation seen.[3]In our study 34.49% cases had onset of AMI in monsoon followed by 28.16% in summer contrary to the observations made by other studies[16] which need further evaluation in our situation.

CONCLUSIONS

316 Cases of acute myocardial infraction admitted to BRIMS Hospital Bidar, during the period from October 2006 to September 2009, were selected for this study. In this particular study undertaken, 43 had atypical presentation of MI. Although there was a notable difference as regards the age and sex, it was statistically insignificant probably because of the limited sample population. With a prospective on past history, atypical presentation was more among hypertensive, but less in patients with angina and similar in diabetics as seen in typical AMI. In this study, a significant observation was that patients with inferior wall MI presented more often with atypical symptoms. As regards the mortality rate, the atypical group had a higher mortality, though being statistically insignificant. Increase in the delay of arrival after onset of MI symptom was associated with 1. Increase in age. 2. Female sex. 3. Atypical symptoms. 4. Increase in the mortality rate were found Statistically not significant, however 5. Decreased thrombolysis was found statistically significant. This study confirms the circadian pattern of onset of AMI with morning peak

between 6:00-12:00 hrs and circannual (seasonal) onset of AMI in monsoon and summer(both statistically significant) in local population, but no circaseptan onset on any particular day of a week. This identification of risk periods allows targeting of therapies to cover the time of highest risk and also identification of high-risk groups that may benefit most from therapy. Similarly, if triggers can be identified, then it may be possible to modify these and so reduce the death rate from ischemic heart disease.

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