North Bengal Medical College Journal
Vol 2 No 1 January 2016

Original Article

Circadian Variations in the Onset of Acute Myocardial Infarction with Their Association of Some Selected Characteristics of Patients

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Revised : August 09, 2015 Accepted : August 20, 2015

Abstract

Introduction: *There is an existence of circadian pattern in the onset of acute myocardial infarction (AMI). The aim of this study was to observe the circadian variations in the frequency of acute myocardial infarction and to identify the relationship between these variations in acute attack and some selected characteristics of the patient.*

Methods*: A retrospective study carried out at cardiology ward of Rajshahi Medical College hospital and included all the patients of myocardial infarction between May 2011 and December, 2011. A total of 350 patients with confirmed acute myocardial infarction were investigated. For analysis of the circadian pattern of onset of symptoms, the day was divided into four time period of six hours interval and patients were categorized into different groups and sub-groups according to their characteristic and risk exposers.*

Results: *This study observed the highest (137, 39.15%) incidence of onset of acute myocardial infarction in the 06.01-12.00 hrs time period followed by 32.85% (115) in the 00.01-06.00hrs time period. Those belongs to age group 40 years and above showed the peak incidence at late morning (06.01-12.00 hours) whereas patients below 40 years revealed no significant circadian variations in the frequency of acute attack. Patients with smoking habit showed their peak incidence in 06.01-12.00hrs time period while high incidence in non-smokers found in 00.01-06.00hrs time period (p <.01.). Statistically significant (p<.05) variations found in the patients with parental history of MI (18.29%) and the previous history of AMI (9.43%). Patients with hyperlipidemia, diabetes and hypertension exhibited their high incidence both in early morning (00.01-06.00 hrs) and late morning (06.01-12.00 hrs).*

Conclusion: *This study observed the existence of circadian variations in the onset of acute myocardial infarction with marked peak incidence in the morning.*

Key words: *Circadian rhythm, Acute myocardial infarction Cardiovascular diseases' risk factors*

North Bengal Med. Coll.J. 2016; 2 (1) : 15-22

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Introduction

An appreciation of the existence of circadian pattern in the onset of acute myocardial infarction (AMI) has been reported in several studies.[1] Both the physiological and pathological functions of cardiovascular organs are closely related to circadian rhythm, an endogenously driven 24-h cycle. Heart rate, blood pressure, and endothelial function show diurnal variations within a day. The onset of cardiovascular disorders such as acute coronary syndrome, atrial arrhythmia, and subarachnoid hemorrhage also exhibits diurnal oscillation.[2]

Serious adverse cardiovascular events, including myocardial infarction, sudden cardiac death exhibit a pronounced circadian rhythmicity, with a marked peak in the morning hours when the patient assumes an upright posture and begins daily activities.[3] Circadian variation has been accepted as a factor in acute myocardial infarction (AMI). An increased incidence of cardiac events in the morning has been reported for a long time. Recent reports have indicated that the onset of AMI shows two peaks, which occur in the morning and evening.[4] The recognition of the morning increase of acute cardiovascular events has convinced many that they may be triggered by morning activities. Trigger factors occur relatively frequently and may play a causative role in up to 20% of cases of acute coronary syndromes. Physical exertion, bursts of anger and sexual activity have been proved to have triggering potential.[5] A general hypothesis of the triggering of coronary thrombosis has been proposed. The process begins with the development of a vulnerable atherosclerotic plaque, which may become disrupted by internal forces or by external hemodynamic or vasoconstrictive changes. Once disrupted, the plaque becomes a thrombogenic focus. From a research standpoint, this new information on triggering provides clues to a mechanism of onset that might lead to more effective preventive therapy.[6] The onsets of myocardial ischaemia, unstable angina, acute myocardial infarction, sudden cardiac death, and strokes have been reported to exhibit a circadian variation, with increased frequency in the second quarter of the day.[7] Since initial observations that the incidence of MI onset was time and activity dependent with circadian, circaseptan, and circannual variation, triggering of MI by heavy exertion, sexual activity, anger, mental stress, cocaine and marijuana use, and exposure to air pollution has been demonstrated.[8] Carlos E D'Negri et al.[9] suggested that recognition of particular regional circadian patterns in myocardial ischaemia is important in planning treatment strategies for patients with coronary artery disease to prevent the occurrence of sudden, catastrophic cardiac events. This retrospective study was designed to explore circadian variations in the onset of symptoms of acute myocardial infarction and

to identify the relationship between these variations and the characteristics of patients with aims to improve the awareness of the risk group about the timing of acute attack and to generate new possibilities for prevention of cardiovascular diseases.

Materials and Methods

This was a descriptive type of retrospective study conducted among the patients of acute myocardial infarction (AMI) admitted in the cardiology department of Rajshahi Medical College hospital between May, 2011 and December, 2011. A total of 350 patients with confirmed acute myocardial infarction were investigated to observe the circadian variations in the onset of acute myocardial infarction and explore any potential association between the circadian variations with some selected patients` characteristics. The variables of the study were age, sex, time of onset of symptoms, physical exercise, smoking habits, taking aspirin, dyslipidemia, diabetes mellitus, hypertension, previous history of ischaemic heart disease, parental history of myocardial infarction. A semi-structured questionnaire was used to obtain data from the patients` admission sheet. The study patients and their relatives (when patients were unable to talk) were also interviewed to ascertain the accuracy of the information recorded in the case sheet. Only the patients with complete information were included in this study. Time of onset of acute attack was recorded from the admission file which was the exact or nearest possible time of onset of severe symptoms of AMI. The common symptoms of AMI were chest pain, sweating, dyspnoea, vomiting. All patients were grouped and sub grouped according to some selected characteristics of the patients. For analysis of the frequency of onset of symptom with their circadian variations, the day was divided into four time period of six hours interval. They were as follows: 00.01 – 06.00 hours, 6.01 – 12.00 hours, 12.01 – 18.00 hours and 18.01 – 24.00 hours. The circadian variation in the frequency of onset of AMI was tested for significance by χ^2 test.

Results

The results have been illustrated in following sections with table and graph. The study revealed that the mean age of the AMI patients was 56 years ($\bar{x}\pm$ SD=55.71±9.39 years) and majority (284, 81.14%) of patients were in the age group of ≥60 years followed by 40-59 years group (57, 16.29%). Out of the 350 patients, 78.29% were male patients. Average age of the male was 56 years ($\bar{x}\pm$ SD = 55.99±9.22 years) and that of female was 55 years ($\bar{x}\pm$ SD = 54.74±9.99 years). Maximum (88%) patients were married and 10.28% were widowed. More details were shown in Table I & II and Figure 1 & 2.

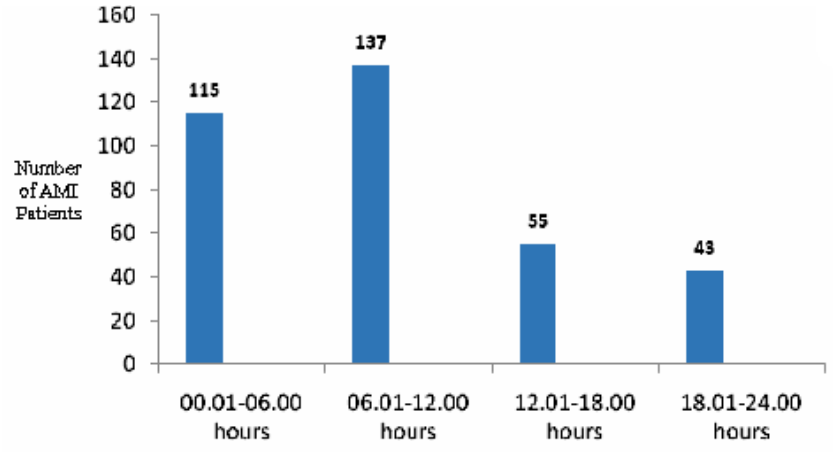

Figure 1: Circadian Variations in the Onset of Acute Myocardial Infarction (N-350)

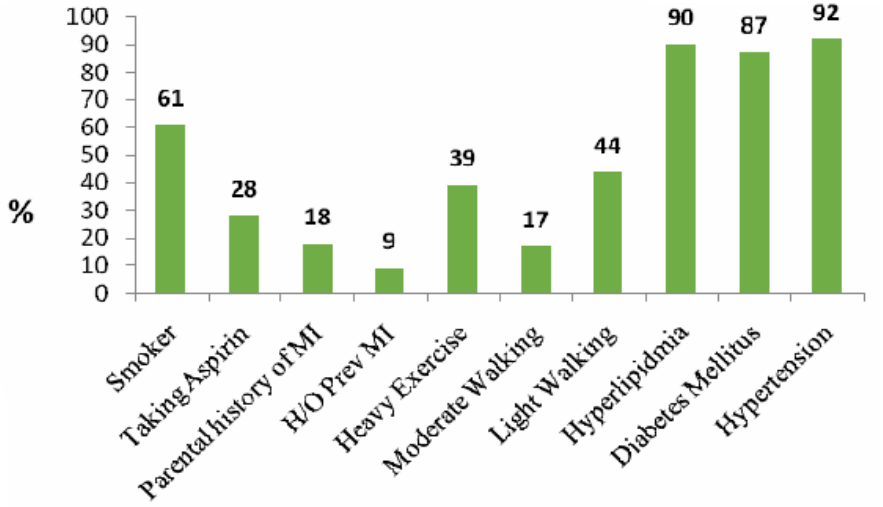

Figure 2: AMI Patients According to their Characteristics and Risk Factors (n-350)

Table I: Age and Gender Distribution of AMI Patients (n-350)

	Gender		
Age Groups	**Total (%)**	**Male Total (%)**	**Female Total (%)**
20-39 years	9(2.57%)	7(2.55%)	2(2.63%)
40-59 years	57(16.29%)	41(14.96%)	16(21.05%)
60-79 years	284(81.14%)	226(82.49%)	58(76.32%)
Total	**350 (100%) $\bar{x} \pm SD = 55.71 \pm 9.39$ years**	**274 (78.29%) $\bar{x} \pm SD = 55.99 \pm 9.22$ years**	**76 (21.71%) $\bar{x} \pm SD = 54.74 \pm 9.99$ years**

Table II: Relationship between Circadian Variations in the onset of Acute Myocardial Infarction and some selected Variables (n-350)

Time of onset of AMI → / Variables ↓	Total (%)	00.01– 06.00 hours (n-115, 32.85%)	06.01 – 12.00 hours (n-137, 39.15%)	12.01 – 18.00 hours (n-55, 15.71%)	18.01 – 24.00 hours (n-43, 12.29%)	p value
Age group:						
20-39 years	9(2.57%)	1(11.11%)	3(33.335%)	3(33.335%)	2(22.22%)	*p >.05.*
40-59 years	57(16.29%)	17(29.82%)	20(35.09%)	12(21.05%)	8(14.04%)	
60-79 years	284(81.14%)	97(34.15%)	114(40.14%)	40(14.08%)	33(11.62%)	
Gender:						
Male	274(78.29%)	87(31.75%)	114(41.61%)	45(16.42%)	28(10.22%)	*p >.05.*
Female	76(21.71%)	28(36.84%)	23(30.26%)	10(13.16%)	15(19.74%)	
Marital Status:						
Married	308(88%)	99(32.14%)	125(40.59%)	49(15.91%)	35(11.36%)	*p >.05.*
Unmarried	3(.86%)	1	1	0	1	
Divorce	3(.86%)	1	0	1	1	
Widow	36(10.28%)	14(38.89%)	11(30.56%)	5(13.89%)	6(16.66%)	
Smoking Habit:						
Smoker	215(61.43%)	66(30.70%)	95(44.19%)	43(20.00%)	11(5.11%)	*p <.01.*
Non-smoker	135(38.57%)	49(36.30%)	42(31.11%)	12(08.89%)	32(23.70%)	
Taking Aspirin:						
Yes	98(28%)	38(38.78%)	52(53.06%)	2(2.04%)	6(6.12%)	*p <.01.*
No	252(72%)	77(30.56%)	85(33.73%)	53(21.03%)	37(14.68%)	
Parental history of MI:						
Yes	64(18.29%)	9(14.06%)	16(25%)	25(39.06%)	14(21.88%)	*p <.01.*
No	286(81.71%)	106(37.06%)	121(42.31%)	30(10.49%)	29(10.14%)	
History of Previous MI:						
Yes	33(9.43%)	7(21.21%)	9(27.275%)	8(24.24%)	9(27.275%)	*p <.05.*
No	317(90.57%)	108(34.07%)	128(40.38%)	47(14.83%)	34(10.72%)	
Physical exercise:						
Light(walking <4 hours/week)	157(44.86%)	55(35.03%)	58(36.94%)	21(13.38%)	23(14.65%)	*p <.01.*
Moderate(walking >4hours/week	58(16.57%)	18(31.03%)	12(20.69%)	16(27.59%)	12(20.69%)	
Heavy(strenuous physical exercise that induce sweat)	135(38.57%)	42(31.11%)	67(49.63%)	18(13.33%)	8(5.93%)	
Lipid Profile:						
Hyperlipidemia= Total Cholesterol > 200mg/dl	316(90.29%)	104(32.91%)	127(40.19%)	50(15.82%)	35(11.08%)	*p >.05.*
Normal= Total Cholesterol < 200mg/dl	34(9.71%)	11(32.35%)	10(29.41%)	5(14.71%)	8(23.53%)	
Diabetes Mellitus:						
Normal= <7.8 mmol/l	46(13.14%)	13(28.26%)	15(32.60%)	9(19.57%)	9(19.57%)	*p >.05.*
Diabetic= >7.8mmol/l	304(86.86%)	102(33.55%)	122(40.14%)	46(15.13%)	34(11.18%)	
Hypertension:						
Normotensive	27(7.71%)	8(29.62%)	7(25.93%)	7(25.93%)	5(18.52%)	*p >.05.*
Hypertensive	323(92.29%)	107(33.13%)	130(40.25%)	48(14.86%)	38(11.76%)	

Discussion

This study observed that the high (137, 39.15%) incidence of onset of acute myocardial infarction was in the 06.01-12.00 hrs time period which was followed by 00.01-06.00 hrs time period (115, 32.85%). Those belong to age group 40 and above showed the peak incidence at late morning hours (06.01-12.00hrs), whereas patients below 40 years distributed equally their frequency of acute attack in all time series. Statistically, we found no significant relation between age groups of patients and circadian pattern of incidence of AMI (p>.05.). In male & female subset of patients, there were circadian variations observed in the incidence of acute MI but it was not statistically significant (p >.05.). This may be due to relatively small size of our female patients (76 patients out of 350). A similar study was conducted by Chowta et al.[10] in India.They observed the statistically significant peak incidence in the second quarter (06.01-12.00hrs) of the day among the female patients within the age group of 60 years and above. They also cited that the frequency of attack in the evening (12.01-18.00hrs) time period and night (18.01-24.00) equally distributed which was also observed with small variations in this study (Table II). In other study, Graham I, et al.[11] quoted that heart attacks are at least three times more likely to occur in the morning than in the late evening.

Patients with smoking habit showed highest frequency (44.19%) of attack in 06.01-12.00 time period where as among non-smoker group high incidence found in the early morning phase (00.01-06.00 hours) (p<.01). This findings are consistent with the study of Juan B López Messa et al.[12] Our study revealed the morning peak incidence of AMI in both diabetes and non-diabetic patients which was also consistent in the research paper of Jamal S. et al.[13]

Periods with highest incidence (06.01-12;00) of onset of MI were same in both aspirin and non-aspirin group. Only 64 (18.29%) patients had the parental history of MI. Their highest periods of onset of acute attack was 12.01 – 18.00 hrs (p<.01.). Patients with the history of previous AMI (33, 9.43%) exhibited their frequency of current acute attack equally in all time period (p<.01.). Those exposure to regular heavy exercise 157 (44.86%) showed their highest incidence of attack at 06.01-12.00 hrs (p<.01). Patients with hyperlipidemia, diabetes and hypertension exhibited their high incidence both in early morning and late morning. Several study findings[12,13,14] documented that smoking, diabetes, hyperlipidemia, hypertension can modify the standard circadian rhythm of onset of myocardial infarction.

Limitations of this study were the reliance on the subjective reports by patient about the timing of acute myocardial infarction, small size of the study population and enrollment of the patients only from a single regional hospital.

Conclusion

In this study, a circadian variations in the onset of AMI was perceived with a morning peak and an early morning and it was more or less apparent in all groups of patients irrespective of their risk exposure. Further study with a much larger sample from the hospital of different regions suggested to ascertain the factors influence the circadian variations in the onset of AMI.

Acknowledgements

We gratefully acknowledge the professors, doctors, clinical assistants, staff nurses of the cardiology department of Rajshahi Medical College Hospital for their active support and dynamic cooperation.

Contribution of the Authors

First author designed and conducted the study, wrote the manuscript. Second author critically reviewed the manuscript. Third and fourth authors helped in data collection.

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