

Circadian Variation In Onset Of Myocardial Infarction : Comparison Between Diabetics (Niddm) And Non-Diabetics

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Abstract : Aims and Objectives : A number of retrospective and prospective studies have demonstrated a peak in the onset of MI in the morning hours and a trough at night. This has led to investigations of the factors which can affect or modify the circadian pattern of onset of MI. The current study was undertaken with an objective of assessing whether the presence of diabetes can or cannot affect the circadian pattern of onset of myocardial infarction in an Indian population. **Material & methods :** 50 non diabetic subjects and 50 diabetic subjects were randomly selected from among patients admitted to cardiac ICU of LTMMC and GH Sion, Mumbai. For all patients the time of onset of MI was noted and the results were tabulated. **Results :** 44% of non-diabetic subjects experienced onset of myocardial infarction in the period between midnight to 6:00 a.m. as compared to 32% in case of diabetics but an application of Chi Square Test, did not come out to be significant. But on comparing diabetics with >5 years and <5 years history, a significant loss of circadian rhythm was observed in case of diabetics of >5 years duration, indicating that autonomic neuropathy may play a role in the loss of circadian rhythm. **Conclusion:** It has important implications for the treatment of myocardial infarction in case of diabetics. This study can be followed up with additional studies to verify other factors which can affect circadian pattern of onset of myocardial infarction. Loss of biorhythms can result in increased incidence of thrombotic events throughout the day leading to increased cardiovascular mortality and morbidity. [Waggiallah H et al NJIRM 2013; 4(6) : 107-110]

Key Words: Circadian Rhythm, Myocardial Infarction

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Introduction: Cardiovascular disease remains one of the major causes of mortality and morbidity in today's world. Contrary to earlier beliefs, acute myocardial infarction, sudden death and stroke do not occur at random over the day and night but rather cluster into an early morning peak(4.00-10.00 am) and a smaller one in the late afternoon.¹

India leads the world with the largest number of diabetic subjects earning the dubious distinction of being termed as the Diabetes capital of the world. According to Diabetes Atlas 2006 published by International Diabetes Federation, the number of people with diabetes in India currently around 40.9 million is expected to increase upto 69.9 million by 2025.² The so called Asian Indian phenotype referring to typical biochemical abnormalities in Indians, makes us more prone to diabetes and coronary artery disease.^{3,4}

Zarisch et. al.⁴ performed autonomic nervous system testing on patients with ambulatory ischaemia and showed that patients with moderate to severe autonomic nervous system dysfunction did not experience a morning peak of ischaemia..Long standing diabetes or poor control

of blood sugar in diabetics is often associated with autonomic neuropathy. The current study was undertaken to determine whether presence of diabetes (NIDDM) and the duration of diabetes can change the time of onset of myocardial infarction in Indian population.

Aims And Objectives: To study the time of onset of pain in myocardial infarction in non-diabetics and patients with diabetes (NIDDM).

Material And Methods: The study design was approved by institutional Ethics Committee.

Place of Study: LTMMC and General Hospital, Sion

Duration of Study: Six months

Study Description: Design: Non Interventional retrospective study

Methodology: Patients admitted in General Medicine wards and Cardiac ICU of the hospital between the study period were included in the study.

Sampling method - 50 randomly selected non-diabetics and 50 randomly selected diabetics who

have been admitted for Myocardial Infarction were interviewed in the study period.

Definition of subject to be studied-

- a) Inclusion Criteria-
 - Patients admitted to General Medicine and Cardiac ICCU at LTMMC between the study period
 - Those consenting to give the interview.
 - Among diabetics, only those having NIDDM were included in the study.
- b) Exclusion Criteria-
 - Patients with IDDM
 - Severely sick patient where he/she is unable to give the interview.

Parameters Studied At The Initiation Of The Study-

Age, Medical history, Investigation, Treatment history, -Medication use, Patient reported time of beginning of discomfort was used as onset time of beginning of MI.

STATISTICAL ANALYSIS-For analysis, the day was divided into four 6 hr. intervals from 00:00-5:59,6:00-11:59,12:00-17:59,18:00-23:59.

Percentage of total subjects in each time group was calculated for both non-diabetics and diabetics, To compare the time of onset of MI. Difference in the circadian variation was tested using Chi-Square Test. Effect of duration of diabetes was compared using Chi-Square Test.

OBSERVATION AND RESULTS :

The data was collected from patients with MI admitted in General Medicine and cardiac ICCU of L.T.M.M.C., Sion. The time of onset of MI was categorized into four time intervals. The number of patients, diabetic and non-diabetic, was calculated and tabulated.

Comparison Of Changes In Incidence Of Onset Of Mi Between Non-Diabetics And Diabetics :

Time	Non Diabetic (N=50)		Diabetic (N=50)	
	No.	%	No.	%
0:00 to 5:59	22	44	15	30
6:00 to 11:59	6	12	10	20
12:00 to 17:59	13	26	10	20
18:00 to 23:59	9	18	15	30

By Chi – Square Test P > 0.05 Not Significant
 44% of non- diabetics had onset of MI before 6:00 a.m. in the morning in comparison to 30% of subjects with diabetes. On comparing using Chi-square test, the difference was not significant.

Association Between Duration Of Diabetes & Onset Of MI :

Time	N = 16 > 5 Yrs		N = 34 < 5 Yrs	
	No.	%	No.	%
00:00-5:59	03	18.8	12	35.3
6:00-11:59	01	06.2	09	26.5
12:00-17:59	07	43.8	03	08.8
18:00-23:59	05	31.2	10	29.4

By Chi – Square Test P < 0.05 Significant

61.8% of cases who had diabetes had MI before noon were significantly more as compared to 25.0% among diabetics of more than 5 years duration ,showing that the duration of disease has an effect on the circadian pattern of onset of MI.

Discussion: In the study, we observed a prominent circadian pattern of acute MI symptom onset in patients without a history of diabetes as compared to those with diabetes. Also those patients who had a history of diabetes for >5 years, had a significant attenuation of the morning peak in acute myocardial infarction. Similar pattern of early morning onset of myocardial infarction with a small peak in 2:00 p.m. also was seen by Mitler et al. ⁶ This early morning peak has also been observed by other workers like Thompson DR et al. , Muller JE et al. ^{7,8} A surge in sympathetic activity and vagal withdrawal in the morning hours alters hemodynamic forces and atherosclerotic plaques to rupture in the morning ⁹. Morning elevation in plasma catecholamine and renin levels, heart rate , blood pressure and coronary blood flow may increase shear forces in the coronary arterial bed , thus promoting plaque disruption and causing unstable angina and acute myocardial infarction. ¹⁰ Epinephrine has a strong proaggregatory effect on platelets , first by causing arachidonic acid release , which leads to thromboxane synthesis and secondly by directly exposing surface glycoprotein IIb/IIIa , the final common path in platelet aggregation.

Graham Thrall et al.¹¹ reviewed studies on prothrombotic effects of an acute change in posture and found that a change of posture from supine to upright has the potential to provoke alterations in blood rheology and hemostasis and such alterations could contribute to the triggering of cardiovascular events occurring within the first 3 hours after awakening.

Hjalmarson et al.¹² showed that the characteristic day-night pattern in the onset of myocardial infarction is altered in patients with diabetes. These findings have also been confirmed by Fava S et al. and Yamamoto et al.^{13,14} Autonomic neuropathy is common in diabetes. In patients with type 2 diabetes, Toyry et al.¹⁵ observed that the risk of developing parasympathetic neuropathy increases sharply after 5 years and prevalence for combined autonomic neuropathy reached 65% after 10 years of follow up.

These factors may account for loss of circadian variation in diabetic patients especially in those who have had diabetes for a duration of >5 years.

Our study also demonstrated that patients with diabetes >5 years duration, have no particular pattern when it comes to the time of onset of myocardial infarction. Biological rhythms can influence the presentation of diseases and study of circadian patterns can definitely help in predictability and management of diseases. The loss of circadian pattern of onset of myocardial infarction in diabetics predisposes these subjects to thrombotic events throughout the day. This has to be borne in mind during management of such cases.

The limitation of the study was the small number of subjects studied. The scope of the study can be validated by increasing the number of subjects.

Conclusion: Our study shows that though a higher percentage of non diabetic subjects showed circadian pattern of onset of MI as compared to diabetic subjects, it was not statistically significant as was deciphered by applying Chi Square Test. It may be because of the smaller sample size. However on comparing the duration of diabetes (>5 years and <5 years) there was a significant loss

of circadian rhythm in case of diabetics of >5 years duration. This shows that autonomic neuropathy which is a complication of long term diabetes may be the reason underlying the loss of circadian pattern of MI onset. These findings can be utilised in clinical practice to modulate the dose of anti-angina drugs. Further studies can be carried out to find out other factors which can disturb the circadian pattern of ischemic events, like effect of beta blockers.

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