IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 20, Issue 4 Ser.4 (April. 2021), PP 43-47
www.iosrjournals.org

Circadian variation of acute coronary syndrome and its correlation with conventional risk factors.

Rabindra Simkhada,[1] Sanjay Singh KC[1]

1. Department of Cardiology, ShahidGangalal National Heart Centre, Kathmandu, Nepal
Correspondence: Dr.RabindraSimkhada
Department of CardiologyShahidGangalal National Heart CentreKathmandu, Nepal

Abstract
Background: *Circadian variation of acute coronary syndrome has been matterof interest for long time in different parts of worldwith variable results. Understanding the time cycle of onset can help in its effective management.*
Material & Methods:*A prospective cross-sectional study conducted at ShahidGangalal National Heart Centre from July 2020 to September 2020. A total of 127 cases of acute coronary syndrome were included. They were interviewed regarding exact time of onset of symptom. It was categorized into 8 groups of 3 hours interval each. Participants were interviewed, examined and investigated for conventional risk factors.*
Results: *Ninety five (74.80%) participants were male. Mean age was 59.07±12.09 years. Among them 40.15% were hypertensive, 31.49% were diabetics, 24.40%were smoker, 30.70%had dyslipidemiaand 7.08% had family history of ischemic heart disease. Highest number, that is 24(18.89%) had symptom onset in between 6 AM to 8:59 AM followed by21(16.53%) had symptom onset in between 9 AM-11:59 AM. During 12 PM-2:59 PM and 3 PM-5:59 PM 17(13.38%)in each group had onset of symptoms. During 9 PM-11:59 PM only 6.29% hadsymptom onset. The morning peak of onset was independent of presence or absence of risk factors.*
Conclusions: *Onset of acute coronary syndrome was most common in morning. As prompt initiation of therapy is always rewarding in acute coronary syndrome, this information will help for further management of patients in our settings.*
Key Words:*Acute coronary syndrome, Circadian variation, Morning peak*

Date of Submission: 25-03-2021 Date of Acceptance: 09-04-2021

I. Introduction:

Acute coronary syndrome (ACS) is the leading cause of mortality across the globe.[1]Although significant improvements have been made in its management; several aspects of ACS are still subject of investigation. Circadian variation in the onset of acute coronary syndrome was topic of scientific interest since long back with variable results. Several studies have shown the incidence of ACS high in morning.[2,3,4]Few other studies have either shown a bimodal pattern or peak during afternoon to evening.[5,6]

To what extent the circadian variation occurs among ACS patients in our part of world is not defined clearly. Also the influence of variables like gender, age, diabetes (DM), hypertension (HTN), smoking, dyslipidemia on the time of onset of ACS has not been described well.

Objective of this study was to see the time variation in the symptom onset in relation to 24 hours circadian rhythm in the ACS participants. We further aimed to see its correlation with gender, age, diabetes, hypertension, dyslipidemia, smoking, family history of ischemic heart disease (IHD) and body mass index (BMI). This will help us to understand ACS more precisely in our patients and formulate better management plan in future.

II. Material And Methods:

This was a cross sectional prospective study conducted at ShahidGangalalNational Heart Centre (SGNHC), Kathmandu Nepal from July 2020 to September 2020. Ethical approval was obtained from institutional review board (IRB)-SGNHC. Informed consent was taken from all the participants and only those participants who voluntarily gave consent were included in the study. Both genders were included. Critically ill patients who couldn't mention the exact time of onset of symptoms and those withoutclassical symptoms of ACS were excluded from the study. Similarly those who did not give consent were excluded. A total of 127 participants of acute coronarysyndrome were enrolled consecutively.

Potential cases of acute coronary syndrome who presented in the hospital were identified and evaluated within 24 hours of presentation. Diagnosis of ACS was confirmed on the basis of history,

electrocardiogram (ECG) and cardiac biomarkers that iscreatine phosphokinase myocardial band (CPK-MB) and/or troponin I. They were categorized into unstable angina, Non-ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI). Those who had 1 mm or moreST elevation in at least 2 anatomically contiguous ECG leads were categorized asSTEMI. However for leads V_2-V_3ST elevation of at least 2 mm or more in male ≥40 years, 2.5 mm or more in male <40 years and 1.5 mm or morein female was considered STEMI. Those with positive cardiac biomarker (more than 2 fold rise in CPK-MB and /or positive troponin I) but no ST elevation was categorized as NSTEMI and those with negative biomarker and no ST elevation in ECG was categorized as unstable angina.

The exact time of onset of chest pain, shortness of breath, palpitation, sweating and other symptoms suggestive of onset of ACS were noted which were categorized into 8 groups of 3 hour interval.Histories weretaken focusing DM, HTN, dyslipidemia, smoking and family history of IHD. Participants' relevant clinical information like blood pressure(BP), height and weight for BMI were obtained. Investigations including sugar F/PP/R, haemoglobinA1c (HbA1c) lipid profile were obtained.

Participants were categorized as hypertensive if they were known case of hypertension or if they had BP ≥140/90 mmHg during examination confirmed by 2nd reading taken 5 minute apart. Diabetes was defined according to American Diabetic Association criteria with a fasting plasma glucose level ≥126 mg/dl (7.0 mmol/l) or a 2 hr. plasma glucose level 200 mg/dl (11.1 mmol/l) or higher during a 75 mg oral glucose tolerance test or a random plasma glucose of 200 mg/dl (11.1mmol/l) or more in a patient of classic symptom of hyperglycaemia or hyperglycaemic crisis or HbA1c level of 6.5% or higher. Both known diabetics and newly diagnosed diabetes were included. Lipid profile was classified according to National Cholesterol Education Program Adult Treatment Panel III to see the prevalence ofdyslipidemia. Both, known dyslipidemic or who had deranged lipid profile were categorized as dyslipidemic.

Data were entered in SPSS version 20 and was analysed. For all variables frequency and percentage of distribution were calculated. Linear regression analysis of independent variables was done with 3 hours time interval category of onset of symptom as dependent variable. P values were calculated and values <0.05 were considered significant.

III. Results:

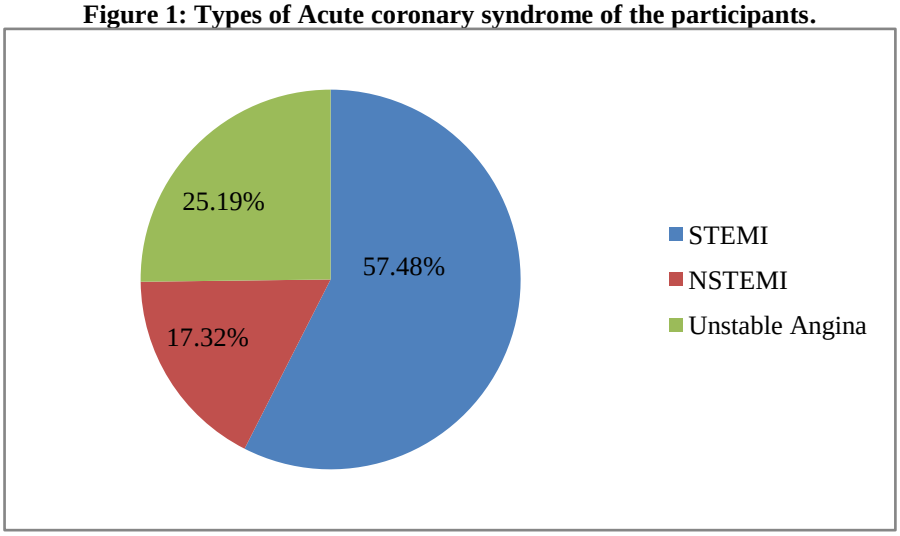
Out of total 127 participants of ACS enrolled, 95(74.80%) were male. The age of the participants ranged from 25 years to 90 years and mean age was59.07±12.09 years. Among them 51(40.15%) were hypertensive, 40(31.49%) were diabetics, 31(24.40%)) were smoker and 39 (30.70%) had dyslipidemia. A total of 9(7.08%) gave family history of ischemic heart disease. One hundred and three (81.10%) of participants had at least 1 risk factor of hypertension, diabetes, smoking, dyslipidemia or family history of IHD. The mean BP and BMI of participants were 131±23.64/84.99±14.46 mmHg and 25.30±3.49 Kg/m^2. The baseline characteristics of enrolled participants are shown in table 1.

Table 1: Baseline Characteristics of the enrolled participants.

Characteristics	**Value**
Male Gender (No./Percentage)	95 (74.80%)
Age (Mean ±SD) years	59.07±12.09
Diabetes (No./ Percentage)	40 (31.49%)
Hypertension (No./ Percentage)	51 (40.15%)
Smoker (No./ Percentage)	31 (24.40))
Dyslipidemia (No./ Percentage)	39 (30.70%)
Family history of IHD (No./ Percentage)	9 (7.08%)
BP(mmHg)	131±23.64/84.99±14.46
BMI (Kg/m^2)	25.30±3.49

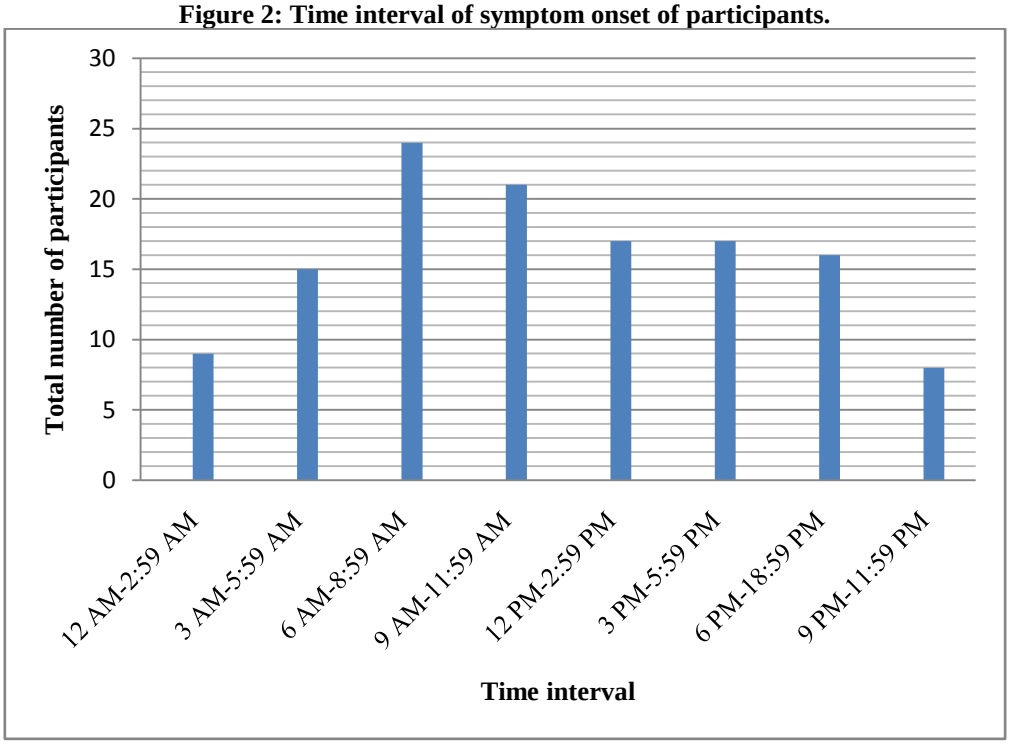
Among the enrolled participants, 73(57.48%) were of STEMI, 22(17.32%) were of NSTEMI and 32 (25.19%) were of unstable angina which is described in figure 1.

Figure 1: Types of Acute coronary syndrome of the participants.



The onset of symptom of ACS was seen most commonly in between 6 AM-8:59 AM. A total of 24(18.89%) had their symptom onset during this time.It was followed by 21(16.53%) participants with symptom onset in between 9 AM-11:59 AM. During each 12 PM-2:59 PM and 3PM-5:59 PM interval 17(13.38%) had onset of their symptoms. Similarly, in between 6 PM-8:59 PM 16 (12.59%) had onset of their symptom. During 3 AM-5:59 AM 15(11.81%) had onset of symptom. In between 12 AM-2:59 AM 9 (7.08%) and 9 PM-11:59 PM 8 (6.29%) had onset of symptom of ACS. The distribution of onset of symptom of ACS in relation to 3 hours of time interval is shown in figure 2.

Figure 2: Time interval of symptom onset of participants.



Linear regression analysis of 3 hourly time categorization of symptom onset as dependent variable with conventional risk factors as independent variables showed no significant correlation indicating the morning time peak of onset of ACS was independent of presence or absence those risk factors. The risk factors and their P values are shown in table 2.

Table 2: Linear regression analysis of time interval with conventional risk factors.

Variables	P value
Gender	0.38
Age	0.63
Diabetes	0.97
Hypertension	0.55
Smoking	0.30
Dyslipidemia	0.96
Family History of IHD	0.47
BMI	0.43

IV. Discussion:

In this study we enrolled 127 participants of ACS, out of which 74.80% were male. The mean age of participants were 59.07±12.09 years. Studies have shown ACS more common in male. In a similar study by MuralikrishnaGopal and colleagues 76% were male.[2]The mean age of participants of similar studies in past were variable. In a study byChhetriet al, the mean age of ACS subjects were 67±18 years.[7] In a study by Junaid Mustafa and colleagues, the mean age was 49±10 years.[6]Studies have shown increasing trend of ACS in young age.[8,9]

On conventional risk factor analysis we found 40.15% hypertensive, 31.49% diabetics, 24.40% smokers and 30.70% dyslipidemic. A total 7.08% gave family history of ischemic heart disease. Prevalence of hypertension was 49.1%, diabetes 28.8%, smoking 34.4%, dyslipidemia 35.3%, family history of IHD 7.8% in a study by Lopez Messa et al on cardiovascular risk factors in the circadian rhythm of acute MI.[10]D'Negri et alfound 53.7%hypertensive, 16.4% diabetic and 44.7% tobacco consumer in MI patients.[5] Thus our study found a comparable proportion of conventional risk factors.

We found the onset of symptom most commonly in between 6 AM to 8:59 AM (18.89%), followed by 9 AM-11:59 AM (16.53%). During 12 PM-2:59 PM and 3 PM-5:59 PM 13.38% had onset of their symptoms in each interval. Inbetween 9 PM-11:59 PMonly 6.29% had onset of symptom. The findings were in consistence with most of the published literatures. Tofler et al had reported higher frequency of onset of MI from 6 AM to noon (34.4%).[11] Cannon CP and colleagues found peak on onset of unstable angina and NSTEMI from 6 AM to noon.[3] We also found a total of 35.42% had their symptom onset from 6 AM-11:59 AM. Similarly Kanth and Colleagues reported a circadian pattern of onset of acute MI with a morning peak.[4]Several possible explanations for morning time increase in onset of ACS includesincrease platelet aggregation and diminished fibrinolytic activities in morning.[12]Moreover increase in sympathetic activities and withdrawal of parasympathetic tone occurs in morning.Morning elevations of catecholamines and change in cortisol level have also been postulated as possible cause. There can be increaseddisruption and rupture of atherosclerotic plaques leading to ACS in morning.[13]D'Negri and colleagues reported two maxima in onset of Acute MI in Argentine and Uruguayan population, 1st between 08-12 hours and second between 15-22 hours.[5]Junaid Mustafa and colleagues however reported highest numbers of cases between 12PM-6PM.[6]

There was no significant correlation of variables likegender, age, diabetes, hypertension, dyslipidemia, smoking, family history of IHD and BMI with categorization of onset of symptom indicating the morning peak of onset was independent of the presence or absence of risk factors.LópezMessa and colleague too have reported the presence of HTN, dyslipidemia, family history and age sex subgroups produced the curve similar to standard curve. They found smoker had lower evening than morning peak.[10]Rana and colleagues reported type 2 diabetes diagnosed within 5 years had similar morning peak as non diabeticMI and somewhat blunted peak in the entire diabetic group. There was no apparent circadian variation in type 1diabetes and type 2 diabetes of 5 years or more duration.[13]

Our study has some limitations. It was a single centre study with limited number of participants. We included only few common conventional risk factors. Larger multi-centrestudies including several other probable new riskfactors is suggested and expected in future.

V. Conclusions:

On analysing 24 hours circadian cycle, onset of acute coronary syndrome was most common during morning hours. It was irrespective of presence or absence of common conventional risk factors. As timely initiation of therapy should always be in priority in managing ACS, this information will help intreating them in our settings. More vigilance and preparedness for management is recommended during these hours.

References:

[1]. Ghous Z, Naseer N, Hassan A. Circadian variation in acute coronary syndromes among patients presenting in a tertiary care hospital in Lahore. ANNALS. 2015;21(4):269-273.

[2]. Gopal M, Boopathy N, Venkatesan R, Jagannathan V. Circadian Variation In Acute Coronary Syndromes. WebmedCentral CARDIOLOGY. 2010;1(9):1-7.
[3]. Cannon CP, McCabe CH, Stone PH, Schactman M, Thompson B, Theroux P, et al. Circadian variation in the onset of unstable angina and non-Q-wave acute myocardial infarction (the TIMI III Registry and TIMI IIIB). Am J Cardiol. 1997;79:253-258.
[4]. Kanth R, Ittaman S, RezkallaS.Circadian Patterns of ST Elevation Myocardial Infarction in the New Millennium. Clinical Medicine & Research. 2013;11(2):66-72.
[5]. D'Negri CE, Nicola-Siri L, Vigo DE, GirottiLA,Cardinali DP.Circadian analysis of myocardial infarction incidence in an Argentine and Uruguayan population. BMC Cardiovasc Disorders. 2006;6:1.
[6]. Mustafa J, Hussain A, Malik MA, Warraich S.Acute coronary syndrome and its sub-types among patients admitted in chest pain unit. JSZMC.2017;8(2):1181-1184.
[7]. Chettri BK, Paudel MS, Dhungana SP, Shamsuddin. Clinical profile of patients with acute coronary syndrome in lumbini medical college and teaching hospital: a prospective study. L M Coll J. 2013;1(2):89-92.
[8]. Poudel N, Alurkar VM, Jha GS, Kafle R, Sapkota S, Lamsal L. Profile of Acute Coronary Syndrome In Young People: A Hospital Based Observational Study in Western Nepal. BJHS. 2018;3(1):361-365.
[9]. Chhabra ST, Kaur T, Masson S, Soni RK, Bansal N, Takkar B, et al. Early onset ACS: An age based clinico-epidemiologic and angiographic comparison. Atherosclerosis. 2018;279:45-51.
[10]. LópezMessa JB, GarmendiaLeiza JR, Aguilar García MD, Andrés de Llano JM, AlberolaLópez C, ArduraFernández J. Cardiovascular risk factors in the circadian rhythm of acute myocardial infarction. Rev EspCardiol. 2004;57(9):850-858.
[11]. Tofler GH, Muller JE, Stone PH, Forman S, Solomon RE, Knatterud GL, et al. Modifiers oftiming and possible triggers of acute myocardial infarction in the thrombolysis in myocardial infarction phase II (TIMI II) study group. J Am Coll Car-diol. 1992;20(5):1049-1055.
[12]. Masuda T, Ogawa H, Miyao Y, Yu Q, Misumi I, Sakamoto T, et al. Circadian variation in fibrinolytic activity in patients with variant angina. Br Heart J. 1994;71:156-161.
[13]. Rana JS, Mukamal KJ, Morgan JP, Muller JE, Mittleman MA. Circadian Variation in the Onset of Myocardial Infarction Effect of Duration of Diabetes. Diabetes. 2003;52:1464-1468.

RabindraSimkhada, et. al. "Circadian variation of acute coronary syndrome and its correlation with conventional risk factors."*IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 20(04), 2021, pp. 43-47.