Original article

J Nepal Health Res Counc 2023 Jan-Mar;21(58): 8-14

Arrhythmias: Its Occurrence, Risk Factors, Therapy, and Prognosis in Acute Coronary Syndrome

Raja Ram Khanal,[1] Ratna Mani Gajurel,[1] Sangam Shah,[2] Chandra Mani Poudel,[1] Hemant Shrestha,[1] Surya Devkota,[1] Sanjeev Thapa[1]

[1]Department of Cardiology, Manmohan Cardio Thoracic Vascular and Transplant Centre, Institute of Medicine, Maharajgunj, Kathmandu, Nepal, [2]Maharajgunj Medical Campus, Institute of Medicine, Tribhuvan University, Maharajagunj, Kathmandu, Nepal

ABSTRACT

Background: Patients with acute coronary syndrome may lead to various metabolic and electrophysiological changes that induce both asymptomatic and symptomatic life-threatening arrhythmias, which increases morbidity and mortality.

Methods: This observational retrospective study was conducted at Manmohan Cardiothoracic Vascular and Transplant Center, Institute of Medicine, Maharajgunj, Kathmandu, Nepal. Three hundred ninety-five patients with a diagnosis of acute coronary syndrome were enrolled in the study.

Results: A total of 395 patients were included in the study with a mean age of patients 61.29± 13.5 years and with male predominance. A total number of 115 cases of arrhythmia were recorded among which the most common were atrioventricular block (10%), reperfusion arrhythmia (9.6%) followed by ventricular premature complex (8%), atrial fibrillation/flutter (6%), and ventricular tachycardia/fibrillation (5%). There was a significant difference in the incidence of arrhythmia in acute coronary syndrome group. STEMI (39.7%), NSTEMI 26(20.8%) and unstable angina11(14.8%) respectively (p=<0.001). Reperfusion arrhythmia was present in 89.47% of STEMI and 10.4 % of NSTEMI/ unstable angina and was statistically significant (p-value <0.001). A total of three patients (0.7%) needed permanent pacemaker insertion in the acute coronary syndrome group. All of these patients were STEMI which was 1.5% of total STEMI, two in inferior wall STEMI (2.6%) and 1 in anterior wall STEMI (0.8%). The total in-hospital mortality was 20 (5.06%), 17(8.6%) among STEMI and 3(2.4%) among NSTEMI, and none in unstable angina (P =<0.001). Pulmonary edema (12.9%) was the most common in-hospital outcome followed by cardiac arrest (7.6%).

Conclusions: Arrhythmia in acute coronary syndrome is a common problem and may lead to structural and functional impairment of myocardial function.

Keywords: Arrythmias; coronary artery disease; STEMI

INTRODUCTION

Acute Coronary Syndrome (ACS) is a global epidemic that is threatening to become the new epidemic affecting people all over the world, particularly in the subcontinent. Coronary Artery Disease (CAD) affects Nepalese more frequently and at a younger age than it does in developed countries. It also affects many other developing countries. ACS are major public health issues since they are a leading source of morbidity and mortality.[1]The development of arrhythmias during periods of myocardial infarction is attributed for most of these deaths.[2]

Certain interactions among structural and functional abnormalities are thought to predict the cascade leading to sudden death from arrhythmias.[3] There is no published evidence of the profile of these arrhythmias in Nepal's current population. Because most arrhythmias arise in the first week of ACS, and notably in the first 24 hours, the goal of this study is to determine the incidence and character of cardiac arrhythmias in ACS in patients at a tertiary hospital in Nepal.

METHODS

A retrospective cross-sectional study was carried out at the Manmohan Cardiothoracic Vascular and Transplant Centre (MCVTC), which is a tertiary cardiac institution and a referral center for cardiac illnesses from all over

Correspondence: Dr Raja Ram Khanal, Department of Cardiology, Manmohan Cardio Thoracic Vascular and Transplant Centre, Institute of Medicine, Maharajgunj, Kathmandu, Nepal. Email: khanalr82@gmail.com, Phone: +9779851082406.

Nepal. The research received ethical approval from the Institute of Medicine's (IOM) Institutional Review Committee. [Approval number: 211 (6-11) e^2 077/078]

The patients with acute coronary syndrome admitted in MCVTC from January 15, 2021 to September 15, 2021 were our study population. The patients with a history of chest pain at rest or other symptoms suggestive of an ACS, with or without new or presumed new significant ST-segment or T-wave changes, left bundle branch block (LBBB) and/or elevated biomarkers of myocardial necrosis (with a rise and/or fall of levels). Arrythmias occurring during the one week was included in the study. We excluded all patients other than Nepalese nationals and those under 18 years of age. We performed simple random sampling among the admitted patients with acute coronary syndrome at MCVTC. The data from the hospital records and patients record file was collected using a structured data sheet. We took written informed consent from the patients that were admitted to MCVTC. The duration of hospital stay was considered as outcome measure.

Among 1550 patients admitted in MCVTC in the year 2020, there were 850 cases of acute coronary syndrome, which accounted for 54.8% of the total cases, with an allowable error of 5% and acceptance level of 95%, the expected sample size is calculated with the following equation,

$N = 4pq/l^2$, where p = prevalence, q = 1-p and l = allowable error

Hence the sample size is 398. However, a total of 395 patients with a diagnosis of acute coronary syndrome were enrolled consecutively and analyzed.

Age and sex of the patient were considered as the independent variable. Acute myocardial infarction was defined according to type 1 myocardial infarction universal definition. STEMI was defined by the presence of persistent ST-segment elevation. All other cases were considered non-ST-segment elevation ACS (NSTACS). Electrocardiogram (ECG), echocardiography, and cardiac markers were used as diagnostic criteria acute coronary syndrome. Serial ECGs and Holter monitoring were done for confirmation of different arrhythmias. Coronary angiography was done for diagnosing coronary artery disease and angioplasty was done in those needed. Both procedures were done in our CATH lab either through radial or femoral artery under local anesthesia. Patients who underwent both primary and elective angioplasty were deployed drug eluting stents. Temporary pacing was done in some patients through right femoral vein during primary PCI.Reperfusion arrhythmia was diagnosed by the presence of arrhythmia (most common being accelerated idioventricular rhythm(AIVR) during or immediately after thrombolysis or PCI.Permanent pacemaker insertion was done via subclavian vein under local anesthesia in patients who had persistent second or third degree atrioventricular block.

Data were collected from the hospital record of the patients. Only selective data required for the research conduction (included in the study variables) were collected. Data was coded and represented in frequency tables. Analysis of quantitative data was done using SPSS version 26 statistical software. Statistical test Chi-Square test was applied wherever applicable.

RESULTS

A total of 395 patients were included in the study and the mean age of the patient was 61.29 ± 13.5 years (Range: 24 to 98). The majority of the patients were male (70.38%). Similarly, 68% of the patients were aged between 41 to 70 years of age. A large portion of patients presented with chest pain (86.58%) followed by shortness of breath (38.23%). The most prevalent risk factor was hypertension (50.38%) followed by smoking (41.77%) and diabetes (38.75%). The detailed clinical and demographical profile of the included patients is shown in Table 1.

Out of 395 patients enrolled in the study,196 (49.62%) had STEMI, 125 (31.65%) had NSTEMI, while 74 (18.73%) had unstable angina. The coronary angiogram revealed single vessel disease (SVD) in 100 patients (25.38%), double vessel disease (DVD) in 85 patients (21.52%), and triple vessel disease (TVD) in 102 patients (25.89%). The number of cases of arrhythmia was 115.

Thirty patients (7.59%) had normal angiogram while only 6 (3.8%) had minor CAD. Primary PCI was done in 87 (22%) patients. 58 (14%) of the patients were treated with antiarrhythmic agents and the common drugs were beta-blockers, amiodarone, and lignocaine. Coronary angiography and angioplasty were done in most of the patients with temporary pacemaker in 17 (4.3%) patients. Among 395 patients, 319 (80.7%) had undergone coronary angiogram while 243 (61.5%) had undergone coronary angioplasty (Table 1 b).

Table 1 (a). Clinical and demographic characteristics of patients.

Characteristics	Number(N)	Percentage (%)
Age(in years) Mean±SD: 61.29± 13.5 (Range: 24 to 98) **Gender**		
Female	117	29.62
Male	278	70.38
Presenting symptom to ED (may have >1)		
Chest pain	342	86.58
Shortness of breath	151	38.23
Jaw, neck, and arm pain	89	22.53
Nausea and vomiting	52	13.16
Diaphoresis	76	19.24
Syncope	14	3.54
Cardiovascular risk factors (may have >1)		
Hypertension	199	50.38
Hypercholesterolemia	28	6.84
Family history of CAD	20	5.06
Diabetes	153	38.73
Smoking	165	41.77
AKI	41	10.38
Chronic Kidney Disease	22	5.5
COPD	38	9.62
Cardiovascular medical history (may have > 1)		
Personal history of CAD	45	11.39
History of unstable angina	13	3.3
Previous acute myocardial infarction	31	7.85
Previous PCI	26	6.58
Previous CABG surgery	4	1.01
Previous history of arrhythmias	14	3.57
History of stroke	21	5.32
Non-ST elevation myocardial infarction	199	50.38
ST elevation myocardial infarction	196	49.62
Anterior wall STEMI	116	29.36
Inferior wall STEMI	76	19.24
Posterior wall MI	4	1.0

ED: Emergency department; CAD: coronary artery disease; AKI: acute kidney injury; COPD: chronic obstructive pulmonary disease; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft; STEMI: ST segment elevated myocardial intervention;

Table 1 (b). Intervention in study participants.

Interventions	Number	Percentage (%)
Thrombolytic medication	19	4.8
Arrhythmia	115	29.11
Interventions during hospitalization		
Coronary angiogram	317	80.76
Normal coronary arteries	32	8.10
PCI	243	61.52
Primary PCI	87	22.03
Treated with anti-arrhythmic medication	58	14.68
TPI	17	4.3
PPI	3	0.75
CABG surgery	21	5.34
Holter monitoring	36	9.11

PCI: percutaneous coronary intervention;CABG: coronary artery bypass graft;PPI: proton pump inhibitors; TPI:

Among 395 patient's arrhythmia was observed in 115 patients (29.11 %) with total 285 arrhythmias recorded. The most common arrhythmia was AV block (10%), reperfusion arrhythmia (9%) followed by ventricular premature complex(VPC)(8%),atrialfibrillation/ flutter(6%),ventricular tachycardia/fibrillation (5%). (Table2)Arrhythmia was present in 78(39.7%), 26 (20.8%), and 11(14.8%) of the patients in STEMI, NSTEMI, and UA respectively. The occurrence of arrythmia was more in inferior wall MI (56%) than in anterior wall MI (28%). Ventricular arrhythmia occurred in 46 patients (23 %) in STEMI, 12patients(9.6%) in NSTEMI and 5patients(6.7%) in UA. The ventricular arrhythmia occurred more in anterior wall MI (26.7%) than in inferior wall MI (19.7%). Similarly, CHB was present in 3% of the total ACS patients of which11 (5.6%)patients in STEMI and 1(0.8%) in NSTEMI. Inferior wall MI patients (11.5%) had more CHB than anterior wall MI (11.5 % and 1.6% respectively).

Among ACS patients, BBB was present in equal proportion between STEMI (11.7%) and NSTEMI/UA (11.1%). Four patients developed BBB after PCI, which was transient. Reperfusion arrhythmia was present in 38 (9.6%) patients with 89.47% in STEMI and 10.4 % in NSTEMI ACS.

The incidence of arrythmias was more common among elderly patients (age≥65 years), patients in cardiogenic shock, LV dysfunction, renal dysfunction, and COPD. Chronic kidney disease (CKD) as a risk factor was singnificantly associated with an increased incidence of arrhythmia (). The details of cardiovascular risk factors with arrythmias are shown in Table 4.

Table 2. Arrhythmia and conduction defects in ACS patients					
Arrhythmia and conduction defects	UA	NSTEMI	STEMI	Total number	Percent (%)
Arrhythmias (may have >1)	11	26	78	115	29.11
Sinus Tachycardia	2	27	47	76	19.29
Sinus bradycardia	0	2	34	36	9.11
PVCs (frequent)	3	8	22	33	8.35
Non-sustained VT	2	4	14	20	5.06
Atrial Fibrillation/Flutter Atrial Tachycardia PSVT	5 0 0	12 0 1	8 1 2	25 1 3	6.3 0.25 0.75
Junctional rhythm	0	10	7	17	4.3
Sustained VT consecutive PVCs	2	4	16	22	5.57
Asystole	0	2	17	19	4.8
Torsade de Pointes	0	0	5	5	1.2
Ventricular Fibrillation	0	0	9	9	2.28
AIVR (Idioventricular rhythm) Reperfusion arrhythmia	2	2	34	38	9.62
Conduction defects (May have >1) Atrioventricular Block (AV block)					
1st Degree	1	2	9	12	3.04
2nd Degree	0	1	10	11	2.58
High Grade	0	0	5	5	1.27
3rd Degree	0	1	11	12	3.04
Right Bundle Branch Block	3	5	17	25	6.33
Left Bundle Branch Block	5	9	6	20	5.06
Bifascicular block	2	0	6	8	2.03

Note: Many patients had more than 1 arrhythmia. The total number of arrhythmia was 285(excluding sinus tachycardia and bradycardia).

Table 3. Acute coronary syndrome and different type of arrythmias		
ACS	Arrhythmia	Percentage
Unstable Angina	11	14.8%
Non-STEMI	26	20.8%
STEMI	78	39.7 %
Anterior wall	33	16.8%
Inferior wall	43	21.9%
Posterior wall	2	1%
Ventricular arrhythmia and ACS		
ACS	Ventricular Arrhythmia	Percentage
Unstable Angina	5	6.7 %
Non-STEMI	12	9.6%
STEMI	46	23.4%
Anterior wall	31	15.8%
Inferior wall	15	7.6.%
Complete heart block and ACS		
ACS	CHB	Percentage
Unstable Angina	0	0
Non-STEMI	1	0.8
STEMI	11	5.6
Anterior wall	2	1.0
Inferior wall	9	4.5

Table 4. Cardiovascular risk factors and arrhythmia		
Risk Factors	Arrhythmia n (%)	P value
Hypertension	62 (31)	0.368
Diabetes	37 (24)	0.086
Family history of CAD	7 (35)	0.552
Chronic kidney disease	16 (72)	0.002
Hypercholesterolemia	8 (29)	0.951
Smoking	45 (27)	0.495
AKI	17 (41)	0.066
COPD	15 (39)	0.139
Elderly (Age≥65years)	45 (27)	0.673

Twenty-six patients developed cardiogenic shock (6.5%), which was more in STEMI than NSTEMI. Six patients died during primary PCI while 14 patients died during hospital admission. There was significant difference in the in-hospital mortality, 17(8.6%) in STEMI, 3(2.4%) in NSTEMI and none in unstable angina (0%), p=<0.001. Among ACS patients with arrhythmia mortality was in 10patients (8.69%, p= 0. 027). None of the NSTEMI-ACS patients required permanent pacemaker insertion. The complications and in hospital outcome among acute coronary syndrome patients are shown in table 5.

Table 5. Complications and in-hospital outcomes of patients

Outcomes	Number	Percentage
In patients' complications AMI post-admission for patients admitted with UA /NSTACS	8	4.02
Cardiac arrest	30	7.59
AMI extension (detected by 2nd rise in CK-MB)	7	3.5
Cardiogenic shock	26	6.58
STEMI	20	5.0
NSTEMI	6	1.5
New severe heart failure/ pulmonary edema	51	12.9
Cardiac tamponade	4	1.01
Stroke	14	3.54
Ischemic stroke	10	2.53
Hemorrhagic stroke	4	1.01
Post PCI stroke	4	1.01
Mortality	20	5.06
Length of hospital stay	6.48 ± 3.45	0-25 days

The mean left ventricle ejection fraction (LVEF) was 44.26 ±12.43 % (Range: 20 to 65 %). Low LVEF was present in 256 patients (64.8%), which was more in STEMI than in NSTEMI/UA (Figure 1).

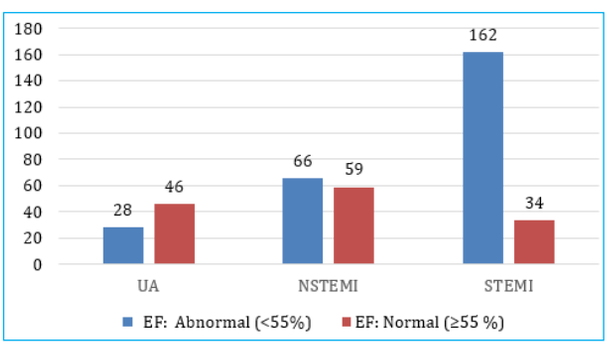

Figure 1. LV function and ACS- Mean LV EF: 44.26 ±12.43 %(Range: 20 to 65 %)

DISCUSSION

Thisstudy was conducted in 395 patients with acute coronary syndrome. The mean age of the patients was 61.29± 13.5 years with male predominance. The majority of patients were in between 41 to 70 years (68%) with 5 % below the age group of 40 years. This was similar to the study conducted by Mhatre MA et al where the majority of patients were in between 41 to 70 years (78%) with 5 % cases below 40 years.[4] The multiple risk factors, life style changes, economic status and stress factor probably could be the cause for age incidence.

A total of 115 patients were found to have arrhythmia (29%) with total of 285 arrhythmias in our study. The most common arrhythmia was AV block (10%), followed by reperfusion arrhythmia (9.6%), VPC (8%) and atrial fibrillation/flutter (6.3%). In the study conducted bySongyun Chu et al a total of 99cases/times of arrhythmia were recorded (23%) with supraventricular tachycardia the most common (19%) followed by VPC (11%) and atrial fibrillation/flutter (9%).[5]

The incidence of arrhythmia varies in different subgroup of ACS patients with high incidence in STEMI and may lead to stroke, heart failure and even sudden death. In our study, arrhythmia was present in 78(39.7%) patients in STEMI, 26(20.8%) in NSTEMI and 11(14.8%) in UA respectively (p value<0.001). This was similar to the study conducted by Songyun Chu et alwhere significant difference in the incidence of arrhythmia were presentbetween STEMI, NSTEMI and UA groups (41.8%,24.8% and 13.8% respectively, p<0.001).[5]

Acute coronary syndrome complicated by ventricular arrhythmia increases both morbidity and mortality. Sudden death can occur due to sustained ventricular arrhythmia if not treated early. In our study ventricular arrhythmia was present in 63 patients (15.9%)with majority in STEMI (73%). Ventricular arrhythmia occurred in 23 % in STEMI, 9.6% in NSTEMI and 6.7% in USA (p value<0.001).In the study conducted by Ahmad Set alventricular arrhythmia was present in 3.3%) with majority in STEMI (74%).[6]The incidence of ventricular arrhythmia was significantly greater in patients with STEMI (majority in anterior wall) than in patients with NSTEMI/UA (6% vs 1.5 %, p value<0.001).

More ventricular arrhythmia was seen in our patients, which might be probably because of lack of adequate treatment and late presentation leading to mor complications.The presence of heart block worsens the in-hospital outcome in ACS patients and may need temporary or permanent pacemaker insertion. The

incidence of AV block in our study population was 10%. Among the totalACS patients CHB was present in 3% cases with majority in STEMI, which was 5.6 % of total STEMI. The incidence of CHB in inferior wall MI and anterior wall MI was 11.5 % and 1.6% respectively.

This was similar to the study conducted byUffeJakobet al where second- and third-degree AV block was present in 3 % of total STEMI patients with CHB in 2.7 %.[7] The incidence of high degree AV block in inferior wall MI and anterior wall MI was 7 % and 1 % respectively.In another study conducted by Kashif Ali et alin Pakistani patients, the incidence of CHB in STEMI was 7 % which was nearly similar to our study.[8]In our study 1 patient with NSTEMI had CHB (0.8%). This was similar to the study conducted by Sean D et al, where high degree AV block among NSTEMI was 0.4%.[9]

Various cardiovascular risk factors increase the risk of arrhythmia in ACS patients. Elderly patients, those with LV dysfunction, renal dysfunction and COPD patients were found to have higher risk of arrhythmias in our study but it was not statistically significant in majority of risk factors. However, in the study conducted by Songyun Chu et al elderly patients, those with COPD, chronic renal dysfunction, cardiac dysfunction and elevated cardiac biomarkers were significantly associated with increased risk of arrhythmia (p value<0.05).[5]

The total mortality in our study was 20(5.06%). Fiftypercentages of the patients who died had one or more arrhythmia. Patients with arrhythmia increase the risk of mortality (p value: 0.027).Thus, the early diagnosis of arrhythmia and its treatment decreases various complications and even death in ACS patients. In the study conducted at SahidGangalal National Heart Center by CM Adhikari et althe in-hospital mortality was 5.7 % in ACS patients.[10] Similarlyin another study conducted byCatherine Winkler et al in ACS patients the total mortality was 4 %.[11]

There was significant difference in mortality between different ACS patients in our study. The in-hospital mortality in STEMI was 8.6 %, 2.4 % in NSTEMI and no mortality in unstable angina (p value<0.001). This was similar to the study conducted by C Jterkelsen et al.[12]In his study the in-hospital mortality among STEMI patients was 10.9%. Similarly in another study done by CM Adhikari et al, the in-hospitalmortality in STEMI was 7.7 %, in NSTEMI was 3.6 % and in unstable angina was 1.8 %.[10]There were three deaths (2.4 %) in NSTEMI patients in our study which was similar to the study conducted by Naoki Misumida et al where the in-hospital mortality of NSTEMI patients without major conduction disorder was 3.8%.[13]Numerous complications can occur in patients with acute coronary syndrome and increases the morbidity and mortality. In our study the most common complication was conduction disturbances (29%) followed by heart failure (12.9 %), cardiogenic shock (6.5%) and stroke (3.5%).

Our study had some limitations. Our study was a single center study done at MCVTC with small sample size. Only the in-hospital outcome was recorded in our study with no follow up of the patients. Hence, a study with larger population size and longer follow up is needed to stratify the risk factors for arrhythmia in ACS patients and its complications.

CONCLUSIONS

The present study provides the incidence of different arrhythmia, their risk factors and in hospital mortality in acute coronary syndrome. It shows that there is high incidence of arrhythmia in these patients and delay in diagnosis of malignant arrhythmia may lead to different complications and even sudden death. So careful attention should be given to these patients to improve the outcome.

CONFLICT OF INTEREST

The authors declare no conflict of interest

REFERENCES

1. The top 10 causes of death. Accessed: January 17, 2022. https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death.
2. Fabijanic D, Culic V, Bozic I, Miric D, Stojanovic Stipic S, Radic M, et al. Gender differences in in-hospital mortality and mechanisms of death after the first acute myocardial infarction. Ann Saudi Med. 2006, 26:455–60.doi: 10.5144/0256-4947.2006.455
3. Armstrong WF, Mchenry PL: Ambulatory electrocardiographic monitoring: Can we predict sudden death? J Am Coll Cardiol. 1985, 5:13B-16B. doi: 10.1016/S0735-1097(85)80519-2
4. Mhatre MA, Sirur FM, Rajpal DR, Shah MR: A clinical study of arrhythmias associated with acute myocardial infarction and thrombolysis. Int J Res Med Sci. 2016, 5:335–43. doi: 10.18203/2320-6012.IJRMS20164574
5. Chu S, Liu L, Shi L, Han X, Meng L, Ding W, Huo Y. Arrhythmia associated with acute coronary syndrome: occurrence, risk factors, therapy and prognosis: a single-centre study. Heart. 2012 Oct 1;98(Suppl 2):E275-. doi: 10.1136/heartjnl-2012-302920v.14

6. Hersi AS, Alhabib KF, AlFaleh HF, Al Nemer K, Al Saif S, Taraben A, et al. Incidence of ventricular arrhythmia and associated patient outcomes in hospitalized acute coronary syndrome patients in Saudi Arabia: findings from the registry of the Saudi Project for Assessment of Acute Coronary Syndrome (SPACE). Annals of Saudi Medicine. 2012 Jul;32(4):372-7. doi: 10.5144/0256-4947.2012.372

7. Bloqueo aurículoventricular de alto grado que complica el infarto de miocardio con elevación ST en la era de la intervención coronaria percutánea primaria. Accessed: January 17, 2022. http://www.scielo.edu.uy/scielo.php?script=sci_arttext&pid=S1688-04202013000200012.

8. Hashmi KA, Shehzad A, Hashmi AA, Khan A: Atrioventricular block after acute myocardial infarction and its association with other clinical parameters in Pakistani patients: An institutional perspective. BMC Res Notes. 2018, 11:1–4.[Article]

9. Pokorney SD, Radder C, Schulte PJ, Al-Khatib SM, Tricocci P, Van de Werf F, et al. High-degree atrioventricular block, asystole, and electro-mechanical dissociation complicating non–ST-segment elevation myocardial infarction. American heart journal. 2016 Jan 1;171(1):25-32 doi:./10.1016/j.ahj.2015.09.004

10. Adhikari CM, Sharma D, Malla R, Rajbhandari S, Raut R, Baidya S, Dhungana M, Prajapati D, KC MB. Trends and in-hospital mortality of acute coronary syndrome at Shahid Gangalal National Heart Centre, Kathmandu, Nepal during 2001-2012. Journal of Advances in Internal Medicine. 2014 Jan 1;3(5):23.[Download PDF]

11. Stanaway JD, Afshin A, Gakidou E. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990-2017: A systematic analysis for the Global Burden of Disease Stu. Lancet. 2018, 392:1923–94. doi: 10.1016/S0140-6736(18)32225-6

12. Terkelsen CJ, Lassen JF, Nørgaard BL, Gerdes JC, Jensen T, Gøtzsche LB, Nielsen TT, Andersen HR. Mortality rates in patients with ST-elevation vs. non-ST-elevation acute myocardial infarction: observations from an unselected cohort. European heart journal. 2005 Jan 1;26(1):18-26.10.[Article]

13. Misumida N, Ogunbayo GO, Kim SM, Abdel-Latif A, Ziada KM, Elayi CS: Frequency and Significance of High-Degree Atrioventricular Block and Sinoatrial Node Dysfunction in Patients With Non-ST-Elevation Myocardial Infarction. Am J Cardiol. 2018, 122:1598–603.doi: 10.1016/J.AMJCARD.2018.08.001