

Original Research Article

Epidemiological profile and predictors of mortality in acute coronary syndrome: a prospective study

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ABSTRACT

Background: India has shown a rising trend in the prevalence of coronary artery disease (CAD) in urban as well as in rural population. Acute coronary syndrome (ACS) is the main reason for the mortality in India. Study of risk factors and biomarkers is important to catch the diagnosis early in order to decrease the mortality. Objective was to study risk factors and brain natriuretic peptide (BNP), troponin I, and CKMB and their effect on outcome in ACS patients in tertiary hospital.

Methods: One hundred and fifty ACS patients were studied in Emergency Department of Medicine, Nehru Hospital, BRD Medical College, Gorakhpur from January 2017 to December 2017. Data on age sex socioeconomic status, medical history, baseline clinical characteristics, time to reach hospital and treatment in hospital, along with biomarkers including BNP, Troponin I and CKMB was estimated. Baseline ECG was obtained at admission and repeated at 12-24 hours and every 24 hours thereafter. A 2D Echocardiogram was performed within initial 48-72 hours for analysis of LVEF and wall motion abnormalities.

Results: Male (58.7%) preponderance was observed with mean age of 60.12 ± 10.58 years. Most of the patients were from rural areas (87.3%) and had hypertension (44.7%). Chest pain was most common symptom (56%). Most of them had duration of symptoms for 6-12 hours (56%). NSTEMI, STEMI and unstable angina were equally distributed between the genders ($p > 0.05$). Out of 150 patients, 15 (10%) were thrombolysed, 78.52% had RWMA. In-hospital mortality was higher; among the patients of age > 75 years (38.5%) ($p = 0.008$), male patient (12.5%) ($p > 0.05$), rural patient (10.7%) ($p > 0.05$), hypertensive patient (17.3%) ($p > 0.05$), patients of Killip class IV (48.3%) ($p = 0.0001$) and patients having severe LVD (33.3%) ($p = 0.0001$). In-hospital mortality was 1.2% and 1.1% among those in whom beta blocker and ACE inhibitors was present ($p > 0.0001$). BNP and CKMB was significantly higher among expired patients (1762.62 ± 1444.89 vs 840.76 ± 1294.82 ; $p = 0.001$) similarly troponin I was significantly higher among expired patients (67.29 ± 45.63 vs 43.99 ± 41.73 ; $p = 0.006$) than alive.

Conclusions: ACS was more prevalent in male, living in fifth to sixth decade of life, had hypertension. STEMI was more common. Patients on ACE inhibitors and beta-blocker had better outcome. Mortality was higher in patients with Killip's class IV, higher value of troponin I, age more than 75 years and had hypertension and dyslipidemia.

Keywords: Acute coronary syndrome, Biomarkers, In-hospital mortality, Killip class, NSTEMI, STEMI

INTRODUCTION

Acute coronary syndrome (ACS) is a significant contributor to mortality and morbidity attributed to cardiovascular diseases (CVD), both in developed and

developing countries. The syndrome encompassing unstable angina, both ST segment elevation and non ST segment elevation myocardial infarction (MI) are common causes of emergency hospital admission.¹

India is undergoing a rapid health transition with rising burden of coronary heart disease (CHD). Among adults over 20 year of age, the estimated prevalence of CHD is around 3-4% in rural areas and 8-10 per cent in urban areas, representing a two-fold rise in rural areas and a six-fold rise in urban areas between the years 1960 and 2000.² To improve the understanding of ACS patient's characteristics and to incorporate evidence based medicine in their treatment and to gather information on long term outcome in these patients, up to date registry data on ACS cases is required in India.³

Recent years have seen a spectacular rise in the importance of biomarker in ACS; the most notable of these biomarkers are troponin, brain natriuretic peptide (BNP) and CK-MB. Their usefulness for diagnosis, decision making and prognostic stratification has been fully validated, and its use in clinical practice is now widespread.⁴

In the study we tried to see the characteristics of hospitalized ACS patients, trends in management of ACS patients, use of guidelines in Indian context and their impact on outcome, correlation of troponin-I, BNP and CK-MB with adverse outcomes.

METHODS

The present prospective study was performed on 150 ACS patients in Emergency Department of Medicine, Nehru Hospital, BRD Medical College, Gorakhpur, between January 2017 and December 2017.

All consecutive patients suspected of ACS having age more than 18 years admitted for chest pain or pressure, at rest or on exertion, radiating to jaw or neck up to occipital region, shoulder or arm pain with shortness of breath and nausea, vomiting was included.

Patients with unrelated disease such as advanced malignancy, surgery or trauma which may limit life expectancy to less than 60 days follow up and patients or relative who did not give written consent were excluded from the present study.

Data collected on different variable including estimation of BNP, troponin I and CKMB. Data on age sex socioeconomic status, medical history, baseline clinical characteristics time to reach hospital, treatment in hospital and outcome in hospital and at 30 and 60 days was collected.

Baseline ECG was obtained at admission and repeated at 12 -24 hours and every 24 hours thereafter. A 2D Echocardiogram was performed within initial 48-72 hours for analysis of LVEF and wall motion abnormalities.

ACS was referred to any constellation of clinical symptoms that are compatible with acute myocardial

ischemia. It encompasses MI (ST- segment elevation and depression, Q wave and non Q wave) and UA and NSTEMI.

Unstable angina is defined as angina pectoris or equivalent ischemic discomfort with at least one of three features; It occurs at rest (or with minimal exertion usually lasting >10 minutes), it is severe and of new onset (i.e. within the prior 4 -6 weeks) and /or it occurs with a crescendo pattern (i.e. distinctly more severe, prolonged or frequent then previously).

NSTEMI

If a patient with clinical features of UA develops evidence of myocardial necrosis as reflected in elevated cardiac biomarkers it is NSTEMI.

STEMI

If a patient with clinical features of UA develops evidence of myocardial necrosis as reflected in elevated cardiac biomarkers with ECG changes i.e. ST- segment elevation, with Q waves, loss of R waves it is MI.

Refractory angina

Appearance of ischemic chest pain at rest associated with ST – segment alteration in patient treated with nitroglycerine, aspirin, beta blockers, and s/c heparin.

All the data analysis was performed using IBM SPSS ver. 20 software, frequency distribution and cross tabulation was used to prepare the tables. Quantitative data is expressed as mean±SD whereas categorical data is expressed as percentage. Significance level was assessed at 5% level.

RESULTS

Mean age of study cohort was 60.12±10.58 years. Most of them belong to age group of 55-64 years [70 (46.7%)]. More than half of patients were males (58.7%).

Majority of patients' belonged to rural areas (87.3%). Hypertension was present in 44.7% patients. The duration of symptoms was 6-12 hours in 56% patients and >12 hours in 30.7% patients.

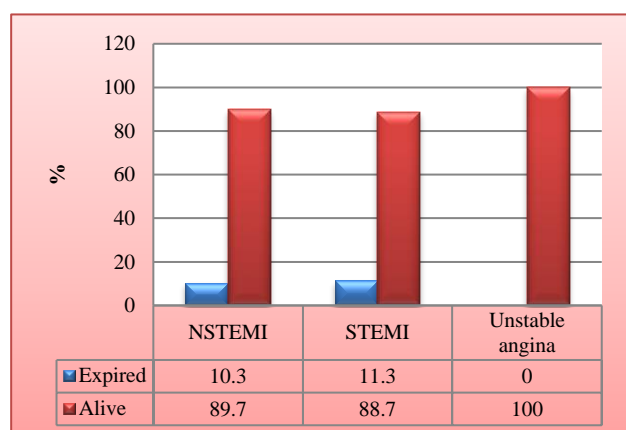
Hypertension and shock was in seen in 21.1% each. Tachycardia and bradycardia were present in 16.7% and 5.3% patients respectively. Chest pain was most common symptom (56%) followed by chest pain and dyspnea (34.7%), dyspnea (6.7%) diarrhea (2.7%). Among risk factors smoking ($p=0.0001$) and alcohol intake ($p=0.0010$) was significantly higher among male compared to female cohort. NSTEMI, STEMI and Unstable angina were equally distributed between the genders ($p>0.05$).

Table 1: Comparing different parameters with diagnosis among study cohort.

Parameters		NSTEMI	STEMI	Unstable angina
Complications	Recurrent angina	22 (75.9)	30 (26.1)	3 (50)
	Cardiogenic shock	6 (20.7)	28 (24.3)	0 (0)
	Arrhythmia	4 (13.8)	15 (13)	0 (0)
	Heart failure	11 (37.9)	57 (49.6)	3 (50)
Killip class	I	19(65.5)	58 (50.4)	6 (100)
	II	14 (13.8)	8 (15.7)	0 (0)
	III	2 (6.9)	14 (12.2)	0 (0)
	IV	4 (13.8)	5 (21.7)	0 (0)
Biomarkers*	TROPI	5.88±3.75	7.38±3.63	5.89±3.88
	BNP	979.24±1441.61	948.16±1354.34	571.17±743.90
	CKMB	43.69±33.88	47.90±45.61	29.96±13.84

Out of 150 patients, 15 (10%) were thrombolysed whereas 135 (90%) were non thrombolysed. Echocardiography revealed that 121 (78.52%) has RWMA whereas 29 (21.48%) had No RWMA. In present study 15(10%) patients were thrombolysed out of which 12(8%) had No RWMA while 3(2%) had RWMA. 135(90%) patients were not thrombolysed out of which 17(11.33%) had no RWMA while 118(78.66%) had RWMA. In-hospital mortality was seen in 10.7% patients.

In-hospital mortality was higher among the patients of age >75 years (38.5%) ($p=0.008$), higher among males (12.5%) ($p>0.05$), higher among rural patients (10.7%) ($p>0.05$), higher among hypertensive patients (17.3%) ($p>0.05$) and was higher among Killip class IV (48.3%) ($p=0.0001$), higher among severe LVD (33.3%) ($p=0.0001$).

**Figure 1: Comparing hospital outcome among different diagnosis.**

In-hospital mortality was 1.2% and 1.1% among those whom beta blocker and ACE was prescribed ($p>0.0001$). There was significant association of in-hospital mortality with BP ($p=0.0001$) and pulse rate ($p=0.02$). In-hospital mortality was higher in patients with troponin between 5-

9 (15%) than ≥ 10 (11%) and < 5 (8.3%). ($p>0.05$), among those whom chest pain and dyspnea was present (13.3%)($p>0.05$), among those whom duration of symptom was > 24 hours (13%)($p>0.05$) and among those whom co- morbidity was present($p>0.05$), among those whom Hb level was 10-12 (16%)($p>0.05$).BNP was significantly ($p=0.001$) higher among expired patients (1762.62±1444.89) than alive (840.76±1294.82) similarly CKMB was significantly ($p=0.006$) higher among expired patients (67.29±45.63) than alive (43.99±41.73).

DISCUSSION

Epidemiological studies have revealed that the prevalence of CAD is increasing in India. ⁵ Present health transition from predominance of infections to the preponderance of cardiovascular disorders, such as hypertension, diabetes, and CAD is now responsible for 53% of all deaths. The disease tends to be more aggressive and manifests at a younger age. Newer studies in India have showed that some of the patients who present with ACS do not have any risk factor for CAD.⁵

In the present study the mean age of presentation was 60.12±10.58 years (range 35 to 85 years) which is comparable to data from the CREATE Registry (mean age 57±12.1 years). The maximum number (about 44%) of patients was in the age group of 55 to 64 years.⁶

In present study authors found that STEMI was more common than NSTEMI/UA. Lakoskiet al also observed that a diagnosis of STEMI was more common in Indians amounting to 60% of all patients presenting with ACS in CREATE registry.⁷ Studies have suggested higher prevalence of ACS in age 60 years or older and predominantly in males which is in agreement to the result obtained in present study.⁸

The skewed gender distribution bias was also a feature in Interheart study and its South Asian cohort.⁹ Also, the male population in CREATE Registry and a study from North India, was, 76.4% and 83.3% respectively.⁸

Hypertension, a conventional risk factor is implicated in CAD. In present study, 31% of patients were hypertensive. The prevalence of hypertension is comparable to that in Create registry (37.7%), and higher than that reported in south Asian cohort of INTERHEART study (17.8%).^{8,9}

Tobacco smoking is a known modifiable risk factor for CAD.⁸ The prevalence of tobacco smoking was low in present study (25.3%). Overall, the mean age of smokers presenting with CAD was younger as compared to non smokers with CAD. Also, STEMI was more common than UA/NSTEMI in smokers than non smokers. Data from Interheart study also suggested that the risk is greater in the young than in the old, and the risk of AMI is even higher in young smokers.⁹

CKMB and troponin I are well known markers of acute cardiac injury and are used in the diagnosis of acute coronary syndrome and to differentiate types of ACS.^{10,11} In present study mean levels of serum CPK, AST, and troponin I were significantly higher in patients with acute STEMI compared with patients with NSTEMI ($p < 0.05$).

CKMB level increases with the extent of myocardial damage; so, it has traditionally been used as an aid in the diagnosis of myocardial injury. While CKMB has been replaced by troponin assays in the work up of many patients with acute chest pain, CKMB may be useful if the initial troponin determination is normal or if a hospitalized patient has a suspected re infarction.¹²

In present study, there was no significant difference in mean CKMB between STEMI and NSTEMI ($p = .8235$). Among total patients with ACS, 36.3% of patients had recurrent angina, 28.3% developed cardiogenic shock, 10% had arrhythmia and 42.5% developed heart failure. According to this, recurrent angina was the most common complication of NSTEMI while heart failure was most common complication of STEMI.

Outcome of Killip class I was better than class II, III, IV. On comparison of outcome of ACS patients who presented in Killip class I and those with higher Killip class (II, III, IV) there was a significant difference observed with p value < 0.001 . This was similar to as found in other studies.^{13,14} EF of 44(29.33%) patients (of which 30% STEMI, 10% NSTEMI and 2.5% of UA) was $> 50\%$.

In a Swedish registry of patients with STEMI from 1996-2007, an increase in the use of evidence-based treatments was reported.¹⁵ The use of aspirin, clopidogrel, beta blockers, statins, and ACE inhibitors were increased. Clopidogrel increased from 0 to 82%, statins increased from 23% to 83%, and various ACE inhibitors increased by a large margin. A decrease was reported in 30-day and 1-year mortality that was sustained during long-term follow-up. By following the proper guidelines in

managing the patients who have experienced STEMI, patients have higher survival rates.

In present study, ACC/AHA based guidelines were used for management of patients. ACE Inhibitor was given to patients if there were no contraindications like cardiogenic shock, intolerance to ACE inhibitors. In case of non tolerability, ARB was used. 63.8% patients were given ACE inhibitor on day 1 of admission and 31.25% patients were not given ACE inhibitor at day one. The hospital mortality was more in patients who were not given ACE inhibitor at day one. There was a significant difference between two group with $p < 0.001$. Similar result was also found for beta-blocker with significant difference ($p < .001$) in between two groups who received beta-blocker then non receivers.

In hospital, patients were treated according to ACC/AHA guideline of pharmacotherapy. In this study, in-hospital mortality was 10.7%. In a Swiss registry, in-hospital mortality varied between 2.4% to 11.8%. showed maximum mortality in older age group (> 75). The Euro Heart Survey expressed mortality risk as per age group as compared to patients below 55 years: the odds ratios of in-hospital mortality due to any type of ACS were 1.9 (age 55-64), 3.7 (age 65-74), 6.2 (age 75-84) and 14.5 (age 85 or higher).¹⁶ In current study, age group mortality was 15.4% (45-54), 7.1% (55-64), 6.2% (65-74), and 38.5% (> 75) which is in agreement to Euro Heart Survey.¹⁶

In Emad et al study, overall in-hospital mortality rate across the 20-year period was higher in women when compared to men (10.6% vs. 4.9%).¹⁷ Among younger patients (< 50 years), the rate of death in women was higher (7.3% vs. 3.1%) and this trend for high mortality was also observed among women of age between 51-70 years (9% vs. 5.4%, $p = 0.001$) and above 70 years of age (17.2% vs. 13.1%) in comparison to men. In present study, mortality in women was lower than in men.

In a Swiss registry, in-hospital mortality varied between 2.4% and 11.8%. In Euro Heart Survey in-hospital mortality was 7% for STEMI and 2.8% for NSTEMI-ACS (total 9.8%).¹⁶ In the GRACE registry in-hospital mortality was 7% for STEMI, 5% for NSTEMI, and 3% for UAP.^{18,19} In this study, in hospital mortality for STEMI was 11.3% and for NSTEMI was 10.3%. In present study, NSTEMI had better outcome than STEMI. In CRUSADE NSTEMI-ACS registry, in-hospital mortality for NSTEMI was 3.9% which is lower than that in present study (10.3%).

In present study, authors found that mortality in ACS patients having hypertension was 17.3 vs. 6.5 (hypertension vs non-hypertension) which was lower than that reported in a study done by Misiriya KJ which showed that higher proportion of NSTEMI/UA cases had hypertension (43% vs. 29.02%), diabetes mellitus

(41.05% vs. 23.95%) and were females (34.96% vs. 21%) in comparison to STEMI cases.²⁰

In present study, authors found that in hospital mortality was higher among Killip class IV 48.3% but there was no mortality in Killip class II and Killip class III. Another study done by Henrique et al.²¹ found that the frequency of death, according to the Killip class, in total long-term clinical follow-up was Killip class I, 17.7%; II, 27.3%; III, 30.4%; and IV, 48.8%.

In present study, authors found that, according to symptoms, maximum mortality was found in patients with chest pain and dyspnea (17.3%) than dyspnea (10.0) or chest pain (7.1) alone. Similar results were found in the study done by Reigel B et al.²² The diffuse symptoms cluster demonstrated higher mortality at 2 years (17%) than the other 3 clusters i.e. chest pain, pain symptoms and stress symptoms (2%-5%), although pre-hospital delay time did not differ significantly.

In present study, authors found that maximum mortality was among severe LVD (33.3%), similar results were found in a study done by Brezinov et al.²³ Mortality rates were highest among patients with severe LV dysfunction (36%), intermediate among those with mild-moderate LV dysfunction (10%), and lowest among those with preserved LV function (4%)

In present study, authors found that maximum mortality was in patients with troponin I value of 5-9 ng/L, but study done by Widimsky et al, the adjusted risk for CV mortality increased three fold in patients with high-sensitivity cardiac troponin I levels between 5 ng/L and 9ng/L and 27 times in those with levels of at least 50 ng/L compared with patients with levels less than 5 ng/L.²⁴

Present study has few limitation; small sample size and cross sectional nature was the main; a large randomized clinical trial is needed to strengthen the presents study findings.

CONCLUSION

Prevalence of ACS was higher in patients who were in fifth to sixth decade of life, were male, who presented within 6-12 hour of start of symptoms, and who had hypertension and diabetes. STEMI was more common than NSTEMI. Among STEMI anterior wall myocardial infarction was more common. Most common complication in NSTEMI was recurrent angina while in STEMI it was heart failure. Patients who were given ACE inhibitors and beta-blocker within 24 hour of onset of symptoms had better mortality and morbidity outcomes. Mortality was higher in patients with Killip's class IV, higher value of Troponin I, age more than 75years and having hypertension and dyslipidemia.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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