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Original Article

Internal Medicine Section

Correlation of Admission Time Blood Glucose, Left Ventricular Function and Regional Wall Motion Index with Occurrence of In-hospital Major Adverse Cardiac Events in Acute Coronary Syndrome

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ABSTRACT

Introduction: Admission time hyperglycaemia is associated with larger infarct size and increased inflammatory process in patients with Acute Coronary Syndrome (ACS). Patients with severe and moderate Left Ventricular (LV) dysfunction are more likely to have triple vessel disease. Admission blood glucose along with conventional Echocardiography (Echo) is a cost-effective and easily feasible method compared to N-terminal proB-type natriuretic peptide (NT-proBNP) in predicting Major Adverse Cardiac Events (MACE) in ACS.

Aim: To study the correlation of admission time blood glucose, LV systolic function and Regional Wall Motion Index (RWMI) with in-hospital MACE in patients with ACS.

Materials and Methods: This was a cross-sectional study which included 100 patients with ACS. Blood samples were taken immediately after admission for plasma blood glucose levels and 2D echo was done within 24 hours to assess LV systolic function and RWMI. All the 100 patients were observed for in-hospital MACE events like cardiac arrhythmias, cardiogenic shock, Congestive Cardiac Failure (CCF), LV dysfunction, recurrent angina and death. Chi-square test was carried out to look for statistical significance between clinical and demographic parameters.

Results: The mean age was 55.4±11.2 years. The incidence of admission time hyperglycaemia was significant in patients with history of Diabetes Mellitus (DM). A total of 55 patients (87.3%) with history of diabetes and 12 patients (32.4%) patients with no previous history of diabetes had admission time hyperglycaemia and five patients had stress hyperglycaemia. There was statistically significant correlation of admission time hyperglycaemia with LV systolic dysfunction (p-value=0.02) and CCF (p-value=0.02). RWMI had statistically significant correlation with LV systolic dysfunction (p-value <0.001), CCF (p-value=0.008) and recurrent angina (p-value=0.02). There was statistically significant correlation of LV systolic function with recurrent angina (p-value=0.04) and death (p-value=0.005).

Conclusion: RWMI and poor LV systolic function can predict the occurrence of in-hospital MACE in patients with ACS. In addition to echocardiography, raised blood glucose levels at the time of admission have a positive predictive outcome with higher incidence of MACE.

Keywords: Arrhythmias, Diabetes mellitus, Echocardiography, Hyperglycaemia

INTRODUCTION

Coronary Artery Disease (CAD) is one of the leading causes of morbidity and mortality in India, resulting into 26% of adult deaths in 2001-2003, which increased to 32% in 2010-2013 [1]. A life-threatening presentation of coronary artery disease is ACS.

ACS includes ST Elevation Myocardial Infarction (STEMI), Non-ST Elevation Myocardial Infarction (NSTEMI) and Unstable Angina (UA). In UA and NSTEMI, partial obstruction of coronary arterial tree causes reduced oxygen supply or increased myocardial oxygen demand due to atheromatous plaque. STEMI occurs due to rupture of the atheromatous plaque and formation of thrombus leading to complete occlusion of the coronary artery, resulting in myocardial necrosis.

The MACE after ACS includes life threatening arrhythmias, cardiac failure, cardiogenic shock, recurrent ischaemia and sudden death.

Admission time hyperglycaemia is common, irrespective of diabetic status in patients with ACS [2]. The prevalence of increased blood glucose in patients with ACS ranges from 51-58% [3]. Increased blood glucose at the time of admission is associated with larger infarct size and increased inflammatory process which leads to increased platelet activation. This explains the impairment in coronary blood flow that reflects a prothrombotic state and endothelial dysfunction leading to a greater stress response. Higher blood glucose may not be the cause for MACE, but an indicator of extent of myocardial damage which influences the occurrence of MACE [3,4].

Progressive dilatation of LV and LV remodelling after ACS have been a strong predictor of MACE [5]. Reduced LV Ejection Fraction (LVEF) is associated with poor short and long term outcomes in patients with ACS. Patients with severe and moderate LV dysfunction are more likely to have triple vessel disease [6].

Regional Wall Motion Abnormality (RWMA) assessed by RWMI using 2D echo correlates with infarct size which in turn predicts the occurrence of MACE in patients with ACS [7].

Early prediction of MACE is essential in patients with ACS [4]. Admission time blood glucose along with conventional echo is a cost-effective and an easy method compared to NT-proBNP in predicting MACE in ACS patients. Although LV function is a good predictor of mortality, there are limited data regarding factors affecting outcomes among ACS patients, presenting with varying degrees of LV dysfunction [8,9]. Hence, in this study, authors evaluated the effect of admission time hyperglycaemia, LV systolic function and RWMI with MACE during hospital stay in patients with ACS.

MATERIALS AND METHODS

This was an observational study which included 100 patients admitted with a diagnosis of ACS in a tertiary care centre in Puducherry, India from January 2018 to June 2019. This study was approved by the Institutional Ethical Committee (PG DISSERTATION/12/2017/120). Informed and written consent was obtained from study participants before proceeding with the study.

Hundred patients who presented in the emergency medicine department with ACS (STEMI, NSTEMI and UA) diagnosed as per clinical presentation, ECG changes and cardiac biomarkers were included in the study. Those patients with chronic kidney disease, anaemia and old myocardial infarction were excluded from the study.

Diagnosis of ACS was confirmed with typical symptoms, ECG findings and laboratory findings. The diagnosis of Acute Myocardial Infarction (AMI) was established by the three criteria accepted by World Health Organisation (WHO): (1) Ischaemic type chest pain; (2) Changes in serial ECG tracings typical for AMI; and (3) Presence of at least two criteria of typical course of rise and fall of serum cardiac biomarkers. The diagnosis of UA pectoris was established by the presence of unstable chest pain and typical electrocardiographic findings in the absence of elevated CK-MB and troponin levels.

The first blood sample during admission was taken for estimating plasma glucose level, cardiac biomarkers and other routine investigations. Samples for fasting blood glucose, post-prandial blood glucose and HbA1c were also obtained in diabetics and non-diabetics to assess the glycaemic control and to rule out diabetes respectively. Admission time hyperglycaemia was defined as blood glucose of more than 140 mg/dL in diabetics and more than 180mg/dL in non-diabetics [10]. A 2D echo was done within 24 hours of admission to assess LV systolic function using modified Simpson rule [11]. According to American College of Cardiology LVEF is assessed as Normal=LVEF 50-70%, Mild LV systolic dysfunction=40-49%, Moderate systolic dysfunction=30-39%, Severe LV systolic dysfunction=LVEF <30% [12]. RWMA was identified using 17 segment model of the LV suggested by American Heart Association by wall motion index score [7]. The LV was divided into 17 segments using the views parasternal long axis or apical long axis view, apical four chamber view, apical two chamber view, short axis of base, mid LV and apex as: 1) Basal anterior; 2) Basal anteroseptal; 3) Basal inferoseptal; 4) Basal inferior; 5) Basal inferolateral; 6) Basal anterolateral; 7) Mid-anterior; 8) Mid-anteroseptal; 9) Mid-inferoseptal; 10) Mid-inferior; 11) Mid-inferolateral; 12) Mid-anterolateral; 13) Apical anterior; 14) Apical septal; 15) Apical inferior; 16) Apical Lateral and 17) Apex.

Each segment was graded as follows: 1-Normal; 2-Hypokinesia; 3-Akinesia; 4-Dyskinesia. Wall motion index score was calculated by dividing the total segmental score by 17. Any score above 1 was considered abnormal and the presence of RWMA. All 100 patients were observed for in-hospital MACE like cardiac arrhythmias, cardiogenic shock, CCF, LV systolic dysfunction, recurrent angina and death.

STATISTICAL ANALYSIS

The data for sample size was calculated based on the study done by Gupta R et al., which came to be 87.6 [1]. Allowing an extra 10% for possible exclusion due to incomplete data, the final sample size was increased to 100. The data was entered in a data collection proforma sheet and MS Excel spreadsheet sequentially. Statistical analysis was carried out using SPSS version 15.0 (IBM SPSS, US) software. Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. Categorical outcomes were compared between study groups using Chi-square test and $p<0.05$ was considered statistically significant.

RESULTS

The study was carried out in 100 ACS patients in a tertiary care centre in Puducherry, India. The mean age was 55.4±11.2 years. Maximum patients were in the age group 51 to 60 years with 44 patients and least in the age group 20 to 30 years and 31 to 40 years with 3 and 5 patients, respectively. In this study 67% were males and 33% were females. The baseline characteristics of the patients are listed in [Table/Fig-1].

Parameters	Values
Mean age	**55.4±11.2 years**
Gender	**Frequency**
Male	67
Female	33
Co-morbidities	
Diabetes	18
Hypertension	13
Both diabetes and hypertension	48
No comorbidities	21
Addictions	
Smoking	33
Alcohol consumption	40
No addictions	27
Diagnosis	
ST elevation MI	64
Non- ST elevation MI	23
Unstable Angina	13
ECG findings	
ST elevation	64
ST depression and other ST changes	29
Normal ECG	7

[Table/Fig-1]: Baseline characteristics of the patients.

Admission time hyperglycaemia was more common in diabetics than non-diabetics. Of the 67% of patients who had admission time hyperglycaemia, 55 patients (87.3%) were known diabetics and 12 patients (32.4%) had no previous history of diabetes mellitus and five patients had stress hyperglycaemia [Table/Fig-2]. Of these 12 non-diabetic patients who had admission hyperglycaemia, seven were newly diagnosed to have diabetes mellitus. In this study 62.7% of STEMI patients, 22.4% of NSTEMI patients and 14.9% UA patients had admission time hyperglycaemia. The echocardiographic findings at the time of admission are summarised in [Table/Fig-3]. MACE during the course of stay in hospital and their frequency are given in [Table/Fig-4].

Features	Frequency
Admission time hyperglycaemia	67
Admission time normoglycaemia	33

[Table/Fig-2]: Admission time blood glucose of study participants (n=100).

RMWI	Frequency
Normal	31
Abnormal	69
LV systolic function	
Normal	41
Mild LV systolic dysfunction	37
Moderate LV systolic dysfunction	20
Severe LV systolic dysfunction	2

[Table/Fig-3]: Echocardiographic findings at the time of admission (n=100).

Among 100 ACS patients, 64 had STEMI (out of which 24

were thrombolysed, 26 patients presented late and 14 had contraindications for thrombolysis), 23 patients had NSTEMI and 13 patients had unstable angina. All the four patients who died had STEMI, of whom one patient was thrombolysed.

Major adverse cardiac events	Frequency and %
Cardiac arrhythmia	12
LV systolic dysfunction	59
Cardiogenic shock	11
CCF	23
Recurrent angina	11
Death	4

[Table/Fig-4]: Major adverse cardiac events developed following admission of study participants (n=100).

Among the 24 patients who met the criteria for thrombolysis, two patients (8.3%) developed Cardiac arrhythmia and recurrent angina, 14 patients (58.3%) developed LV dysfunction, three patients (12.5%) developed cardiogenic shock and one patient died.

There was no statistically significant correlation between admission time Hyperglycaemia and RWMI (p-value=0.08). Admission time hyperglycaemia had statistically significant correlation with LV dysfunction (p=0.02; odd's ratio 2.75) and CCF (p=0.02; odd's ratio- 4.25) [Table/Fig-5]. RWMI had statistically significant correlation with LV systolic dysfunction (p-value <0.001; odd's ratio- 52.2), CCF (p-value=0.008; odd's ratio -6.3448) and recurrent angina (p-value=0.02; odd's ratio -12.38) [Table/Fig-6]. LV systolic function had statistically no significance with cardiac arrhythmias [Table/Fig-7] whereas, it had statistical significance with recurrent angina (p-value=0.04; odd's ratio 8.1633) [Table/Fig-8] and death (p-value=0.005; odd's ratio-6.7297) [Table/Fig-9].

Major adverse cardiac events	Admission time hyperglycaemia		p-value	Odds ratio	95% Confidence
	No n (%)	Yes n (%)			
Cardiac arrhythmia			0.92	0.9831	0.2733 to 3.5354
No	29 (87.9)	59 (88.1)			
Yes	4 (12.1)	8 (11.9)			
LV systolic dysfunction			0.02*	2.756	1.1682 to 6.5040
No	20 (60.6)	21 (31.3)			
Yes	13 (39.4)	46 (68.6)			
Cardiogenic shock			0.80	0.8458	0.2291 to 3.1224
No	29 (87.9)	60 (89.6)			
Yes	4 (12.1)	7 (10.4)			
CCF			0.02*	4.2553	1.1631 to 15.5684
No	30 (90.9)	47 (70.1)			
Yes	3 (9.1)	20 (29.9)			
Recurrent angina			0.80	0.8458	0.2291 to 3.1224
No	29 (87.9)	60 (89.6)			
Yes	4 (12.1)	7 (10.4)			
Death			0.73	1.5	0.1500 to 15.0010
No	32 (97)	64 (95.5)			
Yes	1 (3)	3 (4.5)			

[Table/Fig-5]: Association between admission time hyperglycaemia and major adverse cardiac events among study participants (n=100).
p-value based on Chi-square test, statistically significant (p<0.05) and odd's ratio >1 is statistically significant; CCF- Congestive cardiac failure; LV- Left ventricular

DISCUSSION

In patients with ACS it is essential to predict the occurrence of MACE and identifying a risk model for guiding triage, deciding management and reducing mortality.

Major adverse cardiac events	RMWI		p-value	Odd's ratio	95% Confidence interval
	Normal n (%)	Abnormal n (%)			
Cardiac arrhythmia			0.85	0.8852	0.2454 to 3.1932
No	27 (87.1)	61 (88.4)			
Yes	4 (12.9)	8 (11.6)			
Left Ventricular dysfunction			<0.001*	52.2	11.1584 to 244.1969
No	29 (93.5)	12 (17.3)			
Yes	2 (6.5)	57 (82.6)			
Cardiogenic shock			0.09	5.0847	0.6213 to 41.6112
No	30 (96.8)	59 (85.5)			
Yes	1 (3.2)	10 (14.5)			
CCF			0.008*	6.3448	1.3848 to 29.0608
No	29 (93.5)	48 (69.6)			
Yes	2 (6.5)	21 (30.4)			
Recurrent angina			0.02*	12.3846	1.7061 to 217.2113
No	31 (100)	58 (84.1)			
Yes	0	11 (15.9)			
Death			0.17	4.3282	0.2260 to 82.9056
No	31 (100)	65 (94.2)			
Yes	0	4 (5.8)			

[Table/Fig-6]: Association between Regional Wall Motion Index (RWMI) and major adverse cardiac events.
p-value based on Chi-square test, statistically significant (p<0.05); CCF- Congestive cardiac failure; LV- Left ventricular

LV function	Cardiac arrhythmia		p-value	Odd's ratio	95% Confidence interval
	No n (%)	Yes n (%)			
Normal	38 (92.7)	3 (7.3)	0.06	2.28	0.5776 to 9.0001
Mild	34 (91.9)	3 (8.1)			
Moderate	15 (75)	5 (25)			
Severe	1 (50)	1 (50)			

[Table/Fig-7]: Association between Left Ventricular (LV) function and cardiac arrhythmia (n=100).
p-value based on Chi-square test; Statistically significant (p<0.05)

LV function	Recurrent angina		p-value	Odd's ratio	95% Confidence interval
	No n (%)	Yes n (%)			
Normal	40 (97.6)	1 (2.4)	0.04*	8.1633	1.0020 to 66.5072
Mild LV dysfunction	30 (81.1)	7 (18.9)			
Moderate LV dysfunction	18 (90)	2 (10)			
Severe LV dysfunction	1 (50)	1 (50)			

[Table/Fig-8]: Association between Left Ventricular (LV) function and recurrent angina (n=100).
p-value based on Chi-square test, statistically significant (p<0.05)

LV function	Death		p-value	Odd's ratio	95% Confidence Interval
	No n (%)	Yes n (%)			
Normal	41 (100)	0	0.005*	6.7297	1.3525 to 128.4946
Mild LV dysfunction	35 (94.6)	2 (5.4)			
Moderate LV dysfunction	19 (95)	1 (5)			
Severe LV dysfunction	1 (50)	1 (50)			

[Table/Fig-9]: Association between Left Ventricular (LV) function and death (n=100).
Statistically significant (p<0.05)

Admission time hyperglycaemia was more common in patients with STEMI than NSTEMI and unstable angina with 62.7%, 22.4% and 14.9% respectively which is similar to a study conducted by

Petursson P et al., where admission time hyperglycaemia in STEMI and UA were 62% and 9%, respectively [13]. STEMI usually occurs as a result of occlusion of the coronary artery by a thrombus at the site of ruptured or eroded plaque and the extent of the myocardial injury depends on the area of myocardium supplied by the culprit vessel, duration of occlusion and presence of collaterals. Hence, successful restoration of vessel patency in STEMI is essential which is done by either fibrinolysis or mechanical reperfusion with primary percutaneous coronary intervention, of which the latter is considered superior in reducing the mortality rate [14].

In this study, 67% of the patients had admission time hyperglycaemia and 33% were normoglycaemic similar to a study conducted by Alavi-Moghaddam M et al., where 52.3% had admission time hyperglycaemia and 39.8% were normoglycaemic [4]. In this study, five patients were found to have stress hyperglycaemia. Stress hyperglycaemia is a physiologic response to hormones released secondary to high systemic stress which is an indicator of impaired insulin signalling, systemic and organ specific metabolic dysregulation. Patients with larger infarct size and severe LV dysfunction may have stronger sympathetic activation resulting in higher glucose levels [15].

There was statistically significant correlation of admission time blood glucose with MACE like LV systolic dysfunction and CCF. There were four deaths and out of which 3 patients were known diabetics and all three had admission time hyperglycaemia. In a study conducted by Petursson P et al., admission time hyperglycaemia in non-diabetics led to development of heart failure, atrial fibrillation and cardiac arrest than normoglycemic [13]. However, in a study conducted by Al Jumaily T et al., angiograms were done to assess the severity of ischaemic heart disease and it was found that there was no correlation with admission time hyperglycaemia [16].

There was a statistically significant correlation of RWMA with LV systolic dysfunction, CCF and recurrent angina. A 82.6% of patients with LV systolic dysfunction, 30.4% of patients with CCF and 15.9% of patients with recurrent angina had RWMA during admission. All the four patients who died had RWMA. The greater the wall motion index, the greater the infarct size and the occurrence of complications [7]. RWMA can occur with significant CAD and it can also be normal in CAD with significant ischaemia. Angiographic studies may not correlate well with RWMA because of the tendency of coronary arteriogram, as it may underestimate the degree of stenosis when compared with pathological examination, mainly if it is associated with coronary artery spasm occurring during angiography. Hence the usage of 2D echo has provided a non-invasive method of detecting wall motion abnormality which is a good index of CAD [17].

In the present study, there was statistically significant correlation between LV systolic function and MACE like recurrent angina and death. All the patients who died had LV dysfunction. However, in a study conducted by Popovic B et al., they observed that a low LVEF at admission is not associated with all cause or cardiovascular mortality after one year follow-up [18]. In transmural myocardial infarction, there is alteration in the structure and function of the left ventricle which results in dilatation of LV ventricle and impaired systolic function, referred as LV remodelling. As the LV dilates, the LVEF reduces and the papillary muscles are displaced, rising the degree of mitral regurgitation, resulting in exacerbation of heart failure and increase in mortality rate [7].

Limitation(s)

Due to limited study period, only in-hospital MACE were analysed and long term follow-up could not be done.

CONCLUSION(S)

Admission time blood glucose has correlation with the occurrence of in-hospital MACE. Increased blood glucose at admission has increased risk of occurrence of in-hospital MACE like LV systolic dysfunction and CCF in patients with ACS. High RWMI in ACS is associated with in-hospital MACE like CCF, LV systolic dysfunction and recurrent angina. LV function within 24 hours of admission in patients with ACS is associated with in-hospital MACE like recurrent angina and death. LV systolic function is the single most important predictor of in-hospital mortality. LV systolic function is inversely proportional to in-hospital mortality. Hence admission blood glucose, LV systolic function and RWMI are reliable markers for predicting the occurrence of in-hospital MACE.

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