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Association of HbA1C Level with Extent of Acute Myocardial Infarction and Short-Term Mortality in Patients without Known Diabetes

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ABSTRACT

Objective: To determine the prognostic value of HbA1c levels in relation to the extent of acute myocardial infarction (MI) and short-term mortality in patients without known diabetes.

Methodology: A prospective cohort study was conducted in the Department of Cardiology at Liaquat University Hospital, Hyderabad, over a period of one year, from February 2020 to January 2021. All patients aged 20-75 years, of both genders, with acute myocardial infarction (MI), including STEMI and NSTEMI, were included. MI diagnosis was based on ECG findings and serum cardiac biomarkers such as Troponin-T and Troponin-I. Blood samples were collected from all patients to assess HbA1c levels. Echocardiography was performed to categorize patients according to left ventricular ejection fraction. Short-term mortality was assessed in all patients. Data analysis was conducted using SPSS version 22.0.

Results: A total of 377 patients with acute myocardial infarction (MI) were studied; their mean age was 50.42 ± 11.71 years. The majority of the study subjects were male (83.0%), while females accounted for 17.0%. Among all cases, 59.4% had an HbA1c level of <5.8, and 40.6% had an HbA1c level of ≥5.8. Most study subjects (62.9%) had a left ventricular ejection fraction of <40%. The majority of the cases (77.7%) were diagnosed with STEMI, while NSTEMI was observed in 22.3% of the cases. Overall short-term mortality (30 days) was 14.3%, which was significantly associated with HbA1c level of ≥5.8 (p-<0.05).

Conclusion: Overall short-term mortality (30 days) was 14.3%. Higher HbA1c was observed to be a potential indicator for short term mortality among patients of acute coronary syndrome as well as a predictor for short-term mortality in ACS patients without known diabetes mellitus.

Key words: Acute MI, Hba1c, Unknown diabetes, 30 days mortality

Authors' Contribution:
[1,2]Conception; Literature research; manuscript design and drafting; [3,4]Critical analysis and manuscript review; [5,6]Data analysis; Manuscript Editing.

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Introduction

Acute myocardial infarction (AMI) is a leading cause of both mortality and morbidity worldwide.[1] About 600,000 Americans are admitted to hospitals each year due to an initial episode of acute MI.[1,2] Cardiovascular disease (CVD) is predicted to become twice as common among South Asian populations over the next 20 years.[3,4] Ischemic heart disease (IHD) is a type of cardiovascular disease (CVD), with acute myocardial infarction (AMI) being one of its most common manifestations.[3] The two clinical types of AMI are ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI).[3] The 30-day survival rate has emerged as a important indicator of quality care, and recent findings have shown that the 30-day survival rate for acute myocardial infarction (AMI) ranges from 88.0% to 93.5% when calculated using the hospital catchment method.[5] Type II diabetes is a significant contributing factor to cardiovascular diseases, particularly acute myocardial infarction. Diabetes increases a person's risk of heart attack compared to non-diabetics. Individuals with diabetes are more likely to experience both short- and long-term mortality following a heart attack than those without the disease. Elevated HbA1c levels serve as a potential marker for increased risk of in-hospital mortality among patients with acute coronary syndrome (ACS) and as a predictor of short-term mortality in ACS patients who do not have a history of diabetes mellitus (DM) and are not diagnosed with DM.[6] Each 1% increase in HbA1c is associated with a 30% rise in all-cause mortality and a 40% increase in cardiovascular disease (CVD)-related mortality in individuals with diabetes. Microvascular complications are known to occur long before a person develops overt diabetes mellitus (DM). Hyperglycemia accelerates atherosclerosis by promoting the formation of glycated proteins and products that impair endothelial function, leading to macrovascular complications. HbA1c can be used as a biomarker for glycemic control. Recent studies have also linked elevated HbA1c levels to increased CVD risk and mortality.[7] Multiple investigations have demonstrated that even mild deviations in glucose control (below the diagnostic threshold for diabetes) are associated with an increased risk of cardiovascular disease (CVD), extending the link between adverse CVD outcomes and dysglycemia.[6,7] Therefore, both non-diabetics with stress hyperglycemia and diabetics with uncontrolled blood glucose have a poorer prognosis in cases of acute coronary syndrome (ACS). However, the impact of recently elevated blood glucose, as assessed by HbA1c, has not consistently been recognized as a poor prognostic indicator. There is a correlation between high blood sugar levels upon admission and an increased risk of adverse outcomes, such as cardiogenic shock, congestive heart failure (CHF), and mortality.[8,9] Despite numerous studies exploring this intriguing topic, conclusive findings remain elusive. Therefore, this study aims to investigate the potential association between HbA1c levels and the severity of acute myocardial infarction (AMI), as well as short-term mortality. If a significant correlation between HbA1c levels and both short-term mortality and AMI severity is established, it would support the early and effective management of HbA1c levels to mitigate morbidity and mortality risks.

Methodology

A prospective cohort study was conducted in the Department of Cardiology at Liaquat University Hospital, Hyderabad, over a one-year period from February 2020 to January 2021, following approval of the study protocol and until the target sample size was achieved. Sample size calculation was performed using Raosoft software with a 95% confidence interval and a 5% margin of error, resulting in a sample size of n = 377. Non-probability convenience sampling was used. Patients with acute myocardial infarction (STEMI and NSTEMI), aged 20 to 75 years, of both genders, were included. Patients who did not consent to participate, those with a history of AMI, congestive heart failure, valvular heart diseases, congenital heart diseases, or other severe morbidities with poor prognosis such as chronic liver disease (CLD), chronic kidney disease (CKD), and carcinoma, were excluded. The study was conducted with approval from the ethical committee of Liaquat University of Medical and

Health Sciences (LUMHS). Subjects were selected from the cardiology department's inpatient ward at Liaquat University Hospital, Hyderabad. Following consent, a brief history of the condition's duration was collected. Patients meeting the inclusion criteria were enrolled in the study. Detailed records were kept of the duration, frequency, and intensity of chest discomfort, exercise tolerance, risk factors associated with MI, and any history of prior myocardial infarction. Diagnosis of MI was based on ECG and blood cardiac biomarkers, including Troponin-T and Troponin-I. Blood samples were collected from each patient to determine HbA1c levels. All patients underwent echocardiography and were categorized into three groups based on their left ventricular ejection fraction (LVEF): LVEF > 50%, LVEF 49% to 41%, and LVEF ≤ 40%. Short-term mortality was assessed in all cases and was analysed in relation to HbA1c levels, which were categorized into two groups: HbA1c < 6.8% and HbA1c ≥ 5.8%. Data were recorded in a proforma for analysis. After data collection, analysis was conducted using Statistical Package for Social Sciences (SPSS) software, Version 22.0.

Results

A total of 377 patients with acute myocardial infarction (MI) were studied, with a mean age of 50.42 ± 11.71 years. Males were the majority, accounting for 83.0% of the patients, while females made up 17.0%. Among all patients, 59.4% had an HbA1c level of <5.8, and 40.6% had an HbA1c level of ≥5.8. Most study subjects (62.9%) had a left ventricular ejection fraction (LVEF) of <40%, 30.8% had an LVEF of 41-49%, and 6.3% had an LVEF of >50%. The majority of cases (77.7%) had ST-elevation myocardial infarction (STEMI), while non-ST elevation myocardial infarction (NSTEMI) was observed in 22.3% of the cases. Table I. The data suggest potential correlations between HbA1c levels, the severity of myocardial infarction (MI), and short-term mortality, with some associations showing statistical significance (p < 0.05). Table II. Overall short-term mortality (30 days) was found 14.3% as showed in figure 1In this study, short-term mortality (30 days) was statistically significant according to gender, left ventricular ejection fraction, and type of myocardial infarction (MI) (p < 0.05). Table III.

Table: I Gender distribution of the patients n=377

Variables	Frequency	Percent
Gender		
Male	313	83.0
Female	64	17.0
HbA1c		
≥5.8	153	40.6
<5.8	224	59.4
LVEF		
<40%	237	62.9
41 to 49%	116	30.8
>50%	24	06.4
Types of MI		
ST elevation MI	293	77.7
NST elevation MI	84	22.3

Table: II Association of HbA1c level with severity of acute MI and short-term mortality n=377

Variables	Hba1c		Total	p-value
	≥5.8	<5.8		
LVEF				
<40%	107	130	237	0.059
41 to 49%	39	77	116	
>50	7	17	24	
Total	**153**	224	377	
30 days mortality				
Yes	29	25	54	0.034
No	124	199	323	
Total	153	224	377	

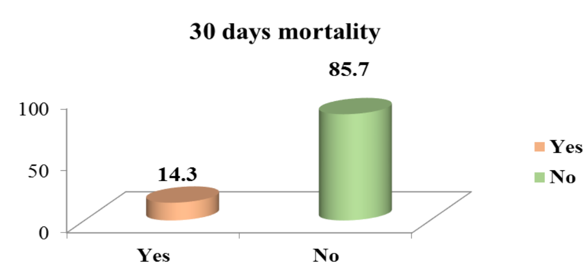

Figure:1 Patient's distribution according to 30 days mortality n=377

Table: III Short term mortality according to gender, HbA1c and LVEF n=377				
Variables		**30 days mortality**		**p-value**
		Yes	**No**	
Gender	Male	36(66.7%)	277(85.8%)	0.001
	Female	18(33.3%)	46(14.2%)	
LVEF	<40%	44(81.5%)	193(59.8%)	0.001
	41 to 49%	10(18.5%)	106(32.8%)	
	>50	00	24(7.4%)	
Type of MI	NST elevation	27(50.0%)	57(82.4%)	0.001
	ST elevation	27(50.0%)	266(17.6%)	

Discussion

Ischemic heart disease (IHD) is the leading cause of mortality globally, and its incidence is rising, although there are variations between different nations.[10] Because of increased use of primary percutaneous coronary intervention (PCI), modern antithrombotic medication, and secondary preventive strategies, both long- and short-term mortality related to ST-elevation myocardial infarction (STEMI) have decreased significantly in recent decades.[10,11] Despite this, mortality rates remain high, with an in-hospital death rate of 4% to 12% among unselected STEMI patients. In this study, short-term mortality (1 month) was found to be 14.3%.[10] Similarly, Aziz F et al[12] found that total mortality in STEMI patients was 5.4% in-hospital, 8.1% at 30 days, and 14.4% after one year. However, McNamara RL et al[13] reported an in-hospital mortality rate of 4.6%. The short-term prognosis of out-of-hospital cardiac arrest (OHCA) patients has improved in the past 15 years due to extensive efforts to enhance both pre-treatment and during hospitalization. [14,15] Despite this, most patients die following OHCA, either before hospitalization due to a lack of return of spontaneous circulation (ROSC) or in-hospital due to cerebral or other complications following ROSC.[16]

In this study, the mean age of the patients was 50.42 ± 11.71 years, and the majority were male (83.0%). In contrast, McNamara RL et al[13] reported a mean age of 64.6 ± 13.8 years, with males comprising 34.8% of the study population. Aziz F et al[12] noted that 87% of the subjects were men in their study. Kvakkestad KM and colleagues[15] found that the average age of the subjects was 63.6 ± 12.5 years, with a majority being male (80.0%). Similarly, in another study reported that out of 74,389 acute myocardial infarction (AMI) admissions, 30.0% were women. In this study, the mortality rate was higher among males compared to females. However, when mortality rates during hospitalization were adjusted for medical history, personal history, age, and initial clinical outcomes, Fabijanić D et al[17] found that being female is an independent predictor of mortality during hospitalization following the first AMI, consistent with some previous research. On the other hand, some researchers argue that after accounting for baseline differences, being female has not been independently associated with an increased in-hospital mortality rate compared to males.

Because variations in mortality risk between women and men were independent of baseline data, it is plausible that other factors are influencing the prognosis. Moshki M et al[18] stated that mortality during hospitalization was higher among females with acute myocardial infarction (AMI) compared to males (10.4% vs. 8.6%). This finding aligns with Anderson and Pepine's results, which indicated that the odds ratio (OR) of in-hospital mortality is approximately 2.65 times higher for females with AMI compared to males.[14,17] Compared to males, the female gender was associated with a significantly higher likelihood of mortality, stroke, MI, urgent revascularization, or definite acute abrupt vessel closure. Even though this discrepancy was reduced in a multivariable model, gender remained associated with all-cause mortality at 30 days.[19] Landmark analysis of events that occurred within the first 2 days and between 2 to 30 days revealed that 38% of females and 36% of males who did not survive the first month died within the first 2 days.[19]

In this study, short-term mortality was significantly higher among patients with HbA1c $\geq$5.8% and an ejection fraction <40%. In contrast to our study, Kapil et al[20] showed a positive predictive association between cardiovascular disease (CVD) and HbA1c (p = 0.001). Furthermore, another study from North Eastern India, which employed the SYNTAX score, found a highly significant link between higher HbA1c levels and the SYNTAX score.[21] Many studies have been conducted over the years to uncover predictors of coronary artery disease (CAD); however, in recent decades, the HbA1c level among diabetics has been explored as a potential predictor. In a recent policy statement, the American Diabetes Association (ADA) suggested that reducing HbA1c may be associated with a decrease in microvascular and neuropathic complications, and possibly macrovascular consequences of DM.[22] Similarly, research associating the severity of CAD and CVD mortality with HbA1c values has been regularly conducted in non-diabetics since 2004.[23] Furthermore, these studies show that even when HbA1c levels are within the standard range, the risk of developing CAD is greatly increased.[24] Several biological mechanisms have been suggested to elucidate a potential causal link between HbA1c and heightened mortality in patients with acute coronary syndrome (ACS).[6] A correlation between baseline plasma fibrinogen levels and HbA1c levels in ACS patients plays a crucial role in coronary thrombosis, aligning with the finding that elevated HbA1c levels were significantly associated with an increased risk of complications in ACS patients.[6,25,26]

Conclusion

As per study conclusion overall short-term mortality (30 days) was noted to be 14.3%. Higher HbA1c was observed to be a potential indicator for short term mortality among patients of acute coronary syndrome as well as a predictor for short-term mortality in ACS patients without known diabetes mellitus. Further large-scale studies are needed on this subject.

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