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Research Article

PROGNOSTIC SIGNIFICANCE OF GLYCEMIC STATUS ON ADMISSION IN DIABETIC AND NON-DIABETIC PATIENTS WITH ACUTE CORONARY SYNDROME

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ABSTRACT

Objectives: The aim is to study the relationship between glycemic status at admission and outcome in diabetic and non-diabetic patients with acute coronary+ syndrome (ACS).

Methods: This prospective, observational study was conducted on all patients admitted to general wards and ICCU at GMCH, Udaipur, from February 2021 to July 2022. Detailed history and clinical examination were done. $HbA_{1c,}$ RBS, CBC, TROP I, and CPK-MB were done. Investigations were collected at the time of admission and discharge.

Results: Among non-diabetic patients, there were 19 patients who had hyperglycemia on admission and 36 had normal sugar. Among diabetic patients, 31 patients had hyperglycemia and 24 patients had normal sugar. 31 patients with hyperglycemia on admission had high HbA_1c. 29 patients had cardiac failure (26.36%), 30 with cardiogenic shock (27.27%), 33 with arrhythmias (30%), and 4 with pulmonary edema (3.63%), making cardiac failure the most common complication in the study population. The mean ejection fraction at admission for the non-diabetics with normal sugar was 44.52, for non-diabetics with hyperglycemia was 43, for diabetics with normal sugar was 41.88 and for diabetics with hyperglycemia was 40.95.

Conclusion: We conclude that non-diabetics presenting with hyperglycemia on admission are at more risk of having complications of ACS and had more mortality compared to diabetics having normal sugar on admission.

Keywords: Glycemic status, Acute coronary syndrome, Acute kidney injury, Diabetic, Non-diabetic.

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INTRODUCTION

It is a well-known fact that diabetes and cardiovascular diseases go hand in hand together. Many patients presenting with cardiovascular diseases are either suffering from diabetes or are in the pre-diabetic state [1]. Coronary artery disease (CAD) which is considered the most significant complication of DM, presents two to four folds greater risk of mortality compared to the non-diabetic population [2,3].

It is well accepted that hyperglycemia is commonly present in patients admitted with acute ST-segment elevation myocardial infarction (STEMI). It is associated with an increased risk of death or adverse cardiovascular events in patients both with and without a previous history of diabetes mellitus [4].

In patients with no prior history of diabetes who present with a macrovascular complication, that is, myocardial infarction, hyperglycemia might be due to a previously undiagnosed diabetes or due to stress hyperglycemia or due to a pre-diabetic state. This can lead to a poor outcome in patients in the form of shock, failure, or arrhythmias [5].

Hence, both stress hyperglycemia in non-diabetic patients and high random blood sugar in diabetic patients are having adverse prognostic effects in patients with ACS. However, the effect of recently elevated blood sugar as measured by HbA_{1c} has still not been consistently reported as a bad prognostic indicator.

Available data suggest that hyperglycemia on admission is an indicator of short-term mortality in patients admitted with acute STEMI, but its efficacy in predicting the long-term mortality is still unclear.

It has been noted that among patients with high-risk Non-ST elevation acute coronary syndrome (NSTE-ACS) also that a substantial proportion of patients admitted with high-risk NSTE-ACS had previously undiagnosed DM (12.2%) or pre-diabetes (10.8%) as defined by HbA_{1c} or FBS after admission.

According to a study done in 2013 by Ashraf, in non-diabetic patients, HbA_{1c} could be utilized for risk stratification of CAD and its severity; independent of traditional cardiovascular risk factors. These factors aroused curiosity, which led to this study, which probes into the prognostic significance of glycated hemoglobin and admission RBS in non-diabetics admitted with acute STEMI.

The Framingham study also confirms that females had a higher occurrence of diabetes compared to males,whereas in India, males have a higher occurrence of diabetes than females, according to a diabetes research study held in India [6]. In acute MI, DM has been a bad prognostic factor with an increased occurrence of heart failure, higher mortality in the hospital, conduction abnormalities including atrial fibrillation, and post-infarction angina among diabetics [7,8]. It has been shown that adequate control of blood sugar brings down the progression of microvascular disorders caused by diabetes. However, its influence on macrovascular complications is not well known [9].

Inadequate glycemic management is shown by elevated HbA_{1c}, and its elevated value during admission for ACS, increases the mortality in 1st month. Furthermore, hyperglycemia at the time of ACS without a history of DM has increased short-term mortality [10].

Diabetes is a significant risk factor for the development of ACS and the adverse outcomes after ACS. “Stress hyperglycemia” has been defined in different ways by various studies transient hyperglycemia has been recognized as a noticeable feature in ACS and is considered to be related to stress [11]. Sometimes, hyperglycemia can denote pre-existing type 2

diabetes or impaired glucose tolerance, which has not been detected before. Studies prove that uncontrolled blood sugar has poor outcome when they develop an ACS, but hyperglycemia at the time of ACS also have a similar prognostic value [12].

Moreover, this study enables risk stratification. Early identification of high-risk groups enables the initiation of specific intervention strategies and it may help us to improve the prognosis of these patients. It also helps in identifying a previously undiagnosed group of diabetics.

This is of importance because there is a global increase in the number of patients suffering from cardiovascular disease with underlying insulin resistance, pre-diabetes, and overt diabetes mellitus, which go unrecognized.

Aims and objectives

1. To compare the glycemic status at admission in diabetic and non-diabetic patients with ACS
2. To study the relationship between glycemic status at admission and outcome in diabetic and non-diabetic patients with ACS in terms of:
   - Duration of hospital stay
   - Discharged or mortality
   - Complications such as arrhythmias, heart failure, or pulmonary edema.

METHODS

This prospective, observational study was conducted on all patients admitted to general wards and Intensive Coronary Care Unit at Geetanjali Medical College and Hospital, Udaipur, during the study period of 18 months from February 2021 to July 2022.

Inclusion criteria

1. Confirmed case of ACS with ECG changes and raised biomarkers (CPK-MB and TROP I) which can be classified into:
   - STEMI: ST-segment elevation 1 mm or more in two or more contiguous leads with reciprocal ST depression in contralateral leads. ST elevation of 1 mm in inferior leads and 2 mm in anterior leads is taken as significant
   - Non-STEMI: ST segment depression in the electrocardiogram (ECG) with elevation of cardiac biomarkers
   - Unstable angina: ST segment depression in the ECG without elevation of cardiac biomarkers
2. Patients with age more than 18 years
3. Patients with informed consent.

Exclusion criteria

Other factors which determine the prognosis of ACS are excluded:

1. Patients with pre-existing renal disease
2. Concurrent systemic infections
3. Patients with Hb < 7 mg/dl
4. Patients with pre-existing pulmonary disease, ischemic heart disease, or cardiac arrhythmias.

Methodology

- Detailed history and detailed clinical examination were done
- HbA_{1c} RBS, CBC, TROP I, and CPK-MB were done
- These investigations were collected at the time of admission and discharge.

a. All patients in the study underwent the following based on a pro forma: A detailed history of
   i. Chest pain - whether present or absent. Duration was not noted
   ii. Palpitation - whether present or absent
   iii. Giddiness - whether present or absent
   iv. Breathlessness - whether present or absent
   v. Past history of hypertension/dyslipidemia/CAD is considered present or absent based on patient history
   vi. History of sedentary lifestyle
   vii. History of smoking
   viii. History of alcoholism
   ix. Family history of coronary artery disease.

b. Detailed examination was done which included:
   i. General examination including JVP
   ii. Vitals including blood pressure and pulse rate
   iii. Examination of the cardiovascular system
   iv. Examination of the respiratory system
   v. Examination of other systems.

c. Investigations done included:
   i. 12-lead ECG
   ii. Complete blood count
   iii. Admission random blood sugar
   iv. HbA_{1c}
   v. Lipid profile.

Transthoracic echocardiogram

- Ejection fraction
  - <40 - Reduced
  - 40–50 - Mid range
  - >50 - Preserved

- Lipid profile
  - S. cholesterol >200 mg/dL - high
  - S. cholesterol <200 mg/dL - low

- Blood sugar (RBS) values:
  - Normal - 70 to 140 mg/dL
  - Pre-diabetes - 140 to 200 mg/dL
  - Diabetes - >200 mg/dL.

Outcome assessment

- Duration of hospital stay
- Discharged or mortality
- Complications such as arrhythmias, heart failure, or pulmonary edema.

Statistical analysis

The data were entered in MS Excel Software version 20 and analyzed using SPSS, IBM Comp, version 21. Descriptive analysis of the data was performed presenting the results as frequency and percent for qualitative variables and as mean and standard deviation for age. The relation between qualitative variables was evaluated by the Chi-square test and Fisher's exact test if needed. The descriptive data were expressed in proportions, mean, and frequency tables. The categorical data were analyzed using Chi-square test. The quantitative data were analyzed using an independent Student's *t*-test. $p<0.05$ was considered statistically significant.

RESULTS

Clinical presentation

DISCUSSION

Our study population included only patients admitted with ACS with or without a history of type 2 diabetes. Comorbidities such as renal disease, patients with Hb <7 mg/dL, and concurrent systemic infections were excluded, so as to study the prognosis related to diabetes and blood sugar alone.

In our study, 43 patients at admission had RBS >140 mg/dL. Among these 30 patients were known as diabetic. 45% of patients had hyperglycemia on admission irrespective of their diabetic status while according to a study done by Timmer *et al*., 34.16% had hyperglycemia on admission irrespective of their diabetic status [13]. Increased levels of free fatty acids (FFA) may also be linked to elevated glucose levels. These FFA have the potential to reduce endothelium-derived vasodilatation in

Table 1: Distribution of history of chest pain, other cardiac symptoms, and other risk factor histories between groups in the study population

Parameter	Non-diabetic with Normal Sugar (NDNS) (n=36)		Non-diabetic with Hyperglycemia (NDS) (n=19)		Diabetic with Normal Sugar (DNS) (n=24)		Diabetic with Hyperglycemia (DS) (n=31)		p-value
	N	%	N	%	n	%	N	%	
History of chest pain*									
Absent	0	0	0	0	0	0	0	0	<0.05
Present	48	100	19	100	24	100	19	100	
History of other cardiac symptoms									
Absent	20	55.5	4	21.05	4	16.67	15	48.3	>0.05
Present	16	44.4	15	78.95	20	83.33	16	51.6	
Family history of CAD									
Absent	34	94.4	19	100	24	100	30	96.7	>0.05
Present	2	5.5	0	0	0	0	1	3.2	
Known cases of CAD									
Absent	33	91.66	19	100	24	100	30	96.7	>0.05
Present	3	8.3	0	0.00	0	0	1	3.2	
Known case of systemic hypertension									
Absent	29	80.55	11	57.89	20	83.3	23	74.19	>0.05
Present	7	19.44	8	42.11	4	16.67	8	25.8	
History of sedentary lifestyle									
Absent	33	91.66	15	78.95	19	79.17	25	80.64	>0.05
Present	3	8.3	4	21.05	5	20.83	6	19.35	
History of cigarette smoking									
Absent	21	58.3	8	42.11	7	29.17	19	61.3	>0.05
Present	15	41.6	11	57.89	17	70.83	12	38.7	
History of alcoholism									
Absent	36	100.00	16	84.21	14	58.33	20	64.5	<0.05
Present	0	0.00	3	15.79	10	41.67	11	35.4	
Random blood sugar*									
Hypoglycemia	13	36.11	0	0.00	9	37.50	0	0.00	<0.05
Normal	23	63.88	0	0.00	15	62.50	0	0.00	
Hyperglycemia	0	0.00	19	100	0	0.00	31	100.00	
Abnormal lipid level*									
Absent	24	66.66	11	57.89	21	87.50	27	87	<0.05
Present	12	33.33	8	42.11	3	12.50	4	13	

CAD: Coronary artery disease

Table 2: Complications of coronary artery disease versus admission RBS

Parameter	Non-diabetic with normal sugar (NDNS) (n=36)		Non-diabetic with hyperglycemia (NDS) (n=19)		Diabetic with normal sugar (DNS) (n=24)		Diabetic with hyperglycemia (DS) (n=31)		p-value
	N	%	n	%	n	%	n	%	
Cardiogenic shock									
Absent	32	88.88	12	63.16	17	70.83	19	61.29	p<0.05
Present	4	11.11	7	36.84	7	29.17	12	38.7	
Cardiac Failure									
Absent	34	94.44	12	63.16	16	66.67	19	61.29	p<0.05
Present	2	5.55	7	36.84	8	33.33	12	38.7	
Pulmonary edema									
Absent	36	100	15	78.95	24	100	31	100	p<0.01
Present	0	0.00	4	21.05	0	0.00	0	0.00	
Arrhythmias									
Absent	29	80.55	8	42.11	16	66.67	24	77.4	p<0.05
Present	7	19.44	11	57.89	8	33.33	7	22.5	

Data are expressed as percentages with absolute numbers

myocardial tissue, expand infarct size, compromise myocardial function during ACSs, and limit myocardial reperfusion. Healthy individuals with elevated glucose levels experience an increase in inflammatory markers, and hyperglycemic individuals with an acute myocardial infarction experience a greater inflammatory response than individuals with normoglycemia that leads to ACS. A stress-induced hyperglycemic environment increases platelet thrombotic characteristics, which can lead to additional cardiovascular complications. The negative effects of hyperglycemia may be reduced by intensive glycometabolic intervention.

In our study, cardiogenic shock was present as a complication in 11.11% of non-diabetic patients presenting with normal sugar, 36.84% of non-diabetic patients presenting with hyperglycemia, 29.17% of diabetic patients presenting with normal sugar, 38.7% of diabetic patients presenting with hyperglycemia. In our study, cardiac failure was present as a complication in 5.5% of non-diabetic patients presenting with normal sugar, 36.84% of non-diabetic patients presenting with hyperglycemia, 33.33% of diabetic patients presenting with normal sugar, 38.7% of diabetic patients presenting with hyperglycemia. In

Table 3: Distribution of major complications of CAD between groups in the study population

Parameter	Normal group (n=40) (HbA_{1c}<5.7%)		Pre-diabetes group (n=15) (HbA_{1c} 5.7–6.4%)		Diabetic group (n=55) (HbA_{1c}>6.4)		p-value
	N	%	N	%	n	%	
Cardiogenic shock							
Present	4	10	7	46.66	19	34.54	p<0.05
Absent	36	90	8	53.33	36	65.45	
Cardiac failure							
Present	6	15	3	20	20	36.36	p>0.05
Absent	34	85	12	80	35	63.63	
Pulmonary edema							
Present	4	10	0	0	0	0	p<0.05
Absent	36	90	15	100	55	100	
Arrhythmias							
Present	7	17.5	11	73.33	15	27.27	p<0.001
Absent	33	82.5	4	26.66	40	72.72	

CAD: Coronary artery disease, Data are expressed as percentages with absolute numbers

Table 4: Ejection fraction and mortality

Parameter	Non-diabetic with normal sugar (NDNS) (n=36)		Non-diabetic with hyperglycemia (NDS) (n=19)		Diabetic with normal sugar (DNS) (n=24)		Diabetic with hyperglycemia (DS) (n=31)	
	N	%	n	%	n	%	n	%
Ejection fraction								
<40 Reduced	8	22.22	3	15.79	8	33.33	12	38.7
40–50 mid-range	24	66.66	16	84.21	16	66.67	15	48.38
>50 preserved	4	11.11	0	0.00	0	0.00	4	12.9
Mortality								
Death	3	8.33	3	15.79	3	12.50	8	25.8
Discharge	33	91.66	16	84.21	21	87.50	23	74.19

p>0.05 (NS), Data are expressed as percentages with absolute numbers

Table 5: Comparison of different parameters between the groups in the study population

Parameter	Non-diabetic with normal sugar (NDNS) (n=36)		Non-Diabetic with hyperglycemia (NDS) (n=19)		Diabetic with normal sugar (DNS) (n=24)		Diabetic with hyperglycemia (DS) (n=31)		ANOVA p-value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
HbA_{1c} (%)	6.55	1.87	6.67	1.88	6.56	1.84	6.55	1.85	>0.05
Random blood glucose at admission (mg/dl)	84.5	78	151	78	144	77	145	77	<0.01
Ejection fraction	44.52	7.49	43.00	5.58	41.88	7.55	40.95	8.02	>0.05

SD: Standard deviations, Data are expressed as mean with standard deviation. One-way ANOVA with *post hoc* multiple comparisons was used to test the level of significant difference

our study, arrhythmia was present as a complication in 19.44% of non-diabetic patients presenting with normal sugar, 57.89% of non-diabetic patients presenting with hyperglycemia, 33.33% of diabetic patients presenting with normal sugar, 22.5% diabetic patients presenting with hyperglycemia. In our study, pulmonary edema was present as a complication only in non-diabetic patients presenting with hyperglycemia. In our study, dyslipidemia was found as a complication in 33.3% of non-diabetic patients with normal sugar at the time of admission, 42.11% of non-diabetic patients with hyperglycemia at the time of admission, 12.50% of diabetic patients with normal sugar at the time of admission, 13% of diabetic patients with hyperglycemia at the time of admission. While in a study done by Liao *et al.,* 10.9% of patients from normal group had cardiogenic shock and 19.8% of patients from diabetic group had cardiogenic shock; 68.4% of patients from normal group had cardiac failure and 75.6% of patients from diabetic group had cardiac failure; and 25.8% of patients from normal group had arrythmia and 30.7% of patients from diabetic group had arrhythmia [14]. Stress-induced hyperglycemia could be a vicious cycle of increasing fatty acids, insulin resistance, chemical inactivation of nitric oxide, and the production of reactive oxygen species, a prothrombotic state, and vascular inflammation. In a study done by Melchior *et al.,* among non-diabetic patients, 33.9% had heart failure, 14% had cardiogenic shock, and 10% had ventricular arrhythmias, among diabetic patients 53.6% had heart failure, 19.6% had cardiogenic shock, and 9.8% had ventricular arrhythmias [15]. These findings simulate our study findings. This means that non-diabetic patients had more complications than diabetic patients who had their blood sugar controlled at the time of admission.

In our study, the mortality was 8.33% in non-diabetic patients with normal sugar on admission and 15.79% in non-diabetic patients with hyperglycemia on admission, mortality was 12.5% in diabetic patients with normal sugar and 25.8% with diabetics having hyperglycemia (uncontrolled diabetes) on admission. In a study done by Zhao *et al.,* the mortality was 5.4% in non-diabetic patients with normal sugar on admission and 6.7% in non-diabetic patients with hyperglycemia on admission, mortality was 1% in diabetic patients with normal sugar and 6.07% with hyperglycemia on admission [16].

In our study, among non-diabetic patients 80% had Left ventricle ejection fraction (LVEF) >40% and 20% had LVEF <40%, among diabetic patients, 63.63% had LVEF >40% and 36.36% had LVEF <40%. In a study done by Kosiborod and McGuire study among non-diabetic patients 83.22% had LVEF >40% and 11.75% had LVEF <40%, among diabetic patients, 87.4% had LVEF >40% and 22.83% had LVEF <40%. Above findings simulate with our study findings [17]. Coronary artery atherosclerosis which is associated with long standing diabetes, is directly related to myocardial ischemia, and consequently, impaired glucose uptake, increased oxidative stress, and vascular endothelial dysfunction, which may promote the progression of diabetic cardiomyopathy, which leads to low ejection fraction.

The study group was small in number. Follow-up of the patients was done only till discharge. Long-term follow-up would have shown further prognostic effects of hyperglycemia on ACS patients.

CONCLUSION

This study indicated that non-diabetics presenting with hyperglycemia on admission are at more risk of having complications of ACS and had more mortality compared to diabetics having normal sugar on admission. In terms of predicting the short-term outcome in ACS, acute glucose metabolism disturbances appear to be more significant than long-term glucose metabolism derangements.

AUTHORS CONTRIBUTION

All Authors had equal contribution in data collection and manuscript writing.

CONFLICTS OF INTERESTS

None.

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