HBA1C-AN INDICATOR OF ADVERSE OUTCOME IN NON DIABETIC PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

Cardiology

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ABSTRACT

BACKGROUND The prevalence of type 2 DM or impaired glucose tolerance by oral glucose tolerance test is about 65% in STEMI patients without history of diabetes. Risk of adverse outcome can be assessed by estimation of admission plasma glucose and glycated haemoglobin (HbA1c) levels. HbA1c level is a reliable biomarker of average blood glucose concentrations and minimally affected by stress hyperglycaemia during AMI.

AIM AND OBJECTIVE To assess whether the HbA1c levels can be used as a prognostic indicator and could be used in identifying risk of adverse outcomes in patients with AMI with unknown diabetes mellitus(DM).

MATERIALS AND METHODS: This study includes 150 non diabetic patients with AMI admitted into the coronary care unit. HbA1c was measured and Patients were graded into three groups by levels of HbA1c: < 5.5%, 5.5–6.4%, >6.4%.Left ventricular ejection fraction (LVEF) was assessed by echocardiography and Continuous monitoring to determine any type of significant arrhythmia. Association between HbA1c groups and classic cardiovascular risk factor and in-hospital adverse outcomes were assessed by chi-square test and one way anova analysis.

RESULTS In-hospital mortality was 5.3% (8/150 patients). Higher HbA1c was associated with Killip's class>1(p .055>0.05), LVEF%.(p .000<0.05), increased heart rate (p .011<0.05), GRACE score(p .017<0.05), bundle branch block14.4%,ventricular tachycardia26.7%,AV block18.9% in group II.

CONCLUSION Increased HbA1c levels was a strong and independent predictor of severity of adverse outcome in patients with acute myocardial infarction without known diabetes mellitus

KEYWORDS

glycated haemoglobin (HbA1c), acute myocardial infarction, diabetes mellitus

INTRODUCTION

There is an increased risk of adverse outcome in patients with acute myocardial infarction (AMI) with Diabetes mellitus (Malmberg, Norhammar, 1999)[1]. Risk of adverse outcome can be assessed by estimation of admission plasma glucose and glycated haemoglobin(HbA1c) levels. Previous studies suggested that elevated HbA1c was associated with a higher risk of mortality in patients without recognized diabetes but had a neutral effect on mortality in patients with diabetes(Liu et al., 2011)[2]. Recent studies shows the increased prevalence of pre diabetes in patients admitted with acute coronary syndrome(AbuShady, Mohamady, Enany, & Nammas, 2015)[3]. It was found that prevalence of type 2 DM or impaired glucose tolerance by oral glucose tolerance test is about 65% in STEMI patients without history diabetes. Hyperglycemia is found in up to 50% of all patients presented with STEMI in emergency department, whereas it is only 20 to 25 % in the patients with previously diagnosed diabetes mellitus (Undas, Wiek, Stępień, Zmudka, & Tracz, 2008)[4]. HbA1c level is a convenient and reliable biomarker of average blood glucose concentrations over the preceding 8-12weeks. HbA1c assay is the preferred investigation for diagnosis of diabetes mellitus and treatment control. It is minimally affected by stress hyperglycemia during AMI and there¬fore reflects previous glycometabolic disturbance(Gustafsson et al., 2007)[5]. The purpose of the present study is therefore to assess whether the HbA1c levels can be used as a prognostic indicator and could be used in identifying risk of adverse outcomes in patients with AMI with unknown diabetes mellitus(DM).

MATERIALS AND METHODS

We performed a single-centre observational prospective study that includes 150 non diabetic patients with Acute Myocardial Infarction admitted into the coronary care unit (CCU) at Govt. KAPV medical college, Tiruchirapalli.The inclusion period was February 2017 to January 2018. The study was approved by the local ethical committee and all patients included gave informed consent to participate in the study. The study population were selected by the following criteria that includes chest pain with ST segment eleva¬tion or depression of at least 1 mm in one or more peripheral leads of the ECG and/or at least 2 mm in one or more precordial leads, or acute left bundle branch block, or ele¬vated levels of troponin according to the criteria established by current guidelines.The following patients with known DM, acute inflammatory diseases, hepatic failure, autoimmunity, cancer ,chronic renal failure and anemia are excluded from the study.DM patients were identified by history of diabetes according to medical his¬tory obtained from hospital records or when the patient reported receiving pharmacological treatment with oral hypo glycaemic drugs or insulin.The present analysis is based on data from 150 AMI patients who were not previously diagnosed DM. Because milder abnormalities of glucose control (below the diag¬nostic threshold of DM) are associated with increased car¬diovascular risk. Patients were graded into three groups according to baseline admission levels of HbA1c: HbA1c levels < 5.5%, 5.5–6.4%, >6.4%.The study design included a medical examination, bio¬chemical analysis and instrumental examinations as well as echocardiography results. Among the main cardiovascular risk factors, the presence of hypertension, dyslipidemia, smoking habits and body mass index were considered. The presence and degree of heart failure was assessed on admission at the emergency department, following the Killip classification. The Global Registry of Acute Coronary Events (GRACE) risk model was obtained to predict probability of hospital death and the level of risk for indi¬vidual patients.

All analytes were measured by conventional laboratory methods. In the CCU department the following analy¬sis were done: serum glucose, glycated haemoglobin, white blood cell count, platelets, haematocrit, electrolytes and cardiac biomarkers (troponin). Hba1c was analysed by ion-exchange high-performance liquid chromatography using the hemocue HbA1c 501 System analyser, biorad.Left ventricular ejection fraction (LVEF) was assessed through two-dimensional echocardiography immediately after admission. Continuous monitoring was performed in all patients during their stay at the CCU in order to determine any type of significant arrhythmia. All patients received recommended stand¬ard management for AMI.

STATISTICAL ANALYSIS

Clinical characteristics of the study population were calcu¬lated according to group of glycated haemoglobin val¬ues.We analysed HbA1c function as a continuous and also as a stratified variable. Continuous data were summarized and given as median values with corresponding SD. Dichotomous data were given as counts and per¬centages. Means between groups were compared by the use of one way ANOVA.Chi-square test done for categorical values.All statistical tests were performed with SPSS 19.0. A value of p<0.05 was considered statistically significant.

RESULTS

150 patients of AMI without prior diagnosis of DM were included in our study population. Three catego¬ries of patients were created according to HbA1c level: Group I (< 5.5%): 47 patients Group II(5.5 to 6.4%): 90 patients ; Group III (>6.4%): 13 patients. Table male patients predominated in this study 77.5%. In all the three groups female patients were present in group I it is higher when compared to others. Cardiovascular risk factors like systemic hypertension, smoking, dyslipidemia were present in all the three groups and not significant as the p value is more than .05(table 1).ST elevation myocardial infarction is 75.6% seen in group II which is higher than other 2 group. Most of the patients age in the study population were 50yrs.The mean BMI in all the three groups was 28 that shows overweight and preobese as per WHO.The mean and standard deviation of heart rate in group II Was 95.46±11.96.In group II and III mean systolic blood pressure was 140. Mean and standard deviation of random blood glucose in group II was 158.48±32.95. In our study total of 8 death 6 in group II and 2 in group III. In-hospital mortality was 5.3% (8/150 patients).Higher HbA1c was associated with Killip's class>1(p.055>0.05), LVEF%.(p=.000<0.05), increased heart rate (p.011<0.05), GRACE score(p .017<0.Arrythmias like Atrial fibrillation, bundle branch block, ventricular tachycardia and AV block are more in group II those were 30%,14.4%,26.7% and 18.9% respectively (table 3).

Table1 clinical and lab characteristics

Variables	HbA1c						Statistical inference
	I (< 5.5%)		II (5.5 to 6.4%)		III (>6.4%)		
	n=47	%	n=90	%	n=13	%	
Male	34	59.6%	80	88.9%	10	76.9%	.000<0.05
Female	23	40.4%	10	11.1%	3	23.1%	.000<0.05
SHT	28	49.1%	45	50.0%	6	46.2%	.966>0.05
SMOK	4	7.0%	10	11.1%	3	23.1%	.232>0.05
DYSLIPID	26	45.6%	49	54.4%	6	46.2%	.548>0.05
STEMI	34	59.6%	68	75.6%	9	69.2%	.125>0.05

Table 2 Baseline characteristics

HbA1C GROUP	Mean	S.D	Statistical inference
AGE I	51.67	5.366	.003<0.05 Significant
II	50.41	5.947	
III	56.23	4.658	
BMI I	28.26	1.768	.863>0.05 Not Significant
II	28.38	1.680	
III	28.15	1.405	
NYHA I	1.67	.852	.587>0.05 Not Significant
II	1.54	.796	
III	1.46	.877	
KILLIP >1 I	1.21	.526	.055>0.05 Not Significant
II	1.41	.685	
III	1.08	.277	
HR I	86.72	11.009	.011<0.05 Significant
II	91.82	11.965	
III	95.46	13.470	
SBP I	138.77	3.311	.001<0.05 Significant
II	140.00	.000	
III	140.00	.000	
LVEF%I	50.12	4.031	.000<0.05 Significant
II	49.60	3.836	
III	44.15	4.930	
RBS I	140.95	29.550	.007<0.05 Significant
II	158.48	32.953	
III	148.31	41.544	
eGFR I	89.16	12.834	.983>0.05 Not Significant
II	89.43	6.529	
III	89.46	1.450	
GRACE I	150.18	25.317	.017<0.05 Significant
II	159.80	22.352	
III	167.69	28.912	

Table 3   Hospital Adverse outcomes

variables	HbA1c						Statistical Inference P value
	I		II		III		
	n=47	%	n=90	%	n=13	%	
Death	0	.0%	6	6.7%	2	15.4%	.039<0.05
AF	18	31.6%	27	30.0%	0	.0%	.061>0.05
BBB	18	31.6%	13	14.4%	1	7.7%	.021<0.05
VT	1	1.8%	24	26.7%	1	7.7%	.000<0.05
AV BLOcK	1	1.8%	17	18.9%	1	7.7%	.007<0.05

DISCUSSION

In this study a substantial proportion of patients suffering from AMI were with underlying pre diabetes (n=90) and unknown overt DM(n=13) after hospital admission. These patients with dysregulated glucose metabolism had worse early outcomes, characterized by progressive increased rates of in-hospital mortality according to HbA1c(Blasco et al., 2014)[7]. In hospital mor¬tality was 15.4%(n=2) in patients with HbA1c >6.4% and 6.7%(n=6) in patients with HbA1c 5.5 – 6.4% . Increased advance glycosylation end product interfere with endogenous fibrinolytic system that may be the cause of coronary artery disease(Peppa, Uribarri, & Vlassara, 2004)[8].In group II the severity of CAD may be due to more generation of AGE product which subsequently attach to the vessel wall that causes endothelial dysfunction and oxidative stress promotion(Milman & Crandall, 2011)[9].Moreover binding of AGE results in release of inflammatory cytokines such as C reactive protein associated with instability of plaque(Koenig, Khuseyinova, & biology, 2007)[10].

Indeed, in our study 8.6% of patients met the HbA1c criteria for newly diagnosed DM and this group represents a particularly high-risk population that has not been recognized or treated. The frequency of 8.6% non-diabetic patients with elevated Hba1c found in the current study is compatible with the findings of undiagnosed diabe¬tes in other studies.It is known that hyperglycaemia and/or hyperinsulinaemia in the acute stage of myocardial infarction are predictors of impaired coronary flow, both before and after reperfusion therapy(Iwakura et al., 2003; Lazzeri et al., 2013; Timmer et al., 2005)[11] .Complications of AMI like Atrial fibrillation, bundle branch block, ventricular tachycardia and AV block are increased in group 2 compared to group I and III and these factors were not independent risk adjusted for in-hospital mortality. An observation in previous studies showed that the association between hyperglycaemia and the high risk of ventricular tachyarrhythmia and initial or complicated bun¬dle branch block in patients with AMI was regardless of diabe¬tes status(Sanjuan et al., 2011)[12].These may be due to the use of free fatty acids instead of glucose by the ischemic myocardium could precipitate regional oxy¬gen or energy crisis, and may lead to damaged cardiac-cell membranes, calcium overload and arrhythmias preceding mortality in many patient

CONCLUSION

There is relation between HbA1c and adverse outcome in patients of AMI without known diabetes and increased HbA1c levels was a strong

and independent predictor of severity of complications in those patients.

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