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Effect of admission glycated hemoglobin on short term outcome of acute ST elevation myocardial infarction in non-diabetic patient

Abstract

Background: Coronary artery disease is one of the most important causes of death in industrialized countries. Diabetes mellitus is a modifiable risk factor for coronary artery disease. It increases the risk of coronary artery disease by 2 to 4-fold.This increased risk occurs in patients with DM and non-diabetic patients with impaired glucose tolerance (IGT). Moreover, increased admission glucose levels may increase mortality rates in patients with acute myocardial infarction (AMI), regardless of diabetic status.

Objective: To assess the relationship between admissions HbA1c level and short term outcomes of acute ST elevation myocardial infarction treated by primary PCI in non-diabetic patients.

Material and Methods: This is an observational study was conducted at Coronary care unit & coronary catheterization lab unit of cardiology department in Ain Shams University hospitals in the period from 1-9-2018 till 1-3-2019.

Results: 100 patients without prior diagnosis of DM were included in our study population Three categories of patients were created according to HbA1c level: Group 1 (<5.7%): 46 patients (46%); Group 2 (5.7 to 6.4%): 38 patients (38%); Group 3 (>6.5%): 16 patients (16%). Baseline characteristics of the study population are shown in Table 1, the mean age of our sample was 55.06±11.73 years and 96% were males, there was highly statistically significant difference found between the 3 groups regarding SYNTAX score with P-value (0.002) & another highly significant difference in EF between the 3 groups.

Conclusion: The present study showed that admission higher HbA1c level in non-diabetic patients presented by acute STEMI is associated with more severe CAD. MACE & thrombus burden were not found in this study to be related to glycated hemoglobin. Introducing measurement of HbA1c in the CCU seems to be a simple method to obtain important information on the expected severity of coronary lesions.

Keywords: admission glycated hemoglobin, angiographic characteristics, myocardial infarction

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Abbreviations: AMI, acute myocardial infarction; MI, myocardial infarction; HbA1c , hemoglobin A1C; CIN, contrast induced nephropathy; MACE, major adverse cardiac events; NS, non-significant; HS, highly significant

Introduction

Coronary artery disease is one of the most important cause of death in industrialized countries. Diabetes mellitus is a modifiable risk factor for coronary artery disease. It increases the risk of coronary artery disease by 2 to 4-fold.This increased risk occurs in patients with DM and non-diabetic patients with impaired glucose tolerance (IGT). Moreover, increased admission glucose levels may increase mortality rates in patients with acute myocardial infarction (AMI), regardless of diabetic status. Up till now there is no agreement about the threshold glycemic level for developing cardiovascular complications.[1–10]

Increased catecholamine levels in acute myocardial infarction (AMI) lead to stress induced hyperglycemia, so looking only at plasma glucose levels at the time of an AMI cannot predict the prognosis.[11] Glycosylated hemoglobin A1C (HbA1c) is a measure of the average blood glucose levels over 2 months[12] and is minimally affected by acute hyperglycemia often observed in myocardial infarction (MI). Elevated HbA1c levels are associated with an increased risk for future micro-vascular and macro-vascular disease.[13] HbA1c can be assessed in the non-fasted state and has higher reproducibility than fasting glucose.[14] There is consistent evidence that optimal glycemic control (defined as HbA1c ≤7%) results in a lower incidence of micro-vascular complications in both type 1 and type 2 DM.[15] Moreover, a report found that elevated HbA1c levels are also predictive for cardiovascular disease and mortality in patients without DM, independent of the fasting glucose value.[16]

Some data suggest a high HbA1c level as a marker of extensive coronary arterial disease.[17] There are some other studies supporting the association between admission serum HbA1c level and increased long-term mortality of non-diabetic patients admitted with STEMI and a higher rate of CAD in these patients.[18,19] There have been few studies which have shown HbA1c to be predictive of CAD in non-diabetes, but only in limited studies HbA1c has been correlated with angiographically proven CAD using Syntax score which was developed as a comprehensive angiographic scoring tool for quantification of coronary lesions with respect to their number, location, and complexity.[20,21]

Aim of the study

The aim of the present study was to assess the effect of admission

HbA1c on outcome of 1ry PCI and short-term outcome of adverse cardiac events in patients without known diabetes mellitus who were admitted with acute ST elevation myocardial infarction.

Patients and methods

a. Type of Study: Observational.

b. Study Setting: Coronary care unit & coronary catheterization lab unit of cardiology department in Ain Shams University hospitals.

c. Study Period: 6 months (From 1-9-2018 till 1-3-2019).

d. Study Population.

Inclusion criteria

i. Chest pain with ECG criteria of STEMI.

ii. New onset left bundle branch block.

iii. Elevated levels of troponin according to the criteria established by current guidelines.

Study population includes patients who came to our hospitals & were directly transported to the catheterization laboratory on arrival, and acute coronary angiography was performed with subsequent PCI when indicated as part of the routine treatment for all STEMI patients in our institute & those who received thrombolysis in other hospitals & referred to us for further management.

Table 1 Demographic data of the study population

		No. = 100
Age	Mean±SD	55.0 ±11.73
	Range	30 – 88
Sex	Female	4(4.0%)
	Male	96(96.0%)
Smoking	Negative	30(30.0%)
	Positive	70(70.0%)
Hypertension	Negative	76(76.0%)
	Positive	24(24.0%)
Family History	Negative	98(98.0%)
	Positive	2(2.0%)
Drug History	Negative	86(86.0%)
	Positive	14(14.0%)
History oh IHD	Negative	88(88.0%)
	Positive	12(12.0%)

Exclusion criteria

i. Anemia.

ii. Acute inflammatory diseases.

iii. Hepatic failure.

iv. Autoimmune diseases.

v. Cancer.

vi. Patients with chronic renal failure in a hemodialysis program.

vii. Known DM.

viii. Previous CABG & previous MI.

Sample size

100 patients who present to Ain Shams University & Specialized hospitals during the study period will be enrolled in the study after fulfilling the inclusion criteria.

Ethical considerations

Ain Shams university ethical committee approval was obtained according to the ethical guidelines of the 1975 declaration of Helsinki as revised in 2008.

Study tools: Checklist for assessment of all the clinical data relevant to the patient. All these sheets were collected then the data entry was carried out through a computer system in order to establish a data-based system for all the patients.

All patients after written informed consent were subjected to the following

i. Proper history taking including clinical, demographic data, risk factors and co-morbidities, duration of hospital stay.

ii. Laboratory investigations especially glycated hemoglobin at admission.

iii. Transthoracic Echocardiography: Ejection fraction measured by 2D eye balling,[22–30] LV dimensions by M-mode, mitral regurgitation, or any other mechanical complications.

iv. Coronary Angiography: angiographic data will be recorded to all patients to calculate Syntax score. (The SYNTAX score has been developed to prospectively characterize the coronary vasculature with respect to the number of lesions and their functional impact, location, and complexity. Higher SYNTAX scores, indicative of more complex disease are hypothesized to represent a bigger therapeutic challenge and to have potentially worse prognosis).[31]

Primary endpoints

a. Correlation of HbA1c level with angiographic finding after primary PCI concerning TIMI flow, thrombus burden & complexity of lesions assessed by SYNTAX score.

b. The correlation of HbA1c level with major adverse cardiac events (MACE) during hospital stay which includes CV mortality, malignant arrhythmia, cardiogenic shock, congestive heart failure & need for mechanical ventilation.

Secondary endpoints

Development of contrast induced nephropathy (CIN).

Statistical analysis

Data was collected, tabulated and all the results will be subjected to adequate statistical analysis using Chi-square test, One Way ANOVA test & Kruskal Wallis test. P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS).

Table 2 Comparison between the 3 groups regarding demographic data

		Normal group	Pre DM group	DM group	Test value	P-value	Sig.
		No. = 46	No. = 38	No. = 16			
Age	Mean±SD	54.22 ± 11.65	57.79 ± 12.81	51.00 ± 7.61	2.154•	0.122	NS
	Range	30 – 82	31 – 88	40 – 60			
Sex	Female	4(8.7%)	0(0.0%)	0(0.0%)	4.891*	0.087	NS
	Male	42(91.3%)	38(100.0%)	16(100.0%)			
Smoking	Negative	12(26.1%)	16(42.1%)	2(12.5%)	5.320*	0.070	NS
	Positive	34(73.9%)	22(57.9%)	14(87.5%)			
Hypertension	Negative	32(69.6%)	32(84.2%)	12(75.0%)	2.457*	0.293	NS
	Positive	14(30.4%)	6(15.8%)	4(25.0%)			
Family History	Negative	46(100.0%)	36(94.7%)	16(100.0%)	3.330*	0.189	NS
	Positive	0(0.0%)	2(5.3%)	0(0.0%)			
Drug History	Negative	36(78.3%)	36(94.7%)	14(87.5%)	4.727*	0.094	NS
	Positive	10(21.7%)	2(5.3%)	2(12.5%)			
History oh IHD	Negative	40(87.0%)	32(84.2%)	16(100.0%)	2.746*	0.253	NS
	Positive	6(13.0%)	6(15.8%)	0(0.0%)			

P-value >0.05: Non significant (NS); P-value <0.05: Significant(S); P-value< 0.01: highly significant(HS)

*:Chi-square test; •: One Way ANOVA test; ‡: Kruskal Wallis test

Table 3 Comparison between DM groups regarding admission HBA1c, pain to first medical contact(FMC), and type of STEMI

		Normal group	Pre DM group	DM group	Test value	P-value	Sig.
		No. = 46	No. = 38	No. = 16			
HBA1C	Mean±SD	5.33 ± 0.25	5.97 ± 0.19	7.84 ± 1.59	85.720•	0.000	HS
	Range	4.8- 5.6	5.7 – 6.4	6.5 – 11.6			
Pain to FMC	Median(IQR)	8(4-12)	6(4 - 11)	4(2.5 - 9.5)	4.117‡	0.128	NS
	Range	2-24	1 – 24	1 – 12			
Type of STEMI	Anterior	32(69.6%)	18(47.4%)	6(37.5%)	22.156	0.014	S
	Lateral	2(4.3%)	2(5.3%)	0(0.0%)			
	Inferior	8(17.4%)	8(21.1%)	6(37.5%)			
	Infroposterior	2(4.3%)	8(21.1%)	2(12.5%)			
	Infrolateral	0(0.0%)	0(0.0%)	2(12.5%)			
	Antroseptal	2(4.3%)	2(5.3%)	0(0.0%)			

P-value >0.05: Non significant(NS); P-value <0.05: Significant(S); P-value< 0.01: highly significant(HS)

*:Chi-square test; •: One Way ANOVA test; ‡: Kruskal Wallis test

Table 4 Comparison between different DM groups regarding SYNTAX score & EF by 2-D eye – balling

		Normal group	Pre DM group	DM group	Test value	P-value	Sig.
		No. = 46	No. = 38	No. = 16			
SYNTAX	Mean±SD	14.96 ± 5.07	16.74 ± 8.19	19.94 ± 4.35	6.458•	0.002	HS
EF	Mean±SD	38.78 ± 9.96	45.79 ± 11.01	45.63 ± 10.22	5.551•	0.005	HS

P-value >0.05: Non significant(NS); P-value <0.05: Significant(S); P-value< 0.01: highly significant(HS)

*:Chi-square test; •: One Way ANOVA test; ‡: Kruskal Wallis test

Table 5 Comparison between the 3 groups regarding Thrombus burden, TIMI flow

		Normal group		Pre DM group		DM group		Test value*	P-value	Sig.
		No.	%	No.	%	No.	%			
Thrombus burden	0	32	69.6%	24	63.2%	6	37.5%	5.215	0.074	NS
	1	14	30.4%	14	36.8%	10	62.5%			
TIMI flow	0	2	4.3%	0	0.0%	0	0.0%	13.346	0.038	S
	1	0	0.0%	0	0.0%	2	12.5%			
	2	16	34.8%	14	36.8%	4	25.0%			
	3	28	60.9%	24	63.2%	10	62.5%			

P-value >0.05: Non significant(NS); P-value <0.05: Significant(S); P-value< 0.01: highly significant(HS)

*:Chi-square test; •: One Way ANOVA test; ‡: Kruskal Wallis test

Table 6 Comparison between the 3 groups regarding MACE & CIN

		Normal group		Pre DM group		DM group		Test value*	P-value	Sig.
		No.	%	No.	%	No.	%			
MACE	Negative	40	87.0%	34	89.5%	14	87.5%	0.129	0.937	NS
	Positive	6	13.0%	4	10.5%	2	12.5%			
CIN	Negative	42	91.3%	32	84.2%	14	87.5%	0.996	0.608	NS
	Positive	4	8.7%	6	15.8%	2	12.5%			

P-value >0.05: Non significant(NS); P-value <0.05: Significant(S); P-value< 0.01: highly significant(HS)

*:Chi-square test

Table 7 Correlation between HB_{A1C} with Age, Pain to FMC, SYNTAX, and EF

	HBA1C	
	R	P-value
Age	0.022	0.829
Pain to FMC	-0.200*	0.046
SYNTAX	0.492**	0.000
EF	0.125	0.215

Results

The Previous table shows that there was no statistically significant difference found between DM groups regarding Demographic data. The Previous table shows that there was highly statistically significant difference found between the 3 groups regarding HBA1C with P-value (0.000) while there was no statistically significant difference found between DM groups regarding pain to FMC. The Previous table shows that there was highly statistically significant difference found between the 3 groups regarding SYNTAX score with P-value (0.002) & another highly significant difference in EF between the 3 groups. In the previous table, there was no statistically significant difference found between the 3 groups regarding Thrombus burden.

The same table shows another statistically significant difference found between the 3 groups regarding TIMI flow with P-value (0.038) being higher in pre-DM group with 63.2% of the pre DM had a better TIMI flow. This table shows no statistically significant difference found between the 3 groups regarding MACE & CIN. The Previous table shows that there was highly statistically significant correlation between level of Hb_{A1c} on admission & SYNTAX score with p- value (0.000) while there was no statistically significant correlation found between groups regarding EF.

Discussion

Stress hyperglycemia commonly occurs in acute myocardial infraction (AMI) secondary to increased catecholamine levels, so looking only at plasma glucose levels at the time of an AMI cannot predict the prognosis.[12] Glycosylated hemoglobin A1c (HbA1c) is a measure of the average blood glucose levels over 2 months[22] and is minimally affected by acute hyperglycemia often observed in myocardial infarction (MI). Using the glucose test, we may fail to identify the undiagnosed DM due to high prevalence of stress hyperglycemia in this population. HbA1c reflects long-term glycometabolic control,[24] and its level as higher than 6.5% is now considered as an alternative category of DM. While according to a recent guideline for DM diagnosis, HbA1c from 5.7% to 6.5% is considered as pre-diabetes.[25] In our study, patients with underlying pre-diabetes and unknown overt DM after hospital admission represent a major portion from the study population (38% for the pre-diabetes & 16 % for newly diagnosed cases). It is reported that 25% of AMI patients had newly diagnosed DM. In our study, 16 newly diagnosed cases of diabetes (16%) were documented.[23]

We found a substantial proportion of patients suffering from AMI with underlying pre-diabetes and unknown overt DM after hospital admission. These patients with disturbed glucose metabolism had worse early outcomes, characterized by progressive increased rates of in-hospital mortality according to HbA1c & higher SYNTAX score

indicating more complex lesions in angiography. Our results showed a highly statistically significant difference concerning the SNTAX score was noted between the 3 groups: in the normal group SYNTAX ranged from 6–22 with Mean±SD 14.96±5.07, while it was 3–34 (Mean±SD 16.74±8.19) in group 2, finally for the DM group (10–28.5 Mean±SD 19.94±4.35).

This was concordant with previous studies by Cakmak et al.[26] and Kassaian et al.[27] This can be explained by insulin resistance in hyperglycemia promoting molecular mechanism by Advanced Glycation End Products (AGEs) which are intimately involved in the pathophysiology of cardiovascular disease by stimulating inflammation, contributing to atheroma formation modulating vascular stiffness and the disturbed endothelial function by reduction of nitric oxide release and increased vascular smooth muscle proliferation [28] and increase of HbA1c one percent is associated with 2.8-fold increase in CAD.

In our study, we found that most of the patients having normal HbA1c had lower LVEF (mean 38.78±9.96) as compared to most of the patients with high normal HbA1c, who had higher LVEF (45.79±11.01) This is discordant with Razzaq et al.,[29] showed that the mean EF was significantly lower in group HbA1c 6.5-8.5 and in group HbA1c >8.5 as compared with that group <6.5. A linear decrease in EF was found with rising HbA1c levels in patients with unstable angina (P=0.0043), with ST-segment elevation myocardial infarction (P = 0.0290) and non-segment elevation myocardial infarction (P=0.0015).

In our study, TIMI flow was found unexpectedly higher in group 2 (Pre-diabetics) with statistically significance as P-value was (0.038) showing 63.2% of the pre DM had TIMI flow III. This finding was not in agreement with Planner et al. who explained the fact that hyperglycemia is associated with higher rate of TIMI 0\1 and lower rate of complete revascularization TIMI and hyperglycemia adversely affect platelets function and endothelial function, promote inflammation, and result in pro-coagulable condition; it is worth mentioning that hyperglycemia per se in STEMI leads to impaired coronary flow on presentation and after primary PCI.[32] The result of MI, however, was still less conclusive as in-hospital managements, such as intervention procedures and medications, may influence the clinical outcomes.

Conclusion

The present study showed that admission higher HbA1c level in non-diabetic patients presented by acute STEMI is associated with more severe CAD. MACE & thrombus burden were not found in this study to be related to glycated hemoglobin. Introducing measurement of HbA1c in the CCU seems to be a simple method to obtain important information on the expected severity of coronary lesions.

Recommendations

The sample size of the study was small mostly due to unaffordability of patients. A larger sample size would have yielded better outlook towards the association of HbA1c with prognosis of patients with acute coronary syndrome.

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None.

Conflicts of interest

Author declares that tier is no conflicts of interest towards the article.

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