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Original Article

Impact of HbA1c levels on coronary SYNTAX score in non-diabetic patients with ST-elevation myocardial infarction undergoing primary angioplasty: A cross-sectional study

Majid Saraei Koushki (MD) [1]
Razieh Parizad (PhD) [1]
Ali Abdollahzadeh (PhD) [1]
Ahmad Separham (MD) [1*]

1. Cardiovascular Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

*** Correspondence:**
Ahmad Separham, Professor, Cardiovascular Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

E-mail: separham@gmail.com
Tel: +98 4133352077

Abstract

Background: Glycated hemoglobin A1c (HbA1c) level is related to increased cardiovascular diseases (CVDs) and death, even in non-diabetic subjects. Although in ST-elevation myocardial infarction (STEMI) cases, the association between HbA1c and coronary artery disease (CAD) remains unclear.

Methods: This cross-sectional study was conducted on 167 non-diabetic STEMI patients undergoing primary percutaneous coronary intervention (PCI). The SYNTAX score was utilized to evaluate CAD severity. Cases were categorized into three groups based on the HbA1c levels: <5%, 5.1-5.9%, and 6-6.5%.

Results: SYNTAX scores significantly increased in the cases with 6 to 6.5 HbA1c levels compared to the other group (28.9±9.5 vs 21.2±5.2 vs 13.7±4.5, P=0.000). Additionally, death was more elevated in this group (4% vs 0% vs 0%, P=0.006).

Conclusion: Higher HbA1c levels are strongly associated with coronary atherosclerosis in non-diabetic patients that present with non-diabetic STEMI. Consequently, in non-diabetic STEMI patients, HbA1c may be able to predict the severity of CAD.

Keywords: Coronary SYNTAX score, HbA1c, Non-diabetic, Myocardial infarction.

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ST-segment elevation myocardial infarction (STEMI) is a critical disease that needs multidisciplinary, immediate, and complex management (1). All types of MI incidence are estimated to be 605,000 and 200,000 new and recurrent MI, respectively, with a 12-billion-dollar cost yearly (2, 3). Coronary heart disease (CHD) treatment progress results in decreasing death numbers (3). The most frequent method to promote myocardial perfusion is percutaneous coronary intervention (PCI). It enhances acute coronary syndrome (ACS) outcomes, especially in emergency management of STEMI cases (4). Currently, in STEMI treatment guidelines, PCI is highly recommended (5). The primary PCI advantages following a short follow-up compared to thrombolysis have been illustrated (6). The SYNTAX score is a valuable visual coronary artery score in cases that underwent PCI, affecting the one-year prognosis. On the other hand, it does not impact the one-year prognosis in the cases that underwent surgical revascularization. Many complex coronary disease cases benefit from SYNTAX score utilization (7). A lower SYNTAX score than a higher score is related to improved cardiovascular outcomes. Thus, the SYNTAX score, as a crucial angiographic technique, is required to be used in daily clinical practice (8). An investigation of the cases with left main coronary artery revascularization coronary artery bypass grafting (CABG) showed a considerable prognostic advantage over PCI at a 10-year follow-up with high anatomic complexity assessed by SYNTAX score. The discriminative SYNTAX score ability on long-term outcomes is better in PCI cases while not valuable for CABG cases (9).

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Higher glycated hemoglobin A1c (HbA1c) levels among non-diabetic adult patients have resulted in more cardiovascular diseases (CVDs) and mortality (10). Research has found a linear relationship between CVD in non-diabetic subjects and HbA1c (11). However, other research on non-diabetic patients found no association between coronary artery disease (CAD) severity and HbA1c (12). Considering that the number of percutaneous coronary intervention (PPCI) patients admitted to the hospital is large and access is easier, and on the other hand, non-PPCI patients leave the hospital the day after angioplasty, but PPCI patients stay in the hospital for several days after angioplasty. Also, few studies have studied the importance of this point in the treatment of non-diabetic patients. Therefore, the present study was designed with the aim of investigating the relationship between HbA1c and SYNTAX score in non-diabetic patients who underwent PPCI following AMI with ST-segment elevation.

Methods

The current study was a descriptive (cross-sectional) study that was conducted in the period from March 2019 to March 2021. The target population included non-diabetic patients diagnosed with STEMI who were hospitalized and underwent primary angioplasty at Shahid Madani Hospital, Tabriz, Iran. According to the formula, the sample size was (P=0.64, q=0.36, Z=1.96, d=0.064), estimated in 217 participants.

$$n = \frac{z^2_{1-\alpha/2} \times p(1-p)}{d^2} \qquad d = 0.1p$$

This study follows the Helsinki Declaration, and the Ethics Committee approved the study protocol (Registration Code: IR.TBZMED.REC.1402.774). After obtaining research ethics approval, permission from the relevant authorities, and informed consent from the patients, the information related to demographic and clinical characteristics of all patients was completed using a checklist designed by a trained individual. The cases' information was gathered from medical records. STEMI was defined as at least two continuous leads with ST-segment elevation of more than 2 millimeters for males older than 40 years old and more than 2.5 mm for less than 40-year-old males and females in leads V2-V3 and/or 1 mm in the other leads. Inclusion criteria included non-diabetic STEMI cases, those who underwent primary PCI with or without stent placement and presented to the emergency room less than 12 hours with more than 30 minutes of chest pain complaint. Exclusion criteria included were no indication for PCI, unavailability of patients' HbA1c percentage, and an HbA1c above 6.4%.All data were gathered in the form of a prepared checklist. These included demographic variables, including sex, age, vital signs, smoking status, and comorbidities, including hypertension (HTN), CVD history, PCI history, sepsis, cardiogenic shock, door-to-balloon, heart failure, and dyslipidemia. Also, SYNTAX score, echocardiographic, and laboratory findings were gathered. During the first 24 hours of hospitalization, the level of HbA1c was checked in all patients, and they were divided into three groups based on HbA1c. Cases in three groups included Ⅰ) HbA1c below five, Ⅱ) HbA1c between 5.1 to 5.9, and Ⅲ) HbA1c between 6 to 6.5 were divided. Data analysis was conducted SPSS Version 26.00 (SPSS INC., IBM Corporation, Chicago, IL). The Kolmogorov-Smirnov test was utilized to evaluate the variables' distribution. Qualitative variables are shown by percentages, and quantitative variables are mean ± standard deviation (SD). The chi-square test was used for comparing the categorical variables. The Mann–Whitney U-test or student's t-test was utilized to compare continuous variables. Statistical significance was determined as a p-value of less than 0.05.

Results

The baseline parameters of all cases are presented in table 1. No statistically significant difference between the three groups was seen in age, gender, and comorbidities. The mean (±SD) age of cases with HbA1c 6 to 6.5, 5.1 to 5.9, and below five were 61.96±10.46, 57.82±11.41, and 56.99±11.79 years, respectively (P = 0.145). In patients with HbA1c 6 to 6.5, one (4%) individual died, whereas other groups were without mortality (P= 0.006), which was statistically significant. As shown in table 1, most of the participants were males. The mean (±SD) duration of hospitalization in cases with HbA1c 6 to 6.5, 5.1 to 5.9, and below five were 4.79±2.40, 4.93±2.77, and 4.36±2.26, respectively (P= 0.066). The mean (±SD) of the SYNTAX score, door-to-balloon time, ejection fraction, ischemic time, and previous PCI history is presented in table 1. The mean (±SD) of ejection fraction of subjects with HbA1c 6 to 6.5, 5.1 to 5.9, and below five were 37.29±6.42, 37.16±7.59, and 37.04±7.2, respectively (P = 0.975). SYNTAX scores were statistically higher in patients with HbA1c 6 to 6.5 compared with patients with 5.1 to 5.9 and below five (mean±SD=28.9±9.5 vs 21.2±5.2 vs 13.7±4.5; P= 0.975). Although the percentage of previous PCI history in patients with HbA1c 6 to 6.5 was higher than in other groups, this difference was not statistically significant (percentage (%) = 13 vs 3 vs 9; P = 0.975).

Table 1.Baseline characteristics, biochemical and cardiac characteristics of all subjects.

Parameter		HbA1c 1 < 5 group	HbA1c 5.1-5.9 group	HbA1c 6-6.5 group	P-value
Sex (N)	Male	144 (86%)	65 (88%)	20 (83%)	0.849
	Female	23 (14%)	9 (12%)	4 (17%)	0.756
Age (year)		56.99±11.79	57.82±11.41	61.96±10.46	0.145
Hypertension (N)		51 (31%)	27 (36%)	6 (25%)	0.50
Hyperlipidemia (N)		23 (14%)	9 (12%)	2 (8%)	0.742
Smoking (N)		72 (43%)	27 (36%)	9 (37%)	0.738
Previous PCI (N)		15 (9%)	2 (3%)	3 (13%)	0.254
Death (N)		0	0	1 (4%)	0.006*
Heart failure (N)		35 (21%)	18 (24%)	5 (21%)	0.837
Sepsis (N)		2 (1%)	2 (3%)	0 (0%)	0.553
Cardiogenic Shock (N)		4 (2%)	7 (9%)	3 (12%)	0.02*
SBP (MmHg)		140.50±24.77	142.26±27.16	129.83±24.20	0.12
DBP (MmHg)		87.22±16.11	88.22±17.14	81.50±15.17	0.393
Heart rate (BPM)		79.97±12.38	80.53±13.16	78.75±10.68	0.437
Ischemic Time (hour)		4.75±4.98	4.81±3.99	7.81±9.85	6.637
Door-to-balloon time (minute)		75.34±49.29	70.21±31.90	65.93±28.14	0.691
Ejection Fraction (%)		37.04±7.2	37.16±7.59	37.29±6.42	0.975
Duration of hospitalization (day)		4.36±2.26	4.93±2.77	4.79±2.40	0.066
SYNTAX Score		13.7±4.5	21.2±5.2	28.9±9.5	0.00**

Mean values (± standard deviation) and number (%) were reported for continuous and categorical variables. HbA1c: Hemoglobin A1c; PCI: Percutaneous coronary intervention; SBP, Systolic blood pressure; DBP, Diastolic blood pressure. Data is shown as n (%) or mean±SD. * Chi-square test. **ANOVA.

Discussion

This study demonstrated that SYNTAX scores were statistically higher in cases with higher HbA1c levels. Also, the number of deaths was statistically higher in subjects with HbA1c 6 to 6.5 compared with other groups. One of the successful scoring systems that demonstrates CAD severity and extent is the SYNTAX score. It provides useful data about revascularization approach choice and prognosis (13). Available guidelines for management with CABG or PCI suggested SYNTAX score (14). Boyraz B et al. (15) revealed that in predicting the revascularization decision, the SYNTAX score was significantly superior to the Gensini score (A score shows the coronary plaque burden) in the stable angina pectoris and NSTEMI cases. So, in this study, we utilized the SYNTAX score. In addition, another research on the cases with NSTEMI demonstrated that the

SYNTAX score has a similar predictive value compared to the systemic immune-inflammatory, platelet–lymphocyte ratio, and the neutrophil-lymphocyte ratio in the NSTEMI subjects' overall mortality (16). The SYNTAX score is an angiographic method used to choose the proper revascularization technique and evaluate the CAD complexity (9). However, it is a vital score for cardiac death prediction (17) and major bleeding risk following drug-eluting stent implantation (18). Gao G et al. (19) demonstrated that the SYNTAX score is negatively associated with myocardial salvage and positively with infarct size. Also, they found that the SYNTAX score for myocardial injury is a valuable independent predictor.

HbA1c is one of the suggested variables for following up the cases with diabetes, which illustrates the last three months' mean plasma glucose level. HbA1c level for diabetes microvascular complications is a considerable risk indicator. ACS cases with higher HbA1c levels have more mortality risk. Also, HbA1c is a short-term predictor of death in ACS patients without DM (20). Several investigations showed a notable correlation between CAD and HbA1c (21, 22). Kayali Y et al. (23) found a strong association between CAD and HbA1c levels in non-diabetic patients, suggesting that HbA1c levels may be valuable for predicting coronary atherosclerosis severity. In our research, as in line with previous research, there was a correlation between STEMI severity and HbA1c level that STEMI severity evaluated by SYNTAX score in non-diabetic patients, indicating HbA1c may be a STEMI severity predictor. At the same time, the mentioned studies showed the relationship between HbA1c level and CAD in non-diabetic patients.

Furthermore, another study in India illustrated that the SYNTAX score is associated with CAD severity, and a higher SYNTAX score is related to the number of diseased vessels (11). A meta-analysis found that post-prandial glucose and fasting glucose in non-diabetic patients were significantly related to CAD risk; however, the correlation between CAD and HbA1c levels was slightly stronger (24). Also, a prospective study that assessed the HbA1c levels and CAD severity in 93 individuals by logistic regression analysis revealed that more HbA1c levels act as severe atherosclerosis-independent predictors (25). Kilic A et al. (26), using SYNTAX score II, found that in NSTEMI cases without diabetes, HbA1c levels are associated with the severity of CAD. Also, in-hospital mortality was correlated with higher levels of HbA1c. The study had some limitations that could impact the strength of evidence compared to other designs. As a cross-sectional study, it cannot prove causation or show the order of relationships between variables. Data from a single center was used, bringing the risk of biased selection and reduced generalizability. Including multiple centers could improve how well the results represent others and where they apply. A larger sample may give stronger, more widely applicable findings. The study also used an earlier version of the SYNTAX score to measure disease complexity. Using the updated version could provide extra insight. Cross-sectional studies only allow limited recorded data, so not all relevant influence factors may have been explored. There was no long-term patient follow-up, preventing seeing how HbA1c impacts the SYNTAX score over time or its potential prognosis importance. The study found that higher HbA1c levels in non-diabetic STEMI patients were associated with more severe coronary artery disease, as shown by higher SYNTAX scores. SYNTAX scores were significantly higher in patients with HbA1c between 6-6.5% versus 5.1-5.9% and below 5%. Mortality was also higher in the highest HbA1c group. These results suggest that HbA1c may predict CAD severity in non-diabetic STEMI patients. Higher HbA1c seemed related to more complex, diffuse coronary atherosclerosis. More significant, more extended studies are needed to validate these findings and better understand the relationships between HbA1c, CAD severity, and outcomes. Future research could explore potential links between higher HbA1c and worse CAD pathology in non-diabetics. If confirmed, HbA1c may help assess prognosis and guide STEMI management even without diabetes. This preliminary cross-sectional study provides evidence linking HbA1c and coronary disease severity, warranting more investigation.

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Ethics approval: This study was performed according to the principles outlined by the World Medical Association's Declaration of Helsinki on experimentation involving human subjects, as revised in 2000, and has been approved by the Ethics Committee of the Tabriz University of Medical Sciences.

Conflict of interests: None declared.

Authors' contribution: Ahmad Separham: Contributed to the conception, designed, and directed the study and

performing patient's angiography and angioplasty. Majid Saraie Koushki: Gathering data of patients, Data curation and performing patient's angiography and angioplasty and writing the manuscript. Razieh Parizad: Performing statistical analyses, writing the manuscript. Writing– review and editing. Ali Abdollahzadeh: Gathering data of patients.

Data availability statement: Data will be made available on request.

Declaration of competing interest: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. This will inform readers that the text has been edited using ChatGPT and artificial intelligence.

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