WHICH PATIENTS HAVE AN ASSOCIATION BETWEEN HBA1C LEVEL AND SEVERITY OF CORONARY ARTERY DISEASE: DIABETIC OR NON-DIABETIC?

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ABSTRACT

Introduction: Diabetes mellitus (DM) has long been recognized as a major risk factor for coronary artery diseases (CAD). Although Hemoglobin A1c (HbA1c) has been widely used as a marker for predicting the severity of DM, there are controversial reports in the literature regarding its association with the severity of CAD. The aim of our study was to determine the association between HbA1c levels and severity of CAD in both diagnosed and undiagnosed diabetic patients with admission hyperglycemia.

Materials and methods: The files of the patients who were admitted to the emergency department of a regional training and research hospital from 2014 to 2015 due to acute coronary syndrome and whose diagnosis was confirmed by coronary angiography and HbA1c levels were analyzed were reviewed retrospectively. Those patients whose HbA1c levels were measured were divided into two groups: diagnosed diabetes (DD) or undiagnosed diabetes (UDD). Gensini score was measured for all patients and the correlation between elevated HbA1c levels and severity of coronary artery disease was subjected to statistical analysis.

Results: Out of 168 patients who met the inclusion criteria, 85.1% (n=143) were male, while 14.9% (n=25) were female. The mean age was 46.6±6.5 years. HbA1c was found to have a significantly positive correlation with the Gensini score in DD group (n=77), whereas no significant correlation was found between HbA1c and the Gensini score in UDD group (n=91) (p<0.001; correlation coefficient: 0.656, p=0.207; correlation coefficient: 0.251, respectively). Linear regression analysis revealed that HbA1c was a significant predictor for gennini score (β: 0.632).

Conclusion: HbA1c can be used as a predictor for the evaluation of diabetic patients with CAD. Moreover, HbA1c was not found to have a significant association with the severity of CAD in undiagnosed diabetic CAD patients with admission hyperglycemia.

Keywords: coronary artery disease, diabetes mellitus, HbA1c, gennini score.

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Introduction

Diabetes Mellitus (DM) is a chronic metabolism disease that is caused by the increased glucose concentration in the blood due to the hereditary and/or acquired deficiency of insulin levels produced by pancreas(5). According to the World Health Organization, the prevalence of DM was 4.7% among persons older than 18 years around the world in 1980 while it rose to 8.5% in 2014. This increase is more rapid in low and middle-income countries(6). The prevalence of DM is higher in elderly people than in young people and higher in females than in males(3,4).

DM is an important risk factor for coronary artery disease (CAD)(5,6). Hemoglobin A1c (HbA1c)
is the most commonly used marker for long-term glycemic control in diabetic patients\(^7\). Elevated HbA1c is considered to be a sign of cardiovascular pathologies\(^8\).

According to the scoring system suggested by Gensini, a numerical value is assigned to the degree of stenosis in a coronary artery, thanks to which CAD can be assessed thoroughly and even very trivial lesions in coronary arteries are not missed\(^9\).

The correlation between HbA1c and severity of stenosis in a coronary artery was explored in some studies that reported contradictory results\(^10,11\). In this study, we investigated the association between stenosis in a coronary artery and HbA1c values using Gensini scoring system in both diagnosed and undiagnosed diabetic patients who had coronary artery disease.

Materials and methods

After the approval was obtained from the ethics committee, the files of patients younger than 55 who presented to the emergency department from 2014 to 2015 and were diagnosed with CAD through angiography (n=660) were reviewed retrospectively, and those patients whose HbA1c levels were analyzed (n=181) were included in the study. The demographic data of the patients, their cardiac enzymes when they were admitted to the emergency department, blood glucose levels on admission, and history of previously diagnosed diabetes as well as other known comorbidities were recorded. Those patients who had a history of liver failure, malignancies, cerebrovascular diseases, active or chronic immunodeficiency, drug or substance use and pregnant patients were excluded from the study (n=13). See the patient flow chart. The coronary angiography findings of the patients included in the study (n=168) were assessed by a cardiologist who was blinded to study. The severity of coronary artery stenosis was determined according to the Gensini score\(^5\).

The study population was divided into two groups:

- diagnosed diabetes (DD) (n=77),
- undiagnosed diabetes (UDD) (n=91).

Moreover, newly diagnosed diabetic patients were assigned to DD group (n=3), while patients with stress-induced hyperglycemia were assigned to UDD group (Figure 1).

Statistical analysis

The data collected in the study were uploaded to Statistical Package for the Social Sciences (SPSS) 22.0 (Armonk, NY: IBM Corp.) software. The data were expressed as numbers and percentage for categorical variables and as mean ± standard deviation for continuous variables. Shapiro Wilk test was performed to analyze the concordance of the continuous variables with the normal distribution. In order to compare the HbA1c values, lipid profile, vital values, cardiac enzyme values and Gensini scores of the groups, Student-t test was used for the normally distributed parameters while Mann-Whitnes U test was used for the parameters that were not normally distributed. Chi-Square test or Fisher test was used for the analysis of the categorical variables. Pearson or Spearman test was used to analyze the correlation between the Gensini score and other variables (HbA1c, lipid profile, cardiac enzyme levels). The significance of variables affecting the severity of coronary atherosclerosis was tested by linear regression analysis. \(P <0.05\) was considered to be statistically significant.

Results

Out of 168 patients included in the study, 85.15% (n=143) were male, while 14.9% (n=25) were female. The mean age of the patients was 46.6±6.5 years. Table 1 presents the comparison between the groups with respect to demographic features, cardiac enzymes, lipid values, HbA1c, Gensini score and vital parameters on admission to emergency department. There were 77 patients in DD group and 91 patients in UDD group. Accordingly, DD group had significantly higher HbA1c, glucose concentrations and Gensini scores.
compared to UDD group (p<0.001; 8.40±2.5 vs 5.53±0.3, p<0.001; 231.2±46.4 vs 109.2±22.2, p<0.001; 39.8±24.3 vs 24.0±21.1, respectively).

Table 2 shows the correlation between the clinical parameters and Gensini scores within each group. Accordingly, it was found that HbA1c had a significantly positive correlation with the Gensini score in DD group, whereas there was no significant correlation between the Gensini score and HbA1c in UDD group (p <0.001; correlation coefficient: 0.656, p=0.207; correlation coefficient: 0.251, respectively).

The linear regression analysis of age, sex, admission systolic blood pressure, admission diastolic blood pressure, admission heart rate, HbA1c, triglyceride, total cholesterol, Low Density Lipoprotein (LDL) and High Density Lipoprotein (HDL) for Gensini score revealed that only HbA1c was a significant predictor (p<0.001; β: 0.632) (Table 3).

Table 1: Comparison between the significance of demographic data, vital parameters at emergency admission, lipid levels, Gensini scores and HbA1c values of the participants included in the study groups.

(Data are expressed as mean ± standard deviation for normally distributed data and percentage for categorical variables.)


Table 2: The correlation between the Gensini score and age, HbA1c, glucose, lipid parameters and cardiac enzyme levels and their significance.

(HbA1c:Hemoglobin A1c, HDL: high density lipoprotein, LDL: Low Density Lipoprotein DD: Diagnosed Diabetes, UDD: Undiagnosed Diabetes)

Table 3: Linear regression analysis showing the significant independent association between the increased HbA1c and Gensini scores.

(β, standardized regression coefficient)

(HbA1c:Hemoglobin A1c, HDL: high density lipoprotein, LDL: Low Density Lipoprotein, B.P: Blood pressure)
Discussion

HbA1c concentration is an established marker of average blood glucose concentration and has been suggested as a diagnostic or screening tool for diabetes\(^{(12)}\). Self-limited studies have demonstrated that HbA1c is a prognostic factor for CAD and also a marker of short and long term mortality in Acute Coronary Syndrome (ACS) patients\(^{(13,14)}\).

One of these studies was conducted by Naito et al. who explored the long-term clinical effects of glucose and elevated HbA1c on non-diabetic ACS patients. In that study, they found that HbA1c and glucose were associated with poor long-term clinical outcomes\(^{(15)}\).

In the sub-group analysis under a meta-analysis of the prognostic effect of HbA1c on mortality, the short and long-term effect of elevated HbA1c on mortality was explored and elevated HbA1c was found to be associated with increased mortality in non-diabetic patients whereas no association was found between elevated HbA1c and mortality in diabetic patients\(^{(16)}\).

Similar to the hypothesis of our study, there are studies exploring the association between HbA1c level and severity of CAD. In a study conducted by Hong et al., they found that HbA1c was associated with three-vessel disease in patients with stable angina and also an independent predictor for the severity of CAD\(^{(17)}\).

Ertem et al.\(^{(18)}\) conducted a study including 65 non-diabetic ACS patients and assessed the correlation between the severity of CAD and HbA1c level using Gensini scores. In that study, no significant association was found between HbA1c levels and severity of CAD \((p=0.299)\). Another study on non-diabetic patients was conducted by Garg et al. In that study, they used the syntax scores to assess the severity of CAD and concluded that HbA1c levels were significantly elevated in patients with increased severity of CAD\(^{(19)}\).

Ozlu et al. assessed the correlation between HbA1c level and severity of CAD using the Gensini scores in diabetic patients. This study showed that there was a significantly positive correlation between the severity of CAD and HbA1c levels.

Another study on the association between HbA1c levels and severity of CAD was conducted in non-diabetic patients with ST-Segment Elevation Myocardial Infarction (STEMI). The patients were divided into two groups depending on HbA1c levels: \(\leq 5.8\%\) and >5.8%.

The group with HbA1c level >5.8% had a higher correlation with the severity of CAD compared to the group with HbA1c level \(\leq 5.8\%\)(20).

Ayhan et al. explored the correlation between HbA1c levels and severity of CAD in premature atherosclerotic patients (<40 years of age). That study showed that HbA1c level was positively correlated with the severity of CAD\(^{(20)}\).

Taking into consideration all of the above-mentioned studies, it seems that the results of studies conducted on diabetic and non-diabetic patients vary. In our study in which we divided the patients into DD and UDD groups, we found that the severity of CAD increased in correlation with the elevated HbA1c levels, which is also consistent with the findings of Ozlu et al. Contrary to the study conducted by Ertem et al., we did not find any prognostic effect of HbA1c level on predicting the severity of CAD in UDD patients. Contrary to the above-mentioned studies, the patients in our study were younger and thus the other risk factors that might affect CAD could be minimized, which was considered as an important advantage. We also observed in our study that stress-induced hyperglycemia was an important reason for hyperglycemia especially in CAD patients, which was consistent with the literature\(^{(22)}\).

Limitations

Our study has several limitations. An important limitation of our study is the low number of the patients in the study group. Moreover, the subjects in our study were enrolled from a single center. Although we tried to ensure homogeneity of the groups for HbA1c analysis by selecting young patients and those who did not have another comorbidity, it is clear that it was not possible to exclude all multifactorial causes affecting CAD process due to the retrospective nature of our study.

Conclusions

The elevated levels of HbA1c were significantly correlated with the severity of CAD in diagnosed diabetic patients with CAD, and HbA1c could be used as a predictor for diabetic patients with CAD. Moreover, HbA1c was not found to have a significant association with the severity of CAD in undiagnosed diabetic CAD patients with admission hyperglycemia.
Which patients have an association between HbA1c level and severity of coronary artery disease: Diabetic or non-diabetic?

References


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