Original Article

Association of Severity of Coronary Artery Disease and HbA1c Levels in Patients with Acute Coronary Syndrome

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ABSTRACT

Objective: To determine the levels of glycosylated haemoglobin (HbA1c) among patients with acute coronary syndrome (ACS) and compare the severity of coronary artery disease (CAD) with glycosylated haemoglobin levels.

Methodology: It was a comparative cross-sectional study carried out in the Department of Cardiology, Rawalpindi Institute of Cardiology, Rawalpindi, from January to July 2020. After taking ethical approval and written informed consent, 100 patients with ACS were recruited by non-probability consecutive sampling. Glycosylated haemoglobin was measured using an immunoassay and patients were labeled as diabetic & non-diabetic. Coronary angiography was done and patients were categorized as having single vessel coronary artery disease (SVCAD), double vessel coronary artery disease (DVCAD) or triple vessel coronary artery disease (TVCAD), minor CAD or normal coronary arteries. The Statistical Package for the Social Sciences (SPSS) version 25 was used to analyze the data.

Results: Patients' mean HbA1c levels were 7.52±2.69%. Thirty seven patients were diabetic. When compared to non-diabetic patients, diabetic patients had significantly higher rates of TVCAD and DVCAD (p-value=0.00003). Single vessel disease and minor CAD were more frequent in non-diabetic patients. Single vessel disease was present in 5(13.5%) diabetic and 30(47.6%) non-diabetic patients. Minor CAD was found in 1(2.7%) diabetic and 8(12.7%) non-diabetic patients. This difference was statistically significant (p-value=0.001).

Conclusion: Diabetes mellitus significantly predicts the severity of coronary artery disease. The severity of CAD is greater in diabetic patients, with the majority of the patients presenting with TVCAD and DVCAD. In contrast, minor CAD or SVCAD is more common among non-diabetics.

Keywords: *HbA1c. Coronary artery disease. Acute coronary syndrome.*

INTRODUCTION

Coronary artery disease is a significant contributor to mortality, morbidity, and financial burden globally. One hundred and ninety seven million cases of CAD were reported in 2019 leading to 17.8 million deaths across the world.[1] The mortality rate due to CAD rose by 21.1% in the last ten years.[2] The prevalence of CAD in Pakistan is reported to be 17%.[3] Diabetes mellitus (DM), the most prevalent chronic disease worldwide, is the most important predictor of CAD. The prevalence of DM is 451 million cases on the global scale and by 2045, it is anticipated to rise to 693 million. About 16.98% of Pakistanis had type 2 diabetes in 2017.[4] Even below the definition of overt diabetes, the risk of CAD increases with glucose intolerance. This is attributed to increased oxidative stress due to inflammation, increased glucose levels, and resistance to insulin in DM.[5] In diabetic patients, CAD is related to greater chances of major adverse cardiac events as compared to non-diabetic patients.[6] Glycosylated haemoglobin is a recognized indicator of long-term glucose levels in diabetic patients. A higher HbA1c level is linked to a higher risk of both microvascular and macrovascular complications. Studies have shown that good glycemic control (HbA1c <7%) results in lesser microvascular complications. Blood glucose levels correlate with CAD severity rather than random or fasting glucose levels.[5] Patients with elevated HbA1c levels are more likely to develop more severe CAD with multiple vessel disease.[6] Literature has reported that higher HbA1c is associated with increased stiffness & calcification in vessels and atherosclerosis. In patients with diabetes mellitus, it is an independent predictor of cardiovascular mortality and morbidity. It has been documented that a 1% increase in HbA1c results in a 30% rise in overall mortality and a 40% rise in cardiovascular mortality in diabetic patients. Patients with decreased HbA1c levels have fewer chances of developing macrovascular as well as microvascular complications.[7]

The present study aimed to establish the association between HbA1c level and the severity of CAD. The number of coronary arteries with significant CAD was used to determine the severity of CAD. Several studies have demonstrated an association between elevated levels of HbA1c and higher CAD severity, morbidity, and mortality but a few studies have also shown controversial results. This study will add useful information to the existing knowledge and aid in establishing a link between the severity of CAD and HbA1c levels in patients with acute coronary syndrome, particularly in our demographic region.

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METHODOLOGY

It was a comparative cross-sectional study carried out in the Department of Cardiology, Rawalpindi Institute of Cardiology, Rawalpindi in seven months from January to July 2020. The hospital ethics committee approved the study. One hundred patients were recruited in this study by non-probability convenient sampling after taking written informed consent. Patients of both genders presenting with ACS with ages ranging from 30-70 years were included. Patients with ACS had symptoms suggestive of CAD such as chest pain, palpitations, apprehension, shortness of breath, nausea, and sweating for >20 mins along with ischemic electrocardiogram changes and/or positive cardiac enzymes (troponin T and troponin I). The patients with ACS had either ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), or unstable angina. The study excluded patients with recent blood transfusion history, hemoglobinopathies, anemia, prior myocardial infarction, or coronary revascularization.

Glycosylated haemoglobin was measured using an immunoassay. Coronary angiography was done during the hospital stay to define the severity of CAD. Patients were categorized as having SVCAD, DVCAD, TVCAD, minor CAD or normal coronary arteries based on the number of coronary arteries involved, and having significant CAD. Patient demographic details, history of risk factors of CAD like hypertension, smoking, dyslipidemia & body mass index (BMI), levels of HbA1c, and coronary angiography findings were collected on a predesigned proforma sheet.

Patients with HbA1c levels ≥6.5% were labeled as diabetics and those with HbA1c levels <6.5% were labeled as non-diabetics. A greater than 50% decrease in the luminal diameter of epicardial coronary arteries was considered to be significant CAD and less than 50% decrease was labeled as minor CAD.

STATISTICAL ANALYSIS

Statistical Package for the Social Sciences (SPSS) version 25 was used to analyze the data. The mean and standard deviation (SD) for continuous variables including age, height, weight, and BMI were calculated using descriptive statistics. Frequency and percentage were calculated for categorical variables including gender, diabetes mellitus, hypertension, and smoking. The severity of CAD was calculated based on the number of coronary arteries having significant CAD on coronary angiogram. The association of severity of CAD was observed between the diabetic and non-diabetic patients by Chi-square test. The association of the severity of CAD was seen with effect modifiers such as gender, body mass index, smoking, and hypertension by applying a poststratification Chi-square test. A p-valve of ≤0.05 was taken significant.

RESULTS

The age of the patients ranged from 30 to 70 years with a mean of 52.14±10.76 years. Distribution of patients according to age groups is shown in Figure 1. Out of 100 patients, 76(76%) were males and 24(24%) were females. Male to female ratio was 3.16:1. The mean BMI was 26.27±2.57 kg/m^2 with minimum and maximum BMI of 20 & 32 kg/m^2, respectively. The mean ejection fraction (EF) of the patients was 41.67±10.72% with minimum and maximum EF of 20% & 80%, respectively. The patients' mean HbA1c value was 7.52±2.69%, while the lowest and highest values were 3.51% and 14.70%, respectively. Diabetes mellitus was found in 37(37%) patients and hypertension in 52(52%) patients. In our study, 47(47%) patients were smokers and 41(41%) patients had dyslipidemia. The family history of ACS was positive in 24(24%) patients.

Out of 100 patients, STEMI type of ACS was found in 79(79%) patients, NSTEMI was noted in 12(12%) patients, and unstable angina was found in 9(9%) patients. Thirty five percent of the patients had single vessel disease, 32(32%) patients had double vessel disease, and 21(21%) patients had triple vessel disease on angiography. Minor CAD was found in 9(9%) patients (Table 1).

In our study, in diabetic patients, TVCAD was found in 13(35.2%) patients, while in non-diabetic patients, TVCAD was found in 8(12.7%) patients. Double vessel disease was found in 17(45.9%) diabetic and 15(23.8%) non-diabetic patients. On the other hand, single vessel disease and minor CAD were more frequent in non-diabetic patients. Single vessel disease was present in 5(13.5%) diabetic and 30(47.6%) non-diabetic patients. Minor CAD was found in 1(2.7%) diabetic and 8(12.7%) non-diabetic patients. This difference was statistically significant (p-value=0.001).

With a significant p-value of 0.00004, the frequency of TVCAD and DVCAD was significantly greater in diabetic individuals (81.1%) compared to non-diabetic patients (36.5%). These results are shown in Table 2.

No significant difference existed in the frequency of TVCAD and DVCAD concerning gender, BMI, type of ACS, hypertension, and smoking (Table 3).

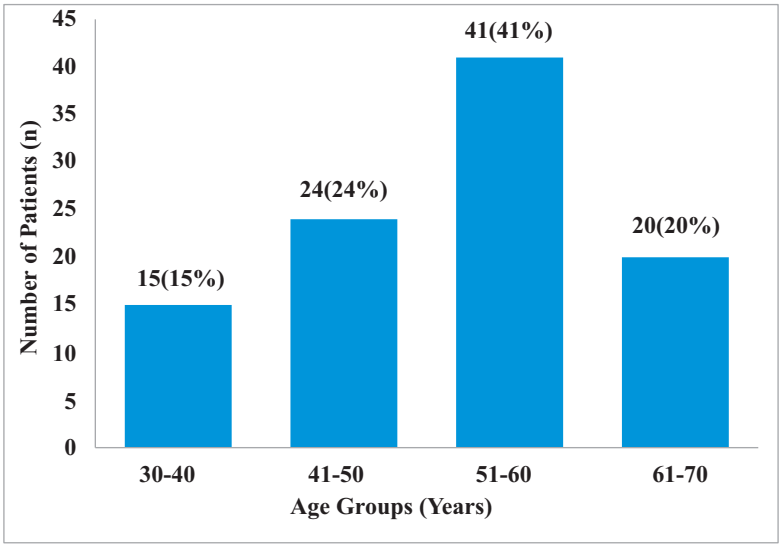

Figure 1: Distribution of Patients according to Age Groups

Table 1: Coronary Arteries Involvement in Diabetic and Non-Diabetic Patients

Angiographic Findings	Diabetic Patients	Non-Diabetic Patients	Total	p-value
TVCAD	13(35.2%)	8(12.7%)	21(21%)	0.0006*
DVCAD	17(45.9%)	15(23.8%)	32(32%)	
SVCAD	5(13.5%)	30(47.6%)	35(35%)	
Minor CAD	1(2.7%)	8(12.7%)	9(9%)	
Normal Coronaries	1(2.7%)	2(3.2%)	3(3%)	

**Significant p-value*

Table 2: Severity of CAD in Diabetic and Non-Diabetic Patients

Angiographic Findings	Diabetic Patients	Non-Diabetic Patients	Total	p-value
TVCAD & DVCAD	30(81.1%)	23(36.5%)	53	0.00003*
SVCAD & Minor CAD	6(16.2%)	38(60.3%)	44	

**Significant p-value*

Table 3: Association of Severity of CAD in Diabetic & Non-Diabetic Patients with various Parameters

Parameters		TVCAD & DVCAD		Total	p-value
		Diabetic	Non-Diabetic		
Gender	**Male**	21(39.6%)	20(37.7%)	41(77.3%)	0.14
	Female	9(17%)	3(5.7%)	12(22.7%)	
BMI (kg/m^2)	**<25**	8(15.1%)	8(15.1%)	16(30.2%)	0.52
	≥25	22(41.5%)	15(28.3%)	37(69.8%)	
ACS Type	**STEMI**	24(45.3%)	19(35.8%)	43(81.1%)	0.52
	NSTEMI	5(9.4%)	2(3.8%)	7(13.2%)	
	Unstable Angina	1(1.9%)	2(3.8%)	3(5.7%)	
Hypertension	**Hypertensive**	21(39.6%)	16(30.2%)	37(69.8%)	0.97
	Normotensive	9(17%)	7(13.2%)	16(30.2%)	
Smoking	**Smoker**	9(17%)	12(22.6%)	21(39.6%)	0.101
	Non-smoker	21(39.6%)	11(20.8%)	32(60.4%)	

DISCUSSION

Coronary artery disease is a leading factor in cardiovascular deaths worldwide. The predictors of coronary artery disease have been the subject of numerous investigations.[8] Diabetic people have 3-4 times increased risk of cardiovascular death.[9] In this study, we compared the severity of CAD in patients with and without diabetes.

In our study, patients had a mean age of 52.14±10.76 years, and 76% of them were males. In another study, patients had a mean age of 55.87±11.04 years and 67.08% were males.[10] In a study by Dar et al., patients had a mean age of 55.8±9 years with 85.1% males.[11] The mean EF of the patients was 41.67±10.72% in our study and 55.86±11.78% in another study conducted by Parkar et al.[10] Our results showed that 52% of the patients were hypertensive and 47% were smokers. Another study revealed that 41.42% of the patients had hypertension and 23.67% were smokers.[10] Thirty seven percent of patients had diabetes mellitus in our study. Similarly, another study reported that 41.8% of the patients were diabetic.[11] In contrast, 94.33% of the patients were diabetic in a study by Parkar et al.[10] The mean HbA1c was 7.52±2.69% in our study, 6.23±1.29% in a study by Basman et al., and 6.84±1.93% in another study.[10,12]

Out of 100 patients in our study, STEMI type of ACS was found in 79(79%) patients, NSTEMI was noted in 12(12%) patients, and unstable angina was found in 9(9%) patients. Another study also reported STEMI in majority of the patients (57.92%) followed by NSTEMI (30.33%) and unstable angina (9%).[10] Dar et al. reported STEMI in 80.77%, NSTEMI in 17.79%, and unstable angina in 1.44% of the patients.[11]

According to our findings, diabetic patients had significantly higher rates of TVCAD and DVCAD than non-diabetic patients (p-value=0.00003). In diabetic patients, TVCAD was found in 35.2% of patients while in non-diabetic patients, TVCAD was found in 12.7% of patients. Single vessel disease, however, was more prevalent in non-diabetics, and 13.5% of patients with diabetes and 47.6% of individuals without diabetes had single vascular disease. So, the severity of CAD and HbA1c levels were found to be positively correlated.

Another study reported that triple vessel disease was found in 45.4% of diabetic and 30.2% of non-diabetic patients with a significant p-value of 0.03. Single vessel disease was significantly more common in non-diabetics (11.6%) than diabetic patients (24.4%) (p-value=0.04).[13] Taimur et al. concluded that the chances of CAD were 6 times higher in diabetic patients than in non-diabetic patients. Thirty eight percent of diabetic patients and 22% of non-diabetic patients had triple vessel disease. Double vessel disease was seen in 26% of diabetics and 20% of non-diabetics, whereas single vessel disease was present in 28% of diabetics and 18% of non-diabetics.[14] On the contrary, HbA1c was not linked to the severity of CAD as measured by the Gensini score, according to a study conducted by Wang et al.[15] Another study conducted in Karachi, Pakistan also reported that HbA1c levels did not significantly correlate with the severity of CAD.[16] In a study by Dar et al., there was a positive association between HbA1c levels and the Gensini score of severity of CAD was reported.[11] A positive correlation was also observed by Basman et al. and Yan et al.[12,17] Another study revealed that patients with diabetes mellitus have more severe CAD than patients without the disease.[18] A study was conducted in China to observe impact of diabetes mellitus and HbA1c level on outcomes of acute coronary syndrome. They concluded that diabetic patients with acute coronary syndrome were associated with increased major cardiovascular events and mortality.[19] Another study concluded that severity of CAD in diabetic patients is positively correlated with HbA1c levels.[9]

CONCLUSION

Diabetes mellitus significantly predicts the severity of coronary artery disease. The severity of CAD is greater in diabetic patients, with the majority of patients presenting with TVCAD and DVCAD. In contrast, minor CAD or SVCAD is more common among non-diabetics.

LIMITATIONS & RECOMMENDATIONS

The study compared the severity of coronary artery disease among diabetic and non-diabetic patients but didn't determine the severity of CAD in patients with impaired glucose tolerance. Furthermore, the duration of diabetes mellitus, glycemic control, and the association of HbA1c levels with various scores such as SYNTAX or Gensini scores were not studied. Further work is recommended to address these limitations.

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