

# Association between HbA1C and Coronary Artery Disease Severity in patients of Diabetes Mellitus Type 2 presented as Acute Coronary Artery Syndrome and Non Diabetic

MAHBOOB QADIR<sup>1</sup>, MUHAMMAD SHAHID NAWAZ KHAN<sup>2</sup>, HUMAYUN RIAZ KHAN<sup>3</sup>, NADEEM ULLAH<sup>4</sup>, MUDDASAR AHMED<sup>5</sup>, HAFIZ MUHAMMAD FARHAN RASHID<sup>6</sup>

<sup>1</sup>Fellow Endocrinology & Senior Registrar of Medicine Dept. Nishtar Medical University & Hospital, Multan.

<sup>2</sup>Assistant Professor of Medicine Dept. Nishtar Medical University & Hospital, Multan.

<sup>3</sup>Senior Registrar of Medicine Dept. Nishtar Medical University & Hospital, Multan.

<sup>4</sup>Assistant Professor of Medicine Dept. Bakhtawar Amin Trust Teaching Hospital, Multan.

<sup>5,6</sup>Assistant Professor of Medicine Dept. Nishtar Medical University & Hospital, Multan.

Correspondence to: Mahboob Qadir, Email: [drmeheboob.qadir@gmail.com](mailto:drmeheboob.qadir@gmail.com), Cell: 0333 6978653

## ABSTRACT

**Aim:** to investigate the prevalence of diabetes mellitus type 2 (T2DM) and association of HbA1c with the severity of coronary artery disease (CAD) in patients presenting at tertiary care center as acute coronary syndrome and non-diabetic.

**Study Design:** Prospective observational study

**Duration and Place Study** was conducted at department of general medicine Nishtar Hospital, Multan from January 2021 to January 2022 in 1 year duration.

**Methodology:** A total of 200 patients were enrolled in study. Main variables of study were BMI, smoking status, dyslipidemia, hypertension, STEMI, angina, HbA1c and treatment strategy. SPSS version 23 was used for data analysis. P value below or equal to 0.05 was taken as significant.

**Results:** Among total 83.5% patients intervened by therapeutic, whereas 48.0% used thrombolytic drug in STEMI. 70.7% patients were thrombolysis in therapeutic intervention and 44.8% were streptokinase in thrombolytic drug. In fasting blood sugar, 53.0% patients were diabetic, whereas in HbA1c levels, 52.3% patients were diabetic.

**Conclusion:** This study highlights the significance of testing for diabetes in individuals in poor nations who report with non-diabetic acute coronary syndrome. One of manifestations of diabetes mellitus may be the acute coronary syndrome.

**Keywords:** Acute coronary syndrome, Coronary angiography, Diabetes, HbA1c.

## INTRODUCTION

Worldwide common cause of morbidity and mortality is acute coronary syndrome (ACS) and is a clinically meaningful presentation of coronary artery disease (CAD)<sup>1</sup>. In ACS patients, cardiovascular prognosis is highly linked to the degree of coronary atherosclerosis<sup>2</sup>. Consequently, it is crucial for the clinical management of this condition to predict and diagnose the degree of coronary lesion in ACS. In developing nations like India, such as the United States, coronary artery disease (CAD) has become largest source of illness as well as mortality<sup>4,5</sup>.

Smoking, family history of coronary artery disease, high blood pressure, dyslipidemia, diabetes mellitus, obesity and obesity are the major risk factors for condition<sup>6</sup>. One of the significant and reliable predictors of death in CAD is diabetes mellitus (DM)<sup>7</sup>. Measuring the serum concentrations of glycated hemoglobin (HbA1c) is a crucial step in determining the glycemic management of diabetes patients in addition to fasting blood sugar levels<sup>8</sup>.

By non-enzymatically condensing glucose molecules with free amino groups on globulin portion of hemoglobin, glycated hemoglobin is created<sup>9</sup>. The level of glycated hemoglobin will increase in direct proportion to ambient blood glucose levels<sup>10</sup>.

## METHODOLOGY

Study was conducted at department of general medicine Nishtar Hospital, Multan from January 2021 to January 2022 in 1 year duration. Patients presented as a non-diabetic acute coronary syndrome met the inclusion criteria for this study. Study included individuals who refused to consent to the treatment, were known to be diabetics, had end-stage renal illness requiring dialysis, had end-stage coronary artery disease with a history of violent reaction to contrast medium, or had kidney transplantation.

Each patient underwent a thorough evaluation as part of the study, which included gathering pertinent histories, performing a general physical and heart examination, conducting all baseline tests, measuring fasting blood sugar levels, level of serum HbA1c and performing an echocardiogram. Using the high-performance liquid chromatography technology, blood HbA1c levels were measured in single facility to standardize test value. Based on

fasting blood sugar and serum HbA1c levels, patients were classified as having diabetes, pre-diabetes, or not having diabetes, as per ADA (American Diabetic Association) criteria. Diabetic patients were those who's HbA1c or fasting blood sugar above 126 mg/dl or 6.4%, respectively. Patients were classified as pre-diabetics if their fasting blood sugar (FBG) was between 100 and 125 mg/dl and their HbA1c were between 5.7 and 6.4%. Patients whose FBG was less than 100 mg/dl and their HbA1c were less than 5.7% were classified as non-diabetics.

Two committed interventionists carried out radial or femoral coronary angiography at the discretion of the operator. Two senior cardiologists were involved to estimate the burden of CAD by interpreting angiographic findings. Gensini score calculation was used to determine the CAD load.

Following compilation in Microsoft Excel, the collected data was entered in software of statistical package for social sciences (SPSS) version 24. The mean  $\pm$  SD were estimated for numerical data and frequency (%) for categorical data. Independent t-test and chi-square were applied to see association among numerical and categorical outcomes respectively. All p values level of 0.05 or less was regarded as statistically significant.

## RESULTS

A total of 200 patients were enrolled 87 (43.5%) females and 113 (56.5%) males. The average age of the patients was  $57.54 \pm 3.47$  years. The average BMI of the patients was  $28.4 \pm 3.88$  kg/m<sup>2</sup>. 85 (42.5%) patients were hypertensive, 56 (28.0%) were smokers, 122 (61.0%) were dyslipidemia, 156 (78.0%) were STEMI, 23 (11.5%) were NSTEMI, and 8 (4.0%) patients were unstable angina. (Table. I). Among total 167 (83.5%) patients intervened by therapeutic, whereas 96 (48.0%) used thrombolytic drug in STEMI. 118 (70.7%) patients were thrombolysis in therapeutic intervention and 43 (44.8%) were streptokinase in thrombolytic drug (Table. II). In fasting blood sugar, 106 (53.0%) patients were diabetic, whereas in HbA1c levels, 105 (52.3%) patients were diabetic. (Figure. I & II). The Gensini score was  $<20$  in 77 (38.5%) patients and  $>20$  in 123 (61.5%) patients. Pearson correlation coefficient between Gensini score and HbA1c was 0.76, showed the positive linear correlation.

Table 1: Demographic and Clinical Characteristics of Both the Groups

Characteristic	Mean±S.D	N (%)
Age (years)	57.54±3.47	
18-30		59 (29.5)
31-60		123 (61.5)
>60		18 (9.0)
BMI (kg/m <sup>2</sup> )	28.4±3.88	
25-27		151 (75.5)
>28		49 (24.5)
Gender		
Male		113 (56.5)
Female		87 (43.5)
Hypertension		85 (42.5)
Smoking status		56 (28.0)
Dyslipidemia		122 (61.0)
STEMI		156 (78.0)
NSTEMI		23 (11.5)
Unstable angina		8 (4.0)

Table 2: Thrombolytic Drugs Interventions Used in Patients of STEMI

Characteristic	Category	N (%)
Therapeutic intervention	Thrombolysis	118 (70.7)
	Primary PCI	16 (9.6)
	Late presentation	27 (16.2)
	Thrombolysis contraindicated	6 (3.6)
Thrombolytic drug	Streptokinase	43 (44.8)
	Tenecteplase	39 (40.6)
	Retepase	14 (14.6)

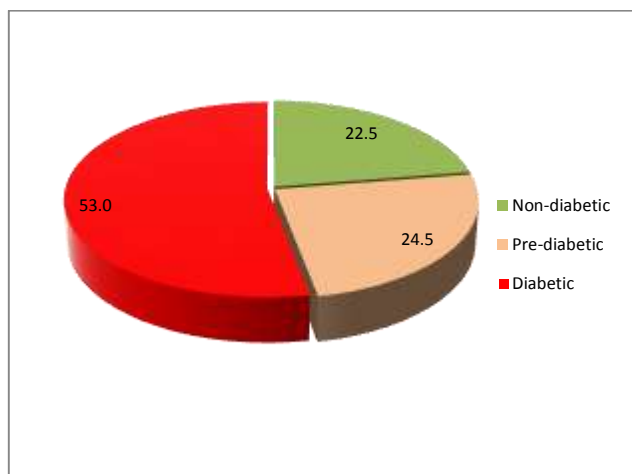


Figure 1: Fasting blood sugar levels of the study patients

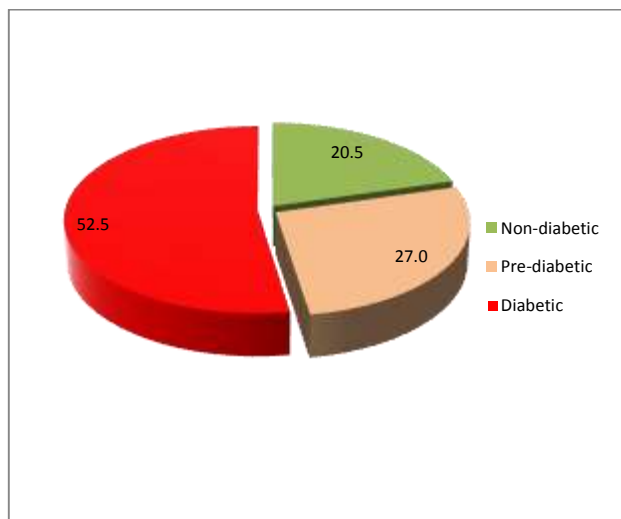


Figure 2: HbA1c levels of the study patients

## DISCUSSION

The burden on healthcare resources around the world is still mostly caused by coronary heart disease. The primary risk factors for developing of CAD are the same everywhere; however the contributions of each particular risk factor to CAD development vary across the developed and developing worlds<sup>11</sup>.

In our study, patients' ages ranged from 18 to 60 years, with the mean patient age being 57.54 ± 3.47 years. The patients in our study had a lower mean age and were generally younger than those in prior studies. This data was in line with earlier Indian research conducted by Sharma et al<sup>12</sup> that has demonstrated that CAD manifests ten years earlier in Indian patients. With a male female ratio of out of 200 patients, 56.5% were males and 43.5% were females a significant male preponderance was seen.

The vast majority of patients had BMIs that were within the normal range. The most frequent risk factor in this patient study group was dyslipidemia. In a trial conducted by Mehraj et al<sup>13</sup> where diabetic and non-diabetic individuals presenting with ACS were not separated, the prevalence of dyslipidemia was significantly greater. The second most common risk factor identified in this investigation was smoking. Prevalence of smoking was also high like other studies conducted by Krishnan et al<sup>14</sup> and Mishra et al<sup>15</sup>.

Acute coronary syndrome's most frequent presentation was ST-elevation myocardial infarction (STEMI) (ACS)<sup>16</sup>. In a study by Ramakrishnan et al<sup>17</sup> reported that due to a lack of infrastructure and knowledge for early patient detection, such as stable chronic angina, ACS is the most prevalent presentation of cardiac illnesses in poor nations compared to industrialized countries.

In our study 52.5% of patients are diabetic and 27% are prediabetic, these findings are comparable with study conducted by Nanayakkara et al<sup>18</sup> reporting 47% diabetic and 53% prediabetics. Nevertheless, efforts are being made to build the necessary infrastructure for implementing the pharmaceutical invasive strategy, which calls for early identification of MI, that encourages the thrombolysis at peripheries whenever necessary early referral of patients to tertiary care center with facility of percutaneous coronary intervention is available. In our study only 9.6 percent of patients who receive primary PCI as the treatment strategy, which was similar with the national statistics from previous studies from the developing countries<sup>19</sup>.

This is in stark contrast to the situation in developed nations like the United States of America, where about 80% of patients receive percutaneous coronary intervention after diagnosis of acute coronary syndrome because there are many PCI-capable centers spread across the nation and the majority of the population lives within a 30- to 60-minute drive of these centres<sup>20</sup>.

## CONCLUSION

In patients presenting with non-diabetic acute coronary syndrome (ACS), this study underlines the significance of determining whether diabetes is present. The ACS may be regarded as one of the diabetes mellitus presentations in poor nations due to the lack of early identification. HbA1c may also be used as a sign of the severity and prevalence of coronary artery disease.

**Limitations:** Most of our patients are residents of rural areas, sample collection is quite difficult because of refused to give consent and withdraw from study participation after giving consent.

**Recommendations:** Further multi center studies on larger sample size, or meta-analysis are recommended to underline the significance of acute coronary disease and its association with diabetic and non diabetic patients.

## REFERENCES

1. Dar MI, Beig JR, Jan I, Shah TR, Ali M, Rather HA, Trambo NA. Prevalence of type 2 diabetes mellitus and association of HbA1c with severity of coronary artery disease in patients presenting as non-diabetic acute coronary syndrome. The Egyptian Heart Journal. 2020;72(1):1-8.

2. Habib S, Ullah SZ, Saghir T, Muhammad AS, Deen ZU, Naseeb K, Sherwani R. The association between hemoglobin A1c and the severity of coronary artery disease in non-diabetic patients with acute coronary syndrome. *Cureus*. 2020;12(1):35-46.
3. Khan FR, Ali J, Ullah R, Hassan Z, Khattak S, Lakhta G, Gul N. Relationship between high glycosylated hemoglobin and severity of coronary artery disease in type II diabetic patients hospitalized with acute coronary syndrome. *Cureus*. 2021;13(3).
4. Mirza A, Mohammad H, Jafer F, Singh J, Lang C. Glycated Hemoglobin Level as a predictor of Severity of Coronary Artery Disease in Non-Diabetic Patients. *J Diabetes Treat*. 2020;5:1084-9.
5. Albashir AA, Elawad OA, Khougali HS. The use of glycosylated hemoglobin (HbA1c) as a predictor of the severity of acute coronary syndrome among diabetic patients. *Irish Journal of Medical Science (1971-)*. 2021;190(2):609-14.
6. Kayali Y, Ozder A. Glycosylated hemoglobin A1c predicts coronary artery disease in non-diabetic patients. *Journal of clinical laboratory analysis*. 2021;35(2):e23612.
7. Güven R, Aykal G, Gungör F, Canakyol K, Bayar N: Which patients have an association between HbA1c level and severity of coronary artery disease: diabetic or non-diabetic?. *Acta Medica Mediterranea*. 2017, 33:123-127.
8. Strisciunglio T, Izzo R, Barbato E, Di Gioia G, Colaiori I, Fiordelisi A, Morisco C, Bartunek J, Franco D, Ammirati G, Pergola V. Insulin resistance predicts severity of coronary atherosclerotic disease in non-diabetic patients. *Journal of Clinical Medicine*. 2020;9(7):2144.
9. Chandel S, Parihar S, Gramani B, Dubey TN. Role of HbA1c with mortality and severity among the patients of Acute coronary syndrome: a prospective study. *International Journal of Advances in Medicine*. 2019 May;6(3):796.
10. Pathak SR, Gajurel RM, Poudel CM, Shrestha H, Thapa S, Thapa S. Angiographic Severity of Coronary Artery Disease in Diabetic and Non-Diabetic Acute STEMI Patients in a Tertiary Care Centre of Nepal. *Kathmandu Univ Med J*. 2021;76(4):410-.
11. Ikeda F, Doi Y, Ninomiya T, Ninomiya T, Hirakawa Y, Mukai N et al. Haemoglobin A1c even within non-diabetic level is a predictor of cardiovascular disease in a general Japanese population: the Hisayama study. *Cardiovasc Diabetol* 2013;12:p164.
12. Sharma M, Ganguly NK (2005) Premature coronary artery disease in Indians and its associated risk factors. *Vasc Health Risk Manag* 2005;1:p217.
13. Mehraj I, Yousuf IW, Aslam K, Masoodi S, Wani YY. Association of HbA1c with prevalence and severity of coronary artery disease in diabetic and nondiabetic patients in Kashmir. *Asian J Sci Technol* 2014;5(3):230–232.
14. Krishnan MN, Zachariah G, Venugopal K, Mohanan PP, Harikrishnan S, Sanjay G et al. Prevalence of coronary artery disease and its risk factors in Kerala, South India: a community-based cross-sectional study. *BMC Cardiovasc Disord* 2016;16:1-5.
15. Mishra TK, Das B. ST-segment elevated acute myocardial infarction: changing profile over last 24 years. *Assoc Phys India* 2016;64:p28.
16. Patil VC, Patil S, Sabale S, Agrawal V, Mhaskar D. Study of percutaneous coronary intervention in patient with coronary artery disease at tertiary care teaching hospital. *JKIMSU*. 2015;4:82–93.
17. Ramakrishnan S, Mishra S, Chakraborty R, Chandra KS, Mardikar HM. The report on the Indian coronary intervention data for the year 2011– National Interventional Council. *Indian Heart J* 2013;65:518–21.
18. Nanayakkara PGCJ, Weeraratna TP, Herath HMM, Kariyawasam AGTA, Ganegoda VR. Value of testing glycosylated hemoglobin in non-diabetic patients presenting with acute coronary syndrome. *Sri Lanka Journal of Diabetes, Endocrinology and Metabolism* 2015; 5(1): 4-7.
19. Dubey G, Verma SK, Bahl VK. Primary percutaneous coronary intervention for acute ST-elevation myocardial infarction: outcomes and determinants of outcomes: a tertiary care Centre study from North India. *Indian Heart J*. 2017;69:294–98.
20. Hsia RY, Shen YC. Percutaneous coronary intervention in the United States: risk factors for untimely access. *Health Research and Education trust* 2016;51(2):592–609.