Original Article ISSN (O):2395-2822; ISSN (P):2395-2814

To Determine the Correlation of HbA1c Level in Patients with Acute Coronary Syndrome.

Sharma T[1], Singh Y[2], Singh M[3], Saxena S.R[4], Joshi A[5]

[1]Junior Resident, Department of General Medicine, STGH Haldwani
[2]Assistant Professor, Department of General Medicine, STGH Haldwani
[3]Associate Professor, Department of General Medicine, STGH Haldwani
[4]Professor, Department of General Medicine, STGH Haldwani
[5]Professor and HOD, Department of General Medicine, STGH Haldwani

Received: January 2020
Accepted: January 2020

ABSTRACT

Background: Acute coronary syndrome (ACS) has emerged most important cause of death worldwide. Diabetes Mellitus (DM) is a major risk factor for ACS. Glycated Hemoglobin (HbA1c) levels are predictive of cardiovascular disease in patients with diabetes mellitus, however, association of HbA1c with in non-diabetics is inconsistent. Aim and Objective: To determine the correlation of HbA1C level in patients with acute coronary syndrome. **Methods:** This observational cross-sectional study included 150 patients who were admitted with symptoms suggestive of ACS. The diagnosis of ACS was made on the basis of Troponin T value, electrocardiogram (ECG), and echocardiograph (2D-Echo). Patients were stratified according to their HbA1c into two groups: Group 1 HbA1c <6.5% (53.3%), Group 2 HbA1c >6.5% (46.7%). Main outcome measures were ECG changes (ST-segment elevation myocardial infarction or non-ST-segment elevation myocardial infarction), troponin T value and left ventricular ejection fraction on echo. Data were analysed using IBS SPSS (statistical package for Social Sciences) Version 24.0. **Results & Conclusion:** The mean age was 59±12 years. Out of 150 patients, 29(19.3%) patients were diabetics, 27(18.0%) patients were hypertensive. The most common complications were shock 27(18.0%) followed by 8(5.5%) patients had congestive heart failure, 7(4.7%). Post ACS complications were seen more with high HbA1c values.

Keywords: ACS, HbA1c, Myocardial Infarction, DM.

INTRODUCTION

Acute coronary syndrome (ACS) is a syndrome due to decreased blood flow in the coronary arteries such that part of the heart muscle is unable to function properly or dies.[1] The most common symptom is chest pain, often radiating to the left shoulder or angle of the jaw, crushing, central and associated with nausea and sweating.[2] Many people with acute coronary syndromes present with symptoms other than chest pain, particularly, women, older patients, and patients with diabetes mellitus.[3] Acute coronary syndrome is commonly associated with three clinical manifestations, named according to the appearance of the electrocardiogram (ECG): ST elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (NSTEMI), or unstable angina.[4,5] Plasma haemoglobin A1c (HbA1c) reflects mean ambient fasting and postprandial glycaemia over a 2–3 months period. HbA1c is formed by the slow irreversible, non-enzymatic glycation of valine and lysine residues in the haemoglobin molecule.[6] It is a useful test for characterising dysglycemia as it is easier to perform than an oral glucose tolerance test and is independent of patients prandial status.[7,8] It has been shown conclusively that a reduction in plasma HbA1c levels below 7%, leads to a lower incidence of microvascular complications in both type 1 and type 2 diabetes mellitus.[9,10] Concomitant occurrence of hyperglycemia in patients presenting with ACS (Acute coronary syndrome) enhances the risk of mortality and morbidity, whether the patient has diabetes or not.[11] Among patients presented with ACS with no prior history of diabetes, hyperglycemia may reflect previously undiagnosed diabetes, stress-related carbohydrate intolerance, or a combination of these.[12]

Name & Address of Corresponding Author
Dr. Yatendra Singh,
Assistant Professor,
Department of General Medicine,
STGH
Haldwani.

MATERIALS AND METHODS

This cross sectional study was done in the department of medicine, Government Medical College and associated Dr. Susheela Tiwari

Government Hospital, Haldwani (Nainital) from September 2017 to August 2019. A total of 150 cases admitted in CCU with complaints of typical chest pain and diagnosed as ACS and divided into two groups: group 1(HbA1c>6.5%) and group 2(HbA1c<6.5%). Patients belonging to age group of 30-95 years were selected. Patients with non-cardiovascular causes for the clinical presentation such as trauma, major surgery aortic aneurysm, CHF, renal insufficiency, hepatic insufficiency, and extensive comorbidities, Patients with past history of ACS, All those patients were excluded who were not properly worked up or who were prematurely discharge (LAMA) were excluded from the study. Acute coronary syndrome includes a) ST-Segment Elevation Myocardial Infarction (STEMI), a condition for which immediate reperfusion therapy should be considered, b) Non-ST-Segment Elevation Myocardial Infarction (NSTEMI), c) Unstable angina. After screening, details of patients with regard to symptoms, medical history, and history of smoking were collected. All patients underwent thorough physical examination and the biochemical investigation. They included HbA1c, serum troponin-T, creatinine kinase-MB (CKMB), electrocardiogram (ECG), and echocardiography. Symptoms of ACS included chest pain, shortness of breath, nausea, vomiting, palpitations, sweating, and anxiety. ACS was established on at least two of the following characteristic symptoms, electrocardiographic changes, troponin-T was measured. Statistical analysis: Mean ± standard deviation was reported for continuous variables, and percentages (number) were reported for categorical variables. Continuous variables were compared using unpaired Student's t-test, and categorical variables were compared using Chi-square tests. All comparisons were two-tailed and P < 0.05 was considered statistically significant. The entire analysis was performed with Statistical Package for the Social Sciences (SPSS) version 24.0.

RESULTS

Table 1: Association between HbA1c and Gender

Gender	HbA1c < 6.5 (n=80)	HbA1c ≥ 6.5 (n=70)	Total (n=150)
Males	58 (72.5%)	46 (65.7%)	104 (69.3%)
Females	22 (27.5%)	24 (34.3%)	46 (30.7%)

Chi Square Value = 0.808; p-value = 0.369

There was no association between gender and HbA1c (p = 0.369). [Table 1]

Table 2: Association between HbA1c and Age

Age (Years)	HbA1c < 6.5 (n=80)	HbA1c ≥ 6.5 (n=70)	Total (n=150)
< 41	6 (7.5%)	6 (8.6%)	12 (8%)
41 – 50	16 (20%)	8 (11.4%)	24 (16%)
51 – 60	24 (30%)	23 (32.9%)	47 (31.3%)
61 – 70	19 (23.8%)	22 (31.4%)	41 (27.3%)
71 – 80	12 (15%)	9 (12.9%)	21 (14%)
> 80	3 (3.8%)	2 (2.9%)	5 (3.3%)

Chi Square Value = 2.882; p-value = 0.718

There was no association observed in age group and HbA1c (p=0.718). [Table 2]

Table 3: Association between HbA1c and Diabetes Mellitus

Diabetes Mellitus	HbA1c < 6.5 (n=80)	HbA1c ≥ 6.5 (n=70)	Total (n=150)
Yes	3 (3.8%)	26 (37.1%)	29 (19.3%)
No	77 (96.3)	44 (62.9)	121 (80.7)

Chi Square Value = 26.693; p-value = 0.0001

In our study, it was observed that patients - 26 (37.1%) had significantly higher diabetes history in HbA1c ≥ 6.5% group as compared to 3 (3.8%) patients in HbA1c < 6.5% group and this difference was statistically significant (p=0.0001). [Table 3]

Table 4: Association between HbA1c and Hypertension

Hypertension	HbA1c < 6.5 (n=80)	HbA1c ≥ 6.5 (n=70)	Total (n=150)
Yes	6 (7.5%)	21 (30%)	27 (18%)
No	74 (92.5%)	49 (70%)	123 (82%)

Chi Square Value = 12.805; p-value = 0.0001

In acute coronary syndrome patients, it was observed that patients - 21 (30%) had significantly higher hypertension history in HbA1c ≥ 6.5% group as compared to 6 (7.5%) patients in HbA1c < 6.5% group and this difference was statistically significant (p=0.0001). [Table 4]

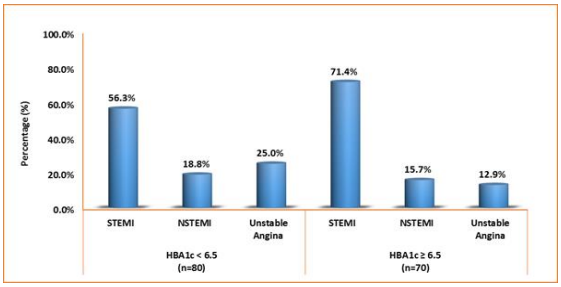

Figure. 1: Association between HbA1c and ACS

Chi Square Value = 4.404; p-value = 0.111

In HbA1c < 6.5 group, 45 (56.3%), 15 (18.8%) and 20 (25.0%) patients were diagnosed with STEMI, NSTEMI and unstable angina respectively whereas in HbA1c ≥ 6.5 group, 50 (71.4%), 11 (15.7%) and 9 (12.9%) were diagnosed with STEMI, NSTEMI and unstable angina respectively. There was no statistically significant difference observed between HbA1c groups on the basis of ACS classification (P=0.111) [Figure 1].

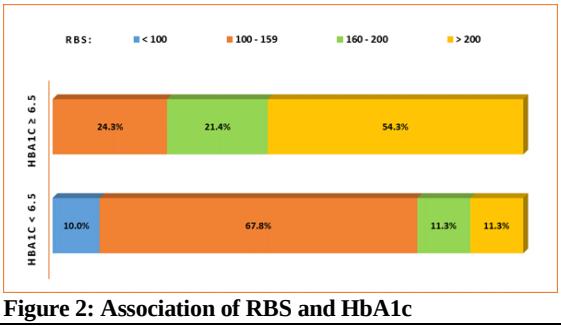

Figure 2: Association of RBS and HbA1c

Chi Square value = 46.214, p-value < 0.0001

Present study revealed that higher RBS value was associated with higher HbA1c value. In HBA1c ≥ 6.5% group, 38 (54.3%) patients had RBS value > 200 whereas 9 (11.3) patients had RBS value > 200 in HBA1c < 6.5% group. [Figure 2]

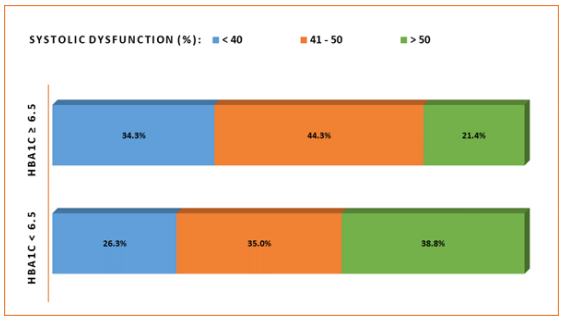

Figure 3: Correlation between Systolic Dysfunction (%) and HbA1c

Chi Square Value = 5.275, p-value = 0.072

Systolic Dysfunction (%) was not associated with HbA1c (p-value = 0.072). [Figure 3]

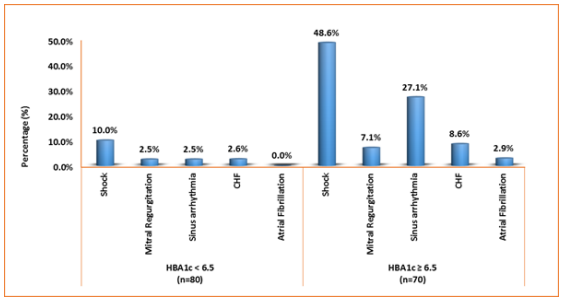

Figure 4: Association between HbA1c and ACS Complications

Chi Square Value = 20.230; p-value = 0.003

In our study, significantly higher complication rate was observed in HBA1c ≥ 6.5 group (36, 51.4% patients) as compared to HBA1c < 6.5 group (14, 17.5% patients). Shock was most common complication in acute coronary syndrome patient, 19 (27.1%) and 8 (10.0%) patients had shock in HBA1c ≥ 6.5 group and HBA1c < 6.5 group respectively. [Figure 4]

DISCUSSION

In our study, 104 (69.3%) were male and 46 (30.7%) were females. The ratio of male and female population was nearly same in our study as in the studies done by Ashraf B.K et al 2019, R. Guven et al 2017, Sebastian T. Lugg et al 2017, Sushil Singh, et al 2016, and Y. Ramesh Naidu, et al 2015. One possible reason for this may be increased propensity of the use of alcohol and smoking by male in our society. Neither there were any previous studies nor present study suggested any correlation between HbA1C and gender (p-value 0.369).[13-16]

In the present study the mean and SD of age was 59 year (30 - 95). In patients having HbA1c < 6.5% their mean value of age was 59.3 year. Patients having HbA1c ≥ 6.5% had mean value of age 59.8 year. While in the studies by Ashraf B.K et al 2019, R. Guven et al Sebastian T. Lugg et al 2017, Sushil Singh et al 2016, Y. Ramesh Naidu et al 2015, Mean age of the patients was 61.5 year ¬, 46.6 years, 65 years, 58.67 years and 57.68 years respectively.[13-15,17] In present study no significant correlation was found between HbA1C and age (p-value 0.718).

In the present study 29 out of 150 were having past history of diabetes mellitus. Out of them 26 (37.1%) had HbA1c >6.5 %. This finding does not need any explanation. As raised HbA1c level was expected in known case of diabetes mellitus. Out of 121 non diabetics, 44 (62.9 %) have HbA1c >6.5 %. All these patients might be having diabetes which was not known to them. The preponderance of non-diabetics was almost 4 times higher than that of diabetics, this finding was surprising. If those patients with HbA1c >6.5% without past history of diabetes should be considered as newly diagnosed diabetes mellitus, the presence of ACS in them was found 62.9%. This finding was similar to study done by Ashraf B.K et al 2019.[14] In his study 58% patients were non diabetics.[15] Our study findings did not match with the study done by Sebastian T. Lugg et al 2017, R. Guven et al 2017. In their study non diabetics were 25.1% and 23% respectively.[15,17] In present study significant statistical correlation found between diabetes mellitus and HbA1c (p value 0.0001).

In the present study, 27 (18.0%) out of 150 patients were hypertensive, out of them 21 (30%) had HbA1c ≥ 6.5%. Our findings were similar to a study done by Sushil Singh et al in year 2016, Y. Ramesh Naidu, et al. in year 2015, in which 33% and 65% were known to be hypertensive respectively.[13,16] In the present study significant correlation was found between hypertension and HbA1c (p value = 0.0001).

In our study majority of the patients 95 (63.4%) were found with STEMI. In group of HbA1c ≥ 6.5% maximum number of patients were having STEMI 50 (71.4%), followed by NSTEMI 11(15.7%) and Unstable Angina 9 (12.9%). Though our study has similar results with the studies done by Sushil Singh et al 2016, Y. Ramesh Naidu et al 2015, patients of STEMI : 74% & NSTEMI : 26%, STEMI: 44(44%) & NSTEMI 27(27%) and Unstable Angina29(29%) respectively.[13,16] But our study results did not match with the study done by Ashraf B.K et al., 2019. He had 12%, 63% and 24.5% patients of Unstable angina, NSTEMI and STEMI respectively.[14] In present study no statistical correlation was found between ACS and HbA1C value (p-value 0.111).

Present study revealed that higher RBS value was associated with higher HbA1c value. In HbA1c ≥ 6.5% group, majority of patients 38 (54.3%) had RBS value > 200. Mean RBS value was significantly higher (223.6±91.7) in HbA1c ≥ 6.5% group as compared to HbA1c < 6.5 group (140.3±42.5). According to a study by P. Karki et al in 2015, The RBS (mg/dl) >200 in 75.00% patients.[18] Present

study found statistically significant correlation between RBS and HbA1c (p-value = 0.0001).

In our study, more systolic dysfunction was found in HbA1c>6.5% group. Out of 70 patients, with HbA1c > 6.5%, 31(44.3%) and 24(34.3%) were having reduce ejection fraction of 41%-50% and <40% respectively, Only 15(21.4%) patients had normal ejection fraction (>50%). In contrast out of 80 patients, with HbA1c < 6.5%, 28(35%) and 21(26.3%) were having reduce ejection fraction 41%-50% and <40% respectively, only 31(38.8) patients had normal ejection fraction (>50%). In present study mean LVEF was found to be 44.8±9.2. According to a study by Sushil Singh et al in 2016, mean LVEF was 42.64%.[13] Higher HbA1c was associated with more reduced ejection fraction but this finding was not statistically significant (p-value = 0.072).

In our study, risk of complication was high in HbA1c>6.5% group. Majority of patients 27(18.0%) were having the complication of shock, followed by other complications such as CHF 8(5.3%), Mitral Regurgitation 7(4.7%), Sinus Arrhythmia 6(4.0%), Atrial Fibrillation 2(1.3%). Hundred (66.6%) patients did not had any complication. Risk of complications in ACS were significantly high in HbA1c ≥ 6.5% group. In high HbA1c group 19 (27.1%) Shock, 6 (8.6%) Congestive heart failure, 5 (7.1%) Mitral regurgitation, 4 (5.7%) Sinus arrythmia, 2 (2.9%) Atrial Fibrillation was seen. As per the study done by Ashraf B.K et al 2019.[14] Y. Ramesh Naidu et al, most common complication was cardiac failure followed by shock.[16] Where as in present study commonest complication was shock followed by congestive heart failure. In both studies complications rate was high in high HbA1c group. Complications of ACS reflect quantum of myocardial damage. Probably Higher HbA1C indirectly reflects more myocardial damage. Our study had significant correlation between complications and HbA1c (p-value <0.03).

CONCLUSION

Cardiovascular disease was commonest cause of death. In whom Raised blood sugar level which was reflected by raised HbA1c promote atherosclerosis and endothelial dysfunction. Raised HbA1c level was found to be a risk factor for acute coronary syndrome (ACS) irrespective of sex (males and females were equally affected). Use of smoking and alcohol may be an added risk factor in males. Although a raised HbA1c level was favouring more possibility of STEMI. However, this was not found to be statically significant. The author recommended a further study with large number of patients to establish any correlation between HbA1c level and NSTEMI. Diabetics were prone for ACS. However, diabetics with raised HbA1c levels were more prone for ACS. The burden of ACS decreased with reduction of HbA1c level even in diabetics, although a significant correlation between HbA1c and hypertension was found. This suggested that usually the various risk factor go together like obesity, raised blood sugar levels, alcohol, smoking etc. Smoking and alcohol was associated with higher HbA1c levels. Again, this suggested that ACS was result of multiple syndromic factors like hypertension, obesity, raised blood sugar etc. The present study suggested some correlation between raised HbA1c level and extent of myocardial damage. It was observed that raised HbA1c was associated with high troponin value. Therefore post ACS complications (shock, CHF, mitral regurgitation, sinus arrythmia) were seen more with high HbA1c values. There was an indirect positive correlation between raised HbA1c and myocardial damage. A further study with large number of patients could throw more light on this scenario. Decision for thrombolysis was independent of HbA1c value. High HbA1c level was also associated with more systolic dysfunction. Again, this support the thought that high HbA1c was somehow related with greater myocardial damage. Poor morbidity was seen in ACS with raised blood sugar level. HbA1c was more precise method of detecting chronically elevated blood sugar and therefore could be substituted for estimation of blood sugar level in patients of ACS.

REFERENCES

1. Amsterdam, E. A.; Wenger, N. K.; Brindis, R. G.; Casey, D. E.; ,Ganiats, T. G.; Holmes, D. R.; et al., "2014 AHA/ACC Guideline for the Management of Patients With Non-ST Elevation Acute Coronary Syndromes: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines". Circulation. 130 (25): e344–e426.
2. Goodacre S, Pett P, Arnold J, Chawla A, Hollingsworth J, Roe D, et al., "Clinical diagnosis of acute coronary syndrome in patients with chest pain and a normal or non-diagnostic electrocardiogram". Emergency Medicine Journal. 26 (12): 866–870.
3. Canto JG, Shlipak MG, Rogers WJ et al (June 2000). "Prevalence, Clinical Characteristics, and Mortality among Patients with Acute Myocardial Infarction Presenting Without Chest Pain". JAMA. 283(24): 3223–3229.
4. Grech ED, Ramsdale DR et al (June 2003). "Acute coronary syndrome: unstable angina and non-ST segment elevation myocardial infarction". BMJ. 326 (7401): 1259–61.
5. Torres M, Moayedi S et al (May 2007) et al "Evaluation of the acutely dyspneic elderly patient". Clin. Geriatr. Med. 23 (2): 307–25, vi. doi:10.1016/j.cger.2007.01.007
6. Krishnamurti, U. and Steffes, M.W.et al Glycohemoglobin: a primary predictor of the development or reversal of complications of diabetes mellitus. Clin Chem. 2001; 47: 1157–1165
7. Khaw, K.T., Wareham, N., Bingham, S., Luben, R., Welch, A., and Day, N. et al Association of hemoglobin A1c with cardiovascular disease and mortality in adults: the European prospective investigation into cancer in Norfolk. Ann Intern Med. 2004; 141: 413–420
8. Barr, R.G., Nathan, D.M., Meigs, J.B., and Singer, D.E. et al Tests of glycemia for the diagnosis of type 2 diabetes mellitus. Ann Intern Med. 2002; 137: 263–272
9. The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med 1993;329:977-86.

10. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood glucose control with sulfonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet 1998;352:837-53.
11. Ceriello A. Acute hyperglycaemia: a 'new' risk factor during myocardial infarction. European Heart Journal 2005;26(4): 328–331.
12. Ertem AG, Bagbanci H, Kilic H et al. Relationship between HbA1C levels and coronary artery severity in nondiabetic acute coronary syndrome patients. Archives of Turkish Society of Cardiology 2013 Jul;41(5):389-395
13. Singh S, Bansal M, Rani K, Gupta V. Prognostic significance of glycosylated hemoglobin in nondiabetic patients in acute coronary syndrome. Heart India 2016;4:17-22
14. Ashraf B.K., Jacob K , George jilse, Samuel suma, Bhagyanath T et al: A study of the relation of HbA1c levels in acute coronary syndrome and its complications, JMSCR Volume 07 Issue 02 February 2019
15. Guven R, Güzinaykal, Gungor F, K. Canakyol, Bayar N et al: Acta Medica Mediterranea, 2017, 33: 123.
16. Naidu YR, Sharmila Y, Nischal Y, Srinivas V, Satyaprasad Vet al: "Study of HbA1c levels in Acute Coronary Syndrome". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 77, September 24; Page: 13274-13278.
17. Lugg et al. HbA1c screening for new onset diabetes following acute coronary syndrome: is it a worthwhile test in clinical practice? Journal of Diabetes & Metabolic Disorders (2017).
18. Vupputuri A, Sekhar S, Krishnan S, Venugopal K, Natarajan KU et al: Heart-type fatty acid-binding protein (H-FABP) as an early diagnostic biomarker in patients with acute chest pain, indian heart journal 67(2015) 538 – 542.

How to cite this article: Sharma T, Singh Y, Singh M, Saxena SR, Joshi A. To Determine the Correlation of HbA1c Level in Patients with Acute Coronary Syndrome. Ann. Int. Med. Den. Res. 2020; 6(2):ME26-ME30.

Source of Support: Nil, **Conflict of Interest:** None declared