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Original Research Article

CORRELATION OF HBA1C LEVELS WITH SEVERITY AND PROGNOSIS OF ACUTE CORONARY SYNDROME

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ABSTRACT

Background: Diabetes remain major cause of cardiovascular diseases on long term. Relationship between cardiovascular atherosclerotic changes and glucose metabolic defects has drawn lot of attention in recent decades. Elevated HBA1c levels associated with increased risk of both microvascular and macrovascular complications. The aim of our study was to investigate the relationship between HbA1c levels with severity, morbidity and mortality in patients with acute coronary syndrome.

Methodology: Observational study was conducted and all patients diagnosing as Acute coronary syndrome was assessed for clinical history and examination. ECG,CPK-MB, Trop -I and 2D -echocardiography were done.HBA1c was send irrespective of diabetes status.

Results: Mean age of patients was 58.34 with male predominance (72%). 56% patients have found HBA1c levels in diabetic range out of which 11% were newly diagnosed. CCF was three times higher in patients with HbA1c level >6.5 as compared to those with Hba1c level <6.5.Mortality rate was no significantly higher in those with higher HBA1c levels.

Conclusion: High level of HBA1c (>6.5) indicating diabetes at the time of admission was associated with multiple morbidities like CCF, Left Ventricular dysfunction and reduced ejection fraction. But, no significant mortality difference was seen at 7 day follow up .

Keywords: ECG: electrocardiography, CCF: congestive cardiac failure

1. INTRODUCTION:

The prevalence of Diabetes mellitus (DM) has increased dramatically worldwide over the last two decades.[1] Compared to non-diabetic population ,diabetic patients have 2 to 4 folds increased risk of benign/malignant coronary artery disease,[2] there is 2 fold higher risk of short term(early) mortality after an acute Myocardial Infarction[3] and poorer outcome when these patients going for angioplasty ,with increased restenosis risk.[4] Pathophysiological basis shows diabetic individuals have reduced response to endothelium dependent vasodilation and markedly increased platelet reactivity, with submaximal response achieved by antithrombotic therapy, all these factors may responsible to development and progression of atherosclerosis, ACS and post ACS complications.[5] Although, traditional CV risk factors including hypertension, dyslipidemia and obesity are more frequent in diabetic population, there are some evidence for an independent role of hyperglycemia on atherosclerosis.[6]

HBA1c is an established marker of previous and long term glycemic status of pts with Diabetes Mellitus(DM), and elevated HBA1c levels are associated with the increased risk for further microvascular and macrovascular complications.[7] Studies have predominantly shown that the optimal glycemic control (defined by as HBA1c 7%) results in lower microvascular

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complications incidence in both DM I and DM II.[8] HbA1c assay measurement has many advantages over plasma glucose measurements, including lower biological variability and the test results are least affected by fasting and acute stress. Diabetic patients with early glucometabolic defects may have normal fasting and deranged post prandial levels, which can be better evaluated by HBA1c. As per guidelines given by American Diabetes Association (ADA) in 2016 following categories subscribed to HbA1c levels: HBA1c <5.7% normal/nondiabetic,HBA1c between 5.7%-6.4% prediabetic and HBA1c ≥6.5 as diabetes. Atherosclerotic coronary artery disease(CAD) is responsible for majority of the increased poor prognosis in diabetes pts and many different studies had recognized cardio-vascular complications as to be partially or mostly dependent on long-standing nearly constant hyperglycemia. The early detection of diabetes by screening as an effective secondary preventive measure for newly admitted patients with acute coronary syndrome(ACS).[9]
Given the high and ever increasing rates of diabetes and cardiac problems in Indian population and lack of enough research in Indian rural area, our study aims at establishing relationship between blood levels of Hba1c with severity , complications and 7 day mortality of patients presenting with ACS.

2. MATERIAL AND METHODS

The observational study was conducted at Index Medical College and Hospital over 12 month duration. All patients diagnosing as Acute coronary syndrome were taken into consideration. The data was collected prospectively and systematically in a pre established proforma after informed written consent. History and thorough clinical examination was done. ECG ,CPK-MB, Trop I, 2D Echocardiography were done in all patients.
Acute Coronary Syndrome includes the following diagnosis: Unstable angina ,Non ST elevation myocardial infarction (NSTEMI), and ST elevation Myocardial infarction (STEMI). Symptoms of ACS includes chest pain, shortness of breath, nausea, vomiting, palpitations, sweating, and anxiety. To diagnose ACS at least two of the following : characterstic symptoms, electrocardiographic changes, and typical rise and fall in biochemical parameters (troponin ,CPK-MB) were taken into consideration.
HBA1c was measured by High performance liquid chromatography (HPLC)method in a NABL accredited laboratory. American Daibetic association guidelines were used to cateroize pts as: HBA1c < 5.7 normal/nondiabetic,5.7-6.4% Prediabetic and ≥6.5 Diabetes. Severity and prognosis of ACS was assessed by 2D echo as wall motion abnormalities (hypokinetic, akinetic, dyskinetic), LVEF and development of complications like CCF, reduced ejection fraction, diastolic dysfunstion including death in 7 days.

Statical analysis:
Data was analysed using a computer based statistical analysis programme, SPSS (Statistical Program for Social Sciences) version 22.0. The Chi-square test was used wherever comparisons were needed between the two groups for categorical variables and Student's T test was used for continuous variables. A p value < 0.05 was considered significant.

3. RESULTS:

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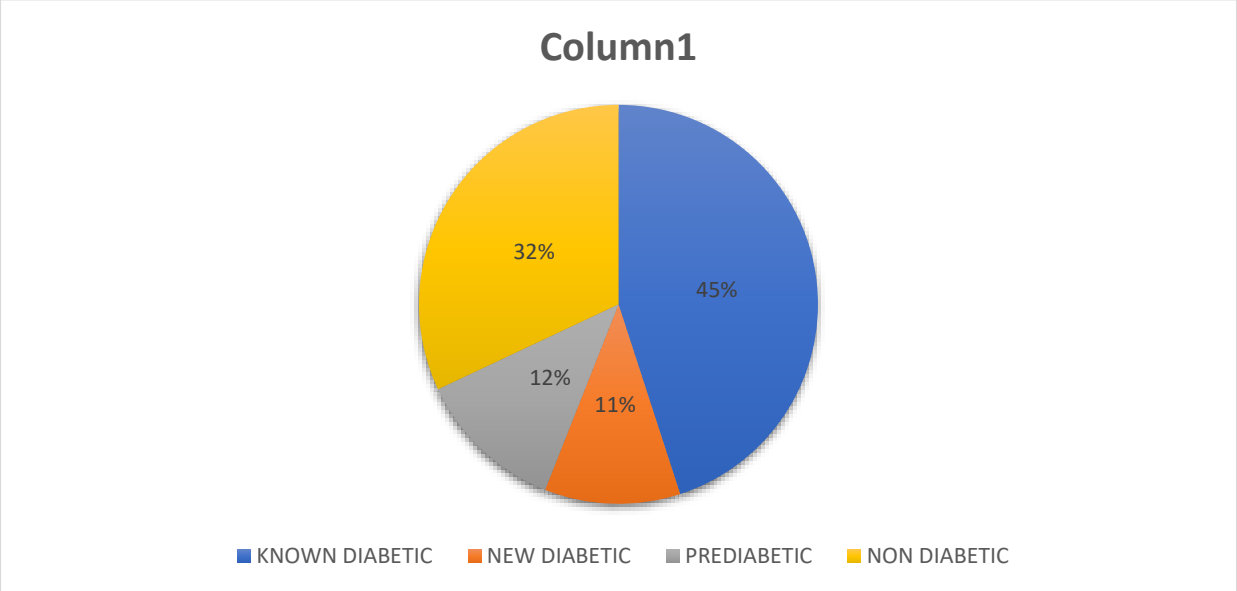
In our study, mean age was found as 58.3 with standard deviation of 9.037 and standard error as 0.904. Median and mode 58 and 54 respectively. Maximum and minimum age of patient diagnosed as ACS was 81 and 42 respectively. Maximum patients (40%) belong to age group 50-59 year with male predominance (72%). We found 5% were hypotensive with systolic BP <90mmHG and 20% were Hypertensive with systolic BP >140 mmHG. Severe hypertension BP >160/100mmHg found in 7% of patients. In our study, irrespective of diabetic status, 60% patient had FBS>126 mg/dl, 5% had Fasting glucose level in range of impaired glucose tolerance i.e. 100-125 mg/dl and 35% had FBS <100 mg/dl while post prandial glucose show similar percentage of diabetics ,there is increase in Impaired glucose tolerance range from 5 % to 8% and 32% were have PPBS <140mg/dl. In our study, most patients had ECG changes showing Anterolateral wall ischaemia (65%) followed by inferolateral(12%) and anteroinferolateral wall ischaemia(8%). 77% patients had positive troponin values suggesting MI and 23 % had negative indicating Unstable angina. STEMI was most common among ACS(53%) following unstable angina(24%) and NSTEMI (23%) with minor difference.

In rural area of our study ,45% were known diabetic, mostly on irregular medication, then 32% were non diabetic. The percentage of newly diabetes were 11% and 12% subjects fall under group of prediabetes.so, overall diabetic status were found in 66%. LV Dysfunction with EF < 40% were found in 39% patients out of which 31 % of patient belong to > 6.5 Hba1c group. When diastolic dysfunction and reduced EF was correlated with HBA1c, LV Dysfunction was significantly associated with diabetes as compared to other group(p value 0.003). Development of CCF as complication secondarily to ACS were seen in only 8% out of which 6% have raised Hba1c levels, and on 7 day follow up frequency of death were found 8% in total with 5 % in raised group and 3% in ≤6.4 group. CCF was three times higher in patients with Hba1c >6.5 as compared to those with hba1c ≤6.4.CCF was significantly found in diabetic population as compared to other(p value 0.005). Mortality rate was no significantly higher in those with higher Hba1c levels(p 0.08).



STATUS OF DIABETES IN ACS PATIENTS

COMPLICATIONS	HBA1C ≤6.4	HBA1C>6.5

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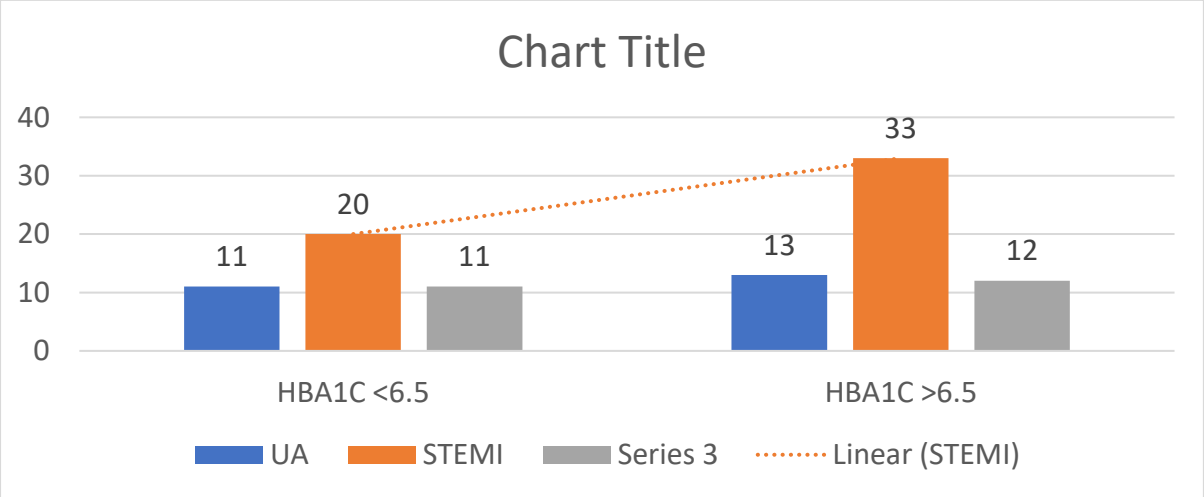
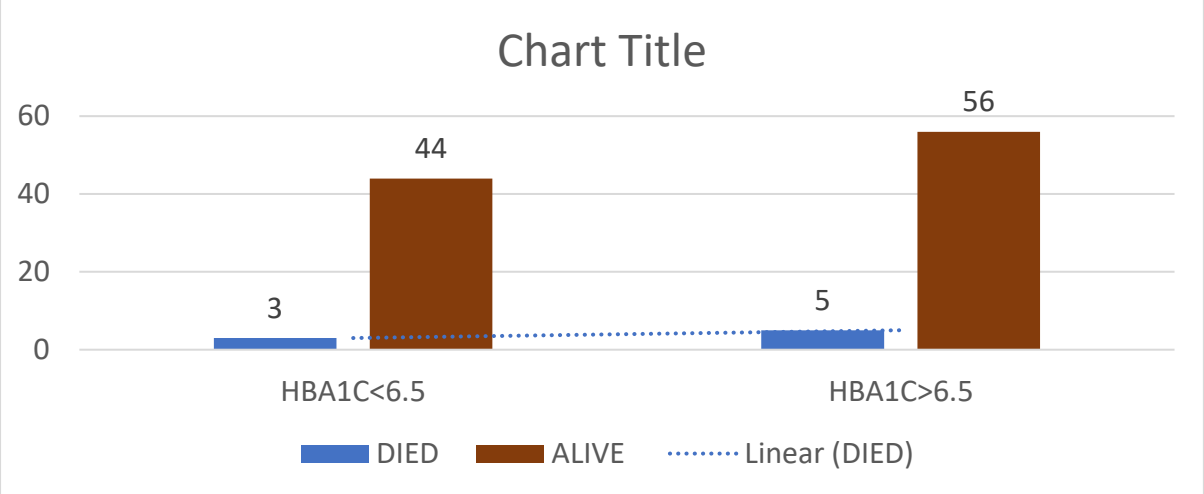
CCF	2%	6%
Reduced EF	8%	31%
Mortality	3%	5%

PERCENTAGE OF COMPLICATIONS IN RELATION TO HBA1C LEVELS



DISTRIBUTION OF DIAGNOSIS IN RELATION TO HBA1C LEVELS



TRENDS OF MORTALITY IN RELATION TO HBA1C

4. DISCUSSION:

Diabetes is associated with an increased risk of MI. Across the broad spectrum of Acute coronary syndrome events, in which diabetes may affect more than 1 in 3 patients, those with diabetes mellitus have worse CVD outcomes after ACS events. Despite overall improvements in and without diabetes, the gradient of risk involved with diabetes persists, although incremental trend of in-hospital mortality risk, associated with diabetes after an ACS event, has declined. Furthermore, the graded association of increased risk seen with diabetes in the presence of ACS extends to glucose values in the range well below the diabetes threshold.

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Apart from CHD, diabetes also increases risk of stroke,cerebrovascular disease and peripheral artery disease.[10] DM is associated independently with two-fold to fivefold increased risk of HF over that in persons without diabetes, and patients with diabetes have worse outcomes once failure has developed. The mechanism by which hyperglycemia may increase atherosclerotic risk remain poorly understood, but given the associations between severity of hyperglycemia in serum and risk for atherosclerosis in both type I and type II DM, it probably directly influences atherosclerosis development, progression and instability. The hyperglycemia cause endothelial vasomotor dysfunction, vascular damage by AGE (advanced glycation end) products, adverse effects of circulating amount of free fatty acids, increased systemic inflammation and a pro-thrombotic state. Endothelial vasomotor dysfunction, a hallmark of diabetic vascular disease, is documented with increased hypertension and adverse CVD outcome.[11,12]

In our study, mean age of patients is 58.3 mode 54 while median is 58. Majority of ACS patients lied in age group of 40-70 years. 72 % were male and 28% were female. In a study by Bornali Dutta et al.,HBA1c correlation in nondiabetic patients, mean age was 58.1 out of these 91.9% were males.[13] Data analysis of our data revealed that FBS in 35% patients were normal,5% level had FBS level in prediabetic level while 60% had diabetes. 32% of patients had PPBS level less than 140, level of 8% was between 149-199,while more than 200 were seen in 60% patients. In our study ,45% were known diabetes with inadequate medication and monitoring while 11% were newly diagnosed as diabetic. In a study by McCune C et al, HBA1c for diabetes screening in acute coronary syndrome: Time for a reappraisal(change) of the guidelines,93of 420 (22%) ACS patients were diagnosed as established diabetes. Out of remaining number of patients ,only 8 individuals (2.4) fulfil nice criteria for DM screening. During this phase of service improvement, 17 out of total 66 screened ACS patients had established DM and the remaining 49 screened patients only 2 met criterion for screening and no patients had tested for fasting glucose. 26 out of 49 ACS patients(52%) were tested for Hba1c and found with mean level of HBA1c 45.1mmol/mol (with range of 31.1 to65 mmol/mol). ECG reports revealed that 5% had anterior wall ischemia , 4% had inferior wall ischemia , 65% had anterolateral ischemia , 12% had inferolateral ischemia, 8% had anteroinferolateral ischemia , 4% had anteroseptal ischemia , and 2 5 had inferoseptal ischemia. Level of troponin were positive in 77% patients.53% patients were diagnosed with STEMI, followed by unstable angina in 24% and NSTEMI in 23% of patients.[14]

In a study by MOHAMMED S. KASEM et al , Value of Glycated Hemoglobin (HbA1c%) as an Indicator of Severity of Acute Coronary Syndrome in Non- Diabetic Adults when patients were distributed according to ACS presentatation, we found that nearly two thirds (65.8%) of them were presented with NSTEMI and one sixth (17.1%) of them presented with Unstable Angina.[15] LVEF was less than 40% in 29% patients. Left ventricular dilatation was diagnosed in 20% patients. CCF (Congestive Cardiac Failure) was diagnosed in 8% of patients . Mohammed s. kasem et al, study revealed that more than half of patients(56.1%) had Efraction (LVEF%) <50% by Simpson method. As regard diastolic dysfunction, grade 1 ,diastolic dysfunction represented 71.5%,grade 2 represented 25.2 %,grade 3 represented 3.3% of study patients.

S Ghaffari,F. Niafar et al. in study, association between HBA1c levels with severity of coronary artery disease and short term outcomes of Acute ST-elevation Myocardial infarction in non-diabetic patients, found out that the median for HBA1c levels was 5.8 % with interquartile range 5.5 % to 6.1%. They selected ,the median 5.8% as the cut off value to make their study comparisons. There were 148 pts in the LOW group (HBA1c <5.8) and 142 pts in the HIGH group (HBA1c >5.8 %).Among inpatients group ,at the time of admission

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RBS were 130+-68 mg/dl .[16] Among those with HBA1c <6.4, 11% had unstable angina ,20% had STEMI ,11% had NSTEMI, while in those patients with high level of hBA1c comparatively greater percentage of patients had these diagnosis in each category. Those with lower level of HBA1c (<6.4%) had 5% rate of left ventricular dilatation in comparence to 15% in the group with high level of HBA1c. 8% of those patients with hba1c <6.4 had ejection fraction less than 40% as compared to 32% of pts with HBA1c level >6.5%. Mortality rate and percentage was no significantly higher in the pts with higher hba1c level. Right ventricular heart failure secondary to left sided damage presenting as CCF was 3 times higher in the patients with HBA1c level >6.5 as compared to those group with HBA1c level <6.4.

Relationship of higher Hba1c level in patients presenting with ACS and its importance in predicting the prognosis of patients remains controversial. There are so many studies with different results. Lazzerri et al. study reported that HBA1c level was not significantly associated with mortality rate in STEMI with already known diabetes undergone for mechanical revascularization either PCI or CABG.[17] Cicek et al. showed that level of HBA1c was an important and independent predictor of in-patient death and high mortality rate in STEMI patients managed with PCI after adjusting baseline characterstics.[18] Timmer et al. study found that increased HBA1c levels were usually associated with increase all mortality rates when followed for an average 3.3 years in 4,176 nondiabetic patients with STEMI managed with PCI.[19] Liu et al. conducted a study as Systemic review on hospiatlized patients with CAD and were not able to detect a direst relationship between the HBA1c levels and its mortality risk increment in diabetes[20]

5. CONCLUSION:

In our current study as many other studies, we conclude that high level of HBA1C (>6.5) indicating diabetes at the time of admission was found to be associated with multiple morbidities like congestive cardiac failure (CCF)and left ventricular dysfunction (LVD) as compared to those with lower HBA1c levels. Although , we were not able to find any significant relationship between high mortality rate , poor outcome in form of death at 7- day follow up and high HBA1c levels.

We think that cause of such finding may be related to a sampling bias since all the samples were taken from a single institute only. Many other biases and limitations might have affected the study and thus we suggest that some prospective longitudinal studies conducted at multiple centers and involving large number of sample size with relatively longer duration (atleast 6month to 2 year) of follow up should be undertaken to resolve the limitations of our study.

We also found that newly diabetic patients may present first time in ACS and diagnosed after work up. Though the fasting blood sugar level may be present high in more numbers of patient than actually diabetic so HBA1c should be taken as diagnostic tool to avoid incorrect diagnosis and to prevent delayed and inappropriate management of blood sugars before diagnosis which eventually going to affect the outcome of the patients.

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