Original Research Article

Clinical implications of Hba1c level in patients with Acute Coronary Syndrome

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ABSTRACT

Background : Coronary artery disease may manifests clinically as Acute coronary syndrome deadly disease worldwide. It is also a major cause of morbidity and death in diabetic population. Levels of hba1c suggest long term glycemic status of the individual. Our aim to make clinical implications of this levels in ACS and to study whether ACS can be initial presentation of Diabetes Mellitus.

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: Out of total ACS patients,53% pts present with STEMI, 23% patient present with NSTEMI and 24 % patients have unstable angina. 45% patients were known diabetic, and 11% were freshly diagnosed with diabetes and 12% had hba1c level in pre diabetic range. When FBS, PPBS and HbA1c compared ,HbA1c had greater utility to rule out stress hyperglycemia and predibetes. Lastly, more frequency of complications like CCF, left ventricular dysfunction and Left ventricular reduced ejection fraction were seen in diabetic persons.

Conclusion: HbA1c have multiple clinical benefits during management of ACS patients. With high level of HbA1c ,more injury to cardiac tissue were seen and significant complications were developed. So, HbA1c also have prognostic value. Also, ACS may be first presentation of diabetes.

Keywords: ACS: Acute coronary syndrome, STEMI: ST elevation myocardial infarction, NSTEMI: Non ST elevation myocardial infarction.

1. INTRODUCTION:

Diabetes mellitus (DM) is the one of the globally public health threat. The overall occurrence has increasingly seen in upright gradation leading to major concern in general population also.[1] Diabetes mellitus (DM) is associated with increased risk of heart diseases especially atherosclerotic coronary diseases and having a much higher risk of death secondary to an event of acute myocardial-infarction (MI).[2] Atherosclerosis alone is responsible for eighty percent of all cause deaths in diabetic patients.[3]

Insulin resistance with relative insulin deficiency characterizes type II diabetes (>90% of all diabetes cases), whereas absolute deficiency of insulin characterizes type I diabetes. There is increasing prevalence and excess of CV risk in type II diabetes as compared to type I diabetes. ACS describe clinical entities on the continuum of myocardial ischemia (unstable

angina pectoris) or infarction(with or without ST segment elevation).[4] Mechanism by which hyperglycemia increase atherosclerotic risk remain poorly understood. Endothelial vasomotor dysfunction , a hallmark of diabetic vascular disease ,is documented with increases hypertension and adverse CVD outcomes.[4,5]

HbA1c is an established marker of previous and long term glycemic status of pts with DM, and elevated HbA1c levels are associated with the increased risk for further microvascular and macrovascular complications.[6] 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. The major disadvantages of Hba1c are lack of standardisation of measurement and the fact that the results can be altered by several non specific factors, such as anaemia, haemoglobinopathies and ureamia.[7,8,9] Patients with an ACS event frequently have diabetes, with approximately ⅓ of ACS patients having diabetes previously diagnosed. In addition, many patients presenting with an ACS event as the first complication of diabetes. The diagnosis of status of diabetes early in hospital course is important because it influences later therapeutic decisions.[8] Taking above mentioned influences of diabetes in consideration , our aim was to evaluate clinical implications of HbA1c levels in pts with ACS with or without diabetes on admission.

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 Diabetic Association guidelines were used to categorize 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 dysfunction including death in 7 days.

Inclusion criteria:
1. Patients who give written and informed consent to take part in the study
2. ACS occurring less than 72 hrs
3. Diagnosis of ACS based on atleast two of the following: characterstic symptoms, electrocardiographic changes, and typical rise and fall in biochemical parameters(troponin,CPK-MB)

Exclusion criteria:
ACS patients having comorbidities and conditions which alters HBA1c levels like anaemia, hemoglobinopathies, sepsis, CKD, CLD, splenectomy, splenomegaly, RA, and on ART /dapsone/ribavirin.

Statistical analysis:

Data was analyzed 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:

Following were the observation made in our study, out of 100 patients, maximum 40 % belong to age group 50-59 years, then 30% were 60-69 years. Remaining 18% were of age group 40-49 years,8% were of 70-79 years and 4% were of 80-89. Most patients lied in 50-69 years(70%).Table 1, Fig 1. There is predominance of male was seen.

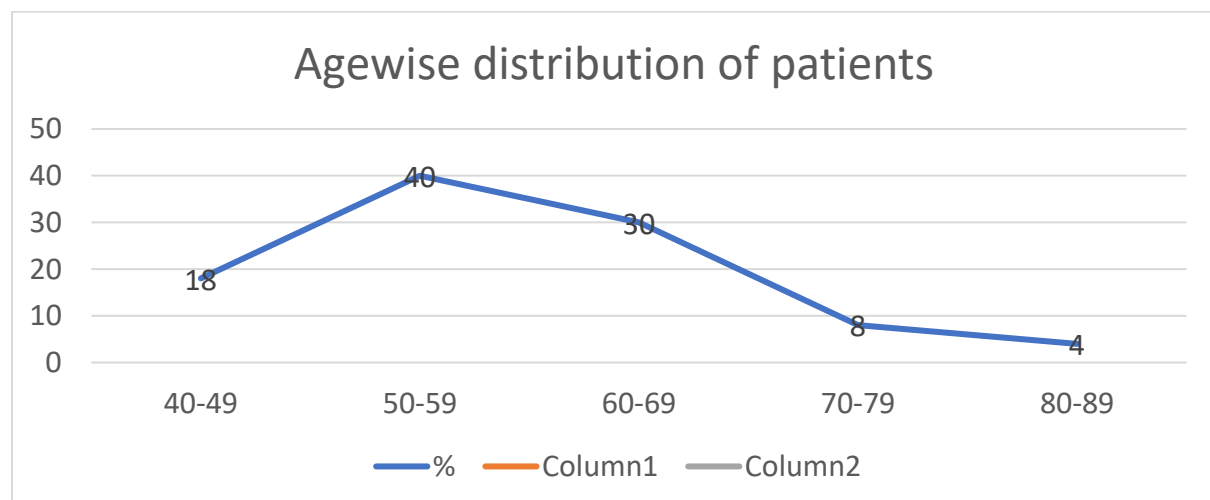| AGE (YEARS)	PERCENTAGE (%)
40-49	18
50-59	40
60-69	30
70-79	8
80-89	4

Table 1 AGE WISE DISTRIBUTION OF PATIENTS

Fig 1. Age wise distribution of patients

Patients blood pressure was found to have variability at admission and follow up. We found at admission 5% were hypotensive with SBP<90 mmhg and diagnosed as cardiogenic shock, 20 % were hypertensive with SBP >140 mmhg .Rest 75 % were considered normotensive. (fig. 2)
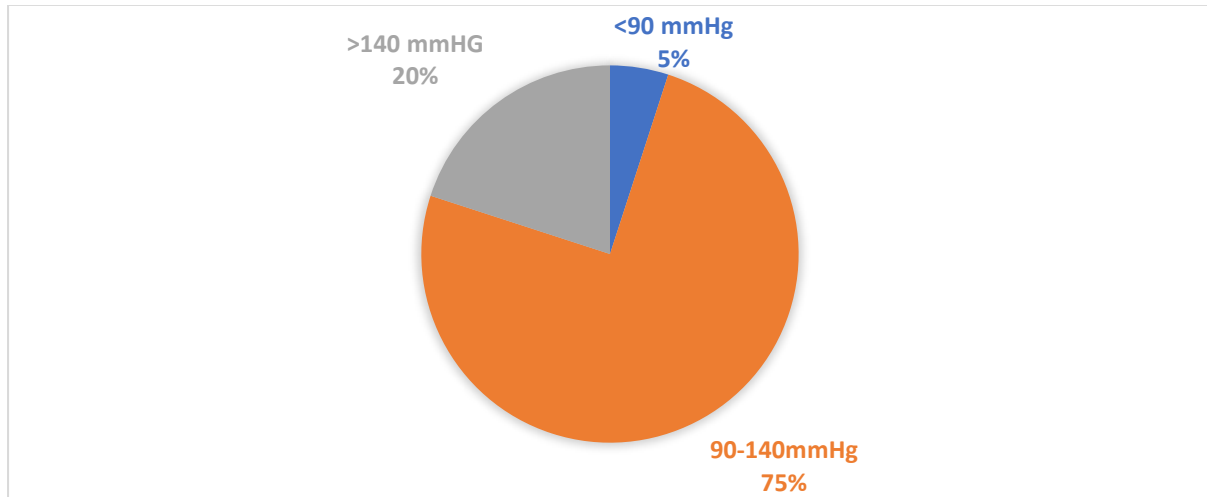

Fig.2 Patients distribution according to systolic blood pressure

Distribution of patients based on diagnosis, ST elevation myocardial infarction was most common among ACS that is 53%,followed by unstable angina then non ST elevation myocardial infarction 24% and 23% respectively.(Fig.3)
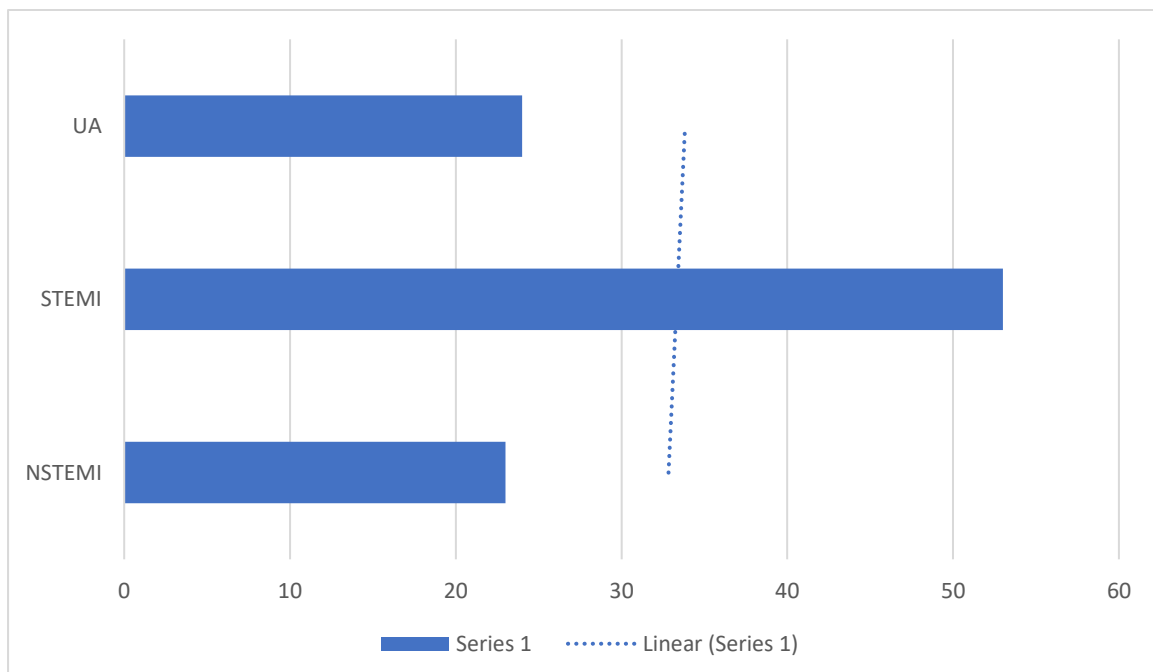

Fig. 3 Distribution of patients based on diagnosis

In our study ,most patients had ECG changes showing anterolateral wall ischaemia-65% followed by inferolateral and anteroinferolateral wall ischaemia ,12% and 8%, respectively. Inferior wall ischaemia was seen in 6% patients.(fig. 4)
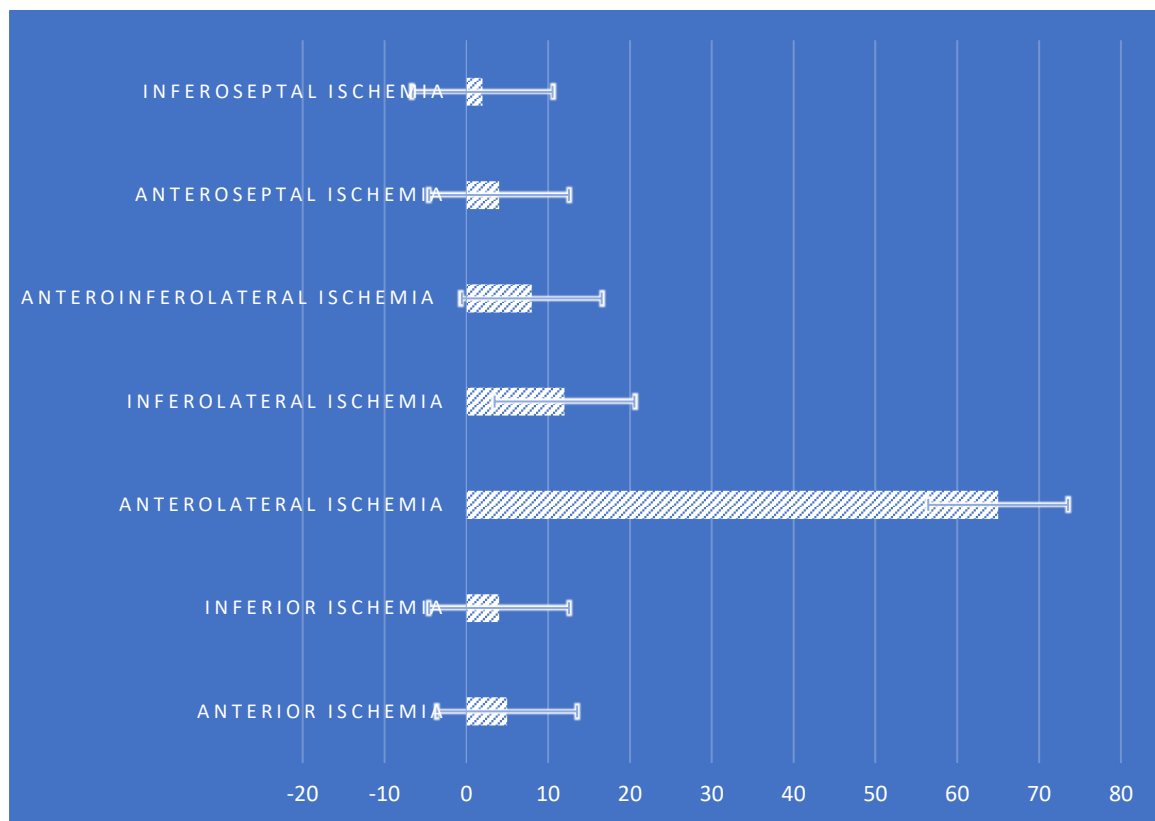
Fig. 4 ECG changes noted at admission

We found following were the frequency in percentage of fasting blood glucose levels, post prandial blood glucose levels and Hba1c levels among patients with ACS. According to FBS levels , person was considered non diabetic-<100mg/dl, prediabetic -101-125mg/dl and diabetic - >125 mg/dl blood sugar levels. Post prandial categorization as nondiabetic-<140mg/dl, prediabetic 140-200 mg/dl and diabetic >200 mg/dl blood sugar levels, and HbA1c considered as per previously mentioned criteria. We found more number of persons had diabetic status according to FBS (60%) and PPBS (60%) as compared to HbA1c levels in which only 46 % were have HbA1c >6.5. These clearly point out at importance of HbA1c to rule out stress hyperglycemia. There are more number of person in prediabetes according to HbA1c than FBS and PPBS. This points out at HbA1c screening could also help in risk quantification of patients with ACS. (Table 2, fig.5)

Status acc. to levels	FBS	PPBS	HbA1c
Non diabetic	35	32	43
Prediabetic	5	8	11
Diabetic	60	60	46

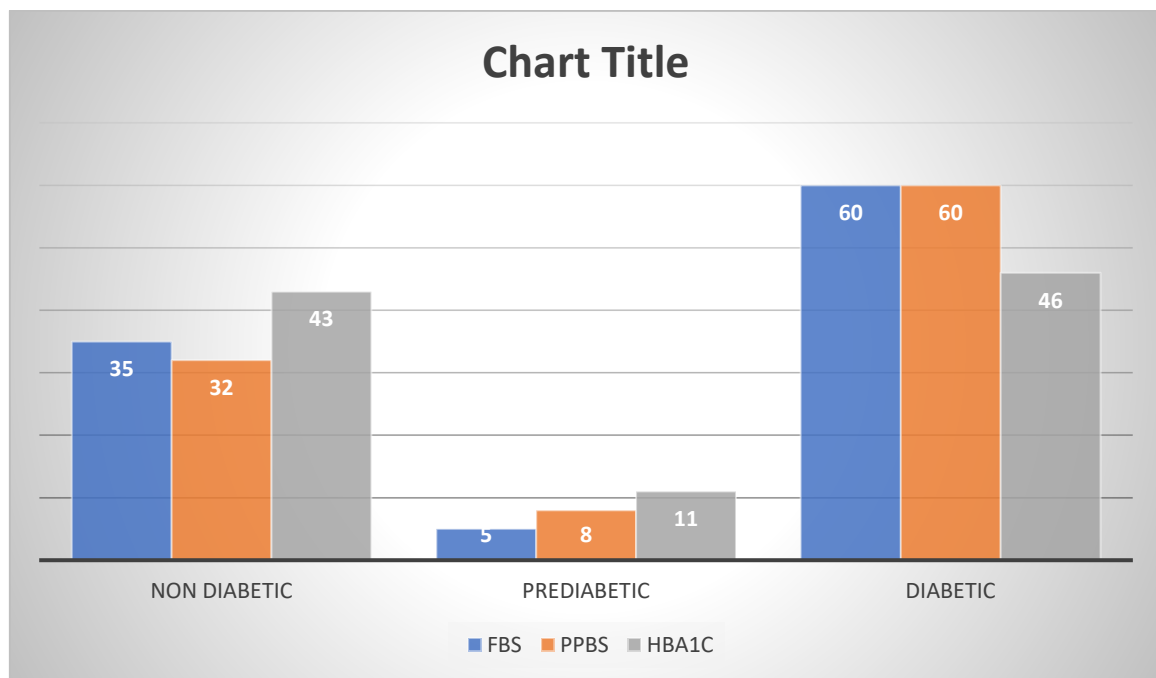Table 2. Glycemic division of patients (in percentage)

Fig. 5 Glycemic status of patients

LV dysfunction was the most common complication found in our study which was much more common in patients with HbA1c >6.5. Out of 40% patients, 28% patients have more deranged HbA1c levels. Similarly, ejection fraction < 40 % was found in 39% of patients out of which 31 % belong to high HBA1c patients group. CCF was found in 8 % patients and 6 % had more hba1c levels. (Fig.6)
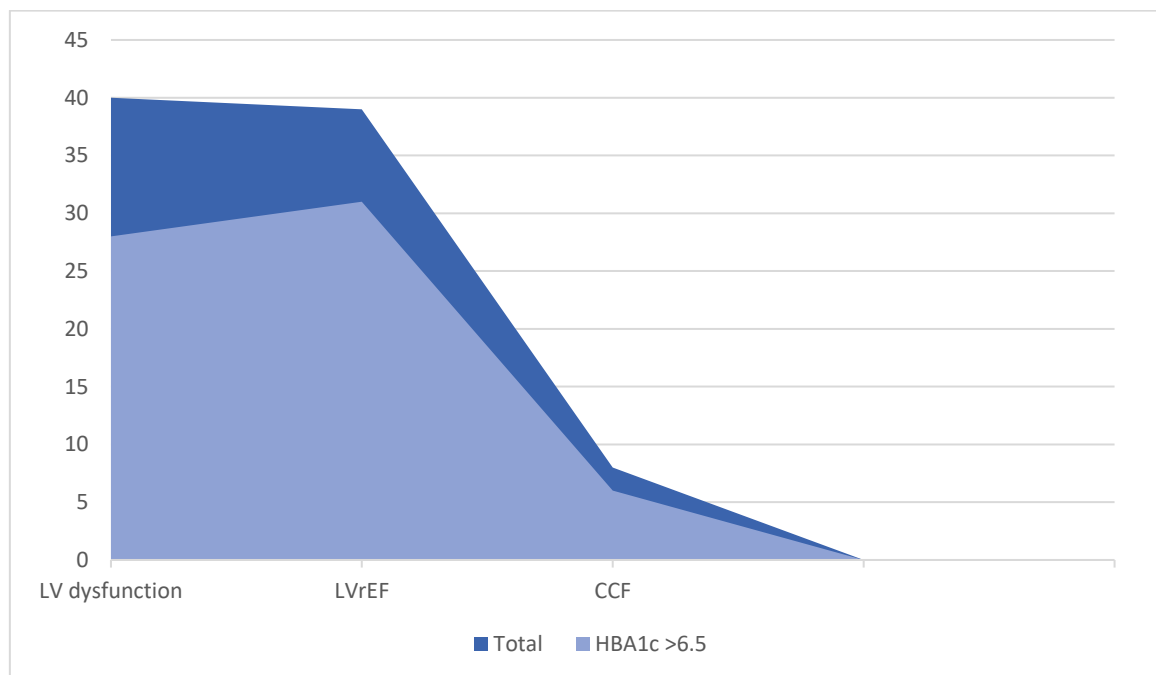

Fig. 6 Complications in ACS patients

4. DISCUSSION:

Elevated Hba1c% levels in diabetic population are not only associated with higher cardiovascular events and mortality, they are also strongly associated and predicts increased altogether mortality.[10] The WHO have recommended HBA1c as the preferred screening tool for the diagnosis of DM type II patients. Others have also highlighted HBA1c testing as an universal screening test in ACS setting.[11] Recently, the ESC/EASD (European Society of cardiology/European Association for the Study of Diabetes) have recommended all ACS pts should be screened for diabetes.[12] There are numerous benefits in the use of HBA1c as a screening method for diabetes. Importantly, it is less influenced by the short-term fluctuations of glycaemic control. It is also not impacted by stress hyperglycemia.[13]

Examine trial of type II Diabetes and Recent ACS showed that in patients having type II DM are at high CV risk, but there was no established relationship seen between MACE(mortality) and baseline HBA1c. Highest CV events rates were observed in between Hba1c level 8% and 9%. DM is associated independently with two-fold to five-fold increased risk of heart failure over that persons without diabetes, and patients with diabetes have worse outcomes once failure has developed.[14]

Glucose management : In general , HbA1c target of below 7% is recommended for most patients with DM. The most recent guidance from ADA/EASD endorses a more personalized approach to determination of the most appropriate HbA1c targets based on patient and drug characteristic, with the consideration of more intensive control for younger patients, shorter duration of diabetes, and/or fewer comorbid conditions, and more liberal HbA1c targets for higher risk patients.[2]

With few exceptions, management should be similar in approach to that of non diabetes. Increased level of evidence for ACE inhibitor use in diabetes is recommended. A higher recommendation value for the adjunctive use of GPIIb/IIIa antagonists for subjects with UA/NSTEMI; and preferential use of coronary artery by-pass grafting(CABG) over per-cutaneous coronary intervention(PCI) for individuals with more extensive coronary artery disease(CAD), independent of left ventricular systolic function.

In addition, recommendations provide guidance for the usefulness of insulin for targeted glucose control, noting a substantial evolution from the original guidelines ,that advocated normal or near normal glucose target levels, to the present targets of permissive hyperglycemia, reserving insulin only to maintain blood/plasma glucose below 180mg/dl.

Numerous trials have demonstrated that blood glucose concentration on admission is one prognostic factor for short term as well as long term mortality in Acute coronary syndrome in both nondiabetes and diabetes.[14,15] There have been few studies which shown HbA1c to be predictive of CAD in non-diabetes.[16] In a study of assam India ,it was concluded that a significant correlation exists between the Hba1c and severity of CAD by Syntax score as well as the number of vessels involved is direct in nondiabetics and HbA1c is found a simple and reliable measure for prediction of severity of CAD, so can be used as a complimentary test to traditional risk factors analysed to predict the severity of CAD.[17]

Timmer et al. demonstrated that elevated HbA1c level was associated with adverse outcome in nondiabetic patients with ST segment elevation MI, an increase in 1% of HbA1c concentration was roughly a 30% increase in all cause and 40% increase in cardiovascular or ischaemic heart disease mortality among individuals with diabetes.[18] Based on the thorough analysis of the pooled data the researcher concluded that undiagnosed diabetes in patients with ACS is not uncommon in Indian population , they also remarked that diabetic status profoundly affects the short term mortality of ACS patients.[19] Universal HbA1c screening

offers a simple ,applicable and effective test for diabetes detection and diagnosis in the ACS population.[20] HbA1c estimation at the time of admission in ICU clearly and quickly differentiates stress induced hyperglycemia in ACS from hyperglycemia seen in undiagnosed DM. However, combination of FGT (fasting blood sugar) and Hba1c significantly enhances the diagnostic accuracy of these individual tests. As the epidemic of diabetes continues to grow worldwide,HbA1c test may continue to be implemented as part of the diagnostic and prognostic tool, leading to better patient care and successful clinical outcomes.[21]

5. CONCLUSION:

In our study, we had found more percentage of deranged blood glucose levels both fasting and post prandial as compared to derangement of HbA1c levels. This may be due to stress hyperglycemia which can be ruled out by measurement of levels of HbA1c and more frequent follow up of blood sugar levels. HbA1c has predictive value for complication development. Lastly , ACS could be initial presentation in asymptomatic diabetic patients and HbA1c easily pick them up. Knowing the diabetic status , therapeutic modifications could be applied which will further improve overall outcome of acute coronary patients.

6. REFERENCES

1. Muhammad R, Masood A, Zaffar J, Butt U. Correlation of mean HbA1c levels with severity of coronary arteries disease in diabetes. PakHeart J 2014;47(4): 184-7
2. Kannel WB, McGee DL. Diabetes and cardiovascular disease: the Framingham Study. JAMA. 1979;241:2035-2038.
3. Roffi M; Topol EJ. Percutaneous coronary intervention in diabetic patients with non-ST-segment elevation acute coronary syndromes. EUR Heart J 2004;25:190-8.
4. Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine, Eleventh Edition Two- Volume Set ISBN: 978-0-323-46342-3 Single Volume ISBN: 978-0-323-46299-0 International Edition ISBN: 978-0-323-55592-0
5. Goldman's Cecil medicine / [edited by] Lee Goldman, Andrew I. Schafer.—24th ed. P. ; cm Cecil medicine Rev. ed. of: Cecil medicine. 23rd ed. c2008.
6. Malmberg K, Ryden L, Wedel H, Birkeland K, Bootsma A, Dickstein K, et al.
7. Goldstein DE, Little RR, Lorenz RA, Malone JI, Nathan D, Peterson CM, Sacks DB: Tests of glycemia in diabetes. Diabetes Care 2004,27(7):1761-1773.
8. International expert Committee report on the role of the A1C assay in the diagnosis of diabetes. Diabetes Care 2009,32(7):1327-1334.
9. Saudek CD, Herman WH, Sacks DB, Bergenstal RM, Edelman D, Davidson MB: A new look at screening and diagnosing diabetes mellitus. J Clin Endocrinol Metab 2008, 93(7):2447-2453.
10. BREWER N., WRIGHT C.S., TRAVIER N., CUNNING-HAM C.W., HORNELL J., PEARCE N., et al.: A New Zealand linkage study examining the associations between A1C concentration and mortality. Diabetes Care; 31 (6):1144-9,2008.
11. Ghopal N, Davies MJ, Mostafa SA, Squire I, Khunti K. A simple strategyfor screening for glucose intolerance, using glycated haemoglobin,in individuals admitted with acute coronary syndrome. Diabet Med.2012;29(7):838-43
12. ESC Guidelines on diabetes,pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD: the Task Force ondiabetes, pre-diabetes, and cardiovascular diseases of the EuropeanSociety of Cardiology (ESC) and developed in

collaboration with the European Association for the Study of Diabetes (EASD). Eur Heart J. 2013;34(39):3035-87

13. SAUDEK C.D., DERR R.L., and KALYANI R.R. Assess-ing glycemia in diabetes using self-monitoring   blood glucose and hemoglobin A1c. Jama; 295 (14): 1688-97,2006

14. Wahab NN, Cowden EA, Pearce NJ, et al. Is blood glucose an independent predictor of mortality in acute myocardial infarction in the thrombolytic era? J Am CollCardiol. 2002; 40:1748-1754.

15. Schiele F, Descotes-Genon V, Seronde MF, et al. Predictive value of admission hyperglycemia on mortality in patients with acute myocardial infarction. Diabet Med. 2006;23:1370-1376.

16. Sianos G, Morel M A, Kappetein AP, Arie Pieter, Morice M C, Keith Dawkins, [4] et al. The SynTAx score: an angiographic for grading the complexity of CAD. Eurointerve. 2005:1:219-27.

17. Bornali Dutta et al. , HBA1C Correlation with severity of Coronary Artery Disease in nondiabetic Patients. Journal of Clinical and Diagnostic research. 2016 Sep, Vol-10(9): OC20-OC2322.

18. K.-T. Khaw, N. Wareham, R. Luben et al., "Glycatedhaemoglobin, diabetes, and mortality in men in Norfolk cohort of European Prospective Investigation of Cancer and Nutrition (EPIC-Norfolk)," British Medical Journal, vol. 322, no. 7277,pp. 15-18,2001.

19. Asheaf, et al, Prevalence of Undiagnosed Diabetes Mellitus in Acute Coronary Syndrome Patients: A Hospital-based Study. International Journal of Scientific Study/May 2016/vol4/Issue 2.

20. McCune C et al, HbA1c for diabetes Screening in Acute Coronary Syndrome: time for a reappraisal of the guidelines? Ulster Med J 2015;84(3):154-156.

21. Sherwani et al. Significance of HbA1c Test in Diagnosis and Prognosis of Diabetic Patients. Biomarker Insights 2016:11 95-104 doi : 10.4137/Bmi.s38440.