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Comparison of Outcomes of ACS in Prediabetes and Nondiabetic In a Tertiary Care Centre

(Original Article)

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ABSTRACT

Background: *Pre diabetes is a definite risk factor in cases of STEMI. This study was aimed to compare various clinical outcomes, coronary angiographic results and incidence of major adverse cardiovascular event (MACE) in prediabetic patients presented with STEMI with those of non prediabetic STEMI patients in a tertiary care centre.*

Methods: *Study was conducted in prediabetic patients presented with STEMI whose fasting serum glucose and glycated hemoglobin level were 100-125 mg/dl and 5.7-6.4%, were respectively. Age and sex matched non prediabetic patients with STEMI was selected as control group. Demographic variables were taken. Further the clinical presentations; findings of coronary angiogram; electrocardiogram (ECG) and 2D echo; morbidity and cardiac mortality were collected and subjected to statistical analysis.*

Results: *Total of 70 patients (35 prediabetic and 35 non prediabetic control) with ACS STEMI were included in the prospective study. The prediabetic patients with ACS STEMI were found with clinical presentation (Killip class III and IV); ECG manifestations (Tachyarrythmia); 2 D echo (Moderate and severe left ventricular dysfunction); angiographic findings (Double and Triple vessel disease, Right coronary artery(RCA), Left circumflex artery (LCX), Long Stents); morbidity (MACE and site hematoma) and cardiac mortality more than the non prediabetic control group.*

Conclusion: *The results showed that prediabetic group had higher Killip class, more multivessel disease, higher MACE and cardiovascular mortality as compared to control group.*

INTRODUCTION

Prediabetic can be defined as those patients without symptoms of diabetes and having fasting blood glucose b/w 100-126mg/dl & b/w Hb (Heamoglobin) A1c 5.7%-6.4%. The American Diabetes Association (ADA) defined the cut off point for normal fasting blood glucose concentrations from 110 mg/dl to 100 mg/dl, thus a value of 100 mg/dl or above would lead to a diagnosis of prediabetes (impaired fasting glucose). [4]

Early diagnosis and treatment of pre diabetes is essential for decreasing the cardiovascular mortality and morbidity in our population. Diabetes is an important modifiable risk factor in cases of STEMI. Secondary prevention of cases with prediabetes can lead us to prevent further cardiovascular complications like MACE.

Diabetes mellitus is a well recognised risk factor for cardiovascular disease and diabetic individuals with acute STEMI have a two to four fold increased risk of adverse cardiovascular events compared to non-diabetic individuals.[1] It is becoming increasingly clear that impaired glucose metabolism and the pre-diabetic state are also associated with adverse clinical outcomes. In this study, admission plasma glucose was an independent predictor of non-fatal reinfarction, hospitalisation for heart failure, and a major adverse cardiovascular event (MACE).

We assessed the impact of the pre-diabetic state on clinical outcomes in patients presenting with acute STEMI. The risk factors of STEMI with prediabetes will be investigated and treated. Along with this secondary prevention for diabetes which could have a major impact on prognosis and treatment of STEMI will be advised.

MACE defined by GUSTO* criteria was major adverse cardiovascular events with death, myocardial infarction, major bleeding and stroke.

BACKGROUND OF STUDY

Diabetes mellitus is an important risk factor of ST elevation myocardial infarction (STEMI).Pre diabetes is a definite risk factor in cases of STEMI.[1] Early recoginition and management of STEMI prevents development of cardiovascular complications. Prevalance of coronary artery disease in prediabetic population in india is 14.9%.[2] No major prospective studies done in a tertiary care centre in cases of pre diabetics with ST elevation MI in India. Thus early diagnosis and treatment of prediabetics could decrease the complications of STEMI.

AIMS & OBJECTIVES

1. To study and compare various clinical outcomes of ACS STEMI in prediabetics to non prediabetics in tertiary care centre.
2. To study and compare the coronary angiographic results and findings of ACS STEMI in prediabetics to non prediabetics.
3. Incidence of MACE* in cases presenting in ACS STEMI with prediabetes.

MATERIALS AND METHODS

Study design: Prospective Cohort study

Study centre/ Population: Single Centre (Department Of Cardiology Amala Institute Of Medical Science And Cardiac Research Centre)

Study period: 2014-2016

Sample size: Total--70 study group (SG)-35/ control group (CG)-35

ST elevation MI defined as ECG showing ST elevation measured at J point found in two contagious leads and ≥0.25mV in men below the age of 40years, 0.2mV in men over the age of 40years, or ≥0.15mV in women in leads V2-V3 and/or ≥0.1 mV in other leads in absence of left ventricular hypertrophy or left bundle branch block (LBBB).[6]

Inclusion criteria

All cases of ACS STEMI with fasting blood glucose ≤126mg/dl with no symptoms of diabetes.

Exclusion criteria

Previously treated and diagnosed cases of diabetes and FBS >126mg/dl

ACS STEMI with 35 prediabetic cases according to definition from ADA were included in the

study group and 35 non diabetic patients with STEMI included in the control group controls. Clinical and angiographic profile of prediabetics with STEMI are studied.

We studied 70 consecutive patients who were admitted to the Department of Cardiology Amala Institiute of Medical Science, Thrissur from Jan 2014 To Jan 2016. The protocol was approved by the institutional review board at Amala institute of Medical science, Thrissur and consent was obtained from all patients.

STATISTICAL ANALYSIS

Univariate statistics are presented as frequency and percentage for categorical variables, and mean (SD) for continuous variables. The p values for comparisons of the distributions of categorical variables between groups were based on Chi Square test. The p values for comparisons of continuous variables between prediabetic and non-diabetic groups were based on paired t tests. A multivariable logistic regression analysis was performed for in-hospital MACE in ACS STEMI patients adjusted for age, sex, ST segment elevation, heart failure, and revascularisation. All analyses were performed using SAS 8.2.

RESULTS

Incidence of pre-diabetes were seen in more in middle aged (52.3±2.3 yrs) men with higher body mass index. Higher incidence of associated peripheral obstructive vascular disease in prediabetic population was statistically insignificant (p=0.01).

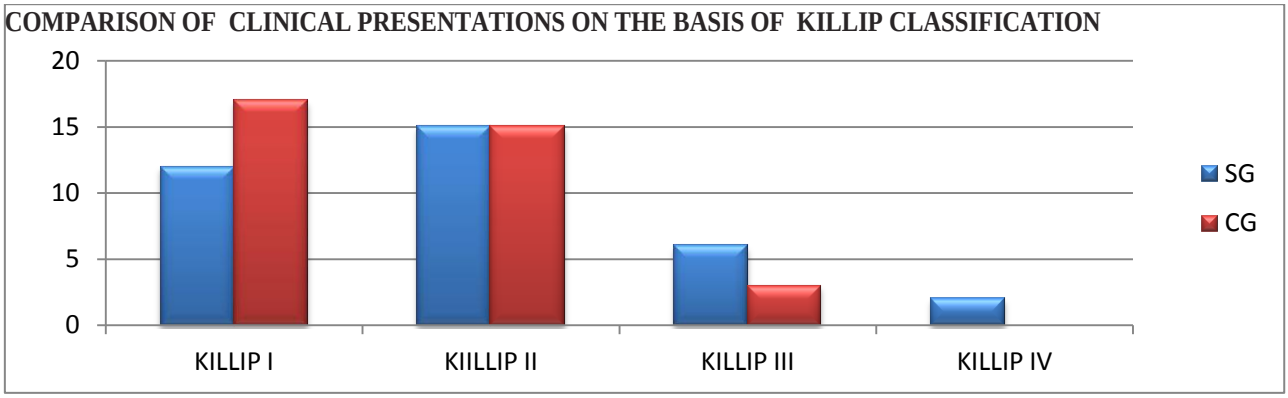
Table No.1 Major Baseline Characterstics

Categories	Prediabetes (%)	Control (%)	P value
N	35	35	
Age	52.0 ± 2.3yrs	50.0 ± 2.5 yrs	
Gender	M:F(8:1)	M:F(3:1)	
HTN	28(80)	29(83)	0.05
DLP	27(77)	33(94)	0.34
PVOD	11(31)	10(29)	0.26
Obesity	33(94)	28(80)	0.32
Smoking	30(87)	24(69)	0.07

Mean average HbA1c was 5.9±0.2 and non diabetic being 5.3±0.3. Major confounding factor that influenced both prediabetic and non prediabetic was smoking which was a major modifiable risk factor in both these groups. Prediabetic patients had chest pain as major presenting complaint as compared to non prediabetic patients. Door to balloon time for prediabetic was more than non prediabetic group due to late presentation that lead to various adverse outcomes in prediabetic group.

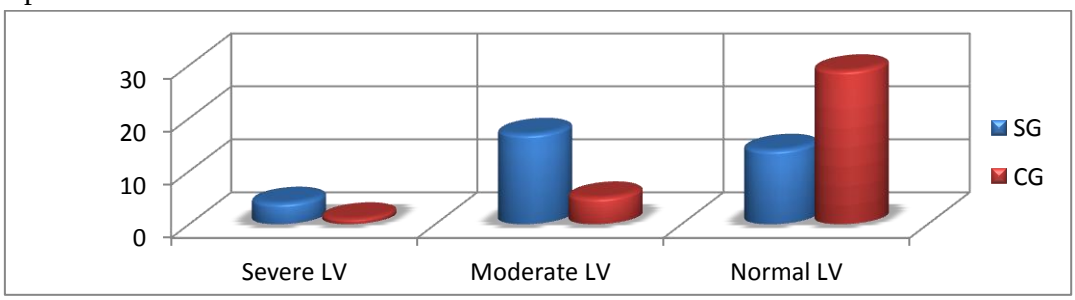
Patients in Killip Class III& IV symptoms were common in prediabetic as compared to non prediabetic and was statistically significant. Major pointer in our study was Prediabetic cases presenting with ST elevation MI with killip class III & IV had poor prognosis and prompt interventions with proper management can improve outcomes in these group.

Graph 1. Comparision of Clinical Presentation On Basis Of Killip Classification



Electrocardiography showed statistically significant higher AV blocks (6%vs3%) and tachyarrythmias (14%vs0%) in prediabetic as compared to non pre diabetic (p=0.032) population. Severe LV dysfunction was found in predominately in prediabetic (11%)as compared to non prediabetic (3%) which was statistically significant (p=0.02).Moderate LV dysfunction was found in 49% cases in prediabetes as compared 14% in non prediabetic. Improvement in LV function was abrupt and prompt in non diabetic as compared to pre diabetic in which the improvement was gradual and even lead to various adverse clinical outcomes.

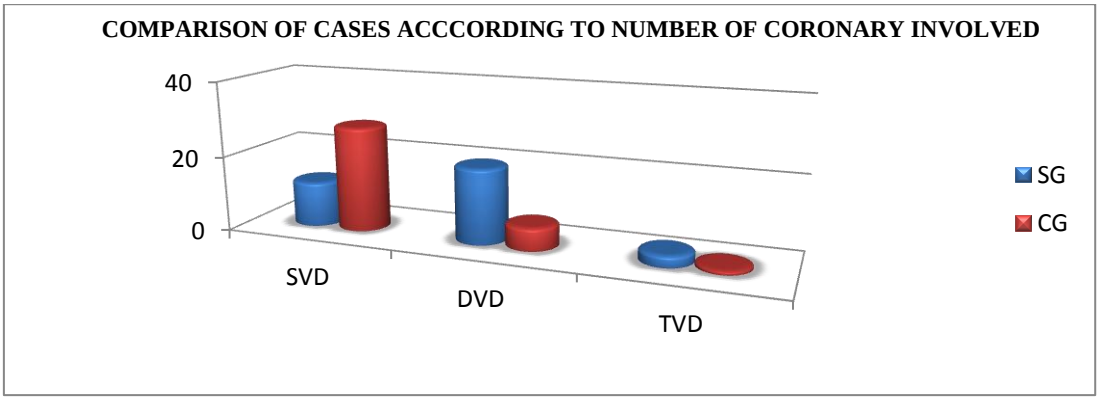
Graph 2. Comparison of LV Function



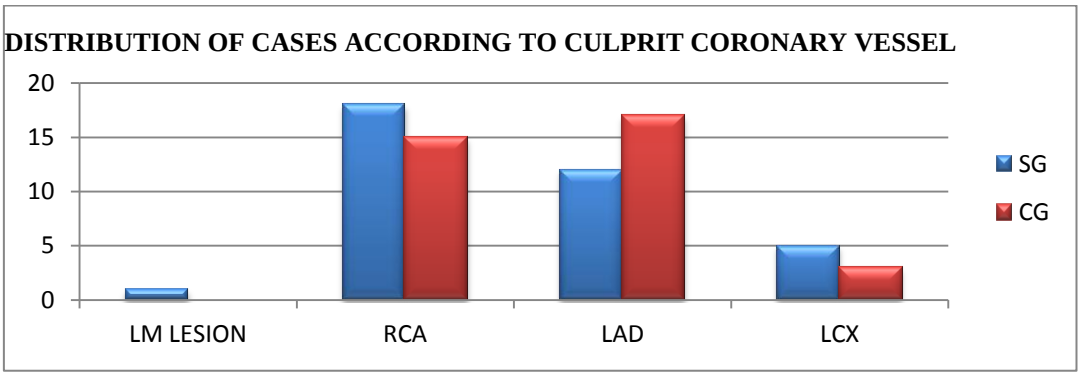
Angiographically 57% of prediabetic population had double vessel disease as compared to non pre diabetic population who had 17% cases of double vessel disease. Almost similar number of cases of triple vessel disease was found in prediabetic (8.5%) and non prediabetic group(2.8%) was stastistically significant (p=0.02).

Percutaneous angioplasty in prediabetic population was challenging. Although drug eluting stents were used in 92% cases of pre diabetes the procedure time and post procedure complications were more in pre diabetic as compared to non prediabetic due to more complex coronary anatomy.BMS was used in only 8% of prediabetes cases in which coronay anatomy was feasible. Predominately long stents (54.2%) were utilized by prediabetes population. Multiple stent deployment was considered in prediabetic as compared to non prediabetic .Although Thrombus load was of Grade 4 & 5 in both groups and thrombus aspiration was underutilized as per ACC/AHA guidelines 2014 and latest evidenced based studies. [7] Ticagrelor was started in 14% cases of prediabetes(0.05). Average Fluro time for primary PCI in prediabetic group was 60±15 mins as compared to 33±12mins in non prediabetic group.

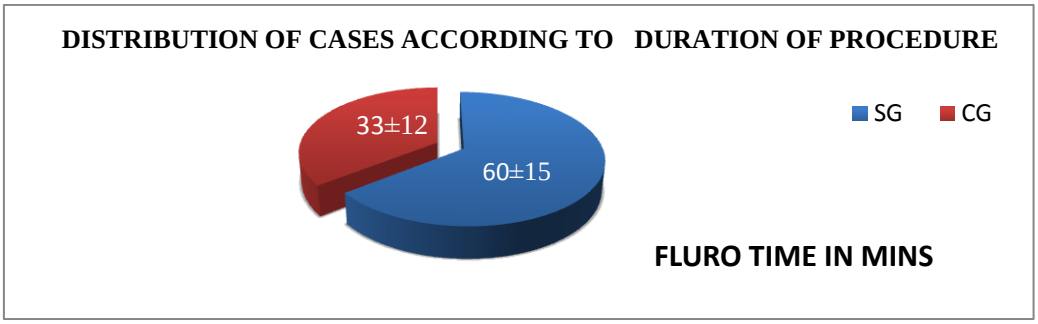
Graph 3 Comparison of Cases Acccording To Number Of Coronary Involved



Graph 4 Distribution of Cases According To Culprit Coronary Vessel



Graph 5 Distribution of Cases According To Duration Of Procedure



Post Thrombolytic era for Prediabetic (15%) was associated with more adverse clinical outcomes as compared to non prediabetic. Although less number of cases encountered with facilitated and failed PCIs in both groups. Post procedure acesses site heamtomas were more common with prediabetes (57%) as compared to non prediabetes (17%).

All cause mortality was more in prediabetic group(8.75%) as compared to non prediabetic (2.8%). Although there were no cardiac deaths in non prediabetic group as compared to pre diabetic which had 2.8% cardiac mortality which was statistically significant. Adverse clinical events including pulmonary oedema (6.7%), cardiogenic shock(12%), and cardiac arrest (3.8%) were all significantly higher in pre-diabetic compared to those with non prediabetic population which was statistically significant(p=0.033)

Table 2. Comparison of other major parameters among SG & CG.

Patient characteristics	Categories	Prediabetes SG (%)	Controls CG (%)	P value
	N	35	35	
Type of MI	AWMI	15(43)	18(51)	0.05
	IWMI	20(57)	17(49)	0.058
ECG				
	AV Blocks	2(6)	1(3)	0.01
	Bradyarrythmia	2(6)	2(6)	0.44
	Tachyarrythmia	5(14)	0	0.049
Type of stent				
	Long Stent	19(54)	12(34)	0.14
	Short stent	16(46)	23(66)	0.11
Morbidity				
	MACE	6(17)	3(9)	0.03
	Site heamotoma	20 (57)	6(17)	0.19
Mortality				
	All cause mortality	3(9)	1(3)	0.02
	Cardiac mortality	1(3)	0	0.01

DISCUSSION

From this study we found that the pre-diabetic state is also a marker for worse prognosis in patients with ACS STEMI. Mukherjee et al in his study had 18.6% cases of prediabetes with higher male predominance (71%). CAG analysis revealed that prediabetic population had double vessel disease (57%) and triple vessel disease (9%) more than the non prediabetic group. Prediabetes with hyperglycemia, free fatty acids, and insulin resistance provokes molecular changes that alter the function and structure of blood vessels. All these conditions affect vasoconstriction and inflammation to promote the coronary atherosclerosis in prediabetics. [8,9]

ACS STEMI is associated with increased microvascular and macrovascular changes which are established in a rapid rate without the symptoms or signs in a prediabetic patients.[8,9,10] Predominance of obesity in middle aged male was an important baseline parameter in prediabetic group indicating the presence of early metabolic syndrome.[8] However, in our study the distribution of obesity was statistically non significant among the control and prediabetic groups.

Majority of prediabetic cases with STEMI were in Killip class II(43%) and Class III (17%) which determined their further prognosis. While relatively more pre diabetic patients were with Killip class III (17%) and IV (6%) indicated the poor prognosis and hence prompt interventions with management needed to improve the outcomes in this group. Moderate LV dysfunction (Killip III-IV class) was significantly observed in prediabetic population (49%) which was only 15.3% prediabetic cases in a previous study by Mukharjee et al.[1,16]

Although ECG was useful in localizing the coronary territory, it was specific only for few cases(54%). There was dilemma in ECG localization in cases with aVR ST elevation MI in prediabetic group. In both the groups, bradyarrythmia (6%) and tachyarrythmias (14%) were only few in number and statistically insignificant (p=0.44). [11] This observation was consistent with the previous report. Various experimental and clinical studies suggested that sudden elevation of FPG itself can increases infarct size.[11]Although abnormal blood glucose is common among patients with ACS STEMI, at admission the hyperglycaemia does not represent abnormal glucose tolerance. Therefore, it was suggested that FPG and HbA1c, but not admission glucose, were independent predictors of abnormal glucose tolerance. Patients with hyperglycaemia at the time of admission were associated with increased risk of mortality in ACS STEMI. [10,11]

This association has been documented not only in diabetic patients but also in non prediabetic

population. Hyperglycaemia activates blood coagulation, aggregates inflammation. We found that the thrombus load detected in CAG was of Grade 4 and 5 in both groups.

Although recent studies have reported that diabetes may not be a predictor for short-term out come after AMI in the PCI era, elevated HbA1c is still an important risk factor for long-term outcome.[7]Taking into account the considerably high prevalence of abnormal glucose tolerance among patients with ACS STEMI and no previous diagnosis of diabetes, HbA1c could be routinely considered for the risk stratification. Various studies have reported that FPG and HbA1c were good measures to predict abnormal glucose tolerance.[14,15] Rapidity of FPG and HbA1c may be useful to predict abnormal glucose tolerance of non diabetic patients who survived ACS STEMI regardless of the presence or absence of admission hyperglycaemia. However, these parameters lacked sensitivity to predict abnormal glucose tolerance.

Kurihara et al [7] demonstrated that the degree of coronary atherosclerosis was more angioscopi-cally in prediabetics (92%) as compared to non diabetic(26%) and diabetic (80%) population. In prediabetic cases with acute STEMI, the major vessels in descending order were RCA (51%)>LAD(34%)>LCX(14%), whereas in the previous study which included prediabetic with CAD, the major vessels were LAD (86%)> LCX(75%)>RCA(68%) in descending order.[7]

In prediabetic population during PCI with long (54%) and multiple DES (44%) stents with prolonged fluro time (60±15min) as compared to non prediabetic (33±12min) population defining the complex coronary anatomy of culprit lesion. The drug eluting stents were used in 92% cases of pre diabetes the procedure time (54%vs34%) and post procedure complications (74%vs26%) were more in pre diabetic as compared to non prediabetic due to more complex coronary anatomy. Although stabilized with optimal medical management, (ACEI/ARB/MRA) an acute improvement in LV function till discharge in post PCI era was documented in this group. Improvements in LV function was abrupt and prompt in non pre diabetic as compared to pre diabetic in which the improvement was gradual and even lead to various adverse clinical outcomes.

This study validates the importance of high risk profile in patients with pre diabetes. Such patients would then be candidates for potential benefits from aggressive acute phase treatment and long term use of optimal secondary prevention treatments, such as aspirin, clopidogrel,

statins, beta blockers, and angiotensin converting enzyme inhibitors. We used ticagrelor in 14% cases of prediabetes.

All cause mortality (9%) and cardiac mortality (3%) was more in prediabetic group. Cardiac free wall rupture was documented in an elderly prediabetic case. Pre PCI(3%) and Post PCI (6%) MACE and all cause mortality was high in prediabetic compared to non diabetic population. Mukherjee et al[1] showed that cardiac mortality and MACE in prediabetic with ACS was 1.23% and 12.4% respectively .Although ACS population taken in previous study included both STEMI/NSTEMI the study group had more mortality and MACE compared to non diabetic similar to our study.(table no:3)

Table 3. Comparison of primary outcomes in trials by Mukharjee *et al* and Thrudeep *et al*

Parameters	Mukharjee etal(STEMI/NSTEMI)		Thrudeep et al(STEMI)	
	Prediabetic(%)	NonPrediabetic(%)	Prediabetic(%)	NonPrediabetic(%)
Death	1.23	1.04	2.8	0
Reinfarction	1.18	0.49	0	0
Stroke	0	0.17	0	0
MACE	12.04	6.74	17.6	9
Cardiogenic shock	1.47	0.52	12.5	4.3
Cardiac arrest	1.97	0.69	3.8	1.2
Pulmonary edema	3.53	2.21	6.7	2.4

This can be due to the complex coronary anatomy and adverse LV remodeling. Cardiac pathophsyiology in prediabetic population has to be defined for estimation of progression of atherosclerosis and severity of LV dysfunction. This has to be confirmed by larger prediabetic population trial which includes CAG, IVUS (intravascular ultrasound) study and cardiac Magentic resonance imaging (cMRI).

CONCLUSION

This study validates the importance of high risk profile in patients with pre diabetes. Such patients would then be candidates for potential benefits from aggressive acute phase treatment and long term use of optimal secondary prevention treatments, such as aspirin, clopidogrel, statins, beta blockers, and angiotensin converting enzyme inhibitors. We used ticagrelor in 14% cases of prediabetes.

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