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Glycemic Abnormalities in Patients of Acute Coronary Syndrome With Type 2 Dm

KEYWORDS: Hyperglycemia, Type 2 DM, Acute coronary syndrome

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ABSTRACT *Introduction- Diabetes Mellitus comprises of a group of common metabolic disorders that share the phenotype of hyperglycemia. Chronic complications of Diabetes Mellitus affect many organ systems of which Ischemic Heart Disease is the most common cause of mortality. DM increases the risk of ACS and of complications after presenting with ACS.*

Aims - Correlation of duration of Diabetes Mellitus and Glycemic abnormalities in patients of Acute Coronary Syndrome with Type 2 Diabetic Patients

Methods- This prospective study was conducted in indoor patients of a General Hospital, with Type 2 Diabetes Mellitus or newly detected Diabetes Mellitus admitted in the Medical ICU with acute coronary syndromes, during a period of 12 months. The study sample consisted of 50 such patients.

Results- Male: Female ratio was 1:1 .More than 70% patients were above 50 years of age. Duration of diabetes had no correlation with ACS. Poor Glycemic control was present in 92% of the patients and its correlation with ACS was statistically significant.

Conclusion- The ADA has suggested glycemic goals based on the premise that glycemic control predicts development of DM related complications of which mortality due to Ischemic Heart Disease is common. Studies have suggested that intensive glycemic control results in a trend for reduced MI. Therefore the glycometabolic state at admission, suggested by the BSL on admission and by HbA1c is an important risk factor for patients with DM and ACS. Adequate glycemic control needs to be stressed upon in all Diabetic patients.

Introduction -
Diabetes Mellitus comprises of a group of common metabolic disorders that share the phenotype of hyperglycemia. Currently India has got the largest number of diabetics and is being called as diabetic capital of the world. Chronic complications of Diabetes Mellitus affect many organ systems of which cardiovascular is the leading cause of morbidity, and Ischemic Heart Disease the most common cause of mortality. Although Diabetes may be a problem of glucose metabolism, the American Heart Association has stated that `Diabetes is a Cardiovascular Disease'

Diabetes is an established major factor of poor prognosis after an acute coronary syndrome .The increased frequency of adverse outcomes among diabetic patients with ACS probably has several explanations in addition to pathophysiologic abnormalities. Patients with diabetes and ACS have higher prevalence of comorbidities including dyslipidemias, hypertension, CHF and renal insufficiency.[1] Recent findings also argue for a direct deleterious effect of hyperglycemia on myocardium.

Further, DM increases the risk of ACS and of complications after presenting with ACS. In a population based study, the 7 year incidence of first MI or death for patients of DM was 20% compared with 3.5% for patients without DM. [2] Type 2 DM patients without prior Myocardial Infarction have similar risk for coronary artery related events as non-diabetics who have had prior Myocardial Infarction. Presence of DM increases the risk of Coronary Artery Disease two to four fold. Approximately 30% of patients hospitalized with MI, 30% will have DM compared with a DM prevalence of 6-8% in the general population. Additional 30% may have undiagnosed DM in the setting of MI. DM increases the risk of ACS and of complications after presenting with ACS[3].

Hyperglycemia remains underappreciated as a risk factor, and it is frequently untreated in ACS patients. Our study has tried to look into this important aspect of hyperglycemia in patients of ACS.

Details of Study:
Aims and Objectives - Correlation of Duration of Diabetes Mellitus and Correlation of Glycemic abnormalities in patients of Acute Coronary Syndrome with Type 2 Diabetes Mellitus.

Materials and Methods-
This prospective study was conducted in indoor patients of a General Hospital, with Type 2 Diabetes Mellitus or newly detected Diabetes Mellitus admitted in the Medical ICU with acute coronary syndromes, during a period of 12 months. The study sample consisted of 50 such patients.

Detailed clinical history was taken of present and relevant past illness specifically the duration of their Diabetes Mellitus. All patients were explained about the nature of the study and written and informed consent was taken from every patient

Inclusion Criteria:
Patients presenting with angina or angina equivalents were considered who were known Type 2 diabetics or had newly detected DM. DM was defined according to ADA criteria.

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Criteria for diagnosing Diabetes Mellitus; [4]
1. Symptoms of diabetes plus random blood sugar >200 mg/dl or

2. Fasting plasma glucose > 126 mg/dl or

3. Two hour plasma glucose > 200 mg/dl during an oral glucose tolerance test.

4. HbA1c >6.5%

Acute Coronary Syndrome (ACS) comprises of;
1. Patients with Acute Myocardial Infarction with ST segment elevation (STEMI)

2. Unstable Angina(UA)

3. Non ST Elevation Myocardial Infarction (NSTEMI)

STEMI patients were defined by acute chest pain or equivalent, ST Segment elevation and raised cardiac enzymes.

Unstable Angina – Angina Pectoris or equivalent chest discomfort with one of the following;

- Occurs at rest usually more than 10 minutes
- Severe and of new onset
- Crescendo pattern

NSTEMI – Clinical features of UA developing evidence of Myocardial Necrosis with raised cardiac biomarkers.

Exclusion Criteria :
- Type I Diabetes Mellitus
- Stable Angina
- BSL on admission done by glucose oxidase method was used to assess short term glycemic control and to detect new patients of Type 2 DM
- HbA1c-was done in all patients from a standardized private laboratory by HPLC (High Performance Liquid Chromatography) method to assess long term glycemic control of all diabetic patients

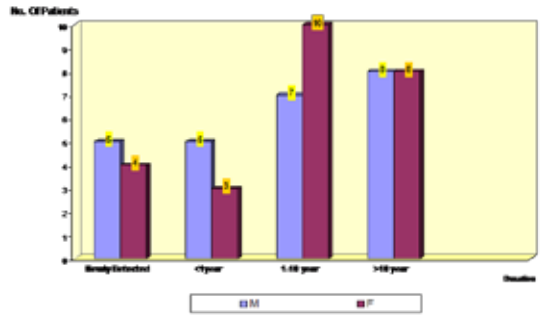
Statistical Analysis was applied for some variables by the chi-square test (X^2) and 'p' value was estimated for statistical significance. Thus entire data collected from examination of all study patients were compiled and conclusions were drawn.

Observations and Results-
50 cases of Type 2 DM with ACS were studied

1. a) Male: Female ratio was 1:1. The number of ACS cases increased as the age increased, i.e. more than 70% patients were above 50 years of age.

1. b) Duration of diabetes had no correlation with ACS. Most patients were equally distributed in the category of 1-10 years (34%) and more than 10 years (32%)

Figure 1.
Sex wise distribution of Duration of DM in patients with ACS



1.c) 18% of the patients had Newly detected Type 2 DM.

2.a) 72% patients had uncontrolled BSL at the time of presentation of ACS and this was statistically significant (p=0.0248). Mean BSL was 254.1mg% suggesting a strong correlation between poor glycemic control and ACS in diabetics.

Table 2 a) Co-relation of HbA1c with BSL on admission

HbA1c	BSL <200	BSL >200	Total
<6.5	2	2	4
>6.5	12	34	46
Total	14	36	50

2.b) 72% patients had both uncontrolled BSL >200 mg% and HbA1c >6.5% at the time of presentation of ACS .

2.c) Poor long term glycemic control was present in 92% of the patients and its correlation with ACS was statistically significant (p = 0.000001)

Mean HbA1c = 8.9 + 1.6

Table 2.
b) HbA1c – Long-term glycemic control and its relation to ACS.

HbA1c (%)	M	F	Total	Percent
<6.5	1	3	4	8%
6.5-8.5	11	5	16	32%
>8.5	13	17	30	60%
Total	25	25	50	100%

X^2=12 p = 0.000001 Mean HbA1c = 8.9% + 1.6

Clubbing the first group <6.5 with second and third group of >6.5 patients i.e. 4 and 46 patients, relation between HbA1c and ACS cases was statistically significant.

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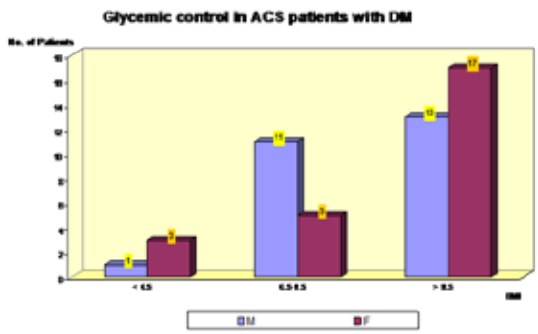
Figure 2.



2.d).24% of patients even though had BSL< 200 mg% on admission but had a poor long term Glycemic control with HbA1c >6.5

Discussion-

Amongst patients with CAD, DM is associated with increased risk of development of ACS and increased risk of death after AMI. Therefore they have greater proportional benefit from proven therapies for acute ischemic heart disease. Short and long-term mortality after STEMI are twice as high among patients of DM. The central contributor to high cardiovascular mortality rates among diabetes is premature development and accelerated progression of atherosclerosis. The underlying metabolic abnormalities in DM are Insulin Resistance, Impaired insulin secretion and increased hepatic glucose production which lead to a state of sustained hyperglycemia which if remains untreated increases the risk of complications in diabetic patients of which cardiovascular is common.

Duration of Type 2 DM and its relation to ACS:

Though long duration of DM is considered a traditional CV risk factor, it was not seen to relate with our study. This may be due to the fact that this was a small study group and that Type 2 diabetes was detected late in them or patients had other associated risk factors leading to occurrence of ACS early in them. Also Type 2 DM may frequently remain undiagnosed until complications occur as was seen in our 18% patients. The absolute risk estimated with charts or Framingham's scores reveal that even newly diagnosed patients have high CV risk.

According to the EPIDIAB (Epidemic of Diabetes) Study. [5]

The risk stratification (%) estimated in 8929 newly diagnosed Type 2 DM patients was

In 14.9% Risk < 10%

In 32.2% Risk 10-20%

In 52.8% Risk > 20%

In an Indian clinic based study it was shown that 17.8% of diabetic subjects had CAD. The prevalence of CAD among diabetic subjects increased with age and duration of diabetes and nearly 40% of subjects with duration more than 20 years had CAD. [6]

The prevalence of atherosclerotic CVD of newly diagnosed DM was in -

UKPDS – 5102 subjects – 8%

EPIDIAB – 26,787 subjects – 31.5% [5]

Level of Glycemic control in Type 2 DM and risk of ACS:

In the last decade a number of studies on glucose control and diabetic complications have been completed and all use HbA1c as a surrogate marker for risk. The standards of care of the ADA were revised based on fasting blood glucose level as well as HbA1c from these studies. However the assays have not been standardized, therefore clinicians should use the same lab to measure HbA1c in the same patient over time. In conditions of sustained hyperglycemia, such as DM, the proportion of haemoglobin that is glycosylated increases substantially. It reflects glycemic control of a patient during a 6-8 week period given the average lifespan of a red blood cell of 120 days.

In standardized assays, the HbA1c approximates the following mean plasma glucose values:

HbA1c (%)	Plasma Glucose (mg/dl)
6%	135
7%	170
8%	205
9%	240

A 1% rise in HbA1c translates into 35mg/dl increase in mean glucose. According to ADA[4], in general target A1C should be < 7%. The ADA has established suggested glycemic goals based on the premise that glycemic control predicts development of DM related complications.In the Framingham study, level of HbA1c correlated with prevalence of CVD, but only in women.

According to the International Diabetes Federation:

HbA1c < 6.5 – low risk; 6.5 to 8.5 – moderate risk; > 8.5 – High risk for cardiovascular disease.

Several observational studies found association between level of glycemic control and total mortality and some authors of these studies attempted to examine the effect of HbA1c on risk of CAD specifically.However interpretations are confounded by 2 issues. First, it is not known whether exposure to hyperglycemia has an impact on early or late stages of CAD. Second, the level of glycemic control determines the risk of diabetic nephropathy which in turn increases risk of CAD. In patients with Type 1 DM in the DCCT, there was less CAD among those receiving intensive therapy than those receiving conventional therapy, but the difference was not statistically significant.

The results of 2 cohort studies showed a positive association between level of hyperglycemia and mortality due to CAD. However it was insulin treatment that was associated with high risk of CAD in several studies. Hyperinsulinemia has been implicated in acceleration of coronary atherosclerosis.

The results of University Group Diabetes Program (UGDP) conducted in Type 2 DM patients and published more than a decade ago showed that fatal and non fatal cardiovascular events occurred with equal frequency in patients who received intensive insulin treatment and had good glycemic control and in patients treated with diet and whose average fasting blood glucose level deteriorated from 120 to 160 after 3 years of the trial, therefore did not demonstrate any important impact of glucose control on

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CVD outcomes.

The UKPDS[7], a prospective study of vascular complications of Type 2 DM with mean follow up of 10 years, demonstrated a 14% reduction in MI for each 1% reduction in threshold for the association between glycemic control and MI .Also a strong association was found between major complications of diabetes and hyperglycemia . Reduction of HbA1c by 1% is likely to reduce risk of any end point by 21%. The UKPDS compared the effects of conventional verses intensive glycemic treatment protocols on both micro and macrovascular complications. This study showed that intensive control resulted in substantial reduction in micro vascular disease. Of the 3867 patients of newly diagnosed type 2 DM studied, compared with the conventional treatment group, the intensive treatment group demonstrated a 16% reduction in risk for fatal and nonfatal MI. In this study intensive therapy resulted in a 0.9% difference in median HbA1c between the intensive (7%) and conventional (7.9%) groups over 10 years. Also in the UKPDS, individuals treated with insulin or sulphonylurea had slightly less CAD than individuals treated with diet, although difference did not reach statistical significance.

In another study, DIGAMI (Diabetes Mellitus, Insulin Glucose infusion in Acute Myocardial Infarction) intensive glycemic control in patients with diabetes with MI was associated with a 52% reduction in 1 year mortality and the survival advantage was maintained for 5 years. [8]In the Whitehall study, subjects who had glucose> 106mg/dl showed a doubling of CAD mortality irrespective of age, blood pressure and other risk factors.

Conclusion-

Identification and appreciation of glycometabolic abnormalities in patients with acute coronary syndromes have the potential to identify patients in whom established management strategies may improve the outcome. Therefore the glycometabolic state at admission, suggested by the BSL on admission and by HbA1c is an important risk factor for patients with DM and ACS and useful as early markers of longstanding glycometabolic disturbance .In addition, impaired glucose tolerance has also been identified as risk factor for CVD, suggesting that mildly elevated hyperglycemia in absence of overt Type 2 DM may contribute to CVD. Since the leading cause morbidity and mortality is atherosclerotic vascular disease, the epidemiology of DM and its associated cardiovascular complications is essential for targeting interventions designed to improve health outcomes in this high risk population.

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