Prognostic value of stress hyperglycemia in acute coronary syndrome in non-diabetic patients

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Abstract

Background: Any kind of stress, physical or emotional leads to increased production of ACTH, thus leading to increased glucocorticoid release and hence, hyperglycemia. Various studies suggest that the treatment of Stress Hyperglycemia has tremendous potential to reduce the morbidity and mortality among hospitalized patients with Stress Hyperglycemia.
Aims: To study the prevalence and prognostic value of stress hyperglycemia in determining the cardiovascular outcome in non-diabetic acute coronary syndrome patients.
Material and Methods: This study was conducted in 100 patients with no previous history of diabetes with Acute Coronary Syndrome over a period of 18 months. Stress Hyperglycemia in the acute phase of Acute Coronary Syndrome was defined as random blood glucose levels greater than or equal to 140 mg/dl. Patients were divided into two groups A and B on the basis of random blood sugar as normoglycemics and those with Stress Hyperglycemia, respectively. These groups were compared to demonstrate the correlation between stress hyperglycemia and cardiovascular outcome of heart failure, arrhythmias, cardiogenic shock or death. The data was collected and statistically analysed.
Results: Out of 100 patients of acute coronary syndrome with no previous history of diabetes, 38 % were found to be having stress hyperglycemia. Heart failure, arrhythmia, shock and death occurred in 57.89%,13.16 % 13.16 %, 21.05% of Stress Hyperglycemic patients as compared to only 16.12%,4.83%, 8.06 %, 6.45 % in normoglycemic patients, respectively.
Summary and Conclusion: There is high prevalence (38%) of Stress Hyperglycemia in Acute coronary syndrome patients and is associated with adverse outcomes such as heart failure, arrhythmia, cardiogenic shock and death.

Keywords: acute phase hyperglycemia, heart failure, arrhythmias, shock, death.

Introduction

Stress hyperglycemia (SH) is present in 25% to 50% of patients admitted with Acute Coronary Syndrome (ACS). SH is associated with the risk of in hospital complications and is a marker of worse prognosis for such outcomes as mortality, heart failure (HF) and cardiogenic shock[1]. At the time of the acute myocardial infarction (AMI), hyperglycemia may be an important risk factor that is potentially modifiable[2, 3].In the past various studies have demonstrated the association between stress hyperglycemia and poorer cardiovascular outcome, but still stress hyperglycemia has been largely overlooked as an important risk factor in ACS patients. This may be due to lack of sufficient studies and poor understanding of the pathophysiology of this association.Presently, there has been a substantial debate on the cut off random blood sugar levels for defining stress hyperglycemia. Biochemical method to be used for measuring blood sugar and protocol to be followed for monitoring of blood sugar has also not been defined.There have been no guidelines regarding target blood glucose levels to be maintained and its subsequent benefit for the patient has also not been established. The most important issue, however, is whether elevated glucose is a direct mediator of adverse outcomes in ACS patients or just a marker of greater disease severity[4].

The Diabetes Insulin-Glucose in Acute Myocardial Infarction (DIGAMI) trial demonstrated significant reductions in mortality when an intensive insulin regimen was administered to hyperglycemic patients hospitalized with AMI[5, 6]. So the present study was carried out to study the prognostic value of stress hyperglycemia in ACS in Non-Diabetic patients

Materials and Methods

Study protocol and participants:

The present study was conducted in the Department of Medicine, Guru Nanak Dev Hospital, Amritsar involving 100 patients of Acute Coronary Syndrome over a period of 18 months. Approval from ethical committee was taken prior to the start of study and informed consent of the patient was taken in their vernacular language before commencing the study.

Patients were selected and defined according to following criteria:

Inclusion criteria:

- Patients with Acute Coronary Syndrome.
- Patients of ACS with complications.

Exclusion criteria

- Diabetic patients [Known case of DM or HbA1c > 6.5]
- Patients on drugs that cause hyper or hypoglycaemia
- Patients with prior history of infarction.
- Patients with ST elevation or depression due to causes other than ACS.
- Patients who do not give the consent.

SH in the acute phase of ACS was defined as random blood glucose levels greater than or equal to 140 mg/dl. Random sugar sample was taken on admission by glucose oxidase method. Patients were divided into 2 groups as:

Group A   -   Normoglycemic patients
Group B   -   Acute phase hyperglycemic (Stress Hyperglycemic) patients.

These groups were compared to demonstrate the correlation between stress hyperglycemia and cardiovascular outcome of heart failure, arrhythmias, cardiogenic shock or death.

Statistical study:

This was a cross sectional type of study. The data collected was analysed with SPSS 21 using ' t' test and Chi square. *P* value of <0.05 was considered significant.

Results

In our study out of 100 patients of acute coronary syndrome with no previous history of diabetes, 38 % of patients were found to be having stress hyperglycemia. Both the groups were matched for age, gender, BMI, history of smoking, alcohol, sedentary lifestyle, hypertension, HbA1c, lipid profile and type of ACS [Table 1].

Table 1: Showing comparison of various factors among Group A and Group B

Variables	Group A	Group B	*P* value
Age	59.02 ± 14.11	56.03 ± 15.29	0.19
Gender			
Male	38 (61.29)	23 (60.53)	
Female	24 (38.71)	15 (39.47)	1.23
BMI	62 ± 0.80	38 ± 0.85	0.91
Smoker	16 (25.8)	11 (28.94)	0.58
Alcohol	13 (21)	8 (21.05)	0.53
Sedentary lifestyle	14 (22.56)	9 (23.68)	0.67
Hypertension	19 (30.6)	12 (31.57)	0.52
RBS	62 ± 11.59	38 ± 12.89	0.001
HbA1c	62 ± 0.54	38 ± 0.51	0.41
Total cholesterol (200 mg/dl)	18 (29.04)	12 (19.46)	0.32
Serum Triglycerides (150 mg/dl)	18 (29.03)	11 (29.95)	0.28
HDL			
Males (40mg/dl)	32 (84.21)	21 (91.32)	0.42
Females(<50mg/dl)	19(79.16)	11(73.33)	0.17
LDL (120 mg/dl)	35 (56.45)	24 (63.16)	0.16
VLDL (30 mg/dl)	18 (29.03)	11 (29.95)	0.28
Type of ACS			
STEMI	26 (41.95)	17 (44.74)	
NSTEMI	6 (9.68)	4 (12.12)	0.44
UA	30 (48.38)	17 (44.74)	

Mean blood sugar in the two groups was found as 111.03±11.59 mg/dl in Group A and 179.47±12.89 mg/dl in Group B. Mean blood sugar was found to be statistically significant in the two groups with (*P*=0.001).Mean HbA1c was found as 5.23±0.54 mg/dl in Group A and 5.25 ±0.51 mg/dl in Group B. Mean HbA1c was found to be statistically insignificant in two groups with (*P*=0.41).

Incidence of heart failure, arrhythmias, cardiogenic shock and death was found to be significantly greater among stress hyperglycemic patients.Heart Failure was found in 16.12% patients of Group A and 57.89% patients of Group B which was statistically significant (*P*=0.002).Arrhythmia was found in 4.83% patients of Group A and 13.16% patients of group B which was also statistically significant (*P*=0.02).Cardiogenic shock was found in 8.06% patients of Group A and 29.95% patients of Group B .This was statistically significant (*P* 0.001).Death was found in 6.45% patients of Group A and 21.05% patients of Group B. This was also statistically significant (*P*=0.02) [Table 2].

Table 2: Showing comparison of various cardiovascular outcomes among Group A and Group B

	Group A		Group B		x^2-value
	No. of cases	%age	No. of cases	%age	
Heart failure					$x^2 = 9.19$ P value = 0.002
• Present	10	16.12	22	57.89	
• Absent	52	83.88	16	42.11	
Arrhythmia					$x^2 = 4.82$ P value = 0.02
• Present	3	4.83	7	13.16	
• Absent	59	95.17	31	86.84	
Shock					$x^2 = 21.79$ P value = 0.0001
• Present	5	8.06	11	29.95	
• Absent	57	91.94	27	71.05	
Death					$x^2 = 4.82$ P value = 0.02
• Yes	4	6.45	8	21.05	

Discussion

Our study was undertaken to identify the true prevalence of stress hyperglycemia in acute coronary syndrome patients in non- diabetic population as not many studies have been done in this population. Stress hyperglycemia is a poorly recognized entity in these patients. In the past majority of the studies have established the prognostic importance of diabetes on cardiovascular outcomes in ACS patients but the importance of stress hyperglycemia in non-diabetic patients has been essentially underrated. This study appraises the prognostic significance of stress hyperglycemia in non- diabetic ACS patients.

During severe stress there is increased ACTH release from hypothalamus leading to increased glucocorticoid production. Cortisol causes stimulation of gluconeogenesis and decreased glucose utilization by the cells. This causes a rise in blood glucose levels. Extent of myocardial injury directly correlates with the degree of adrenergic stress and hence the amount of glucocorticoid production and hyperglycemia. Thus, acute phase hyperglycemia associated with acute coronary syndrome can be considered as an epiphenomenon leading to poor outcomes.

Whether there is a direct role of stress hyperglycemia in the adverse prognosis of ACS patients' outcome has not been established. Various studies have suggested that treating stress hyperglycemia may improve ACS sequel[17], thus pointing towards a straight role of Stress Hyperglycemia in the pathogenesis of ACS.

In our study out of 100 patients of acute coronary syndrome with no previous history of diabetes, there was found to be a 38 % prevalence of stress hyperglycemia.Similarly, Zhou Na and Li Zhen found 37% prevalence of stress hyperglycemia in AMI patients who were not diabetics[7].Also Nordin et al in a retrospective study found 38 % of patients of acute coronary syndrome having stress hyperglycemia without evidence of prior diabetes mellitus[8].

In a study conducted by Abbas Ali Mansour, patients with ACS were divided into 3 groups out of which 36.2 % were non-diabetic patients without acute phase hyperglycemia, 27.2 % were Non-diabetic patients with acute phase hyperglycemia and 36.6 % were diabetic patients[9].High prevalence of stress hyperglycemia was found in similar studies conducted by Kosiborod et al [1].

In the present study, difference between the mean blood sugar of two groups was found to be statistically significant with a *P* value of <0.001.Similarly,Modenesi et al in 2012[10] found statistically significant difference in the mean admission blood sugar of two groups (p = 0.03). This is in concordance with our study.In present study, mean HbA1c was found 5.23 + 0.54 % in group A and 5.25 + 0.51 % in group B.

Mean HbA1c was found to be statistically non-significant in two groups with (p=0.41; NS).

Similarly, Lakhdaret al[11] and Soler et al[12] found that hyperglycaemia was common after acute AMI, whereas high HbA1c was less common. This is in concordance with our study.

Occurrence of STEMI, NSTEMI and UA in two different groups was statistically insignificant (*P*=0.44).Similarly, Abbas Ali Mansour et al in 2011[9] found no significant difference in occurrence of Acute Coronary Syndrome in different groups which is in concordance with our study.

Significant difference was found in the outcomes of heart failure (*P* =0.002), arrhythmias (*P*= 0.02), cardiogenic shock (*P*= 0.05) and death (*P*= 0.02).

This shows that irrespective of previous history of diabetes admission blood sugar if 140 mg/dl is associated with adverse outcomes such as heart failure, arrhythmia, cardiogenic shock and death.

Similarly, Lakhdar et al in 1986[11] observed high blood sugar values and high serum cortisol levels in patients with complications like left ventricular failure and in those who expired. This is consistent with the findings of our study.

Also Meisinger C et al in 2006[13] showed admission hyperglycemia was also associated with complications during hospital stay among 28-day survivors. This study is in concordance with our study.

Petursson P et al in 2007[14] studied admission glycaemia and outcome after acute coronary syndrome. In this study, they found that, admission hyperglycaemia is a strong risk factor for mortality in patients with acute coronary syndrome and may be even stronger than a previous history of diabetes which is consistent with our study.

Likewise Taysir et al in 2009[15] found that that the stress hyperglycemia on admission is a powerful predictor of increased major adverse events and hospital mortality and cardiac failure in patients with acute coronary syndrome. This is in keeping with the findings of our study.

Ameer et al in 2010[16] found that admission hyperglycemia more than 200mg/dl was associated with higher incidence of cardiogenic shock, recurrent ischemic events, heart failure, and death in non-diabetic patients (P=0.009, 0.022, 0.025, 0.026 respectively) but no more arrhythmias.

Zhou Na, Li Zhen[7] concluded in their study that heart failure, arrhythmias, cardiogenic shock and mortality were significantly higher in high blood sugar patients. This is in keeping with the findings of our study.

Modenesi[10] in 2012 found in their study that SH was associated with such events as death, HF, and left ventricular systolic dysfunction during the in hospital follow up period. This is in keeping with our study.

The benefits of strict control of blood sugar levels in critical patients have been demonstrated and include reduced rates of organ dysfunction and mortality with the maintenance of blood glucose levels between 80 and 110 mg/dL instead of the old target, which was between 180 and 200 mg/dL. The benefits seem to be related not only to lower blood glucose levels but also to the anti-inflammatory effects of insulin, which reduce the production of substances related to oxidative stress and lower glucotoxicity[17].

Conclusion

One fair conclusion based on the findings of this study is that there is high prevalence (38%) of stress hyperglycemia in ACS patients and is associated with adverse outcomes such as heart Failure, arrhythmia, cardiogenic shock and death.

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