EVALUATION OF ADMISSION TIME HYPERGLYCAEMIA IN ACUTE CORONARY SYNDROME PATIENTS

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ABSTRACT

BACKGROUND

Hyperglycaemia, in both diabetic and nondiabetic patients, has a significant negative impact on the morbidity and mortality of patients presenting with an Acute Myocardial Infarction (AMI). Contemporary evidence indicates that persistent hyperglycaemia after initial hospital admission continues to exert negative effects on AMI patients. There have been a number of studies demonstrating the benefit of tight glucose control in patients presenting with AMI, but a lack of convincing clinical data has led to loose guidelines and poor implementation of glucose targets for this group of patients.

MATERIALS AND METHODS

100 patients who came with Acute Coronary Syndrome who had admission time hyperglycaemia during October 2012 to September 2014 were studied in this study. Hyperglycaemia was defined in the current study as random blood glucose at admission more than 200 mg/dL. We studied patients of more than 18 years of age who were diagnosed as Acute Coronary Syndrome- ST Segment Elevation Myocardial Infarction (STEMI), Non-ST Segment Elevation Myocardial Infarction (NSTEMI) and Unstable Angina (UA).

RESULTS

Mean age for diabetic patients was 57.40 years and for non-diabetic patients was 56.09 years. Males were more susceptible to develop ACS in both the groups. Incidence of STEMI and NSTEMI was more in diabetics than non-diabetics. Incidence of Unstable Angina was more in non-diabetics than diabetics.

CONCLUSION

Incidence of complications is higher (surprisingly) in non-diabetics as compared to diabetics. Incidence of death is much higher in diabetics as compared to non-diabetics with stress hyperglycaemia (on admission). Hence, blood glucose level and HbA1c levels should be routinely measured in every patient with Acute Coronary Syndrome.

KEYWORDS

Hyperglycaemia, Diabetes Mellitus, Arrhythmia, Cardiogenic Shock, Cardiac Arrest.

BACKGROUND

High admission blood glucose levels after acute coronary events are common and are associated with an increased risk of death in subjects with and without diabetes.[1]

Elevated admission glucose levels in non-diabetic patients with ACS are independently associated with larger infarct sizes and higher long-term mortality rates when compared with patients with normal glucose levels. Glycometabolic state at hospital admission is an important risk marker for long-term mortality in patients with acute coronary syndrome.

Stress plays an important role in the regulation of insulin secretion. A variety of common clinical illnesses lead to stress, which are commonly associated with increased blood glucose levels. Acute insulin response is inhibited by catecholamines by alpha adrenergic receptor stimulation. The stress effect is probably an index of sympathetic nervous system overactivity. Epinephrine blocks insulin secretion, stimulates glucagon release, activates glycogen,[2] breakdown and impairs insulin action in target tissues such that capacity to dispose off an exogenous glucose load is impaired.

Several studies have shown that abnormally inhibited acute insulin secretion during stress can be improved by alpha blockage and have supported the concept that inhibition of insulin secretion during stress is attributed to overactivity of the adrenergic nerves.[3]

The reaction to stress operates primarily through two basic endocrine mechanisms, one relating to the adrenal medulla and the other to the adrenal cortex.[4] The adrenal medulla combined with other components of the sympathetic nervous system serves as an "alarm" mechanism to mobilise

glucose as well as fatty acids and lactic acid. The means by which the rise in glucose occurs is by -

1. Increased glycogenolysis in the liver.
2. Direct inhibition of glucose uptake by the muscle.
3. An inhibitory effect of epinephrine upon pancreatic insulin release lessening any rise in serum insulin.

The second principal endocrine mechanism of sustaining or raising blood glucose is through stimulation of pituitary adrenocortical axis, clinical studies are not clear in delineating how much or what type of stress gives this corticoid response.[4]

One third of all individuals with hyperglycaemia admitted to an urban general hospital do not have a previous diagnosis of diabetes in these patients. Hyperglycaemia is a risk factor for adverse outcomes during acute illness like acute myocardial infarction. Patients with stress hyperglycaemia were at increased risk of Congestive Heart Failure and cardiogenic shock when compared to patients with diabetes mellitus. Stress hyperglycaemia after myocardial injury is associated with an increased risk of in-hospital mortality. During acute myocardial insult, hyperglycaemia is associated with increased levels of inflammatory markers and enhanced expression of cytotoxic T-cells.[5] An increased inflammatory immune process leads to poor cardiac outcome, especially in acute myocardial infarction patients. So stress hyperglycaemia amplifies inflammatory immune reaction and worsens functional cardiac outcome. The relation between infarct size and plasma glucose concentration confirms that stress hyperglycaemia is a real phenomenon in patients with acute myocardial infarction, which leads to poor patient outcome. Larger infarctions results in more pronounced sympathetic nervous system activation and catecholamine secretion that leads to hyperglycaemia on one hand and higher mortality on the other.[6,7]

G A Oswald et al in 1986 showed a correlation between plasma concentrations of adrenaline in the early stages of the infarction and the size of the infarct. Hyperglycaemia measured on admission in most non-diabetic patients with acute MI is determined both by the extent of infarction, mainly through the secretion of adrenaline and through secretion of other stress hormones that are independent of infarct size.[7] In experimental MI, it has been suggested that the stimulus to adrenaline release is reflex arising from receptors at the site and boundary of the infarct. The relation of plasma concentration of adrenaline early in the course of infarction to infarct size in the patients studied is compatible with a similar mechanism existing in man.[8]

MATERIALS AND METHODS
We Studied Patients of more than 18 Years of Age who were Diagnosed as Acute Coronary Syndrome -
- ST Segment Elevation Myocardial Infarction (STEMI).
- Non-ST Segment Elevation Myocardial Infarction (NSTEMI).
- Unstable Angina (UA).

With their Supportive Evidences from -
- Clinical history.
- Examination.
- ECG changes.
- Biochemical markers.

Inclusion Criteria
Patients having age above 18 years with features of Acute Coronary Syndrome.

Exclusion Criteria
- Age less than 18 years.
- Non-cardiac chest pain patients.

Study Design
100 patients presenting with Acute Coronary Syndrome who had admission time hyperglycaemia and who fulfilled inclusion/exclusion criteria were enrolled for the study.

Data Analysis
Hyperglycaemia was defined in the current study as random blood glucose at admission more than 200 mg/dL.[9] Patients were stratified based on their history of diabetes mellitus and the blood glucose levels at the admission.
- Admission time hyperglycaemia with diabetes mellitus.
- Admission time hyperglycaemia without diabetes mellitus.

Instruments, Materials Required and Used -
1. ECG.
2. Blood Sugar Level by GOD-POD method. Semi Auto Analyser (ERBA CHEM-5 PLUS) Semi Auto Analyser (ERBA CHEM-7 PLUS).
3. Troponin I by Ami-check Kit.

RESULTS

Age in Years	Diabetic Patients		Non-Diabetic Patients	
	Male	Female	Male	Female
< 30	1	0	0	0
31 - 40	2	0	4	1
41 - 50	6	4	6	4
51 - 60	8	6	9	5
61 - 70	10	4	7	6
71 - 80	6	1	3	2
> 80	1	1	2	1
Total	**34 (68%)**	**16 (32%)**	**31 (62%)**	**19 (38%)**
Mean ± SD	58.52 ± 9.87	56.29 ± 10.04	56.61 ± 11.25	55.58 ± 10.59

Table 1. Age and Sex Wise Distribution in Patients with Acute Coronary Syndrome in Diabetic Patients and Non-Diabetic Patients

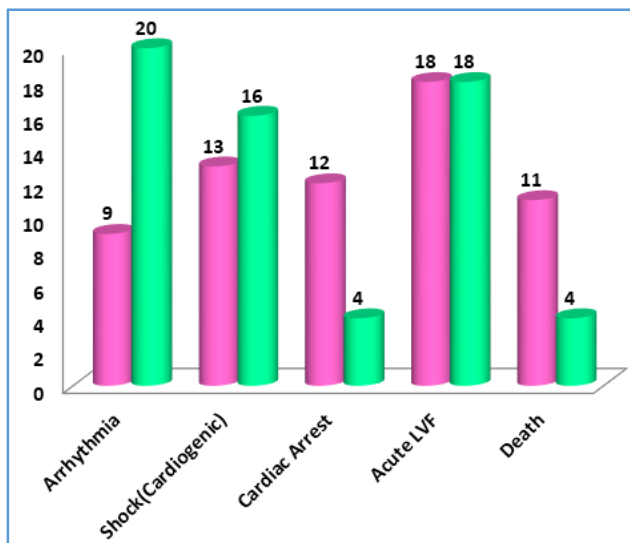| Diagnosis	Diabetic Patients	Non-Diabetic Patients
	No. (%)	No. (%)
NSTEMI	9 (18%)	6 (12%)
STEMI	23 (46%)	15 (30%)
UA	18 (36%)	29 (58%)
Total	**50**	**50**

Table 2. Association between Diagnosis and Diabetic and Non-Diabetic Patients

Complications	Diabetic Patients	Non-Diabetic Patients
	No. (%)	No. (%)
Arrhythmia	9 (18%)	20 (40%)
Shock (Cardiogenic)	13 (26%)	16 (32%)
Cardiac Arrest	12 (24%)	4 (8%)
Acute LVF	18 (36%)	18 (36%)
Death	11 (22%)	4 (8%)

Table 3. Association between Complications and Diabetic and Non-Diabetic Patients

Value of $\chi^2 = 11.411$, p = 0.0223, significant.

By applying Chi-Square test, there is significant association between complications and diabetic and non-diabetic patients (p = 0.0223).

Final Outcome	Diabetic Patients	Non-Diabetic Patients
	No. (%)	No. (%)
Recovered	39 (78%)	46 (92%)
Death	11 (22%)	4 (8%)
Total	**50**	**50**
Table 4. Association between Final Outcome and Diabetic and Non-Diabetic Patients		

Value of χ^2 = 2.824, p = 0.0929, significant.

By applying Chi-Square test, there is significant association between final outcome (recovered and death) and diabetic and non-diabetic patients (p = 0.0929).

DISCUSSION
Hyperglycaemia at the time of hospital admission predicts increased mortality in patients with Acute Coronary Syndromes (ACS) including ST-Segment Elevation Myocardial Infarction (STEMI),[10-15] revascularisation procedures such as thrombolysis or Percutaneous Coronary Intervention (PCI),[16-19] and other critical illnesses.[20-22] The relationship between blood glucose and mortality appears linear with escalating risk associated with increasing blood glucose levels and is independent of a diagnosis of diabetes.[23]

There are three main hypotheses as to why hyperglycaemia portends higher mortality in acutely ill patients. First elevated blood glucose can be a physiologic response to hormones, such as epinephrine or cortisol that are released under high systemic stress and hence may indicate greater overall illness severity.[24] For example, those subjects with larger areas of myocardial ischaemia and more impaired left ventricular function may have stronger sympathetic activation leading to higher glucose levels. Second, hyperglycaemia may be an indicator of systemic and organ-specific metabolic dysregulation, especially impaired insulin signalling. In this regard, insulin resistance causes not only hyperglycaemia but also may lead to a reduction in energy production in the heart and other organs producing a lower tolerance to hypoperfusion. In a similar vein, reduced insulin signalling may increase vulnerability to ischaemic injury, because downstream molecules in the insulin signalling cascade have well-established cytoprotective effects and these are lost when insulin-signalling pathways are disrupted.[25,26] Third, acute hyperglycaemia is implicated in the activation of other pathologic processes that could contribute to cellular and tissue injury, such as increasing free radical formation and oxidative stress, inducing of a prothrombotic state and worsening endothelial function.[27-29]

- 100 patients who came with Acute Coronary Syndrome who had admission time hyperglycaemia during October 2012 to September 2014 were studied in this study.
- 50 patients who were non-diabetic, but had admission time hyperglycaemia > 200 mg/dL with HbA1c < 6.5% were labelled as stress hyperglycaemia. Their blood sugar came to normal levels after 2nd/3rd day.
- 4 patients who were diabetic, but had admission time hyperglycaemia > 200 mg/dL with HbA1c < 6.5%. Their blood sugar also came to normal levels after 2nd/3rd day. (i.e. diabetics with good glycaemic control).
- Remaining 46 patients who were diabetic, but had admission time hyperglycaemia > 200 mg/dL with HbA1c > 6.5%, they had uncontrolled sugar levels (i.e. diabetics with poor glycaemic control).
- Mean age for diabetic patients was 57.40 years and for non-diabetic patients was 56.09 years.
- Males were more susceptible to develop ACS in both the groups.
- Incidence of STEMI and NSTEMI was more in diabetics than non-diabetics.
- Incidence of Unstable Angina was more in non-diabetics than diabetics.
- Complications like Arrhythmia and Cardiogenic Shock were seen more in non-diabetics than in diabetics. Cardiac arrests and Death were seen more in diabetics than non-diabetics. Acute LVF was equally common in both diabetics and non-diabetics.
- In diabetics 28/50 (56%) patients developed complications and in non-diabetics 34/50 (68%) patients developed complications.
- Deaths occurred in 15 patients. Out of it, 11 (22%) were diabetic and 4 (8%) were non-diabetic.
- Deaths were more due to Cardiogenic shock, Cardiac arrest and Acute LVF in diabetics than non-diabetics.
- 4 patients who were diabetic with controlled HbA1c i.e. HbA1c < 6.5%, but had admission time hyperglycaemia developed arrhythmias.

CONCLUSION
Incidence of complications is higher (Surprisingly) in non-diabetics as compared to diabetics. Incidence of death is much higher in diabetics as compared to non-diabetics with stress hyperglycaemia (on admission). Hence, blood glucose level and HbA1c levels should be routinely measured in every patient with Acute Coronary Syndrome.

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