

## Stress Hyperglycemia and its Relation to Acute Coronary Syndrome Complications

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### Abstract

**Introduction:** Stress hyperglycemia has been associated with increased acute coronary syndrome complications.

**Objectives:** We aimed to study the relationship between stress hyperglycemia and myocardial infarction complications.

**Methods:** Demographic and cardiovascular risk factors were obtained from ninety-nine patients with acute coronary syndrome admitted to the coronary care unit at King Khalid Hospital during the period from June 2014 to April 2015. Tests included plasma glucose estimation, post-admission plasma sugar, Glycosylated haemoglobin, electrolytes, and lipid profile. Diabetic patients with high admission plasma sugar (known or newly discovered) were excluded.

**Results:** Stress hyperglycemia was present in 24.4% of patients, of whom ventricular arrhythmia was detected in 33.3% and low ejection fraction in 50%, while in non-stress hyperglycemia, ventricular arrhythmia and low ejection fraction patient was detected in 12.2%, and 16.2% respectively. A significant statistical correlation was found between stress hyperglycemia and coffee intake, method of transportation to the hospital, and thrombolysis administration. No significant correlation was evident between hyperglycemia and acute coronary risk factors and complications.

**Conclusion:** A significant statistical correlation was found between stress hyperglycemia and coffee intake, method of transportation to the hospital, and thrombolysis administration. There was no evident correlation between stress hyperglycemia and myocardial infarction complications.

**Keywords:** Stress hyperglycemia; Coronary complications

**Abbreviations:** hs-CRP: High Sensitive C-Reactive Protein; HbA1c: Glycosylated Haemoglobin; SPSS: Statistical Package for Social Science; STEMI: ST-Segment Elevation Myocardial Infarction; NSTEMI: Non ST-Segment Elevation Myocardial Infarction

### Introduction

During stressful conditions like myocardial infarction, the sympathetic discharge increase, resulting in adrenaline, noradrenaline, and other counter-regulatory hormone releases. Stress hyperglycemia is the outcome. The high level of these hormones also leads to insulin resistance, at receptor and post receptors levels [1,2]. Claude Bernard, a French physiologist, recorded stress hyperglycemia in 1855 [3].

Coronary heart disease is a common illness, causing much morbidity and mortality worldwide. Risk factors for the coronary disease like diabetes mellitus are alarmingly increasing, due to rapid urbanization, bad eating habits, and lack of physical activity [4,5].

Hyperglycemia has been associated with platelets and thrombotic factors activation that favour thrombus formation [6,7].

Although numerous studies have confirmed the association between stress hyperglycemia in patients with acute coronary syndrome, and increased mortality, and morbidity, however such patients were shown to be actually latent diabetic patients, in whom the stress of myocardial injury worsened their glycaemic status [8]. No studies have assessed hyperglycemia in Tabuk Area, Saudi Arabia.

In the current study, we studied hyperglycemia among patients with the coronary syndrome, excluding patients with known or latent diabetes mellitus, according to their HbA1c% at the time of coronary care unit admission.

### Materials and Methods

A total of 99 patients admitted to King Khalid Hospital coronary care unit, with the diagnosis of the acute coronary syndrome were

invited to sign a consent form then, interviewed using a structured questionnaire. On admission, blood samples were drawn from an antecubital vein with a 19-gauge needle and collected in two tubes (redtop one for plasma sugar, lipid profile, liver function test, serum magnesium, uric acid, serum calcium, serum albumin, high sensitive C-reactive protein (hsCRP), and 25-hydroxy vitamin D level, and glycosylated haemoglobin HbA1c% was collected in pink top venipuncture tube.

Blood glucose was determined by the timed endpoint method using hexokinase enzyme, the change in absorbance is measured at 340 nm. It was performed on Synchron CX9 autoanalyzer [9]. Total cholesterol and triglycerides were measured using enzyme colorimetric assay [10].

HbA1c% was measured using glycohemoglobin reagent set from Pointe scientific Inc. [11] Basic clinical information and traditional risk factors, including dyslipidaemia, were extracted from patients admission charts, then patients were categorized into 2 groups, diabetics (from history, use of oral hypoglycaemic drugs, insulin or the result of their admission HbA1c%), and non-diabetics, according to American Diabetes Association guidelines 7 (diabetes HbA1c >6.5, prediabetes 5.8-6.4, normal 5.7 or less) [12]. Those with admission plasma glucose value of 140mg or more were considered to have stress hyperglycemia [13], after excluding known or newly discovered diabetes mellitus (those not known to have diabetes, but their admission HbA1c% was

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more than 6.5 according to American Diabetes Association) [12]. Arrhythmias were extracted from patient's follow-up charts, and the ejection fraction was obtained from the echocardiography report. The ethical committees of the University of Tabuk and King Khalid Hospital approved the research, and the Statistical Package for Social Science (SPSS-version 16) was used for data analysis. A descriptive study was done, Pearson chi-square (X2) test for categorical variables P-value ≤ 0.05 was considered significant.

## Results

The mean age of 99 patients with the acute coronary syndrome was 51.8 years (SD ±11.3), 84.8% were males. The majority (73.3%) had ST-segment elevation myocardial infarction (STEMI). Diabetes mellitus was present in 37.4%, hypertension in 33.3% while 52% were cigarettes smokers. High admission plasma sugar was evident in 57.7% while stress hyperglycemia was present in 24.4%. Table 1 illustrates other clinical characteristics of participants.

The mean admission plasma sugar was 190.1 mg ± 104.6, post-admission plasma sugar 153.4 ± 103.2, and serum creatinine 110.3 ± 109.9. Table 2 showed other investigations, among coronary syndrome patients.

Table 3 shaded light that: Among stress hyperglycemia patients, ventricular arrhythmia (tachycardia and fibrillation) was detected in 33.3% and low ejection fraction in 50%, while in non-stress hyperglycemia patient, 12.2%, and 16.2% had ventricular arrhythmia, and low ejection fraction respectively.

A direct positive correlation was found between admission hyperglycemia, coffee intake, method of transportation to the hospital, and thrombolysis administration. No significant statistical correlation was found between age, sex, hypertension, smoking. Moreover, vitamin-D deficiency (Table 4).

## Discussion

In patients with suspected myocardial infarction, stress (admission)

Character	No %
<b>Age range( years )</b>	
29-44	26 (27%)
45-75	70 (72.9%)
<b>Sex</b>	
Males	84 (84.8%)
Females	15 (15.2%)
<b>Vascular risk factors</b>	
diabetes mellitusKnown	37 (37.4%)
Newly discovered diabetes	11 (11.1%)
Prediabetes	23 (23.2%)
Hypertension	33 (33.3%)
Prior myocardial infarction	13 (13.1%)
Smoking	51 (52%)
Obesity	20 (20.2%)
Overweight	25 (25.2%)
Central adiposity	29 (29.2%)
<b>Type of MI</b>	
STEMI	73 (73.3%)
NSTEMI	21 (21.6%)
Stable angina	3 (3.1%)
High plasma sugar including diabetics	57 (57.3%)
Stress hyperglycemia	24 (24.5%)

Table 1: Basic clinical characteristics of coronary syndrome patients.

Investigation	Mean± SD
Plasma sugar on admission	190.1±104.6
Plasma sugar post-admission	153.4±103.2
Serum creatinine	110.3±109.9
blood urea	5.97±2.5
Sodium	138.1±4.4
Potassium	3.8±0.47
Serum calcium	2.1±0.2
Serum albumin	34.3±4.6
Magnesium	0.86±0.13
Uric acid	325.9±101.1
Cholesterol	5.1±1.6
Triglyceride	1.99±1.1
Positive high sensitive- CRP	0.65±0.47

Table 2: Investigations of coronary syndrome patients.

Complications No%	Arrhythmias	Ejection fraction<50	P value
Stress hyperglycemia	8 (33.3%)	12 (50%)	0.43
No stress hyperglycemia	9 (12.2%)	12 (16.2%)	
Total	17 (35.5%)	24 (66.2%)	

Table 3: Complications among the study group.

Character	Stress hyperglycemia	P value
<b>Age range</b>		
29-44 years	14 (25.1%)	0.92
45-75	40 (74.9%)	
<b>Sex</b>		
Males	48 (87.3%)	0.42
Females	7 (12.7%)	
High blood pressure	22 (40%)	0.13
Smokers	23 (42.6%)	
Coffee intake (No)	15 (28.3%)	0.02
<b>Method of transportation to hospital</b>		
Private car	46 (85.2%)	0.009
Ambulance	8 (14.8%)	
<b>Thrombolysis</b>		
Done	41 (74.5%)	0.03
Not done	14 (25.5%)	
Hypokalemia	11 (20%)	0.31
Hypomagnesaemia	10 (20.8%)	
Vitamin-D deficiency	25 (65.8%)	0.47
Positive hs-CRP	36 (69.2%)	0.45
Hypercholesterolemia	11 (20%)	0.43
Hypertriglyceridemia	18 (32.7%)	0.19

Table 4: Correlation of stress hyperglycemia to different patient's parameters.

hyperglycemia appears more important than long-term glucose abnormality, in determining prognosis [14].

In the present study 24.4% of coronary syndrome patients had admission hyperglycemia, in accordance with previous study [1] who stated that: hyperglycemia is present in 5-30% of critically ill patients, including myocardial infarction, trauma, sepsis, and apoplexia. Similarly, Alajbegovic et al. [14] concluded hyperglycemia in 27.4% of patients not known to be diabetics.

The mean age of our sample was 51.8 years (SD ± 11.3), ranging

from 29-75 years. Twenty-six (27%) of the present sample were young (age range 29-44), and higher than other studies [15,16] (63.8 years  $\pm$  10.65), this can be explained by the high rate of smoking (52%) and high prevalence of other risk factors in our sample. Interestingly more than two-thirds of the present sample (71.7%) had abnormal sugar profile (diabetes, and prediabetes), in accordance with Norhammar et al. [13] who concluded, diabetes or prediabetes was present in up to 65% of myocardial patients without history of diabetes mellitus.

Prediabetes was found in 23.2% of patients similar to its epidemiology in Saudi population (25.5%) [17], the relationships between prediabetes, endothelial dysfunction, and atherosclerosis had been previously documented by Ciccone et al. [18] and Pannaciulli et al. [19], Acute hyperglycemia had an adverse effect on the heart; it can lead to fatal arrhythmias [20], and QT prolongation in normal subjects [21]. Furthermore, hyperglycemia was found to be an independent variable in the prediction of ventricular arrhythmias [22]. In the current study, the arrhythmia was higher (33.3%) in patients with stress hyperglycemia, compared to the patient without hyperglycemia (12.2%).

Trough inactivation of sarcoplasmic reticulum calcium ATPase, stress hyperglycemia can impair cardiac dysfunction leading to a reduction in contractility [23], moreover persistent hyperglycemia was found to be associated with left ventricular dysfunction, defined as pre-discharge ejection fraction [24]. In the present study: 50% of patients with stress hyperglycemia had low ejection fraction while 16.2% of patients without stress hyperglycemia showed low ejection fraction.

A significant statistical correlation was found between stress hyperglycemia, coffee intake ( $P < 0.02$ ), method of transportation to hospital ( $P < 0.009$ ), and thrombolysis administration ( $P < 0.03$ , similarly Yamauchi et al. showed that coffee exerts a suppressive effect on hyperglycemia in mice, by improving insulin sensitivity [25].

The main strength of our study is the use of HbA1c% for the detection and hence the exclusion of those with undiagnosed diabetes mellitus.

## Limitations of the Study

There are many limitations of this study, first the small size of our sample, second the reliance on a questionnaire for data collection, third the study was conducted in a single hospital, so generalization cannot be guaranteed, and finally the lack of control group is a major limitation. Further larger case-controlled studies are needed.

## Conclusion

The study gave a sample of young Saudi patients in their productive years of life, who acquire a serious disabling, and fatal disease. This sample of patients had many unwanted lethal health problems, including smoking, undiagnosed diabetes, prediabetes, and stress hyperglycemia. It appears prudent for clinicians to monitor for hyperglycemia, and checking the HbA1c% of at risk, for earlier detection and prevention prediabetes.

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