

## FREQUENCY OF STRESS HYPERGLYCEMIA AMONG PATIENTS WITH ACUTE LEFT VENTRICULAR FAILURE

Muhammad Abbas Khan<sup>1</sup>, Muhammad Sadiq<sup>2</sup>, Umair Ali<sup>3</sup>, Sifat Ullah<sup>4</sup>,  
Syed Aman Shah<sup>5</sup>, Hafiz Muhammad Jamil Gul<sup>6</sup>

<sup>1,2,4,5</sup>Department of Cardiology, Hayatabad Medical Complex, Peshawar, Pakistan.

<sup>3</sup>Department of Cardiology, Khyber Teaching Hospital, Peshawar, Pakistan

<sup>6</sup>Department of Cardiology, Services Hospital, Peshawar, Pakistan.

Address for Correspondence:

**Umair Ali**

Department of Cardiology, Khyber Teaching Hospital, Peshawar, Pakistan.

Emails: dr.umair85@gmail.com

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### Contribution

MAK and MS conceived the idea and designed the study. SU and SAS did data collection and manuscript writing. UA and HMJG did final review. All authors contributed equally to the submitted manuscript.

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### ABSTRACT

**Objective:** To determine the frequency of stress hyperglycemia among patients with acute left ventricular failure

**Methodology:** This cross-sectional study was conducted in the in the department of cardiology, Hayatabad Medical Complex, Peshawar from September 2013-August 2014. Patients presenting acute left ventricular failure were included in the study in a consecutive manner and subjected to measurement of blood glucose level and observations were recorded data was analysis on SPSS 22 with  $p < 0.05$  taken as significant.

**Results:** In this study 171 patients were included, 60.2% were male. Mean age of the patients was  $58.7 \pm 7.9$  years. Most of the patients (71.4%) were between 50.01 to 70.00 years. Of the whole sample, 46.8% were hypertensive, 39.8% had history of coronary artery disease and 53.8% were having BMI beyond 22.9. Mean admission plasma glucose level of the sample was  $133 + 24.1$  mg/dl with 33.3% patients having stress hyperglycemia.

**Conclusion:** Stress hyperglycemia is frequent occurrence in our population with left ventricular failure.

**Key Words:** Stress hyperglycemia, left ventricular failure, heart failure, body mass index, obesity, hypertension, diabetes mellitus.

## INTRODUCTION

Acute heart failure (AHF) remains a major cause of cardiovascular morbidity and mortality, in part because of the lack of optimal patients risk stratification and management strategies.<sup>1</sup> It is an increasing cause of admission in emergency departments worldwide, with most patients being hospitalized because of worsening chronic heart failure.<sup>2</sup>

Elevation of glucose could be due to pre-existing, but not yet detected type 2 diabetes, impaired glucose tolerance, or it can be a marker of existing insulin resistance and/or beta-cell failure that through different mechanisms other than diabetes contributed to worse outcome after myocardial infarction.<sup>3</sup> Acute hyperglycemia is independently associated with impaired left ventricular function; it abolishes ischemic pre-conditioning, generating oxidative stress, it worsens endothelial function, increases platelet activation, and amplifies inflammatory immune reactions after acute coronary syndrome and subsequent mortality.<sup>4</sup> Furthermore, it exerts a profound negative impact on the development of the coronary collateral circulation in vivo.<sup>5</sup>

It has been previously shown that screening with an oral glucose tolerance test (OGTT) in an outpatient HF clinic reveals a substantial proportion with unrecognized DM associated with poor prognosis and a more severe HF phenotype.<sup>6</sup> Also, abnormal glucose metabolism (AGM) below the diabetic threshold has been associated with increased mortality and exercise intolerance.<sup>7</sup>

The present study is designed to determine the frequency of stress hyperglycemia in patients presenting with acute left ventricular failure. Heart failure is not uncommon in our population and the as mentioned above, significant morbidity and mortality in patients with Left ventricular failure are due to abnormal glucose metabolism in non-diabetic or unknown diabetic patients.

## METHODOLOGY

It was a cross sectional study carried out in the department of cardiology, Hayatabad medical complex, Peshawar from September 2013-August 2014. Patients were selected through consecutive (non-probability) sampling technique. All patients with age 18-60 years presenting to the department/ ER with acute

left ventricular failure irrespective of gender were included in this study. Patients having previous history of diabetes mellitus, atrial fibrillation and chronic kidney disease were excluded from this study. Patients having history of steroids intake in last one week and patients having symptomatic peripheral arterial diseases were also excluded.

The study was conducted after taking approval from hospital ethical committee. The purpose and benefits of the study were explained to the participants and an informed written consent was obtained. A pre designed proforma was made and all information's regarding this study were documented.

All patients were subjected to detailed history and clinical examination. All patients were subjected to extraction of 3cc of blood under strict aseptic conditions and were immediately sent to hospital laboratory for measuring blood glucose level. Another sample for HbA1c was sent before discharge. All the laboratory investigations were done under supervision of an expert pathologist with minimum of 5 years' experience post fellowship. Data was analyzed using SPSS version 22. Chi square test was applied keeping P value significant at <0.05.

## RESULTS

Out of 171 patients there were 60.2% male and 39.8% female. Mean age of the participants was  $58.7 \pm 7.9$  years. 36.3% were in age group 61-70 years. The age distribution is shown in table 1. Hypertension as seen in 46.8% and coronary artery disease in 39.8% patients. Mean BMI was  $24.7 + 2.89$ . While distributing the sample on the basis of BMI cut off values defined for Asian population, we observed that none of the patient was underweight in our study (BMI < 18.5), 46.2% of patients were of healthy weight range (BMI 18.5-22.9). (Table 2). In our study, the mean blood glucose level observed was  $133 + 24.1$  mg/dl. Using the cut-off point of 140mg/dl, stress hyperglycemia was recorded in 57 (33.3%) of patients (Table 2).

After applying chi square test for stratifying hyperglycemia with age groups and gender, we found p value of 0.029 and 0.581 respectively. Cross tabulation of HTN and hyperglycemia found  $p = 0.017$  and for CAD ( $p = 0.00$ ). Stratification of hyperglycemia with BMI categories found  $p = 0.00$ , which is statistically significant.

**Table 1: Age Distribution of study population (n = 171)**

Age group	Frequency/ Percentage
Up to 50 years	17% (n=29)
51 to 60 years	35.1% (n=60)
61 to 70 years	36.3% (n=62)
71 years & above	11.7% (n=20)

**Table 2: Base Line Characteristics of study population (n=171)**

BMI	Frequency/ Percentage
Healthy Weight Range	46.2% (N=79)
Overweight	33.9% (n=58)
Obese	19.9% (n=34)

## DISCUSSION

Heart failure (HF) with left ventricular (LV) systolic dysfunction is a common disease with a poor prognosis. This is particularly true for patients with co-existent diabetes mellitus (DM), in whom the mortality rate is elevated 1.5-2 times.<sup>8-10</sup> Additionally, diabetic HF patients appear more susceptible to exercise intolerance.<sup>11,12</sup> It has previously been reported that screening with an oral glucose tolerance test (OGTT) in an outpatient HF clinic reveals a substantial proportion with unrecognized DM associated with poor prognosis and a more severe HF phenotype.<sup>6</sup> Also, abnormal glucose metabolism (AGM) below the diabetic threshold has been associated with increased mortality and exercise intolerance.<sup>7,13</sup>

In our study, the admission plasma glucose of 140 mg/dl and above was chosen to select the group of stress hyperglycemia. In some of the largest observational studies to date, as well as in epidemiological analyses of randomized clinical trials, the initial mean 24-hour and mean hospitalization glucose levels above ~120-140 mg/dL appear to be associated with the greatest increase in short-term mortality risk, when the entire cohort of patients (including those with and without established diabetes) is considered.<sup>14</sup> It would appear reasonable to consider random glucose levels >140 mg/dL as the definition of stress hyperglycemia in the acute heart failure setting.<sup>15</sup>

In some instances, hyperglycemia may occur in AHF as the response to myocardial dysfunction, without previously known diabetes. However, most of the experts consider impaired glucose tolerance among patients with AHF a sign of adverse outcome.<sup>16</sup> It is mostly stress-induced and represents a transient increase in blood glucose concentration during AHF episode. This may occur in patients with undiagnosed diabetes, or only with impaired glucose tolerance.

The studies investigating HbA1c in AHF are lacking. In chronic HF, the relationship between mortality and HbA1c in diabetic patients with HF seems to be U-shaped, with the lowest risk of death in patients with humble glucose control (7.1% < HbA1c ≤ 7.8%), making this area attractive for the further prospective studies.<sup>17</sup>

Several prior and smaller studies evaluated the association between admission glucose and mortality in hospitalized patients with HF but had important limitations<sup>18-20</sup>. The largest of these observational studies analyzed the medical record data from 1122 patients hospitalized with HF and did not identify a significant relationship between admission glucose and longer-term (6-month and 1-year) mortality, consistent with our findings.<sup>18</sup> The authors found an association between higher admission glucose and increased risk of in-hospital and 60-day mortality.<sup>18</sup> Two additional studies also suggested a possible association between admission glucose and mortality in hospitalized patients with HF; however, these studies analyzed younger patient cohorts with fewer coexisting illnesses and were limited by small patient samples and single-center experience.<sup>19,20</sup>

The present study was an attempt to report a stress hyperglycemia among patients with LVF in nondiabetic patients. In the Acute Decompensated Heart Failure National Registry (ADHERE) of patients hospitalized with a primary diagnosis of acute HF (33 046 hospitalizations), admission hyperglycemia was not tested as a potential predictor of in-hospital death.<sup>21</sup> 2

previous studies have attempted to investigate the relationship between hyperglycemia and clinical outcome in nondiabetic patients with HF. Suskin et al showed that in nondiabetic patients with HF, impaired fasting glucose level was associated with more severe symptoms, worse NYHA functional class, and a shorter 6-minute walk distance<sup>28</sup>. Newton and Squire analyzed data of 528 patients hospitalized with HF and found that elevated glucose level was associated with increased all-cause mortality<sup>22</sup>. In survivors of the index admission, the relationship was stronger for patients not classified as diabetic.

## CONCLUSION

Stress hyperglycemia is frequent occurrence in our population with left ventricular failure. We recommend further studies on its control, treatment and follow up complications before designing future recommendations.

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