ORIGINAL ARTICLE

Study of Stress Hyperglycaemia as an In-Hospital Prognostic Factor in Acute ST Elevation Myocardial Infarction Patients

Sureshkumar Nagocha[1], Ashok Gagiya[2], Vivek Gurjar[3]

[1]Department of General Medicine, SMIMER, Surat, India
[2]Department of General Medicine, SMIMER, Surat, India
[3]Department of General Medicine, SMIMER, Surat, India

ABSTRACT

Introduction: According to the American Diabetes Association and American Association of Clinical Endocrinologists' consensus on inpatient hyper glycemia, any blood glucose level higher than 7.8 mmol/l (140 mg/dl) without symptoms of preceding diabetes is considered stress hyper glycemia or hospital-related hyper glycemia.

Methodology all patient admitted with acute onset of ST elevation myocardial infarction within 12 hours of onset, age more than 18 and less than 80 years at tertiary care hospital were included in this study.

Result In case group mean age was 55.4 years while in control group mean age 57.5 years was In case group mean Hba1c 5.6 and SD 1.0 was while in control group mean Hba1c 5.3 and SD was 1.1 with p value 0.234.

Conclusion Mortality was commonly noted in the stress hyperglycemic groups. 5(25%) deaths were noted in group, while in euglycemic group 4 (11.4%) death were noted in group.

INTRODUCTION

Stress hyper glycemia or hospital-related hyper glycemia was defined by the American Diabetes Association and American Association of Clinical Endocrinologists consensus on inpatient hyper glycemia as any blood glucose level greater than 7.8 mmol/l (140 mg/dl) without signs of prior diabetes. [1] As early as 1931, it was discovered that non-diabetic patients with acute myocardial infarction had an extremely high incidence of glycosuria. [2] Stress hyper glycemia usually goes away once the stress of acute sickness or surgery wears off. [3]

When a hba1c is measured when a patient is in the hospital, it is possible to distinguish between individuals who have stress hyper glycemia and those who have diabetes but have not yet been diagnosed. [4] After a MI, stress hyper glycemia is linked to a higher risk of in-hospital mortality in both diabetic and non-diabetic patients. [5] An increase in in-hospital mortality and subsequent heart failure was associated with blood glucose levels greater than 120 mg/dl (6.1 mmol/L) in the management of MI (myocardial infarction), according to a meta-analysis of 15 studies. This association held true whether or not diabetes had previously been diagnosed. [5]

Higher troponin I levels were linked to hyper glycemia, perhaps as a result of more extensive myocardial injury. In line with this interpretation, they also discovered that patients with hyper glycemia had infarcts that were larg-

er than those of normoglycemic patients, however there is no definitive link between blood glucose levels and infarct size. [6] Patients without a history of diabetes who present with a major vascular problem, such as a myocardial infarction, may have hyper glycemia that was either undiagnosed diabetes, hyper glycemia brought on by stress, or a pre-diabetic condition. A bad prognosis for the patient may result from this in the form of shock, failure, or arrhythmias. [7]

Therefore, high random blood sugar in diabetic individuals as well as stress hyper glycemia in non-diabetic patients both have negative predictive implications in patients with ACS. A basic survival reaction known as stress hyper glycemia occurs when the body is aroused by powerful events including infection, trauma, or surgery. In the body's neuroendocrine system, stress could cause an increase in the secretion of a number of metabolic hormones like glucagon, epinephrine, and growth hormone. This increase could either directly or indirectly antagonise insulin, causing a lack of it, insulin resistance [9], and high blood sugar [10].

By maintaining blood glucose levels, intervention in individuals with stress hyper glycemia can lower the risk of complications developing and mortality [11]. However, there isn't currently a single accepted protocol for treating stress hyper glycemia [12, 13]. In this study, the predictive importance of the admission RBS in non-diabetics admitted with acute STEMI is investigated.

METHODOLOGY

After taking ethical committee permission cohort of patients admitted in ICU who had following inclusion criteria were participated in to study those criteria were as follow   the study was conducted on patients admitted in the medicine ward/ICU of our tertiary care hospital, all patient admitted with acute onset of ST elevation myocardial infarction within 12 hours of onset, age more than 18 and less than 80 years. while following patients were exclude from study who had MI patients undergoing cardiac intervention procedures or known case of diabetes mellitus or patient on steroids or those with acute pancreatitis or those admitted 12 hours after the onset of symptoms or those with disorders like acute/chronic renal failure or hepatic failure or age less than 18 or more than 80 years or those patients not willing for study. Sample size was calculated by considering the proportion of stress hyperglycemia among acute myocardial infarction cases by 6-months data record among all admitted Patients at medicine department at tertiary care hospital is 3.16%, N = z2 PQ / L2, Z= level of significance 95% =1.96, P= 3.61%, Q= 1-p, L= Allowable error = 5%, Sample size= 49 (10% extra on sample size due to drop out) So, our sample size was 55. patients were divided in to two groups A and B, A Group included patients hyperglycemia, while Group B was included patients without hyperglycemia, patients were enrolled after informed written consent. Detailed history

was taken. General and Systemic examination was carried out and all findings were recorded in the Patient's Performa. Blood investigations, other relevant investigations, on admission RBS and FBS on next 2 consecutive days were noted, and appropriate treatment will be given to patient for myocardial infarction under consultant of the treating unit. Data were collected and entered into MS EXCEL spread sheet, descriptive statistics were analyzed by frequency and percentages, while quantitative data were presented in to mean and SD and compared by unpaired t test.

RESULTS

Table 1 shows that demographic and clinical variables of stress hyperglycemic group (case) and euglycemic group (control), in stress hyperglycemic group (case) out of total 20 cases majority of cases 8 (40%) were belonged from 60 to 69 years age group and mean age was 55.4 years, while in euglycemic group (control) out of total 35 controls majority of cases 12 (34.28%) were belonged from 50 to 59 years age group and mean age was 57.5 years. with p value 0.154 which was statistically not significant which indicates that there was not any association between case and control groups for age groups.

In stress hyperglycemic group (case) out of total 20 cases majority of cases 16 (80%) were male, while in euglycemic group (control) out of total 35 controls majority of cases 21 (60%) were male. With p value 0.128 which was statically not significant, which indicates that there was not any association between case and control groups for gender groups.

In the Stress Hyperglycemic Group (case) out of total 20 cases in majority of cases Inferior wall 9 (45%) was affected, while in Euglycemic Group (control) out of total 35 controls in majority of cases Anterior wall 18 (51.42%) was affected. With p value 0.356 which was statically not significant

In Stress Hyperglycemic Group (case) out of total 20 cases in majority of cases 12 (60%) were belonged from Killip class 1 from, while in Euglycemic Group (control) out of total 35 controls in majority of cases 23 (65.71%) were belonged from Killip class 1. With p value 0.356 which was statically not significant

In Stress Hyperglycemic Group (case) out of total 20 cases in majority of cases had complication was Arrythmia which was noted in 7(35%) of cases. While in Euglycemic Group (control) out of total 35 controls in majority of cases had complication was Cardiogenic shock which was noted in 8 (22.85%) of cases. With p value 0.346 which was statically not significant

In Stress Hyperglycemic Group (case) out of total 20 cases 5 (25%) cases were death while in Euglycemic Group (control) out of total 35 controls 4 (11.42%) cases were death. With p value 0.190 which was statically not significant.

Table 1 Comparison of Demographic and clinical variables of Stress Hyperglycemic group & Euglycemic group

Variables	Stress Hyperglycemic Group (n=20)	Euglycemic Group (n=35)	OR (95% CI)	P – value
Age (in years)				
Less than 40	1 (5%)	2 (7.7%)	Ref	0.154
40-49	2 (10%)	8 (22.85%)	0.5 (0.02, 8.70)	
50-59	6 (30%)	12 (34.28%)	1 (0.07, 13.36)	
60-69	8 (40%)	4 (11.42%)	4 (0.27, 58.55)	
70 & above	3 (15%)	9 (25.71%)	0.67 (0.04, 10.25)	
Mean ± SD	55.4 ± 9.8	57.5 ± 12	-	
Gender				
Male	16 (80%)	21 (60%)	2.66 (0.74, 9.66)	0.128
female	4 (20%)	14 (40%)	Ref	
Affected wall in MI				
Anterior wall MI	5 (25%)	18 (51.42%)	0.14 (0.01 – 1.86)	0.356
Inferior wall MI	9 (45%)	10 (28.57%)	0.45 (0.03 – 5.84)	
Antero-lateral wall MI	2 (10%)	3 (8.57%)	0.33 (0.02 – 6.65)	
Antero-septal wall MI	2 (10%)	3 (8.57%)	0.33 (0.02 – 6.65)	
Lateral wall MI	2 (10%)	1 (2.85%)	Ref	
Posterior wall MI	0 (0%)	0 (0%)	-	
Killip class				
1	12 (60%)	23 (65.71%)	Ref	0.937
2	4 (20%)	7 (20%)	1.09 (0.27 – 4.50)	
3	2 (10%)	3 (8.57%)	1.28 (0.19 – 8.72)	
4	2 (10%)	2 (5.71%)	1.92 (0.24 – 15.35)	
Complication				
LVF	5 (25%)	7 (20%)		0.346
Arrythmia	7 (35%)	3 (8.57%)		
Cardiogenic shock	6 (30%)	8 (22.85%)		
Heart block	5 (25%)	2 (5.71%)		
Out come				
Discharge	15 (75%)	31 (88.57%)	Ref	0.190
Death	5 (25%)	4 (11.42%)	2.58 (0.60 – 11.04)	

Table 2 comparison of clinical and biochemical variables of of Stress Hyperglycemic group & Euglycemic group

Variables	Stress Hyperglycemic Group (Mean ± SD)	P value	Euglycemic Group (Mean ± SD)	P Value
Blood sugar level				
On admission	265.55 ± 90.1	0.005	106 ± 13	0.302
2 days	99.7 ± 19.1		96.3 ± 15	
3 days	103.3 ± 12.5		102.6 ± 16	
On discharge	110.7 ± 21.6		106 ± 18	
HBA1c	5.6 ± 1.0		5.3 ± 1.1	0.234
Hospital stays	7.8 ± 2.1		6.3 ± 1.3	0.126
Ejection fraction	38 ± 0.12		43 ± 0.1	0.345

Table 2 shows that comparison of blood sugar level with stress hyperglycemic group on admission mean was 265.55 and SD was 90.1, while at discharge mean was 110.7 and SD was 21.6, p value was calculated by Anova test 0.005 which indicate that in stress hyperglycemic group at admission blood sugar level significantly higher compared with blood sugar level at discharge.

comparison of blood sugar level with euglycemic group on admission mean was 106 and SD was 13, while at discharge mean was 106 and SD was 18, p value was calculated by Anova test 0.302 which indicate that in euglycemic group at admission blood sugar level was not significantly higher compared with blood sugar level at discharge.

DISCUSSION

In the context of STEMI, hyperglycemia may be momentary and stress-induced rather than an indication of the patient's underlying glucometabolic status. While the processes have not been completely explored, stress hyperglycemia is most likely caused by the sudden re-

lease of catecholamine, cytokines, and cortisol in the initial stage of myocardial infarction. Moreover, the assessment and therapy of these individuals remain difficult and unknown. [14]

In individuals with STEMI, stress hyperglycemia seems to be a transitional condition with negative repercussions rather than a simple glucose metabolism. [15] Heart failure, hemodynamic instability, and greater infarct sizes are all linked to this autonomic nervous system reaction. [16]

Acute increases in plasma glucose have been linked to several negative consequences, including oxidative stress, endothelial dysfunction, inflammation, apoptosis, and hypercoagulability, which may worsen outcomes in STEMI patients, according to several clinical trials. [15-17] Esposito and other Several studies have shown that hyperglycemia in the presence of acute myocardial infarction, regardless of the presence of diabetes, is an independent predictor of death. [18, 19, 20] According to two of these studies, people without diabetes who have hyperglycemia die at a greater rate than those with diabetes who have the same condition. [18, 20] According to Capes et al. [21], diabetic patients with ACS are at risk for in-hospital complications at admission blood glucose concentrations equal to or above 180 mg/dL, while non-diabetic patients with ACS are at risk for in-hospital problems for blood glucose levels over 110 mg/dL.

Timmer et al. [22] have showed that the increase in mortality was not only restricted to individuals with pre-existing diabetes and have classified blood glucose levels exceeding 140 mg/mL as stress hyperglycemia for nondiabetic patients. In the HI-5 research, individuals with acute myocardial infarction who maintained mean blood glucose concentrations exceeding 144 mg/dL had a higher six-month death rate. [23]

In this investigation, we included 55 instances of myocardial infarction that met the inclusion criteria and presented within 12 hours after symptom start. The patient's medical history was recorded, as well as the results of a physical examination. During the patient's hospital stay, an electrocardiogram, cardiac enzymes, and echocardiography were performed. During their hospital stay, the individuals were monitored, and any difficulties were reported. The 55 Patients Included in This Study Were Further Stratified into Two Groups, Based on Random Blood glucose Levels at Admission. GROUP A: Patients with Stress Hyperglycemia GROUP B: Patients without stress hyperglycemia

In the current research, 36% of patients had stress hyperglycemia at the time of admission. While the precise threshold for stress hyperglycemia (SH) has not yet been established, epidemiological studies have shown that it affects 25% to 50% of patients who are hospitalized with ACS. [24,25] In the Nazli Gormeli Kurt [26] investigation, it was discovered that 141 (45.9%) of the patients had stress hyperglycemia. In the Renata de Faria Modenesi study [27], 96 patients (26.4%) had stress hyperglycemia. [4] In research by Marfella et al [28], 31

(29%) individuals had stress hyperglycemia. In a retrospective review of patients hospitalized with ACS, Nordin et al [29] found a prevalence of stress hyperglycemia of 38%.

First, a comparison was made between individuals who had stress hyperglycemia and those who did not. The age distribution in the stress hyperglycemic group was 55.4-9.8 years, while the age distribution in the non-stress hyperglycemic group was 57.5-12 years. 60% of those who were not hyperglycemic under stress and 80% of those who were men. The age difference between the two groups was negligible. In both categories, men are more impacted than women. In the research conducted by Rafael et al. [30, 31] on 834 patients, the mean age was 64 years.

The mean lifespan in different research was 63.3 13.8. In the Raffaele Marfella et al. study [32], the mean age was 57. 2 in the stress hyperglycemic group and 59 5 in the euglycemic group. in Hayri Cinar's [33] research the research comprised a total of 259 patients whose data could be obtained in full. Patients made up of 80.3% men (n = 208) and 19.7% women (n = 41). The patients' average age was 60 years. Male patients' median ages ranged from 32 to 104 years old, while female patients' median ages were 70 and 58, respectively (37–90 years). The mean patient age in Nazli Gormeli Kurt's research [26] was determined to be 52.61+15.93 years.

The majority of cases included in both groups (60% of stress hyperglycemic and 65.7 % of non-stress hyperglycemic) had a Killip class I. The mean blood sugar of the stress hyperglycemic group was 265.5 mg/dl and the non-stress hyperglycemic group was 106 mg/dl on admission. The difference was statistically significant. (P-value ≤0.001 by t-test). In Raffaele Marfella et al. [32] the mean glucose of stress hyperglycemic group had 216mg/dl and non-stress hyperglycemic group had 108mg/dl.

Out of 55 patients enrolled in the study 23 (41.8%) patients presented with acute IWMI, 19 (34.5%) patients presented with acute AWMI, 5 (9%) patients presented with acute ASMI, 3 (5.4%) patients presented with LWMI, and 5 (9%) patients presented with ALMI. In Hayri Cinar [33] 30.9% of patients presented with AWMI, 30.1% with IWMI, 0.8% with PWMI, 0.4% with AIWMI, and 0.4% with ALWMI. In Nazli Gormeli Kurt study [26] it was found that 23.1% of patients were presented with AWMI, 27.8%% with IWMI, 5.5% with PWMI, 4.5% with AIWMI, and 3.9% with ALWMI.

The mean HBA1C of the stress hyperglycemic group was 5.6 % and that of the non-stress hyperglycemic group was 5.3 %, which is not significant.

There were 20 patients under group A and 35 patients in group B out of which 12 patients in group A (60%) and 14 (40%) patients in group B developed complications during hospital stay. The incidence of complications was found to be higher in subjects with stress hyperglycemia than the non-stress hyperglycemic Group. Among the

stress hyperglycemic group 25% patients developed LVF, 35% developed arrhythmia, 30% developed cardio genic shock, and 25% developed heart block as compared to euglycemic patients in which 20% patients developed LVF, 8.5% developed arrhythmia,22.8% developed cardio genic shock, and 5.7% developed arrhythmia.

In Carlos Passos Pinheiro study [34] in-hospital complications were observed in 24 stress hyperglycemic patients (35.8%) as compared to only 11 non-stress hyperglycemic patients' patients (12.9%) (p = 0.001). Patients with hyperglycemia had more cardiac and noncardiac complications. It was noted from this study that the in-hospital complication rate was higher in the stress hyperglycemic group as compared to non-stress hyperglycemic patients.

The stress hyperglycemia group had lower left ventricular ejection fraction (MEAN LVEF=38%) as compared to the non-stress hyperglycemic patients (MEAN LVEF=43%). The difference was statistically significant. (P-value ≤0.001 by t-test). In Raffaele Marfella study [32] it was found that hyperglycemia was associated with higher troponin I levels, probably because of more extensive myocardial damage. Consistent with this interpretation, they also found that patients with hyperglycemia were presented with larger infarct size compared with normoglycemic patients. Regarding mean ejection fraction calculated on echocardiography, both groups showed no difference.in Carlos Passos Pinheiro study. [34] Mean ejection fractions were 57.4 ± 12.9% and 57.1 ± 13.5% for groups I (stress hyperglycemic) and II(non-stress hyperglycemic), respectively (p = 0.881).

In this study some of the group a patients need to stay in the hospital for a prolonged period, because these stress hyperglycemic groups develop more complications during their hospital stay. In Carlos Passos Pinheiro study [34] the mean length of hospital stays in group I patients was 8.3 ± 10.2 days, and in group II patients, 7.2 ± 5.7 days (p = 0.403).

Mortality was commonly noted in the stress-hyperglycemic groups. 5 (25%) deaths were noted in group A & 4 (11.4%) death were noted in group B patients. Several studies demonstrate an association between hyperglycemia and death in populations with ACS. In the CREATE-ECLA study, [35] group with stress hyperglycemia, the mortality rate was 14%. In the HI-5 study, [36] mortality was significantly higher in the group with average blood glucose levels greater than or equal to 144 mg/dL. Suleiman et al. [37] observed in a cohort of 735 nondiabetic patients with AMI that the blood glucose levels on admission were correlated with higher mortality in the first 30 days. Svensson et al. [38] demonstrated that patients with blood glucose levels greater than or equal to 120 mg/dL had 46% higher mortality compared with patients whose blood glucose levels were between 56 and 119 mg/dL. In Hayri Cinar study [33] 10.1% of stress hyperglycemic and 1.3% non-stress hyperglycemic were died 89.9% and 98.7% discharged

respectively. In Renata de Faria Modenesi study [27] There was a statistically significant difference between the groups regarding mortality (p<0.001); 21% of the patients with SH died during hospitalization compared with 3% of the patients without SH.

Several hypotheses have been put forward to explain the relation between stress hyperglycemia and poor outcome. Stress hyperglycemia may be a marker of extensive myocardial damage, reflecting a surge of stress hormones such as catecholamine's and cortisol that produce or augment an insulin resistant state. Relative insulin deficiency and excess catechol amines reduce glucose uptake by the ischemic myocardium and promote lipolysis and increased circulating free fatty acids. The latter inhibit glucose oxidation (the "glucose-fatty acid cycle") and are toxic to ischemic myocardium, resulting in increased membrane damage, arrhythmias, and reduced contractility. [39-42]

Alternatively, elevated blood glucose levels per se adversely affect outcome through the cumulative effects of several mechanisms, including induction of endothelial dysfunction, oxidative stress, hypercoagulability, and impaired fibrinolysis. Admission hyperglycemia may not only be the cause of more severe myocardial damage but also its consequence. Large infarcts are more likely to cause catecholamine release, which affect acid and glucose homeostasis.

LIMITATION OF STUDY

Small sample size. Mortality and complication rates are also influenced by factors such as the presence or absence of co-morbidities, infarct sites, the time from disease onset to treatment, Killip's classification at admission, ST segment elevation resolution, left ventricular function and number of vessels involved. The study was done till the patient was discharged from the hospital. Further follow up is required for assessing the long-term morbidity. Angiographic evidence was not obtained since the procedure was not available in the institution.

CONCLUSION

Subjects with stress hyperglycemia had a higher incidence of complications during hospital stay and a lower left ventricular ejection fraction. There was a significant negative correlation between stress hyperglycemia and left ventricular ejection fraction. The incidence of complications was found to be higher in subjects with stress hyperglycemia Than the Euglycemic Group. In this study some of the group A patients need to stay in the hospital for a prolonged period. Mortality was commonly noted in the stress-hyperglycemic groups. 5(25%) deaths were noted in group A and 4 (11.4%) death were noted in group B patients.

RECOMMENDATION

Our study results suggest that stress hyperglycemia is independent predictors of adverse outcome after acute ST elevation myocardial infarction. Hence, measurement of both blood glucose enables identification of these high-risk groups for aggressive management.

REFERENCES

1. Farrokhi F, Smiley D, Umpierrez GE. Glycemic control in non-diabetic critically ill patients. Best Pract Res Clin Endocrinol Metab 2011; 25:813-24.

2. Cruikshank N: Coronary thrombosis and myocardial infarction with glycosuria. BMJ 1:618-619, 1931 FREE full text.

3. Garber AJ, Moghissi ES, Bransome ED Jr., Clark NG, Clement S, Cobin RH, et al. American college of endocrinology position statement on inpatient diabetes and metabolic control. Endocr Pract 2004; 10 Suppl 2:4-9.

4. DiNardo MM, Korytkowski MT, Siminerio LS. The importance of normo glycemia in critically ill patients. Crit Care Nurs Q 2004; 27:126-34.

5. Capes SE, Hunt D, Malmberg K, Gerstein HC: Stress hyperglycemia and increased risk of death after myocardial infarction in patients with and without diabetes: a systematic overview. Lancet 355: 773–778, 2000

6. Oswald GA, Smith CCT, Bette ridge DJ, Yudkin JS: Determinants and importance of stress hyperglycemia in nondiabetic patients with myocardial infarction. BMJ 293: 917–922, 2008

7. Vora SD, Chaudhary KS, Parmar HK, Modi PJ. A Study of Glycosyl-atedHemoglobin (HbA1c) in Acute Coronary Syndrome. Ntl J Community Med 2016; 7(2):106-110.

8. Wernly B, Lichtenauer M, Hoppe UC, Jung C. Hyperglycemia in septic patients: an essential stress survival response in all, a robust marker for risk stratification in some, to be messed in none. J Thorac Dis. (2016) 8: E621–4. 10.21037/jtd.2016.05.24.

9. Kaibori M, Ishizaki M, Matsui K, Ishizaki M, Iwasaka J, Miyauchi T, et al. Perioperative exercise for chronic liver injury patients with hepatocellular carcinoma undergoing hepatectomy. Am J Surg. (2013) 206:202–9. 10.1016/j.amjsurg.2012.07.035.

10. Marik PE, Bellomo R. Stress hyperglycemia: an essential survival response! Critical Care. (2013) 17:305. 10.1186/cc12514.

11. Godinjak A, Iglica A, Burekovic A, Jusufovic S, Ajanovic A, Tancica I, et al. Hyperglycemia in critically ill patients: manage-ment and prognosis. Med Arch 2015; 69(3): 157-60.

12. Koracevic GP. Proposal of a new approach to study and categorize stress hyperglycemia in acute myocardial infarction. J Emerg Med. (2016) 51:31–6. 10.1016/j.jemermed.2015.03.047.

13. Koraćević G, Mićić S, Stojanović M, Tomašević M, Kostić T, Koraćević M, et al. Single prognostic cut-off value for admission glycemia in acute myocardial infarction has been used although high-risk stems from hyperglycemia as well as from hypoglycemia (a narrative review). Prim Care Diabetes. (2020) 14:594–04. 10.1016/j.pcd.2020.09.004.

14. Barth, E, Albuszies, G, Baumgart, K, et al. Glucose metabolism and catecholamines. Crit Care Med 2007; 35: S508–S518.

15. Qaseem, A, Humphrey, LL, Chou, R, et al. Use of intensive insulin therapy for the management of glycemic control in hospitalized patients: a clinical practice guideline from the American College of Physicians. Ann Intern Med 2011; 154: 260–267.

16. Petersen, CL, Nielsen, JR, Petersen, BL, et al. Catecho-laminergic activation in acute myocardial infarction: time course and relation to left ventricular performance. Cardiology 2003; 100: 23–28.

17. Esposito, K, Nappo, F, Marfella, R, et al. Inflammatory cytokine concentrations are acutely increased by hyperglycemia in humans: role of oxidative stress. Circulation 2002; 106: 2067–2072.

18. Wahab, NN, Cowden, EA, Pearce, NJ, et al. Is blood glucose an independent predictor of mortality in acute myocardial infarction in the thrombolytic era. J Am Coll Cardiol 2002; 40: 1748–1784.

19. Bolk, J, van der Ploeg, T, Cornel, JH, et al. Impaired glucose metabolism predicts mortality after a myocardial infarction. Int J Cardiol 2001; 79: 207–214.

20. Kosiborod, M, Rathore, SS, Inzucchi, SE, et al. Admission glucose and mortality in elderly patients hospitalized with acute myocardial infarction: implications for patients with and without recognized diabetes. Circulation 2005; 111: 3078–3086.

21. Capes SE, Hunt D, Malmberg K, Gerstein HC. Stress hyperglicaemia and increased risk of death after myocardial infarction in patients with and without diabetes a systematic overview. Lancet. 2000;355(9206):773-8

22. Timmer JR, van der Horst IC, Ottervanger JP, Henriques JP, Hoorntje JC, de Boer MJ, et al; Zwolle Myocardial Infarction Study Group. Prognostic value of admission glucose in non-diabetic patients with myocardial infarction. Am Heart J. 2004;148(3):399-404.

23. Cheung NW, Wong VW, McLean M. The Hyperglycemia Intensive Insulin Infusion in Infarction (HI-5) study: a randomized controlled trial of insulin infusion therapy for myocardial infarction. Diabetes Care. 2006;29(4):765-70.

24. Kosiborod M, Rathore SS, Inzucchi SE, Masoudi FA, Wang Y, Havranek EP, et al. Admission glucose and mortality in elderly patients hospitalized with acute myocardial infarction: implications for patients with and without recognized diabetes. Circulation. 2005;111(23):3078-86.

25. Meier JJ, Deifuss S, Klamann A, Launhardt V, Schmiegel WH, Nauck MA. Plasma glucose at hospital admission and previous metabolic control determine myocardial infarct size and survival in patients with and without type 2 diabetes: the Langendreer Myocardial Infarction and Blood Glucose in Diabetic Patients Assessment (LAMBDA). Diabetes Care. 2005;28(10):2551-3.

26. Gormeli Kurt et al., Stress Hyperglycemia in Acute Myocardial Infarction / doi: 10.14744/ejmo.2018.49469

27. Modenesi RF, Pena FM, Faria CA, Carvalho RV, Souza NR, Soares JS, et al. Influence on prognosis and prevalence of stress hyperglycemia in a cohort of patients with acute coronary syndrome August 28, 2012/2012; 24(4):352-356

28. Marfella R, Siniscalchi M, Esposito K, Sellitto A, De Fanis U, Romano C, et al. Effects of stress hyperglycemia on acute myocardial infarction: role of inflammatory immune process in functional cardiac outcome. Diabetes Care. 2003;26(11):3129-35. 15.

29. Nordin C, Amiruddin R, Rucker L, Choi J, Kohli A, Marantz PR. Diabetes and stress hyperglycemia associated with myocardial infarctions at an urban municipal hospital: prevalence and effect on mortality. Cardiol Rev. 2005;13(5):223-30.

30. Sanjua R, Nunez J, Blasco ML, et al. Prognostic implications of stress hyperglycemia in acute ST elevation myocardial infarction. Prospective Observational Study. Rev Esp Cardiol. 2011; 64:201–7.

31. Pinheiro CP, Oliveira MD, Faro GB, et al. Prognostic value of stress hyperglycemia for in-hospital outcome in acute coronary artery disease. Arq Bras Cardiol. 2013; 100:127–34.

32. Katherine Esposito, Raffaele Marfella, Dario Giugliano. Stress Hyperglycemia, Inflammation, and Cardiovascular Events. DIABETES CARE 2003; 26 (11): 1650-1651

33. Cinar H, Avci A, Gulen M, Avci BS, Comertpay E, Satar S. Does stress hyperglycemia affect mortality? Acute myocardial infarction - case control study. Arch Med Sci Atheroscler Dis. 2019 Aug 14;4:e201-e207. doi: 10.5114/amsad.2019.87303.

34. Pinheiro, Prognostic Value of Stress Hyperglycemia for In-Hospital Outcome in Acute Coronary Artery Disease// Arq Bras Cardiol. 2013;100(2):127-134

35. Mehta SR, Yusuf S, Diaz R, Zhu J, Pais P, Xavier D, Paolasso E, Ahmed R, Xie C, Kazmi K, Tai J, Orlandini A, Pogue J, Liu L; CREATE-ECLA Trial Group Investigators. CREATE-ECLA Trial Group. Effect of glucose-insulinpotassium infusion on mortality in patients with acute ST-segment elevation myocardial infarction: the CREATE-ECLA randomized controlled trial. JAMA. 2005;293(4):437-46. 17.

36. Cheung NW, Wong VW, McLean M. The Hyperglycemia: Intensive Insulin Infusion in Infarction (HI-5) study: a randomized controlled trial of insulin infusion therapy for myocardial infarction. Diabetes Care. 2006;29(4):765-70.

37. Suleiman M, Hammerman H, Boulos M, Kapeliovich MR, Suleiman A, Agmon Y, et al. Fasting glucose is an important independent risk factor for 30-day mortality in patients with acute myocardial infarction: a prospective study. Circulation. 2005;111(6):754-60. 19.

38. Svensson AM, McGuire DK, Abrahamsson P, Dellborg M. Association between hyper- and hypoglycaemia and 2-year all-cause mortality risk in diabetic patients with acute coronary events. Eur Heart J. 2005;26(13):1255-61.

39. Oliver MF, Kurien VA. Serum free fatty acids and arrhythmias after acute myocardial infarction. Lancet 1969; 2:1077-1078.

40. Lopaschuk GD, Stanley WC. Glucose metabolism in the ischemic heart. Circulation 1997; 95: 313-315.

41. Taegtmeyer H, McNulty P, Young ME. Adaptation and maladaptation of the heart in diabetes, part I: general concepts. Circulation 2002; 105: 1727 – 1733.

42. Depre C, Vanoverschelde JL, Taegtmeyer H. Glucose for the heart. Circulation 1999; 99: 578-588.