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VALUE OF HIGH SENSITIVE CRP IN HYPERGLYCEMIC PATIENTS WITH ACUTE CORONARY SYNDROME.

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ABSTRACT

Background: Hyperglycemia on admission in patients with acute coronary syndromes is common, and it is a powerful predicator of increased risk of in hospital complications in patients with and without diabetes mellitus, high sensitivity c- reactive protein (hs- CRP) is a cardiovascular risk marker in patients with acute coronary syndrome. **Objectivs:** 1. To determine the levels of high-sensitivity C-reactive protein (hs-CRP) in subjects of acute coronary syndrome with admission hyperglycemia whatever diabetic or not. 2. To determine the levels of high-sensitivity C-reactive protein (hs-CRP) in subjects of acute coronary syndrome without admission hyperglycemia. 3. To compare the results of the above two groups and assess the prognostic value of admission glucose and hs -CRP levels in hyperglycemic patients with acute coronary syndromes. **Design and Setting:** Prospective study, at Sohag university hospital in Egypt. **Methods:** We measured the blood glucose, hs -CRP, cardiac enzymes and HBAIClevels at admission in 100 consecutive patients with ACS. Glucose was categorized as ≤11.1mmol=<200 mg/ dl and ≥ 11.1 mmol=>200 mg/ dl. hs -CRP negative <1 and positive >3 mg, HBAIC ≤ 6.5% or ≥ 6.5). **Results:** In our study reveals a statistically significant relation between levels of admission glucose and left ventricular function (LVfailure, pulmonary edema and cardiogenic shock) or arrhythmias in hyperglycemic patients with ACS (P< 0.0001). Also there is a significant relation between level of hs- CRP and LVF and type of myocardial infarction in-hospital complications. Also there is insignificant relation between HBAIC levels and left ventricular function in ACS at admission. **Conclusion:** We conclude that elevated admission glucose appears a more important in predicting in-hospital and short term complications particularly left ventricular failure and cardiogenic shock in patients with acute coronary syndromes. Also the increased levels of hs- CRP are a predictor for severity and extent of myocardial damage and left ventricular function especially in STEMI. The synergistic effect of associated both stress hyperglycaemia and hs- CRP is a strong predictor for poor ACS outcome.

KEYWORDS: High-sensitivity C-reactive protein level, Hyperglycemia, Inflammatory marker, Atherosclerosis, Acute coronary syndrome.

INTRODUCTION

Over the last decades, evidence has accumulated that systemic inflammatory activity plays a key pathogenic role in atherosclerosis and cardiovascular disease (CVD).[1]

This rationale has led to a search for clinically useful inflammatory biomarkers to improve CVD risk prediction. Prominent among possible candidates is C-reactive protein (CRP) as measured by a highly sensitive assay.[2]

C-reactive protein represents the classical acute-phase protein produced in the liver in response to inflammatory stimuli and plasma levels of high-sensitive C reactive protein (hs-CRP)provide a sensitive marker of increased inflammatory activity in the arterial wall.[3]

Insulin resistance correlates closely with the risk of CVD, explaining some of the excess mortality in type 2 diabetes patients. There appears to be more-or-less linear relationship of cardiovascular risk to insulin resistence across the spectrum of normoglycemic patients with insulin resistence up to presenting with overt type 2 diabetes.[4]

Different studies revealed that hyperglycemia on admission in patients with acute coronary syndromes is

common, and it is a powerful predicator of survival and increased risk of in-hospital complications in patients with and without diabetes mellitus.[5]

Diabetic patients have generalized higher inflammatory state compared with nondiabetic patients, even in the context of ACS. The level of HS CRP correlates significantly with severity of myocardial lesion in ACS.

METHODS

Patients

The study included 100 consecutive patients admitted with acute coronary syndrome in Sohag university hospital from December 2016 to April 2017. It included 48 patients with ST segment elevation myocardial infarction (STEMI) and 30 Patients with Non ST segment elevation myocardial infarction and 22 patients with unstable angina.

***Inclusion Criteria**; a. Above 18 years. b. Hyperglycemic patients with ACS (whatever previously diagnosed diabetic or not).

*** Exclusion Criteria**; Patients with preexisting or acute inflammatory process, malignancy or collagen diseases were excluded.

Measurements

For all patients, full history taking, clinical examination and serum glucose level assessment on admission were done. Serial cardiac enzymes (troponin I and CKMB), glycosylated haemoglobin (HBAIc), hs CRP, serial ECG and complete echo-Doppler study were obtained. Follow up clinical examination and assessment of complication was done for one month after admission.

Diabetes was defined as the use of insulin or glucose-lowering medication on admission, or a diet for diabetes documented in medical history. Patients were categorized according to glucose level at admission (< 200 mg or > 200 mg/ dl = > 11.1 mmol/ l), based on values reported by the world health organization for diagnosing diabetes and according to admission HbA1c (<6.5% and ≥ 6.5%). Statistical Analysis of all Results was done using descriptive statistics Analysis.

RESULTS

Patients included in the study have a mean age of 61.07 ± 7.36 years. All patients were diabetics with admission glucose ranged from (103 - 430) a mean 239.08± 85.82 mg/ dl. Admission glucose was categorized as (< 200 mg/ dl and ≥200 mg/ dl).

HbAIClevel was also included as a continuous and categorized (≤6.5% and ≥6.5%).
Hs C-reactive protein levels were measured in all patients including STEMI & NSTEMI.

In the studied patient with acute coronary syndromes the incidence of left ventricular failure increased incrementally with the levels of admission hyperglycemia either clinically as assessed by killip classification or by echocardiographic ejection fraction (EF%) which is statistically significant. Also there is a significant relation between increased level of hs-CRP with STEMI versus NSTEMI (P<0.0001). There is no significant relationship between level of glycosylated haemoglobin level and left ventricular function at admission or short term complications.

Statistcs

Table (1): Relation between hyperglycemia and characteristics of studied population.

Variable	Group1 Nohyperglycmia N=26	Group II Hyperglycemia N=74	P value
Age/ years			
Mean ± SD	61.38±8.68	60.95±6.90	0.80
Median (range)	65 (48-75)	61 (48-75)	
Gender			
Females	8 (30.77%)	28 (37.84%)	0.52
Males	18 (69.23%)	46 (62.16%)	
Smoking			
Current smoker	8 (30.77%)	22 (29.73%)	0.92
Ex-smoker	6 (23.08%)	20 (27.03%)	
Non-smoker	12 (46.15%)	32 (43.24%)	
Hypertension and Treatment			
Non-hypertensive	18 (6923%)	42 (56.76%)	
ACEIS	4 (15.38%)	8 (10.81%)	
B-blocker & diuretics	0	2 (2.70%)	0.48
B-blocker	2 (7.69%)	16 (21.62%)	
CCB	2 (7.69%)	4 (5.41%)	
Diuretics	0	2 (2.70%)	
Diabetes and treatment			
Not	26 (100%)	0	
Stress hyperglycemia	0	22 (29.73%)	
1st diagnosed	0	16 (21.62%)	
Insulin	0	14 (18.92%)	<0.000
Metformin	0	2 (2.70%)	1
Metformin & pioglitazone	0	6 (8.11%)	
Sulfonylurea			

Table (2): Relation between hyperglycemia and pattern of ACS.

Pattern of ASCs	Group I No hyperglycemia N=26	Group II Hyperglycemia N=74	P value
UA	10 (38.46%)	12 (16.22%)	
NSTEMI	6 (23.08%)	24 (32.43%)	0.06
STEMI	10 (38.46%)	38 (51.35%)	

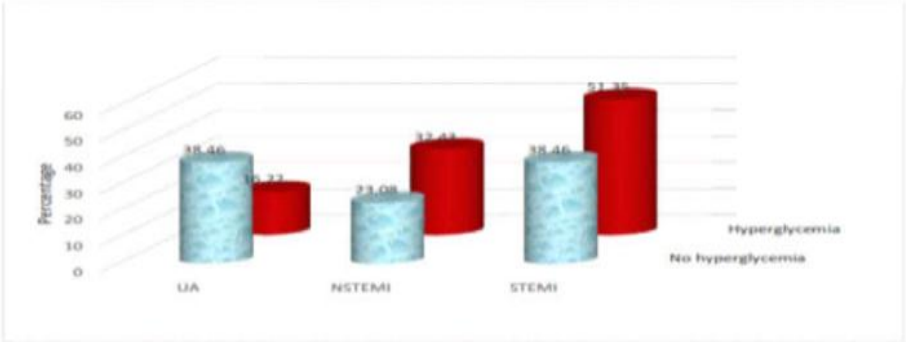
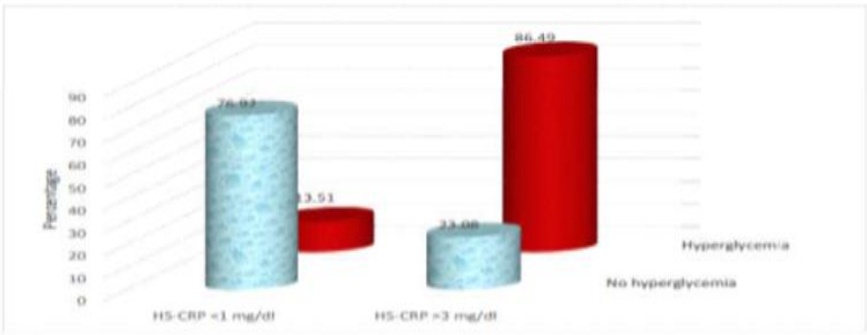


Figure (1): Comparison between patients with and without hyperglycemia as regard pattern of ACS.

Table (3) & Figure (2) Relation between hyperglycemia and HS-CRP.

HS-CRP	Group I No hyperglycemia N=26	Group II Hyperglycemia N=74	P value
HS-CRP <1 mg/ dl	20 (76.92%)	10 (13.51%)	<0.0001
HS-CRP >3 mg/ dl	6 (23.08%)	64 (86.49%)	



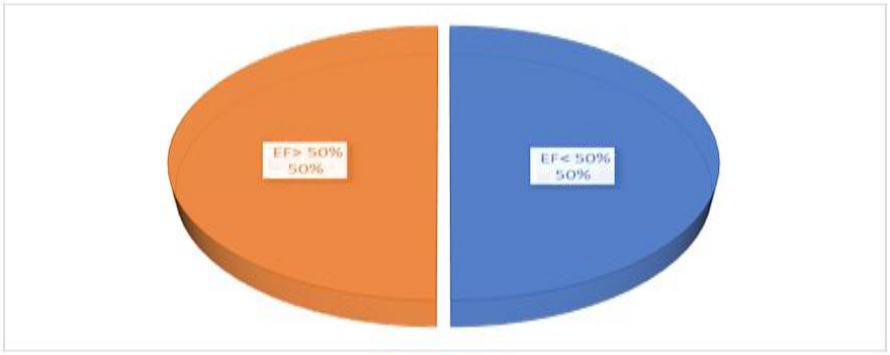


Figure (3): Distribution of studied population according to ECHO-EF%.

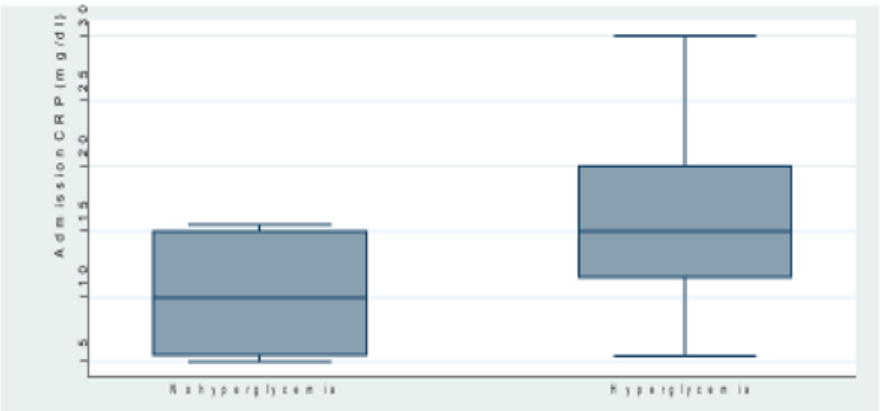
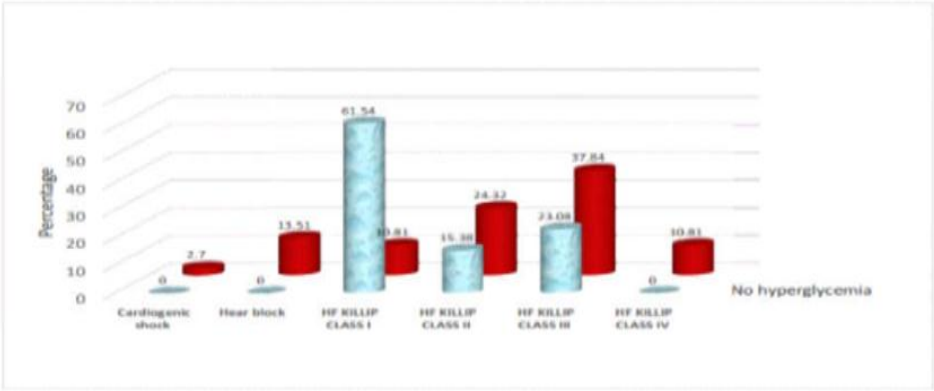


Figure (4): Comparison between patients with and without hyperglycemia as regard Admission CRP (mg/dl).

Table (4): Relation between hyperglycemia and In- hospital complications.

In hospital complications	Group I No hyperglycemia N=26	Group II Hyperglycemia N=74	P value
Cardiogenic shock	0	2 (2.70%)	
Hear block	0	10 (13.51%)	
HF KILLIP CLASS I	16 (61.54%)	8 (10.81%)	<0.0001
HF KILLIP CLASS	4 (15.38%)	18 (24.32%)	
II HF KILLIP	6 (23.08%)	28 (37.84%)	
CLASSIIIHFKILLIP	0	8 (10.81%)	
CLASS IV			



Comparison between patients with and without hyperglycemia as regard In- hospital complications.

DISCUSSION

The patient enrolled in this study allowed us to explore the relation between admission hyperglycemia and outcomes across a broad range of glucose concentration in patients presented by acute coronary syndromes. We found evidence a linear trend between admission glycemia and complications, particularly left ventricular failure. This result is similar with a large study's findings.[6,8]

Also elevated admission glucose is an important and significant predictor of in hospital outcome after STEMI and this is similar with the result of study by Rasoul et al.[9]

But the prior long term glucose dysregulation detected by HbAIC is a covariate of other high risk clinical characteristics of interest and significant observation in our study.[10,11]

The synergistic relationship between glucose level, c-reactive protein (hs-CRP) and risk of clinical events remained statistically significant.

These findings suggest that the important deleterious biological interactions between glucose and C - reactive protein observed in vitro could also be of clinically relevance in ACSpatients.[12]

Although both HbA1cand admission glucose may be associated with impaired prognosis, our results indicate that increased admission glucose is more important.

Higher admission glucose is associated with higher Killip class, larger infarct size and lower ventricular function.[13] HbA1c may have limited predictive power for short-term outcomes in patients with ACS, but its association with long-term outcome may be stronger.[14]

Although stress-induced hyperglycaemia can partly explain the relation between admission glucose and outcome, hyperglycaemia itself can also be harmful. The thrombotic properties of platelets are increased in a hyperglycaemic environment, and this can result in additional cardiovascular complications.[15]

Moreover, recent reports suggest that glucose may be an important mediator in inflammatory responses. Elevated glucose levels induce an increase in inflammatory markers in healthy people, and hyperglycaemic patients with an acute myocardial infarction have an augmented inflammatory response compared to normoglycaemic patients.[16]

Similarly, Duarte et al[17], studying patients with ACS and complications, have found higher mean blood glucose levels, which were significantly associated with in-hospital events.

Our results showed a significant difference of mean CRP levels in patients of NSTEMI, STEMI as compared to UA patients and are in consistence with Zebrack et al[18] and Kazmierezak et al,[19] who identified increase in the CRP levels in patients of STEMI and NSTEMI versus UA, mainly due to myocardial necrosis and release of cytokines mediated CRP response.

A limited increase in the CRP levels in patients with UA could be due to low grade myocardial necrosis by ischemia.[20]

Our results are in agreement with Rubins et al[21] who showed that the major coronary risk factors were more common in patients with STEMI compared to UAand NSTEMI.

However, Perski et al[22] found smoking to be most common and significant risk factor in young patients with CHD.

CONCLUSION

Elevated admission hyperglycaemia in patients with acute coronary syndromes of is an important predictor of in-hospital left ventricular failure especially in STEMI.

ACSdiabetic patients have more inflammation than non-diabetic patients. Increased inflammatory markers have the highest risk of adverse events.

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