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IMPACT OF COMBINED WHITE BLOOD CELL COUNT AND PLASMA GLUCOSE FOR PREDICTING IN-HOSPITAL OUTCOMES AFTER ACUTE MYOCARDIAL INFARCTION

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ABSTRACT

Objective: To determine the combined effects of WBC count and Plasma Glucose levels on predicting in-hospital outcomes in patients with acute myocardial infarction.

Methodology: This cross-sectional study was conducted at Liaquat University of medical and health sciences Hyderabad between the periods of 12 months (1st January 2011 to 31st December 2011). All consecutive patients with acute myocardial infarction with age $\geq$ 18 years of either sex were included. White blood cell count and plasma glucose levels were measured and compared their relationship with in-hospital mortality rates. SPSS version 16 was used for data entrance and analysis. A p value of <0.05 were considered statistically significant.

Results: Among 916 patients, the mean age of the patients $\pm$ standard deviation was 60 $\pm$ 2 years with predominant male proportion (74%). Majority of them (60%) were diagnosed as acute anterior wall myocardial infarction. Overall in-hospital mortality rate was 109 (12%). In-hospital mortality rate was significantly higher observed in patients with a higher count of WBC and elevated levels of plasma glucose ($p<0.05$).

Conclusion: Patients with hyperglycemia and raised WBC count at the time of hospitalization with acute myocardial infarction had an increased in-hospital mortality rate. A step wise increase in peak creatinine kinase level and a step wise decrease in left ventricular ejection fraction were also observed in patients with high PG levels with high WBC count.

Key Words: Acute Myocardial Infarction, Raised White Blood Cell Count and Plasma Glucose Levels, In-Hospital Mortality Rate

INTRODUCTION

An increase in white blood cells (WBC) count and high plasma glucose (PG) levels in patients with acute myocardial infarction (AMI) is associated with high morbidity and mortality.[1] Although the mechanism responsible for these associations is unknown, several suppositions have been postulated, including a WBC-mediated prothombotic state, leukocyte mediated no-reflow, and indirect cardiotoxicity mediated through proinflammatory cytokines.[2-4] Hyperglycemia on admission in patients with acute coronary syndrome is common, and it is reported to be independently associated with poor prognosis even in the primary intervention era.[5] Hyperglycemia is associated with large infarct size, left ventricular dysfunction, and short-term mortality after AMI regardless of diabetic status.[6]

The actuality that WBC count and PG is low-cost and universally measured investigations makes possibly them useful investigations to determine prognostic value. Objective of this study was to determine the combined effects of WBC count and PG levels on predicting in-hospital outcomes in patients with AMI admitted in the cardiology department of Liaquat University of Medical and Health Sciences (LUMHS).

METHODOLOGY

This cross sectional study was conducted at Liaquat University of Medical & Health Sciences Hospital (LUMHS), section of Cardiology, Hyderabad between 1st January 2011 to 31st December 2011 through a consecutive sampling technique in patients with a diagnosis of AMI who were admitted in coronary care unit of either sex and age $\geq$ 18 years. Informed consent was taken from patient/relative and this study was critically reviewed and approved by the ethical committee of the hospital.

During the acute phase, all patients were kept in coronary care unit and after stabilization, were shifted to Cardiology ward. A detailed examination was performed both at the time of admission and before discharge including 2-D Echocardiography.

A 12 leads electrocardiogram (ECG) was recorded at the time of admission (ECG machine of cardimax Fx-2III, Fakuda Denshi) for the diagnosis of AMI. Serial ECGs for the following three days were done to look for the evidence of AMI as S-T segment elevation along with pathological Q-waves of 0.04 second wide and 2 mm in height and also for the concomitant arrhythmias and type of myocardial infarction.

A blood sample was obtained for determining the WBC count and plasma glucose levels. All patients were also screened for Diabetes mellitus and were labeled as Diabetic when the fasting blood glucose was $\geq$ 126 mg/dl and random $\geq$ 200 mg/dl or if they were already taking anti-diabetic medication. Patients were classified as low, medium, and high WBC count on the basis when they have WBC count <9 x 109/L (Low WBC tertile), $\geq$9-11 x 10^9/L (medium WBC tertile), and $\geq$12 x 10^9/L (high WBC tertile).

Most of the patients were given bolus dose of Aspirin 300 mg and Clopidogrel 300 mg orally at the time of presentation and 75mg maintenance dose of coated Aspirin and Clopidogrel given daily. Streptokinase was the only thrombolytic therapy used unless contraindicated. Concomitant standard drugs recommended for the management of AMI i.e. beta blockers, ACE inhibitors, Statin, and Nitrates were also used where needed except if the patient has had a contraindication to these drugs.

Data was entered and analyzed using statistical package for social sciences (SPSS) version 16. Quantitative variables were presented as mean ± SD and t-test was performed for comparison between them. Categorical variables were presented as frequency and percentage and Chi-square test was performed for comparison between them. The nominal regression model was used for in-hospital mortality rate determination. In this model, WBC count and PG levels were used as continuous variables. Differences were considered statistically significant at $p < 0.05$.

RESULTS

A total of 916 patients of AMI were included for final analysis. The mean age of the patients ± standard deviation was 60±12 years. Male proportion was higher than the female, 74% and 26%, respectively. Majority of the study participants were hypertensive (59%) and presented with ST segment elevation MI (89%). Rest of the basic

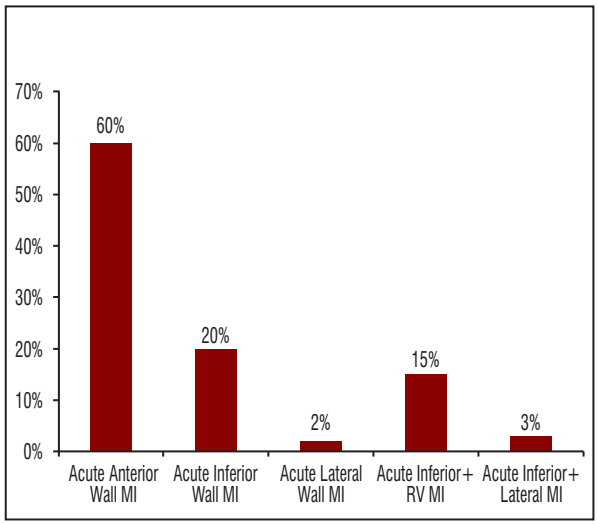
Table 1: Baseline Characteristics of Study Participants with AMI

Characteristics	No: of Patients	Percentage
Age-yrs	60 ± 12	
Male	678	74%
Diabetics	303	33%
Hypertensive	541	59%
Current Smoker	431	47%
Previous History of Infarction	110	12%
ST Segment Elevation	815	89%
Thrombolytic Therapy Given	715	78%
Time to Admission Within 6 Hours	669	73%

demographic shown in Table 1.

Among 916, 550 (60%) of admitted patients were diagnosed as acute anterior wall MI, 183 patients (20%)

Figure 1: Case Distribution According To Type of Infarction



Types of acute myocardial Infarction
MI = Myocardial infarction, RV = Right ventricular

were of Inferior wall MI, and 137 patients (15%) were of Inferior + right ventricular MI. (Figure 1)

Overall in-hospital mortality rate was 109 (12%). In-hospital mortality rate was observed higher in patients with a higher count of WBC (15.6%) as compare to those with moderate (12.4%), and low WBC count (7.8%), respectively, (p <0.001) (Table 2).

As WBC count increased so did the creatinine kinase concentration. Peak creatinine kinase concentration were 2,240±2,277 IU/L in the low WBC tertile, 2,849±2,751 IU/L in the medium tertile, and 3,260±3,110 IU/L in high tertile (p <0.001). It was also observed that low left ventricular ejection fraction occurs in patients with AMI and high WBC counts. Pre-discharge left ventricular ejection fraction was 55±11% in the low WBC tertile, 54±12% in the medium WBC tertile, 50±12% in the high WBC count group (p<0.001) (Table 2).

Table 2: Effect of WBC Count on In-Hospital Mortality, Peak CK, and Left Ventricular EF

Variable	Low WBC Count (n=305)	Medium WBC Count (n=309)	High WBC count (n=302)	P-value
In-hospital Mortality n=109 (12%)	24 (7.8%)	38 (12.4%)	47 (15.6%)	<0.001
Peak Creatinine Kinase (IU/L)	2240±2277	2849±2751	3660±3110	<0.001
Pre-discharge Left Ventricular EF	55±12	54±12	50±12	<0.001

WBC = White blood cell,
EF = Ejection fraction,
IU/L = International Unit per Liter,

In our study we have also observed that patients who had higher levels of PG were also associated with raised rates of in-hospital mortality (7.2% in low PG count, 9.2% in moderate count, and 19.2% in high count (p < 0.001) (Table 3).

Table 3: Effect of PG Levels on In-Hospital Mortality, Peak CK, and Predischarge Left Ventricular EF

Variable	Low PG (n=301)	Medium PG (n=306)	High PG (n=308)	P-value
In-hospital Mortality n=109 (12%)	22 (7.2%)	28 (9.2%)	59 (19.2%)	<0.001
Peak Creatinine Kinase (IU/L)	2240±2236	3000±2800	3260±3000	<0.001
Pre-discharge Left Ventricular EF	58±12	54±12	50±12	<0.001

PG = Plasma glucose,
IU/L = International unit per liter,
EF = Ejection fraction

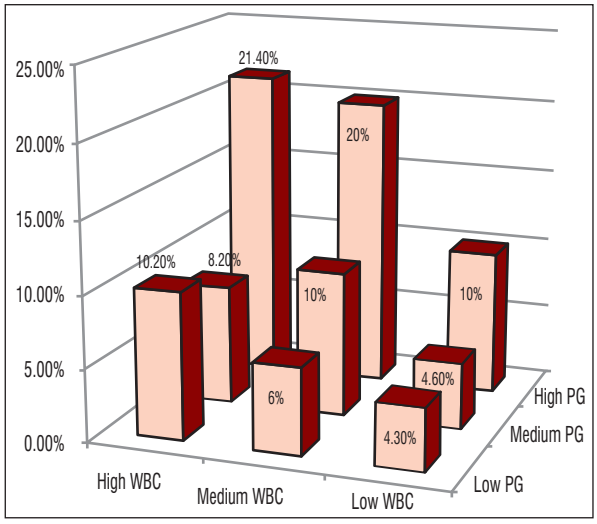
The combined effect of WBC count and levels of PG on predicting in–hospital outcomes were also observed. 25 died out of 122 patients with high WBC count and high PG levels, while there were 5 deaths out of 123 patients with a low WBC count and low PG levels. It was noticed that patients with raised WBC count and PG levels have five folds increased risk of in hospital mortality when comparing it with normal values (p= <0.001) (Figure 2).

DISCUSSION

In 1974, Friedman et al, initially explained the relationship between WBC count and coronary artery disease.[7] What they have found that raised the levels of WBC count has direct association with increased risk of AMI and in 1982 Schlant et al, were the first to document an elevation in WBC count as a predictor of all-cause mortality in patients who survived an AMI.[8] Numerous other studies subsequently confirmed this observation.[9,10] However, there is a lack of data to completely describe the short term prognostic significance of the WBC count measured during the acute phase of myocardial infarction.

In this study we have found a physically powerful alliance between high plasma glucose levels and weaken left

Figure 2: In-Hospital Mortality among Patients With High WBC Count & PG Levels



PG = Plasma Glucose

ventricular function, and high mortality after an AMI. It is unclear whether so-called stress hyperglycemia predisposes to a worse outcome or is simply a marker of poor prognosis. Though inconclusive, studies suggest that stress hyperglycemia may be a marker of extensive myocardial damage.[11] Better established through both in-vitro and in-vivo studies is the fact that an elevated blood glucose levels, whether acute or chronic, adversely affects endothelium-dependent vasodilation and impairs macrophage and lymphocyte function.[12] Hyperglycemia during AMI may reflect a compromised metabolic state and is associated with a surge of serum catecholamine and decreased insulin sensitivity that increases the turnover of potentially harmful free fatty acids.[13,14] As well, hyperglycemia may promote an osmotic dieresis, leading to a reduced circulating volume and decreased end-diastolic and stroke volumes through interference with the Frank-Starling mechanism of myocardial contractility.[15]

Previous studies suggest that harmful effect of raised WBC count and higher plasma glucose levels exists which may interfere with the overall outcome of patients with AMI. There are certain limitations in our study which should be fulfilled in the newer multicenter studies. These limitations such as only measuring and comparing the effects of higher WBC and raised PG levels at the time of admission can cause a difference in overall outcome when comparing with those patients who had persistent elevated PG or WBC levels during hospitalization, and also due to lack of facilities we could not assess the efficacy of insulin therapy during hospitalization. Thing should be remember that patients with AMI but without documented diabetes mellitus were not undergone insulin treatment due to short term raised in the levels of plasma glucose.

CONCLUSION

Patients with hyperglycemia and raised WBC count at the time of hospitalization with acute myocardial infarction had an increased in-hospital mortality rates. A step wise increase in peak creatinine kinase level and a step wise decrease in left ventricular ejection fraction was also observed in patients with high PG level with high WBC count ($p < 0.001$).

These markers i.e. WBC count and Plasma Glucose levels in patients with AMI at admission may help improve risk stratification, initial management and further planning for future management of patients to decrease mortality.

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