Original Research Article

ROLE OF NLR IN CONJUNCTION WITH CORONARY ARTERY INVOLVEMENT AS A BIOMARKER FOR THE MAGNITUDE OF CURRENT OF INJURY, TYPE OF INTERVENTION AND CLINICAL OUTCOMES IN STEMI

ABSTRACT

Background: The potential prognostic biomarker—Neutrophil-Lymphocyte Ratio (NLR) can be used to predict the severity of STEMI. We conducted an Observational study using this parameter together with the extent of coronary artery involvement from Angiogram and magnitude of ST elevation on electrocardiogram (ECG) to determine the prognosis, length of hospital stay. The effect of early reperfusion with Fibrinolysis was also observed.

Methods and Results: 30 subjects (Age 56.43 ± 13.982), with ST-elevation on ECG at admission, treated with Streptokinase and undergoing Angiogram were taken for the study. ECG and Complete blood picture (CBP) on admission, day 3, and day of discharge and on follow-up were obtained respectively.

Out of 30 subjects, 15 received Fibrinolysis out of which 12 (80%) survived compared to the other 15 subjects who presented late, out of which 10 (66.6%) survived. ST elevation on ECG on day-1 was found to be (0.3933 ± 0.11725), day-3 (0.1759 ± 0.12437), day of discharge (0.0500 ± 0.07) and on follow up (0.000 ± 0.00000). NLR values on day-1 were (7.890 ± 4.9831), day-3 (6.243 ± 5.0531), day of discharge (4.340 ± 2.7427) and on follow up (1.714 ± 1.3977) indicating the association of high NLR values and magnitude of current of injury on admission. NLR values >4 and as high as 18.5 were observed in expired subjects. Length of hospital stay was found to be (6.43 ± 5.029).

Conclusion: There was a linear decrement in ST resolution with decrease in NLR and can be attributed to natural course of disease and type of intervention provided. Nevertheless the univariate correlation between ECG and NLR on various days of treatment was not significant.

Keywords: STEMI, neutrophil to lymphocyte ratio, electrocardiogram, reperfusion, mortality, pharmacotherapy

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INTRODUCTION

Atherosclerosis is a major cause of cardiovascular disease and ST elevated myocardial infarction (STEMI) in particular. It is a chronic inflammatory process which leads to plaque formation. The rupture of the unstable plaque and consequent thrombosis leads to occlusion of the coronary arteries and necrosis of the myocardial tissue (1). STEMI is a leading cause of morbidity and mortality and has several risk factors including hypertension, diabetes, smoking, alcohol consumption, etc. Leukocytes and its subtypes are considered as markers of inflammation as the injury to the tissues leads to infiltration of these cells, neutrophils in particular at the site of injury (2). Recently Neutrophil to Lymphocyte ratio (NLR) has emerged as a potential inflammatory biomarker to assess the prognosis of coronary artery disease (CAD) (3,4). The ratio can be easily calculated from complete blood picture (CBP) reports, which is inexpensive and available widely. There is strong evidence about the negative impact of elevated NLR. Arbel et al. (2012) in a study with three-year follow-up of patients with cardiovascular diseases reported that NLR is associated with more severe CAD (5). The reference values of NLR vary depending upon race and ethnicity. These variations need to be

considered while proposing a cut-off value in particular race (6).

According to a number of studies, in patients undergoing coronary angiography or percutaneous coronary intervention, NLR has been associated with adverse outcomes (7, 8). Diagnosis of STEMI is made with the evidence of ST elevation on electrocardiogram. The extent of infarction and number of infarct related arteries (IRA) involved in STEMI is determined using Angiogram and the need for percutaneous coronary intervention (PCI) is assessed (9). The European and American guidelines for STEMI recommend primary percutaneous intervention (PPCI) over fibrinolysis for early reperfusion and better prognosis (10). However, restoration of the normal blood flow immediately with thrombolytic therapy has been observed to be the most effective in patients with STEMI which can be observed from ST segment resolution on ECG. This is referred to as "Electrocardiographic sign of spontaneous reperfusion (SR)" (11). Nearly 30 deaths out of 1000 patients are prevented when patients are treated with fibrinolysis within 6 hours of onset of symptoms. One of the most used fibrinolytic is streptokinase. It is a non-fibrin selective fibrinolytic which acts on the occluding thrombus and causes lysis to restore the blood flow or patency in the affected artery (12). Residual thrombus can occur after mechanical thrombectomy or thrombolytic therapy. This thrombus can be removed via a more aggressive anti-platelet therapy together with thrombolytic therapy (13, 14).

MATERIALS AND METHODS

A prospective observational study was conducted between October 2018 and March 2019. Firstly, informed consent of all subjects was obtained by giving a brief explanation about the study and the lab tests to be performed in the informed consent form. Demographic data (age, gender) and cardiovascular disease risk factors (hypertension, diabetes, smoking, and alcohol consumption) were extracted from all patients.

Study Patients

A total of 30 patients above 18 years of age with a diagnosis of STEMI on admission (mean age 56.43 ± 13.98) were enrolled in the study. STEMI was diagnosed according to typical symptoms of chest pain and shortness of breath prior to admission and with cumulative ST-segment elevation of ≥0.2mV in limb leads or ≥0.1mV in at least two consecutive chest leads. Patients with ongoing infection or systemic inflammatory condition, severe renal or liver disease, haematological disease and pregnant women were excluded from the study. Also patients with ECGs showing Left bundle branch block or patients with cardiogenic shock were excluded.

ECG of all patients on admission, day 3, on the day of discharge and on first follow-up was obtained and the magnitude of ST elevation was measured at the J point from leads II, III, aVF for Inferior myocardial infarction, leads I, aVL, V5-V6 for Lateral wall myocardial infarction, leads V3-V4 for Anterior myocardial infarction, and V1-V2 for septal myocardial infarction.

Laboratory Measurements

Venous blood samples were collected from all patients at the time of admission, on day 3, at the time of discharge and on the first follow-up from the antecubital vein while the patient was in supine position. Complete blood count was obtained from which neutrophils and lymphocyte counts were analysed. NLR was calculated by dividing neutrophil count by lymphocyte count.

Out of 30 subjects, only 12 of them underwent Angiogram for suspected coronary artery atherosclerosis on the 3rd day after admission. Each coronary angiography was performed through the femoral artery access by two interventional cardiologists. A thorough review of angiogram established the location of the lesions and the percentage of stenosis caused by the lesions. PCI was advised for stenosis >50% in any of the main arteries. The angiography reports revealed the need for PCI in almost all patients, with some requiring a single stent to some requiring as many as 3

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stents or CABG. Geriatric patients who couldn't undergo PCI were advised medical management.

STATISTICAL ANALYSIS

Statistical tests were performed using the SPSS 17.0 statistical package for windows. The data was separated into continuous and categorical type. Continuous data is expressed as mean and standard deviation (SD), while categorical data is represented by number and percentages. Whether there is a significant difference in the NLR was determined by recording the baseline parameters during the analysis which include age, gender, hypertension, diabetes, smoking, alcohol consumption, thrombolytic therapy, type of MI, type of coronary artery involvement, ST segment elevation, NLR, type of intervention, and length of hospital stay. Analysis of this data was performed by three different tests, Pearson's correlation test, repeated measures ANOVA, Mauchly's test of sphericity and Freidman test. The p values were determined and significance was fixed at $p \leq 0.005$.

RESULTS

Baseline demographics

Over a period of 8 months (October 2018 - March 2019), there were 30 patients presenting to the hospital with a primary diagnosis of STEMI. The mean age was 56.43 ± 13.98, among them 20 (66.67%) patients were males and 10 (33.33%) were females. Overview of baseline characteristics, comorbidities are given in the table 1.

Table 1: Baseline characteristics and clinical data of the study population

DATA	CASES (n=30)
Age (years)	56.43 ± 13.98
Male	20 (66.67%)
Female	10 (33.33%)
Coronary risk factors	
Hypertension	15 (50%)
Diabetes	8 (26.66%)
Smoker	7 (23.33%)
Alcoholic	5 (16.66%)

Complete blood picture characteristics

Hematological analysis was carried out to calculate the inflammation associated with the injury based on neutrophil and lymphocyte count on day of admission, day 3, day of discharge and on first follow-up. The hematological parameters are included in the table 2.

Table 2: Hematological characteristics of the study population

HEMATOLOGICAL PARAMETERS	CASES (n=30)
Haemoglobin (g/dl)	12.74 ± 2.76
RBC count (million cells)	4.49 ± 1.01
WBC (thousand/cumm)	12.03 ± 3.03
NEUTROPHIL TO LYMPHOCYTE RATIO	
On day of admission	7.890 ± 4.9831
Day-3	6.243 ± 5.0531
Day of discharge	4.340 ± 2.7427
Follow up	1.714 ± 1.3977

Electrocardiographic (ECG) Characteristics

The diagnostic determination of cardiac disease is purely based on ECG changes and this parameter confirms the diagnosis of STEMI in subjects. The 30 subjects that were included in the study show a significant elevation in the ST segment on the day of admission. The changes in ST segment were also noted on day-3, day of discharge and pn follow up. The changes in the ST segment on the following days are represented in the table 3.

Table 3: Electrocardiographic characteristics of the study population

ELECTROCARDIOGRAM	CASES (n=30)
On day of admission	0.3933 ± 0.11725
Day-3	0.1759 ± 0.12437
Day of discharge	0.0500 ± 0.07
Follow up	0.000 ± 0.00000

Angiographic (CAG) Characteristics

8 (26.67%) patients presented with anterior wall MI, 10 (33.33%) patients presented with inferior wall MI, 1 (3.33%) patient presented with lateral wall MI, 5 (16.67%) patients presented with anterolateral MI, 1 (3.3%) patients presented with anteroseptal MI, 3 (10%) patients presented with inferolateral MI and 2 (6.66%) patients presented with anterior with lateral wall MI. The data based on vessel involvement in the patients is given in table 4. Among the 30 patients, 16 (53.33%) patients

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had not undergone CAG due to unstable health condition and financial problems.

Table 4: Angiographic characteristics of the study population

TYPE OF VESSEL	NUMBER OF PATIENTS
Single Vessel Disease	
RCA	3 (10%)
LAD	3 (10%)
LMCA	1 (3.33%)
Double Vessel Disease	
RCA + LCx	2 (6.66%)
RCA + LAD	2 (6.66%)
LAD + LMCA	1 (3.33%)
Triple Vessel Disease	
RCA + LCx + LAD	1 (3.33%)
LMCA + RCA + LCx	1 (3.33%)

DISCUSSION

Clinical consequences of STEMI range from none or minimal sequelae to early death and patients may have a mortality risk that cannot be neglected. STEMI can be treated with a number of therapeutic interventions, including pharmacologic treatments and invasive approach. Different combinations of pharmacologic treatments and invasive strategies are associated with different benefits and risks, which depend upon patients' baseline clinical profile and risk (15).

A meta-analysis published in the International Journal of Cardiology (Dentali et al.) explored the impact of NLR on clinically important outcomes in ACS, pooled data from 23 studies, for a total of >16,000 patients who met the predefined criteria. Pooled results of included studies in ACS patients found that high NLR, measured on-admission, was associated with a higher mortality rate and with major clinical adverse outcomes. Overall in-hospital and long-term mortality appeared to increase in patients with higher NLR (15).

Findings of our study displayed similar outcomes with higher NLR value on admission. The cut-off value for our study was set to be >3.8 which indicated severity. Patients with NLR value higher than 3.8 required immediate intervention. Patients with NLR as high as 9 or above did not survive. It was also noted that patients who presented to the hospital within 12h of onset of symptoms and were subjected to thrombolytic therapy had relatively lower NLR when compared to those who presented late. The NLR in some of these patients only increased with their hospital stay until they expired.

In patients with high NLR, early identification of major adverse cardiovascular events can be achieved by strict surveillance which can help in making treatment decisions, preventing complications and reducing hospital stay (15).

It is important to perform serial ECGs while the patient is still in the cardiac intensive care unit to identify high-risk ECG which can expedite the treatment decisions, thereby, minimizing total ischemic time (16).

Our study involved collection of ECG at 3 different times of the hospital stay and also at the first follow-up. The first ECG was obtained at the time of admission, which showed significant ST-elevation. The next two ECGs were collected on the 3rd day and on the day of discharge which showed relatively less to no elevations in the leads. ECG obtained on the follow-up almost never had any significant elevations.

We correlated the ECG findings and NLR and found that, Significant ST-elevation at admission was associated with high NLR.

High NLR and ST-segment elevation was also associated with >50% stenosis of the coronary arteries which required immediate intervention. Correlating these three parameters was found to be helpful in determining the severity of STEMI and observation was made that the course of treatment could be decided considering these parameters at the earliest.

CONCLUSION

There is a linear decrement in ST resolution with decrease in NLR and can be attributed to natural course of disease and type of intervention provided. Nevertheless the univariate correlation between ECG and NLR on various days of treatment was not significant. This study confirms the prospective use of NLR along with the extent

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of coronary artery involvement and magnitude of ST elevation to predict the severity of STEMI. Time of admission has a great impact on mortality and length of hospital stay with Fibrinolysis within 12 hours of the onset of symptoms proving beneficial effects.

LIMITATIONS

This study had a few flaws. Convenient sampling and the sample was relatively small to produce profound results. Moreover, it was a prospective observational study conducted for a short period.

INSTITUTIONAL REVIEW BOARD (IRB)

Institutional Review Board approval was received for this study (Reference number: 2018/25/011).

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