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Research Article

TO GOVERN THE INCIDENCE OF IN-HOSPITAL MORTALITY IN ACUTE CORONARY SYNDROME PATIENTS WITH RAISED NEUTROPHIL TO LYMPHOCYTE RATIO

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Abstract:

Background: Coronary heart disease (CHD) is the leading cause of mortality in the world. ACS is caused by the rupture of the atherosclerotic plaque & inflammation plays a key role. White blood cells (WBCs) are the major mediators of inflammation and WBCs and their differentiation have been studied for prediction of cardiovascular outcomes and early risk assessment.

Aim: To determine the in-hospital mortality rate in patients with acute coronary syndrome with elevated neutrophil to lymphocyte ratio (NLR).

Study design: A cross-sectional study.

Place and Duration: In the Medicine Unit-II of Bahawal Victoria Hospital (BVH) Bahawalpur for one-year duration from May 2019 to May 2020.

Method: 550 patients who met the inclusion criteria were enrolled in the study. A history of ischemic heart disease, smoking and diabetes was taken. On admission, a white blood cell count was taken and used to calculate the ratio of neutrophils to lymphocytes. Patients with increased NLR were followed for 7 days with inpatient mortality after admission. The information obtained was recorded on a standardized display.

Results: The results showed that in patients with increased NLR on admission, in-hospital mortality increased after 7 days. Diabetes has not been found to have a major influence on the NLR. In addition, patients who suffered from myocardial infarction and smoking patients had a higher NLR compared to other patients.

Conclusion: NLR can be used to identify patients at high risk of early mortality after acute coronary syndrome, but its usefulness may be limited by its non-specificity. More research is needed to determine exactly what level of NLR is to be significant.

Key words: Acute Coronary Syndrome, Neutrophils, Lymphocytes, Mortality.

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INTRODUCTION:

Coronary artery disease (CHD) is the leading cause of death in the world, causing 1 in 5 deaths in the United States in 2004 [1-2]. In 2008, it was estimated that approximately 770,000 Americans had a new coronary attack, and approximately 430,000 had a recurrent attack. The most common symptom of CHD in the emergency room is acute coronary syndrome (ACS), which is a clinical unit involving unstable angina, non-ST segment elevation and non-ST segment elevation myocardial infarction [3-4]. ACS is caused by rupture of the plaque and inflammation plays a key role. White blood cells (WBCs) are one of the major mediators of inflammation, therefore WBC and their differentiation have been studied to predict cardiovascular outcomes. Neutrophils can facilitate the rupture of atherosclerotic plaques by releasing proteolytic enzymes, arachidonic acid derivatives and superoxide radicals. Increased neutrophil counts are associated with poor functional recovery after coronary angioplasty and an increase in infarct size following reperfusion in patients with ACS. On the other hand, studies have shown that absolute and relative lymphocyte concentrations are significantly lower in patients with cardiac events and that such patients are at greater risk of future cardiac events. In ACS, relative lymphopenia is a stress response⁵⁻⁶. Increased (greater than 2) neutrophil to lymphocyte count (NLR) on admission has been shown to be independently associated with increased early, ie 7-day mortality (5.6%). Such an elevated NLR as an independent predictor integrates the predictive risk of these two WBC subtypes with a single risk factor.

Early risk assessment is useful both in predicting the risk of recurrent cardiac events and in identifying the patients who would benefit most from aggressive interventions. Risk assessment can be performed using clinical scoring systems derived from the GRACE scoring system or myocardial thrombolysis (TIMI) studies [7-8].

In our country, the level of C-reactive protein (CRP) in relation to increased mortality from ACS was tested, but no studies on the prognostic significance of NLR were carried out. CRP is expensive and not widely available. By contrast, WBC with Difference is a routinely performed, inexpensive test from which the NLR can be easily calculated. It is important to conduct a study in our country to determine the usefulness of NLR in predicting short-term mortality in ACS, so that we can aggressively deal with such patients with early angiographic intervention.

MATERIAL AND METHODS:

This cross-sectional study was conducted at the Medicine Unit-II of Bahawal Victoria Hospital (BVH) Bahawalpur for one-year duration from May 2019 to May 2020. The sample size of 550 cases was calculated with a 95% confidence level, a 2% margin of error and assuming the expected percentage of early mortality, ie 5.96% in ACS patients with increased NLR (> 2). The sampling technique was pointless probability sampling. Both men and women, 35–65 years of age, who had their first acute coronary syndrome event (according to the operative definition) and an NLR > 2 within 12 hours, were included in the study.

Exclusion criteria:

Patients with pneumonia as evidenced by effusion or cloudiness on the chest X-ray (CXR). Patients with urinary tract infection as evidenced by more than 5 white blood cells / HPF in the urine. Patients with a history of stroke. Acute pericarditis as manifested by a concave ST segment elevation.

Data collection:

After informed consent, 550 patients who met the inclusion criteria were enrolled in the study. The demographic profile (name, age, gender) has been recorded. A patient history of smoking and diabetes was taken and blood was drawn to calculate random blood sugar levels for patients who were not known to have diabetes (random blood sugar (BSR) > 200 mg / dL was taken as diabetes). All patients were treated in a closed ward according to the standard acute coronary syndrome protocol. Patients with increased NLR (as defined by operative definition) were followed in hospital for a mortality of up to 7 days. All information obtained was recorded on the attached standard Performa (Annex 1).

Data analysis procedure:

All data was processed and analyzed using SPSS version 18.0 for Windows. Numeric variables such as age are represented by calculating the mean and standard deviation. Categorical variables such as gender and in-hospital mortality are calculated based on frequency and percentage. Data were stratified by diabetes (known diabetics taking diabetes medications or BSR > 200 mg / dL) and smoking (at least 5 packs years), calculated by multiplying the average number of packs of cigarettes smoked per day by the total number of years of smoking) to take with effect modifiers.

RESULTS:

The results were compiled after studying certain variables. 550 cases of acute coronary syndrome were

obtained from the emergency department of Bahawal Victoria Hospital (BVH) Bahawalpur. Acute coronary syndrome was diagnosed by typical chest pain or shortness of breath combined with a ST-segment deviation > 2 mm and / or T-wave inversion in at least two consecutive ECG leads or elevated CK-MB > 25 IU / L. Simultaneously, a differential white blood cell count was performed and the neutrophil to lymphocyte ratio was calculated simply by dividing the neutrophil count by the lymphocyte count. The mean age of the

patients enrolled in the study was 54.7 ± 8.3 years. 83 patients (15.09%) were in the age range 35 to 45 years and 189 patients (34.36%) of all 550 were in the age range 46 to 55 years. The most numerous groups were people aged 56 to 65, which included 278 patients (50.55%). The youngest patient in our study was 35.7 years old and the oldest 65 years old. The mean age of men was 58.2 ± 6.1 years, and of women 53.3 ± 5.3 years. Age details are provided in Table 1 and Fig. 1.

Table 1: Age distribution of patients (n=550)

Age (Years)	No. of patients
35-45	83 (15.09%)
46-55	189 (34.36%)
56-65	278 (50.55%)
Mean \pm SD	54.7 \pm 8.3 years

Fig. 1: Analysis of patients according to age (n=550) Fig. 2: Analysis of patients according to their presentation (n=550)

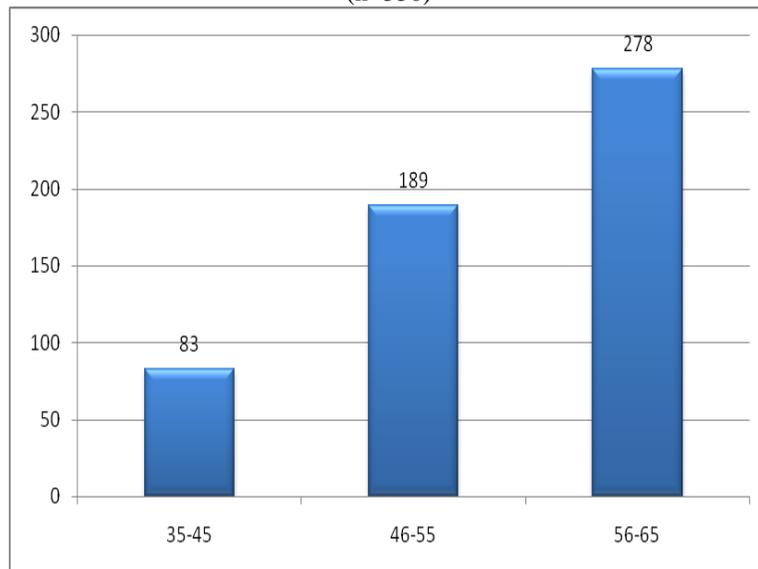
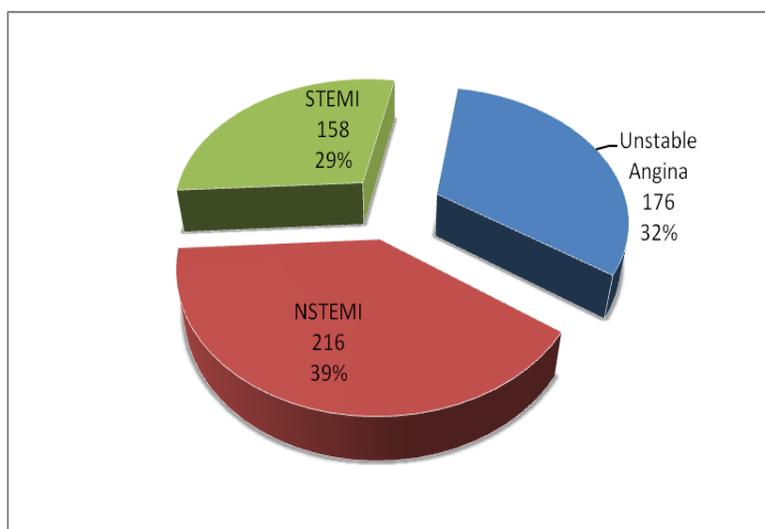


Fig. 2: Analysis of patients according to their presentation (n=550)



Out of 550 patients, 337 (61.27%) patients were male and 213 (38.72%) were female. The male to female ratio was 1.58: 1. The gender distribution is shown in Table 2.

Table 2: Sex distribution of patients (n=550)

Sex	No. of patients
Male	337 (61.27%)
Female	213 (38.72%)
Total	550 (100%)
M: F ratio	1.58: 1

Data were also analyzed by smoking and diabetes. Smoking as a risk factor has been found to be present in 167 patients, of which 167.9 are female smokers. Diabetes mellitus as a risk factor was present in 207 patients, including 141 men and the rest of the women. Out of all 49 patients, they had diabetes and smoking as risk factors. In 225 patients with acute coronary syndrome, no risk factor was identified. The results

also showed that most patients with acute coronary syndrome had a non-ST segment elevation myocardial infarction. 216 (39.27%) had NSTEMI and 176 (32%) patients had unstable angina. Out of 550, 158 (28.72%) patients had ST-segment elevation myocardial infarction (Fig. 2). The NLR according to their presentation is also presented in Table 3.

Table 3: Mean NLR of Study Variables

Study variable	NLR (Mean)
Males	3.9
Females	3.2
Smokers	4.1
Unstable Angina	2.9
NSTEMI	3.8
STEMI	5.6
Alive at 1 week	4.4
Expired Patients	5.8

Forty-six (8.36%) patients died while in hospital within 7 days. The ratio of neutrophils to lymphocytes was calculated for all patients at admission. Interestingly, the neutrophil to lymphocyte count ratio was found to be greater than 4.9 in all but three patients who died, with an average of 5.8 compared with

patients who survived seven days. The mean neutrophil to lymphocyte count ratio among the surviving patients was 3.9. The highest NLR was mainly observed among smoking patients. The mean ratio of neutrophils to lymphocytes among smokers was 4.1. There was no significant difference in the

NLR compared to those without diabetes. Overall, male patients were found to have a higher mean NLR of 3.9 compared to women who had a mean NLR of 3.2. NLR by patient presentation and study variables is presented in Table 3.

DISCUSSION:

Coronary heart disease (CHD) is the leading cause of death worldwide, causing 1 in 5 deaths in the United States in 2004. Acute coronary syndrome (ACS) is a generic term used to describe one spectrum of myocardial ischemia involving the coronary arteries: ST-elevation myocardial infarction (30%), non-ST segment elevation myocardial infarction (25%), or unstable angina (38 %) [9-10]. Early risk assessment is useful both in predicting the risk of recurrent cardiac events and in identifying the patients who would benefit most from aggressive interventions. Doctors have long sought to identify a population prone to mortality in which timely intervention can prevent the death or accompanying disability associated with ACS. Patients admitted to our hospital with acute coronary syndrome were not representative of any particular area or socioeconomic class, but mainly belonged to the middle and lower socioeconomic strata. A total of 550 consecutive patients with acute coronary syndrome participated in the study; all had unstable angina or history of ST-segment / non-ST-elevation myocardial infarction, ECG, or elevated MBC. Our study found that white blood cell count, specifically the NLR, which is a cheap and simple test, is not only an independent marker, but likely can predict the risk of complications, including mortality after ACS¹¹⁻¹². The results are consistent with many studies that have found predictive value for total leukocyte count and its subtypes in patients with coronary artery disease. Hitinder *et al.* From the University of Michigan retrospectively examined 2,833 patients with ACS and divided the patients into low, medium and high-risk groups at admission. They concluded that patients with high NLRs were significantly more likely to die both in hospital and 6 months after discharge. In-hospital mortality was 8.5% in the high NLR group compared to the lowest NLR group which was 1.8%. The 6-month mortality was also higher by 11.5% compared to 2.5%, respectively. The results of this study and the results are quite similar to our study, as the mortality rate in our study was 8.36% in patients with an NLR above 4.9 and a mean of 5.8. In addition, the mean NLR was 3.9 in patients who survived ACS after 1 week. Basem *et al.* Concluded that NLR is an independent predictor of short-term and long-term mortality in NSTEMI patients with mean NLR greater than 4.7. Our study included patients not only with NSTEMI, but also with

unstable angina and STEMI. However, we also concluded that the NLR was greater than 4.9 in all patients who died. In this respect, the results are quite similar to the studies conducted by Basem *et al.*

In the CAPRIE study, neutrophilia was an independent marker of cardiovascular risk, although it was not the main measure. Indirectly, the results of our study also showed an increased number of neutrophils compared to the number of lymphocytes in patients with ACS who were at higher risk of complications and death. A study by Munir *et al.*¹² at the Shifa International Hospital in Islamabad found that the neutrophil to lymphocyte ratio was the highest among patients with STEMI compared to patients with NSTEMI and unstable angina, and showed that NLR is a better predictor of ACS mortality than another leukocyte subtypes¹³⁻¹⁴. The sample size was smaller than in our study (550 patients) and included only 130 patients with ACS. Huang G *et al.* Conducted a study to look at the usefulness of WBC count and differentiation in patients with CAD. These included 623 patients, the sample size was slightly larger than in our study, and the study endpoint was the major adverse cardiac events (including death, CCF, and stroke) compared to our data as we only studied early mortality after ACS and its relationship with NLR. They concluded that an elevated neutrophil count after ACS is a predictor of serious adverse coronary events, and in this respect the results were similar to our studies. Papa A11 and all of them conducted a study on the relationship between WBC counts and mortality after ACS. Acute mortality was not analyzed in this study and the endpoints were fatal and non-fatal MI at 3 years. Although they did not investigate the 1-week mortality, the results were similar as the NLR emerged as an independent predictor of cardiac death. Nunez J *et al.* Analyzed 515 patients with STEMI and concluded that the neutrophil to lymphocyte ratio is a useful marker for predicting later mortality in STEMI patients, but only analyzed long-term mortality. We only analyzed in-hospital mortality at 1 week¹⁵. Outcome variables (long-term vs. hospital) were different in the two studies, but the NLR proved to be a useful adjunct in predicting mortality in patients with ACS.

CONCLUSIONS:

The results of this study and a review of the literature indicate that NLR may be an inexpensive and easy-to-use method of predicting patients at high risk for ACS. However, its usefulness may be limited due to its non-specificity and low sensitivity. We recommend more studies to determine the usefulness of NLR as a predictor of mortality in patients with ACS.

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