ORIGINAL ARTICLE

Frequency of High Neutrophil and Lymphocyte Ratio (NLR) among NSTEMI/USA patients and to Compare Frequency of Mortality in patients of NSTEMI/USA having high NLR with those without high NLR

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ABSTRACT

Background: Neutrophil to lymphocyte ratio (NLR) is comparatively a new prognostic marker used in patients with chronic stable angina (CSA). NLR can help in predicting short and long term moralities in NSTEMI patients.
Aim: To evaluate the frequency of high neutrophil and lymphocyte ratio among NSTEMI/USA patients and to compare frequency of mortality in patients of NSTEMI/USA having high NLR with those without high NLR.
Study design& duration: Descriptive, case series study from 25th November 2020 to 24th May 2021.
Study settings: Department of Medicine and Cardiology, Fatima Memorial Hospital, Lahore.
Methods: 185 patients having non ST elevation myocardial infarction (NSTEMI) and/or unstable angina (UA) having 30 to 70 years age and both males and females were included. Patients with sepsis having total Leucocyte count (TLC>11,000/<4000), history of surgery or on steroids in the past three months, history of hematological malignancy, late for fibrinolysis or those with contraindication to fibrinolysis were excluded were excluded. Demographic information (name, age, address, and education) was also noted.
Results: Mean age of the participants was 57.99 ± 6.10 years while the age range was from 30 to 70 years. Most of patients 164 were included in the age group of 51 to 70 years. 110 (59.46%) patients were male and 75 (46.54%) of them were females. Frequency of neutrophil and lymphocyte ratio among NSTEMI/USA patients was found in 91 (49.19%) patients. My study has shown higher frequency of mortality in patients of NSTEMI/USA having high NLR 26 (28.57%) compared to normal NLR 06 (6.38%) with p value = 0.0001.
Conclusion: Frequency of high neutrophil and lymphocyte ratio among NSTEMI/USA patients is very high with higher mortality in high Neutrophil-to-lymphocyte ratio group as compared to low NLR group.
Keywords: Myocardial infarction, Non ST elevation, Neutrophil-to-lymphocyte ratio

INTRODUCTION

Worldwide, Myocardial Infarction (MI) and Coronary artery disease (CAD) areconsideres as a major cause of death and morbidity. Atherosclerosis is one of the major risk factor of cardiovascular diseases (CVD)[1]. Cardiovascular diseases are thenumber one cause of death overall on global level. Most common complications include fatal heart attack and heart failure[2]. Patient whose ECG shows no ST segment elevation but who presentwith acute coronary syndrome are labelled as unstable angina/NSTEMI. Due to its heterogeneous nature thesepatients have high probability of death and other cardiac events of different types.[3] Neutrophil to lymphocyte ratio (NLR) is a relatively new prognostic marker used in patients with chronic stable angina (CSA).[4]NLR can help in predicting short and long term moralities in NSTEMI patients. There is an increased risk of downstream events in patients having peri-infarction morbidity[6].

Atherosclerosis is considered as a diverse inflammatory disease.[7] Neutrophil-to-lymphocyte ratio (NLR) is an inflammatory marker at systemic level. It is directly related to the cardiovascular outcome of the patients[8]. In different studies, it has been seen that the White blood cell count and its subtypes can be used as inflammatory biomarkers with a predictive value for adverse cardiovascular outcomes.Inflammation has been shown to underlie many cardiovascular diseases, especially those involving atherosclerosis as pathogenic mechanism like coronary artery disease[13,14,15].

Lymphocytes play role in remodeling following inflammation example Cluster differentiation (CD4+) T involve in capture of proangiogenic macrophages and also collateral artery formation[18]. NLR is an inexpensive, widely available test and can be easily calculated in comparison to other inflammatory markers[19]. High NLR has proven to be associated with poor angiographic findings, larger infarct sizes and increased rate of long and short term mortality. NLR has incremental prediction independent of other risk scores, Global Registry of Acute Coronary Events (GRACE) score is one example[20].

Rationale of our study was to find the frequency and mortality related to NLR among NSTEMI/USA patients. It has been known that there may be various complications related to NSTEMI patients. The above stated studies were obtained from local and international literature which contains ambiguity in results separately for the variables. So this study is being conducted to ratify the association of NLR with mortality in local population suffering from NSTEMI and implement the results of this study in future. Furthermore strategies could be made to detect positive cases at risk earlier to decrease the long term morbidity.

The objective of the study was to evaluate the frequency of high neutrophil and lymphocyte ratio among NSTEMI/USA patients presenting in a tertiary care hospital and to compare frequency of mortality in patients of NSTEMI/USA having high NLR with those without high NLR. "

Operational definitions:

NSTEMI: Patient with acute coronary syndrome include prolonged chest pain (>60 min), ST segment depression, deviation or temporary elevation, new or recent onset of angina in past month. Elevation in troponin I or T (>3 times normal), contractile protein released form necrotic cardiac myocytes

Unstable Angina: Unstable angina was diagnosed in patients with symptoms of acute coronary syndrome (ACS) with normal cardiac enzymes, with or without Electrocardiography (ECG) changes.

METHODOLOGY

This descriptive, case series study was conducted in the Department of Medicine and Cardiology Fatima Memorial Hospital, Lahore during six months from 25th November 2020 to 24th May 2021. 185 NSTEMI/USA patients was calculated. Confidence level of 95% and 7% margin of error was calculated**.** Sample technique was Non-probability, Consecutive sampling. All patients with unstable angina (UA) or non ST elevation myocardial infarction (NSTEMI) having 30 to 70 years age and both males and females were included while patients with sepsis having total Leucocyte count (TLC>11,000/<4000), history of surgery or on steroids in the past three months, history of hematological malignancy, late for fibrinolysis or those with contraindication to fibrinolysis were excluded were excluded.

Data collection procedure: There were total of 185 NSTEMI/USA patients meeting the inclusion criteria coming to department of medicine and endocrine at Fatima Memorial hospital, Lahore were enrolled in the study. Informed consent was taken from all the patients. Demographic information (name, age, address, and education) was also noted. Then complete blood count was done by taking blood from the patient to note high neutrophil to lymphocyte ratio (as per-operational definitions). Patients were followed up to know the outcome/mortality of the patients after 7 days of admission. Responses were noted in the questionnaire. All this information was recorded in well-structured proforma.

Data analysis procedure: SPSS version 25.0 was used for data entry and analysis. Quantitative variables were shown as mean and standard deviation for example, age, BMI and NLR. The qualitative variables were demonstrated as frequency and percentage like gender, high NLR and mortality. Chi square test was calculated to measure association of high NLR with mortality. p value < 0.05 was considered as significant.

RESULTS

Mean age of the participants was 57.99±6.10 years while the age range was from 30 to 70 years. Most of the patients 164 were included in the age group of 51 to 70 years. (Table I). 110 (59.46%) patients were male and 75 (46.54%) of them were females with ratio of 1.5:1. Mean BMI was 29±3.0kg/m^2 (Table II). Mean NLR was 2.64±1.09. Frequency of neutrophil and lymphocyte ratio among NSTEMI/USA patients was found in 91(49.19%) patients. Our study has shown higher frequency of mortality in patients of NSTEMI/USA having high NLR 26(28.57%) compared to normal NLR 06 (6.38%) with p value=0.0001 (Table III). Table IV & V can be seen for stratification of Neutrophil-to-lymphocyte ratio with respect to age groups and genders respectively, while the stratification with respect to BMI is shown in Table VI

Table-I: Distribution of patients as per age (n=185)

Age (years)	n	%age
30-50	21	11.35
51-70	164	88.65
Total	185	100.0

> Mean ± SD = 57.99 ± 6.10 years

Table-II: Distribution of patients according to BMI (n=185).

BMI (kg/m^2)	n	%age
<30	114	61.62
>30	71	38.38
Total	185	100.0

> Mean ± SD = 29.09 ± 3.09 kg/m^2

Table III: Comparison frequency of mortality in patients of NSTEMI/USA having high NLR with those without high NLR.

Neutrophil-to-lymphocyte ratio	Mortality		p-value
	Yes	No	
Low	06 (6.38%)	88 (93.62%)	0.0001
High	26 (28.57%)	65 (71.43%)	

Table IV: Stratification of high Neutrophil-to-lymphocyte ratio with respect to age groups

Age (years)	High Neutrophil-to-lymphocyte ratio		P value
	Yes	No	
30-50	08	13	0.280
51-70	83	81	

Table V: Stratification of high Neutrophil-to-lymphocyte ratio with respect to gender.

Gender	High Neutrophil-to-lymphocyte ratio		P value
	Yes	No	
Male	61	49	**0.039**
Female	30	45	

Table VI: Stratification of high Neutrophil-to-lymphocyte ratio with respect to BMI.

BMI (kg/m^2)	High Neutrophil-to-lymphocyte ratio		P-value
	Yes	No	
<30	54	60	0.530
>30	37	34	

DISCUSSION

Inflammation plays a vital role in the incidence of atherosclerosis.[22]The neutrophil to lymphocyte ratio (NLR) is a prime indicator of systemic inflammation. It is also a valuable prognostic marker in such patients and also in those who plan to undergo percutaneous coronary intervention (PCI).[23,24]Moreover, the NLR has been associated with in-hospital cardiovascular mortality in ST segment elevation myocardial infarction (STEMI) patients.[25,26]We have carried out this study to evaluate the frequency of high neutrophil and lymphocyte ratio among NSTEMI/USA patients and to compare frequency of mortality in patients of NSTEMI/USA having high NLR with those without high NLR.

Mean age of the participants was 57.99±6.10 years while the age range was from 30 to 70 years. Most of the patients 164 were included in the age group of 51 to 70 years. Frequency of neutrophil and lymphocyte ratio among NSTEMI/USA patients was found in 91(49.19%) patients. My study has shown higher frequency of mortality in patients of NSTEMI/USA having high NLR 26(28.57%) compared to normal NLR 06(6.38%) with p value=0.0001. In a study by Naoki and others showed that in the study population, the mean NLR was 3.43. Total study population was 396 patients, out of these, 244 patients had an NLR >2.8.[21] In another study by Zahoor and his colleagues showed that the mean age was 51.6+12.5 years while 78(31.20%) patients had a high neutrophil to lymphocyte ratio[27].

There is a significant relationship between high NLR and cardiovascular mortality in STEMI patients. The same has been demonstrated by various studies completed on a global level[28-30]. Moreover, other studies have also shown a relation between higher NLR and low ejection fraction after event of STEMI[31,32]. Another association noted and observed has been with complex coronary arteries of the patients.[33,34] Left ventricular apical thrombus and remodeling are other pathologies linked with high NLR[35,36]

Muniret al[43] and Azab et al[45] showed in their study a trend to increased mortality (8.7%) in patients with high NLR which is consistent with our results. Tamhaniet al[46] investigated relation betweenShort term mortality and admission NLR in patients with acute coronary syndrome. Their results showed that high NLR is an independent predictor of In Hospital and 30 day mortality in ACS patients which correlate with our results. Azabet al[45] studied the relation of Atrial Fibrillation and high NLR in NSTEMI patients and showed a frequency of 13%, which was statistically significant. Yilmaz et al. reported that the NLR is a non-dependent predictor of coronary thrombus formation in patients with non-ST segment elevation ACSs (NST-ACS) (sensitivity=93%; specificity=62%, AUC-ROC=0.86)[47].

Ozturk et al. found that NLR levels were raised in NST-ACS than in the control group[48]. That study differs from the present study in some respects: It was a retrospective study; patients under the age of 45 only were recruited; the sample size was quite low (44 patients with UA, 40 with NSTEMI and 40 controls, 124 participants totally), and the NLR was not evaluated for DTC. In a study by Mehmet Gul showed that patients with NSTEMI were

evaluated. The study population, which was 308 in total had a mean age of 59.22+11.93. Follow up for the patients continued for upto 3 years post discharge date and their clinical outcomes were assessed in follow up visits. The Kaplan-Meier survival analysis showed interesting results, where 3-year mortality was found to be 21.6% in patients who had a high NLR versus 3% in the low-NLR group (P <0.001)[49].

CONCLUSION

This study concluded that frequency of high neutrophil and lymphocyte ratio among NSTEMI/USA patients is very high with higher mortality in high Neutrophil-to-lymphocyte ratio group as compared to low NLR group. So, we recommend that Neutrophil-to-lymphocyte ratio should be used in all patientsof NSTEMI for early evaluation of this group who are at high risk and proper treatment can be offered to these patients.

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