ORIGINAL ARTICLE

USEFULNESS OF NEUTROPHILS TO LYMPHOCYTES RATIO FOR PREDICTING TROPONIN-I ELEVATION IN PATIENTS PRESENTING WITH SUSPECTED NSTE-ACUTE CORONARY SYNDROME

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Background: Most of the admissions to the coronary care unit are patients who are having Non-ST-segment elevation acute coronary syndrome (NSTE-ACS). Inflammation has an important role in the pathogenesis of the acute coronary syndrome. Inflammatory marker such as Leukocyte counts & most importantly Neutrophils to Lymphocyte Ratio (NLR) has been found an important predictor of cardiovascular events. Few studies show the diagnostic role of Neutrophils to Lymphocyte ratio in the patient presenting with NSTE-ACS. The objective of this study was to determine the diagnostic role of Neutrophils to Lymphocytes ratio to predict the elevation of Troponin-I in patients presenting with suspected NSTE-acute coronary syndrome. **Methods:** This was a Descriptive Case Series study, conducted in Cardiology department Ayub Teaching Hospital/Ayub Medical College Abbottabad, from 15th May 2017 to30th December 2018. A total of 203 patients with suspected NSTE-ACS were inducted in the study by non-probability, consecutive sampling. **Results:** Results of this study shown a strong correlation between Neutrophils to Lymphocyte ratio (NLR) & rise in Troponin-I levels. Furthermore, results shown that at 4th quartile of Neutrophils to Lymphocyte ratio (NLR) there is high Specificity (97.8%) and very high positive predictive of value 96.7% for predicting the rise in Troponin-I levels. **Conclusion:** We concluded that there is a strong correlation between rising Neutrophils to Lymphocyte ratio (NLR) and cardiac Troponin-I elevation in patients presenting with suspected NSTE-acute coronary syndrome. Therefore, this parameter can be used to predict the rise in troponin level in patients presenting with suspected NSTE-ACS.

Keywords: Non-ST segment elevation myocardial infarction (NSTEMI); ST-segment depression; Neutrophils to Lymphocytes ratio; Non-ST elevation acute coronary syndrome; Electrocardiogram

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INTRODUCTION

Ischemic heart disease is the leading cause of cardiovascular mortality. It accounts 1/3rd of all global deaths. Mortality due to cardiovascular diseases will further increase to 24.2 million by year 2030.[1] Studies have shown that in the United States more than 1 million people have acute coronary syndromes (ACS) annually, with 0.4 million people die each year due to coronary artery disease.[2]Similarly there is increased prevalence (approximately 6.25%) of ischemic heart disease in our country.[3]

Acute coronary syndrome (ACS) is a clinical spectrum in which patients have symptoms that are consistent with acute myocardial ischemia. If there is no ST segment elevation on Electrocardiogram (ECG) and cardiac biomarkers are raised this is termed as Non-ST elevation MI (NSTEMI), on the other hand it is called as Unstable Angina if cardiac biomarkers are normal.[4] Cardiac biomarkers are released into circulation as a result of myocardial damage.[5]

As compared to ST elevation Myocardial Infarction (STEMI) the incidence of NSTE-acute coronary syndrome is increasing, because of increased incidence of diabetes mellitus and elderly population.[6] Non-ST elevation acute coronary syndrome is the common presentation of ischemic heart disease, presenting to emergency room of hospitals[7] and it accounts for 1/3 cases of Acute Coronary Syndrome.[8]

Inflammation plays very important role in the initiation of at atherosclerosis and presentation of patients with Acute Coronary Syndrome.[9] White blood cells (WBC's) are important mediator of inflammation, various studies have demonstrated their role in different cardiovascular diseases. In patients who present with NSTE-ACS, Neutrophils (a specific type of WBC) counts on admission has been found important predictor of outcome during hospital stay.[10] In Patients having UA/NSTEMI, a raised total leukocyte count predicts mortality and recurrent presentation with myocardial infarction.[11]

More recently, Neutrophils to Lymphocytes Ratio (NLR) which is obtained by dividing absolute neutrophils count by absolute lymphocytes count, is found more specific in predicting cardiovascular events. Various Studies have shown that raised NLR; shows a strong correlation with severity of coronary heart disease on angiographic assessment of coronaries,[12] correlates well with SYNTAX Score in assessment of coronary artery disease.[13] Similarly raised NRL works as predictor of: restenosis in bare-metal stents,[14] thrombus formation in patients presenting with NSTE-ACS.[15] Short-term and long-term mortalities in patients presenting with Non-ST elevation MI can be predicted with raised NLR.[16] Similarly playing its role as important predictor NLR can be useful and in patients presenting with decompensated heart failure.[17]

Objective of this study was to determine the usefulness of Neutrophils to Lymphocytes (NLR) for predicting elevation of Troponin-I levels, in patients presenting with suspected Non-ST Elevation (NSTE) acute coronary syndrome.

MATERIAL AND METHODS

Patients were inducted from department of Cardiology, Ayub Teaching Hospital/ Ayub Medical College Abbottabad through non-probability consecutive sampling, the design of study was Descriptive Case Series. Informed consent was taken. Patients from 25–85 years of age, both male and female, presenting with chest pain of more than 10 minutes duration suggestive of acute coronary syndrome were included in the study.

Patients diagnosed with infectious illnesses (based on history of fever, clinical findings and laboratory investigations suggestive of infective illness), recent accidental or surgical trauma, history of malignancy and immune-compromised patients were excluded.

Standard 12-leads Electrocardiography was done on patients who presented with chest pain. Blood samples were taken to analyse complete blood count with its differentials.

From same automated blood sample NLR was calculated by dividing absolute neutrophils count to the absolute lymphocytes count. Cardiac specific troponin-I was measured six hours after the onset of anginal symptoms. These Patients who were suspected of having acute coronary syndrome, based on symptoms of angina, risk factors of coronary artery disease and/or ECG changes, were started on standard treatment of ACS within 10 minutes of landing into emergency department of Ayub Teaching Hospital Abbottabad, without waiting results of blood test.

Statistical analysis was done using SPSS 20. Descriptive & inferential analysis were done. Sensitivity, specificity and positive predictive value of NLR was calculated using ROC curve analysis.

RESULTS

Total two hundred & three patients were recruited in this study, comprising 64% (n=130) male and 36% (n=37) female. Mean age of the study population was 60.67±11.86. In this study population 40.4% (n=82) patients were having diabetes mellitus while remaining 59.6% (n=121) were having no diabetes. Similarly, 65.5% (n=133) were hypertensive while 34.5% (n=70) were normotensive.

While considering the percentage of NSTEMI and unstable angina, 63.5% (n=129) were turned out NSTEMI and 36.5% (n=74) were diagnosed with unstable angina.

Bivariate analysis showed that there is a strong correlation between Neutrophils to Lymphocyte ratio (NLR) and Troponin-I levels with two tailed Pearson Correlation value of 0.406.

These results show that at 4th quartile of NLR (Mean NLR: 10.35±4.44, with minimum NLR: 6.00 & maximum: 23.35) there is high Specificity (97.8%) for predicting rise in cardiac troponin-I levels, however sensitivity is low (34.9%). At 4th quartile of Neutrophils to Lymphocytes Ratio (NLR) the positive predictive value of NLR for rise in troponin levels is highly significant (96.7%).

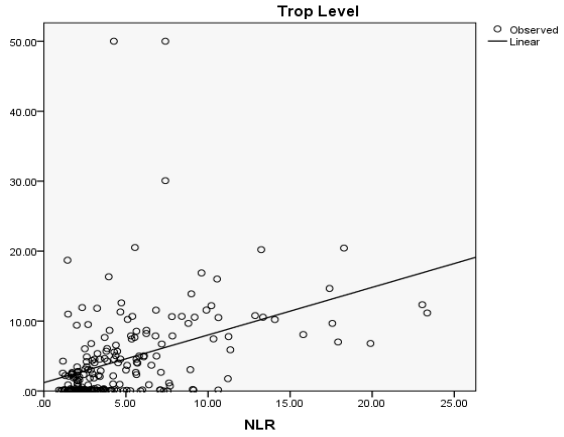

Figure-1: Correlation between Neutrophils to Lymphocyte Ration (NLR) & Troponin-I Levels

Table-1: ACS

	Frequency	Percent	Cumulative Percent
NSTEMI	129	63.5	63.5
Unstable Angina	74	36.5	100.0
Total	203	100.0	

Table-2: For Analysis purpose values of NLR were segregated into four percentile/quartile groups

Percentile Group of NLR	Mean	n	SD	Minimum	Maximum
1	1.7076	50	.35023	.92	2.21
2	2.7763	52	.36357	2.24	3.46
3	4.6042	50	.73099	3.49	5.89
4	10.3543	51	4.44722	6.00	23.35
Total	4.8671	203	4.03775	.92	23.35

Table-3: Using Receiver–operating characteristic (ROC) curve analysis Sensitivity, Specificity & predictive values of NLR (at its 4th quartile) for predicting rise in troponin-I levels were calculated

Statistic	Interpretation	Value	[95% Confidence Interval]	
Prevalence	Pr(A)	63.5%	56.5%	70.2%
Sensitivity	Pr(+|A)	34.9%	26.7%	43.8%
Specificity	Pr(-|N)	93.2%	84.9%	97.8%
ROC area	(Sens.+Spec.)/2	0.64	0.59	0.69
Likelihood ratio (+)	Pr(+|A)/Pr(+|N)	5.16	2.14	12.43
Likelihood ratio (-)	Pr(-|A)/Pr(-|N)	0.70	0.61	0.80
Odds ratio	LR(+)/LR(-)	7.39	2.86	19.01
Positive Predictive Value	Pr(A|+)	90.0%	78.2%	96.7%
Negative Predictive Value	Pr(N|-)	45.1%	37.1%	53.3%

DISCUSSION

Acute coronary syndrome is most commonly caused by disruption of atherosclerotic plaque with superimposed thrombus formation; thus, inflammation plays very important step in the pathogenesis of acute coronary events. Inflammatory markers such as white blood cells count and C - Reactive Protein (CRP) have shown correlation with poor prognosis in patients presenting with acute coronary syndrome.[18] Most importantly Neutrophils to Lymphocyte ratio (NLR) is found important predictor of cardiovascular morbidity and mortality.[12–17] For patients diagnosed with stable coronary artery disease, NLR has a predictive role in determining mortality.[19]

Study done by Zazula AD *et al* showed patients who presented with suspicion of acute coronary syndrome (ACS) a higher quartile of NLR has 91.1% Specificity for final diagnosis of acute coronary syndrome.[20] Our study showed that there is strong correlation between increasing neutrophils to lymphocytes ratio (NLR) and rising Troponin-I levels. Furthermore, at higher quartile (4th quartile) of NLR (10.35±4.44) there is very high Specificity of 97.8% (CI: 95%) with positive predictive value of 96.7% for rising Troponin-I levels. In other words, patients who present to emergency room with ischemic chest pain suggestive of acute coronary syndrome, a high NLR at the time of presentation can be useful to predict elevation of troponin levels & therefore diagnosis of Non-ST elevation -ACS.

CONCLUSION

We concluded that there is a strong correlation between rising Neutrophils to Lymphocyte ratio (NLR) & cardiac Troponin I elevation in patients with suspected NSTE-ACS. Therefore, NLR being a simple, inexpensive, readily available & cost-effective tool, can be used as a predictor of rise in cardiac Troponin-I levels in patients with suspected NSTE-ACS. We can simply conclude that patients who present with chest pain of cardiac origin, a high NLR value can be used as a predictive tool for raised troponin levels.

AUTHORS' CONTRIBUTION

MSA: Data collection, literature search. MYD: Data analysis. MK: Data interpretation. ARJ: Proof reading. Adnan: Study design. SJ: Write-up.

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