ORIGINAL RESEARCH PAPER

Cardiology

SIGNIFICANCE OF NEUTROPHIL LYMPHOCYTE RATIO AS PREDICTOR OF IN-HOSPITAL MORTALITY IN ACUTE CORONARY SYNDROME

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INTRODUCTION: Atherosclerosis is a low-grade inflammatory disease that results in atherosclerotic plaque formation and progressive stenosis of the coronary arteries. Inflammation plays an important role in all stages of atherosclerosis, from initiation and growth to complication of plaque including unstable angina pectoris (USAP), non-ST-elevation myocardial infarction (non-STEMI) and ST-elevation myocardial infarction (STEMI). Increased neutrophil to lymphocyte ratio (NLR) has been shown to play a role in the pathophysiology of atherosclerotic disease. It has been reported that increased values of NLR is associated with cardiovascular diseases. In addition, these parameters have been shown to be a predictor of morbidity and mortality in patients with ACS. However, few reports have investigated so far the relationship between these parameters and the complexity in patients with ACS, with contrasting results. Therefore, the aim of the current study is to evaluate the prognostic significance of NLR in patients with ACS.

METHOD: We did an observational study on consecutive 200 patients diagnosed with ACS from January 2018 to June 2019 in our department. On admission day, once the ACS is diagnosed, included patients are investigated for NLR and their morbidity and mortality upto discharge.

OBSERVATION AND RESULTS: Patients were divided on the basis of pre-treatment, on-admission NLR into ≤2, 2.1-3, 3.1-4, 4.1-5, 5.1-6, 6.1-7, ≥7.1. As NLR value increases, Survival rate is decreasing and mortality rate is increasing with significant P value of 0.0003.

CONCLUSION: NLR value is a useful, easily calculable, simple tool , available from routine CBC which is done in every patient regularly in all hospitals and can be used independently of other parameters to risk stratify patients of Acute coronary syndrome.

INTRODUCTION:

Acute coronary syndrome(ACS) is the most common cause of death worldwide both in developed and developing countries for the last few decades. Still It's incidence is increasing worldwide. Atherosclerosis is a low-grade inflammatory disease that results in atherosclerotic plaque formation and progressive stenosis of the coronary arteries[1]. Inflammation plays an important role in all stages of atherosclerosis, from initiation and growth to complication of plaque including unstable angina pectoris (USAP), non-ST-elevation myocardial infarction (non-STEMI) and ST-elevation myocardial infarction (STEMI)[2].

Increased neutrophil to lymphocyte ratio (NLR) has been shown to play a role in the pathophysiology of atherosclerotic disease. It has been reported that increased values of NLR is associated with cardiovascular diseases[3]. In addition, these parameters have been shown to be related to the development of acute coronary syndrome (ACS) and found to be a predictor of morbidity and mortality in patients with ACS[4]. However, few reports have investigated so far the relationship between these parameters and the complexity in patients with ACS, with contrasting results[5].

There are many demographic, clinical, laboratory and biochemical parameters used for prognostic purpose for example Cardiac troponin, CK-MB, hsCRP, NTproBNP, Cystatin-c. The tests to detect these markers are expensive and available only in limited centers in our country. Inflammatory markers like Lipid profile, Absolute neutrophil counts, Neutrophil-lymphocyte ratio and Hemoglobin level are significantly associated with prognosis in ACS as atherosclerosis is considered to be due to chronic inflammatory process and can be easily done even in remote setup[6].

MATERIALS AND METHOD:

This is an observational study done from April 2018 to March 2019 in ICCU, Department of medicine, Shyam shah medical college and Sanjay Gandhi hospital, Rewa, MP . We will study consecutive 200 cases of chestpain patients aged more than 15 years and diagnosed to have ACS fulfilling Inclusion criteria, excluded by exclusion criteria.

INCLUSION CRITERIA:

- Patients more than 15 years of age diagnosed with ACS as per latest ACC/AHA guidelines.

EXCLUSION CRITERIA:

- Patients who are less than 15 years of age.
- Past history of CAD, CVA, Peripheral vascular disease, connective tissue diseases.
- History of fever, trauma, surgery, neoplasm, or infectious disease prior to/ on admissions.
- Patients currently using immunosuppressant (including corticosteroids).
- Consent denied.

DATA COLLECTION AND METHODS:

A detailed history was taken and recorded. The patients were thereafter subjected to complete clinical examination, Laboratory investigations including ECG and troponin-T or I levels. Patient were appropriately treated and monitored for complication and once stabilised patients were discharge and phone numbers were collected. Patients are monitored till discharge for the morbidity and mortality.

STATISTICAL ANALYSIS:

SPSS software version 19 was used to analyse the data. Pages and Numbers from MacBook Air were used for data recording and analysis . Continuous variables were analysed using unpaired 't' test for normally distributed data. Discrete variables were studies using Wilcoxon rank sum test. Categorical variables were analysed using Chi square test. Odds ratio (OR) and 95% confidence intervals (CI) were calculated. A P value < 0.05 was taken as significant.

RESULTS:

During the study period , total 200 patients were enrolled after considering the inclusion and exclusion criteria.

As shown in table 1, Mean age group in the Survivors group was 59.6 ± 9.1 and in the Non-survivors group was 61.9 ± 11.6. In both the groups most of the patients were in the age group of 40-64 (67.47% vs 67.65%) followed by ≥65 years age group (30.72% vs 32.35%).There was no statistical difference in age and gender between ACS patients who survived and those who died.

As shown in table 2, Even though patients who were smoking were higher in the non-survivors group, there was no significant statistical difference (P= 0.144). Statistically significant alcohol (P=0.002) and tobacco use (P=0.007) were present in non-survivors group.

As shown in table 3, Statistically significant features associated with high mortality were decreased Left ventricular ejection fraction (45.60 ± 9.34 vs 36.12 ± 11.84, P-value<0.00001), decreased haemoglobin levels (10.73 ± 1.45 vs 9.68 ± 1.18, P-value=0.0001), increased absolute neutrophil counts (8004.11 ± 1930.94 vs 9606.38 ± 2703.09, P-value=0.00006), increased Neutrophil-lymphocyte ratio (4.56 ± 1.51 vs 6.11 ± 3.32, P-value= 0.00002).

As shown in Table:5, although, in-hospital morbidity like Left ventricular failure, cardiogenic shock , Ventricular Arrhythmias like ventricular tachycardia and ventricular fibrillation were occurred more in non-survivors group, statistical significance was present only in cariogenic shock (P=0.000007) and Left ventricular failure (P= 0.000749).

As shown in Table:6 & Figure:1, Mortality rates observed with various NLR ranges were as follows: ≤2 (0%), 2.1-3 (8.3%), 3.1-4 (3.5%), 4.1-5 (9.3%), 5.1-6 (28.3%), 6.1-7 (18.7%), ≥7 (54.5%). Thus with increasing NLR value on admission were associated with increasing in-hospital mortality with half of patients more likely to die when the NLR value was ≥7.

		Survivors	Non-survivors	
	15-19	0 (0%)	0 (0%)	
	20-39	3 (1.81%)	0 (0%)	
	40-64	112 (67.47%)	23 (67.65%)	
	≥65	51 (30.72%)	11 (32.35%)	
Gender	Male	117 (70.48%)	24 (70.59%)	0.99012
	Female	49 (29.52%)	10 (29.41%)	
Total		166	34	

Table 4: ACS type			
Variable	Survivors	Non-survivors	P value
STEMI	86 (51.81%)	16 (47.06%)	0.613843
NSTEMI / UA	80 (48.19%)	18 (52.94%)	
Total	166	34	

Table 5			
Variable	Survivors	Non-survivors	P value
LVF	23 (13.86%)	13 (38.24%)	0.000749
Cardiogenic shock	20 (12.05%)	15 (44.12%)	0.000007
Ventricular arrhythmia	14 (8.43%)	6 (17.65%)	0.102796
Total	166	34	

Table 2: Risk factors and co-morbidities			
Variables	Survivors	Non-survivors	P value
Smoking	43 (25.90%)	13 (38.24%)	0.144565
Alcohol	23 (13.86%)	12 (35.29%)	0.002724
Tobacco	33 (19.88%)	14 (41.18%)	0.007624
Diabetes Mellitus	45 (27.11%)	8 (23.53%)	0.666613
Hypertension	68 (40.96%)	18 (52.94%)	0.198727
Dyslipidemia	68 (40.96%)	12 (35.29%)	0.538685
Total	166	34	

Table 3: Investigations			
Variable	Survivors	Non-survivors	P value
Hemoglobin	10.73 ± 1.45	9.68 ± 1.18	0.000106
ANC	8004.11 ± 1930.94	9606.38 ± 2703.09	0.0006
NLR	4.56 ± 1.51	6.11 ± 3.32	0.000029
LVEF	45.60 ± 9.34	36.12 ± 11.84	<0.00001
Total	166	34	

Table 1: Age and gender				
Variable		Survivors	Non-survivors	P-value
Age	Mean age	59.6 ± 9.1	61.9 ± 11.6	0.5892

Table 6							
NLR	≤2	2.1-3	3.1-4	4.1-5	5.1-6	6.1-7	≥7
Survivors	6 (100%)	22 (91.7%)	28 (96.5%)	49 (90.7%)	43 (71.7%)	13 (81.3%)	5 (45.5%)
Non-survivors	0 (0%)	2 (8.3%)	1 (3.5%)	5 (9.3%)	17 (28.3%)	3 (18.7%)	6 (54.5%)
Total	6	24	29	54	60	16	11

Figure 1

In-hospital mortality associated with various NLR ranges
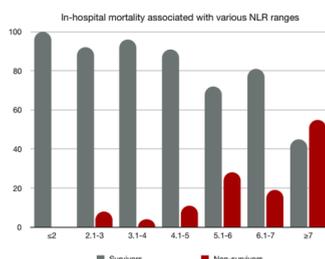
DISCUSSION:

Early stratification of patients is important in the evaluation and management of patients with cardiac disorders especially in acute coronary syndrome.There are various prognostic indicators like Biomarkers Cardiac troponin T/I, CK-MB isoenzyme, hsCRP, NTproBNP, Cystatin-c[7]. Clinical grading scales like TIMI Risk scoring system are validated previously in various studies. The tests to detect these markers are expensive and available only in limited centers in our country and difficult to interpret. Inflammatory markers like Lipid profile, Absolute neutrophil counts, Neutrophil-lymphocyte ratio are significantly associated with prognosis in ACS as atherosclerosis is considered to be due to chronic inflammatory process and can be easily done even in remote setup.

Neutrophil-to-lymphocyte ratio (NLR) is an inexpensive, easy to obtain, widely available marker of inflammation, which can aid in the risk stratification of patients with various cardiovascular diseases in addition to the traditionally used markers[7,8].

Ample research databases from Indian subcontinents have supported a potential of NLR as a prognostic and diagnostic index of coronary artery disease (CAD) and disease associated mortality[8-10]. An elevated NLR, irrespective of other biomarker levels, independently indicates an increased long term risk of mortality not only in patients with stable CAD but also in acute coronary syndrome (ACS) patients[9,10].

The purpose of this study was not to develop a new ACS outcome prediction model or to test whether various

prediction models were more accurate with regard to predicting individual patient outcome. Rather, the point of this study was to assess the significance of an existing, simple, and NLR value in patients of ACS in patients.

The previously conducted studies were concluded with different NLR cut-off value for ACS risk stratification are as follows: Sawant AC et al(2014)[11] cutoff was 7.4, Arbel Y et al(2014)[12] cutoff was 3, Choi DH et al(2019)[13] cut off was 2.8, Qureshi M.I et al(2017)[14] cutoff was 3.04, Bajari R et al(2017)[15] cutoff was 5.25, Azab B et al(2010)[16] cutoff was 4.7.In all these studies, increased NLR value more than the given cutoff value was significantly associated with increased morbidity and mortality in ACS patients.

In our study , rather than giving cutoff value for NLR, we like to conclude that Increasing NLR value is significantly associated with increasing in-hospital mortality and decreasing survival. Other parameters significantly associated with increasing mortality are decreased Hemoglobin level, increased absolute neutrophil count, decreased ejection fraction, complications like Left ventricular failure, Cardiogenic shock.

CONCLUSION:
Admission day NLR value is a useful tool to stratify and predict the outcome for in-hospital mortality and increasing NLR value is significantly associated with mortality. Decreased Hemoglobin level, Increased Absolute neutrophil count also associated with increased mortality which is also available from simple CBC. We suggest that NLR value assessment and documentation should become standard procedure in acute care of patients with Acute coronary syndrome.

LIMITATION:
• Impact of duration from "symptom onset-to-blood prick" time.
• Single centre study.
• Study on Pre-ACS and Post-ACS percentage increase in NLR value is warranted to know the causal association.
• Other factors like DM, HTN, Dyslipidemia, Smoking are not significantly different from survivors which may be due to less number of non-survivors in our study.

CONFLICT OF INTEREST:
None

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