DOI: 10.7860/JCDR/2021/51766.15719

Original Article

General Medicine Section

Role of Neutrophil-lymphocyte Ratio as Short-term Outcome Prognostic Indicator Following an Acute ST Segment Elevation Myocardial Infarction-A Prospective Observational Study

CATHERINE T PAUL[1], VIJAYASHREE THYAGARAJ[2], SWATI HEGDE[3]

ABSTRACT

Introduction: The ratio of Neutrophils to Lymphocytes (NLR) has recently arisen as a likely biomarker to forecast clinical outcomes in Ischaemic Heart Disease (IHD). The NLR in cases of ST Elevation Myocardial Infarction (STEMI) with respect to survival outcomes and complications is not well established in literature and was evaluated in the present study.

Aim: To study the association of NLR with complications and mortality following acute STEMI.

Materials and Methods: A short-term prospective observational study was conducted in 102 participants diagnosed with STEMI. The study was conducted at tertiary care hospital from October 2015 to September 2017. Haematological, serological and radiographical findings were obtained and compared between survivors and non survivors. Receiver Operator Curve (ROC) and Area Under the Curve (AUC) analysis were performed to analyse the utility of NLR in predicting mortality and major complications.

Results: The mean age of patients was 64.12±14.82 years and 75.5% of them were male. Non survivors (9.8%) had a greater incidence of cardiogenic shock (p-value <0.00049), pulmonary oedema (p-value <0.01199) and tachyarrhythmia (p-value <0.00049) compared to survivors. The ROC and AUC analysis showed that a higher NLR had a sensitivity of 80% in detecting mortality, 77.78% in detecting cardiogenic shock and 80% in detecting pulmonary oedema.

Conclusion: Higher NLR can be a useful prognostic marker for predicting short-term mortality and acute complications following an acute STEMI.

Keywords: Acute coronary syndrome, Complication, Morbidity, Mortality, Prognosis

INTRODUCTION

Cardiovascular Diseases (CVDs) that include IHD and stroke account for 17.7 million deaths and are leading causes of death [1]. In India the prevalence of coronary artery disease is 21.4% for diabetics and 11% for nondiabetics and this prevalence in rural population is half than that in urban population [2]. IHD comprises of Silent Ischemia (SI), Stable Angina Pectoris (SAP) and Acute Coronary Syndromes (ACS) [3]. The acute manifestation of IHD is ACS, subdivided into sudden cardiac death, Non ST Segment Elevation ACS (NSTE ACS) and STEMI. The NSTE ACS is further subdivided into NSTEMI and Unstable Angina Pectoris (UAP) [3,4].

Inflammation has shown to underlie many CVDs, especially those involving atherosclerosis as a pathogenic mechanism, such as coronary artery disease [3,4]. Lymphocytes and monocytes are found in the early phases of plaque formation, whereas neutrophils are involved in acute plaque disruption and thrombotic occlusion. The atherosclerotic plaque is formed under the direction of activated monocytes, sections of blood platelets, proliferating endothelial cells and foam cells (from unsafe Low Density lipoprotein Cholesterol or LDL-C). The neutrophils which release Reactive Oxygen Species (ROS), oxidise LDL-C and contribute to plaque disruption. In established atheromata, the neutrophils undergo apoptosis and thereby the migration of monocytes/macrophages occurs into the site to maintain function of phagocytosis [4].

Inflammatory markers such as C-Reactive Protein (CRP) and neutrophil rise in the acute phase of cardiac diseases such as Acute Heart Failure (AHF), and ACS (especially in STEMI) is an established phenomenon [5,6]. Studies have observed that various haematological indices such as total leukocyte count, neutrophil count and NLR are predictive of survival in STEMI [7-9].

NLR ratio can be calculated as the absolute count of neutrophils divided by the total count of lymphocytes. NLR has been proved to be a useful prognostic indicator in various conditions like major cardiac events, cancers, infectious diseases and postoperative complications. In a study by Forget P et al., the normal NLR value in adult, non geriatric healthy population was between 0.73 and 3.53 [10]. NLR is an inexpensive, widely available test and can be easily calculated in comparison to other inflammatory markers in developing countries such as India.

Given the paucity of NLR based survival prediction studies, occurrence of higher frequency of STEMI in Indian population, and because STEMI is associated with high early and late morbidity and mortality [11], the current study was undertaken. Also, the documented NLR could contribute to future risk stratification of admitted patients with acute STEMI [12,13]. The previous studies also support the role of NLR in predicting complications and death in myocardial infarction patients [14-16]. Thus, prognostic value of NLR in STEMI with respect to survival outcomes was evaluated in the present study.

MATERIALS AND METHODS

A hospital based short-term prospective observational study was conducted under the Department of General Medicine in a tertiary care hospital (MS Ramaiah Medical College, Bengaluru, Karnataka, India) from October 2015 to September 2017. The study was approved by Institutional Ethics and Scientific committee, prior to the start of the study (Reference number: STD-1/EC/027/2015). A written informed consent was obtained from all the participants before starting the study.

Sample size calculation: The study was conducted on a sample of 102 participants. In the present study, sample size was calculated, assuming the sensitivity of NLR in predicting in-hospital mortality after STEMI to be 60%, with the precision of 1.5% and desired confidence level of 95% based on a previous study by Ghaffari S et al., [14].

Inclusion criteria: All patients aged more than 18 years and admitted to the Coronary Care Unit (CCU) with a diagnosis of STEMI were included.

Exclusion criteria: Those participants with active infections, active hepatobiliary disease, patients on steroids, patient with human immunodeficiency virus infection, pre-existing haematological malignancies or chronic inflammatory conditions were excluded.

Study Procedure

The diagnosis of STEMI was made as per the definition by American College of Cardiology/American Heart Association (ACC/AHA) i.e., STEMI is a clinical syndrome defined by characteristic symptoms of myocardial ischaemia in association with persistent electrocardiographic ST elevation and subsequent release of biomarkers of myocardial necrosis. The ST segment elevation corresponds to a new ST elevation at the J point in at least 2 contiguous leads of >2 mm in men or >1.5 mm in women in leads V2-V3 and/or >1 mm in other contiguous chest leads or limb leads [17].

A detailed history was obtained, and physical examination was performed on all patients. Complete Blood Counts (CBC), levels of troponin I, Creatinine Phosphokinase Myocardial Band (CPK-MB), ECG, 2D Echocardiography (2D ECHO) and Coronary Angiography (CAG), were performed when found necessary. All patients received treatment as per the standard of care. All complications were documented and patients were followed-up until discharge or death.

STATISTICAL ANALYSIS

Data were analysed using statistical software R version 4.0.3. Continuous variables were presented as Mean±SD/Median (minimum, maximum) and categorical variables were presented as absolute counts and frequency. The association between categorical variables was measured using Chi-square test. To compare the difference between groups, t-test/Mann-Whitney U test was applied. The p-value ≤0.05 was considered statistically significant. The NLR data was analysed with respect to mortality and major complications using ROC analysis. The AUC, sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of NLR were reported. The cut off value for NLR in predicting in-hospital mortality and various complications was calculated using Area Under Curve-Receiver Operator Characteristic (AUC-ROC) Curve analysis.

RESULTS

Mean age of the study sample was 64.12±14.82 year and 75.5% were men. Around 72,70% of the participants had Type 2 Diabetes Mellitus (T2DM), 69 (67.6%) had hypertension and 40 (39.2%) had dyslipidaemia. The inferior wall MI was observed in 60 (58.8%), anterior wall MI in 32 (31.3%) and lateral wall MI in 10 (9.8%) of the study sample [Table/Fig-1].

Variables	Mean±SD/Range	Number of subjects (%)/ Median (Min, Max)
Age (years)	64.12±14.82	65 (36, 90)
	>18-<40	3 (2.94%)
	41-50	22 (21.57%)
	51-60	21 (20.59%)
	61-70	20 (19.61%)
	71-80	18 (17.65%)
	81-90	18 (17.65%)
Gender	Female	25 (24.51%)
	Male	77 (75.49%)
Heart Rate (beats/minute)	106.86±10.04	104 (86, 132)
RR (cycles/minute)	26.17±4.2	26 (16, 34)
SpO_2 (%)	92.91±3.48	94 (84, 99)
Hb (gram%)	11.62±2.38	11.53 (5.8, 19.71)
Total leukocyte count (cell/cumm)	4000-11000	43 (42.16%)
	>11000	59 (57.84%)
Neutrophils (%)	77.09±11.91	80 (41, 96)
Lymphocytes (%)	16.05±9.79	13 (2, 48)
Platelets (cells/cumm)	204591.37±75403.78	183500 (90730, 489130)
RBS (gram%)	183.15±48.72	181 (82.7, 340)
NLR	7.74±7.71	6.35 (0.85, 48)
Troponin (ng/mL)	604.67±1941.15	239.5 (34, 19356)
CPK-MB (IU/L)	29.93±19.03	27.5 (4.6, 103)
Creatinine (mg/dL)	1.23±0.52	1.2 (0.4, 3)
T2DM	No	30 (29.41%)
	Yes	72 (70.59%)
Hypertension	No	33 (32.35%)
	Yes	69 (67.65%)
Dyslipidemia	No	62 (60.78%)
	Yes	40 (39.22%)
Death	No	92 (90.2%)
	Yes	10 (9.8%)
Cardiogenic shock	No	84 (82.35%)
	Yes	18 (17.65%)
Pulmonary oedema	No	77 (75.49%)
	Yes	25 (24.51%)
Tachyarrhythmia	No	82 (80.39%)
	Yes	20 (19.61%)
ECG	AWMI	32 (31.37%)
	IWMI	60 (58.82%)
	LWMI	10 (9.8%)
EF (%)	35	29 (28.43%)
	40	20 (19.61%)
	50	2 (1.96%)
	56	51 (50%)
CAG	DVD	24 (23.53%)
	SVD	52 (50.98%)
	TVD	26 (25.49%)

[Table/Fig-1]: The characteristics of study participants along with summary of variables.
AWMI: Anterior wall ST segment elevation myocardial infraction; CAG: Coronary angiography; CPK-MB: Creatinine phosphokinase; ECG: Electrocardiogram; DVD: Dual vessel disease; EF: Ejection fraction; Hb: Haemoglobin; HTN: Hypertension; IWMI: Inferior wall myocardial infarction; LWMI: Lateral wall ST segment elevation myocardial infraction; NLR: Neutrophil to lymphocyte ratio; PWMI: Posterior wall ST segment elevation myocardial infraction; RR: Respiratory rate; RBS: Random blood sugar; SpO_2: Blood oxygen saturation; SVD: Single vessel disease; T2DM: Type 2 diabetes mellitus; TVD: Triple vessel disease

Ten patients (9.8%) succumbed in the hospital following STEMI during the study period. The mean age of survivors was 64.76±15.15 years and the mean age of non survivors was 58.20±10.58 years. The presence of comorbidities though higher in non survivors, was not statistically significant. The LV systolic dysfunction was seen in 39 (41.3%) survivors, whereas all the non survivors (100%) had LV systolic dysfunction. In the current study, 7 (70%) of non survivors had Triple Vessel Disease (TVD) and 3 (30%) non survivors had Double Vessel Disease (DVD). Among survivors, 52 (56.5%) patients had SVD, 21 (22.8%) patients had DVD and 19 (20.6%) patients had TVD. The non survivors had a worse angiographic picture as compared to the survivors [Table/Fig-2].

There was no significant difference in age, gender, comorbidities and ECG changes between patients who died and survived STEMI. No significant difference in mean total count, mean neutrophil count, mean NLR, troponin I, CPK-MB and creatinine values was observed between survivors and non survivors. The development of

Variables		Outcome		p-value
		Death (n=10)	Survived (n=92)	
Age (in years)	<40	0 (0%)	3 (3.26%)	0.5297[MC]
	41-50	3 (30%)	19 (20.65%)	
	51-60	3 (30%)	18 (19.57%)	
	61-70	3 (30%)	17 (18.48%)	
	71-80	1 (10%)	17 (18.48%)	
	81-90	0 (0%)	18 (19.57%)	
Mean age (in years)		58.2±10.56	64.76±15.12	0.1851[t]
Gender	Female	2 (20%)	23 (25%)	1[MC]
	Male	8 (80%)	69 (75%)	
Heart rate (beats/minute)		101.6±11.5	107.43±9.76	0.08074[t]
RR (cycles/minute)		23.6±4.2	26.45±4.12	0.02053*#[t]
SpO_2 (%)		94.9±3.14	92.7±3.46	0.05683[t]
Hb (gram%)		10.99±3.74	11.69±2.21	0.3776[t]
Total count (cells/cumm)		14306± 4505.38	12170.65± 6148.78	0.2893[t]
Total leukocyte count (cell/ cumm)	4000-11000	3 (30%)	40 (43.48%)	0.5312[MC]
	>11000	7 (70%)	52 (56.52%)	
Neutrophils (%)		83.3±6.78	76.41±12.17	0.08246[t]
Lymphocytes (%)		10 (3 ,24)	13 (2 ,48)	0.1294[MW]
Platelets (cell/cumm)		177915 (113100, 361720)	183500 (90730, 489130)	1.0[MW]
RBS (gram %)		190.25±73.37	182.38±45.78	0.63[t]
NLR		8.35 (3, 31.67)	6.2 (0.85, 48)	0.1138[MW]
Troponin (ng/mL)		244 (34 ,945)	235.5 (37 ,19356)	0.593[MW]
CPK MB (IU/L)		28.54±15.38	30.09±19.45	0.8087[t]
Creatinine (mg/dL)		1.47±0.66	1.2±0.5	0.1211[t]
T2DM	No	1 (10%)	29 (31.52%)	0.2879[MC]
	Yes	9 (90%)	63 (68.48%)	
HTN	No	2 (20%)	31 (33.7%)	0.5107[MC]
	Yes	8 (80%)	61 (66.3%)	
Dyslipidemia	No	5 (50%)	57 (61.96%)	0.5237[MC]
	Yes	5 (50%)	35 (38.04%)	
Cardiogenic shock	No	2 (20%)	82 (89.13%)	0.00049*[MC]
	Yes	8 (80%)	10 (10.87%)	
Pulmonary oedema	No	4 (40%)	73 (79.35%)	0.01199*[MC]
	Yes	6 (60%)	19 (20.65%)	
Tachyarrhythmia	No	3 (30%)	79 (85.87%)	0.00049*[MC]
	Yes	7 (70%)	13 (14.13%)	
ECG	AWMI	5 (50%)	27 (29.35%)	0.2644[MC]
	IWMI	5 (50%)	55 (59.78%)	
	LWMI	0 (0%)	10 (10.87%)	
EF (%)	35	9 (90%)	20 (21.74%)	0.001*[MC]
	40	1 (10%)	19 (20.65%)	
	50	0 (0%)	2 (2.17%)	
	56	(0%)	51 (55.43%)	
CAG	DVD	3 (30%)	21 (22.83%)	0.001*[MC]
	SVD	(0%)	52 (56.52%)	
	TVD	7 (70%)	19 (20.65%)	

[Table/Fig-2]: Comparison of variables between survivors and non survivors of STEMI. AWMI: Anterior wall ST segment elevation myocardial infraction; CAG: Coronary angiography; CPK MB: Creatinine phosphokinase MB; ECG: Electrocardiogram; DVD: Double vessel disease; EF: Ejection fraction; Hb: Haemoglobin; HTN: Hypertension; LWMI: lateral wall ST segment elevation myocardial infraction; NLR: Neutrophil to lymphocyte ratio; PWMI: Posterior wall ST segment elevation myocardial infraction; RR: Respiratory rate; RBS: Random blood sugar; SpO_2: Blood oxygen saturation; SVD: Single vessel disease; T2DM: Type 2 diabetes mellitus; TVD: Triple vessel disease; MC: Monte-carlo's simulation; t: t-test; #:one-tailed test; MW: Mann-whitney U test; *p-value <0.05 was considered as statistically significant

complications like cardiogenic shock (p-value <0.00049), pulmonary oedema (p-value <0.01199) and tachyarrhythmia (p-value <0.00049) were found to be significantly higher in the patients who succumbed to STEMI [Table/Fig-2].

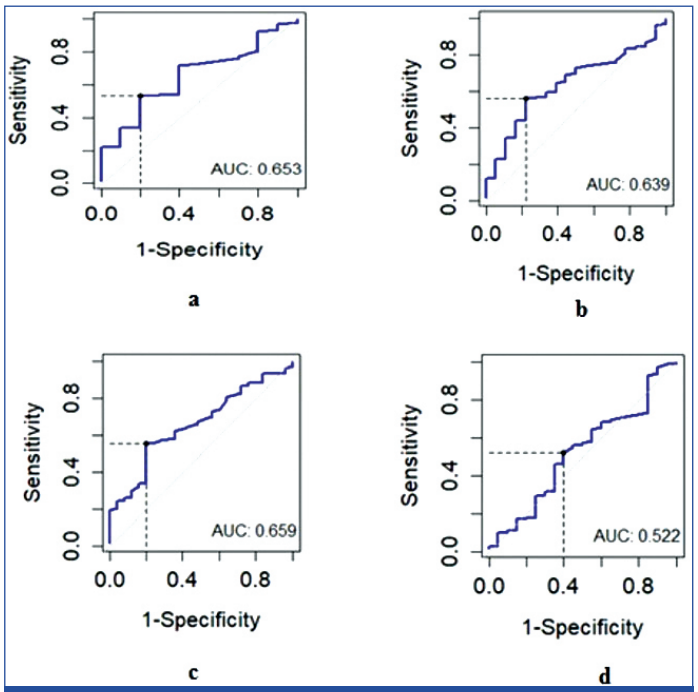
The NLR in relation with mortality, cardiogenic shock, pulmonary oedema and tachyarrhythmias was evaluated by Receiver Operating Curve (ROC) plots for specific variables and AUC were used to determine the cut-off values for respective parameters. The cut-off for NLR was predicted to be 6.3, above which the incidence of cardiac mortality was high. NLR demonstrated 80% sensitivity in detecting mortality, 77.78% sensitivity in detecting cardiogenic shock and 80% sensitivity in detecting pulmonary oedema (80%). The association between NLR and tachyarrhythmia was not statistically significant [Table/Fig-3-5].

Variables		NLR {Median (Min, Max)}	p-value (Mann-whitney test)
Cardiogenic shock	No	5.85 (0.85, 48)	0.06523
	Yes	7.83 (1.94, 31.67)	
Pulmonary oedema	No	5.47 (0.85, 48)	0.01709
	Yes	7.27 (2.64, 31.67)	
Tachyarrhythmia	No	6.28 (0.85, 48)	0.768
	Yes	6.75 (1.14, 46.5)	

[Table/Fig-3]: Association between complications and NLR in patients with STEMI. NLR: Neutrophil-lymphocyte ratio; *p-value <0.05 was considered as statistically significant

Variables	Mortality	Cardiogenic shock	Pulmonary oedema	Tachyarrhythmia
Cut-off	>6.31	>6.31	>6.15	>6.31
Specificity	53.26%	55.95%	55.84%	52.43%
Sensitivity	80%	77.78%	80%	60%
PPV	96.07%	92.16%	89.58%	84.31%
NPV	15.68%	27.45%	37.03%	23.53%
AUC	0.653	0.639	0.659	0.522

[Table/Fig-4]: Neutrophil- lymphocyte ratio in relation to mortality and complications. PPV: Positive predictive value; NPV: Negative predictive value



[Table/Fig-5]: a) AUC-ROC: NLR in relation to mortality; b) AUC-ROC: NLR in relation to cardiogenic Shock; c) AUC- ROC: NLR in relation to pulmonary oedema; d) AUC-ROC: NLR in relation to tachyarrhythmia.

DISCUSSION

The CVDs are a global burden and the incidence and mortality associated with them are very high especially in Indian subcontinent [2,3]. The patients presenting with acute chest pain and persistent

(>20 min) ST-segment elevation often develop STEMI [4,5]. The risk factors such as smoking, life style habits (sitting in working for long hours, fat rich diet and minimal exercise activity) and associated comorbidities such as diabetes mellitus, hypertension and hyperlipidaemia often progress to atherosclerosis resulting in IHD or myocardial infarction [3,6]. Inflammatory markers {raised Erythrocyte Sedimentation Rate (ESR), CRP, and Interleukin-6 (IL-6)}, total leukocyte count and NLR are predictors of STEMI and associated cardiovascular mortality [7-9]. The current study compared the various parameters between survivors and non survivors with STEMI.

A NLR of more than 6.30 predicted mortality with a sensitivity of 80% and specificity of 53.26%. With the cut-off value we considered for NLR [Table/Fig-4], there was a positive correlation with the development of complications such as cardiogenic shock and pulmonary oedema. In this study, higher NLR demonstrated 80% sensitivity in detecting mortality, 77.78% sensitivity in detecting cardiogenic shock and 80% sensitivity in detecting pulmonary oedema (80%).

Han YC et al., reported that high NLR group was associated with a significantly higher rate of 12-month Major Adverse Cardiac Events (MACE) (19.1% vs 3.7%), 12-month death (18.2% vs 2.8%), in-hospital MACE (12.7% vs 2.8%) and in-hospital death (12.7% vs 1.9%) compared to the low NLR group. The same study had reported that, raised values of NLR were independent predictor for 12-month MACE after adjustment for confounders and factors encompassed in the Thrombolysis In Myocardial Infarction (TIMI) risk score for STEMI [16]. This is in line with a recent study by Luke K et al., where in-addition to NLR ratio, parameters associated to platelet counts was also considered [18]. The NLR (6.29 vs. 2.18) and Platelet to Lymphocyte Ratio (PLR) (173.88 vs. 122.46) significantly predicted ACS. An ROC curve analysis was performed as in the current study and showed Mean Platelet Volume (MPV) had the highest AUC (95%) for ACS diagnosis with an optimum cut-off point at ≤8.35 (sensitivity 93.6% and specificity 97.3%) [18].

Yalcinkaya E et al., found that Grade 3 Ischemia (G3I) and raised NLR in STEMI patients were considerably associated and that NLR has a prognostic value for risk stratification STEMI patients. The death rate amplified proportionally with rise in grade of ischemia on electrocardiogram (OR=1.254, CI: 1.120-1.403) [19].

NLR is not just a cardiac specific marker, but also showed to be an indicator of prognosis and major events after major coronary surgery. Wang Z et al., evaluated the relationship between NLR and prognosis of patients with Non-ST-Elevation Acute Coronary Syndrome (NSTE-ACS) undergoing elective PCI within 1 year. They showed that preoperative NLR and postoperative NLR (within 24 hours) had predicted the MACE in NSTE-ACS patients who underwent elective coronary intervention [20].

The additional role of NLR in AHF patients was shown by Cho JH et al., [21]. The patients, in this study, having highest NLR quartile had the highest in-hospital and postdischarge mortality. A cut-off NLR value of 7.0 and 5.0 indicated augmented hazard of in-hospital and postdischarge death in patients with and without aggravated infection or ischemia, respectively. Raised NLR in AHF patients during hospitalisation was an independent predictor for in-hospital and postdischarge three-year mortality.

The PLR and NLR correlated with TIMI frame count (R: 0·372 and R: 0·301) with a positive correlation in another study by Vakili H et al., [22]. The PLR just as NLR is an efficient biomarker of STEMI. The current study showed that NLR is a useful and inexpensive tool that may be used at bedside to determine complications and mortality in non survivors of STEMI. The CPK-MB (AUC= 0.498) was only variable that was found to be just significant in differentiating between survivors and non survivors. In a similar study, Machado G et al., had reported high NLR to be an independent predictor of distal embolization, no-reflow, and procedural complications in patients with STEMI who had undergone primary surgical intervention. A low NLR value has demonstrated an excellent NPV (92.1-97.8%) for these procedural outcomes [23]. The usefulness of NLR is further validated by reports of an Indian study which showed that higher mortality was seen in high NLR (42/135, 34.1%; NLR >5.25) compared to low NLR (5/265, 1.9%; NLR ≤5.25) group with difference between them for prediction of mortality as found in the current study [24].

Since, NLR is not affected by risk factors (HTN, T2DM and hyperlipidaemias) and is superior to other peripheral blood cells determining morbidity and mortality risk in patients with STEMI, it can be recommended as a routine investigation to identify patients who are likely to develop complications with STEMI.

Limitation(s)

The limitations of the study were that it was conducted in a small subgroup of population while strengths lie in the methodology and ROC analysis. Further multicentric studies with larger samples on mortality rates may contribute to the further understanding and application of NLR ratio in predicting morbidity and mortality in STEMI patients.

CONCLUSION(S)

Neutrophils to Lymphocytes (NLR) is a simple and easily available blood test that can be used for risk stratification of patients presenting with acute STEMI. Higher NLR seems to be associated with higher mortality and higher incidence of major complications like acute pulmonary oedema and cardiogenic shock following an episode of acute STEMI. This will help in early identification and more aggressive management of these patients.

REFERENCES

[1] WHO. World Health Organization; Geneva: 2016. Global Health Estimates 2015: Deaths by Cause, Age, Sex, by Country and by Region, 2000-2015.

[2] Sreeniwas Kumar A, Sinha N. Cardiovascular disease in India: A 360 degree overview. Med J Armed Forces India. 2020;76(1):01-03. Doi: 10.1016/j.mjafi.2019.12.005.

[3] Huffman MD, Prabhakaran D, Osmond C, Fall CH, Tandon N, Lakshmy R, et al. New Delhi Birth Cohort. Incidence of cardiovascular risk factors in an Indian urban cohort results from the New Delhi birth cohort. J Am Coll Cardiol. 2011;57(17):1765-74.

[4] Gaul DS, Stein S, Matter CM. Neutrophils in cardiovascular disease. European Heart Journal. 2017;38(22):1702-04.

[5] Sidhu NS, Rangaiah SKK, Ramesh D, Veerappa K, Manjunath CN. Clinical characteristics, management strategies, and in-hospital outcomes of acute coronary syndrome in a low socioeconomic status cohort: An observational study from urban India. Clin Med Insights Cardiol. 2020;14:1179546820918897.

[6] Jaffe AS, Lindahl B, Giannitsis E, Mueller C, Cullen L, Hammarsten O, et al. ESC study group on cardiac biomarkers of the association for acute cardiovascular care: A fond farewell at the retirement of CKMB. Eur Heart J. 2021;42(23):2260-64.

[7] Sugizaki Y, Shinke T, Doi T, Igarashi N, Otake H, Kawamori H, et al. Impact of the angiographic burden on the incidence of out-of-hospital ventricular fibrillation in patients with acute myocardial infarction. Heart and Vessels. 2019;34(1):52-61.

[8] Vaccarezza M, Balla C, Rizzo P. Atherosclerosis as an inflammatory disease: Doubts? No more. Int J Cardiol Heart Vasc. 2018;19:01-02.

[9] Chen H, Li X, Liu S, Gu L, Zhou X. MircroRNA-19a promotes vascular inflammation and foam cell formation by targeting HBP-1 in atherogenesis. Sci Rep. 2017;7(1):01-10.

[10] Forget P, Khalifa C, Defour JP, Latinne D, Van Pel MC, De Kock M. What is the normal value of the neutrophil-to-lymphocyte ratio?. BMC Res Notes. 2017;10(1):12. Doi: 10.1186/s13104-016-2335-5.

[11] Dai J, Fang C, Zhang S, Hou J, Xing L, Li L, et al. Not all plaque erosions are equal: novel insights from 1,660 patients with STEMI: A clinical, angiographic, and intravascular OCT study. Cardiovascular Imaging. 2020;13(2_Part_1):516-18.

[12] Smilowitz NR, Mahajan AM, Roe MT, Hellkamp AS, Chiswell K, Gulati M, et al. Mortality of myocardial infarction by sex, age, and obstructive coronary artery disease status in the ACTION Registry-GWTG (Acute Coronary Treatment and Intervention Outcomes Network Registry-Get With the Guidelines). Circulation: Cardiovascular Quality and Outcomes. 2017;10(12):e003443.

[13] Ghadri JR, Wittstein IS, Prasad A, Sharkey S, Dote K, Akashi YJ, et al. International expert consensus document on Takotsubo syndrome (part I): Clinical characteristics, diagnostic criteria, and pathophysiology. Eur heart J. 2018;39(22):2032-46.

[14] Ghaffari S, Nadiri M, Pourafkari L, Sepehrvand N, Movasagpoor A, Rahmatvand N, et al. The predictive value of total neutrophil count and neutrophil/lymphocyte ratio in predicting in-hospital mortality and complications after STEMI. J Cardiovasc Thorac Res. 2014;6(1):35-41.
[15] Gul U, Kayani AM, Munir R, Hussain S. Neutrophil lymphocyte ratio: A Prognostic marker in acute ST elevation myocardial infarction. J Coll Physicians Surg Pak. 2017;27(1):04-07.
[16] Han YC, Yang TH, Kim DI, Jin HY, Chung SR, Seo JS, et al. Neutrophil to lymphocyte ratio predicts long-term clinical outcomes in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. Korean Circulation Journal. 2013;43(2):93-99.
[17] O'Gara PT, Kushner FG, Ascheim DD, Casey DE Jr, Chung MK, de Lemos JA, et al. American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. ACCF/AHA guideline for the management of ST-elevation myocardial infarction: A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2013;127:e362-e425.
[18] Luke K, Purwanto B, Herawati L, Al-Farabi MJ, Oktaviono YH. Predictive value of hematologic indices in the diagnosis of acute coronary syndrome. Open Access Maced J Med Sci. 2019;7(15):2428-33.
[19] Yalcinkaya E, Yuksel UC, Celik M, Kabul HK, Barcin C, Gokoglan Y, et al. Relationship between neutrophil-to-lymphocyte ratio and electrocardiographic ischemia grade in STEMI. Arq Bras Cardiol. 2015;104(2):112-19.
[20] Wang Z, Wang J, Cao D, Han L. Correlation of neutrophil-to-lymphocyte ratio with the prognosis of non ST-segment elevation in patients with acute coronary syndrome undergoing selective percutaneous coronary intervention. J Int Med Res. 2020;48(10):300060520959510.
[21] Cho JH, Cho HJ, Lee HY, Ki YJ, Jeon ES, Hwang KK, et al. Neutrophil-Lymphocyte ratio in patients with acute heart failure predicts in-hospital and long-term mortality. J Clin Med. 2020;9(2):557.
[22] Vakili H, Shirazi M, Charkhkar M, Khaheshi I, Memaryan M, Naderian M, et al. Correlation of platelet-to-lymphocyte ratio and neutrophil-to-lymphocyte ratio with thrombolysis in myocardial infarction frame count in ST-segment elevation myocardial infarction. Eur J Clin Invest. 2017;47(4):322-27.
[23] Machado G, Araujo GN, Carpes CK, Lech MC, Mariani S, Valle FH, et al. Elevated neutrophil-to-lymphocyte ratio can predict procedural adverse events in patients with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention. Coron Artery Dis. 2019;30(1):20-25.
[24] Bajari R, Tak S. Predictive prognostic value of neutrophil-lymphocytes ratio in acute coronary syndrome. Indian Heart J. 2017;69(Suppl 1):S46-50.

PARTICULARS OF CONTRIBUTORS:
1. Senior Resident, Department of General Medicine, Jubilee Mission Medical College, Thrissur, Kerala, India.
2. Professor, Department of General Medicine, MS Ramaiah Medical College, Bengaluru, Karnataka, India.
3. Assistant Professor, Department of General Medicine, MS Ramaiah Medical College, Bengaluru, Karnataka, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Swati Hegde,
Assistant Professor, Department of General Medicine, Ramaiah Medical College, Bangalore, Karnataka, India.
E-mail: swatihegde2006@yahoo.co.in

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Aug 06, 2021
- Manual Googling: Oct 23, 2021
- iThenticate Software: Nov 15, 2021 (11%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Aug 05, 2021**
Date of Peer Review: **Sep 28, 2021**
Date of Acceptance: **Oct 26, 2021**
Date of Publishing: **Dec 01, 2021**