

Predictive Value of Neutrophil Lymphocyte Ratio and Platelet Lymphocyte Ratio in Immediate Outcomes of ST-elevation Myocardial Infarction: A Cross-sectional Study

SNEHA BARKUR SADASHIVA¹, KS CHENTHIL²

ABSTRACT

Introduction: There have been various inflammatory markers implicated in the pathogenesis of Acute Coronary Syndromes (ACS). However, the role of the Neutrophil Lymphocyte Ratio (NLR) and Platelet Lymphocyte Ratio (PLR) as prognostic markers in ST-elevation Myocardial Infarction (STEMI) remains poorly researched.

Aim: To determine the prognostic value of NLR and PLR to predict the immediate outcomes in patients with acute STEMI, and if any association exists between NLR/PLR and Thrombolysis in Myocardial Infarction (TIMI) risk score.

Materials and Methods: This was a cross-sectional study conducted at a tertiary care centre, Puducherry, India, where 190 patients who presented to casualty with STEMI were enrolled. The patient co-morbidities, personal and family history were obtained. The routine laboratory parameters including platelets, lymphocytes, neutrophils and their corresponding ratios were calculated. Patients were grouped into low and high NLR/PLR

groups and were assessed for occurrence of in-hospital mortality or Major Adverse Cardiovascular Events (MACE). Analysis was made to see if there is an association between NLR/PLR and MACE. Chi-square test and one-way ANOVA test was used for statistical significance.

Results: Among 190 subjects, 157 male and 33 female with mean age of 55.72 ± 11.24 years were included. A total of 8.94% patients had MACE. NLR was positively associated with MACE (p -value=0.0006), whereas PLR was not associated with MACE. Patients with high NLR had 1.45 times higher odds of having MACE. NLR was significantly associated with TIMI risk score. Both NLR (F ratio=6.341) and PLR (F ratio=4.600) showed significant association with Killip classification, however NLR showed higher association (p -value <0.001).

Conclusion: NLR can be used as a powerful prognostic marker for predicting immediate MACE and death in STEMI patients. In addition, NLR showed positive correlation with Killip classification and TIMI risk score.

Keywords: Acute coronary syndrome, Inflammatory markers, Killip classification, Major adverse cardiovascular events, Prognostic markers

INTRODUCTION

Acute STEMI is one of the most common emergencies seen worldwide. The underlying pathophysiological mechanism is atherosclerotic plaque rupture and thrombus formation. Inflammation has been found to be the basis of many cardiovascular diseases, especially those that involve atherosclerosis, a mechanism seen in Coronary Artery Disease (CAD) [1-3]. The body responds to inflammation by producing white blood cells, especially neutrophils from the bone marrow. Lymphocytes and monocytes play a key role in the early stages of plaque formation [4].

One of the most selective markers to detect myocardial damage is troponin. There is ambiguity in the use of troponin in emergency setting, as there can be a prolonged elevation in serum troponin levels and there is a need to measure it at successive intervals to see the increasing trend. Although, the fundamental flaw against it is an increase in its serum level 3-4 hours after the onset of symptoms. Thus, in most centers, these markers should be reviewed in consecutive times. And in this case, its application in rapid triage of patients with Myocardial Infarction (MI) is faced with ambiguity [5]. Hence, there is a need to find novel biomarkers. D-dimer level is expected to increase in acute ischemic events faster than other cardiac markers [6]. CD40 ligand is known to regulate the thrombotic potential of human atherosclerotic lesion by inducing the expression of tissue factor [7].

Therefore, there is increasing need to find prognostic markers capable of accelerating diagnostic and decision making processes for STEMI patients [8]. NLR and PLR are the two indices which have attracted attention as inflammatory markers capable of predicting

poor prognosis and MACE [9,10]. There are many advantages of NLR such as being cost effective and high speed of testing, hence, saves a lot of time in the decision process and planning for a referral to a higher ICU centre if worse prognosis is predicted [11]. Moreover, there is inadequate research regarding the prognostic value of NLR and PLR when compared to the standard Thrombolysis in Myocardial Infarction (TIMI) scoring, which is a well established tool that analyses the 30 days mortality of patients with STEMI. The effect of NLR on cardiovascular diseases is still unclear and prognostic significance of NLR in patients with STEMI is not established.

Hence, this study aimed to determine the prognostic value of NLR and PLR to predict the immediate outcomes (one week) in patients with acute STEMI.

MATERIALS AND METHODS

It was a prospective cross-sectional study, conducted at a tertiary care centre, Puducherry, India from January 2019 to June 2020 after approval from Institutional Ethical Committee Board (Reg no. ECR/451/inst/PO/2013/RR-16, project number- 02/2019/16). Informed consent was obtained in local language from the participants.

Sample size calculation: Sample size was calculated using the statistical formula for estimating a proportion with 5% absolute precision and 5% level of significance. The study included a total sample size of 190 participants.

Inclusion criteria: Study participants, aged more than 18 years who presented to casualty with STEMI. The STEMI was diagnosed based

on the criteria laid by the American Heart Association as a new ST-elevation measured from the J point in two or more contiguous leads with a cut-off point of 0.1 mV in all leads except V2,V3, whereas a cut-off >2 mm >40 years of age, >2.5 mm <40 years of age, >1.5 mm in leads V2, V3 in a woman irrespective of age, during the first 12 hours after the onset of symptoms were included in the study. [12].

Exclusion criteria: Patients with unstable angina, non-STEMI, severe liver disease, autoimmune disease, haematological disorders, inflammatory and infectious disease, pre-existing valvular disease and whose laboratory blood investigations were not available were excluded from the study.

Study Procedure

The basic demographics of patients like age, sex, co-morbidities (diabetes mellitus, hypertension, dyslipidaemia), personal history (smoking and alcohol consumption) and family history of CAD were obtained. Two mL of venous blood sample was drawn at the time of admission in casualty and sent for estimation of complete blood counts. NLR and PLR were calculated. Patients were grouped into low and high NLR groups based on a cut-off of 3.53, whereas the cut-off for PLR was 172 [13].

All patients were assessed for occurrence of MACE which includes arrhythmias, cardiogenic shock, cardiac rupture, re-infarction and in hospital mortality. Data was analysed to find out if there is an association between NLR/PLR and MACE and the correlation between NLR/PLR and TIMI risk score.

TIMI risk score is a well researched score that analyses the 30 day mortality and 1 year mortality of patients with STEMI-ACS. The total is 7 points, and each variable is assigned 1 point. Variables includes age over 65 years, the presence of three or more CAD risk factors, previous coronary artery stenosis more than 50%, changes in ECG ST segment elevation, angina attacks greater than or equal to 2 in the past 24 hours, ingestion of aspirin and raised cardiac enzymes in the past 7 days [14]. Patients were also grouped into clinical severity based on Killip classification and data was analysed. Killip class I- no clinical signs of failure; Killip class II- rales/crackles in the lung; Killip class III- pulmonary oedema; Killip class IV- cardiogenic shock [15].

STATISTICAL ANALYSIS

Descriptive analysis was carried out by calculating mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. Chi-square test and one-way ANOVA test was used for statistical significance. Statistical Package for the Social Sciences (SPSS) version 25.0 was used for statistical analysis.

RESULTS

There were 157 males and 33 females; their co-morbidities, risk factors and haematological parameters are shown in [Table/Fig-1]. Logistic regression analysis was carried out to find out the association of the NLR and PLR with MACE [Table/Fig-2]. This analysis found that both NLR and PLR were associated with the MACE as an outcome. However, the NLR showed a higher association than PLR. It was again proved by the odds ratio. Patients with high NLR had 1.45 times higher odds of having MACE, whereas patients with high PLR had 0.9917 times higher odds of having MACE. Based on this analysis, it was concluded that the percentage of cases correctly classified by NLR was 92.63% [Table/Fig-3]. NLR was observed as a high value in MACE positive than negative group which was statistically significant (p-value=0.0042).

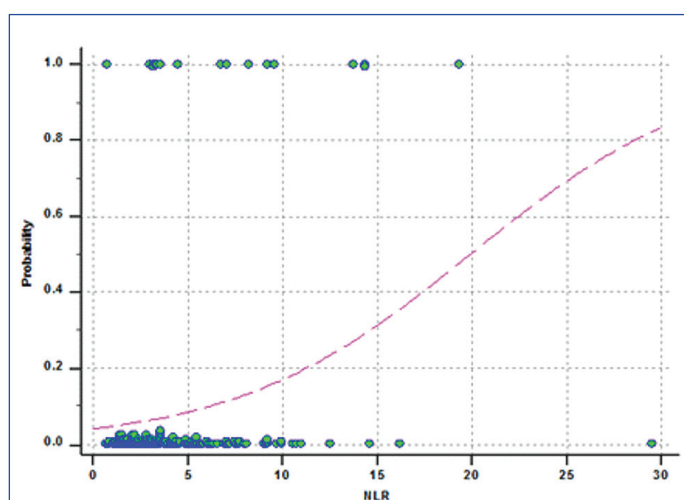
The one-way ANOVA was conducted to confirm the above results. The ANOVA showed that NLR had a close association with MACE while PLR was not associated with MACE [Table/Fig-4]. In the total population, NLR has shown a prognostic value to identify the cardiovascular outcomes appropriately

Baseline variables	Mean±SD, N=190	95% CI
Demographic variables		
Age in years	55.72±11.24	54.112 to 57.331
Gender (Male: Female)	157:33	
Haematological variables		
Lymphocytes %	22.07±10.32	20.597 to 23.552
Neutrophils %	70.62±12.25	68.870 to 72.377
NLR %	4.50±3.64	3.980 to 5.024
Platelet count (×10 ⁹ /L)	284.1±84.5	271.9 to 296.2
PLR %	165.94±109.06	150.338 to 181.554
Co-morbidity status		
Type 2 diabetes mellitus	124 (65.26%)	
Systemic hypertension	87 (45.78%)	
Dyslipidaemia	14 (7.36%)	
Family history	13 (6.84%)	
Smoking	90 (47.36%)	
Risk stratification variables		
TIMI score (Thrombolysis in myocardial infarction)		
0-2 (Low risk)	22 (11.57%)	
3-5 (Intermediate risk)	128 (67.36%)	
>5 (High risk)	40 (21.05%)	
Killip classification		
I	98 (51.57%)	
II	77 (40.52%)	
III	10 (5.26%)	
IV	5 (2.63%)	
MACE (Major Adverse Cardiac Events)		
No	173 (91.05%)	
Yes	17 (8.94%)	

[Table/Fig-1]: Basic characteristics of the study population.

Blood indices	Coefficient	p-value	Odds ratio	95% CI	Percent of case correctly classified	ROC-AUC
NLR	0.37704	0.0006	1.45	1.1747 to 1.8096	92.63%	0.713
PLR	-0.0083	0.234	0.9917	0.9846 to 0.9989		

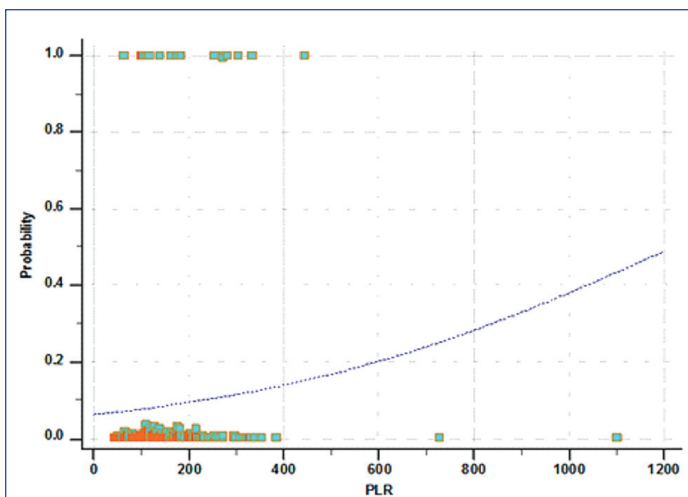
[Table/Fig-2]: Logistic regression analysis of NLR, PLR with MACE.



[Table/Fig-3a]: Prognostic probability of NLR.

Both NLR and PLR showed significant association with Killip Classification [Table/Fig-4]. However, NLR showed higher association with Killip (p-value <0.001).

The NLR has shown significant differences and associations with the TIMI risk score. The one-way ANOVA showed that the NLR has significantly differed among the three groups of TIMI risk Score



[Table/Fig-3b]: Prognostic probability of PLR.

Outcome parameters	Variables	F Ratio	p-value
MACE	NLR	3.13	0.006
	PLR	1.22	0.297
KILLIP class	NLR	6.341	<0.001
	PLR	4.6	0.004
TIMI Risk Score	NLR	2.168	0.039
	PLR	0.878	0.525

[Table/Fig-4]: One-way ANOVA analysis.

MACE: Major adverse cardiac events; TIMI risk score: Thrombolysis in myocardial infarction

(p-value=0.039). The PLR did not show any significant difference (p-value=0.525) [Table/Fig-4].

DISCUSSION

Even though various studies showed NLR as a good prognostic marker in STEMI, there was lack of evidence of comparison between NLR and established TIMI mortality risk score [16-20]. NLR combines two subtypes of leukocytes, which have opposite effects on inflammation. Therefore, the ratio is more predictive than using any one parameter alone. The aim of this study was to determine the predictive value of NLR and PLR with the in-hospital mortality and MACE in patients with acute STEMI and also to evaluate the association between TIMI risk score with NLR and PLR in patients with STEMI. The results showed that higher NLR was significantly associated with MACE, KILLIP classification and TIMI risk score in STEMI.

A study among patients with ACS found that NLR at admission was an independent predictor of hospitalisation and six month mortality [21,22]. Similar to this study results, other studies also have shown that the NLR is a prognostic marker in patients with CAD [23]. In addition, the maximum NLR can effectively predict the subsequent mortality of STEMI hospitalised patients, and has a high discriminative ability [24].

Platelets have a significant role in production of inflammatory mediators [25]. However, platelets are known to be an important factor in the formation of a thrombus, thus play a key role in the pathogenesis of ACS [26]. The association between low lymphocyte count and MACE has also been shown in several studies [27,28]. Subsequently, PLR has been proposed to be a useful prothrombotic and inflammatory marker [29,30]. It has been reported that higher platelet and lower lymphocyte counts are associated with poor cardiovascular prognosis [31].

The present study found a significant association between Total Leukocyte Count (TLC) and NLR, which was concordant with results of previous study [32,33]. Several studies have found that TLC provides independent predictive value for short-term mortality in patients with acute myocardial infarction [33,34]. This can be explained

by mechanisms such as leukocyte mediated hypercoagulability and indirect cardiotoxicity mediated by proinflammatory cytokines [35,36].

The prognostic significance of different WBC subtypes varies in patients with acute myocardial infarction [37-42]. High neutrophil count was associated with a larger infarction size, worse angiographic outcomes and poor short-term prognosis in patients with acute STEMI [37]. Neutrophils produce certain inflammatory mediators like elastase, myeloperoxidase, and acid phosphatase that cause acute myocardial injury or further tissue damage after STEMI [42]. In addition, lymphopenia is associated with a high risk of adverse consequences and mechanical complications after acute myocardial infarction [28].

In a study, a comparison was made between NLR and complexity of CAD, it was found that complex CAD had a NLR of 2.3, which was higher than others which had NLR of 1.6 [43]. Another study proved that the severity of CAD increased with increasing NLR [44].

There was no statistically significant correlation between the age and NLR which was also manifested in a previous study, whereas in few previous studies, it was observed that patients who had higher NLR were older than those with lower NLR [21,45]. Hence, based on the risk stratification, the association of age with NLR could vary.

A non significant association was seen in patients, between NLR and diabetes mellitus in previous studies which is similar to our results [32,45]. Also, we found no significant association between Hypertension (HTN) and NLR, similar to previous studies [32,45].

A meta-analysis study explored the impact of NLR on clinically important outcomes in ACS. It was found high NLR measured at admission, was associated with a higher mortality rate and with major clinical adverse outcomes. Overall, the risk of in-hospital and long-term mortality increased in patients with higher NLR [46].

Many ACS studies now support the use of NLR as a biomarker of admission, which can be used to determine prognosis [21-23]. NLR can be easily calculated at the time of care, thereby helping STEMI patients with short-term and long-term risk prediction, even before revascularisation occurs. In patients with high NLR, early identification of MACE can be achieved by strict surveillance which can help in making treatment decisions, preventing complications and reducing hospital stay [46].

Limitation(s)

Although NLR, a combined surrogate marker for both acute inflammatory reactions and activated neurohormonal system, might be more potent than these other surrogate markers, there is lack of comparison studies with these markers and NLR. Also, it was a cross-sectional study, not a cohort study. Therefore, the derived cut-off value of the study could not be applied to the general population.

CONCLUSION(S)

NLR is used as a good prognostic indicator for predicting short-term MACE and death in STEMI patients, whereas PLR did not show a positive association with MACE. In addition, NLR showed positive correlation with Killip classification and TIMI risk score, which can predict prognosis in STEMI patients. It is a widely used, easy to calculate, inexpensive, immediately available and effective blood index, hence it can be used as a reliable admission biomarker to determine prognosis in acute STEMI patients.

REFERENCES

- [1] Rosenfeld ME. Inflammation and atherosclerosis: Direct versus indirect mechanisms. *Curr Opin Pharmacol.* 2013;13(2):154-60.
- [2] Recio-Mayoral A, Rimoldi OE, Camici PG, Kaski JC. Inflammation and microvascular dysfunction in cardiac syndrome X patients without conventional risk factors for coronary artery disease. *JACC Cardiovasc Imaging.* 2013;6(6):660-67.
- [3] Yayan J. Emerging families of biomarkers for coronary artery disease: Inflammatory mediators. *Vasc Health Risk Manag.* 2013;9:435-56.
- [4] Soehnlein O. Multiple roles for neutrophils in atherosclerosis. *Circ Res.* 2012;110(6):875-88.
- [5] Wu AHB, Smith A, Christenson RH, Murakami MM, Apple FS. Evaluation of a point-of-care assay for cardiac markers for patients suspected of acute myocardial infarction. *Clin Chim Acta.* 2004;346(2):211-19.

- [6] Reihani H, Sepehri Shamloo A, Keshmiri A. Diagnostic value of D-Dimer in acute myocardial infarction among patients with suspected acute coronary syndrome. *Cardiol Res.* 2018;9(1):17-21.
- [7] Mach F, Schönbeck U, Fabunmi RP, Murphy C, Atkinson E, Bonnefoy JY, et al. T lymphocytes induce endothelial cell matrix metalloproteinase expression by a CD40L-dependent mechanism: Implications for tubule formation. *Am J Pathol.* 1999;154(1):229-38.
- [8] Ghaderi F, Eshraghi A, Shamloo AS, Mousavi S. Association of epicardial and pericardial fat thickness with coronary artery disease. *Electron Physician.* 2016;8(9):2982-89.
- [9] Besli F, Ilter A, Gungoren F. The link between mean platelet volume to lymphocyte ratio and complexity of coronary artery disease. *Angiology.* 2018;69(4):358-59.
- [10] Bressi E, Mangiacapra F, Ricottini E, Cavallari I, Colaioni I, Di Gioia G, et al. Impact of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio on 5-year clinical outcomes of patients with stable coronary artery disease undergoing elective percutaneous coronary intervention. *J Cardiovasc Transl Res.* 2018;11(6):517-23.
- [11] 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.
- [12] Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, et al. Fourth Universal Definition of Myocardial Infarction (2018). *Circulation.* 2018;138(20):e618-51.
- [13] Seaoud E, Mohamed AAHA, Elkot MA. The role of the Platelet/Lymphocyte ratio and Neutrophil/Lymphocyte ratio in predicting high-risk heart score in patients admitted with Non-ST elevation acute coronary syndrome. *Pulse (Basel).* 2020;8(1-2):66-74.
- [14] de Mello BHG, Oliveira GBF, Ramos RF, Lopes BBC, Barros CBS, Carvalho E de O, et al. Validation of the Killip-Kimball classification and late mortality after acute myocardial infarction. *Arq Bras Cardiol.* 2014;103(2):107-17.
- [15] Azab B, Zaher M, Weiserbs KF, Torbey E, Lacossiere K, Gaddam S, et al. Usefulness of neutrophil to lymphocyte ratio in predicting short- and long-term mortality after non-ST-elevation myocardial infarction. *Am J Cardiol.* 2010;106(4):470-76.
- [16] Tavares F, Moraes PIM, Souza JM, Barbosa AH, Santos EM, Marcondes JA, et al. Prognostic role of neutrophil-to-lymphocyte ratio in patients with ST-elevation myocardial infarction undergoing to pharmaco-invasive strategy. *Cardiovascular Revascularisation Medicine [Internet].* 2021 Jan 29 [cited 2021 Jun 5]; Available from: <https://www.sciencedirect.com/science/article/pii/S1553838921000786>.
- [17] Machado GP, Araujo GN de, Maltauro D, Custodio J, Milan V, Wainstein M. Comparação entre a Relação Neutrófilo-Linfócito Precoce e Tardia na Predição de Eventos Adversos em Pacientes com IAMCSST submetidos à ICP Primária. *Arquivos Brasileiros de Cardiologia.* 2021;116(3):504-06.
- [18] Ahmed WMK, Samy E, Radwan WA, Moharrar AN. Association between leukocytes: Absolute and differential ratios with major adverse cardiac cerebrovascular events in st-elevation myocardial infarction patients: Egyptian PCI-capable center experience. *Egyptian Journal of Critical Care Medicine.* 2020;7(2 and 3):86-91.
- [19] Lin G, Dai C, Xu K, Wu M. Predictive value of neutrophil to lymphocyte ratio and red cell distribution width on death for ST segment elevation myocardial infarction. *Scientific Reports.* 2021;11(1):11506.
- [20] Yoon GS, Choi SH, Woo SI, Baek YS, Park SD, Shin SH, et al. Neutrophil-to-Lymphocyte ratio at emergency room predicts mechanical complications of ST-segment elevation myocardial infarction. *J Korean Med Sci.* 2021;36(19):e131.
- [21] Bajari R, Tak S. Predictive prognostic value of neutrophil-lymphocytes ratio in acute coronary syndrome. *Indian Heart J.* 2017;69 Suppl 1:S46-50.
- [22] Tamhane UU, Aneja S, Montgomery D, Rogers EK, Eagle KA, Gurm HS. Association between admission neutrophil to lymphocyte ratio and outcomes in patients with acute coronary syndrome. *Am J Cardiol.* 2008;102(6):653-57.
- [23] Muhammed Suliman MAR, Bahnacy Juma AA, Ali Almadhani AA, Pathare AV, Alkindi SSA, Uwe Werner F. Predictive value of neutrophil to lymphocyte ratio in outcomes of patients with acute coronary syndrome. *Arch Med Res.* 2010;41(8):618-22.
- [24] Núñez J, Núñez E, Bodí V, Sanchis J, Miñana G, Mainar L, et al. Usefulness of the neutrophil to lymphocyte ratio in predicting long-term mortality in ST segment elevation myocardial infarction. *Am J Cardiol.* 2008;101(6):747-52.
- [25] Wagner DD, Burger PC. Platelets in inflammation and thrombosis. *Arterioscler Thromb Vasc Biol.* 2003;23(12):2131-37.
- [26] Eisenberg EHAM, van Werkum JW, van de Wal RMA, Zomer AC, Bouman HJ, Verheugt FWA, et al. The influence of clinical characteristics, laboratory and inflammatory markers on 'high on-treatment platelet reactivity' as measured with different platelet function tests. *Thromb Haemost.* 2009;102(4):719-27.
- [27] Zouridakis EG, Garcia-Moll X, Kaski JC. Usefulness of the blood lymphocyte count in predicting recurrent instability and death in patients with unstable angina pectoris. *Am J Cardiol.* 2000;86(4):449-51.
- [28] Ommen SR, Hammill SC, Gibbons RJ. The relative lymphocyte count predicts death in patients receiving implantable cardioverter defibrillators. *Pacing Clin Electrophysiol.* 2002;25(10):1424-28.
- [29] Smith RA, Ghaneh P, Sutton R, Raraty M, Campbell F, Neoptolemos JP. Prognosis of resected ampullary adenocarcinoma by preoperative serum CA19-9 levels and platelet-lymphocyte ratio. *J Gastrointest Surg.* 2008;12(8):1422-28.
- [30] Wang D, Yang JX, Cao DY, Wan XR, Feng FZ, Huang HF, et al. Preoperative neutrophil-lymphocyte and platelet-lymphocyte ratios as independent predictors of cervical stromal involvement in surgically treated endometrioid adenocarcinoma. *Oncol Targets Ther.* 2013;6:211-16.
- [31] Nikolsky E, Grines CL, Cox DA, Garcia E, Tchong JE, Sadeghi M, et al. Impact of baseline lymphocyte count in patients undergoing primary percutaneous coronary intervention in acute myocardial infarction (from the CADILLAC Trial). *American Journal of Cardiology.* 2007;99(8):1055-61.
- [32] Gazi E, Bayram B, Gazi S, Temiz A, Kirilmaz B, Altun B, et al. Prognostic value of the neutrophil-lymphocyte ratio in patients with st-elevated acute myocardial infarction. *Clin Appl Thromb Hemost.* 2015;21(2):155-59.
- [33] Furman MI, Gore JM, Anderson FA, Budaj A, Goodman SG, Avezum A, et al. Elevated leukocyte count and adverse hospital events in patients with acute coronary syndromes: Findings from the Global Registry of Acute Coronary Events (GRACE). *Am Heart J.* 2004;147(1):42-48.
- [34] Barron HV, Cannon CP, Murphy SA, Braunwald E, Gibson CM. Association between white blood cell count, epicardial blood flow, myocardial perfusion, and clinical outcomes in the setting of acute myocardial infarction: A thrombolysis in myocardial infarction 10 substudy. *Circulation.* 2000;102(19):2329-34.
- [35] Ott I, Neumann FJ, Kenngott S, Gawaz M, Schömig A. Procoagulant inflammatory responses of monocytes after direct balloon angioplasty in acute myocardial infarction. *Am J Cardiol.* 1998;82(8):938-42.
- [36] Lee HY, Kim JH, Kim BO, Kang YJ, Ahn HS, Hwang MW, et al. Effect of aspiration thrombectomy on microvascular dysfunction in ST-segment elevation myocardial infarction with an elevated neutrophil count. *Korean Circ J.* 2011;41(2):68-75.
- [37] Kirtane AJ, Bui A, Murphy SA, Barron HV, Gibson CM. Association of peripheral neutrophilia with adverse angiographic outcomes in ST-elevation myocardial infarction. *Am J Cardiol.* 2004;93(5):532-36.
- [38] Baldus S, Heeschen C, Meinertz T, Zeiger AM, Eiserich JP, Münzel T, et al. Myeloperoxidase serum levels predict risk in patients with acute coronary syndromes. *Circulation.* 2003;108(12):1440-45.
- [39] Ommen SR, Gibbons RJ, Hodge DO, Thomson SP. Usefulness of the lymphocyte concentration as a prognostic marker in coronary artery disease. *Am J Cardiol.* 1997;79(6):812-14.
- [40] Widmer A, Linka AZ, Attenhofer Jost CH, Buergi B, Brunner-La Rocca HP, Salomon F, et al. Mechanical complications after myocardial infarction reliably predicted using C-reactive protein levels and lymphocytopenia. *Cardiology.* 2003;99(1):25-31.
- [41] Blum A, Sclarovsky S, Rehavia E, Shohat B. Levels of T-lymphocyte subpopulations, interleukin-1 beta, and soluble interleukin-2 receptor in acute myocardial infarction. *Am Heart J.* 1994;127(5):1226-30.
- [42] Tousoulis D, Antoniadis C, Koumalos N, Stefanadis C. Pro-inflammatory cytokines in acute coronary syndromes: From bench to bedside. *Cytokine Growth Factor Rev.* 2006;17(4):225-33.
- [43] Sönmez O, Ertaş G, Bacaksız A, Tasal A, Erdoğan E, Asoğlu E, et al. Relation of neutrophil-to-lymphocyte ratio with the presence and complexity of coronary artery disease: An observational study. *Anadolu Kardiyol Derg.* 2013;13(7):662-67.
- [44] Arbel Y, Finkelstein A, Halkin A, Birati EY, Revivo M, Zuzut M, et al. Neutrophil/lymphocyte ratio is related to the severity of coronary artery disease and clinical outcome in patients undergoing angiography. *Atherosclerosis.* 2012;225(2):456-60.
- [45] Soyulu K, Gedikli Ö, Dagasan G, Aydin E, Aksan G, Nar G, et al. Neutrophil-to-lymphocyte ratio predicts coronary artery lesion complexity and mortality after non-ST-segment elevation acute coronary syndrome. *Revista Portuguesa de Cardiologia.* 2015;34(7):465-71.
- [46] Dentali F, Nigro O, Squizzato A, Gianni M, Zuretti F, Grandi AM, et al. Impact of neutrophils to lymphocytes ratio on major clinical outcomes in patients with acute coronary syndromes: A systematic review and meta-analysis of the literature. *International Journal of Cardiology.* 2018;266:31-37.

PARTICULARS OF CONTRIBUTORS:

1. Junior Resident, Department of Internal Medicine, Mahatma Gandhi Medical College and Research Institute, Puducherry, India.
2. Professor, Department of Internal Medicine, Mahatma Gandhi Medical College and Research Institute, Puducherry, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. KS Chenthil,
Professor, Department of Internal Medicine, Mahatma Gandhi Medical College and Research Institute, Piliyarkuppam-607403, Puducherry, India.
E-mail: chenthil21@gmail.com

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

PLAGIARISM CHECKING METHODS: [Jan H et al.]

- Plagiarism X-checker: Mar 04, 2021
- Manual Googling: Jun 10, 2021
- iThenticate Software: Jul 22, 2021 (25%)

ETYMOLOGY: Author Origin

Date of Submission: **Mar 03, 2021**
Date of Peer Review: **Apr 26, 2021**
Date of Acceptance: **Jun 11, 2021**
Date of Publishing: **Aug 01, 2021**