

Association of Neutrophils and Lymphocytes Ratio with Respect to Severity of Coronary Artery Disease

Dr. Pritish Prashant Paricharak¹, Dr. Anil Bhattad^{2*}¹Post Graduate Resident, ²Assistant Professor, Department of Medicine, Krishna Medical College and Research Center, Karad Maharashtra, IndiaDOI: [10.36347/sjams.2022.v10i04.027](https://doi.org/10.36347/sjams.2022.v10i04.027)

| Received: 15.03.2022 | Accepted: 21.04.2022 | Published: 25.04.2022

*Corresponding author: Dr. Anil Bhattad

Assistant Professor, Department of Medicine, Krishna Medical College and Research Center, Karad Maharashtra, India

Abstract

Original Research Article

Background: Cardiovascular diseases caused an estimated 17.3 million deaths in a year. Around 40% of these cardiovascular deaths are due to coronary heart disease. It is projected that coronary heart diseases will remain a leading cause of morbidity and mortality for many years to come. Atherosclerosis, the main underlying pathologic process for coronary heart diseases, is a chronic disease state of the coronary arteries that slowly develops over decades before becoming clinically significant. Its pathophysiology is complex, including inflammatory and immunological events which are considered to be of central importance in the initiation and progression of atherosclerotic plaques. Gradual chronic progression of coronary atherosclerosis may result in luminal narrowing causing symptoms of angina. **Aim:** To study neutrophils to lymphocyte as inflammatory markers in long standing (chronic) coronary artery disease. **Material and methods:** A Cross sectional Observational study was conducted at outpatient department of Medicine in Krishna Hospital and research centre. For a period October 2019- October 2021. Registration of patients was from October 2019. Such 72 cases were studied. They were registered when admitted under Medicine department. At the time of registration, the patients with exclusion criteria were not enrolled for study. The main objective of this study was to study clinical and laboratory parameters of patients with coronary artery disease, to do Coronary angiographic evaluation of cardiac functions. **Results:** Mean Age in Years Was 56.72 ± 5.5 . Majority 77.77% were in age group of 50 to 60 years and 70.83% were males. Patients mainly complained of chest pain 97.22%, followed by breathlessness 86.11%, palpitation 15.27%, retrosternal burning 13.88%, sweating 15.27%, tightness in chest 13.88% and tremors 13.88%. **Conclusion:** Study concluded that there is a strong association between NLR and severity of coronary artery disease. Among Cases having positive family history majority had NLR in range of 2 to 3. Statistical significance was also noted between NLR and family history ($p=0.02$). Smoking and NLR also had statistical significance ($P=0.009$). But no statistical significance was seen between Hb and NLR ($p=0.84$). Positive association was seen between NLR and Hs CRP, CPK MB, troponin and ESR. Patients having impaired CRP levels all had NLR level > 3 i.e more severity of CAD. ($p<0.0001$). Similar findings were seen for troponin and NLR ($p<0.0001$). Patients having raised ESR had raised NLR also. Which shows a direct relation between two.

Keywords: neutrophils and lymphocytes ratio, severity of coronary artery disease.

Copyright © 2022 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY-NC 4.0) which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

INTRODUCTION

Cardiovascular diseases are responsible for 30% of all deaths worldwide and are the number one cause of deaths globally [1, 2].

The inflammatory markers like neutrophil, lymphocyte and Neutrophil to lymphocyte ratio (NLR) have been associated with increased adverse clinical outcomes in ST elevation myocardial infarction (STEMI) [3], non-ST elevation myocardial infarction (N-STEMI) [4]. The role of inflammatory markers in the development and progress of atherosclerosis has been

clarified and several biological markers of inflammation predict cardiovascular risk [5]. Since it is an inflammatory disease, some inflammatory markers have been proposed for the evaluation of the cardiovascular risk. Red cell distribution width (RDW) and neutrophil-to-lymphocyte ratio (NLR) are the two markers of inflammation that are used to determine risk of morbidity and adverse cardiovascular outcomes in patients with acute myocardial infarction (AMI) [6]. Inflammatory markers are also known as classic markers of inflammation in cardiovascular diseases [7]. NLR was taken to be a potential marker to determine

inflammation in cardiac and non-cardiac disorders, and to predict long-term mortality in patients who underwent percutaneous coronary intervention in patients with ST-segment elevation myocardial infarction (STEMI). As these inflammatory marker values are readily available in routine blood count analysis, NLR may be used as a cost-effective predictor of inflammation and cardiovascular complications [8].

The ratio between the absolute number of neutrophils and the number of lymphocytes (NLR) has recently emerged as a potential new biomarker predicting worse clinical conditions ranging from infectious disease to cardiovascular disease. Prognostic significance of NLR in patients with ST-elevation myocardial infarction (STEMI) is not established. This study aimed to investigate prognostic impact of NLR in patients with STEMI.

Aim

To study neutrophils to lymphocyte as a inflammatory markers in long standing (chronic) coronary artery disease.

MATERIAL AND METHODS

A Cross sectional Observational study was conducted at outpatient department of Medicine in Krishna Hospital and research centre. For a period October 2019- October 2021. Registration of patients was from October 2019. Such 72 cases were studied. They were registered when admitted under Medicine department. At the time of registration, the patients with

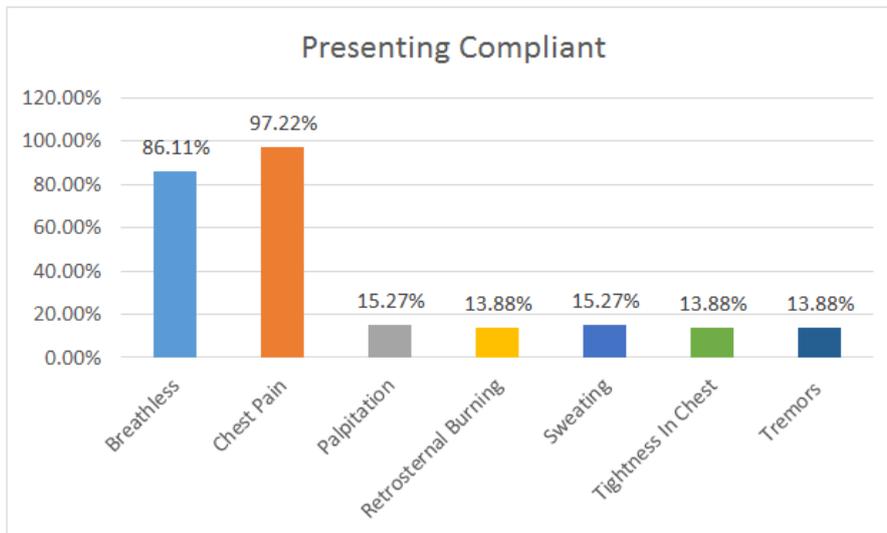
exclusion criteria were not enrolled for study. The main objective of this study was to study clinical and laboratory parameters of patients with coronary artery disease, to do Coronary angiographic evaluation of cardiac functions (LV systolic function, diastolic function and resting RWMA), to assess neutrophils to lymphocytes ratio on admission and to study the levels of neutrophils and lymphocytes to find out its relation with chronic coronary artery disease. At the time of registration, the baseline information was taken especially with respect to sociodemographic factors, clinical findings, and other investigations. The data thus collected was analyzed to study neutrophils to lymphocyte as an inflammatory marker in long standing (chronic) coronary artery disease.

Exclusion criteria

- The presence of any active or recent infections.
- Patients with other haematopathology.
- Patients with severe anaemia.(Hemoglobin <7 g/dl)
- Patients with Cerebrovascular Accident.
- Patients who have refused consent to the study.

RESULTS

Mean Age in Years Was 56.72+5.5. Majority 77.77% were in age group of 50 to 60 years and 70.83% were males. Patients mainly complained of chest pain 97.22%, followed by breathlessness 86.11%, palpitation 15.27%, retrosternal burning 13.88%, sweating 15.27%, tightness in chest 13.88% and tremors 13.88%.



Graph-1: Presenting Compliant seen among the study population

Table-1: Blood parameters among study population

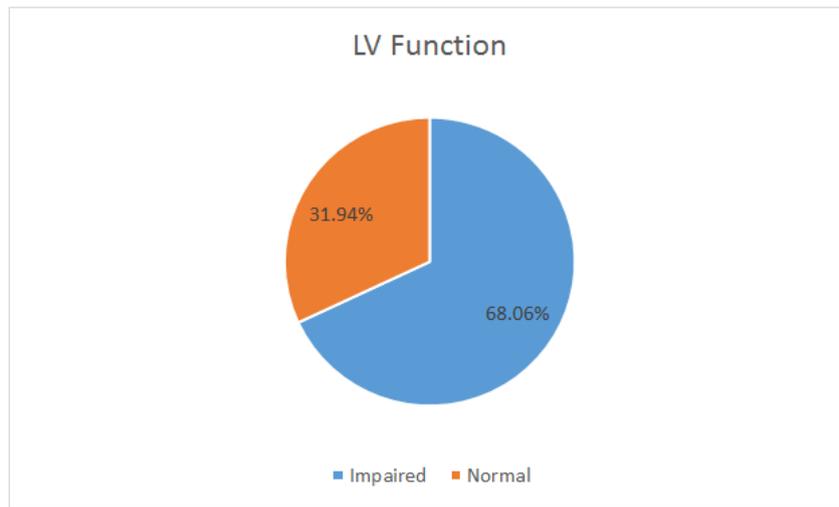
Parameter	Mean	SD
WBC count	9.5	1.67
Neutrophil	61.27	22.6
Lymphocyte	34.63	27.6
Platelet	161.5	3.89
Neutrophil lymphocyte ratio	2.23	0.93

Mean WBC count was 9.5+1.6, neutrophil was 61.27+22.6, lymphocyte was 34.63+27.6, platelet was 161.5+3.89 and NLR was 2.23+0.93.

Table-2: Neutrophil To Lymphocyte Ratio among study population

NLR	Frequency	Percentage
1-2	40	55.56%
2-3	18	25%
>3	14	19.44%
Total	72	100%

It was seen that Majority 55.56% had NLR between 1 to 2, 25% had between 2 to 3 and only 19.44% had >3.



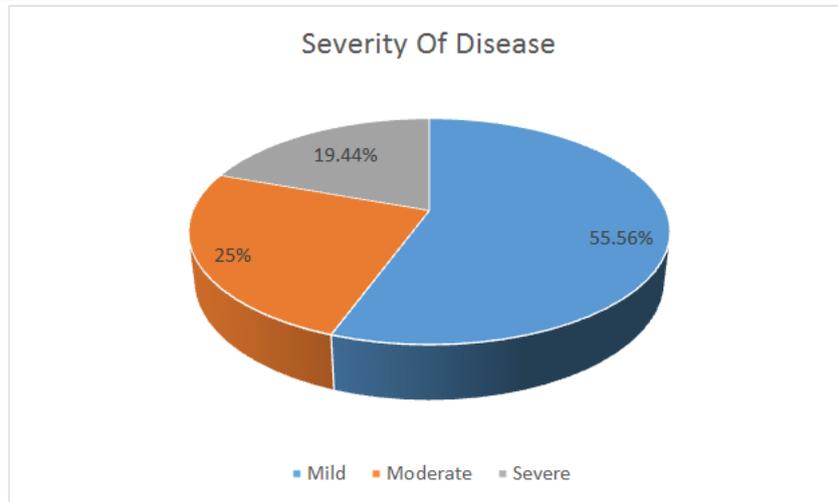
Graph-2: On 2D ECHO, LV Function among study population

In present study, Majority 68.06% cases had impaired LV function.

Table-3: Distribution of study population depending on Ejection Fraction %

EF%	Frequency	Percentage
<40	19	26.38%
40 to 50	25	34.72%
50 to 60	23	31.94%
>60	5	6.94%
Total	72	100%

Present study showed that Mean EF% was 46.65+11.3. Majority 34.72% had EF% in range of 40 to 50, followed by 31.94% in 50 to 60, 26.38% <40 and 6.94% >60%.



Graph-3: Severity of Disease On 2D ECHO among the study population

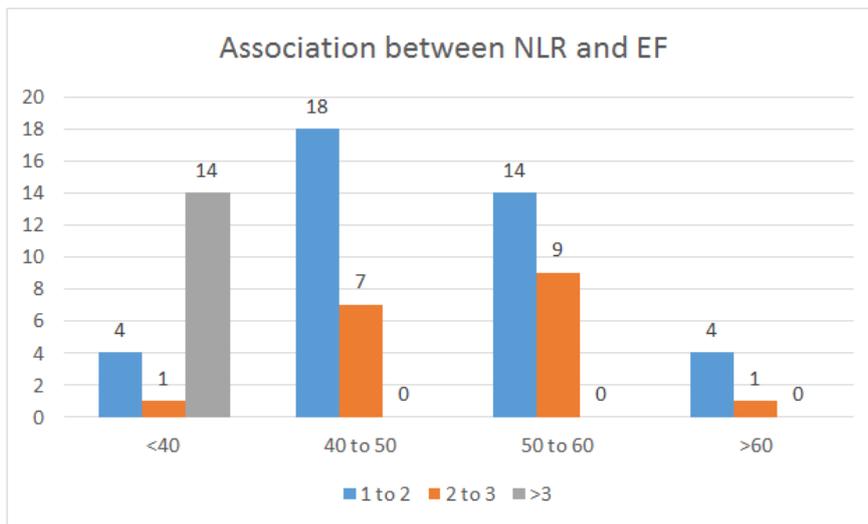
It was seen that, on severity of disease on 2 D ECHO, majority 55.56% had mild disease, 25% had moderate and only 19.44% had severe disease.

Table-4: Association between NLR and LV functioning

NLR / LV func	Impaired	Normal	Total
1-2	19	21	40
2-3	17	01	18
>3	13	01	14
Total	49	23	72

Among 49 cases having impaired LV functioning, 19 had NLR 1-2, 17 had 2-3 and 13 had

ratio >3. Applying chi square test, $p < 0.0001$, as p value is < 0.05 , data shows statistical significance.



Graph-4: Association between NLR and EF

Among 19 cases having EF<40, 4 had NLR 1-2, 1 had 2-3 and 14 had ratio >3. Applying chi square test, $p < 0.0001$, as p value is < 0.05 , data shows statistical significance.

DISCUSSION

Mean Age in Years Was 56.72 ± 5.5 . Majority 77.77% were in age group of 50 to 60 years and 70.83% were males. Pinheiro Machado G *et al.* [9] included 664 patients with a mean age of $60.5 (\pm 12.1)$ years and

66.3% were male. Study by Sari I *et al.* [10] showed that mean age was 60.6±12.6 years, 78% were males.

Patients mainly complained of chest pain 97.22%, followed by breathlessness 86.11%, palpitation 15.27%, retrosternal burning 13.88%, sweating 15.27%, tightness in chest 13.88% and tremors 13.88%.

Mean WBC count was 9.5±1.6, neutrophil was 61.27±22.6, lymphocyte was 34.63±27.6, platelet was 161.5±3.89 and NLR was 2.23±0.93. Park JS *et al.* [11] analyzed the data and found that mean NLR was 4.7±5.2. Study by Sari I *et al.* [10] showed that mean WBC was 9.16±2.93, neutrophils was 6.20±2.85, lymphocyte was 2.03±0.75, platelet was 220.4±48.3, and mean NLR was 3.7±2.6.

It was seen that majority 55.56% had NLR between 1 to 2, 25% had between 2 to 3 and only 19.44% had >3. Study by Misumida N *et al.* [12] showed that of the 396 patients, 244 patients (62%) had NLR ≥2.8.

Mean EF% was 46.65±11.3. Majority 34.72% had EF% in range of 40 to 50, followed by 31.94% in 50 to 60, 26.38% <40 and 6.94% >60%. Study by Kamal Sharma *et al.* [13] showed that mean EF was 5.55±5.04.

It was seen that, on severity of disease on 2 D ECHO, majority 55.56% had mild disease, 25% had moderate and only 19.44% had severe disease. Among 49 cases having impaired LV functioning, 19 had NLR 1-2, 17 had 2-3 and 13 had ratio >3. Applying chi square test, $p < 0.0001$, as p value is < 0.05 , data shows statistical significance. Among 19 cases having EF<40, 4 had NLR 1-2, 1 had 2-3 and 14 had ratio >3. Applying chi square test, $p < 0.0001$, as p value is < 0.05 , data shows statistical significance. Study by Misumida N *et al.* [12] showed that 44 patients (62%) had NLR ≥2.8. Patients with NLR ≥2.8 were older and had a higher prevalence of LM/3VD. Study by Song M *et al.* [14] showed that majority had single vessel disease and had statistical significance with NLR ratio. Similar results were seen in present study.

CONCLUSION

Study concluded that there is a strong association between NLR and severity of coronary artery disease. Among Cases having positive family history majority had NLR in range of 2 to 3. Statistical significance was also noted between NLR and family history ($p=0.02$). Smoking and NLR also had statistical significance ($P=0.009$). But no statistical significance was seen between Hb and NLR ($p0.84$). Positive association was seen between NLR and Hs CRP, CPK

MB, troponin and ESR. Patients having impaired CRP levels all had NLR level > 3 i.e more severity of CAD. ($p<0.0001$). Similar findings were seen for troponin and NLR ($p<0.0001$). Patients having raised ESR had raised NLR also. Which shows a direct relation between two.

REFERENCES

1. Kuklina, E. V., & PhD, M. D. (2006). PaulaW. yoon, scd, MPH and Nora L. Keenan, PhD. *Prevalence of Coronary Heart Disease Risk Factors and Screening for High Cholesterol Levels Among Young Adults*, 8(4), 327-33.
2. Libby. (2002). P, Ridker PM, Maseri A. Inflammation and athero 鄧 sclerosis. *Circulation*, 105(9), 1135.
3. Usefulness of Neutrophil to lymphocyte ratio in predicting long term mortality in ST elevation myocardial infarction Nunen J. *AM J Cardiol* 2008;101:747-52
4. Bekler, A., Erbag, G., Sen, H., Gazi, E., & Ozcan, S. (2015). Predictive value of elevated neutrophil-lymphocyte ratio for left ventricular systolic dysfunction in patients with non ST-elevated acute coronary syndrome. *Pakistan journal of medical sciences*, 31(1), 159.
5. Osadnik, T., Strzelczyk, J., Hawranek, M., Lekston, A., Wasilewski, J., Kurek, A., ... & Poloński, L. (2013). Red cell distribution width is associated with long-term prognosis in patients with stable coronary artery disease. *BMC cardiovascular disorders*, 13(1), 1-8.
6. Horne, B. D., Anderson, J. L., John, J. M., Weaver, A., Bair, T. L., Jensen, K. R., ... & Intermountain Heart Collaborative (IHC) Study Group. (2005). Which white blood cell subtypes predict increased cardiovascular risk?. *Journal of the american college of cardiology*, 45(10), 1638-1643.
7. Arbel, Y., Finkelstein, A., Halkin, A., Birati, E. Y., Revivo, M., Zuzut, M., & Banai, S. (2012). Neutrophil/lymphocyte ratio is related to the severity of coronary artery disease and clinical outcome in patients undergoing angiography. *Atherosclerosis*, 225(2), 456-460.
8. Yilmaz, M., Tenekecioglu, E., Arslan, B., Bekler, A., Ozluk, O. A., Karaagac, K., & Akgumus, A. (2015). White Blood Cell Subtypes and Neutrophil-Lymphocyte Ratio in Prediction of Coronary Thrombus Formation in Non-ST-Segment Elevated Acute Coronary Syndrome. *Clinical and Applied Thrombosis/Hemostasis*, 21(5), 446-452.
9. Pinheiro Machado, G., Araujo, G. N., Carpes, C. K., Lech, M. C., Mariani, S., Valle, F. H., ... & Wainstein, M. V. (2019). Elevated neutrophil-to-

- lymphocyte ratio can predict procedural adverse events in patients with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention. *Coronary Artery Disease*, 30(1), 20-25.
10. Park, J. S., Seo, K. W., Lim, H. S., Choi, B. J., Choi, S. Y., Yoon, M. H., ... & Shin, J. H. (2015). Importance of Prognostic Value of Neutrophil to Lymphocyte Ratio in Patients with ST-elevation Myocardial Infarction. *Journal of the American College of Cardiology*, 65(10S), A143-A143.
 11. Park, J. S., Seo, K. W., Choi, B. J., Choi, S. Y., Yoon, M. H., Hwang, G. S., ... & Shin, J. H. (2018). Importance of prognostic value of neutrophil to lymphocyte ratio in patients with ST-elevation myocardial infarction. *Medicine*, 97(48).
 12. Misumida, N., Kobayashi, A., Saeed, M., Fox, J. T., & Kanei, Y. (2015). Neutrophil-to-lymphocyte ratio as an independent predictor of left main and/or three-vessel disease in patients with non-ST-segment elevation myocardial infarction. *Cardiovascular Revascularization Medicine*, 16(6), 331-335.
 13. Sharma, K., Patel, A. K., Shah, K. H., & Konat, A. (2017). Is neutrophil-to-lymphocyte ratio a predictor of coronary artery disease in Western Indians?. *International Journal of Inflammation*, 2017.
 14. Song, M., Graubard, B. I., Rabkin, C. S., & Engels, E. A. (2021). Neutrophil-to-lymphocyte ratio and mortality in the United States general population. *Scientific Reports*, 11(1), 1-9.