ORIGINAL ARTICLE

Frequency of Poor & Good Coronary Collateral Circulation in patients of Non-ST Segment Elevation MI & to compare mean Platelet –Lymphocyte ratio with good & poor coronary collateral circulation

AHMAD RAZA¹, ASMA SHARIF², MUHAMMAD FAYYAZ ZAFAR³, MUHAMMAD SHAHZAD AZEEM⁴, MUHAMMAD ARSLAN ASLAM⁵ ^{1,34}Senior Registrar, Cardiology Department Mayo Hospital Lahore

^{2,5}Assistant Professor, King Edward medical University Lahore

Correspondence to Dr Asma Sharif Email: drasmaehsan11@gmail.com, Cell: +92 300 4117741: 03004117741

ABSTRACT

Background: Coronary collateral circulation (CCC) is a secondary source of blood supply to an ischemic myocardial area in coronary artery disease. One of the most important protective responses of the cardiac against ischemia is the development of CCC. Recently, platelet to lymphocyte ratio has emerged as a major inflammatory marker & a new predictor of serious unfavorable cardiovascular outcomes.

Aim: To find the frequency of poor & good coronary collateral circulation in patients of Non-ST Segment Elevation Myocardial Infarction & to compare mean platelet–lymphocyte ratio in patients with poor & good coronary collateral circulation of Non-ST Segment Elevation Myocardial Infarction.

Methodology: This cross Sectional study was conducted in Cardiology Department, Mayo Hospital Lahore

After taking informed consent 150 patients meeting inclusion criteria was taken in this study. The patients were enrolled from Department Cardiology, Mayo Hospital Lahore. Their basic demographical information like age, gender and contact detail was obtained. Patients were labeled as according to CCC, one with Poor CCC and second with good CCC [as per operational definition]. All procedure was done by consultant cardiologist having more than 5 years of experience after post-graduation. Venous blood was collected from patients in sterilized manners by experienced staff nurse and was sent to hospital laboratory for analysis of PLR. PLR was compared in cases with good and poor CCC.

Results:1The average age of cases was 52.41 ± 18.12 years with minimum and maximum age of 20 and 80 years. There were 96(64%) male and 54(36%) female cases in this study. A total of 33 (22%) cases had poor and 117(78%) cases had good CCC. The mean Platelet-to-lymphocyte ratio (PLR) was 122.16 \pm 30.10 with minimum and maximum PLR was 80.64 and 201.60. The mean PLR in cases with poor and good CCC was 165.95 \pm 21.93 and 109.81 \pm 18.21 respectively, the mean PLR was highly significant in cases with Poor CCC when compared with good CCC, p-value < 0.0001.

Conclusion: This study concludes that cases with poor CCC have higher PLR when compared to good CCC, so in future cases with higher PLR at admission can be predict for high risk patients for poor CCC. Using PLR (inexpensive and readily available) test we can hence, patients with NSTEMI can be prevented from morbidity & mortality by early and appropriate medications or interventions.

Keywords Cardiology, Angiography, coronary artery disease, Low ejection fraction, coronary collateral circulation.

INTRODUCTION

In developed countries, cardiovascular disease is the leading cause of death. Atherosclerosis is a progressive condition defined by the accumulation of lipids, fibrous materials in the major arteries, or it is the leading cause of cardiac disease¹. Inflammation, that is a key component in the progression & initiation of atherosclerosis, may play a role in the collateralization variability, because inflammation and the development of new blood vessels have a complicated relationship^{2,3}.

The platelet-to-lymphocyte ratio (PLR), which may be derived from a full blood count, is a new measure that combines predictive values of a person's platelet & lymphocyte counts to suggest a systemic inflammatory burden⁴. The ratio of PLR is an independent predictor of death in individuals with non-ST-elevation myocardial infarction (NSTEMI) & ST-elevation myocardial infarction (STEMI)^{5,6}. Coronary collateral circulation is a secondary source of flow of blood to an ischemic myocardial area in coronary artery disease. One of the most important protective responses of the cardiac against ischemia is the development of CCC. Platelet-to-lymphocyte ratio has emerged1recently as a major inflammatory marker & a new predictor of serious unfavorable cardiovascular outcomes. ⁷ The CCC has been shown to predict myocardial survival after total blockage of the coronary arteries³.

Recently a study reported among 386 cases 201(52.07%) had good Coronary collateral circulation and 185(47.93%) cases had poor Coronary collateral circulation. Further they reported that the value of platelet-to-lymphocyte ratio of the patients with poor CCC were highly significant than those patients with good CCC

Received on 24-08-2021 Accepted on 13-01-2022 (152.8 \pm 27.7 vs. 128.8 \pm 23.4, p< *0.00001*). As a result, they came to the conclusion that the high PLR is linked with poor coronary collateral circulation in individuals with ANSTEMI⁸.

We aimed to compare to coronary collateral circulation & platelet–lymphocyte ratio in patients with non-ST segment elevation myocardial infarction. As, there is no local study available and international data is also not widely available on this comparison though a retrospective study reported that poor CCC has higher values of PLR when compared to good CCC, p-value < 0.05.⁹ This study can be helpful in future to screen high risk patients poor CCC on basis of PLR i.e. a practical, inexpensive, and important tool. Hence, patients with NSTEMI can be prevented from morbidity and mortality by early and appropriate medications and interventions.

METHODOLOGY

After permission from Institutional Ethical Review Board, this cross sectional study was conducted at Cardiology Department, Mayo Hospital, Lahore. of 150 patients are estimated using good Coronary collateral circulation in 47.93% patients with NSTEMI9. We used 95% confidence level and 8% level of significance. All patients with 20-80 years of age either gender having NSTEMI, the presence of ischemic (>12 hours), a troponin-I level of greater than 0.01ng/ml & absence of ST segment elevation (of 1mm) on 12.0-lead electrocardiography were included from the study. Angiography of the coronary arteries reveals an 80% stenosis lesion (on angiography), as well as a background of percutaneous coronary intervention or coronary artery bypass grafting, significant hemodynamically ventricular arrhythmias (on Echocardiography) & malignancies related patients were excluded. Their basic demographical information like age, gender and

contact detail was obtained. Patients were labeled as according to CCC, one with Poor CCC and second with good CCC [as per operational definition]. All procedure was done by consultant cardiologist having more than 5 years of experience after post-graduation. Venous blood was collected from patients in sterilized manners by experienced staff nurse and was sent to hospital laboratory for analysis of PLR. PLR was compared in cases with good and poor CCC. All data was collected by researcher himself.

All the data was analyzed with SPSŚ V20. Age and PLR were presented as mean \pm S.D. Gender and good or poor CCC frequencies and percentages was calculated. To compare PLR in poor and good CCC group independent sample t-test was used. Data was stratified for age, gender, smoking (> 5 years), diabetes (BSR > 20 mg/dL), hypertension (BP>160/90), Obesity (BMI>29.9 and \leq 30kg/m2) and duration of NSTEMI to address the effect modifiers. A post-stratification independent sample t-test was used, with a p-value of 0.05 considered significant.

RESULTS

Total 150 patients included. The mean age of cases was 52.41±18.12 years. The mean Platelet-to-lymphocyte ratio (PLR) was 122.16±30.10. The mean PLR in cases with poor and good CCC was 165.95±21.93 and 109.81±18.21 respectively, the mean

PLR was high significant in cases with Poor CCC when compared with good CCC, p-value < 0.001 (Table: 1).

There were 96(64%) male and 54(36%) female. There were 44(29.3%) patients belong to < 40 years of age and 86(57.33%) were > 40 years of age. A total of 33(22%) cases had poor and 117(78%) cases had good CCC (Table 2). Obesity, diabetes, and hypertension was found in 50(%), 46(%) and 46(%) patients respectively. When data was stratified for age, gender, diabetes, hypertension, smoking and duration of NSTEMI, the mean PLR was higher significantly in cases having poor CCC when compared with Good CCC, p-value < 0.001 (Table 3).

Table 1:	Descriptive Statistics
----------	-------------------------------

	Mean±_SD
Age	52.41 <u>+</u> 18.12
Platelets to lymphocyte ratio	122.16 <u>+</u> 30.10
Poor CCC	1651 <u>+</u> 21.93
Good CCC	109.81 <u>+</u> 18.21

Table 2: Frequency of Gender & Coronary Collateral Circulation

			Frequency (%)
Gender		Male	96(64.0%)
		Female	54(36%)
Coronary	Collateral	Poor	33(22.0%)
Circulation		Good	117(78%)

Table 3 Comparison of PLR with Age Gender, Hypertension, Diabetes, Smoking etc...

		Poor CCC	Good CCC	P value
		Frequency(Mean ±SD)	Frequency (Mean±SD)	
Platelets to lymphocyte ratio		33(195.95 <u>+</u> 21.93)	117(109.81+18.21)	0.0001
Age Groups	<40	8(169.60 <u>+</u> 10.29)	36(10.8.44 <u>+</u> 19.87)	0.002
	>40	25(164.79 <u>+</u> 24.59)	81(110.42 <u>+</u> 17.51)	0.001
	Male	28(165.28+22.47)	68(110.21 <u>+</u> 17.83)	0.0003
Gender	Female	5(169.75 <u>+</u> 20.44)	49 (109.25 <u>+</u> 18.89)	0.000
Obesity	Yes	9(176.06 <u>+</u> 10.82)	41(108.72 <u>+</u> 21.20)	0.001
	No	24(162.16 <u>+</u> 23.94)	76 (110.40 <u>+</u> 1 6.49)	0.0001
	Yes	24(163.25 <u>+</u> 23.62)	37(110.96 <u>+</u> 19.15)	0.005
Smoking	No	9(173.15 <u>+</u> 15.47)	80(109.28 <u>+</u> 17.85)	0.009
Diabetes	Yes	8(174.89 <u>+</u> 10.94)	38(110.51 <u>+</u> 20.97)	0.001
	No	25(163.09 +23.90)	79(109.48 <u>+</u> 16.85)	0.00
	Yes	10(164.81 <u>+</u> 19.18)	36 (109.73 <u>+</u> 17.60)	0.001
Hypertension	No	23(166.45+23.45)	81(109.85 <u>+</u> 18.58)	0.002
Duration d	of <4 week	11(170.90+20.80)	52(111.75 <u>+</u> 18.52)	0.0009
NSTEMI	>4 week	22(163.48+ 22.53)	65(108.26+ 17.95)	0.00

DISCUSSION

Inflammation is known to play a key role in the progression & initiation of the complicated atherosclerotic procedure that underlying cardiovascular disease. Inflammation's role in CVD has been researched in the past, and the association between several inflammatory indicators has been established. ¹⁰ Leukocytes & Platelets are crucial components of these procedures linked to atherosclerosis formation¹¹. Increased platelet counts could indicate an increase in the release of inflammatory mediators, an increase in activation of thrombocyte, which produces a damaging inflammatory response, as well as a pro thrombotic state^{12,13}.

Increased platelet activity has been linked to main negative cardiovascular outcomes in previous investigations. A low red blood cells count, on the other hand, has been related to low cardio-vascular outcomes in patients with heart disease. ¹⁴ The platelet-to-lymphocyte ratio is a newer prognostic index that combines these two parameters' risk predictions. Increased values of PLR have emerged as a useful predictor of long-term unfavorable cardiovascular outcomes in some forms of acute coronary disorders, as well as critical limb ischemia in patients with peripheral artery disease^{12,14}.

In coronary heart disease, CCC is a secondary source of blood flow to an ischemic myocardial area. One of the most important defensive answers of the heart towards ischemia is the development of CCC. Presence of good or poor CCC is linked with infarct size, survival & ventricular1functions.¹⁵ Collaterals that are

well-developed decrease the size of ischemic area, decrease the formation of ventricular aneurysms & function. Improvement¹⁶.

In patients with non-ST elevation myocardial infarction, a recent study was conducted to investigate the association between PLR & coronary collateral circulation (NSTEMI). In one study, the complete blood count was used to compute the PLR. The value of PLR patients with poor CCC were significant than those patients with strong CCC.⁷

The PLR has emerged as just a simple & practical inflammatory state measure in a variety of cardiovascular disorders, including NSTEMI. ^{4, 17} Lymphocytes, on the other hand, constitute a calm and controlled immune response that causes less cardiac damage. A low lymphocyte count has been linked to a higher risk of cardiovascular disease and mortality¹⁸.

In current study we found a total of 33 (22%) cases had poor and 117(78%) cases had good CCC. A study reported among 386 cases 201 (52.07%) had good Coronary collateral circulation and 185(47.93%) cases had poor Coronary collateral circulation. ⁹ We found higher rate of good CCC.

Further they reported that the value of platelet-to-lymphocyte ratio of the poor CCC patients were highly significant than that patients with good CCCC (p < 0.001). ⁹ We also found that mean PLR was significantly higher in cases with Poor CCC when compared with good CCC, p-value < 0.001 i.e. mean PLR in cases with poor and good CCC was 165.95±21.93 and 109.81±18.2.

In another study multiple logistic regression tests, PLR & hs-CRP p value was <0.05 found to be an independent factor of poor CCC. According to AROC curve research, the area under the Curve for PLR to predict poor CCC with 79.0 percent sensitivity & 71.0 percent specificity was 0.782. As a result of the study, it was found that a high PLR is associated with coronary collateral circulation in individuals with NSTEMI¹⁹.

Another study looked into the clinical factors linked to the development of CCC in patients with non-ST-elevation myocardial infarction & developed a score model for predicting bad collateralization upon admission, to the hospital. A total of 224 patients with NSTEMI were enrolled in this study, all of whom were hospitalized in CCU. Patients were split into two CCC groups: poor & good²⁰. We only compared their mean levels in this study, therefore more research is needed to prove PLR's diagnostic accuracy in predicting CCC.

CONCLUSION

This study concludes that cases with poor CCC have higher PLR when compared to good CCC, so in future cases with higher PLR at admission can be predict for high risk patients for poor CCC. Using PLR (inexpensive and readily available) test we can hence, patients with NSTEMI can be prevented from morbidity and mortality by early and appropriate medications and interventions. **Conflict of interest:** Nil

REFERENCES

- Ferrucci L, Fabbri E. Inflammageing: chronic inflammation in ageing, cardiovascular disease, and frailty. Nature Reviews Cardiology. 2018;15(9):505-22.
- Demir K, Avci A, Altunkeser BB, Yilmaz A, Keles F, Ersecgin A. The relation between neutrophil-to-lymphocyte ratio and coronary chronic total occlusions. Bmc cardiovascular disorders. 2014;14(1):1-6.
- Açar G, Kalkan ME, Avci A, Alizade E, Tabakci MM, Toprak C, et al. The relation of platelet–lymphocyte ratio and coronary collateral circulation in patients with stable angina pectoris and chronic total occlusion. Clinical and Applied Thrombosis/Hemostasis. 2015;21(5):462-8.
- Balta S, Ozturk C. The platelet-lymphocyte ratio: a simple, inexpensive and rapid prognostic marker for cardiovascular events. Platelets. 2015;26(7):680-1.
- Afari ME, Bhat T. Neutrophil to lymphocyte ratio (NLR) and cardiovascular diseases: an update. Expert review of cardiovascular Therapy. 2016;14(5):573-7.
- Küçük E, Kocayiğit İ, Günel C, Düzenli H. Neutrophil-to-lymphocyte ratio in occlusive vascular diseases: the literature review of the past 10 years. World journal of emergency medicine. 2016;7(3):165.

- Akdag S, Akyol A, Asker M, Ozturk F, Gumrukcuoglu HA. The relation of platelet–lymphocyte ratio and coronary collateral circulation in patients with non-ST segment elevation myocardial infarction. Postępy w Kardiologii Intervencyjnej= Advances in Interventional Cardiology. 2016;12(3):224.
- Delgado GA, Abbott JD. Acute Coronary Syndromes. Evidence-Based Cardiology Consult: Springer; 2014. p. 15-36.
- Akdag S, Akyol A, Asker M, Ozturk F, Gumrukcuoglu HA. The relation of platelet–lymphocyte ratio and coronary collateral circulation in patients with non-ST segment elevation myocardial infarction. Postępy Kardiol Interwencyjnej. 2016;12(3):224-30.
- Dai W, Zhang Ž, Zhao S. Baseline levels of serum high sensitivity C reactive protein and lipids in predicting the residual risk of cardiovascular events in Chinese population with stable coronary artery disease: a prospective cohort study. Lipids in health and disease. 2018;17(1):1-8.
- 11. Bronze L. SCUBE 1: a novel biomarker related to platelet activation and atherothrombosis. Rev Port Cardiol. 2018;37(5):383-5.
- Ozcan Cetin EH, Cetin MS, Aras D, Topaloglu S, Temizhan A, Kisacik HL, et al. Platelet to lymphocyte ratio as a prognostic marker of in-hospital and long-term major adverse cardiovascular events in ST-segment elevation myocardial infarction. Angiology. 2016;67(4):336-45.
- Çelik O, Demirci E, Aydın M, Karabag T, Kalçık M. Evaluation of ghrelin levels and endothelial functions in patients with coronary slow flow phenomenon. Interventional Medicine and Applied Science. 2017;9(3):154-9.
- Yüksel M, Yıldız A, Oylumlu M, Akyüz A, Aydın M, Kaya H, et al. The association between platelet/lymphocyte ratio and coronary artery disease severity. Anatolian journal of cardiology. 2016;15(8):640.
- Möbius-Winkler S, Uhlemann M, Adams V, Sandri M, Erbs S, Lenk K, et al. Coronary collateral growth induced by physical exercise: results of the impact of intensive exercise training on coronary collateral circulation in patients with stable coronary artery disease (EXCITE) trial. Circulation. 2016;133(15):1438-48.
- Fagiani E, Christofori G. Angiopoietins in angiogenesis. Cancer letters. 2013;328(1):18-26.
- Azab B, Shah N, Akerman M, McGinn JT. Value of platelet/lymphocyte ratio as a predictor of all-cause mortality after non-ST-elevation myocardial infarction. Journal of thrombosis and thrombolysis. 2012;34(3):326-34.
- Mansiroglu AK, Sincer I, Gunes Y. Assessment of neutrophil and neutrophil/lymphocyte ratio in coronary collateral developed patients with acute coronary syndrome. Revista da Associação Médica Brasileira. 2020;66:954-9.
- Akdag S, Akyol A, Asker M, Ozturk F, Gumrukcuoglu HA. The relation of platelet–lymphocyte ratio and coronary collateral circulation in patients with non-ST segment elevation myocardial infarction. Postepy Kardiol Interwencyjnej. 2016;12(3):224.
- İleri M, Güray Ü, Yetkin E, Gürsoy HT, Bayır PT, Şahin D, et al. A new risk scoring model for prediction of poor coronary collateral circulation in acute non-ST-elevation myocardial infarction. Cardiol J. 2016;23(1):107-13.