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Original Research Article

Prognostic Significance of Hematological Parameters in Assessing Risk of Myocardial Infarction: Comparative Study in Myocardial Infarction Patients and Healthy Controls

Dr. Byna Syam Sundara Rao[1*], Dr. Kavali Samanth Kumar[2], Dr .Vissa Shanthi[1], Dr. Nandam Mohan Rao[1], Dr. Bhavana Grandhi[3], Dr Jyothi Conjeevaram[4]

[1]Professor, Department of Pathology, Narayana Medical College, Nellore (Andhra Pradesh), India
[2]Tutor, Department of Pathology, Narayana Medical College, Nellore (Andhra Pradesh), India
[3]Associate professor, Department of pathology, Narayana Medical College, Nellore (Andhra Pradesh), India
[4]Professor Department of social and preventive medicine, Narayana Medical College, Nellore (Andhra Pradesh), India

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***Corresponding author:** Dr. Byna Syam Sundara Rao

Abstract

Background: Coronary artery disease (CAD) is caused by atherosclerosis and its complications. Total leukocyte count and platelet have different roles in the pathogenesis of ST- segment elevation myocardial infarction (STEMI). ***Aims and Objective:*** To evaluate the prognostic significance of haematological parameters in myocardial infarction patients by comparing with healthy subjects. ***Materials and Methods:*** This prospective study was carried out on 48 cases diagnosed with ST elevation myocardial infarction (STEMI) and 48 normal healthy subjects from June 2018 to July 2019 in department of pathology and cardiology at Narayana Medical College & Hospital. ***Results:*** Of the total, 48 cases, 35 (72.91%) are men, 13(27.09%) are women with myocardial infarction and 48 controls of which 32(66.67%) are men and 16(33.33%) are women. Neutrophil-lymphocyte ratio (NLR) and platelet –lymphocyte ratio (PLR) were found to be significantly higher in STEMI group than the controls ($p<0.005$), 8.669±2.06 vs 2.09±0.45 and 210.05 ± 40.93vs 117.01±29.41. Mean platelet volume (MPV), Platelet distribution width (PDW) are higher in cases when compared to healthy subjects (13.79±3.36 vs 8.48±1.23) and (15.85±0.96 vs 14.71±1.16)**.** ***Conclusion:*** Mean platelet volume (MPV), platelet distribution width (PDW), Neutrophil - lymphocyte ratio (NLR), Platelet-lymphocyte ratio (PLR) are considered to be an independent risk factors for myocardial infarction.

Keywords: Myocardial infarction, Neutrophil - lymphocyte ratio, platelet indices, Platelet-lymphocyte ratio.

INTRODUCTION

Myocardial infarction is an important sign of coronary artery disease which may cause mobility and mortality [1]. Family history, smoking, obesity, hypertension, hyperlipidemia and inactivity have been proposed as risk factors for MI [2]. Neutrophils are the first leukocytes to be found in the damaged myocardial infarction area [3]. Lymphocytes have been shown to modulate the immunologic response at all stages of atherosclerotic process. The association between low lymphocyte count and adverse cardiovascular outcomes is shown in several studies [5]. The circulating white blood cell count is a biomarker with potential utility in cardiovascular risk prediction [4]. The relationship between the Total leukocyte count (TLC) and the risk of symptomatic or fatal coronary heart disease has been found in various observational epidemiological studies [6]. The Neutrophils -Lymphocyte ratio (NLR) is a combination of two independent marker of inflammation which is regarded as simple non specific marker of inflammation [7]. It is regarded as marker for body immune response to offending agents. In previous studies of Coronary artery disease (CAD), neutrophil – Lymphocyte ratio (NLR) emerged as a new inexpensive risk assessment in patients with ST-Segment elevation Myocardial Infarction (STEMI) prior to revascularization [8]. Platelets play a crucial role in the pathogenesis of artherosclesois and thrombosis formation after coronary plaque rupture. Total leukocyte count and platelets have different roles in the pathogenesis of ST- segment evaluation myocardial infarction. Increased Total leukocyte count is associated with high morality in patients with STEMI [9]. MPV is a potentially useful biomarker of platelet activity. Apart from total Leukocyte count, other blood count

parameters such as neutrophil count, High neutrophil - lymphocyte ratio and Platelet to lymphocyte ratio seem to have prognostic value in STEMI [10].

AIM AND OBJECTIVE

To evaluate the prognostic significance of haematological parameters in myocardial infarction patients by comparing with healthy subjects.

MATERIALS & METHODS

STUDY DESIGN

A prospective study was conducted in the department of pathology and cardiology from the period of June 2018 to July 2019 at Narayana Medical College & Hospital in Nellore. Ethical clearance for study was obtained from ethics committee of Tertiary care Hospital. An informed consent was taken from all participants in our study.

Inclusion Criteria

All patients with diagnosis of acute myocardial infarction with symptoms of ischemia and ECG changes are included as cases in our study. Controls included patients who admitted to Tertiary care Hospital for general health check-up and who are Non–diabetic, Non-hypertensive, non smoker without significant symptoms.

Exclusion Criteria

- Patients age < 20 years
- Cases with hepatic or renal impairment
- Where the blood sample either taken had micro-thrombi or a marked coagulant effect
- Patients taking anticoagulants or antiplatelets drugs
- Lymphoproliferative disorders and malignancy
- Patients not giving consent

DATA COLLECTION AND LABORATORY STUDY

Clinical details of patients which included age, sex, symptoms, smoking, diabetes, dyslipidemia, hypertension, relevant past history, family history and treatment history etc are taken from hospital records (Cardiology). An informed consent was taken from all cases and controls. Blood sample was taken within 6hrs of symptoms before administration of any anticoagulant. Blood samples are collected for complete blood count parameters including haemoglobin, total leukocyte count, neutrophils, lymphocyte, platelets, Neutrophil- lymphocyte ratio, Platelet - lymphocyte ratio and platelet volume indices which are measured using a auto analyzer SYSMEX XN 1000. NLR and PLR were calculated from the neutrophil, platelet and lymphocyte counts obtained from hemogram. PLR and NLR were calculated by dividing platelet count by lymphocyte count, the number of neutrophils by the number of lymphocytes respectively. Two levels of internal quality controls were done.

Statistical Analysis

- Data entered into Microsoft Excel and analysed with SPSS version 22.0. Data was tested for normality using Kolmogorov-Smirnov and as they were not normally distributed; Mann Witney U test was administered to see the differences between cases and controls.
- The P-value < 0.005 was considered as significant association between the parameters. Data were expressed as Mean ± Standard Deviation.

RESULTS

Study included 96 cases of which 48 patients were suffering with ST elevation myocardial infarction (STEMI) - Group 1 and 48 healthy subjects – Group 2

Both in controls and cases predominant age group of 51-60 years (Table-1).

Table-1: Age wise distribution between cases and controls

Age in years	No.of cases subjects (48)	%	No.of control Subjects (48)	%
20-30	0	0	00	0
30-40	0	0	06	12.5
40-50	04	8.34	13	27.08
50-60	23	47.91	15	31.26
60-70	17	35.41	14	29.16
>70	04	8.34	00	0

The mean and standard deviation of age distribution in controls is 53.41±9.03 as compared to 60.25±7.56 in cases as shown in (Table-2).

Table-2: **Comparison of risk factors between cases and controls**

Parameter	cases (n=48)	Control (n= 48)
Age (Years) mean±SD	60.25±7.56	53.41±9.03
Male (%)	35(72.91%)	32(66.67%)
Female (%)	13(27.09%)	16(33.33%)
Family history of CAD (%)	17 (35.4%)	4 (8.3%)
Hypertension (%)	36 (75%)	0(0%)
Diabetics (%)	18 (37.5%)	0(0%)
Smoking (%)	32 (66.7%)	0(0%)
Dyslipidemia	11 (22.92%)	0 (0%)

Males are predominantly affected in both cases and controls when compared to females. Regarding risk factors of patients with STEMI and control subjects, family history of coronary artery disease, hypertension, diabetes and smoking and Dyslipidemia are predominant in STEMI subjects than healthy subjects

seen in Table-2. The mean and standard deviation of haemoglobin is slightly lower in patients as compared to control group while slightly increased in total leukocyte count in patients as compared to control (Table-3). There is not much significant changes in RBC count and platelet count between cases and controls subjects.

Table-3: Comparison of Hb, RBC, TLC and platelet count between Group –I and Group –II

Parameter	Cases (n=48) Mean±SD	Control (n= 48) Mean±SD
Hb (gm%)	10.4208 ± 0.672	13.236± 0.317
RBC (M/Cmm)	4.678 ± 1.225	4.82±2.28
TLC (T/Cumm)	13.208 ± 0.45	8.22±0.5
Platelet (Lacs/Cumm)	277 ± 79.32	276± 50.81

Hb – Haemoglobin, RBC – Red blood cells, TLC – Total leukocyte count

There is not much significant changes in MCV, MCH, MCHC between patient and control group (Table-4).

Table-4: Comparison of blood indices between group I and group II

Parameters	Cases (n=48)	Control (n=48)
	Mean ± SD	Mean ± SD
MCV (fi)	83.23±7.43	85.16±8.38
MCH (pg)	27.63±3.63	28.43±4.13
MCHC (gm%)	32.91±1.72	32.93±7.67

MCV – Mean corpuscular volume, MCH – Mean corpuscular Haemoglobin, MCHC – Mean corpuscular Haemoglobin concentration

There is significant increase in neutrophils in patients compared to controls where as lymphocytes shows significant decrease in patients when compared with controls (Table-5).

Table-5: Comparison of differential leucocyte count, NLR and PLR ratio between case and controls

Parameter	Cases (n= 48) Mean±SD	Control (n=48) Mean±SD
Neutrophils (%)	68.60±6.48	45.39±5.20
Lymphocytes (%)	14.12±4.19	34.16±4.53
NLR ratio	8.669±2.06	2.09±0.45
PLR ratio	210.05±40.93	117.01±29.41

NLR – Neutrophil lymphocyte ratio; reference range 1.2 - 4.4 (11)
PLR – Platelet lymphocyte ratio; reference range 75 – 199 (11)

Neutrophil - lymphyocte ratio (NLR) and platelet - lymphocyte ratio (PLR) are slightly higher in patients when compared with controls.

Platelet parameters are presented in Table-6.

Table-6: Comparison of platelet parameters values in patients with STEMI and controls

Platelet Parameter	Cases (mean ± SD)	Control (mean ± SD)	P Value
Platelet count (x10^3L)	289±79.32	276±50.81	0.583
Mean platelet volume (FL)	13.79±3.36	8.48±1.23	< 0.0001
Platelet distribution width (FL)	15.85±0.96	14.71±1.16	< 0.0001

Comparative results showed Mean Platelet Volume is higher in cases compared to controls (13.79±36) vs (8.48±1.23). The PDW was also significantly higher in cases compared to controls (16.85±0.96) vs (14.71±1.16) as shown in (Table-6). Platelet count was not significantly different among groups (P value 0.583) although its value is slightly higher in cases than the control.

DISCUSSION

Acute coronary syndrome is becoming the leading cause of morbidity and mortality in developing countries like India. The spectrum of presentation is from unstable angina to myocardial infarction [12]. Sudden occlusion of the coronary artery by a thrombus leads to myocardial infarction. Myocardial infarction is almost always due to the formation of occlusive thrombus at the site of rupture or erosion of an atheromatous plaque in coronary arteries. Chest pain is the most common symptom of acute myocardial infarction and described as pressure sensation of tightness or squeezing. Clinically a myocardial infarction can be classified into a ST segment elevation MI versus a non ST segment elevation MI based on ECG changes [13]. Electro cardiography may show acute changes with elevations in the ST segment and T wave inversion. The role of inflammation in coronary artery disease has been widely recognised [14]. Elevated leukocyte count play important role in the atherogenesis, vascular injury, the development of an atherosclerotic plaque rupture and thrombosis.

In our study both in controls and cases predominant age group of 50-60 years with predominance of males (47.91%). This finding was correlated with study carried out by Reddy *et al.*, [15]. Risk factors like smoking, hypertension, diabetes and family history of Coronary artery disease and Dyslipidemia are predominantly noted in STEMI subjects than healthy subjects. This finding was correlated with Reddy *et al*., [15].

In the present study the mean total leukocyte count is significantly higher in myocardial infarction group than in control group. Khalid Al-partosis *et al.*, [16] found significantly higher level of total leukocyte count in STEMI group as compared to control group and that is comparable with present study. In the present study, mean haemoglobin significantly lower in STEMI group as compared to control group. Gajera N *et al.*, [17] found significantly lower level of haemoglobin in STEMI groups as compared to control group. In the present study MCV, MCH an MCHC found no statistically significant change in STEMI group as compared to control group. The finding was correlated with study carried out by Gajera *et al*., [17]. In the present study, the mean neutrophil count is significantly higher and lymphocyte count is significantly lower in STEMI group than in control group. Similar findings found in studies carried out by Gajera *et al*., [17] and Chafil *et al*., [18]. Neutrophil to lymphocyte ratio and platelet to lymphocyte ratio are elevated and statistically significant in STEMI patients when compared to normal healthy subjects. This finding was correlated with study carried out by Mehmet Erturk *et al*., [19] (Table-7).

Table-7: Comparison of Platelet lymphocyte ratio and Neutrophil lymphocyte ratio of previous studies

Publisher	Parameter	Cases	P value
Mehmet Erturk *et al*., [19]	Platelet lymphocyte ratio	156.37±78.56	< 0.001
	Neutrophil lymphocyte ratio	6.13± 4.34	< 0.001
Present study	Platelet lymphocyte ratio	210.1±40.9	< 0.0001
	Neutrophil lymphocyte ratio	8.69±2.06	< 0.0001

Activated neutrophils aggravate the inflammatory response through secretion of inflammatory mediators including oxygen free radicals and arachidonic acid metabolites. These neutrophils mediated inflammatory process that occur during STEMI cause tissue damage, plaque disruption, activate coagulation system thrombosis, myocyte necrosis and microvascular plugging [20]. Inflammatory process occurring during course of STEMI is mediated by the complex interaction between neutrophils mediated reactive innate immune response and subsequent lymphocyte mediated adaptive immune response.

Present study examined the relationship between platelet parameters mainly Mean platelet volume, Platelet count, and Platelet distribution width and the occurrence of STEMI. We found mean MPV and mean PDW are higher in patients with STEMI patients than control group, while no statistically significance was detected regarding the platelets between the two groups (Table-8). The results of

present study are comparable with studies carried by Reddy *et al*., [15], Cetin *et al.*, [21] and, except Adel *et al*., [22] study (Table-8). Adel *et al*., [22] study revealed all platelet parameters statistically significant.

Table-8: Comparison of platelet parameters of previous studies

Publisher	Parameter	Cases	Controls	P value
Reddy *et al.*, [15]	Platelet count	273.7	257.1	0.017
	MPV	10.2	8.5	< 0.005
	PDW	17.8	16.3	< 0.001
Cetin *et al*., [21]	Platelet count	278.1	277.1	0.532
	MPV	8.8	8.6	0.003
	PDW	17.2	16.4	< 0.001
Adel *et al.*, [22]	Platelet count	261	252	0.002
	MPV	10.4	10.2	0.041
	PDW	15.3	15.5	0.030
Present study	Platelet count	277	276	0.583
	MPV	13.79	8.48	< 0.0001
	PDW	15.83	14.79	< 0.0001

There were two hypotheses developed in assessing these parameters. In the first hypothesis activated platelets have an increase in size. Second more platelet activation and aggregation will lead to release of younger platelet in circulation from bone marrow. Platelet play a crucial role in the thrombus formation after the rupture of an atherosclerotic plaque in the pathogenesis of myocardial infarction. Larger platelets have higher thrombotic potential and are metabolically and enzymatically active than smaller platelets. These have a greater prothombotic potential as well as increasing levels of procoagulant surface proteins [23]. Platelet function and activity can be best assessed by platelet volume indicators like PDW and MPV rather than platelet count. MPV is the most accurate measurement of the size of platelets and associated with platelet count. PDW directly measures the variability in platelet size and its high values could suggest larger production of larger reticulated platelets. However platelet indices as good prognostic marker with simple, not requiring any expensive technology and can be adopted as routine testing in clinical setup.

CONCLUSION

Most common hematological parameters altered are high total leukocyte count, neutrophil count, lymphocyte count, neutrophil - lymphocyte ratio and Platelet- lymphocyte ratio, mean platelet volume and platelet distribution width. Neutrophil - lymphocyte ratio and Platelet -lymphocyte ratio are cheap and easy to use markers in the diagnosis and assessing prognosis of patients. Platelet indices has the potential to be used as preliminary test to identify high risk patients for myocardial infarction along with other support clinical investigations.

Source of Support: Nil
Conflicts of Interest: Nil

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