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Original Research Article

A comparative study of platelet to lymphocyte ratio as novel biomarker to predict severity and association with prognosis in COVID–19 patients

Bahuddeen M. Mulla, Mumtaz A. Khan, Ravi Krishnegowda, Ramesh Maddimani*, Karthik C., Naazim Javed Khan

Department of Medicine, Bangalore Medical College and Research Institute, Bangalore, Karnataka, India

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***Correspondence:**
Dr. Ramesh Maddimani,
E-mail: rameshmaddimani@gmail.com

ABSTRACT

Background: Influenza-like illness (ILI) and severe acute respiratory infection (SARI) are the important manifestations in day today clinical practice in COVID era. A number of clinical investigations including haematological parameters are used for the risk stratification of the patients. This study was undertaken in order to find the applicability of platelet to lymphocyte ratio in risk stratification.
Methods: A prospective study was undertaken in Victoria hospital and Bowring and Lady Curzon hospitals attached to BMCRI tertiary care hospitals in Bangalore for a period of one and half years. All the patients were subjected for clinical and haematological evaluation and appropriate ratios were calculated. A total of 266 patients were enrolled in the study, out of which 144 were COVID negative and 122 were COVID positive. The data was analyzed using appropriate statistical methods using statistical package for social sciences (SPSS) version 24.
Results: The mean age of the COVID negative patients was 43.37 years and COVID positive patient was 49.08 years. Males outnumbered females. There was statistically significant difference in mean platelet to lymphocyte ratio between the COVID positive and negative cases (226.4 versus 399.38). The area under curve was 0.614 for the platelet to lymphocyte ratio (PLR) in patients with severe and non-severe ILI and SARI cases. Majority of the haematological parameters were significantly different in SARI patients who were COVID positive and negative.
Conclusions: PLR can be used as an indicator for risk stratification in ILI and SARI patients.

Keywords: COVID–19, ILI, SARI, Platelet to lymphocyte ratio, Hematological parameters

INTRODUCTION

COVID–19 infection is declared as pandemic by World Health Organization (WHO) in March 2020. Different waves have resulted in heavy death tolls especially in a country like India. As per WHO estimates of June 2021, the number of confirmed COVID–19 cases surged above 180 492 131 cases with 3 916 771 deaths.[1] This disease has posed a great threat to human health consuming most of the resources of efficient healthcare systems. The published reports have found that, 26–33% of the patients required intensive care and 4–15% died.[2, 3] Even state of the art centres presently suffering from lack of intensive care unit (ICU) beds for critically ill COVID–19 patients.[4]

Early diagnosis and prompt management is the most effective way to improve the curative efficacy which is a challenge for the clinicians. Nasopharyngeal swab for reverse transcriptase-polymerase chain reaction (RT-PCR) and chest computerized tomography (HRCT) are the important tools in determining the progression and prognosis of COVID–19.[5]

But their clinical application is limited by many factors including time consumption, restricted medical resources

and high examination costs. It is the time find out convenient and cost effective markers which are widely applicable in order to evaluate the clinical severity.

Haematological markers including neutrophils, lymphocytes, monocytes, platelets, neutrophil–to–lymphocyte ratio (NLR), monocyte to lymphocyte ratio (MLR) and platelet to lymphocyte ratios (PLR) have been proposed as indicators in order to assist in the diagnosis, early warning and risk stratification of the infectious diseases.[6,7] MLR and PLR are often used as surrogate markers in diagnosis of influenza virus infection in patients with respiratory tract infection. But the studies are scant in this regard. Hence this study was undertaken in order to examine the usefulness of platelet to lymphocyte ratio in prognosis of patients presenting with influenza like illness and severe acute respiratory tract infection.

METHODS

A prospective study was undertaken in Victoria hospital and Bowring and Lady Curzon hospitals attached to BMCRI tertiary care hospitals in Bangalore from March 2020 to August 2020. All admitted cases with COVID-19 and influenza-like illness (ILI) in Victoria and Bowring and Lady Curzon hospitals were enrolled by universal sampling method due to lack of pilot study. Patients aged above 18 years, fitting into the WHO criteria for influenza like illness, undergoing throat swab/nasopharyngeal swab for RT-PCR for COVID-19 were included in to the study. Asymptomatic COVID-19 patients and presenting with chronic respiratory infections were excluded from the study. A total of 266 patients were enrolled in the study, out of which 144 were COVID negative and 122 were covid positive.

After obtaining ethical clearance and approval from the institutional ethics committee of BMCRI, the data of all cases of influenza like illness admitted in the specified hospitals during the specified period was collected and studied for the clinical and biochemical profiles. The patients were subjected for complete blood count, renal function tests, liver function tests, serum electrolytes and other relevant investigations. The data thus obtained was analyzed using appropriate statistical methods using statistical package for social sciences (SPSS) version 24.

RESULTS

The mean age of the COVID negative patients was 43.37 years and COVID positive patient was 49.08 years. Males outnumbered females in both the groups. There was no statistically significant difference in pulse rate and respiratory rates in both the groups. The oxygen saturation was significantly lower in COVID positive patients when compared to the negative patients (Table 1).

The total white blood cells (WBC) count was significantly lower in COVID positive patients when compared to negative patients. The neutrophil, lymphocyte percentage and platelet count was not significantly different between the COVID positive and negative patients. The PLR was significantly higher in COVID positive patients (Table 2).

The area under curve for the severe disease was 61.3% which was statistically significant (Figure 1). The cut off level of PLR was 176.87 with a sensitivity of 62.7% and specificity of 50.3% (Table 3).

The area under curve for moderate diseased patients using PLR for the categorizing the moderate COVID disease was 53.5% which was statistically not significant (Figure 2 and Table 4).

The haematological parameters have shown that, there was no statistically significant difference in mean total WBC count, neutrophil%, lymphocyte%, platelet count and PLR (Table 5).

There was a statistically significant difference in total WBC count, neutrophil%, lymphocyte% and PLR between the COVID positive and negative SARI patients (Table 6).

Table 1: Distribution of the study groups as per demographic and vital characteristics.

Baseline characteristics	COVID negative (n=144)	COVID positive (n=122)	P value
Age (mean±SD)	43.37±17.18	49.08±17.7	0.008
Male, %	63.2	66.4	0.296
Pulse rate	93.78±13.8	95.15±13.4	0.417
Respiratory rate	20.08±5.1	20.22±6.26	0.843
Oxygen saturation	90.97±10.79	87.74±12.81	0.027

Table 2: Distribution of the study groups according to haematological parameters.

Hematological parameters	COVID negative (n=144)	COVID positive (n=122)	P value
Total count	9408.5±4354.56	7153.6±3054.33	0.000
Neutrophil %	71.95±13.96	72.12±15.42	0.925
Lymphocyte %	19.53±12.0	18.92±11.87	0.674
Platelet count	2.62±1.14	2.67±1.01	0.732
Platelet to lymphocyte ratio	226.4±161.46	399.38±850.2	0.017

Table 3: Area under curve for platelet to lymphocyte ratio for severe diseased patients.

Area	Standard error[a]	Asymptotic sig[b]	Asymptotic 95% confidence interval	
			Lower bound	Upper bound
0.614	0.038	0.003	0.539	0.688

The test result variable (s): platelet to lymphocyte ratio has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased. [a]Under the nonparametric assumption, [b]null hypothesis: true area=0.5

Table 4: Area under curve for platelet to lymphocyte ratio for moderate diseased patients.

Area	Standard error[a]	Asymptotic sig[b]	Asymptotic 95% confidence interval	
			Lower bound	Upper bound
0.535	0.036	0.350	0.463	0.606

The test result variable(s): platelet to lymphocyte ratio has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased. [a]Under the nonparametric assumption, [b]null hypothesis: true area=0.5

Table 5: Hematological parameters of ILI patients in the study groups.

Hematological parameters	COVID negative (n=54)	COVID positive (n=57)	P value
Total count	7929.44±3821.25	6926.49±2569.81	0.106
Neutrophil %	65.63±135.72	62.7±14.41	0.276
Lymphocyte %	25.15±12.03	26.18±11.07	0.64
Platelet count	2.55±1.29	2.6±0.71	0.827
Platelet to lymphocyte ratio	170.18±91.71	348.06±1209.4	0.284

Table 6: Hematological parameters of SARI patients in the study groups.

Hematological parameters	COVID negative (n=90)	COVID positive (n=65)	P value
Total count	10295.89±4432.62	6926.49±2569.81	0.000
Neutrophil %	75.74±12.73	80.38±10.95	0.019
Lymphocyte %	16.17±10.7	12.55±8.44	0.025
Platelet count	2.66±1.05	2.73±1.21	0.716
Platelet to lymphocyte ratio	260.12±183.88	445.75±285.14	0.000

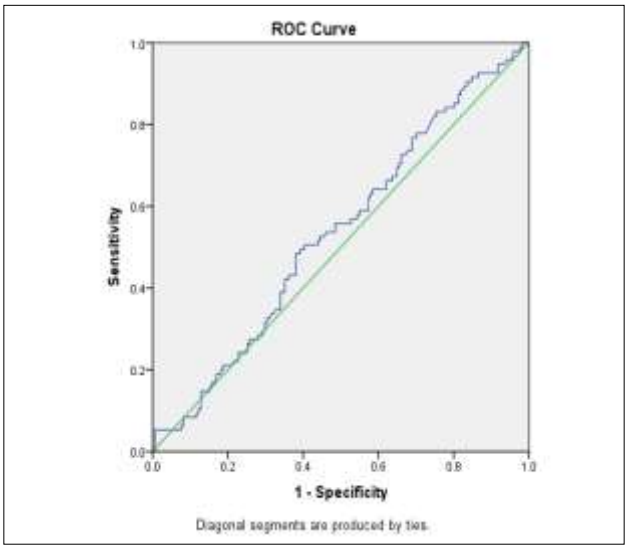

Figure 1: Receiver operator characteristic curve for platelet to lymphocyte ratio for moderate diseased patients.

DISCUSSION

This study was mainly undertaken to study the usefulness of PLR in stratification of clinical severity in COVID positive and negative ILI and SARI patients. Recent literature reports that, hematologic markers have drawn attention as potential indicators to assist in early diagnosis and stratification of severity of the diseases as in other infectious disease including cirrhosis of liver, coronary artery disease and solid tumours. PLR is a cost effective method of predicting COVID-19 severity. PLR has been used as a predictor of inflammation and mortality in various diseases. Patients have demonstrated elevated PLR levels due to involvement of inflammatory process in COVID-19. PLR reflects the degree of cytokine storm which might be useful as a novel sign in monitoring of patients with COVID-19.[8-10] This study has shown that, total WBC count was significantly lower in COVID positive patients and neutrophil, lymphocyte percentage and platelet count was not significantly different between positive and negative patients. The PLR was significantly higher in COVID positive patients. A study by Peng et al had noted that, significant difference in WBC counts,

neutrophil%, lymphocyte%, platelet counts.[11] In a study by Hashem et al, the PLR was significantly higher in admitted to ICU patients when compared to non ICU patients.[4] In a meta–analysis, high PLR was associated with severe COVID-19.[12] The area under curve for the severe disease was 61.3% which was statistically significant. The cut off level of platelet lymphocyte ratio was 176.87 with a sensitivity of 62.7% and specificity of 50.3%. The area under curve for moderate diseased patients using platelet lymphocyte ratio for the categorizing the moderate COVID disease was 53.5% which was statistically not significant. In a study by Hashem et al, the area under curve for PLR was 0.7 between non ICU and admitted to ICU cases.[4] A study by Yang et al have reported AUC of 0.784 with a sensitivity of 77% and sensitivity of 44%.[13] Sun et al have reported a cut off PLR value of 226.67, with AUC of 0.746 with sensitivity of 59.26% and specificity of 80.9%.[14] The haematological parameters have shown that, there was no statistically significant difference in mean total WBC count, neutrophil%, lymphocyte%, platelet count and PLR. There was a statistically significant difference in total WBC count, neutrophil%, lymphocyte% and PLR between the COIVD positive and negative SARI patients. In a study by Peng et al, the lymphocyte, platelet counts and PLR were lower in ARDS group than non ARDS group.[8]

Limitations

Further follow up of COVID ILI patients is required to establish that the platelet to lymphocyte ratio as early indicator to detect SARI cases.

CONCLUSION

This study had shown that, PLR can be used as an indicator of severity in COVID patients. Also, there was a significant difference in PLR of SARI patients where it can be used.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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