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PLATELET TO LYMPHOCYTE RATIO (PLR) IN PREDICTING SEVERITY OF COVID-19 PNEUMONIA

Medicine

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ABSTRACT

The PLR has been used for the past two decades to assess prognosis in acute and systemic inflammatory conditions. Thrombocytopenia and lymphopenia have individually been found to correlate with severity and outcome of COVID-19 pneumonia. PLR can act as a potential marker of deteriorating clinical condition in patient of COVID-19, thereby proving to be an important marker to use, in prospective triaging of patient in resource and time limited settings.

KEYWORDS

INTRODUCTION:

COVID has reached almost all countries in the world, and even through the rate of spread of COVID-19 has slowed down considerably over the past few months, transmission continues and many countries internationally are now facing the threat of another wave of COVID-19 caused by one of the many genetic variants of the virus.1

Platelet-to-lymphocyte ratio (PLR): PLR is the ratio of the platelet to lymphocyte count in the venous blood. Similar to NLR, PLR has also been found to be useful as a prognostic marker in severe inflammatory conditions and physiological stresses such as acute infections, myocardial infarction, systemic inflammatory conditions such as rheumatoid arthritis and giant-cell arteritis. The value of PLR as an inflammatory marker increases when its fluctuations are interpreted along with other complementary haematologic indices, particularly the neutrophil-to-lymphocyte ratio (NLR), which provides additional information about disease activity, presence of neutrophilic 5 inflammation, infectious complications, and severe organ damage in diseases such as systemic lupus erythematosus .2

AIMS AND OBJECTIVE

- To correlate the Platelet-to-Lymphocyte ratios with severity of COVID-19 pneumonia on its presentation
- To use the PLR in low resource settings to prioritise and triage attribution of health care services in view of prognosis based on the PLR.

MATERIAL & METHODS

A cross-sectional study was done from May 2020 to May 2021 on 300 COVID positive patients (100 of mild, moderate and severe category each), with the aim of correlating Platelet o lymphocyte (PLR), with the severity of COVID-19 disease on presentation of participants.

All the patients who came to SSG Hospital with either signs and symptoms suggestive of COVID-19 infection, or those who were asymptomatic for COVID, but radiological evidence of pneumonia were screened, and subsequently enrolled according to the inclusion/exclusion criteria.

Rapid Antigen Test (RAT) was conducted to identify patients with SARS-CoV-2 infection, with those testing positives considered as COVID-19 positive and directly admitted to the COVID Positive Isolation Ward or COVID Intensive Care Unit (as required). Those who tested negative on RAT but were still suspected to be COVID positive based on clinical/radiological findings were ruled out using RT-PCR. RAT negative suspected patients were admitted in COVID Suspect Isolation Ward/ COVID ICU till confirmed reports were obtained. RT-PCR Positive patients were shifted to COVID Positive Isolation Ward/COVID ICU and subsequently approached for participation in the study.

Patients were classified into mild, moderate and severe pneumonia based on the severity of the illness. All medical record information including demographics, symptoms, underlying comorbidities, clinical examination and laboratory data were obtained and recorded. Patients were subjected to detailed investigations comprising of

- Complete blood counts (CBC) (including NLR (Neutrophils to lymphocytes ratio), PLR (Platelets to lymphocytes ratio), Platelet indices)
- Renal Function Tests
- Liver Function Tests (including PT-INR, APTT)
- Chest x-ray PA view or HRCT Thorax
- RBS
- ECG
- Other investigations (as deemed necessary).

A-Drop Score (For assessment of severity of pneumonia)

Criteria	Score 0	Score 1
Age	In Males <70 In Females <75	In Male >70 In Female>75
Dehydration	BUN <21 mg/dl	BUN=>21 mg/dl
Respiratory failure	Spo2>90% on Room Air	Spo2 <or=90% on Room Air
Orientation	Conscious	Confused
Blood Pressure	>90mm hg Systolic pressure	<or=90mm hg Systolic Pressure

Based on A-Drop score

Score	Risk	Preferred treatment modality	Mortality
0-1	Low	Home isolation with frequent monitoring or hospitalization if comorbidities are present or symptoms not resolving even on treatment	<5%
2	Immediate	Hospital Admission	<20%
3-5	High	ICU admission	>40%

Inclusion And Exclusion Criteria

Inclusion Criteria:

Participation in the study was solicited from all the patients who:

- Age 12 years and above
- Diagnosed case of COVID-19 Pneumonia
- Admitted in the COVID isolation ward or the COVID ICU in the hospital.

Exclusion Criteria:
Potential participants were excluded from the study if they met any of the following conditions:
- Hemoglobinopathies;
- Bleeding disorders;
- Viral infections like dengue, chikungunya, acute and chronic hepatitis, HIV;
- Patients who are already on some anti platelet medications like Aspirin, CPG;
- Malignancy;
- Chronic kidney disease;
- Pregnant and postpartum females;
- Unwilling to participate in the study.

RESULT:

Table 1:comparison Of Platelet Indices (plateletcrit, Platelet-larger Cell Ratio, And Mean Platelet Volume) With Severity Of Clinical Manifestation During Admission Of Participants (n = 300)

Platelet indices		Df	F	Sig.
Platelet-large cell ratio	Between Groups	2	0.630	0.533
	Within Groups	297		
	Total	299		
Mean platelet volume	Between Groups	2	0.461	0.631
	Within Groups	297		
	Total	299		
Plateletcrit	Between Groups	2	1.648	0.194
	Within Groups	297		
	Total	299		

Table 2: Categorization Of Participants On The Basis Of Total Neutrophil Count (n = 300)

Particular	n	%
Lymphopenia	206	68.7
Normal Lymphocyte count	90	30.0
Lymphophilia	4	1.3
Total	300	100

Table 3: AUC For Platelet-lymphocyte Ratio (PLR) (n=300)

	Area	Std. Error	95% CL Lower Bound	Upper Bound
Platelet-Lymphocyte Ratio	0.731	0.030	0.672	0.790

The AUC for PLR was found to be 0.731 (95%CI = 0.672 – 0.790).It was found that for PLR, if we consider a cut-off value of 160.37, it is able to differentiate between mild and moderate/severe cases with a sensitivity of 70% and a specificity of 66%. for PLR, if we consider a cut-off value of 160.37, it is able to differentiate between mild and moderate/severe cases with a sensitivity of 70% and a specificity of 66%.

Table 4: AUC For Platelet Indices (Plateletcrit, MPV, PLCR) (n=300)

Test Result Variables	Area	Sig.	Lower Bound	Upper Bound
Plateletcrit	0.506	0.871	0.435	0.576
Mean platelet volume	0.420	0.420	0.403	0.540
Platelet-larger cell ratio	0.299	0.299	0.465	0.609

As can be seen from table 4, the AUC (area under curve) for all three indices, viz. plateletcrit, MPV and PLCR are insignificant, i.e. the p-value for all three AUCs is above 0.05. It is indicative of the poor sensitivity and specificity of platelet indices in correctly differentiating mild from moderate/severe cases of COVID-19.

DISCUSSION

Although in our study, the mean platelet count was not found to be significantly associated with clinical severity of COVID-19, other studies conducted elsewhere have found that an increasing severity is usually associated with decreased platelet count, with thrombocytopenia being a predictor for poor outcome in COVID-19 patients. A study published from China found that out of 178 participants enrolled in their study the group with severe disease had significantly lower platelet count [186.00 (103.50–249.00)×109 /L] than that of the non-severe group [251.00 (202.00–317.00)×109 /L] (p = 0.000) (3) . Another study, also from China, found that with 150,000/mm3 as the reference platelet count, platelet counts of 100,000 – 150,000/mm3 , 50,000 – 100,000/mm3 , and less than 50,000/mm3 groups had a relative risk of 3.42 (95% confidence interval [CI] 2.36-4.96), 9.99 (95% CI 7.16-13.94), and 13.68 (95% CI 9.89-18.92), respectively of not surviving (4). Higher mortality in patients with thrombocytopenia was again seen in yet another study from China, where older age, lower platelet count and longer activated partial thromboplastin time at admission were determined to be risk factors of 28-day mortality, and all three, together with higher white blood cells were risk factors of 180-day mortality. The researchers also observed that patients with thrombocytopenia had significantly higher mortality not only in 28 days, but also in 90 days and 180 days, with Kaplan-Meier analysis indicating that patients with thrombocytopenia had much lower probability of survival (p< 0·1%)(5) . A meta-analysis of 25 studies which reported on platelet counts in a total of 7613 severe and non-severe patients of COVID-19 found that the pooled standardized mean difference (SMD) revealed a lower platelet count in severe patients than non-severe patients (SMD = −0·36, 95% CI −0·48 to − 0·23, I2 = 56·9%). They also found that the pooled SMD revealed a much lower platelet count in non-survivor COVID-19 patients than survivor patients (SMD = −0·60, 95% CI −0·72 to − 0·47, I2 < 0·1%) (135) (6).

Thrombocytopenia which is associated with severe COVID-19 may either be a manifestation of sepsis-induced DIC, or may be due to direct platelet-viral interaction. For thrombocytopenia associated with SARS-CoV – the virus most closely related to COVID-19, multiple possible mechanisms have been mooted, autoantibody or immune complexes mediated clearance, direct infection of hematopoietic stem/progenitor cells and the megakaryocytic lineage via CD13 or CD66a resulting in decreased production of platelets, increased thrombomodulin levels leading to pathologic activation of the coagulation pathway and consumption of platelets, and increased plasma concentrations of tissue-plasminogen activator reflecting increased fibrinolysis (7,8) . However, the exact pathway by which SARS-CoV-2 leads to thrombocytopenia remains unknown. Additional research is therefore warranted to elucidate the causal and pathophysiologic mechanisms of DIC and thrombocytopenia associated with COVID-19 with insight into the innate immune response to this virus (9).

Similarly, lymphopenia has also been found to be associated with higher mortality and more severe outcomes of COVID-19 in many studies. Decreased lymphocyte count was found to be associated with severe outcomes in COVID19 by Huang et al (10), and Li Tan et al (11) . A meta-analysis by Henry et al also found that lymphopenia was associated with higher mortality increased severity during COVID-19 . The inflammatory cytokine storm is likely a key factor behind the observed lymphopenia. The serum level of pro-inflammatory cytokines, such as TNF-α and IL-6, have been closely correlated with lymphopenia . It has also been speculated that the numbers of suppressive immature neutrophils and/or G-MDSCs expanded during severe COVID-19 infection are associated with lymphopenia and disease severity . Recent works that identified the presence of G-MDSCs (HLA-DRneg , Linneg , 67 CD33+ , CD11b+ , CD15+ , CD14neg) by flow cytometry in the peripheral blood of COVID-19 patients provided mechanistic insights by which these cells can impair T cell activity and cause lymphopenia.

In our study, AUC for PLR, being 0.731(95%cl: 0.672-0.790).It was found that cut-off of 160.37 for PLR , we got sensitivity of 70% and specificity of 66%. Given that our findings are based on haematological findings in the participants on admission, PLR can act as a potential marker of deteriorating clinical condition in patients of COVID-19, thereby aiding in prospective triaging of patient.

CONCLUSION

The PLR yielded high AUCs and had a high cut-off point of discerning presence of mild versus moderate/severe disease. This indicates that PLR can to be used as prognostic indicators for identifying patients who would develop moderate or severe disease, thereby helping in triaging of patients for admission in resource-limited settings.

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