Original Article

DOI: 10.7860/NJLM/2021/49397:2545

Pathology Section

Role of Impedance-Based Platelet Parameters and Related Ratios in Screening for Coronavirus Infection- An Institutional Experience

PREETHI A RAI[1], JAYAPARKASH CHANDRASHEKAR[2]

ABSTRACT

Introduction: Impedance based platelet parameters can be easily obtained from most automated haematology analysers. Few of these parameters, especially Platelet Count (PLT), Mean Platelet Volume (MPV) and Plateletcrit (PCT), have been shown to predict disease progression in Coronavirus Disease 2019 (COVID-19). However, data on usefulness of these parameters as predictors of COVID-19 infection, in suspected cases, is limited.

Aim: To evaluate the role of impedance-based platelet parameters, like PLT, MPV, PCT, Platelet-Distribution Width (PDW), and related ratios, as predictors of COVID-19 infection in suspected cases, using real-time Reverse Transcription Polymerase Chain Reaction (rRT-PCR) as standard.

Materials and Methods: Retrospective analytical cross-sectional study was conducted in September 2020, at a teaching hospital located in Mangalore, Karnataka, India. The study parameters were retrieved and/or calculated, from the medical records of 328 patients (from July 2020 to August 2020) who had undergone COVID-19 rRT-PCR testing of their respiratory samples, comprising equal number (n=164) of patients with positive and negative test results, matched for age and sex. The data were compared and analysed. Statistical Package for Social Sciences (SPSS) version 23.0 was used in statistical analysis of this study. The significance level (p-value) was set to 0.05.

Results: Data of total 328 subjects (age range: 18-85 years, 164 COVID positive and 164 COVID negative subjects) was collected and analysed for comparison. Differences in PLT, PCT, and most of the calculated ratios were statistically significant between the two groups; however, Area Under Curve (AUC) for all were <0.7. PCT values were significantly lower in COVID-19 positive group, despite normal PLT (p-value=0.005).

Conclusion: Impedance based platelet parameters have limited role as predictors of COVID-19 infection in suspected patients, despite of their established prognostic value. Decrease in PCT values possibly precedes occurrence of thrombocytopenia following COVID-19 infection.

Keywords: Blood platelet counts, Haematological tests, Mean platelet volume, Predictive value of tests, Sensitivity and specificity, Thrombocytopenia

INTRODUCTION

The PLT is a component of routine haematological investigation, which can be estimated using various cost-effective manual and automated methods. Among automated methods, the one using impedance technology is popularly employed. Along with PLT, most of the automated haematology analysers working on the principle of impedance, also simultaneously derive other related parameters like the MPV, PCT and PDW, collectively referred to as Platelet indices. With regard to COVID-19, various studies have been conducted to determine the characteristics and prognostic implications of PLT and related indices like MPV, in COVID-19 patients [1-4]. Most of these studies have suggested an association of decreased PLT with increased disease severity and mortality in COVID-19 disease, thus serving as a prognostic biomarker [1,2].

This study was primarily conducted to compare, and determine if there are statistically significant differences in, PLT and related impedance based indices and ratios, between patients who were positive and negative for 'Severe Acute Respiratory Syndrome Corona virus 2' (SARS-CoV-2) Ribonucleic Acid (RNA) in respiratory samples, tested by COVID-19 rRT-PCR test. The study variables included MPV, PCT, PDW, Platelet-to-Lymphocyte ratio (PLR), Red Blood Cells-to-PLT ratio (RBC-PLT ratio), ratio of MPV to PCT (MPV/PCT ratio), ratio of PDW to PLT (PDW/PLT ratio), ratio of MPV to PLT (MPV/PLT ratio), ratio of PDW to PCT (PDW/PCT ratio) and ratio of product of MPV and PDW to product of PLT and PCT {(MPVxPDW)/(PLTxPCT) ratio}. The secondary objective of the study was to determine the sensitivity and specificity of the above parameters that had statistically significant differences among the two groups of patients, in predicting the results of the COVID-19 rRT-PCR test.

MATERIALS AND METHODS

This study was a retrospective analytical cross-sectional study conducted at a teaching hospital catering to all clinical specialties, located in Mangalore, Karnataka, India. Patient data that were available from the hospital medical records from July 2020 to August 2020 (two months period), were used for the study. Data analysis was done in September 2020. Ethical clearance was obtained for the study from the Institutional Ethics Committee (Reference number: FMIEC/CCM/446/2020).

Sample size calculation: The minimum sample size needed for the study, as derived by the formula, $n=\{2(Z\alpha+Z\beta)\ p\ (1-p)\}/(p1-p2)^2$, with reference to study by Li Q et al., was 139 per group [5]. The values used in the formula were $Z\alpha=1.96$ at 95% confidence interval; $Z\beta=0.841$ at 80% power; p1=4.3%; p2=14%.

Inclusion criteria: First group (n=164) included all patients above 12 years of age, whose upper respiratory samples were tested and reported positive for SARS-CoV-2 Ribonucleic Acid(RNA) using COVID- 19 rRT-PCR test in the Microbiology Department of the hospital laboratory, and also had haematological analysis of their venous blood sample done as a part of routine investigation, using Coulter™ LH 750 automated haematology analyser (manufactured by Beckman Coulter, Canada L.P., Mississauga), in the Haematology Department of the hospital laboratory, within a span of maximum two days prior or after the day of RT-PCR testing, irrespective of the clinical indication for the testing.

The second group (n=164) enrolled included whose upper respiratory samples were tested and reported negative for SARS-CoV-2 infection using the COVID-19 rRT-PCR test, during the same time-frame, and were age- and sex-matched with the previous group.

Exclusion criteria: Positives cases where haematological data were unavailable and/or where age and sex-matched 'COVID-19 Negative' controls were not available were excluded from the study.

Study Procedure

The institutional standard operating procedures were followed for the sample collection and for conducting the tests. The venous blood samples for haemograms were collected in standard 4 mL Becton Dickinson (BD™) Dipotassium Ethylene Diamine Tetraacetic Acid (K2 EDTA) vacutainer tubes and were run in Complete Blood Count (CBC) mode in the automated haematology analyser within two hours of collection. Values of PLT, Red Blood Cells Count (RBC), MPV, PCT, PDW, Total Leukocyte Count (TLC) and Absolute Lymphocyte Counts (ALC) were noted retrospectively from the computer database of the analyser using the 'unique identification number' of the test sample, from which parameters like PLR, RBC-PLT ratio, MPV/PCT ratio, PDW/PLT ratio, MPV/PLT ratio, PDW/PCT ratio and (MPVxPDW)/(PLTxPCT) ratio were calculated for each subject and the results were compiled and analysed. The haematology laboratory adheres to internal and external quality control checks, participates in the National external quality assurance program, and is accredited by the National Accreditation Board for Testing and Calibration Laboratories (NABL), as per ISO 15189 standards. Reference ranges used were 150×10^9/L to 450×10^9/L for PLT, 7.2-11.7 fL for MPV, 0.22-0.24% for PCT and 10.0%-17.9% for PDW [6,7].

STATISTICAL ANALYSIS

The data analysis was done using International Business Machines (IBM) SPSS Statistics 23.0 software (Statistical Product and Service Solutions, developed by International Business Machines corporation). The numerical variables were expressed as mean, median, standard deviation and Inter-Quartile Range (IQR), and compared between the two study groups using Mann-Whitney U test. Categorical data were compared using Chi-squared test/Fisher's-exact test. Receiver Operating Characteristic (ROC) curve analysis was done for the parameters that showed statistically significant differences between the two study groups, to estimate the AUC, to identify the best threshold for these variables with their sensitivity and specificity, and to evaluate their discriminative ability in predicting the results of the COVID-19 rRT-PCR test. A $p<0.05$ was considered statistically significant, with $p<0.01$ being statistically highly significant.

RESULTS

Over a period of two months during which this study was conducted, a total of 8149 patients were tested for SARS-CoV-2 RNA by rRT-PCR. Out of these, SARS-CoV-2 RNA was detected in 1388 cases, not detected in 6750 cases, and, the result was inconclusive in 10 cases. After application of inclusion and exclusion criteria, statistical analysis was carried out using haematological data collected from A total of 328 subjects (164 COVID-19 positive and COVID-19 negative subjects) were analysed and results were tabulated. The age of the subjects in the study ranged from 18-85 years, with a mean age±standard deviation of 40.7±15.6 years in each group. Each group had 87 females (53%) and 77 males (47%).

[Table/Fig-1] compares the values of PLT, MPV, PCT, PDW, PLR, RBC-Platelet ratios, MPV/PCT ratios, PDW/ PLT ratio, MPV/PLT ratio, PDW/PCT ratio and (MPV×PDW)/(PLT×PCT) ratio between both the groups.

Statistically significant differences were found in values of PLT, PCT, TLC, ALC, RBC-PLT ratio, MPV/PCT ratio, PDW/PLT ratio, MPV/PLT ratio, PDW/PCT ratio and (MPV×PDW)/(PLT×PCT) ratio between the two study groups, with all except MPV/PLT ratio being highly significant (p-value <0.01). No statistically significant

Parameter	Group	N	Mean	SD	Mann-whitney U test p-values	Interquartile Range (IQR)		
						50th Percentile (Median)	25th percentile	75th percentile
Platelet (PLT) (×10⁹/L)	CP	164	239.28	80.93	0.001	228.150	190.025	270.625
	CN	164	266.42	89.69		262.550	204.400	317.475
Plateletcrit (PCT)	CP	164	0.20 %	0.06	<0.001	0.187	0.159	0.228
	CN	164	0.22 %	0.06		0.218	0.174	0.251
Mean Platelet Volume (MPV)	CP	164	8.34fL	1.14	0.753	8.180	7.590	8.858
	CN	164	8.31fL	0.99		8.195	7.710	8.865
Platelet Distribution Width (PDW)	CP	164	16.79 %	0.77	0.103	16.655	16.220	17.200
	CN	164	16.89 %	0.78		16.765	16.393	17.245
Platelet-Lymphocyte ratio	CP	164	200.2	183.74	0.702	115.6025	150.800	215.035
	CN	163	193.1	147.73		110.7900	146.700	207.550
Red Blood Corposcules-Platelet Lymphocyte Ratio (RBC-PLR) ratio	CP	164	21.30	8.39	<0.001	19.200	16.084	25.156
	CN	164	19.28	15.31		16.621	13.771	21.457
Mean Platelet Volume/ Plateletcrit (MPV/PCT) ratio	CP	164	47.00	19.94	0.001	44.041	36.984	52.792
	CN	164	44.53	37.70		38.196	31.575	48.940
Platelet Distribution Width/ Platelet count (PDW/PLT) ratio	CP	164	0.08	0.04	0.002	0.074	0.060	0.089
	CN	164	0.08	0.06		0.064	0.052	0.082
Mean Platelet Volume/ Platelet count ratio	CP	164	0.04	0.02	0.010	0.036	0.028	0.044
	CN	164	0.04	0.03		0.032	0.024	0.041
Platelet Distribution Width/ Plateletcrit (PDW/PCT)	CP	164	94.92	40.72	0.001	89.156	73.858	104.609
	CN	164	89.80	68.69		78.115	65.354	97.866
(Mean Platelet Volume×Platelet Distribution Width)/ (Platelet count×Plateletcrit) [(MPV×PDW)/(PLT X PCT)]	CP	164	4.46	6.94	0.001	3.216	2.228	4.532
	CN	164	3.91	7.00		2.479	1.604	4.032

[Table/Fig-1]: Group-wise Mean, Median, Standard Deviation, Interquartile Range (IQR) And Mann-Whitney p-value of Platelet-related study parameters.
PLT: Platelet count; PCT: Plateletcrit; MPV: Mean platelet volume; PDW: Platelet-distribution width; RBC=RBC count, PLR: Platetet-lymphocyte ratios; CP: COVID-19 positive; CN: COVID-19 negative, N: Number of subjects in the group; SD: Standard deviation, p-values are significant; p<0.05 was considered statistically significant and p<0.01 being statistically highly significant

Parameters		Group				Chi-square/Fisher's-exact test p-values
		COVID-19 Positive		COVID-19 Negative		
		N	%	N	%	
PLT	Within normal range (150-450×10⁹/L)	147	89.6	147	89.6	0.927
	Mild thrombocytopenia (100-149.9×10⁹/L)	11	6.7	10	6.1	
	Moderate thrombocytopenia (50-99.9×10⁹/L)	2	1.2	1	0.6	
	Severe thrombocytopenia (<50×10⁹/L) (lowest value in brackets)	1 (49.1*)	0.6	1 (21.5*)	0.6	
	Thrombocytosis (>450×10⁹/L) (highest value in brackets)	3 (731.6*)	1.8	5 (710.0*)	3.0	
MPV	Within normal range (7.2-11.7 fL)	138	84.1	144	87.8	0.470
	Below normal range (lowest value in brackets)	23 (6.45 fL)	14.0	19 (6.11 fL)	11.6	
	Above normal range (highest value in brackets)	3 (13.57 fL)	1.8	1 (11.71 fL)	0.6	
PCT	Within normal range (0.22-0.24%)	28	17.1	28	17.1	0.005
	Below normal range (lowest value in brackets)	110 (0.043%)	67.1	86 (0.019%)	52.4	
	Above normal range (highest value in brackets)	26 (0.537%)	15.9	50 (0.456%)	30.5	
PDW	Within normal range (10.0%-17.9%)	149	90.9	146	89.0	0.582
	Above normal range (highest value in brackets)	15 (19.64%)	9.1	18 (19.39%)	11.0	
TLC	Within normal range (3.5-11×10⁹/L)	140	85.4	108	65.9	<0.001
	Below normal range (lowest value in brackets)	11 (1.64*)	6.7	0	0.0	
	Above normal range (highest value in brackets)	13 (17.12*)	7.9	56 (40.43*)	34.1	

[Table/Fig-2]: Distribution of normal and abnormal result values among the study groups.
PLT: Platelet count; MPV: Mean platelet volume; PCT: Plateletcrit; PDW: Platelet-distribution width, TLC: Total leucocyte count; N: Number of subjects in the group; %: Percentage of subjects in the group; *(×10⁹/L)

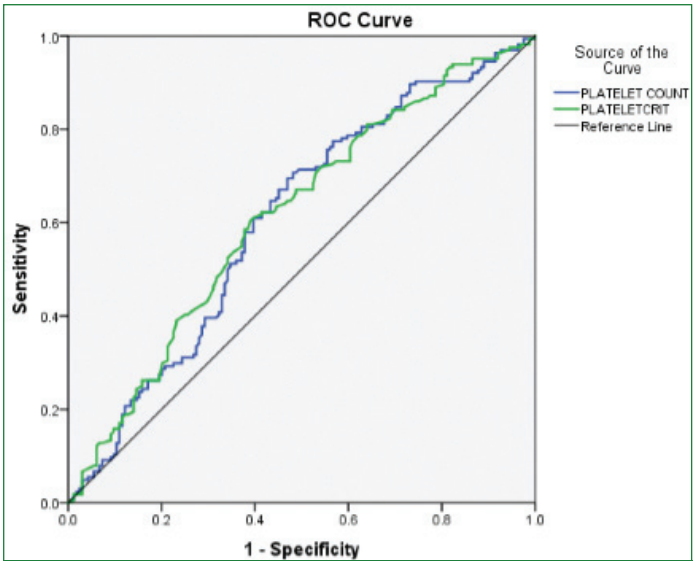
difference was found in the PLR, MPV and PDW values between the two groups. In both the groups, PLT were within normal range in 89.6% of the study population. Distribution of the normal and abnormal result values of PLT, MPV, PCT, PDW, RBC count and TLC in both the study groups were compared [Table/Fig-2]. The proportion of subjects with normal PLT, mild, moderate and severe thrombocytopenia, and thrombocytosis in both the groups were comparable (p-value=0.927).

With regard to the values of MPV and PDW, the proportion of subjects with result values falling within the normal reference range, below the lower limit of normal and above the upper limit of normal respectively were also comparable between the two study groups, with p-values of 0.47 for MPV, and 0.582 for PDW. With regard to PCT, both the groups had equal percentage of subjects having result values within normal reference range (17.1%). However, a relatively higher percentage (67%; n=110) of COVID-19 positive subjects were having result values below the lower limit of normal reference range compared to the COVID-19 negative subjects (52.4%; n=86), and, a relatively higher percentage (30.5%; n=50) of COVID-19 negative subjects were having result values above the upper limit of normal reference range compared to the COVID-19 positive subjects (15.9%; n=26). These differences in distribution of PCT values among both the study groups were found to be statistically highly significant (p-value=0.005). Within each of the study groups, the proportion of subjects with lower than normal PCT levels was not dependent on the proportion of subjects with low PLT levels (thrombocytopenia) (p-value >0.05 for each group). With regard to the TLC, majority of the subjects in both the groups had TLC values within normal reference range; however, a significantly higher percentage of COVID-19 negative subjects (34.1%; n=56) had leucocytosis (TLC>11×10⁹/L), and a significantly higher percentage (6.7%; n=11) of COVID-19 positive subjects had leucopenia (TLC<3.5×10⁹/L), compared to the other group, respectively [Table/Fig-2].

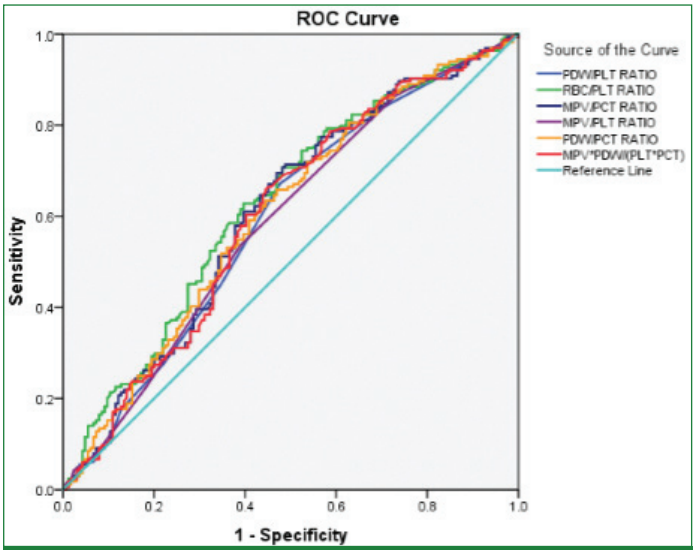
On analysing the platelet related variables further with ROC curve, PLT values of less than or equal to a cut-off value of 2,50,550/cumm had a sensitivity of 64.6% and a specificity of 57.2% for predicting cases positive for SARS-CoV-2 RNA by RT-PCR (AUC=0.61). PCT values of less than or equal to a cut-off value of 0.2% had a sensitivity of 61% and specificity of 62% (AUC=0.62), PDW/PLT ratio values of greater than or equal to a cut-off value of 0.068 had a sensitivity of 60.4% and specificity of 57.3% (AUC=0.597), (MPV×PDW)/(PLT×PCT) ratio values of greater than or equal to a cut-off value of 2.87 had a sensitivity and specificity of 60% (AUC=0.602), RBC-PLT ratio values of greater than or equal to a cut-off value of 16.67 had a sensitivity of 70.7% and specificity of 50.6% (AUC =0.628), MPV/PCT ratio values of greater than or equal to a cut-off value of 38.6 had a sensitivity of 69.5% and specificity of 51.8% (AUC=0.607), MPV/PLT ratio values of greater than or equal to a cut-off value of 0.035 units had a sensitivity of 53.7% and specificity of 61% (AUC=0.588), and PDW/PCT values of greater than or equal to a cut-off value of 78.3 had a sensitivity of 66.5% and specificity of 50.6% (AUC=0.605) for predicting cases positive for SARS-CoV-2 RNA by RT-PCR. The standard error, asymptotic significance (p-value), and asymptotic 95% confidence interval for these parameters are depicted in [Table/Fig-3]. The ROC curves of PLT and PCT values are shown in [Table/Fig-4]. The ROC curves of PDW/PLT ratio, RBC/PLT ratio, MPV/PCT ratio, MPV/PLT ratio, PDW/PCT ratio and MPV*PDW/(PLT*PCT) ratio are shown in [Table/Fig-5]. An AUC values below 0.7 for all these parameters suggests that these tests have a poor discriminative ability in predicting the positivity for SARS-CoV-2 RNA by RT-PCR, individually [8].

Test result variable (s)	AUC	Standard error*	Asymptotic significance† (p-value)	Asymptotic 95% confidence interval	
				Lower bound	Upper bound
Platelet count	0.610	0.032	0.001	0.548	0.672
PCT	0.618	0.031	<0.001	0.557	0.680
PDW/PLT ratio	0.597	0.031	0.002	0.536	0.659
RBC/PLT ratio	0.628	0.031	<0.001	0.567	0.688
MPV/PCT ratio	0.607	0.031	0.001	0.546	0.668
MPV/PLT ratio	0.588	0.031	0.006	0.527	0.650
PDW/PCT ratio	0.605	0.031	0.001	0.544	0.666
MPV*PDW/(PLT*PCT)	0.602	0.031	0.001	0.541	0.664

[Table/Fig-3]: The Area Under the Receiver Operating Characteristic (ROC) curve (AUC) of the platelet-related parameters for predicting cases with positive RT-PCR for COVID-19 infection.
PCT: Plateletcrit; PDW: Platelet-distribution width, MPV: Mean Platelet volume; RBC: RBC count; PLR: Platetet-lymphocyte ratios; PLT: Platelet count; *Under the non parametric assumption; †Null hypothesis: true area: 0.5



[Table/Fig-4]: Receiver Operating Characteristic (ROC) curves of Platelet count (PLT) and Plateletcrit (PCT) for predicting cases with positive RT-PCR for COVID-19 infection.



[Table/Fig-5]: Receiver Operating Characteristic (ROC) curves of the various studied platelet-related ratios for predicting cases with positive RT-PCR for COVID-19 infection. PDW: Platelet-distribution width; PLT: Platelet count; RBC: Red blood cell count; PCT: Plateletcrit; MPV: Mean platelet volume

DISCUSSION

Prior studies have shown prognostic value of PLT, PCT and the ratios of MPV-to-PCT, PDW-to-PLT and MPV-to-PLT, in predicting disease progression and/or mortality in COVID-19 disease [1,9-11]. However, studies on differences of these parameters between the patients with and without COVID-19 infection are limited. In this study, we found that platelet related parameters like PLT, PCT, RBC/PLT ratio, MPV/PCT ratio, PDW/PLT ratio, MPV/PLT ratio, PDW/PCT ratio and (MPVxPDW)/(PLTxPCT) ratio were significantly different for patients who were tested positive for SARS-CoV-2 RNA by rRT-PCR compared to those who were negative for the same. However, none of the parameters had a best cut-off value with a good combination of sensitivity and specificity in predicting positivity for coronavirus infection, precluding their use as good early screening tools for the same.

In general, thrombocytopenia have been reported to be one of the common haematological changes seen in patients with COVID-19, apart from reduced lymphocyte count with normal white blood cell count, prolonged activated partial thromboplastin time and elevated D-dimer levels [12]. However, it is important to realise that many patients with COVID-19 do not present with thrombocytopenia, and PLT level abnormalities are more significant in severe cases where serial follow-up may help predict worsening disease severity and/or mortality.

The present study revealed that majority (89.6%; n=147) of the COVID-19 positive patients present with normal PLT levels, indicating that thrombocytopenia is not a sensitive biomarker of COVID-19 infection per se. In keeping with that, even a study done exclusively on 215 COVID positive patients who were admitted in hospital, observed thrombocytopenia in only 25.1% patients on the hospital admission day and in 24.1% patients on the third follow-up day [10]. In other studies, done on 41, 99 and 1099 patients, thrombocytopenia was observed in 5%, 12% and 36.2% patients on admission, respectively [13-15]. These variations in reported rates of thrombocytopenia in COVID-19 may be attributed to variations in study sample sizes and proportions of patients with severe disease manifestations in the study. Platelet activation and aggregation secondary to the damage to pulmonary endothelial cells have been implicated as cause for increased platelet consumption or thrombogenesis in severe COVID-19 disease. This along with bone marrow suppression and immune mediated destruction of the platelets has been hypothesised to cause thrombocytopenia in severe COVID-19 disease [3,4].

While some studies have reported correlation between decreasing platelet level and increasing disease severity or mortality in COVID-19 disease, few others did not find any such correlation [1,2,10]. The established association of thrombocytopenia with severe or advanced COVID-19 disease suggests that most of the COVID-19 positive patients in the present study had milder disease severity and/or were likely in early course of COVID-19 infection with non severe disease.

Occassionally, even thrombocytosis may be seen in COVID-19 positive patients. In the present study, three (1.8%) patients had PLT above normal reference range, and, Chen N et al., in their study observed the same in four (4%) COVID-19 positive patients on admission [14]. However, as the frequency of thrombocytosis in COVID-19 positive group was not significantly different from the COVID-19 negative group in this study, it is possible that thrombocytosis was just a coincidental finding in these patients, with no direct causal relationship with COVID-19 infection.

The finding in this study of abnormally low PCT values (below the lower-limit of normal reference range) in significantly higher proportion of COVID-19 positive patients compared to the negative group, despite of normal PLT levels in the majority and comparable rates of thrombocytopenia in the two groups, suggests possibility that alterations in PCT becomes evident earlier in the course of COVID-19 disease than thrombocytopenia [Table/Fig-2]. However, as there was no follow-up of these parameters in the study subjects, there is lack of data on what proportion of these subjects, with low PCT and normal PLT levels at the time of presentation, indeed developed thrombocytopenia later on. Hence, the utility of PCT as early predictor of impending thrombocytopenia cannot be conclusively established with the available study findings. Moreover, PCT can vary with variation in MPV, leading to significant overlap of PCT between thrombocytopenic patients and patients with normal PLT values [16]. However, there were no statistically significant differences in MPV values among the two study groups, in this study.

Güçlü E et al., in their study, reported an association of increase in MPV and PDW with increased disease severity and/or mortality rate in COVID-19 patients [10]. PLR has also been reported as a parameter that indicates the severity of the infection some studies [11,17,18]. Yun H et al., in their study comparing 32 patients with COVID-19 and 2337 negative patients, reported significantly higher levels of MPV in COVID-19 positive patients [19]. In contrast, no statistically significant differences were found in the PLR, MPV and PDW values, between the patients with and without COVID-19 infection in this study, with majority of subjects in both the groups having MPV and PDW values within normal reference range [Table/Fig-2]. This suggests a possibility that parameters like PLR, MPV and PDW may be minimally altered in the early course of the COVID-19 infection and/or in non severe version of the disease.

The study findings of significantly higher levels of all the studied platelet related ratios, i.e., PDW/PLT ratio, RBC-PLT ratio, MPV/PCT ratio, MPV/PLT ratio, PDW/PCT ratio and (MPVxPDW)/(PLTxPCT) ratio, in COVID-19 positive subjects compared to the negative group, can be attributed to their inverse relationship with PLT and PCT, as all of these ratios have either PLT, PCT or both as their denominators. However, in the study by Ozcelik N et al., which compared platelet indices in patients with COVID-19 pneumonia and influenza pneumonia, MPV/PLT ratio was reported to be statistically significantly lower in the COVID-19 group [20]. Overall, this study revealed poor performance of these parameters as independent predictors of COVID 19 infection. In a case-control study done on paediatric patients by Golwala ZM et al., MPV/PCT ratio, PDW/PLT ratio and MPV/PLT ratio, in the first sample after hospital admission, were shown to be predictors of in-hospital paediatric mortality and could predict 65% to 67% of deaths accurately [9]. Studies on these ratios in COVID-19 patients are limited in the literature. Whether these parameters are better or early predictors of COVID 19 disease severity/mortality, than the PLT, PCT, PDW or MPV alone, needs further evaluation involving follow-up of patients.

Limitation(s)

The study had few limitations, apart from the small sample size and lack of follow-up of the study parameters in all the subjects. Factors like patient symptomatology, duration of illness, degree of disease severity, type of clinical manifestations at the time of testing and on follow-up, and presence or absence of any other illness/ co-morbidities in the participants of both the study groups, were not considered in the study. Certain co-morbidities that evoke systemic inflammatory response and/or impair immunity, may behave as potential confounding factors, as they may be associated with both alterations in platelet related parameters as well as an increased risk of acquiring the COVID 19 infection.

CONCLUSION(S)

To conclude, though some of the platelet related parameters have been shown to have prognostic values in COVID-19 disease, they have a poor role as predictors of COVID-19 infection in suspected patients. The finding of normal platelet counts in majority of patients who were found positive for SARS-CoV-2 infection, suggests possibility that effects of COVID-19 disease on platelets, in early coarse of infection, is often not significant enough to be reflected as alterations in platelet counts and related ratios. However, abnormally low plateletcrit values may be seen earlier, compared to thrombocytopenia. More complex study designs involving study of serial follow-up data of platelet related parameters in COVID-19 positive subjects may provide insight on the average time period taken for the occurrence of alterations in platelet related lab parameters, following initial detection of SARS-CoV-2 infection, with and without treatment.

REFERENCES

[1] Lippi G, Plebani M, Henry BM. Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A meta-analysis. Clin Chim Acta. 2020;506:145-48. Doi: 10.1016/j.cca.2020.03.022.

[2] Yang X, Yang Q, Wang Y, Wu Y, Xu J, Yu Y, et al. Thrombocytopenia and its association with mortality in patients with COVID-19. J ThrombHaemost. 2020;18(6):1469-72.

[3] Zhang Y, Zeng X, Jiao Y, Li Z, Liu Q, Ye J, et al. Mechanisms involved in the development of thrombocytopenia in patients with COVID-19. Thromb Res. 2020;193:110-15. Doi: 10.1016/j.thromres.2020.06.008.

[4] Fu Y, Cheng Y, Wu Y. Understanding SARS-CoV-2-Mediated Inflammatory Responses: From Mechanisms to Potential Therapeutic Tools. Virol Sin. 2020;35(3):266-71.

[5] Li Q, Ding X, Xia G, Chen HG, Chen F, Geng Z, et al. Eosinopenia and elevated C-reactive protein facilitate triage of COVID-19 patients in fever clinic: A retrospective case-control study. E Clinical Medicine [Internet]. 2020 May 25 [cited 2020 Aug 15];23:100375. Available from: https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(20)30119-X/fulltext. Doi: 10.1016/j.eclinm.2020.100375.

[6] Farias MG, Schunck EG, Dal Bó S, de Castro SM. Definition of reference ranges for the platelet distribution width (PDW): A local need. Clin Chem Lab Med. 2010;48(2):255-57.

[7] Budak YU, Polat M, Huysal K. The use of platelet indices, plateletcrit, mean platelet volume and platelet distribution width in emergency non-traumatic abdominal surgery: A systematic review. Biochem Med (Zagreb). 2016;26(2):178-93.

[8] Šimundić AM. Measures of Diagnostic Accuracy: Basic Definitions. EJIFCC. 2009;19(4):203-11.

[9] Golwala ZM, Shah H, Gupta N, Sreenivas V, Puliyel JM. Mean Platelet Volume (MPV), Platelet Distribution Width (PDW), Platelet Count and Plateletcrit (PCT) as predictors of in-hospital paediatric mortality: A case-control Study. Afr Health Sci. 2016;16(2):356-62.

[10] Güçlü E, Kocayiğit H, Okan HD, Erkorkmaz U, Yürümez Y, Yaylacı S, et al. Effect of COVID-19 on platelet count and its indices. Rev Assoc Med Bras. 2020;66(8):1122-27.

[11] Khartabil TA, Russcher H, van der Ven A, de Rijke YB. A summary of the diagnostic and prognostic value of hemocytometry markers in COVID-19 patients. Crit Rev Clin Lab Sci. 2020;57(6):415-31.

[12] Xu P, Zhou Q, Xu J. Mechanism of thrombocytopenia in COVID-19 patients. Ann Hematol. 2020;99(6):1205-08.

[13] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497-506.

[14] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study. Lancet. 2020;395(10223):507-13.

[15] Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX et al. Clinical characteristics of 2019 novel coronavirus infection in China. N Engl J Med. 2020;382:1708-20.

[16] Chandrashekar V. Plateletcrit as a screening tool for detection of platelet quantitative disorders. Journal of Hematology. 2013;2(1):22-26.

[17] Qu R, Ling Y, Zhang YH, Wei LY, Chen X, Li XM, et al. Platelet-to-lymphocyte ratio is associated with prognosis in patients with coronavirus disease-19. J Med Virol. 2020;92(9):1533-41.

[18] Gong J, Ou J, Qiu X, Jie Y, Chen Y, Yuan L, et al. A Tool for Early Prediction of Severe Coronavirus Disease 2019 (COVID-19): A Multicenter Study Using the Risk Nomogram in Wuhan and Guangdong, China. Clin Infect Dis. 2020;71(15):833-40.

[19] Yun H, Sun Z, Wu J, Tang A, Hu M, Xiang Z. Laboratory data analysis of novel coronavirus (COVID-19) screening in 2510 patients. Clin Chim Acta. 2020;507:94-97. Doi: 10.1016/j.cca.2020.04.018. Epub 2020 Apr 18.

[20] Ozcelik N, Ozyurt S, Yilmaz KB, Gumus A, Sahin U. The value of the platelet count and platelet indices in differentiation of COVID-19 and influenza pneumonia. J Med Virol. 2021;93(4):2221-26.

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Pathology, Father Muller Medical College, Mangalore, Karnataka, India.
2. Professor and Head, Department of Pathology, Father Muller Medical College, Mangalore, Karnataka, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Preethi A Rai,
Assisrtant Professor, Department of Pathology, Father Muller Medical College, Kankanady, Manglore-575002, Karnataka, India.
E-mail: drpreethirai@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Mar 13, 2021
- Manual Googling: Jun 16, 2021
- iThenticate Software: Jul 13, 2020 (18%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? No
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Mar 12, 2021**
Date of Peer Review: **May 17, 2021**
Date of Acceptance: **Jun 25, 2021**
Date of Publishing: **Oct 01, 2021**