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Original research article

STUDY OF PLATELET PARAMETERS IN COVID 19 PATIENTS

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Abstract

Background: Platelets are anucleate blood cells that play a crucial role in maintaining hemostasis and thrombosis. Viruses directly can interact with platelets and modulate their function contributing to platelet activation resulting in consumption or destruction often leading to thrombocytopenia. Thrombocytopenia has been implicated in patients infected with SARS Cov 2, while the dynamic changes of platelets and its association with severity remains unclear.

Methods: The demographics, clinical data and platelet parameters in 140 patients were analyzed and correlated with Disease severity using appropriate statistical analysis.

Results: Among 140 patients, majority were males with mild severity. PDW levels were higher in severe cases when compared to mild and moderate severity cases and found to be statistically significant ($p<0.05$). Platelet count and PCT levels were decreased in severe cases when compared to mild and moderate severity cases and found to be statistically significant ($p<0.05$).

Conclusions: platelet count was an independent risk factor for COVID 19 patients. Role of platelets and their dynamic changes in SARS Cov2 related immunothrombosis is an area of active research and thrombocytopenia is biomarker of poor outcome and increased disease severity.

Keywords: Platelets, platelet indices, SARS Cov2

Introduction

Novel corona virus disease (COVID19) caused by severe acute respiratory syndrome corona virus 2(SARS CoV-2) struck China in December 2019 and spread all over the world posing a threat to global public health and increased clinical burden [1].

Studies have shown that most patients of COVID 19 infection developed mild

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symptoms, however few have developed severe pneumonia, acute respiratory distress syndrome (ARDS) or even death [2, 3].

In severe novel corona virus pneumonia, the number of platelets and their dynamic changes were a concern. Thrombocytopenia has been implicated in patients infected with severe acute respiratory syndrome, while the association of platelet count and changes with subsequent severity remains unclear [2].

Platelets are small, anucleate cell fragments of megakaryocytes. The role of platelets is not only limited to haemostatic process but also modulates host response and virus survival via release of soluble inflammatory mediators, further leading to platelet activation and also contribute to weak adaptive response there by creating an immune response imbalance [4, 5, 6].

Viruses can modulate platelet production at various steps of development. Megakaryopoiesis is triggered by a variety of cytokines released during inflammation (GM CSF, IL 3, IL6 and FGF4) along with thrombopoietin which acts on megakaryocytes development. IL-6 causes increase in ploidy of megakaryocytic nuclei and their by increasing the cytoplasm volume leading to production of large platelets [7].

Platelets display several pattern recognition receptors and serve as first line responders in the defence against pathogens including viruses. Viral infections cause platelet activation through different pathophysiological mechanisms, including direct interaction with pathogen and release of various inflammatory mediators such as IL-3, IL-6. Platelets also release chemokines which in turn promote endothelial signalling and leukocyte tissue migration [8].

Viruses also possess enzymes which can modulate platelet functions (Example-Influenza virus) exhibits neuraminidase (Sialidase) which hydrolyses the terminal sialic acid residues from host cell receptors and thereby decreases the life span of platelets by targeting platelets for rapid clearance in the liver and spleen and further alters megakaryocytic ploidy and size of platelets [9, 10].

Platelet parameters are deranged in laboratory reflecting platelet activation are potential biomarkers in various disorders including critical illness, venous thrombosis and malignancies. There are several ways to monitor platelet activation including platelet activation markers, flow cytometric analysis. However, platelet parameters like MPV, PDW, PCT are simple and they are readily available biomarkers can represent inflammation which is needed for monitoring the disease severity and prognosis of the patient [11, 12].

Materials and Methods

It is cross sectional prospective study with 140 cases conducted at department of pathology, Bangalore medical college and research institute for a period of 6 months (May-October 2020).

Aims & Objective

1. To study the platelet parameters in Covid 19 patients.
2. To correlate the disease severity with platelet parameters.

Inclusion criteria: All CBC samples of covid 19 positive patients.

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Exclusion criteria

- Patients who have declined to participate in the study.
- Patients who lost follow up due to unforeseen causes.
- Pediatric population.

All CBC samples received at central laboratory; Department of pathology was included in the study. EDTA blood samples received was checked for the details of the patient and was processed by Beckman LH 780 analyzer to obtain platelet indices. Platelet indices include Platelet count (PLT), Platelet distribution width (PDW), Mean platelet volume (MPV), Platecrit (PCT) are standard indicators of platelet function. Clinical severity of the patients is graded as mild, moderate and severe based on established criteria. Statistical tools are applied to look for any evidence of association between platelet indices and clinical severity.

Clinical severity: categorized as mild, moderate and severe.

Patient with mild illness may exhibit variety of signs and symptoms (e.g.: fever, cough, sore throat, malaise, headache etc. They do not have shortness of breath, dyspnoea on exertion or abnormal imaging. Moderate illness is defined as evidence of lower respiratory disease during clinical assessment or imaging with Spo2≥94% on room air at sea-level. Respiratory rate <30breaths /min. Patient with covid 19 is considered to have Severe illness, if they have Spo2<94% on room air at sea-level, Pao2/Fio2 <300mmHg and Respiratory rate >30 breaths /min or lung infiltrates >50%.[13]

Statistical analysis

Statistical analysis will be performed by SPSS software version. All data of the demographic and clinical characteristics were analysed by descriptive statistics such as mean, standard deviation and percentage. Tables and graph were added wherever applicable. We used Student t-test and ANOVA to determine significant difference between two or more groups. A P value of < 0.05 was considered statistically significant.

Results

1. Demographic and epidemiological features

Overall, 140 laboratory -confirmed covid 19 patients were enrolled in our study, among which 107(76%) patients were mild, 26 (18.5%) was moderate, and 7(5%) were severe. In our study, 105(75%) were males, 35(25%) were females, Age ranged from 20-91years. Majority of the mild severity cases presented as asymptomatic with myalgia, fever and sore throat, Moderate and severe cases presented as cough, fever and breathlessness. One severe case developed septicemia and acute kidney injury. (Table 1)

Table 1: Demographic details with Disease severity

Variables	Mild	Moderate	Severe	P value
Male	77(72%)	24(92%)	4(57%)	0.05
Female	63(28%)	2(7.7%)	3(42.9%)	0.05

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2. Laboratory findings

Platelet distribution width (PDW-fl) in mild cases was 16.8, moderate cases (17.5) and in severe cases (18.0). PDW levels were higher in severe cases when compared to mild and moderate severity cases and found to be statistically significant (p<0.05).

Plateletcrit (PCT-%) in mild cases was (0.24), moderate cases (0.20) and in severe cases (0.09). PCT levels were decreased in severe cases when compared to mild and moderate severity cases and found to be statistically significant (p<0.05).

Mean platelet volume (MPV-fl) in mild cases was (8.8), moderate cases (9.2) and in severe cases (9.0). MPV levels were increased in moderate and severe cases when compared to mild severity and had no significant difference (p > 0.05).

Table 2: Association of platelet parameters with disease severity

Laboratory Findings	Mild (N-107) Mean ± SD	Moderate (N-26) Mean ± SD	Severe (N-07) Mean ± SD	P-value
MPV	8.85±1.15	9.22±1.52	9.05±0.85	0.36
PCT	0.24±0.08	0.20±0.11	0.09±0.059	0.0001
PDW	16.7±1.72	17.55±1.01	18.0±0.59	0.02

Platelet parameters: MPV (Mean platelet volume), PCT (Plateletcrit), PDW (Platelet distribution width

Discussion

Covid 19 is a novel infectious disease caused by coronavirus (SARS Cov2), produces respiratory and systemic illness which progress to develop ARDS, multiorgan failure followed by intravascular coagulopathy. Majority of the studies revealed a decrease in number of platelets with severe COVID 19, very few studies has investigated the dynamic changes of platelets and its association with severity of patients infected with SARS Cov 2 [14, 15].

The present study was done to document the role of platelet parameters in covid 19 patients and to look for any association between platelet indices and clinical severity in covid 19 patients. We analyzed the demographic, epidemiological, clinical and laboratory characteristics of 140 patients who were hospitalized.

Yanli Liu *et al*. conducted study on 383 patients showed that platelet parameters revealed that patients with thrombocytopenia had lower levels of platelets and PCT and higher levels of MPV than those without thrombocytopenia [16]. A study done by Xiude Fan *et al*. on PDW in patients with Hantaan virus showed that PDW levels were positively correlated with the severity of disease (p<0.05) while PCT and PLT were negatively correlated with severity of HFRS [17].

Platelets play a crucial role in maintenance of hemostasis; besides this they also assist and modulate inflammatory reactions by direct interactions or via release of soluble mediators that trigger platelet activation. Thrombocytopenia is a most common laboratory finding following viral infections and they use various strategies to decrease the level of circulating platelets [4-8].

Dynamic changes of platelets which includes MPV, PDW, PCT are standard indicators of platelet function. MPV represents variation in average size of platelets. PDW is an

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indicator of heterogenicity in platelet size. Increase in MPV and PDW suggests increase in average diameter of the platelets due to destruction or immaturity.[18-20] PCT is a ratio of total platelets in the blood. Decrease in Platelets and PCT indicate that platelets are undergoing destruction or consumed. It is recognized that when platelets undergo destruction, bone marrow responds by producing immature platelets which have larger volume than mature platelets, there by altering the platelet parameters [21].

Mechanism of thrombocytopenia in SARS COV 2 is poorly understood, however there are several explanations. Diffuse alveolar damage by virus would cause platelet activation, aggregation, and thrombi formation at the site of injury resulting in consumption of platelets and megakaryocytes. In addition, SARS Cov2 directly infect hematopoietic precursor cells and inhibit their growth and may induce growth inhibition by binding to CD13 OR CD66a of hematopoietic cells and bone marrow stromal cells, resulting in abnormal hematopoiesis [22, 23].

We analysed whether platelet parameters could predict disease severity. In our study platelet count and PCT reduced as the severity increased and found to be statistically significant. PDW showed increasing trend with disease severity and was statistically significant, whereas MPV showed increasing trend in mild and moderate cases but was not statistically significant. Although platelet count, PCT, PDW correlated well with the severity of the COVID 19 patients.

Platelet parameters are simple, readily available biomarkers. Platelet activation can be seen in various conditions including inflammatory diseases, trauma, malignancy resulting in changes in platelet parameters. Thrombocytopenia is a significant feature in SARS Cov2, analysis of all platelet parameters instead of only platelet count may provide a more accurate and comprehensive information for the disease severity and patient prognosis.

Our study had few limitations. First, Since the study was done in first wave, majority of the cases had mild severity. Second, the study is limited by relatively small number of critical patients (severe). Third the sample size was less and we couldn't follow up the patients.

Conclusion

Current study showed that PDW, PCT may be used as a valuable parameter for assessing the severity in COVID 19 patients. Hence monitoring of platelets during hospitalization may be important in the prognosis of patients with SARS Cov2.

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Conflict of interest: Nil.

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