## Original Research Article

# Study to determine the correlation of platelet-lymphocyte ratio in COVID 19 positive and negative severe acute respiratory infections cases

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## ABSTRACT

**Background:** Severity of COVID 19 disease is related to the systemic inflammatory response triggered by the respiratory virus. Hematological alterations triggered by inflammation can be used as a marker to predict the severity of COVID 19 infection.
**Methods:** 155 patients of severe acute respiratory infections (SARI) defined by World Health Organization (WHO) criteria of which 65 were COVID positive and 90 COVID negative were taken for the study. Demographic profile of the population and platelet count, lymphocyte count and platelet lymphocyte ratio was compared between COVID 19 positive and negative SARI cases using appropriate descriptive statistics. Correlation analysis done for the same parameters between severe and moderate COVID 19 SARI cases.
**Results:** Median platelet count in COVID positive group (2.47 L) was lower than that of COVID negative group (2.65 L) and was not statistically significant between 2 groups. Median lymphocyte count in COVID positive group (651) was lower compared to the negative group (1250) and difference was statistically significant. PLR in COVID positive group was higher (353) than COVID negative group (198) and was statistically significant (p value 0.00). PLR was higher in severe COVID disease compare to moderate disease but difference was not statistically significant. No significant correlation was found in platelet count, lymphocyte count in moderate and severe COVID positive SARI cases.
**Conclusions:** Lower lymphocyte counts was observed in SARI caused by COVID 19 infection than other causes of SARI. No significant correlation was found in platelet count between COVID positive and negative SARI cases. PLR was significantly higher in COVID positive SARI cases as compared to COVID negative SARI cases. Platelet lymphocyte ratio (PLR) was higher in severe COVID disease when compared to moderate disease but levels did not reach statistical significance.

**Keywords:** Platelet-lymphocyte ratio, COVID 19, Severe acute respiratory infections

## INTRODUCTION

The COVID 19 infection which started off in Wuhan, China has spread all across and in March 2020, World Health Organization (WHO) had declared COVID 19 infection as a pandemic. It's been proven that severe systemic inflammation associated with cytokine storm is the key determinant of severe COVID 19 disease.[1]

Evidence of inflammation is shown by raised inflammatory markers such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), serum ferritin and lactate dehydrogenase (LDH) and levels of these markers have correlated with severity of the COVID 19 infection.[2] Platelets, neutrophils and lymphocytes are immune system elements in the blood and these components control the level of inflammation as well as undergo changes

secondary to the inflammatory process.[3] Systemic inflammation bring about changes in the blood composition such as thrombocytosis, neutrophilia, lymphopenia and normochromic anemia.[4] So the components of the circulating blood can be used as markers of systemic inflammation. Absolute lymphocyte count and platelet count are sensitive markers in infections and inflammation and the platelet lymphocyte ratio (PLR) of patients indicates the degree of cytokine storm, which might provide a new indicator in the monitoring of patients with COVID-19.

PLR reflects both aggregation and inflammatory pathways, and may be more valuable in predicting various inflammations than platelet or lymphocyte counts alone.[5]

Recently neutrophil to lymphocyte ratio (NLR) and PLR have been shown to be useful prognostic markers in various inflammatory conditions like rheumatoid arthritis, ankylosing spondylitis, solid tumours and acute respiratory distress syndrome (ARDS).[6-9]

Severe acute respiratory illness (SARI) is an acute respiratory infection with history of fever of more than 38 degrees with onset within last 7 days and requires overnight hospitalization and it can be mild with no evidence of pneumonia or hypoxia, moderate where oxygen saturation is 90-94% and severe where saturation falls below 90%.[10]

This study is done to determine whether platelet to lymphocyte ratio has a clinical value in differentiating SARI caused by SARS-CoV-2 infection and non COVID SARI cases and also to determine PLR variation in severe and moderate COVID 19 disease.

## METHODS

This study is a cross sectional study conducted at Bowring and Lady Curzon hospital attached to Bangalore Medical College and Research Institute, Bangalore from May 2020 till October 2020. The study was approved by the Institutional ethical committee and written informed consent was taken from all patients who were included in the study.

### Inclusion criteria

Patients admitted as a case of COVID positive and negative SARI with age more than 18 years were included in the study.

### Exclusion criteria

Patients not willing to give informed consent, less than 18 years of age, with chronic inflammatory diseases, liver disease, malignancy, undergoing chemotherapy and radiotherapy, and patients with bone marrow pathology were excluded.

65 patients who were confirmed to have COVID 19 infection but real-time reverse transcription–polymerase chain reaction (RTPCR) or rapid antigen test and 90 patients who are negative for COVID 19 but diagnosed as SARI due to non COVID illness.

SARI patients are selected based on WHO case definition and these patients were grouped based on WHO COVID 19 disease severity criteria into severe and moderate disease as mild SARI cases were not admitted to the hospital.[10]

Mild SARI included symptomatic patients meeting the case definition of COVID-19 without evidence of viral pneumonia or hypoxia.

Moderate SARI (pneumonia) included adolescent or adult with clinical signs of pneumonia (fever, cough, fast breathing) but no signs of severe pneumonia, including $SpO_2$ more than or equal to 90% in room air.

Severe SARI included adolescent or adult with clinical signs of pneumonia (fever, cough, dyspnea, fast breathing) plus one of the following respiratory rate >30 breaths/min; severe respiratory distress or $SpO_2$ <90% in room air.

Details of patients were obtained and clinically examined as per the study proforma. Complete hemogram was done for the patients. Lymphocyte count, platelet count and PLR was determined and analysis done between COVID 19 positive SARI and COVID 19 negative SARI groups.

Correlation analysis of lymphocyte count, platelet count and PLR with severity the severity COVID 19 infection was also done.

### Statistical analysis

SPSS (statistical package for social sciences) version 20 (IBM SPASS statistics [IBM corp. released 2011] was used to perform the statistical analysis.

Data was entered in the excel spread sheet. Descriptive statistics of the explanatory and outcome variables were calculated by median and interquartile range (IQR) (based on data distribution- normalcy test-Shapiro Wilk test) for quantitative variables, frequency and proportions for qualitative variables. Inferential statistics like Mann-Whitney test (based on data distribution) was applied to check the statistical difference of platelet count, lymphocyte count and P/L ratio between groups. The level of significance is set at 5%.

## RESULTS

### Demographic characteristics

Sample size of the study was 155 in which 65 patients were COVID positive and 90 were COVID negative. The mean age was 53.9 in COVID positive group and 49.9 in COVID

negative group. There were 37 males and 28 females in COVID positive SARI group and 55 males and 35 females in COVID negative group.

There were 46 severe COVID cases and 19 moderate COVID cases. Among the non-COVID SARI cases 47 were severe and 53 were moderate cases.
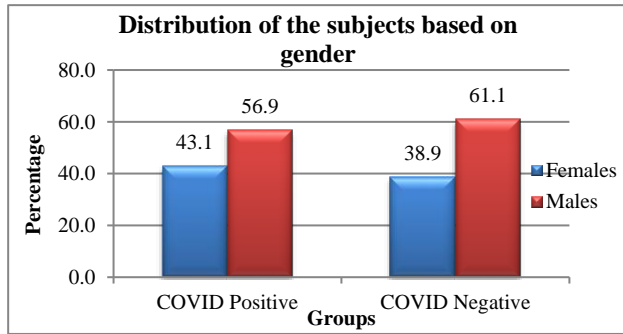


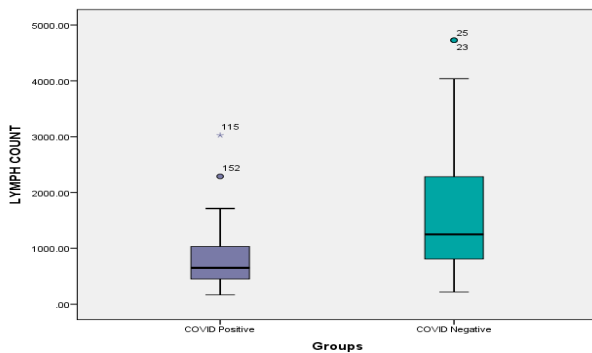**Figure 1: Distribution of the subjects based on gender.**



**Figure 2: The distribution of lymphocyte count between COVID positive and negative cases.**

*Correlation analysis between COVID positive and COVID negative SARI patients*

The median platelet count in SARI COVID positive group was 2.47 L and that of SARI COVID negative group was 2.65 L which was higher .The correlation analysis showed that the difference in platelet count observed was not statistically significant between the groups. The median lymphocyte count in SARI COVID positive group was 651 which was very low compared to that of SARI COVID

negative group that had median lymphocyte count of 1250. The correlation analysis showed that the difference in the lymphocyte count observed was statistically significant between the groups (p value 0.00).

Analysis on PLR showed that the median PLR was higher in COVID positive patients with a value of 356 which was 198 in COVID negative patients and the difference was statistically significant (p value 0.00).

*Correlation analysis between severe and moderate COVID positive SARI cases*

The median platelet count in severe COVID patients was 2.64 L which is lower than that of moderate COVID cases was 2.28 L. The correlation analysis showed that the mean platelet count was not statistically significant between the groups (p value 0.35).

The median lymphocyte count in severe COVID disease was observed to be 587 and that in moderate COVID disease was 703. As expected lymphocyte count which was lower in severe COVID infection than non-severe disease. However, this difference was not statistically significant (p value 0.33).

Analysis on PLR showed that the median PLR was higher in severe COVID disease with a median value of 428 which was 363 in moderate disease but this difference observed was not statistically significant (p value 0.48).
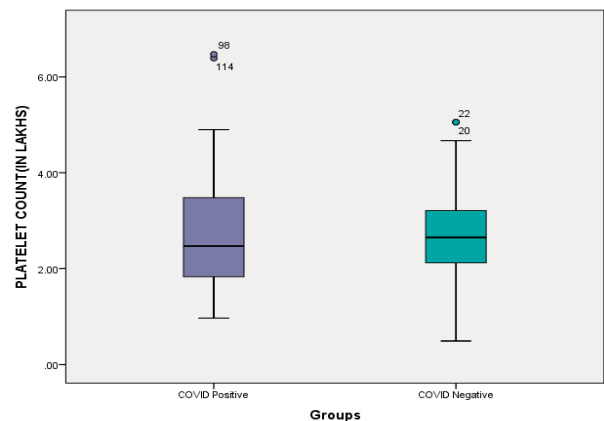


**Figure 3: The distribution of platelet count between COVID positive and negative SARI cases.**

**Table 1: Comparison of the clinical parameters between the groups using Mann-Whitney test.**

| Clinical parameters | Groups | N | Minimum | Maximum | Median | IQR | P value |
|---|---|---|---|---|---|---|---|
| **Platelet count (in lakhs)** | COVID +ve | 90 | 0.97 | 6.47 | 2.47 | 1.67 | 0.63 |
| | COVID -ve | 65 | 0.49 | 5.06 | 2.65 | 1.11 | |
| **Lymphocyte count** | COVID +ve | 90 | 167.54 | 3027 | 651 | 600.7 | 0.00* |
| | COVID -ve | 65 | 218 | 4728 | 1250 | 1524.5 | |
| **P/L ratio** | COVID +ve | 90 | 66.8 | 1383 | 356 | 418.97 | 0.00* |
| | COVID -ve | 65 | 30.8 | 860 | 198.05 | 239.73 | |

**Table 2: Comparison of the clinical parameters based on severity within the groups using Mann-Whitney test.**

| Clinical parameters | Groups | Severity | N | Minimum | Maximum | Median | IQR | P value |
|---|---|---|---|---|---|---|---|---|
| **Platelet count** | COVID +ve | Moderate | 45 | 0.97 | 6.47 | 2.64 | 2.09 | 0.356 |
| | | Severe | 20 | 1.02 | 4.5 | 2.28 | 1.21 | |
| **Lymphocyte count** | COVID +ve | Moderate | 45 | 306 | 3027 | 703.15 | 901 | 0.334 |
| | | Severe | 20 | 167.54 | 2289 | 587.76 | 594 | |
| **P/L ratio** | COVID +ve | Moderate | 45 | 117 | 1383 | 324.25 | 362 | 0.48 |
| | | Severe | 20 | 66.8 | 1348 | 363.5 | 428.42 | |

## DISCUSSION

SARS-CoV-2 causes a severe form of pneumonia evolving towards adult respiratory distress syndrome (ARDS) due to extensive inflammation in the lungs and occasionally associated with multiorgan failure carrying high mortality rates.[11] Severe systemic and pulmonary inflammation contributes to development and progression of ARDS.[12,13]

PLR indirectly reflect a patient's inflammatory state and the degree of cytokine storm, which might provide a new indicator in the monitoring of patients with COVID-19.The advantage of PLR selection is that it reflects both aggregation and inflammatory pathways, and maybe more valuable in predicting various inflammations than platelet or lymphocyte counts alone.[5]

In this study we tried to correlate the platelet count , lymphocyte count and PLR between SARI caused by SARS CoV2 and other causes of SARI at admission and whether these indices varied with the severity of COVID 19 SARI infection.

We found that median platelet count and lymphocyte count was lower in COVID-19 SARI as compared to covid negative SARI patients. Presence of lymphopenia in COVID SARI cases was statistically significant, indicating that COVID-19 disease progressing to moderate or severe SARI were having marked lymphopenia and can be a useful predictor of COVID-19 infection in the setting of a patient with pneumonia.

Although platelet count was lower in COVID SARI cases PLR was higher compared to COVID negative cases. This result points that PLR is would be a better market of inflammation than platelet count alone. It also suggests that in a SARI patient with higher PLR, likely that the patient is infected with SARS CoV2.

Platelet count was higher in moderate COVID 19 illness than severe illness but Lower median lymphocyte count was noted in severe COVID disease compared to non-severe COVID infection. PLR in severe COVID illness was significantly higher than moderate illness. But lower lymphocyte count and a higher PLR in severe COVID SARI was not statistically significant. The reason for it may be that all the COVID positive patients included were SARI cases which means that the moderate illness will also be having a higher degree of inflammation although not as severe as severe cases but obviously more than mild disease or Influenza like illness (ILI). From the results it is likely that a higher the PLR more likely is the patient go for a severe illness as PLR values are indirect marker of underlying severity of infection.

Single-center case series of the 30 hospitalized by Qu et al, patients with confirmed COVID-19 in Huizhou Municipal Central Hospital comparing the correlation between the difference of PLR at the time of admission and the maximum of PLR during treatment, and the length of hospital stay found that the patients' ΔPLR was correlated with the length of hospitalization. If PLR increased more during treatment, the patient had longer hospital stay and a greater possibility of severe pneumonia, suggesting that the number of platelets and their dynamic changes during the treatment may have a suggestion on the severity and prognosis of the disease.[14]

Meta-analysis done by Chan and Rout on NLR and PLR in severe and non-severe COVID 19 illness, they have observed that NLR and PLR was high in severe illness and statistically significant when compared to non-severe disease.[15]

## CONCLUSION

Presence of lymphopenia and higher PLR is a simple cost effective and reliable marker that can give clue to the etiology of SARI. It indicated as to whether a patient is infected with SARS-CoV-2 so that early therapy which has mortality benefit in SARI COVID 19 infection can be started before the RTPCR reports are available.

Platelet count, lymphocyte count or PLR can't be taken as marker of severity once the patients has developed SARI.

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