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A Study of haematological parameters, Neutrophil-Lymphocyte Ratio (NLR) and Platelet-Lymphocyte Ratio (PLR)as biomarkers in COVID-19 cases

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ABSTRACT

Introduction: COVID-19 produces marked inflammatory and immune responses that can influence hematological parameters. Among these, neutrophil–lymphocyte ratio (NLR) and platelet–lymphocyte ratio (PLR) have emerged as accessible and economical indicators for assessing disease severity and prognosis.
Aim: To evaluate the role of hematological parameters, platelet indices, Neutrophil–Lymphocyte Ratio (NLR), and Platelet–Lymphocyte Ratio (PLR) in assessing COVID-19 severity, and to study the impact of comorbidities such as diabetes mellitus, hypertension, and ischemic heart disease.
Materials and Methods: This retrospective study was conducted in the Department of Pathology from May to December 2020. A total of 330 RT-PCR-confirmed COVID-19 cases were included and categorized into survivors and non-survivors based on hospital records. Patients with platelet disorders or other systemic infections were excluded. Hematological parameters, NLR, and PLR were compared between the two groups.
Results: Of the 330 cases, 68% were males and 32% females (male:female ratio 2.1:1). Most cases and deaths occurred in the 61–70 years age group, followed by 51–60 years. Total leukocyte count, NLR, and PLR were significantly higher in non-survivors ($p < 0.05$). Platelet count, platelet indices, hemoglobin levels, and comorbidities showed no significant differences between the groups.
Conclusion: Elevated leukocyte count, NLR, and PLR are associated with poor prognosis in COVID-19 patients. NLR and PLR may serve as early, accessible biomarkers for predicting disease severity and guiding clinical management.

Keywords*: Covid -19, Neutrophil to Lymphocyte Ratio, Platelet to Lymphocyte Ratio.*

INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), emerged as a global public health emergency and significantly affected healthcare systems worldwide. The disease exhibits a broad clinical spectrum ranging from asymptomatic infection to severe pneumonia, acute respiratory distress syndrome (ARDS), multiorgan failure, and death. Early identification of patients at risk of severe disease became essential during the pandemic, particularly in resource-limited healthcare settings such as India, where rapid and cost-effective prognostic markers were urgently needed.[1-3]

Several laboratory biomarkers have been investigated for predicting disease severity and prognosis in COVID-19 patients. Among these, hematological parameters derived from routine complete blood count (CBC) testing have gained considerable attention because they are inexpensive, rapidly available, and widely accessible. Several studies have demonstrated that abnormalities such as lymphopenia, neutrophilia, thrombocytopenia, and leukocytosis are commonly associated with severe COVID-19 infection and poor clinical outcomes. [1,2]

Inflammatory indices derived from CBC parameters, particularly the Neutrophil–Lymphocyte Ratio (NLR) and Platelet–Lymphocyte Ratio (PLR), have emerged as potential biomarkers for assessing disease severity and prognosis in COVID-

19 patients. NLR reflects the balance between innate and adaptive immune responses, where elevated neutrophil counts indicate systemic inflammation while reduced lymphocyte counts suggest impaired immune regulation. Similarly, PLR serves as an indicator of inflammatory and thrombotic activity, both of which play a significant role in the pathogenesis of COVID-19.[2]

Indian studies have also highlighted the clinical relevance of these hematological markers. A prospective observational study conducted at All India Institute of Medical Sciences (AIIMS) reported significantly elevated NLR values in patients with severe COVID-19 and concluded that NLR was a better predictor of disease severity and mortality compared to PLR.[3] Another study from Armed Forces Medical College, Pune, observed that both NLR and PLR were significantly associated with disease progression and intensive care requirement among hospitalized COVID-19 patients.[2]

Similarly, Pujani et al. demonstrated that hematological biomarkers such as neutrophilia, lymphopenia, and elevated NLR were strongly associated with adverse outcomes in Indian COVID-19 patients.[4] A study from Ramaiah Medical College, Bengaluru, further emphasized the utility of platelet indices and PLR in predicting disease severity and mortality.[5]

One of the major advantages of NLR and PLR is that they are inexpensive, easily obtainable and can be calculated from routinely performed laboratory tests without additional financial burden. This makes them serve as practical biomarkers for early risk stratification and monitoring of COVID-19 patients in busy hospitals and peripheral healthcare centers where advanced inflammatory markers may not be readily available. This can improve patient management and optimize healthcare resources. Therefore, the present study aims to evaluate hematological parameters with special emphasis on Neutrophil–Lymphocyte Ratio (NLR) and Platelet–Lymphocyte Ratio (PLR) as biomarkers in COVID-19 cases and to determine their association with disease severity and clinical outcomes.

MATERIALS AND METHODS

We conducted a retrospective study in Department of Pathology of a tertiary care hospital in South Karnataka after taking Institutional Ethical Committee approval for the study. We collected the details of RTPCR positive Covid-19 cases admitted in our hospital over a period of 8months from the hospital records section. Data included 330 covid-19 cases and grouped into survivors and non-survivors. Their haematological parameters like total leucocyte count, differential leucocyte count, platelet count, mean platelet volume (MPV), platelet distribution width (PDW) and plateletocrit (PCT)were collected. Neutrophil-Lymphocyte Ratio (calculated by dividing absolute neutrophil count to absolute lymphocyte count) and Platelet-Lymphocyte Ratio (calculated by dividing platelet count to absolute lymphocyte count) were calculated. All of these parameters were compared between survivors and non-survivors group.

Statistical Analysis:

All the data were entered in MS excel and analysed in SPSS 20.0.
Continuous variables were reported as mean values, standard deviation (SD) or median with interquartile range (IQR), while categorical variables were expressed as count and percentage. The statistical significance of intergroup differences was compared through Mann-Whitney *U* test for continuous variables and through Pearson's $\chi 2$ test for categorical variables. p-value of <0.05 is considered statistically significant.

RESULTS

This study included 330 Covid patients. Of which 225 cases were males and 105 cases were females, with male to female ratio of 2.1:1. (Figure 1)

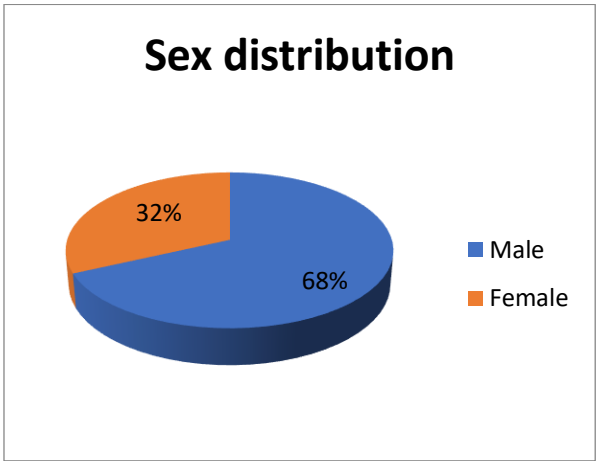

Figure 1: Sex distribution of cases

Out of 330 cases, majority of them were above 40 years of age (>40years:265 cases, <40years:65cases). Among 225 males, 177 (79%) survived and 48 (21.3%) died. Among 105 females, 92 (87.6%) survived and 13 (12.4%) died.

Mortality was high in the age group between 91-100years(100%) followed by 81-90years(37.5%), 61-70years (27.3%), 51-60years (23.9%) (Figure 2) (Table 1).

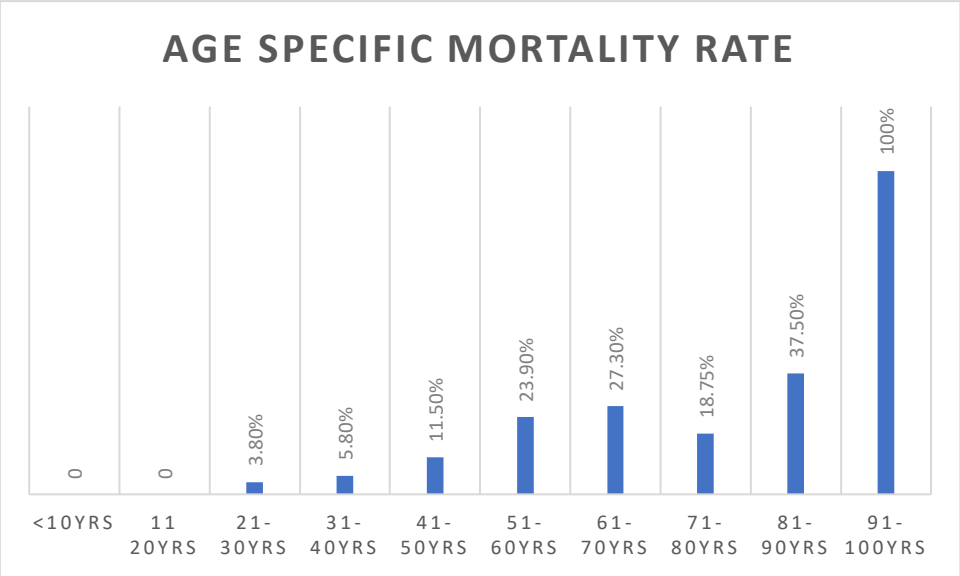

Figure 2: Age specific mortality rate

Table 1: Age wise distribution of cases and age specific mortality rate

Age in years	No. of patients	Male	Female	Deaths	Age specific mortality rate
<10yrs	3	2	1	0	0%
11- 20yrs	2	1	1	0	0%
21-30yrs	26	14	12	1	3.8%
31-40yrs	34	28	6	2	5.8%
41-50yrs	69	49	20	8	11.5%
51-60yrs	71	48	23	17	23.9%
61-70yrs	84	56	28	23	27.3%
71-80yrs	32	21	11	6	18.75%
81-90yrs	8	5	3	3	37.5%
91-100yrs	1	1	0	1	100%

Among non-survivors (n=61), 25 cases had Diabetes Mellitus, 20 cases had Hypertension and 5 cases had Ischemic heart disease. Among survivors(n=269), 112 cases had Diabetes Mellitus, 84 cases had Hypertension and 17 cases had Ischemic heart disease. In this study there is no statistical association between the presence of additional comorbid conditions and mortality (Table 2).

Table 2: Clinical characteristics of the study subjects.

Attributes	**Survivors (n=269)**	**Non-survivors (n=61)**	**Total (n=330)**	**Chi-square**	**p-value**
Diabetes mellitus					
Yes	112 (41.6%)	25 (41%)	137 (41.5%)	0.008708	0.92565
No	157 (58.4%)	36 (59%)	193 (58.5%)		
Hypertension					
Yes	84 (31.2%)	20 (32.8%)	104 (31.5%)	0.056075	0.81281
No	185 (68.8%)	41 (67.2%)	226 (68.5%)		
IHD					
Yes	17 (6.3%)	5 (8.2%)	22 (6.7%)	Fisher exact test	0.57365
No	252 (93.7%)	56 (91.8%)	308 (93.3%)		

In the present study, Hemoglobin, platelet count and platelet indices (MPV, PDW, PCT) between survivors and non-survivor groups showed no statistical difference(Table 3).

Table 3: Haematological parameters of the study subjects among survivors and non-survivors.

	Group	Mean	SD	p-value
Hb	Survivors	13.05	2.29	0.545
	Non-survivors	13.22	2.31	
PLT	Survivors	2,22,851	99,830	0.652
	Non-survivors	2,05,508	71,235	
MPV	Survivors	7.94	0.91	0.665
	Non-survivors	8.07	0.99	
PCT	Survivors	0.17	0.07	0.895
	Non-survivors	0.16	0.05	
PDW	Survivors	13.84	2.77	0.190
	Non-survivors	14.52	4.07	

Total leucocyte count, NLR and PLR showed statistical significance among survivors and non-survivors, with p value of <0.05 (Table 4). The total leucocyte count, NLR and PLR among survivors is 7200 cells/cumm, 3.6, 165.9 respectively. While among non-survivors it is 11,700cells/cumm, 9.41 and 203 respectively.

Table 4: Haematological parameters of the study subjects among survivors and non-survivors

	Group	Mean	SD	p-value
TC	Survivors	8488.85	5179.79	*<.05*
	Non-survivors	12370.49	6028.69	
NLR	Survivors	5.51	5.26	*<0.05*
	Non-survivors	10.78	7.66	
PLR	Survivors	188.26	122.45	*0.0048*
	Non-survivors	231.67	131.46	

DISCUSSION

Individuals infected with covid -19 are having varied clinical course and outcome. In the current study the significance of lab parameters in prognosticating the severity of illness is presented.

Early diagnosis of the severity of COVID 19 illness is crucial for appropriate allocation of medical resource and triaging. As the clinical picture at time can be confusing and physicians remain undecided about the need for intensive care, certain laboratory parameters might be of help in such situations.

Various hematological abnormalities such as leucopenia, lymphopenia, thrombocytopenia etc in covid 19 have been reported. Studies showed that a greater number of lymphopenic patients had reactive lymphocytes, of which a subset appeared to be lymphoplasmacytoid.[6,7]

As most of the individual hematological parameters have low specificity in identifying severity of illness, many authors have studied combination of hematological and biochemical parameters like low lymphocyte-to-C-reactive protein ratio, platelet-to-lymphocyte ratio and thrombocytopenia to improve the specificity in critical illness.[8] Present study is one such exercise where NLR and PLR have been the primary focus. It has shown in this study that increased NLR and PLR are associated with high mortality.

The results of this study provide significant insights into the demographic and hematological predictors of mortality in COVID-19 patients. By analyzing 330 cases, this study highlights the critical roles of age, gender, and specific inflammatory markers—Total Leucocyte Count (TLC), Neutrophil-to-Lymphocyte Ratio (NLR), and Platelet-to-Lymphocyte Ratio (PLR)—in determining clinical outcomes.

Demographic Predictors: Age and Gender

The demographic data in this study revealed a male preponderance (2.1:1 ratio) and a significant increase in mortality associated with advancing age, particularly in patients over 60 years. This aligns with external research, such as the study by Singh et al., which reported an even higher male-to-female ratio of 3.7:1 and identified a median age of 50 years among their cohort.[9] The literature suggests that the elderly are a primary risk group due to their vulnerability to a severe course of infection, which often leads to respiratory failure and death.[10] The observed 100% mortality rate in the 91–100 age group in this study further underscores that age is one of the most powerful predictors of an unfavorable clinical outcome.

Comorbidities and Mortality

Interestingly, this study found no statistical association between mortality and comorbid conditions such as Diabetes Mellitus, Hypertension, or Ischemic Heart Disease. This finding contrasts with some literature which suggests that individuals with pre-existing comorbidities are at a substantially higher risk. For instance, Singh et al. observed that hypertension was the most common comorbidity in their severe group. The discrepancy in these results may be due to the specific demographic makeup of the study or variations in the severity of the comorbidities themselves. [9]

Hematological Markers and the Inflammatory Response

The most significant laboratory findings in this study were the elevated levels of TLC, NLR, and PLR among non-survivors, all of which showed statistical significance ($p < 0.05$).

- **Total Leucocyte Count (TLC):** Non-survivors exhibited a significantly higher TLC (11,700 cells/cumm) compared to survivors (7,200 cells/cumm). This increase is typically driven by an activation of the non-specific cellular response, where neutrophils are released into the bloodstream to combat the viral infection, often contributing to a "cytokine storm".[10]
- **Neutrophil-to-Lymphocyte Ratio (NLR):** The NLR was markedly higher in non-survivors (9.41) than in survivors (3.6). This confirms findings in the literature where NLR is identified as an excellent predictor of COVID-19 severity and mortality.[9,10] The mechanism behind this is the combination of neutrophilia (increased neutrophils) and lymphopenia (decreased lymphocytes) caused by the hyperactivation of the immune system and subsequent lymphocyte apoptosis.[10] Study conducted by Jingyuan Liu et al, compared NLR with MuLBSTA and CURB-65 scoring models. The results showed that NLR was better than the other two models for predicting the early incidence of Covid-19 critical illness. They found that the prediction effects of the NLR-MuLBSTA and NLR-CURB-65 models were better than those of the original models.[8]
- **Platelet-to-Lymphocyte Ratio (PLR):** Non-survivors also showed a higher PLR (203) compared to survivors (165.9). As supported by the meta-analysis by Simadibrata et al., severe cases often demonstrate elevated PLR levels because the decrease in absolute lymphocyte counts is typically more significant than the decrease in platelet counts.[11] The role of Platelet-lymphocyte ratio has been studied by Rong Qu et al, in their study and found that larger the PLR, the more severe the cytokine storm, and the longer the hospital stay, the worse the prognosis. They also calculated the cut-off value of PLR. When PLR > 126.7, they told that intervention is must to prevent further deterioration of the disease.[12] We also found PLR to be having similar prognostic value in our subjects.

Clinical Utility of Inflammatory Ratios

The study's findings on NLR and PLR are particularly valuable because these markers are inexpensive, readily available, and easily interpreted from a routine complete blood count. [10,11] While hemoglobin and platelet indices (MPV, PDW, PCT) did not show statistical significance in this specific cohort, the strong predictive value of NLR and PLR provides clinicians with a rapid tool for early stratification of high-risk patients.

In conclusion, these results reinforce the understanding that systemic inflammation, reflected through hematological ratios, is a primary driver of COVID-19 mortality. Monitoring NLR and PLR upon admission is recommended to identify high-risk patients and implement aggressive treatment strategies to prevent disease progression.

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