ORIGINAL RESEARCH

Evaluation of hematological parameters in prediction of covid- 19 disease severities: A cross sectional study

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ABSTRACT

Background: The severity of COVID-19 could be evaluated by examining several blood parameters mainly white blood cell (WBC) count, granulocytes, platelet, and novel hemocytometric markers neutrophil to lymphocyte ratio (NLR), platelet-to-lymphocyte (PLR), and lymphocyte to monocyte ratio (LMR). **Aim:** The current study was conducted to investigate alteration in blood parameters and their association with the severity and mortality of COVID-19 patients. **Material and Method:** This retrospective cross-sectional study was conducted in the Department of pathology, in a tertiary care centre, India. A total of 300 RT-PCR COVID-19 positive patients of age group between 18-80 years were enrolled in our study. The hematological parameters were compared between different grades of severity. The following parameters were assessed: hemoglobin, platelets count, total leukocyte counts (TLC), relative neutrophil count, relative lymphocyte count, neutrophil-to-lymphocyte ratio (NLR), and absolute eosinophil counts (AEC). **Results:** The overall mean age observed in our study was 52.35 years, majority of the patients were male (57.6%). Associated co morbidities found in 83.6% of cases. Our results showed that COVID-19 survivors exhibited lower hemoglobin (Hb) and hematocrit (HCT), while showed higher Red Cell Distribution Width (RDW), neutrophil lymphocyte ratio (NLR), and lymphocytes. Logistic regression analysis showed that age greater than 40 years old, neutrophilia and high NLR were associated with more deaths. **Conclusion**: Routine hematological parameters are cost-effective and fast predictive markers for severe COVID-19 patients, especially in resource-constrained health care settings to utilize limited ICU resources more effectively.

Keywords: Complete blood count, COVID-19, hematological parameters, severe disease

INTRODUCTION

The corona virus disease 2019 (COVID-19) caused by Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2) was first described in the late December 2019 in Wuhan, China.[1,2] The COVID-19 is a high contagious disease and spread around the globe within a short time, and the world health organization (WHO) has declared it a pandemic on March 12, 2020 [3]. COVID-19 has varied clinical manifestations, ranging from mild flu-like symptoms and asymptomatic phase to life-threatening acute respiratory distress syndrome (ARDs), and organ failure that may lead to death [4]. The initial symptoms of COVID-19 are shortness of breath, cough, fatigue, fever, dyspnea, myalgia, and muscle pain. However, they could progress to acute respiratory distress syndrome (ARDS), multi-organ dysfunction, shock, and metabolic acidosis when the condition becomes worsened [5]. At the start of an infection and in the incubation period, there are mild flu-like symptoms. According to the National Health Commission of China, the protocol published (version 7) for diagnosis and treatment for COVID-19, the COVID-19 severity is classified into four levels based on the clinical manifestations: critical, severe, moderate, and mild disease [6]. Different respiratory factors such as oxygen saturation rate, lesion progression in pulmonary rate, and respiratory rate were the key factors considered during the classification of the severity levels of COVID-19.[7]

Patients with severe COVID-19, mostly critical individuals, usually have dysfunction complications of other organs, such as shock, septic, disseminated intravascular coagulation (DIC), and heart failure. Except for clinical symptoms and pulmonary computed tomography (CT) findings, most confirmed COVID-19 patients revealed laboratory fluctuations in different serological parameters, including renal and liver function tests, coagulation parameters, and inflammatory, biochemical and hemocytometric parameters.[8,9]. To show the prognosis and hyperinflammation state, a combination of laboratory tests has been evaluated. The combination of the various test includes platelet-to-lymphocyte (PLR) and neutrophils to lymphocyte ratio (NLR). COVID-19 leads to variation in the hematological parameters, including lymphocytes, white blood cells, platelets, neutrophils, etc.[10-12]. Moreover, knowledge about the risk of infections along with other comorbid conditions would provide valuable insights on risk stratification and making a clinical decision in severe COVID-19 patients.[13]. CBCs are the most appropriate and potent laboratory examination. The main objective of this research was to evaluate and review the variations among CBC level of COVID-19 patients with the disease severity level and how the CBC level changes after the onset of disease to identify the stage and disease's key indicator to provide information for the diagnosis and treatment basis for health professionals [14].

Aims & objectives: Moreover, this study aimed to explore novel inflammatory markers NLR, PLR as a valuable marker in predicting severity and outcome of COVID-19 infection as they were previously reported in different infections and inflammatory conditions

MATERIAL AND METHODS

This is a retrospective cross-sectional study was conducted in the Department of pathology, in a tertiary care centre, India, over a period of 12 months from April 2021 to March 2022. All patients, who were ≥ 18 years of age with COVID-19 confirmed on SARS-CoV-2 reverse transcription-polymerase chain reaction (RT-PCR) and whose routine hematology counts were sent within 24 h of admission were included in the study.

For each patient, Demographic data, clinical history, and laboratory results during hospitalization were collected. Patients The parameters collected upon admission regardless their levels included a complete blood profile in addition to measurements of C-reactive protein (CRP), procalcitonin (PCT), ferritin, and lactate dehydrogenase (LDH). Blood samples were collected in vacationers containing EDTA (ethylenediamine tetraacetic acid) for CBC. CBC of the patients was done on automated six parts Sysmex hematology analyzer. The following parameters were assessed: hemoglobin, platelets count, total leukocyte counts (TLC), relative neutrophil count, relative lymphocyte count, neutrophil-to-lymphocyte ratio (NLR), and absolute eosinophil counts (AEC).

Routine clinical hematology laboratory data obtained on the day of patients' positive COVID-19 test were utilized as candidate predictors for the model. The outcome recorded for each patient was the need for subsequent ICU care during hospitalization.

EXCLUSION AND INCLUSION CRITERIA

All those individuals who were tested positive for the SARS-CoV-2 according to the WHO and CDC guidelines for the detection and diagnosis of COVID-19 were included in this study. Individuals below 18 years of age and those with missing data were excluded.

STATISTICAL ANALYSIS

The IBM SPSS Ver. 23 statistical package programs and Microsoft excel 2016 for data analysis. Continuous variables mean, standard deviation and categorical variables were measured as frequency and percentage. We determined the comparison between multiple groups by using the chi-square and continuous variable by independent t-test. The 95% CI having a two-tailed tests and $p < 0.05$ considered statistically significant

RESULTS MOSTLY

A total of 300 COVID-19 positive individuals confirmed by RT-PCR were examined in this study. The age of the patients ranged from 18 to 82 years with a mean age of 52.35 years. There were 173 males and 127 female patients, Male individuals were more affected than female individuals. Most of the participants belonged to rural areas (54%). Majority of the participant had one or more co morbidities (83.6%). Fate of Covid 19 disease patients 89% were improved

Table 1: Distribution of Escherichia coli Isolates from various clinical samples. (n=215)

Characteristics		Frequency (%)
Age groups	< 40 Years	63 (21%)
	40-60 Years	103 (34.4%)
	60-80 Years	116 (38.6%)
	>80 Years	18 (6%)
	Mean ± SD	52.35 ± 17.17
Gender	Male	173 (57.6%)
	Female	127 (42.4%)
Residential status	Urban	138 (46%)

	Rural	162 (54%)
Co morbidities	Present	251 (83.6%)
	Absent	49 (16.4%)
Outcomes	Improvement	267 (89%)
	Death	33 (11%)

Hematological parameters included the mean ± SD of Hb, total mean leucocyte count, lymphocytes, lymphocyte percentage, and neutrophil/lymphocyte ratio (NLR), which were 12.42 ± 2.10 g/dL, 8.67 ± 5.62×10^9/µL, 1.96×10^3 ± 0.961, 27.35 ± 15.12, and 4.54± 5.52, respectively.

Measurements indicated a C-reactive protein (CRP) concentration of 23.45 ±3 4.98 mg/L and a ferritin concentration of 534.70 ± 519 ng/mL (Table 2). We observed that survivors had higher hemoglobin (Hb), hematocrit (HCT), and normal red cell distribution width (RDW) values (12.65 ± 1.87, 37.21 ± 4.8, and 14.16 ± 1.91, respectively) compared with non- survivors (10.91 ± 2.85, 32 ± 8.4, and 16.29 ± 3.94, respectively). In addition, survivors had statistically significant higher ages compared with non-survivors (49.5 ± 17.44 and 64.5 ± 11.72, respectively) (Table 3). We also found that the survivors exhibited higher levels of lymphocytes, neutrophil count (2056.20 ± 940.65, 5285 ± 4313.9, respectively compared to non- survivors (1385.70 ± 912.47, 11690 ± 9888.92, respectively). The results showed that 14.3% and 52.5% of survivors and non survivors showed high leukocytic count while 78.5% and 47.1% of survivors and non survivors showed normal total WBCs count respectively, 29.5% and 58.8 % from survivors and non survivors respectively had lymphopenia, 17% and 64.75% of survivors and non survivors showed neutrophilia respectively, while 29.5% and 70.6 % of survivors and non survivors had high NLR respectively (Table 4).

Table 2: Hematological parameters of the studied sample

Parameters	Mean	SD
CRP (mg/L)	23.45	34.98
Ferritin (ng/ml)	534.70	519.21
LDH (U/L)	489.35	182.78
Na+	141.75	13.52
K+	4.04	0.78
Ca++	4.45	0.37
INR	1.10	0.13
Prothrombin Time(s)	14.34	1.82
SGOT	40.09	19.82
SGPT	41.55	31.95
hs CRP (mg/L)	7.83	4.29
Control time PTT(s)	28.51	6.12
PTT	40.38	6.27
Albumin	3.83	0.77

Table 3: Red Blood indices and platelets according to cases fate

Title	Survivors		Non-Survivors		*p*-value
	Mean	SD	Mean	SD	
Hemoglobin	12.65	1.87	10.91	2.85	0.03
Age	49.5	17.44	64.5	11.72	0.001
Hematocrit PCV	37.21	4.84	32.48	8.40	0.04
MCH	27.84	2.67	27.84	4.20	0.99
MCHC	33.92	1.46	33.59	1.32	0.36
MCV	81.96	5.86	82.65	10.47	0.79
Red Cell	4.57	0.68	4.03	1.25	0.10
RDW	14.16	1.91	16.29	3.94	0.04
Platelet	271.5	1.142	271.2	1.132	0.99

Table 4: Leucocytes and cases fate

Title	Details	Survivors				Non-Survivors				*p*-value
		No.	%	Mean	SD	No.	%	Mean	SD	
	Low	8	7.1			0	0.0			0.03
WBCs	Normal	88	78.6	7.92	4.20	8	47.1	13.61	10.02	0.00

	High	16	14.3			9	52.9			
Lymphocytes	Low	33	29.5	2.05	0.9	10	58.8	1.3	0.9	0.01
	Normal	79	70.5			7	41.2			0.03
	Low	11	9.8			0	0.0			
Neutrophils	Normal	68	60.7	5.285	4.3	3	17.6	11.69	9.8	0.03
	High	19	17.0			11	64.7			0.00
	Missed	14	12.5			3	17.6			
	Normal	64	57.1			2	11.8			0.01
NLR	High	33	29.5	3.62	4.05	12	70.6	10.91	9.33	0.00
	Missed	15	13.4			3	17.6			

DISCUSSION

To manage COVID-19 infection, early diagnosis, appropriate treatment, and future control measures are all essential to limit the spread of the virus. Laboratory parameters play an indispensable role in the early assessment of disease etiology, diagnosis, treatment, and follow-up.

The COVID-19 cause low deaths in young adults less than 40 years but more death in aged patients above 40 years (Wu and McGoogan et al). Researchers grouped the patients having confirmed COVID- 19 cases. About 75% of cases were above 50 years of age (Saddique et al). Our study aligned with the previous reports and about 78.6 % of patients were older than 40 years of age. Age is considered a significant indicator of COVID-19 outcomes. As in my study about 57.8% were males and 42.3% were females. The mortality rate was 15.8% among admitted patients (Khalid et al) [15-17].

Patients have a normal leukocytic count, later on, leukopenia or leukocytosis can occur, although leukopenia is more frequently observed [18].

In our study, the mean leukocytic count was 7.9×103, and the mean of the lymphocyte count was 2×103 for survivors, whereas the mean of the total leukocytic count increased in non-survivors to 13.61×103 with a decreased mean of the total lymphocytic count to 1.3 × 103 ($p = 0.034$* and 0.010*, respectively). Huang et al. and Xu et al. found that 63% of patients in Wuhan, China, and 42% of patients outside of Wuhan presented with lymphopenia [19-20].

Current study observed, non-survivors exhibited neutrophilia with a mean value of 11.69×109/L compared with 5.2×109/L in survivors ($p = 0.032$). The same results were observed by Fan et al [21]. in a cohort of 69 COVID19 patients. They reported that ICU patients were more likely to develop neutrophilia during their hospital stay with a median peak of absolute neutrophil count of 11.6×109/L compared with 3.5×109/L in the non-ICU group ($p < 0.001$).

In the present study, the non-surviving patients who experienced severe COVID-19 had prominent laboratory abnormalities compared with those of survivors who experienced clinical improvement. Lymphopenia is a reliable indicator of the severity and hospitalization of COVID-19 patients, similar results reported by Awale RB et al [22].

The TLC was observed to be gradually increasing with the disease severity and during the hospital stay. Similarly, the study by Terpos et al.[23] found normal or slightly reduced TLC during the first week while during the second week of illness there was a decreased lymphocyte count. This decrease in the lymphocyte count was seen in the present study also. These findings were more pronounced in the patients who died due to illness. Contrary to this, Fan et al.[24] in their study on COVID-19 patients found leucopenia on admission (19/67) 29.2%. The TLC has been studied as a biomarker for COVID-19 and Peng et al.[25] in their study on 190 healthy and COVID-19 patients found a lower TLC in the patients with COVID-19 than the healthy subjects.

The platelet count was observed to be within range with a slight marginal decrease in the patients with severe disease in the present study. Thrombocytopenia was seen in the non-survivors while the normal platelet count was seen in the survivors in the study by other authors.[26-27], Similarly, the severe patients had a lower platelet count as compared to the non-severe patients. The platelet count was found to be an independent risk factor for mortality in COVID-19.

Present study revealed an increased neutrophil-to-lymphocyte ratio and decreased lymphocyte-to-C-reactive protein ratio in patients with survivors COVID-19 infection compared with non-survivors patients, High NLR values were associated with more death, accordance to L –Rangel et al [28].

Non-survivors had increased levels of total leukocytic count, absolute lymphopenia, absolute neutrophilia, and increased NLR compared with clinically improved patients. A retrospective study in Hong Kong and Singapore showed that lymphopenia was observed in patients who suffered from SARS-CoV in 2003 and was associated with adverse outcomes and ICU stay [29-30]. Monitoring lymphopenia may help to categorize patients who may require ICU care.

CONCLUSION

The CBC is an easily available, inexpensive, and reliable investigation that can help in providing insights into the patients' COVID-19 status. The combinations of ratio and serial trends of hematology parameters along with clinical assessment can aid in precise decision-making in COVID-19 patient management. With an increase in severity, there is an increase in the TLC and absolute neutrophil count while the absolute lymphocyte count decreases.

Monitoring of lymphopenia and NLR may help categorize patients who may need ICU care. It is important to identify the laboratory abnormalities early and act to prevent complications.

CONFLICTS OF INTEREST

None

SOURCE OF FUNDING

None

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