

A Hospital Based Observational Study to Assess the Role of Hematological Biomarkers, Coagulation Profile and CRP (C-Reactive Protein) in Covid-19 Patients

Ram Ugrah Prasad¹, Vivek Kumar Pandey²

¹Tutor, Department of Pathology, SKMCH, Muzaffarpur, Bihar, India

²Tutor, Department of Pathology, SKMCH, Muzaffarpur, Bihar, India.

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Corresponding author: Dr. Vivek kumar Pandey

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Abstract

Aim: In this study, the roles of biomarkers from a peripheral blood sample were used in the diagnosis of COVID-19 patients who have history of fever and have been admitted to hospital are examined.

Methods: The present study was conducted Department of Pathology, SKMCH, Muzaffarpur, Bihar, India where the patients having history of fever were admitted during the period of 3 months. A total of 100 patients were included who were suspected cases of corona. RTPCR was done for all the patients and were categorized into covid negative and covid positive patients.

Results: Out of 100 patients included in the study that came with history of fever and was admitted in hospital, RTPCR was done and 65% patients were positive. Out of which 66.2% were male patients and 33.8% were female patients. Hematological parameters were recorded and presented in a tabular data as described in Table 1. Parameters included were total leukocyte count, neutrophils, hemoglobin, lymphocytes, NLR, PLR, SII, and Platelets. In patient with negative test results, it was found that total leukocyte count, neutrophils, platelet, NLR and SII values were higher. Whereas, haemoglobin, lymphocytes and PLR was found to be higher in patients with positive test results.

Conclusion: In our study, low values of leukocytes, neutrophils, platelets and high values of hemoglobin, Lymphocytes were found with a CBC test which is easily available are found to be valuable in terms of the initial diagnosis of COVID 19. In addition, low values of NLR and SII and high value of PLR and CRP are also indicative of COVID-19.

Keywords: SARS- CoV- 2, RT-PCR, Neutrophil lymphocyte ratio, Platelet lymphocyte ratio, Coagulation factor

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Introduction

Coronavirus disease 2019 was first reported in Wuhan city, Hubei, China, in the last week of December 2019. [1] The disease reported in a cluster of atypical

pneumonia cases and primarily transmitted through respiratory and body contact. [2] Patients with coronavirus disease demonstrated a series of clinical

symptoms, including raised body temperature, cough, headache, nausea, vomiting, anorexia, diarrhea, dyspnea, multiple organ dysfunctions. [3] A large proportion of infected patients reported mild symptoms of the disease and recover. [4] Some patients progressively develop serious complications, including sepsis, acute respiratory failure, metabolic acidosis, heart failure, kidney injury, hypoxic encephalopathy, and eventually die of the illness. [3] A recent report reported a few new symptoms, including anosmia and ageusia. [5] Considering high transmission and infectivity patterns, World Health Organisation announces it as an emergency of public health concern on March 31, 2020. [6] In the initial phase of the disease outbreak, the mortality ranges from 2 to 5%, much higher in the elderly. [3] The mortality in coronavirus cases admitted in Wuhan city reached 7% in the outbreak's initial days. [7]

Various inflammatory markers were associated with COVID-19 progression [8], but the hallmark of hyper inflammatory response is interleukin-6 (IL-6) acting as a central player in immune regulation, inflammation, and infection. [9] Raised levels of IL-6 precede the development of acute lung injury due to increased permeability of lung capillaries driving the ARDS development and stimulation of coagulation and micro thrombi formation in the lungs. [10] Patients with higher IL-6 levels have more rapid progression and a higher complication rate so it was proposed that the levels of IL-6 may be used as a biomarker to help assist clinicians in recognizing patients with severe COVID-19 early in the disease course. [11,12] The importance of identifying this elevated biomarker also lies in selecting patients who can benefit from the use of antibodies against IL-6 such as tocilizumab. IL-6 also induces the synthesis of another sensitive biomarker of inflammation and infection,

CRP, which increases during inflammatory response. [13]

Due to the fact that it is very critical to identify patients with high chances of worsening clinical symptoms or poor clinical outcomes, it is very helpful to find laboratory parameters, which can predict disease worsening.

Blood tests have an important role in early diagnosis of the disease, considering the information they provide to physicians regarding the inflammatory process. Complete blood counts (CBC) are easily performed and cheap. Included in the CBC are values such as white blood count, neutrophil, lymphocyte and platelet count (PLTs). These parameters may be used as inflammatory markers by themselves, their ratios to one another may also be indicators of early inflammation. [14] Considering previous research, the use of circulating biomarkers in lieu of inflammation and the immune system have been considered as a prognostic indicator in COVID-19-positive patients.

In this study, the roles of biomarkers from a peripheral blood sample were used in the diagnosis of COVID-19 patients who have history of fever and have been admitted to hospital are examined.

Methods

The present study was conducted Department of Pathology, SKMCH, Muzaffarpur, Bihar, India where the patients having history of fever were admitted during the period of 3 months. A total of 100 patients were included who were suspected cases of corona. RTPCR was done for all the patients and were categorized into covid negative and covid positive patients.

Methodology

All the blood parameters, Systemic inflammatory index (SII) = thrombocyte count neutrophil count/lymphocyte count. Neutrophil lymphocyte ratio (NLR) = absolute neutrophil count/absolute

lymphocyte count. Platelet lymphocyte ratio = absolute platelet/absolute lymphocyte count were calculated. Coagulation factor (prothrombin time(PT), activated partial thromboplastin time (aPTT), international normalized ratio(INR) and C-Reactive protein

(CRP) were compared between negative and positive COVID-19 cases.

The analysis of the data was done using the SPSS 25 statistical package programs. A Chi-square test was used to analyze the resounding variables of the patients, which were expressed as a number and percentage. The independent samples t-test

was used for analysis for parametric continued variables and they were presented as a mean as well as standard deviation. The Binary Logistic Regression test was used to assess the diagnostic utility of several biomarkers to define risk ratios, including the SII. A receiver-operating characteristic (ROC) curve was formed, the Youden's index (J) used for cut-off values in the diagnosis of COVID-19 and the area under the curve (AUC) was calculated, $p < 0.05$ was considered statistically significant.

Results

Table 1: Covid suspected patients vs sex

	Covid Positive	Covid Negative
Male	43	18
Female	22	17
Total	65	35

Out of 100 patients included in the study that came with history of fever and was admitted in hospital, RTPCR was done and 65% patients were positive. Out of which 66.2% were male patients and 33.8% were female patients. The mean age of positive patients was 43.03years with standard deviation of 16.1.

Table 2: Comparison of haematological parameters according to RTPCR test results

Hematological parameters	Covid Positive n=65	Covid Negative n=35
Total leukocyte count	9.7±5.7 7.7 (3.8-26.1)	12.5±5.3 13.1 (5.3-23.2)
Neutrophils	6.2±1.3 6.2(3.2-9.3)	6.8±1.3 6.7 (3.5-9)
Hemoglobin	13.3±1.5 13.4 (9.7-16.5)	11.8±2.6 12.4 (6-16)
Lymphocytes	2.6±1.2 2.7 (0.4-5.8)	2.2±1.1 2 (0.5-5.3)
NLR	3.6±3.6 2.3 (0.55-23.25)	4.6±3.9 3.2 (0.66-18)
PLR	130.27±85.87 112.17 (20.4-383.26)	119.89±63.7 104.6 (29.5-262.3)
SII	861.4±120 457 (111-862.5)	999.6±78.67 748 (311-4014)
Platelet	224.2 ± 92.7 212.0 (79- 458)	241±97.8 212 (95-510)

Hematological parameters were recorded and presented in a tabular data as described in Table 1. Parameters included

were total leukocyte count, neutrophils, hemoglobin, lymphocytes, NLR, PLR, SII, and Platelets. In patient with negative test

results, it was found that total leukocyte count, neutrophils, platelet, NLR and SII values were higher. Whereas haemoglobin, lymphocytes and PLR was found to be higher in patients with positive test results. Since there was a statistically significant disparity between negative and positive

groups according to parameters (leukocyte, neutrophil hemoglobin, platelet, NLR, PLR and SII), they were then studied with ROC analyses. Regarding the observations made by ROC analyses, the following information concerning patients with COVID-19 diagnoses were found.

Table 3: Comparison of results according to cut-off points

Hematological parameters		Negative	Positive	p value
Hemoglobin	<11.25	14(40%)	6(9.2%)	0.05
	>11.25	21(60%)	59(90.76%)	
lymphocytes	<22.5	18(51.4%)	20(30.7%)	0.04
	>22.5	17(48.57%)	45(69.2%)	
PLR	<201.8	29(82.85%)	52(80%)	0.02
	>201.8	6(17.14)	13(20%)	

The optimal cut-off values were 11.25, 22.5 and 201.8 for hemoglobin, lymphocytes and PLR. Comparisons were made between these two groups that were formed according to the cut-off values and correlation was established with PLR where p value was <0.05.

Table 4: Comparison of coagulation profile and CRP

Coagulation profile and CRP	Positive	Negative	P value
PT (Prothrombin time)	14.33±.44	14.54±0.644	.180
APTT (Activated partial thromboplastin time)	30±0.01	31.50±1.3	.110
INR	1.3±0.07	1.1±0.05	.07
CRP	7.9±0.26	6.03±0.5	.05

Further coagulation profile (PT, APTT, INR) and CRP was compared between negative and positive group. P value was assessed and there was strong correlation noted with CRP.

Discussion

On March 11, 2020, the World Health Organization (WHO) declared the novel coronavirus (COVID-19) outbreak a global pandemic. To date (May 4th, 2022), there have been 515.82 million confirmed cases of COVID-19 worldwide, with 6.24 million reported deaths; whereas in Kosovo, 228,098 cases were confirmed and 3,138 deaths reported. In patients, COVID-19 results in a wide range of clinical manifestations, including asymptomatic infection, mild upper respiratory syndrome, severe pneumonia, acute respiratory distress syndrome (ARDS), multiple organ dysfunction

syndrome, and even death. The most prevalent symptoms are fever, cough [15,16] headache, loss of smell, and nasal obstruction [17], whereas gastrointestinal disorders are uncommon. [15,16]

With the continuous spread of COVID-19 cases worldwide and different speculations of its effect on the human body are also flashing every day, we are still inexperienced in understanding a few aspects of COVID-19. However, we still have a lot to know about the effect of COVID-9 on different biochemical and hematological profiles in patients who survived or died due to COVID-19. Taking into account that COVID 19 is highly infective and has high mortality rates early diagnosis of the disease is essential. The authoritative diagnosis of this disease is made by a viral presence in real-time PCR analyses. Due to factors such as the high

number of samples, limited number of staff trained in performing the aforementioned tests insufficient lab capacities, the time it takes to receive results can be prolonged. Therefore, every parameter allowing for early diagnosis is vital. Therefore, in this study, the possibility of diagnosing COVID-19 early by a simple, inexpensive, easily accessible test, such as a CBC, has been examined.

Patients who came with history of fever and were admitted in the hospital, RTPCR was performed during the arrival and was found that 65% patients were covid positive and 35% patients were negative out of 100 patients examined.

Comparison of hematological findings showed that the death cohort had higher neutrophils count, white blood cells, higher prothrombin time, and activated partial thromboplastin time. Besides, the death cohort had lower lymphocyte count, platelets, and lower hemoglobin than survivors' cases. This conclusion mostly matches earlier studies conducted on patients with COVID-19. [2,18,19] However, the role of platelet count in the mortality cohort should be described concerning the development of sepsis complications. Earlier work on sepsis patients in the intensive care unit discussed the role of platelet count in prognosis. [2,20]

An obvious relationship, although not definitely proven, exists between a bacterial infection and neutrophilia, and a viral infection and lymphocytosis. Accordingly, NLR of peripheral blood has been used to distinguish between these types of infections. In few studies NLR is higher in those with fever due to bacterial infections than those with fever due to a viral etiology¹⁴ however in our study NLR was reduced in COVID-19 positive cases. SII has been proposed as a prognostic indicator in the follow-up of sepsis patients. [21] In this study, SII was found to be significantly low for COVID-

19-positive patients, meaning that it can also be used while diagnosing COVID-19. [22]

Conclusion

The definitive diagnosis of COVID-19 was made by RT-PCR analysis, but this is a time-consuming and less accessible test. In our study, low values of leukocytes, neutrophils, platelets and high values of hemoglobin, Lymphocytes were found with a CBC test which is easily available are found to be valuable in terms of the initial diagnosis of COVID 19. In addition, low values of NLR and SII and high value of PLR and CRP are also indicative of COVID-19.

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