Original Article

Comparison of Biochemical and Hematological Parameters Among COVID-19 Patients With and Without Vaccination in a Tertiary Care Hospital: A Retrospective Study

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ABSTRACT

Background: The availability of the COVID-19 vaccine during the pandemic has changed the disease course in the entire world. The current study aimed to compare various hematological parameters among COVID-19 patients with and without vaccination.

Methods: The present retrospective study included 26 vaccinated and 26 non-vaccinated COVID-19 patients. Various clinical and biochemical parameters of RT-PCR-positive patients were collected. The values are expressed in Mean±SD or median values IQR. Mann-Whitney U test was used for comparison between the groups.

Results: Among the vaccinated individuals, 17 cases (65.4%) were asymptomatic, one patient (3.8%) had moderate, eight cases (30.8%) had mild COVID-19 infection and all 26 patients were completely recovered. Among non-vaccinated COVID-19 patients, 25 cases (96.2%) had severe, one case (3.8%) had moderate COVID-19, and 16 patients (61.5%) recovered but ten cases succumbed to COVID-19. There were statistically significant differences in SpO2, total leucocyte count, and differential counts of neutrophils, lymphocytes, eosinophils, monocytes, and basophils between vaccinated and non-vaccinated patients (P<0.001). The neutrophil/ lymphocyte ratio was found to be at a higher level (P<0.01) among non-vaccinated patients [10.9(4.28-23.63)] compared to vaccinated [1.55(1.09-2.28)]. The blood urea, total and direct bilirubin, serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), and inflammatory markers, like C-reactive protein (CRP), D-dimer, ferritin, and lactate dehydrogenase (LDH) were highly elevated in non-vaccinated patients (P<0.001). Moreover, lower values of total protein, serum albumin, and albumin and globulin (A/G) ratio were noted in the non-vaccinated compared to vaccinated individuals (P<0.001).

Conclusion: Vaccinated patients had milder disease with fewer derangements of hematological parameters compared to non-vaccinated patients. It can be concluded that vaccine has played a vital role during the COVID-19 pandemic in reducing mortality.

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Introduction

Coronaviruses are a large family of viruses that are known to cause illnesses ranging from the common cold to more severe diseases, such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS) [1]. A novel coronavirus (SARS-CoV-2 causing COVID-19) was identified in 2019 in Wuhan, China, and has not been previously identified in humans. In case of critical illness, patients progress rapidly to acute respiratory failure, metabolic acidosis, coagulopathy, and septic shock. Early identification of risk factors for critical illness facilitates the appropriate provision of supportive care and rapid access to the intensive care unit [2].

Many laboratory parameters make it possible to assess the severity of the COVID-19 infection and predict the risk of evolving toward more serious diseases, such as acute respiratory distress syndrome (ARDS). Laboratory parameters, like absolute neutrophilia, thrombocytopenia, hypoalbuminemia, the elevation of liver enzymes, creatinine, and nonspecific inflammatory markers, such as C-reactive protein (CRP) and interleukin-6 (IL-6) are associated with unfavorable disease course. The neutrophil-to-lymphocyte ratio (NLR) has proven its prognostic value in infections, inflammatory diseases, and several types of cancers [3]. NLR is a fast and inexpensive tool that may be useful in the early screening of COVID-19 patients.

India started vaccination against COVID-19 with AstraZeneca's COVISHIELD and Bharat Biotech's COVAXIN on January 16, 2021 [4]. The vaccine trials have found that they are effective in reducing disease severity and mortality [5, 6]. Hence, the present retrospective study was undertaken to compare biochemical and hematological parameters among COVID-19 patients with and without vaccination in a tertiary care hospital.

Materials and Methods

Study setting and design: The study was carried out from February 2021 to June 2021 in Yenepoya Medical College Hospital, Yenepoya (deemed to be university), Mangalore, India. Various clinical and biochemical parameters, like oxygen saturation (SpO_2), Complete Blood Count (CBC), platelet count, liver function tests (LFT), Renal Function Tests (RFT), C-reactive Protein (CRP) d-dimer, ferritin, Lactate Dehydrogenase (LDH), and disease outcome of RT-PCR-positive COVID-19 patients with and without COVID-19 vaccination were collected from central laboratory and medical record department of our institution. The NLR was calculated for each study participant. All the details were entered into an excel sheet and analyzed. The patient's details, like name, address, and contact numbers were anonymized.

Inclusion criteria: The following COVID-19 patients who were admitted to our institutional hospital were included in this study:

COVID-19 patients who have not received any COVID-19 vaccine in the past.

COVID-19 patients who have received at least one dose of the COVID-19 vaccine (Covishield) one month before the onset of COVID-19 symptoms/RT PCR report.

Exclusion criteria: COVID-19 patients with incomplete details were excluded from our study.

Sample size: The study results were statistically analyzed using descriptive statistics, with the acceptance of statistical significance at a 5% level and 80% power with a standard effect size of 0.8; the total sample size in each group was 26. Thus, we included the details of 26 vaccinated and 26 non-vaccinated COVID-19 patients in this study making the total sample 52 (n=52) for this study.

Sampling method: Simple random sampling method was followed using computer-generated numbers. The details of 26 vaccinated and 26 non-vaccinated COVID-19 patients were randomly selected from the medical record department.

Statistical analysis: The values are expressed in Mean±SD and Median/IQR. Frequency and percentage were used for categorical data. Mann-Whitney U test was used for variables with no normal distribution for comparison between vaccinated and non-vaccinated groups. Analysis was performed using SPSS software, version 23.

Results

The present study included a total of 52 COVID-19 patients (26 vaccinated and 26 non-vaccinated). Among vaccinated individuals, the majority were females (24, 92.3%). Regarding the severity of COVID-19 among vaccinated patients, 17 cases (65.4%) were asymptomatic, one patient (3.8%) had moderate disease, and the remaining eight cases (30.8%) had mild COVID-19. The mean age of the vaccinated individuals was 25.46±5.85

Table 1. Demographic details and disease outcome among study participants

Vaccination Status (n=52)	No. (%)	Mean±SD	No. (%)	
	Gender	Age (y)	Severity of COVID-19	Outcome
Yes (n=26)	Male 2(7.7) Female 24(92.3)	21-44 (25.46±5.85)	Asymptomatic: 17(65.4) Mild: 8(30.8) Moderate:1(3.8%)	Recovered: 26(100)
No (n=26)	Male: 16(61.5) Female: 10(38.5)	32-92 (57.08±14.38)	Moderate: 1 (3.8%) Severe: 25 (96.2%)	Recovered: 16(61.5) Expired: 10(38.5)

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Table 2. Comparison of various parameters between vaccinated and non-vaccinated COVID-19 patients

Parameters	Vaccination Status	Mean±SD/Median (IQR)	Mann Whitney U	P
SpO_2 levels (%)	Yes	96.38±1.29	129	<0.001
	No	91.35±5.59		
Hemoglobin (gm/dl)	Yes	12.25±1.83	327.5	0.848
	No	12.01±2.61		
Total leucocyte count (103 /µl)	Yes	7.57±3.48	135	<0.001
	No	13.61±6.61		
Neutrophils (%)	Yes	54.33±11.62	28	<0.001
	No	82.56±10.62		
Lymphocytes (%)	Yes	32.51±10.6	42	<0.001
	No	8 (4-16.85)*		
Neutrophil/ lymphocyte ratio (Number)	Yes	1.55(1.09-2.28)*	35	<0.001
	No	10.9(4.28-23.63)*		
Eosinophils (%)	Yes	2.45(0.77-3.77)*	70.5	<0.001
	No	0.05(0.0-0.22)*		
Monocytes (%)	Yes	9.92±2.64	102	<0.001
	No	4.8 (3.75-8.1)*		
Basophils (%)	Yes	0.40(0.3-0.7)*	149.5	<0.001
	No	0.2(0.1-0.3)*		
Platelet count (103 /µl)	Yes	259.19±70.92	312.5	0.641
	No	226(171-348.5)*		
ESR (mm/1hr)	Yes	14(0.75-27)*	190.5	0.007
	No	30.5(17.5-46.25)*		

n=52; * Median values with IQR; Mann Whitney U test was applied for all the parameters.

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Table 3. Comparison of hepatic and renal parameters between vaccinated and non-vaccinated COVID-19 patients

Parameters	Vaccination Status	Mean±SD/Median (IQR)	Mann Whitney U	P
Creatinine (mg/dl)	Yes	0.65±0.14	213	0.02
	No	0.78(0.60-1.22)*		
Urea (mg/dl)	Yes	19.24±7.17	72	<0.001
	No	37(29.50-59.50)*		
Total bilirubin (mg/dl)	Yes	0.4(0.3-0.5)*	118.5	<0.001
	No	0.65(0.50-1.05)*		
Direct bilirubin (mg/dl)	Yes	0.1(0.0-0.1)*	54	<0.001
	No	0.2(0.20-0.40)*		
Indirect bilirubin (mg/dl)	Yes	0.3(0.2-0.4)*	243	0.077
	No	0.5(0.30-0.72)*		
SGOT (U/L)	Yes	27.5(21-33.5)*	128.5	<0.001
	No	51.5(31-69.5)*		
SGPT (U/L)	Yes	14.5(12-27.25)*	108.5	<0.001
	No	37(23.75-61.50)*		
ALP (U/L)	Yes	63.88 ±17.89	199.5	0.011
	No	85.50(59.25-123)*		
Total proteins (gm/dl)	Yes	7.66±0.56	145	<0.001
	No	6.72±0.98		
Albumin (gm/dl)	Yes	4.26±0.32	30	<0.001
	No	3.30±0.59		
Globulin (gm/dl)	Yes	3.40±0.31	333.5	0.934
	No	3.38±0.57		
Albumin and globulin (A/G) ratio (Number)	Yes	1.25±0.12	72	<0.001
	No	0.99±0.22		

n=52; * Median values with IQR; Mann Whitney U test was applied for all the parameters.

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SGOT: Serum glutamic oxaloacetic transaminase; SGPT: Serum glutamic pyruvic transaminase; ALT: Alanine aminotransferase.

years with an age range of 21- 44 years. All 26 vaccinated COVID-19 patients completely recovered from the infection. Among non-vaccinated COVID-19 patients, the majority were males (16, 61.5%). Regarding the severity of COVID-19 among non-vaccinated patients, 25 cases (96.2%) had severe and one patient (3.8%) had moderate COVID-19. The mean age of the vaccinated individuals was 57.08±14.38 years with an age range of 32- 92 years. Regarding COVID-19 outcomes among the non-vaccinated patients, 16 patients (61.5%) recovered from the COVID-19 infection but ten patients succumbed to infection (Table 1).

Various details of biochemical parameters in study participants are mentioned in Table 2. The values are expressed as mean/median values (±SD/IQR). The present study found statistically significant differences in oxygen saturation (SpO2), total leucocyte count, and

Table 4. Comparison of inflammatory markers between vaccinated and non-vaccinated Covid patients.

Parameters	Vaccination Status	Mean±SD/Median (IQR)	Mann Whitney U	P
C-reactive protein (CRP) levels (mg/dl)	Yes	8.85(5.07-12.85)*	57	<0.001
	No	56.35(36.72-100.45)*		
D-dimer (ng/ml)	Yes	132(84.45-205.34)*	34.5	<0.001
	No	1387.25(578.25-4221.75)*		
Ferritin (µg/L)	Yes	16.65(12.27-26.82)*	27	<0.001
	No	546.50(222-898.25)*		
LDH (U/L)	Yes	167.85±34.44	65	<0.001
	No	367(242.75-529.5)*		

n=52; * Median values with IQR; Mann Whitney U test was applied for all the parameters.

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differential counts of neutrophils, lymphocytes, eosinophils, monocytes, and basophils (P<0.001) between vaccinated and non-vaccinated COVID-19 patients. NLR was found to be at a higher level among non-vaccinated COVID-19 patients [10.9 (4.28-23.63)] compared to vaccinated COVID-19 patients [1.55(1.09-2.28)] with a P<0.01.

Regarding renal and hepatic parameters in study participants (Table 3), the blood urea, total and direct bilirubin, serum glutamic oxaloacetic transaminase (SGOT), and serum glutamic pyruvic transaminase (SGPT) levels were highly elevated in non-vaccinated COVID-19 patients with a P<0.001. Moreover, lower values of total protein, serum albumin, and albumin and globulin (A/G) ratio were noted in the non-vaccinated group compared to vaccinated individuals (P<0.001).

Table 4 shows the details of various inflammatory markers in the study groups. Our data clearly showed higher levels of CRP, D-dimer, ferritin, and lactate dehydrogenase in the non-vaccinated group compared to the vaccinated group.

Discussion

COVID-19 is a systemic infection with a significant impact on the hematopoietic and immune systems. Biochemical and hematological parameters have been investigated to assess their role in diagnosis and prognosis. In this study, we documented the levels of CRP, ferritin, D-dimer, and hematological parameters in addition to disease outcome.

NLR is a simple parameter to assess the inflammatory status of a subject. In a study by Forget P et al., it was identified that normal NLR values in an adult, non-geriatric, and population in good health, are between 0.78 and 3.53 [3].

Several studies have described the clinical characteristics of patients with the novel coronavirus (SARS-CoV-2) infected pneumonia, indicating severe patients tended to have higher NLR.

A study by Jingyuan et al. showed that NLR was the most significant factor affecting severe illness incidence and it had a significant predictive value. NLR may also have prognostic value in determining severe cases and risk stratification [2, 7].

Another study by Kesari et al. showed that severe COVID-19 cases had higher leukocytes, lower lymphocytes, lower eosinophil count, and high NLR [8]. All these study findings are similar to your study results. Our study also reported higher leukocytes, lower lymphocytes, lower eosinophil count, and high NLR in non-vaccinated COVID-19 patients compared to vaccinated patients.

In a study by Smilowitz et al., initial high CRP concentrations were associated with worse clinical outcomes. Patients with the highest quartiles of CRP had the greatest likelihood of venous thromboembolism, acute kidney injury, critical illness, and mortality [9]. In our study, there were higher levels of CRP in non-vaccinated individuals with high mortality compared to the vaccinated group.

D-dimer is a sign of ongoing active fibrinolysis and, consequently coagulation. It assesses the severity of the host response. A study by Zhang et al. showed that the higher the D-dimer levels, the greater the risk of sepsis and septic shock for the patient. D-dimer was found to be especially predictive of disease progression [10]. These findings are consistent with our study results, wherein a significant difference was noted in levels of D-dimer of the non-vaccinated group compared to vaccinated cases.

D-dimer, ferritin, and CRP play an important role in the risk stratification of patients, predicting prognosis, and improving clinical management. Their routine monitoring would appear advisable in patients with COVID-19. Monitoring all the hematological and biochemical parameters, including novel hemograms and NLR, can aid clinicians to identify potentially severe cases at early stages and initiate effective management in time, which may reduce the overall mortality of COVID-19 patients [11].

The present study is one of its own kind in comparing hematological and biochemical parameters among vaccinated and non-vaccinated COVID-19 patients in the Indian population. Limitations of our study are lack of details, like co-morbidities and medications given were not taken into consideration. However, this study is a reflection of a real-life clinical setting wherein a proportion of asymptomatic patients may not have significant abnormalities.

5. Conclusions

The progression of illness seems to be prevented by vaccination; thus, the severe illness and mortality were lower in the vaccinated group. Raised NLR and increased D-dimer, ferritin, and CRP were associated with severe COVID-19.

Ethical Considerations

Compliance with ethical guidelines

The present study was initiated after the approval of the Scientific Review Board and Yenepoya Ethics Committee (Approval Number: YEC-2/916). The ethics committee gave approval with a waiver of consent because it was a retrospective study. The study is registered at the Clinical Trial Registry of India (Code: cCTRI/2021/12/038934).

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Authors' contributions

All the authors equally contributed to preparing, conducting, and analyzing this study.

Conflict of interest

All related research's ethical principles are considered in this article.

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