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Original Article

Comparison Between Haematological Parameters and Clinical Disease Severity in Covid-19 Infection Patients at a Tertiary Care Diagnostic Centre in Pakistan

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ABSTRACT

Objective: To determine the comparison between haematological parameters and clinical disease severity in patients with COVID-19 infection at a Tertiary Care Hospital in Pakistan.

Study Design: Cross-sectional study.

Place and Duration of Study: Pathology Department of the Armed Forces Institute of Pathology, Rawalpindi Pakistan, from Mar to Aug 2021.

Methodology: A total of 183 patients fulfilling the selection criteria were enrolled after taking written informed consent, and investigations to assess haematological parameters were carried out, such as the complete blood count, PT, APTT, and D-Dimers. The severity of the illness was determined according to the criteria set, and findings were recorded and subjected to statistical analysis.

Results: The mean age of the patients was 34.5410.12 years. Using blood tests, there was a strong link between the severity of the COVID-19 infection and the total WBC count (p=0.041), PCV (p=0.05), neutrophil count (p=0.02), lymphocyte count (p=0.001), eosinophil count (p=0.001), and D-Dimers (p=0.001).

Conclusion: Total WBC count, neutrophil, lymphocyte, eosinophil, and eosinophil count, as well as D-Dimers, were all strongly linked to how bad the condition was and can be used to predict how bad a COVID-19 infection will be early on.

Keywords: COVID-19, Haematological parameters, Total WBC count.

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INTRODUCTION

A global pandemic developed from a coronavirus disease (COVID) causes severe Acute Respiratory Distress Syndrome (ARDS).[1] Although it was primarily diagnosed as a respiratory tract infection, new research shows that COVID-19 can cause a wide range of clinical symptoms, including mild to moderate upper respiratory tract infections and severe systemic diseases that affect the immune, gastrointestinal, cardiovascular, neurological, and hematopoietic systems in addition to the respiratory system.[2]

Patients with clinical symptoms frequently develop pneumonia and exhibit radiographic signs of parenchymal disease.[3] Around 80.9% of patients have mild symptoms, 13.8% have severe symptoms, and 4.7% have critical disease.[4] Patients admitted to critical care units had high plasma levels of pro-inflammatory cytokines such as interleukins and tumour necrosis factor, suggesting that those with severe disease may suffer a cytokine storm impact. It is important to recognise COVID-19 and determine the severity of the condition as soon as possible, since patients may have ARDS immediately after the start of the illness.[5]

The severity of pneumonia secondary to COVID-19 and haematological abnormalities in such patients are linked by multiple echanisms.[6] In COVID-19, haematological abnormalities are associated with disease severity, mortality, and disease progression.[7] Patients with COVID-19 have a very well-documented history of thrombocytopenia, an abnormal coagulation profile, lymphopenia, and sepsis that results in disseminated intravascular coagulation (DIC).[8] In the intensive care unit, platelet count, a straightforward and easily accessible haematological parameter, correlates independently with the severity of the disease and also relates to the risk of mortality.[8] COVID-19 has been linked to coagulopathies including arterial thrombotic problems, thrombo-inflammation, venous thromboembolism (VTE), local microthrombi, and sepsis-induced coagulopathy

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(SIC).[9] As this pandemic develops, it is important to constantly monitor any haematological symptoms caused by this specific virus.[10]

These blood and inflammation markers, like the complete blood count, D-dimer, coagulation profile, ferritin, and C-reactive protein, can help a lot in figuring out how bad a disease is early on. They can also help doctors treat patients more quickly, which can lower the number of people who get sick or die from the disease. Therefore, the current study aimed to determine the comparison between haematological parameters and clinical disease severity in patients with COVID-19 infection at a tertiary care hospital in Pakistan.

METHODOLOGY

The cross-sectional study was carried out at the Armed Forces Institute of Pathology, Rawalpindi, Pakistan from April to September 2022, after receiving approval from the Ethical Review Committee (IRB/22/873 dated 01-Mar-2022).The sample size of was calculated taking the expected frequency of severe COVID-19 infection in patients as 13.8%3. The non-probability consecutive sampling technique was used.

Inclusion Criteria: Patients, aged 18 to 70 years, of either gender, who were confirmed to have COVID-19 infection through a Real Real-time reverse transcriptase Polymerase Chain Reaction (RT-PCR) test (conducted on a nasopharynx smear) were included.

Exclusion Criteria: Patients who had chronic liver disease or any haematological disorder were excluded.

The study included 183 patients; patients' clinical characteristics were divided into four categories: mild, moderate, severe, and critical. Fever, a sore throat, a cough, and the absence of a consolidation patch on X-rays were regarded as signs of a mild infection. A moderate infection was indicated by a fever, respiratory symptoms, and an oxygen saturation of <93% with less than 50% involvement of the lung on radiological imaging. Patients with respiratory distress (breathing rate above 30 bpm, oxygen saturation below 93%, and greater than 50% lung infiltration) were classified as having severe disease, whereas patients with respiratory failure necessitating mechanical ventilation, shock, or other organ failure were classified as having a critical infection.[11,12]

After receiving written informed consent from all patients who fulfilled the selection criteria, participants were enrolled in the study. A thorough patient history and clinical examination of all participants were done, and findings were noted down on a proforma. Safety measures as given by the World Health Organisation (WHO) were followed for assessing every patient with a COVID-19 infection. To check the levels of different blood components, tests were done, including a full blood count to find out the amount of haemoglobin, total white blood cells, red blood cells, and platelets, as well as the mean corpuscular volume (MCV), packed cell volume (PCV), and coagulation profile to find out the prothrombin time (PT), activated partial thrombin time (APTT), and D-dimer levels. The severity of the illness was determined according to the criteria set, and findings were noted on the proforma and subjected to statistical analysis.

The data was analysed through the Statistical Package for Social Sciences (SPSS) version 25.0. Quantitative data was presented as mean and standard deviation. Qualitative data was presented as frequencies and percentages. We used the Analysis of Variance (ANOVA) test and the chi square test for inferential statistics. The *p*-value of ≤ 0.05 was considered statistically significant.

RESULTS

A total of 183 patients were enrolled. The patients' average age was 34.5410.12, their average WBC count was 5.91.89 x 109/L, their average RBC count was 5.20.53 million/mm3, their average haemoglobin level was 15.491.64 g/dl, their average PCV was 42.683.88%, their average MCV was 81.037.78 femtoliter, their average MCH was 29.612.45 picograms, and their average MCHC was 35.812.27 grams/decilitre (Table-I).

There were 174(95.1%) males and 9(4.9%) females in the study. In 123(67.2%) patients, the D-Dimer value was 200, and in 60(32.8%), it was >200. In terms of clinical features, low-grade fever was seen in 50(27.3%) patients, moderate fever was seen in 99(54.1%) patients, and high-grade fever was present in 34(18.6%) patients. Mild disease was present in 123(67.2%) patients, moderate disease was seen in 37(20.2%) patients, severe disease was seen in 18(9.8%) patients, and critical disease was present in 5(2.7%) patients (Table-II). In terms of ongoing blood tests, there was a strong link between the total leucocyte count (p=0.041), PCV (p=0.05), neutrophil count (p=0.02), lymphocyte count (p<0.001), and eosinophil count (p<0.001) (Table-III). Furthermore, a statistically significant correlation was seen between D-Dimers

and the clinical severity of COVID-19 (p<0.001) (Table-IV).

Table-I: Descriptive Statistics of Quantitative Variables (n=183)

Variables	Mean±Standard deviation
Age (in year)	34.54±10.12
Total WBC count (x109/L)	5.9±1.89
RBC count (million/mm3)	5.2±0.53
Hemoglobin (g/dl)	15.49±1.65
PCV (%)	42.68±3.88
MCV (femtoliter)	81.03±7.78
MCH (picograms)	29.62±2.45
MCHC (grams/deciliter)	35.82±2.27
Platelet count (platelets per microliter)	201.78±60.51
Neutrophil (%)	56.49±10.30
Lymphocyte (%)	36.84±10.02
Monocyte (%)	3.59±1.24
Eosinophil (%)	2.81±0.98
PT (seconds)	14.14±0.59
APTT (seconds)	33.80±5.88

DISCUSSION

Haematological parameters from this study showed a strong link between the severity of the disease and the total WBC count (p=0.041), PCV (p=0.05), neutrophil count (p=0.02), lymphocyte count (p<0.001), eosinophil count (< 0.001), and D-Dimers (p<0.001). The majority of the patients in our study were males, had mild disease, and did not have lung involvement.

The majority of COVID-19 infections have mild to moderate symptoms, and those who receive the right medical care recover quickly.[11, 12] The majority of COVID-19 patients' primary cause of death is ARDS.[13] The cytokine storm, a fatal and uncontrolled systemic inflammatory reaction brought on by the production of large amounts of proinflammatory cytokines, is one of the main causes of ARDS.[14] When a patient has a more severe clinical course, the haematological parameters are typically more noticeable and severe.[15]

In our study, all patients had a mean hemoglobin level within the normal range. Past studies have revealed no correlation between haemoglobin levels and the severity of COVID-19 infection, a finding that our study also supports. Most individuals with bacterial or viral infections have raised WBCs, which is a typical bodily reaction to systemic infection.16,17 In our patients, the WBC count was within the normal range; however, it was seen that with increasing severity of infection, there was an associated increase in the mean value of WBC, and this was statistically significant. Similar findings were revealed by Ahmed *et al*.[18]

Table-II: Frequency Distribution of Qualitative variables (n=183)

Variables	n (%)
D-Dimers:	
≤200	123(67.2%)
>200	60(32.8%)
Fever grade:	
Low grade (up to 1000F)	50(27.3%)
Moderate grade (>100 to 1030F)	99(54.1%)
High grade (>1030F)	34(18.6%)
Cough:	
Yes	135(73.8%)
No	48(26.2%)
Type of cough:	
Productive	50(27.4%)
Non-productive	85(46.4%)
Body Aches:	
Yes	171(93.4%)
No	12(6.6%)
Nausea:	
Yes	33(18%)
No	15(82%)
Headache:	
Yes	102(55.7%)
No	81(44.3%)
Anosmia:	
Yes	27(14.8%)
No	156(85.2%)
Loss of taste:	
Yes	27(14.8%)
No	156(85.2%)
Weakness:	
Yes	165(90.2%)
No	18(9.8%)
Loose motion:	
Yes	14(7.7%)
No	169(92.3%)
Oxygen saturation <93%	
Yes	50(27.3%)
No	133(72.7%)
Degree of lung involvement:	
No involvement	123(67.2%)
≤50% involvement	37(20.2%)
>50% involvement	23(12.6%)
Severity of disease:	
Mild	123(67.2%)
Moderate	37(20.2%)
Severe	18(9.8%)
Critical	5(2.7%)

In terms of differential count, our study revealed that there was a significant increase in the neutrophil

Table-III: Comparison of Hematological Parameters with Clinical Severity of COVID-19 Infection (n=183)

Hematological parameters	Mild disease n=123	Moderate disease n=37	Severe disease n=18	Critical disease n=5	*p* - value
	Mean±Standard deviation				
Total WBC count (x109/L)	5.84±1.82	5.64±1.91	6.47±1.89	7.94±2.89	0.041
RBC count (million/mm3)	5.27±0.54	5.09±0.48	5.12±0.44	5.34±0.64	0.264
Hemoglobin (g/dl)	15.55±1.67	14.97±1.45	16.05±1.31	15.4±2.74	0.105
PCV	0.43±0.04	0.41±0.03	0.43±0.03	0.43±0.05	0.052
MCV (femtoliter)	80.91±8.66	80.41±5.91	83.28±5.32	80.60±2.7	0.622
MCH (picograms)	9.59±2.51	29.09±2.65	30.92±0.91	29.40±2.15	0.075
MCHC (grams/deciliter)	35.73±2.25	35.83±2.26	36.35±2.31	35.92±3.21	0.763
Platelet count (platelets per microliter)	200.28±58.53	214.59±70.77	183.50±52.70	210.00±45.65	0.326
Neutrophils (%)	55.89±9.77	54.94±10.2	59.27±10.8	72.60±9.96	0.002
Lymphocytes (%)	37.83±9.13	38.86±10.31	30.33±10.5	20.80±4.87	< 0.001
Monocytes (%)	3.68±1.28	3.54±1.21	3.27±1.01	2.80±0.45	0.269
Eosinophils (%)	2.76±0.89	2.54±0.77	3.44±1.14	4.20±1.78	< 0.001
PT (seconds)	14.17±0.66	14.08±0.36	14.11±0.47	14.00±0.58	0.794
APTT (seconds)	33.94±4.82	34.35±9.67	32.22±0.65	32.00±0.05	0.543

Table-IV: Association of D-Dimers with Clinical Severity of COVID-19 Infection (n=183)

Hematological Parameter	Mild disease (n=123)	Moderate disease (n=37)	Severe disease (n=18)	Critical disease (n=05)	*p*-value
	Frequency (percentage)				
D-Dimer					
≤200	123(67.2%)	0(0%)	0(0%)	0(0%)	
>200	0(0%)	37(20.2%)	18(9.8%)	5(2.7%)	

and eosinophil count with increasing severity of infection and a significant decline in the lymphocyte count in patients with increasing severity. Ahmed *et al*.[18] revealed that there was a significant increase in the neutrophil count and a decrease in lymphocyte count with increasing infection severity. However, in the study by Ahmed *et al*.[18] monocytes and disease severity correlated significantly; however, in our study, no significant correlation could be elicited.

In terms of D-Dimers, the correlation between severity of infection and the levels of D-Dimers was statistically significant in our study, i.e., lesser levels were seen in mild infection and higher levels were seen in individuals with moderate to critical COVID-19 infection. These findings are similarly supported by the studies by Taj *et al*.[2] and Islam *et al*.[4]

LIMITATIONS OF STUDY

There were certain limitations to the study. The correlation of haematological parameters in asymptomatic patients was not assessed, and it cannot be commented on if such parameters were also deranged in those without any symptoms.

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CONCLUSIONS

The current study concluded that total WBC count, neutrophil, lymphocyte, and eosinophil count, and D-dimer count correlated significantly with the severity of the condition and can be used as a predictor of early detection of the severity of infection and prompt treatment in patients with COVID-19 infection.

Conflict of Interest: None.

Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

IA & HMR: Data acquisition, data analysis, drafting the manuscript, critical review, approval of the final version to be published.

KA & NAR: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

SI & MS: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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