Haematological Profiles of Patients Suffering from Severe and Non-Severe COVID-19 infection

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Abstract

Background: The current COVID-19 pandemic has had devastating effects on the lives of people all over the globe. Thus, it is important to identify differences between the severity levels of the disease to understand pathophysiology better and therefore, come up with more efficient ways to diagnose and combat it. The objective of this study is to analyze the hematological profile of non-severe & severe patients at the time of presentation in tertiary health care set up and identify any differences between them.

Material and Methods: A comparative retrospective study was carried out among patients visiting the Infectious Diseases Department at Holy Family Hospital, Rawalpindi through systematic random sampling. The self-structured questionnaire consisted of 1) Sociodemographic details and 2) Hematological profile (samples taken at the time of admission). The hematological profile consisted of hemoglobin (Hb), white blood cell count (WBCs), platelets (PLT), neutrophils, prothrombin time (PT), and activated partial thromboplastin time (APTT). Continuous variables were compared by the Mann–Whitney U test and enumeration variables were compared by Pearson χ² or Fisher exact test, where appropriate.

Results: Out of 106 patients, 58 (54.7%) were non-severe while 48 (45.3%) were severe at the time of presentation. In our study, there was a lower level of platelets and consequently, more thrombocytopenia in severe patients comparatively. A significantly longer PT time was also observed in severe patients. Our results showed a marked difference in the levels of hemoglobin between the two groups, along with an increased incidence of neutrophilia in patients with severe outcomes.

Conclusion: Thrombocytopenia, neutrophilia, and falling hemoglobin levels are the hematological factors that differ significantly between severe and non-severe forms of the disease.

Keywords: Blood platelets, COVID-19, neutrophils, leukocyte count, partial thromboplastin time, prothrombin time, thrombocytopenia.
Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), causing coronavirus disease 2019 (COVID-19) has rapidly evolved from an epidemic outbreak in the food market of Wuhan, China. On January 30, 2020, the World Health Organization (WHO) declared COVID-19 outbreak as the sixth public health emergency of international concern (PHEIC) and a pandemic on March 11, 2020. Although it is a well-established fact that COVID-19 is primarily manifested as a respiratory tract infection, emerging data and studies indicate that it should be regarded as a systemic disease involving multiple systems, including cardiovascular, respiratory, gastrointestinal, neurological, hematopoietic and immune system. The early phase of this disease was found to have marked lymphopenia, involving a dramatic loss of CD4+ T and CD8+ T cells. Several studies on SARS-CoV-2 infection have investigated the correlation between abnormalities on laboratory indices including leukocytes, lymphocytes, and eosinophils counts, serum inflammatory cytokine levels, and the severity or mortality of the diseases. Studies from China have shown various changes in blood cell counts. 83.2% of patients presented with lymphocytopenia, 36.2% with thrombocytopenia, and 33.7% with leucopenia. In contrast, a study in Singapore showed only 36.9% of patients with lymphopenia, 29.2% of patients with leukopenia, and 20% with mild thrombocytopenia on admission. Aggravation of lymphopenia correlated with disease severity. Increased neutrophil count, and increase neutrophil-to-lymphocyte ratio, and decreased hemoglobin levels have been identified as risk factors for the severe illness of SARS-CoV-2 infection.

The current COVID-19 pandemic has had devastating effects on the lives of people all over the globe. Although most of those affected remain asymptomatic or show mild symptoms, the disease can progress rapidly to manifest severe complications and even death. As Pakistan is a third world country, identification of any possible factor that may lead to better understanding of disease, management of resources and prompt provision of health care is invaluable in the current healthcare setup.

Thus, the objective of our study is to compare the hematological profile of the patients suffering from severe and non-severe disease, and identify possible factors that can be further investigated as potential risk factors for developing severe SARS-CoV-2 infection.

Materials and Methods

Ethical Statement

Approval to carry out the study was given by the ethics and research committee of Rawalpindi Medical University. The confidentiality and anonymity of all participants were fully maintained. The participants’ personal information (names, identity numbers, and addresses) were not collected.

Study Design

A comparative retrospective study was conducted from April 2020 to June 2020. The study was carried out among patients visiting the Infectious Diseases Department at Holy Family Hospital, Rawalpindi. Systematic sampling was done where data were collected from every fourth patient who was diagnosed with COVID-19. A self-structured questionnaire was used which consisted of sociodemographic details and hematological profile (samples taken at the time of admission) of the patients. The hematological profile consisted of hemoglobin (Hb), white blood cell count (WBCs), platelets (PLT), neutrophils, prothrombin time (PT), and activated partial thromboplastin time (APTT). Only confirmed COVID-19 patients, through laboratory testing (PCR) and chest X-ray findings, were included in this study.

When COVID-19 disease was suspected by WHO, its severity was defined according to the degree clinical management required for acute respiratory infection. Patients with COVID-19 are considered to have severe illness if they have fever or suspected respiratory infection, plus one of the following: respiratory rate >30 breaths/min; severe respiratory distress; or pulse oximeter oxygen saturation ≤ 93% on room air. Non-severe patient represent patients except for the above conditions.

Data Collection

The data was collected from notes taken by doctors and nurses of patients admitted at the department of infectious diseases, Holy Family Hospital, Pakistan.

Statistical Analysis

Continuous variables were described as mean (standard deviation) and median (interquartile range), while categorical variables were presented as counts (frequencies and percentages). Sociodemographic characteristics were described in terms of frequencies and percentages. Continuous variables were
compared by the Mann–Whitney U test and enumeration variables were compared by Pearson χ² or Fisher exact test, where appropriate. A two-tailed p < .05 was considered statistically significant. The analysis was carried out using the Statistical Package for Social Sciences (SPSS) v.23.0 (IBM, Armonk, US).

**Results**

In our study of 106 patients, the mean age is 45 years (SD=18.68) with the majority 31 (38.27%) lying in the 41 to 60 years old age group. Out of 106 patients, fifty-eight (54.7%) were non-severe while 48 (45.3%) were severe at the time of presentation. The mean duration between onset of symptoms and appearing at the hospital for non-severe and severe patients was 2 (SD=2.50) days and 6 (SD=4.99) days, respectively. Eleven patients (13.6%) were referred from other hospitals in Rawalpindi and Islamabad. Table 1 shows details of the patient's profile.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total (N=106)</th>
<th>Status Non-severe (N=58)</th>
<th>Status Severe (N=48)</th>
<th>P-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>74 (69.8)</td>
<td>42 (72.4)</td>
<td>32 (66.7)</td>
<td>0.521</td>
</tr>
<tr>
<td>Females</td>
<td>32 (30.2)</td>
<td>16 (27.6)</td>
<td>16 (33.3)</td>
<td></td>
</tr>
<tr>
<td>Contact History</td>
<td></td>
<td></td>
<td></td>
<td>0.287</td>
</tr>
<tr>
<td>Yes</td>
<td>80 (75.5)</td>
<td>44 (75.9)</td>
<td>36 (75)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>13 (12.3)</td>
<td>6 (10.3)</td>
<td>4 (8.3)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>13 (12.3)</td>
<td>8 (13.8)</td>
<td>8 (16.7)</td>
<td></td>
</tr>
<tr>
<td>Travelling History</td>
<td></td>
<td></td>
<td></td>
<td>0.764</td>
</tr>
<tr>
<td>Yes</td>
<td>28 (26.4)</td>
<td>16 (27.6)</td>
<td>12 (25)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>78 (73.6)</td>
<td>42 (72.4)</td>
<td>36 (75)</td>
<td></td>
</tr>
<tr>
<td>Hospital visit within the last 14 days</td>
<td></td>
<td></td>
<td></td>
<td>0.337</td>
</tr>
<tr>
<td>Yes</td>
<td>18 (17)</td>
<td>8 (13.8)</td>
<td>10 (20.9)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>88 (83)</td>
<td>50 (86.2)</td>
<td>38 (79.1)</td>
<td></td>
</tr>
</tbody>
</table>

*Note:* *P*<0.05

Haematological profile:
Table 2 shows the hematological findings of COVID-19 patients taken at the time of the presentation.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total (n=106)</td>
</tr>
<tr>
<td>WBCs (× 10⁹/L)</td>
<td>Median (IQR)</td>
</tr>
<tr>
<td>7.08 (5.51-9.06)</td>
<td>7.065 (5.80-9.00)</td>
</tr>
<tr>
<td>Leukocytosis (&gt;9.5x10⁹/L), n (%)</td>
<td>18 (16.98%)</td>
</tr>
<tr>
<td>Hemoglobin (g/L)</td>
<td>14.4 (12.93-15.10)</td>
</tr>
</tbody>
</table>
In this study, we have come across some commonly assessed hematological factors, such as thrombocytopenia, neutrophilia and declining hemoglobin levels, that can guide us about the level of severity the disease will achieve in the particular individual. The first finding of note is the median number of days between the onset of symptoms and the presentation at the hospital. Our results showed that those in the severe condition presented very late after the initial onset of symptoms which suggests that the people seeking help early on in the course of the disease show considerably less dangerous outcomes than those who wait for the situation to get worse. This also highlights the importance of quick diagnosis and prompt provision of care in the control and subsequent treatment of COVID-19. A study by Cheng et al. similarly shows that the time between the onset of symptoms and admission was higher for those who suffered from severe respiratory distress.13 One of the main findings in our study was thrombocytopenia in severe cases. A meta-analysis study by Terpos et al. has suggested that thrombocytopenia is significantly associated with the severity of the COVID-19 disease. Most of the severe cases 90/156 (57.7%) presented with a platelet count of less than 150,000/mm3 (thrombocytopenia) as compared to non-severe cases, where only 225/713 (31.6%) have thrombocytopenia (P < .001).11 A review article by Liu et al. also shows more severe thrombocytopenia and elevated PT in severe patients compared to non-severe patients (p < 0.001). Thrombocytopenia was present in 57.7% of severe cases and 31.6% of non-severe cases, (31.6%), and the median platelet count in severe type was markedly lower 137.5 (IQR 99.0-179.5) ×109/L than that in non-severe type 172.0 (IQR 139.0-212.0) ×109/L, (p < 0.001).12 A study from Cheng et al., however, showed increased platelets in patients suffering from pneumonia and COVID-19 (median =209.20×109 cells/L) as compared to just COVID-19 alone (median = 143.50×109 cells/L).13 Our results also show an increased incidence of neutrophilia in patients with severe outcomes. The study by Wu et al. confirmed that neutrophilia was associated with an increased risk of both developments of ARDS and death.14 Activation of neutrophils to generate an immune response to fight the virus is a possible explanation for this finding.12 Finally, our results also showed a marked difference in the levels of hemoglobin between the two groups, i.e., 14.85 mg/dL in non-severe patients compared to 13.80 mg/dL in severe patients. The study by Guan et al. also shows a considerable difference in the hemoglobin levels between the severe (median = 12.8 mg/dL) and non-severe (median = 13.5 mg/dL) groups.15 On the other hand, Huang et al. found no marked difference in the fall of hemoglobin between severe and non-severe patients.16 Liu et al. state the possibility that the decrease in hemoglobin could be due to disruption of erythropoiesis, which in turn is
caused due to the inflammatory changes brought about by the virus. Based on the studies they reviewed, they also suggest using reduced hemoglobin levels as a marker for disease progression. This study shows the reliability of some hematological markers in the local setting that were previously identified on an international level. They might serve as quick, inexpensive ways to identify possible patients who may require critical care.

This is a retrospective study, and thus, contains all of the inherent drawbacks of this study design. In addition to this, the analysis has not been adjusted for multiple comparisons. Hence, given the potential for type 1 error, and as the study can not be generalized, it should be interpreted as a simple descriptive study. However, this study may be a stepping stone for further, more extensive studies that might explore this avenue in a detailed manner.

Further longitudinal studies must be done to confirm whether these factors are potential risk factors for the severity of disease or whether the severe infection itself causes these changes.

Conclusion

Thrombocytopenia, neutrophilia, and falling hemoglobin levels are the hematological factors that differed significantly between the two groups. In addition to this, the time between the onset of symptoms and presentation at the hospital is also important.

References