White Blood Cell Profile among Different Clinical Stages of COVID-19 Patients

Khushbun Nahar Layla, Shahanara Yeasmin, Sharif Ahmed Khan, Khyrun Nahar Shaila, Afrina Binte Azad, Rahnuma Ahmad and Samina Rahman

ABSTRACT
Coronavirus is affecting millions of people world-wide. Coronavirus disease 2019 (COVID-19) is declared a pandemic by WHO. Severe acute respiratory syndrome corona virus 2(SARS-CoV-2) is the causative agent. The clinical presentations of SARS-CoV-2 infection range from febrile illness to pneumonia, ARDS and multi organ failures. Increasing scientific evidences have shown that abnormalities in routine laboratory test, particularly haematological parameters influence the outcome of the disease. Here variations in WBC profile in several clinical forms of COVID-19 patients are observed, The clinical course of the disease may change with haematological parameters such as lower total count of WBC, lymphocyte, higher neutrophil count, eosinophil count etc.

By investigating haematological parameters of different clinical stage of RT-PCR positive 100 COVID-19 patients, statistically significant association (p value 0.001) of lymphocyte count with disease severity was found. It is also found that higher level of total count WBC, neutrophil count in severe group in comparison to mild and moderate groups but failed to reach any statistical significance. Moreover total count WBC and neutrophil count showed positive correlations but lymphocyte count, eosinophil count and monocyte count showed negative correlation with severity of disease. So, complete analysis of the haematological parameters will be very much helpful for early detection of complications & better control of the disease.

Keywords: COVID-19, SARS-C0-V-2, RT-PCR, WBC.

I. INTRODUCTION
Coronavirus belongs to the Coronaviridae family. It is a zoonotic RNA envelope virus. This virus has a pleomorphic or spherical shape with glycoprotein in the viral envelope. World Health Organization (WHO) declared novel corona virus-2 (SARS-Cov-2) on February 12, 2020. The pneumonia caused by novel coronavirus was named COVID-19. The third corona virus identified is the novel Corona virus (SARS-CoV-2) that causes pneumonia (COVID-19) which first broke in China in December 2019 [1].

Currently the pandemic COVID-19 is leading to millions of infections and thousands of deaths worldwide [2],[3]. Recently, more than 4 million people have been infected and about 300,000 have died due to coronavirus infection [4].

First case of COVID-19 was identified in Bangladesh on 8th March 2020 [5].

Coronavirus first affects the respiratory epithelium though angiotensin converting enzyme 2 (ACE2) [2], [6]. The main mechanism for organ damage and inflammation is cytokines storm, especially in endothelial cells of pulmonary vessels with increased inflammatory cytokines such as macrophage chemo attractant protein-1, interleukin-1, 6, 10 and 12 [7]. This virus initially undergoes viral replication in the respiratory tract. Then spread to other organs. At the bone marrow level, the virus causes cellular death and resulting in lowering formation of blood cells [8]-[10].

The presence of circulating viral particles induces the activations of neutrophils and macrophages and leads to
production of pro-inflammatory substances like cytokines. These cytokines act on bone marrow, responsible for inactivation of thrombocyte, leukocytes and other components [9]. These inflammations cause changes in the function of several organs, leading to several changes in haematological parameters among different clinical stages of COVID-19 patients [11], [12]. COVID-19 has been shown to exert significant effects on the hematopoietic system.

II. METHODS & MATERIALS

A. Study Design
Cross-sectional study

B. Study Population
Total 100 RT-PCR positive COVID-19 patients.

C. Inclusion Criteria
- COVID-19 patients evidenced by positive RT-PCR
- Age: 18 – 65 years
- Gender: Male & Female
- Ethnicity: Bengali

D. Exclusion Criteria
- RT-PCR positive but critically ill COVID-19 patients
- RT-PCR negative COVID-19 patients
- Known case of malignancy, hepatic & renal diseases.
- Pregnant and lactating mother

E. Ethical Clearance
Approved by the director and ethical committee of Dhaka Medical & Health Sciences College & hospital, Dhaka.

F. Data analysis
All the parameters were implied as mean ± SD and range. Kruskal-Wallis test & ANOVA followed by Bonferroni test were performed to compare between groups. p value <0.05 was taken as level of significance. Statistical analysis was performed by SPSS (Statistical Package for Social Science) version 25.0.

III. RESULT

TABLE I: DEMOGRAPHIC PROFILE AMONG DIFFERENT CLINICAL STAGES OF COVID19 PATIENTS (N=100)

<table>
<thead>
<tr>
<th></th>
<th>Mild (n=25)</th>
<th>Moderate (n=38)</th>
<th>Severe (n=37)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 30</td>
<td>7 (28.0)</td>
<td>3 (7.9)</td>
<td>7 (18.9)</td>
<td></td>
</tr>
<tr>
<td>31 – 40</td>
<td>7 (28.0)</td>
<td>11 (28.9)</td>
<td>8 (21.6)</td>
<td></td>
</tr>
<tr>
<td>41 – 50</td>
<td>3 (12.0)</td>
<td>9 (23.7)</td>
<td>6 (16.2)</td>
<td></td>
</tr>
<tr>
<td>51 – 60</td>
<td>7 (28.0)</td>
<td>9 (23.7)</td>
<td>12 (32.4)</td>
<td></td>
</tr>
<tr>
<td>&gt;60</td>
<td>1 (4.0)</td>
<td>6 (15.8)</td>
<td>4 (10.8)</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD (Range)</td>
<td>41.52±13.48</td>
<td>47.32±12.10</td>
<td>45.24±13.97</td>
<td>0.236a</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>18 (72.0)</td>
<td>26 (68.4)</td>
<td>23 (62.2)</td>
<td>0.702b</td>
</tr>
<tr>
<td>Female</td>
<td>7 (28.0)</td>
<td>12 (31.6)</td>
<td>14 (37.8)</td>
<td></td>
</tr>
</tbody>
</table>

N= Total number of subjects, *p value reached from ANOVA test, **p value reached from chi squared test.

TABLE II: WBC FINDINGS IN DIFFERENT CLINICAL STAGES OF COVID19 PATIENTS (N=100)

<table>
<thead>
<tr>
<th></th>
<th>Mild (n=25)</th>
<th>Moderate (n=38)</th>
<th>Severe (n=37)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC (k/cumm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(4.34-11.97)</td>
<td>(8.26-15.2)</td>
<td>(6.80-14.93)</td>
<td>0.085a</td>
<td></td>
</tr>
<tr>
<td>Neutrophils (%)</td>
<td>72.52 ± 13.02</td>
<td>11.31 ± 11.17</td>
<td>56.4-96 (9.93-4)</td>
<td>0.089a</td>
</tr>
<tr>
<td>Lymphocytes (%)</td>
<td>23.01 ± 11.64</td>
<td>17.33 ± 10.70</td>
<td>11.87 ± 7.86</td>
<td>&lt;0.001a</td>
</tr>
<tr>
<td>Monocytes (%)</td>
<td>2.90 ± 2.29</td>
<td>2.89 ± 3.73</td>
<td>2.88 ± 2.33</td>
<td>1.000a</td>
</tr>
<tr>
<td>Eosinophils (%)</td>
<td>1.81 ± 1.92</td>
<td>0.96 ± 0.92</td>
<td>1.48 ± 1.54</td>
<td></td>
</tr>
</tbody>
</table>

a: p value achieved from chi squared test
b: p value achieved from Kruskal-Wallis test & results were expressed as Mean ± SD

TABLE III: DISTRIBUTION COUNT AMONG WBC COUNT IN DIFFERENT CLINICAL STAGES OF COVID19 PATIENTS (N=100)

<table>
<thead>
<tr>
<th></th>
<th>Mild (n=25)</th>
<th>Moderate (n=38)</th>
<th>Severe (n=37)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukopenia (&lt;4,000)</td>
<td>6 (24)</td>
<td>3 (7.9)</td>
<td>6 (16.2)</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WBC (&gt;11,000)</td>
<td>12 (48)</td>
<td>14 (36.8)</td>
<td>17 (45.9)</td>
<td>0.19</td>
</tr>
<tr>
<td>Leukocytosis (&gt;11,000)</td>
<td>7 (28)</td>
<td>14 (55.3)</td>
<td>21 (37.8)</td>
<td></td>
</tr>
</tbody>
</table>

p value achieved from chi squared test

TABLE IV CORRELATION OF WBC PARAMETERS WITH DIFFERENT CLINICAL STAGES OF COVID-19 PATIENTS

<table>
<thead>
<tr>
<th></th>
<th>r value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total count of WBC</td>
<td>+0.083</td>
<td>0.410</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>+0.074</td>
<td>0.467</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>-0.385</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Monocytes</td>
<td>-0.017</td>
<td>0.869</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>-0.015</td>
<td>0.882</td>
</tr>
</tbody>
</table>

Spearman’s correlation coefficient (r) test was done to see WBC finding in different clinical stages of disease. Finding shows statistically significant (p-value<0.05) negative correlation with lymphocytes count.
IV. DISCUSSION

This study was carried out to evaluate the findings of haematological parameters of different clinical stages of COVID-19 patients. For this purpose, a total 100 number of RT-PCR positive COVID-19 patients with age ranging from 18 to 65 years were included in this study. In this study, the number of mild, moderate and severe COVID-19 cases were 25, 38 and 37 respectively. Based on COVID-19 interim guidance by World Health Organization [14], the cases were categorized as mild, moderate and severe COVID-19 cases.

WBC profiles were done to assess the haematological changes. Moreover, correlations of all above mentioned haematological parameters were done to observe the relationship among different clinical stages of COVID-19 patients. In this study, the mean total count of WBC, differential count of neutrophil, eosinophil and monocyte were not statistically significant. But lymphocyte count was statistically significant. Similar types of observations were found by some scholar [5], [15]-[17]. On the contrary, [18] found statistically significant raised neutrophil, total count of WBC. [19] also found higher WBC count, neutrophil and eosinophil count. In the present study, the range of total count of WBC and neutrophil were very high, similar types observations were found by [15]. It is probably due to associated secondary bacterial infections.

There are few advanced mechanisms recommended by various investigators. They suggest some possible mechanisms regarding haematological changes of COVID-19 patients. COVID-19 induces cytokine storm that produces a chain of immune responses that is responsible for changes in different peripheral leukocytes such as lymphocytes [17], [20]. Lymphopenia and leucopenia in COVID-19 result in part from the effect of the inflammatory cascade and viral activity at the bone marrow level. It may occur due to cytokine storm syndrome. Coronavirus can direct attack the lymphocytes and devastation of lymphoid organs [21].

The prevalence of lymphopenia found in COVID-19 indicate that COVID-19 might act on lymphocytes, mainly T lymphocytes, as SARS-CoV-2 may causes reduction of CD4 and CD8 cells. [15]. Lymphopenia is one of the routine findings in viral infection. In a different study in China, among 1,099 patient’s lymphopenia was present in 83.2% of COVID-19 patients [22]. Lymphopenia was commonly seen in hospitalized COVID-19 patients and has a correlation to different clinical stages of COVID-19 and might have a prognostic value in hospitalized patients [21]. SARS-CoV-2 invades lymphocytes, proliferates within cell and causes the lymphocytes to cease or become declined when they reach the immune organs especially in the spleen. Lymphopenia has been revealed by many articles [15], [21]-[23].

Our study had some limitations, Samples were taken purposively so that there may be chance of bias which can influence the results. Blood tests were not done in specific time of natural history of illness of the study subjects.

V. CONCLUSION

This study showed that low lymphocyte count was more common in severe COVID-19 group than other two groups. Thus, complete and extensive analysis of the haematological parameters in COVID-19 patients can provide valuable information for the clinicians so that they can predict the prognosis of the disease and manage the patients with success.

REFERENCES


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