Peripheral Blood Smear Findings of COVID-19 Patients Provide Information about the Severity of the Disease and the Duration of Hospital Stay

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Abstract. Background: Data about the morphological changes in peripheral blood smears during COVID-19 infection and their clinical severity association are limited. We aimed to examine the characteristics of the cells detected in the pathological rate and/or appearance and whether these findings are related to the clinical course by evaluating the peripheral blood smear at the time of diagnosis in COVID-19 patients.

Methods: Clinical features, laboratory data, peripheral blood smear of fifty patients diagnosed with COVID-19 by PCR was evaluated at diagnosis. Peripheral smear samples of the patients were compared with the age and sex-matched 30 healthy controls. Pictures were taken from the patient's peripheral blood smear. Patients were divided into two groups. Mild and severe stage patient groups were compared in terms of laboratory data and peripheral smear findings. The relationship between the laboratory values of all patients and the duration of hospitalization was analyzed.

Results: The number of segmented neutrophils and eosinophils were low, pseudo-Pelger-Huet, pseudo-Pelger-Huet/mature lymphocyte ratio, atypical lymphocytes, monocytes with vacuoles, bands, and pyknotic neutrophils rates were higher in the peripheral blood smear of the patient group (p <0.05). Increased pseudo-Pelger-Huet anomaly, pseudo-Pelger Huet/mature lymphocyte ratio, a decreased number of mature lymphocytes, and eosinophils in peripheral blood smear were observed in the severe stage patients (p <0.05). A negative correlation was observed between hospitalization duration and mature lymphocyte and monocytes with vacuoles rates (p <0.05).

Conclusion: A peripheral blood smear is an inexpensive, easily performed, and rapid test. Increased Pseudo-Pelger-Huet anomaly/mature lymphocyte rate suggests a severe stage disease, while high initial mature lymphocyte and monocytes with vacuoles rates at the time of diagnosis may be an indicator of shortened duration of hospitalization.

Keywords: Pseudo-Pelger Huet anomaly; Mature lymphocytes; Monocytes with vacuoles; Severe COVID-19.

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Introduction. Coronaviruses (CoV) are a large family of viruses that cause diseases in a broad clinical spectrum, from mild common flu infection to Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV-1). The new coronavirus disease was first identified as a result of research in a group of patients who developed respiratory tract symptoms such as fever, cough, shortness of breath in Wuhan Province in China at the end of December.1,2 On 02/11/2020, the disease caused by a new coronavirus (SARS-CoV-2) was officially named COVID-19 by the World Health Organization (WHO).3 SARS-CoV-2 was initially detected in people working at the seafood and animal market in this region. It spread from person to person and other cities such as Hubei, and finally, other world countries.5,6 Ultimately, it was declared a pandemic disease by WHO on March 11, 2020.3

Viral infections can change the cell numbers and morphology in the peripheral blood smear. In addition to numerical changes like leukocytosis, leukopenia, neutrophilia, neutropenia, monocytes, monocytopenia, lymphocytosis, lymphopenia, thrombocytopenia, it can also change the morphology of the cells like atypical lymphocyte, inclusion bodies, vacuolization. Atypical lymphocytes, which are sometimes difficult to distinguish from the blasts, can be seen in many viral infections such as infectious mononucleosis, viral hepatitis, cytomegalovirus infections, human immunodeficiency virus infections (HIV), and COVID-19 infection.6,7 Some viruses can produce intracytoplasmic or intranuclear inclusions when they grow either in vivo and in vitro (in cell cultures). It is possible to see them easily under a microscope in painted smears. The number of monocytes with vacuoles may increase with infections, malignancies, alcohol use, toxic situations as evidence of active immune response.8,9,10 Pyknosis and karyorrhexis are known as death phases of cells and appear with rounding and opacity of infected cell nuclei due to the virus infection's cytopathic effect. The cells' band size (club, stab) varies between 10 and 16 microns, and their nuclei are undivided, seen like a horseshoe. Their numbers may increase in infections and bleeding. Two or single lobe neutrophils that have defects of lobulation or maturation are called pseudo-Pelger-Huet anomalies. The hereditary type of pseudo-Pelger-Huet is autosomal dominant, but the acquired type is mostly associated with different pathological states like myelodysplastic syndrome, certain infections, and drug use.11,12,13

While it is impossible to obtain the presence, percentage, or counts of some cells with a unique pathological appearance by complete blood count, they can be easily distinguished by peripheral blood smear. Those cells with prognostic significance in several diseases are illustrated as a pseudo-Pelger-Huet anomaly in myelodysplastic syndrome, smudge cells in chronic lymphocytic leukemia, and vacuolar lymphocytes in metabolic diseases.14,15,16 Cells suggesting viral infection in peripheral blood smears in COVID-19 patients are limited, and a small number of studies showed an association between peripheral blood smear findings and clinical severity of the disease. In our study, we aimed to define cells with the pathological appearance and/or rates in peripheral blood smear at the time of diagnosis and whether these cells are associated with clinical severity in COVID-19 patients.

Materials and Methods.

Patients. The data of laboratory-confirmed COVID-19 patients diagnosed between June 01, 2020, and June 20, 2020, were analyzed retrospectively in the Malatya Training and Research Hospital. Fifty COVID-19 patients and 30 healthy controls were included in this study. Peripheral blood smear samples of the patient group were compared with the healthy controls initially. All peripheral blood smear samples were obtained with the same techniques. The patient group was divided into two as mild and severe disease groups. Both mild and severe disease groups were compared in terms of age, gender, leukocytes, neutrophils, hemoglobin, hematocrit, lymphocytes, eosinophils, monocytes, platelets in complete blood count, segmental, bands, pseudo-Pelger-Huet anomalies, mature lymphocytes, pseudo-Pelger Huet /mature lymphocytes, atypical lymphocytes, monocytes, monocytes with vacuoles, eosinophils, basophils, pyknotic neutrophils in peripheral blood smear, duration of hospitalization and mortality rates. The relationship between the baseline laboratory characteristics of the patients and the duration of hospitalization was also examined.

Laboratory Analysis. Real-time reverse transcriptase-polymerase chain reaction (PCR) tests for SARS-CoV-2 RNA were performed using nasopharyngeal swabs. Total nucleic acid extraction of nasopharyngeal swabs of viral isolates was performed using a biospeedy and coyote extraction system (Bioeksen Ltd and Coyote Bioscience Ltd.). Real-time PCR (RT-PCR) assays for SARS-CoV-2 RNA detection were performed using Biospeedy COVID-19 RT-qPCR Detection Kit (Bioeksen, Istanbul, Turkey).

Disease Severity. Patients were divided into four stages according to their clinical status. Stage 1; asymptomatic
(without any symptoms), stage 2; symptomatic without lung involvement, stage 3; symptomatic with lung involvement, stage 4; acute respiratory distress syndrome, intubated, multiorgan failure. Stage 1, 2 patients were classified as a mild stage, and 3, 4 patients were classified as a severe stage.

Collection of Peripheral Smear. For cases meeting the study criteria, the Wright stained smear was subsequently examined by two hematologists (Dr. Aydogdu I, Dr. Berber I). Hematologists evaluated peripheral blood smear preparations blinded in terms of patients, controls, and laboratory results of the subjects. Peripheral blood smears of the patients were prepared with a blood sample taken from an EDTA tube. A peripheral blood smear was performed, using the same technique, in 30 healthy controls. One hundred leukocyte counts were performed on each peripheral blood smear. Pictures were taken from the peripheral blood smears of the patients (Figure 1-5). Lymphocytes divided into two groups; mature lymphocytes and atypical or reactive lymphocytes, which have an eccentric nucleus, dark basophilia of the cytoplasm and pale sunflower region adjacent to the nucleus, cells similar to the plasma cell, and single-core lymphocyte-monocyte, dark basophilia or vacuoles in the cytoplasm and sometimes with nucleoli (Figure 1). Neutrophils were divided into three subgroups; (I) the nuclei composed of 3-4 segments connected with thin chromatin as segmented neutrophils, (II) single-lobe or bilobed neutrophils as a pseudo-Pelger-Huet anomaly (Figure 2), (III) cell size ranging from 10 to 16 microns with horseshoe-shaped undivided nuclei resembling the C, U, S letters as bands (club, stab) (Figure 3). The cells with a nucleus having features like loose chromatin network, curved, resembling kidney and located in the middle or edge of the cell, with gray-blue colored cytoplasm, and thin granules were evaluated monocytes. Monocytes containing vacuoles in their cytoplasm were recorded as monocytes with vacuoles (Figure 4). Pyknosis is the shrinkage of the cell nucleus. Karyolysis is the melting of nucleus chromatin with enzymes (nucleases) released from the dead cell’s lysosomes. Karyorrhexis is the rupture of the nuclear membrane, chromatin division into small basophilic granules, and spreading into the cytoplasm (Figure 5). Cells with a bilobed nucleus and large pink granules in their cytoplasm were recorded as eosinophils.

**Figure 1.** Atypical lymphocytes in patients’ peripheral blood smear A, B, C. There were lymphocytes with a broad cytoplasm, loose chromatin network and lobulated appearance. Lymphocytes were larger than they should be. The cytoplasm of the lymphocytes was scattered looking adherent to the erythrocytes. Their appearance was particularly similar to stimulated lymphocytes seen in viral infections, and especially “Downey” cells. D. Blast-like lymphocytes.
Figure 2. Different degrees of abnormal maturation (Pseudo-Pelger Huet type). There may be single or double lobed neutrophils. A. Neutrophil granulocytes with unsegmented nucleus with coarsely clumped chromatin. B. Toxic granulations are suggestive of infection in the cytoplasm. C. The bilobed neutrophil with vacuoles, which we are accustomed to seeing mostly in patients with myelodysplastic syndrome. D. Bilobed neutrophil with dysplasia.

Figure 3. A. Band cell that we are accustomed to seeing in bacterial infections whose nucleus is "C" shaped. They are also known as club or stab cells. B. A dysplastic neutrophil that we see mostly in patients with myelodysplastic syndrome. Hypogranulation is at the forefront of the neutrophil's cytoplasm. C. Cell group consisting of bands and dysplastic neutrophils.

Statistical Analysis. Data analysis was performed using IBM SPSS v26 software. Descriptive statistics were used to summarize data. Variables were assessed for normal distribution with the Kolmogorov Smirnov test. Categorical data were presented as number-percentages, and numerical data were presented as median, minimum, and maximum. Differences between categorical variables were analyzed with the Chi-Square test, and numeric variables were compared with the Mann-Whitney U test. A two-sided p-value ≤ 0.05 was considered statistically significant.

Roc analysis was performed to find a cut-off point for differential morphological aspects between mild and severe disease stages.
Figure 4. A, B. The monocytes with vacuoles that generally increased during infections. Vacuoles are often considered to be evidence of the fight against infectious agents. C. A picture to show the severity of vacuolization in patients. D. Beside a monocyte with vacuole, a neutrophil with dysplasia and vacuole.

Figure 5. Pyknosis, karyolysis and karyorrhexis are the death steps of the cell nucleus as a result of the cytopathic effect of the virus. A. Pyknosis is the shrinkage of the cell nucleus. Neutrophils with concentrated and basophilic nuclei showing pyknosis. Toxic granulations are suggestive of infection. B. Karyolysis is the melting of nucleus chromatin with enzymes (nucleases) released from the lysosomes of the dead cell. The nuclear membrane is preserved. C, D. Karyorrhexis is the rupture of the nuclear membrane, division of chromatin into small basophilic granules and spreading into the cytoplasm. Neutrophils that have undergone karyorrhexis are seen. Moreover, a dysplastic neutrophil with increased basophilic staining in one part of the cytoplasm and vacuolization in the other part.
Table 1. Clinical features, laboratory values, and peripheral blood smear findings of all the patients and healthy controls.

| Characteristics and laboratory values | All patients median (min-max) | Controls median (min-max) | P |
|--------------------------------------|-----------------------------|--------------------------|---|
| Total number of patients             | 50                          | 30                       | >0.05 |
| Gender                               |                             |                          |    |
| Male (%)                             | 25 (50)                     | 15 (50)                  |    |
| Female (%)                           | 25 (50)                     | 15 (50)                  |    |
| Stage                                |                             |                          |    |
| Early (Stage I)                      | 1 (2)                       |                          |    |
| Stage II                             | 23 (46)                     |                          |    |
| Severe (Stage III)                   | 24 (48)                     |                          |    |
| Peripheral blood smear (%)           |                             |                          |    |
| Leukocyte                            | 5.19 (2.83-20.36)           | 5.21 (2.4-11.3)          | >0.05 |
| Neutrophil                           | 3.27 (0.86-18.81)           | 3.22 (1.1-10.3)          | >0.05 |
| Hemoglobin                           | 13.95 (8.5-17.9)            | 14.03 (10.2-17.1)        | >0.05 |
| Hematocrit                           | 40.75 (25.6-52.7)           | 42.09 (30.6-51.3)        | >0.05 |
| Lymphocyte                           | **1.28 (0.39-2.53)**        | **2.12 (2.2-5)**         | **0.008** |
| Monocyte                             | 0.47 (0-1.16)               | 0.41 (0-0.9)             | >0.05 |
| Eosinophil                           | 0.02 (0-0.6)                | 0.02 (0-0.42)            | >0.05 |
| Platelet                             | 210 (116-389)               | 216 (110-344)            | >0.05 |
| Band                                 | 7.5 (0-44)                  | 2.5 (0-8)                | **0.019** |
| Mature Monocyte                      | 28 (0-65)                   | 30.5 (24-49)             | 0.126 |
| Atypical lymphocyte                  | **8 (0-26)**                | **0 (0-3)**              | **<0.001** |
| Mature Monocyte with vacuoles        | 5.5 (0-20)                  | 5 (0-10)                 | 0.486 |
| Pseudo-Pelger Huet                   | 2 (0-22)                    | 0 (0-0)                  | **0.002** |
| Basophil                             | 0 (0-4)                     | 0 (0-2)                  | 0.592 |
| Eosinophil                           | 0 (0-7)                     | 4 (0-5)                  | **0.001** |
| Pyknotic neutrophils                 | 0 (0-67)                    | 0 (0-0)                  | 0.014 |
| Pseudo-Pelger Huet/ Mature lymphocyte ratio | **0.44 (0.00-7.00)**        | **0.12 (0-18)**          | **<0.001** |
| Length of hospital stay (day)        | 5 (1-17)                    |                          |    |
| Mortality (Number/Percent)           | 2 (4)                       |                          |    |

Spearman correlation coefficient correlates with hospital stay length and baseline laboratory values and morphological findings in the peripheral blood smears. The study was approved by the research ethics committee of Inonu University, Faculty of Medicine (date/reference number: 30-06-2020/892). All analyses were performed in accordance with the principles of the Declaration of Helsinki.

Results. Patients and healthy controls were similar in terms of age and sex. In the peripheral blood smear, the number of segmented neutrophils, eosinophils were low; the band, pseudo-Pelger-Huet, atypical lymphocytes, monocytes with vacuoles, pseudo-Pelger-Huet/mature lymphocyte ratio, and pyknotic neutrophils were higher in the patient group (Table 1) (p<0.05).

Twenty-four patients in the mild-stage and 26 patients in the severe stage were compared in terms of clinical features and laboratory values (Table 2). No statistically significant difference was found between mild and severe stage in terms of complete blood count. In peripheral blood smears of severe-stage patients, it was observed that the number of mature lymphocytes and eosinophils decreased, and pseudo-Pelger-Huet anomaly, pseudo-Pelger Huet anomaly/mature lymphocytes ratio increased when compared with the mild stage group (p< 0.05). The number of band cells, mature monocytes, and monocytes with vacuoles were increased in the severe stage, although they did not reach the statistical significance (p>0.05). The length of hospital stay was significantly higher in severe-stage patients (p<0.05). A cut-off point for differential morphological aspects between the mild and severe stages of the disease was tried to be determined by Roc analysis. Unfortunately, a specific value could not be found because the area under the curve (AUC) was not significant. While none patients died in the mild stage group, two patients died in the severe stage (p> 0.05).

Laboratory values of all patients were compared with the duration of hospitalization. A significant positive correlation between a longer hospitalization duration and an increased number of neutrophils in the complete blood count was observed. A negative correlation between the duration of hospitalization and lymphocyte count in hemogram, mature lymphocyte, and monocytes with vacuoles rates in peripheral blood smear was observed (p<0.05) (Table 3).
vacuolated monocytes, whose entity correlates with patient outcome. They phenotypic changes in peripheral blood monocytes, detectable morphological and inflammation peripheral blood smears and the significance of these morphological changes of COVID the peripheral blood smear. Information about the monocytes with vacuol manifested by atypical lymphocytes, inclusion bodies, duration.

The peripheral blood smear had a short hospitalization of mature lymphocytes and monocytes with vacuoles in onset of the disease, patients with an patients with severe diseases stage. Moreover, at the rates in peripheral blood smear were found in COVID ratio, and decreased mature lymphocyte and eosinophil Discussion. This study shows that an increased pseudo-Pelger Huet, pseudo-Pelger Huet/ mature lymphocyte ratio, and decreased mature lymphocyte and eosinophil rates in peripheral blood smear were found in COVID patients with severe diseases stage. Moreover, at the onset of the disease, patients with an increased number of mature lymphocytes and monocytes with vacuoles in the peripheral blood smear had a short hospitalization duration.

In general, viral infections are known to be manifested by atypical lymphocytes, inclusion bodies, monocytes with vacuoles, and pyknosis in leukocytes of the peripheral blood smear. Information about the morphological changes of COVID-19 infection in peripheral blood smears and the significance of these changes on the disease's clinical course is limited.

Dan Zhang et al. reported COVID-19 induces readily detectable morphological and inflammation-related phenotypic changes in peripheral blood monocytes, whose entity correlates with patient outcome. They detected an increased number of larger, atypical, vacuolated monocytes, not generally seen in healthy individuals' peripheral blood smear. We confirmed the presence of the same vacuolated monocytes in our previous study. Delphine Gérard et al. reported that peripheral blood film examination revealed a highly pleomorphic atypical lymphocyte population, and many cells were large (15–30 μm). The cytoplasm was sometimes granulated. Cytoplasmic basophilia was sometimes generalized and sometimes confined to the cytoplasmic margins. Some cells had one or more nucleioli and could have been mixed with blast cells. Alia Nazerullah et al. reported peripheral blood examination findings in SARS-CoV-2 infection. They showed that the pseudo-Pelger-Huet anomaly was recorded in all cases of COVID-19, affecting more than 5% of granulocytes in most cases. Yunus Murat Akcabelen et al. reported dysplastic changes in peripheral blood cells of COVID-19 patients. We also observed atypical lymphocytes, pseudo-Pelger-Huet anomaly, and dysplastic changes in peripheral blood cells in a previous study.

Maryame et al. found neutrophil granulocyte with dysmorphic morphology marked by hypogranular

| Characteristics and laboratory values | Mild Stage Median (min-max) | Severe Stage Median (min-max) | P |
|--------------------------------------|-----------------------------|-----------------------------|---|
| Total number of patients             | 24                          | 26                          | <0.001 |
| Median Age (year)                    | 27.5 (18-52)                | 57.5 (27-88)                | 0.396 |
| Gender                               | Female (number/percent)     | 10 (41.7)                   | 15 (57.7) |
|                                     | Male (number/percent)       | 14 (58.3)                   | 11 (42.3) |
| Stage (Number. %)                    | Early                       | 1 (4.2)                     | 24 (92.3) |
|                                     | Stage I                     | 23 (95.8)                   | 2 (7.7) |
|                                     | Stage II                    |                             |     |
|                                     | Stage III                   | 24 (92.3)                   |     |
| Complete blood count                 | Leukocyte                   | 5.54 (3.25-9.09)            | 5.13 (2.83-20.36) | 0.398 |
|                                     | Neutrophil                  | 3.33 (1.63-6.84)            | 3.26 (0.86-18.81) | 0.614 |
|                                     | Hemoglobin                  | 14.3 (10.5-17.2)            | 13.65 (8.5-17.9) | 0.244 |
|                                     | Hematocrit                  | 41.25 (35.2-52.2)           | 40.25 (25.6-52.7) | 0.541 |
|                                     | Lymphocyte                  | 1.21 (0.61-2.53)            | 1.39 (0.39-2.32) | 0.778 |
|                                     | Monocyte                    | 0.49 (0.00-1.12)            | 0.43 (0.32-1.16) | 0.122 |
|                                     | Eosinophil                  | 0.05 (0.00-0.60)            | 0.01 (0.00-0.21) | 0.058 |
|                                     | Platelet                    | 221 (152-389)               | 196 (116-309) | 0.062 |
| Peripheral blood smear (%)           | Segmental                   | 23.5 (0-55)                 | 17 (0-57) | 0.062 |
|                                     | Band                        | 5 (0-40)                    | 9 (0-44) | 0.094 |
|                                     | Pseudo-Pelger Huet          | 6 (0-46)                    | 18.5 (0-36) | 0.007 |
|                                     | Neutrophil                  | 31 (0-65)                   | 17 (4-44) | 0.010 |
|                                     | Mature lymphocyte           | 9 (1-21)                    | 8 (0-26) | 0.366 |
|                                     | Reactive lymphocyte         |                             |     |
|                                     | Lymphocyte                  | 5 (0-20)                    | 6.5 (1-18) | 0.271 |
|                                     | Monocyte                    | 0 (0-22)                    | 4 (0-16) | 0.159 |
|                                     | Monocyte with vacuoles      |                             |     |
|                                     | Basophils                   | 0 (0-2)                     | 0 (0-4) | 0.234 |
|                                     | Eosinophils                 | 1 (0-7)                     | 0 (0-4) | 0.008 |
|                                     | Pyknosis                    | 1 (0-18)                    | 0 (0-67) | 0.162 |
|                                     | Pseudo-Pelger Huet/ Mature | 0.1538 (0.00-1.44)          | 0.7305 (0.00-7.00) | 0.002 |
|                                     | lymphocyte                  |                             |     |
| Lenght of hospital stay (day)        | 5 (1-17)                    | 10 (1-16)                   | 0.037 |
| Mortality (Number. %)                | 0 (0)                       | 2 (7.7)                     | 0.491 |

Table 2. Comparison of laboratory values, peripheral blood smear findings, and clinical features of Mild and severe stage patients.
cytoplasm and hyposegmented nucleus, atypical eosinophils containing multiple vacuoles, rare, activated lymphocytes, and large monocytes in some peripheral blood films in COVID-19 patients. They did not show any association of these changes with the clinical course of the disease. In this study, we observed a large number of dysplasia, hypolobular, hypergranular neutrophils, and a small number of hypogranular neutrophils. It was observed that atypical lymphocytes increased compared to the control group but did not significantly affect hospitalization duration. Cantu MD et al. reported blue-green neutrophil and monocyte cytoplasmic inclusions in peripheral blood smear of critically ill SARS-CoV-2 positive patients; these inclusions were still present 20 days after the diagnosis of COVID-19. They showed that blue-green inclusions might correlate with short-term mortality. Similar inclusions were found by us in one patient's lymphocytes with a severe stage (Figure 1H), showing that they are not specific for myeloid lineage. Alterations of granulocytes can be different in COVID-19; Christian Salib et al. showed hypersegmented granulocytes infected patients; in our study, we found that pseudo-Pelger-Huet anomalies were significantly present, especially in severe patients. Similarly, Gina Zini et al. reported morphological anomalies of circulating blood cells in COVID-19 patients. These anomalies were unsegmented or bilobular nuclei like pseudo-Pelger-Huet, hypergranular with basophilic cytoplasm, hypogranular and agranular areas, multiple vacuoles in neutrophil granulocyte, immature circulating cells with blasts-like reticular chromatin and rare thin azurophilic granules, likely pre-apoptotic, circulating apoptotic neutrophil, apoptotic cells with blue cytoplasm, of possible lymphocyte origin, large polyploid reactive lymphocyte with hyperbasophilic cytoplasm, giant vacuolated platelets. Anupam Mitra et al. reported a leukoerythroblastic reaction in a 46-year-old previously healthy female with COVID-19 infection. In peripheral blood smear, they found nucleated erythroid, rare blast, with prominent nucleoli and immature chromatin pattern, a left-shifted myeloid series with immature promyelocytes and metamyelocytes, and occasional monocytes. Chuan Qin et al. reported 452 patients with COVID-19 infection, 286 of whom were diagnosed as a severe infection. Severe cases tend to have lower lymphocyte counts, higher leukocyte counts, neutrophil-lymphocyte ratio (NLR), and lower percentages of monocytes, eosinophils and basophils. Man Kong et al. reported a higher level of neutrophil-to-lymphocyte is associated with severe COVID-19. Ai-Ping Yang et al. reported that elevated neutrophil-to-lymphocyte ratio could be considered independent biomarkers for indicating poor clinical outcomes.

The cells we examined in peripheral blood smear were morphologically similar to the others published in the literature. We did not see a leukoerythroblastic reaction in any of our patients. Especially in severe patients, we found a higher number of band cells and a lower number of segmented neutrophils, but these
results did not reach statistically significant levels, and that could be due to increased cytokine levels in the severe stage. We observed an increased pseudo-Pelger Huet anomaly, pseudo-Pelger Huet anomaly/mature lymphocyte ratio, decreased mature lymphocytes, and eosinophils rates in the severe stage patients. Impaired immunity due to decreased lymphocyte count and an increase in dysfunctional neutrophil count due to pseudo-Pelger Huet anomaly may be the answer to why these patients are admitted to the hospital at a severe stage.

The morphological abnormalities in all cell lines may be a prognosticator for increased mortality of this disease. There was a negative correlation between monocytes with vacuoles, lymphocyte counts, and duration of hospitalization. These observations can be explained by the degree of suppressing the SARS-CoV-2 virus through inflammatory mechanisms on hematopoiesis and the immune system that reduce these cells' number.

Our study has some strengths. To our knowledge, this is the first article showing an association between peripheral blood smear morphology with the Pelger Huet anomaly and the immune system that reduce these cells' number.

Our study has some strengths. To our knowledge, this is the first article showing an association between peripheral blood smear morphology with the Pelger Huet anomaly and the immune system that reduce these cells' number.

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