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Evaluation of hematological parameters in covid-19 patients in district Hapur

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Abstract
Objective: The coronavirus disease (COVID-19) sparked from Wuhan city of China and rapidly developed into a pandemic. The critically ill patients of COVID-19 exhibit features of hyper inflammation, and the particular blood tests may be rewarding for prognosis. Our aim was to investigate the CBC, which includes total leukocyte, lymphocytes and granulocytes count, Hemoglobin, MCV, MCH, MCHC, RBCs and Platelet count, NLR etc. The current study was conducted to conclude the alteration in blood parameters and their association with the severity and mortality of COVID-19 patients.
Methods: An observational cross-sectional study was conducted retrospectively, a total of 100 COVID-19 positive patients were examined: 50 were mild, 25 were moderate, 10 were severe, and 15 were critically diseased patients. Unfortunately, we recorded 6 deaths among the critical group. The overall mean age observed in our study was 48.94 years, where the mean age for critical individuals was 62.12 ± 14.35 years.
Results: A significant association between the disease severity and elevation in blood parameters were observed. The total WBC's and Neutrophils count were significantly decreased (p value<0.001). The lymphocyte count was increased in critical patients (1.40 × 109 /L) compared to mild patients (1.92 × 109 /L) (p = 0.28).
Conclusion: These blood parameters could be used as a suitable biomarker for the prognosis and severity of COVID-19. Evaluating novel hemograms, NLR can aid clinicians to identify potentially severe cases at early stages, initiate effective management in time, and conduct early triage which may reduce the overall mortality of COVID-19 patients.

Keywords: Biomarkers, COVID-19, hematological parameters, corona Viru

Introduction
The coronavirus disease 2019 (COVID-19) ranges from mild illness to Severe Acute Respiratory Syndrome. Corona Virus 2 (SARS-CoV-2) was first described in the late December 2019 in Wuhan, China [1, 2]. The COVID-19 is a high contagious disease and spread around the globe within a short time, and the world health organization (WHO) has declared it a pandemic on March 12, 2020 [3].
COVID-19 symptoms can vary from person to person, leading to a clinical manifestation of disease ranging from asymptomatic to mild infections, through to serious, life threatening cases requiring admission to the intensive care unit (ICU) [4, 5]. The severity of COVID-19 depends on several factors including age, gender, and the presence of existing comorbidities such as diabetes, hypertension, or respiratory disease [6-8]; however, it is difficult to predict the future severity of COVID-19 infection at the time of the patients' admission to the hospital.
Early diagnosis is vital when considering the short time of onset of acute respiratory distress syndrome after admission to hospital and the high mortality rates in COVID-19 [9].
Blood tests have an important role in early diagnosis of the disease, considering the information they provide to physicians regarding the inflammatory process. This information includes leukocyte count and characteristics such as neutrophil- or lymphocyte-dominance, inflammation (CRP), collateral organ damage (acute renal failure, acute liver failure) and the severity of the disease.
Complete blood counts (CBC) are easily performed and inexpensive. Included in the CBC are values such as white blood count, neutrophil, lymphocyte and platelet count (PLT), mean platelet volume and certain ratios of these values.

These can be used as inflammatory markers. Neutrophils are the most characteristic cell type among the white blood cells and are an important component of the immune system.

Except for clinical symptoms and pulmonary computed tomography (CT) findings, most confirmed COVID-19 patients revealed laboratory fluctuations in different serological parameters, including renal and liver function tests, coagulation parameters, and inflammatory, biochemical and hemocytometric parameters [10, 11].

To show the prognosis and hyper inflammation state, a combination of laboratory tests has been evaluated. The combination of the various tests includes platelet-to-lymphocyte (PLR) and neutrophils to lymphocyte ratio (NLR). COVID-19 leads to variation in the hematological parameters, including lymphocytes, white blood cells, platelets, neutrophils, etc [11-13]. These variations are different from case to case and level of the disease severity. Neutropenia has been previously reported in about 35%-85% of patients and was the most common blood count abnormality [10-12].

The main objective of this research was to evaluate the variations of CBC levels of COVID-19 patients with the disease severity. How the CBC level changes after the onset of disease. This would help the clinician to ascertain both the diagnosis and prognosis.

Materials and Methods

Study design: A retrospective cross-sectional study was conducted from May 2020 to July 2020.

Patients

Our study participants include n = 100 patients who were tested positive for CoVid-19 through real-time reverse transcriptase PCR and admitted in isolation wards of District Hapur. Among them, 70 were males while 30 were females. The overall average age was 18–78 years. The demographic information such as gender, age, and co-morbidities was also recorded from each individual as shown in Tables 1.

Table 1: Demographic information of various disease groups

Demographics	Total N=100	Mild N=50	Moderate N=25	Severe N=10	Critical N=15
Age	48.9	43.24	49.1	56.6	62.1
Gender					
Male	70 (70%)	38 (38%)	15 (15%)	70 (70%)	10 (10%)
Female	70 (30%)	12 (12%)	10 (10%)	3 (3%)	5 (5%)

Sample processing

The blood routine indicators included lymphocyte count (LYM), lymphocyte %, platelet count (PLT), white blood cell count (WBC), platelet volume distribution width (PDW), PDW%, red blood cell count (RBC), red blood cell volume distribution width (RDW), red blood cell volume distribution width (RDW), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular-hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), mean platelet volume (MPV), hemoglobin (HGB), PLT-I, granulocytes count, Granulocyte ratio (G%), neutrophil ratio, and neutrophil count.

Exclusion and inclusion criteria

All the individuals who were tested positive for the COVID-19by RT PCR test (according to U.P. govt. guidelines) were included in this study.

Individuals below 18 years of age and those with not having RT-PCR positive report were excluded.

Model development

According to the MOHFW guidelines for novel corona virus pneumonia diagnosis and treatment protocol, COVID-19 patients have been classified into different groups i.e. mild, moderate, severe, and critical based on the severity of the disease. Severe disease is defined as patients having less than 90% of saturation rate at rest, per min breaths is ≥30, >50% lesion progression in pulmonary imaging, the arterial pressure of oxygen (PaO2)/fractional concentration of oxygen (FiO2) is 100 mmhg. Moderate disease is defined as patients having <94% spo2 on room air, respiratory rate ≥ 24/minute. The mild disease level is defined as patients with slight clinical manifestations but no appearance of pneumonia on radiological imaging. Biochemical and hematological parameters were assessed by automated hematology analyzer. Leukopenia was defined as a value lower than 4000 leukocytes/mm3 and lymphopenia as a value lower than 1000 lymphocytes/mm3.

Results

A total of 100 COVID-19 positive individuals were examined in this study. The patients were previously screened through RT-PCR for the SARS-CoV-2 infection and were found positive for the viral infection. Among the total individuals (n = 100), 70 (70%) were male individuals while 30 (30%) were female individuals. Male individuals were more affected than female individuals. The severe and critical diseased patients were mostly older individuals compared with mild and moderate groups. The overall mean age was 48.94 years where the mean age for critical individuals was 62.12 ± 14.35 years. Comorbidities were also present in all patients such as hypertension, diabetes, COPD. e. The most common complaints at the time of admission were fever (62%), cough (45%), sore throat (43%), shortness of breath (18%) and myalgia (16%) (Table 2)

Table 2: Comparisons of Patient Features according to PCR test results. N = 100

Patient features	Positive	Negative
Fever	62 (62%)	38 (38%)
Cough	45 (45%	55 (55%)
Sore throat	43 (43%)	57 (57%)
Dyspnea	17 (17%)	83 (83%)
Myalgia	16 (16%)	84 (84%)
Malaise and fatigue	4 (4%)	96 (96%)
Shortness of breath	18 (18%)	82 (82%)
Headache	2 (2%)	98 (98%)
Chest pain	4 (4%)	96 (96%)
Rhinorrhea	1 (1%)	99 (99%)

The hematological parameters such as white blood cells, lymphocyte count, granulocytes, hemoglobin, mean corpuscular hemoglobin, mean corpuscular-hemoglobin concentration, red blood cells, mean corpuscular volume,

hematocrit, red cell distribution width, percentage of red cell distribution width, platelets, mean platelet volume, platelet distribution width, platelet count, platelet large cell ratio were examined across the comparative groups.

The white blood cells were significantly decreased (p value =<0.001) in mild patients compared to critical individuals (6.76 × 109 /L). Similarly, significant difference (p value =<0.001) of white blood cells was observed between the moderate patients (8.25 × 109 /L) and severe patients (7.77 × 109 /L), and between moderate (8.25 × 109 /L) and critical patients (11.79 × 109 /L) (p value = 0.039). The mean platelets count was significantly decreased in critical group (165.0 × 109 /L) compared to moderate group (223.73 × 109 /L), mild group (217.03 × 109 /L) and severe group (205.55 × 109 /L) (p value = 0.16). No significant association between gender and platelet count elevation was observed in COVID-19 patients. The red blood cell count was increased in the severe group (5.1 × 1012/L); however, it was similar in other groups (mild group 4.95 × 1012/L, moderate group 4.97 × 1012/L) (p value = 0.91). The critical diseased individuals represented the highest value of lymphocyte compared to other diseased groups. The red cells distribution width was significantly decreased (57.86%) in critical patients compared to mild patients (177.3%) (P value = 0.83). The granulocyte count was decreased in critical patients (1.40 × 109 /L) compared to mild patients (1.92 × 109 /L) (p value = 0.28). The mean corpuscular hemoglobin was also observed similar across the different comparative groups (p value = 0.1). Similarly, the mean corpuscular-hemoglobin concentration was also not elevated with the severity of the disease (p value = 0.31). The mean corpuscular volume was similar between mild patients (82.63 fl) and moderate patients (83.65 fl) however a little increase was observed in severely diseased patients (86.45 fl).

The platelet large cell ratio was increased in critical patients (26.49%) compared to severe patients. A significant decrease was also observed in NLR in various disease groups.

Discussion

Considering the high infectivity and mortality rates of COVID-19, early diagnosis of the disease is essential. There is a need to assess the disease severity and mortality risk associated with COVID-19 in the current pandemic for the optimal management of the patients [14, 15]. Therefore, every parameter allowing for early diagnosis is vital. In this study, the possibility of diagnosing COVID-19 early in hospital visits by a simple, inexpensive, easily accessible test, such as a CBC, has been examined.

In this study, we demonstrated that simple parameters from a routine hematological workup have the capacity to be useful predictors of hospital admission in COVID-19 patients on the day of positive COVID-19 swab. Recently, several studies describing predictive modeling for COVID-19 have been published, focusing on prediction models for COVID-19 diagnosis [16], COVID-19 severity [17], and patient mortality [18]. A common disadvantage of many proposed models is the requirement of detailed patient information including CT scans [19, 20], other imaging data [21, 22], extensive specialist knowledge, that is, APACHE II score [23], additional protein marker tests [24], or extensive patient history and clinical workup [25, 26], and the need for rapid AI-based diagnostic and prognostic system for COVID-19 remains an unmet challenge [27]. In contrast to these studies, our proof-of-concept modeling indicated that routinely available hematological parameters such as wbc, NLR and platelet count are powerful predictors of severity of COVID-19 in patients at the time of the positive COVID-19 test (admission to the hospital).Several studies have examined neutrophil-to-lymphocyte ratio (NLR) as a biomarker for COVID-19 severity and have proposed a significant prognostic value on NLR for the prediction of disease severity, decreased NLR being associated with the severe course of COVID-19 (28–30).

Out of 100 patients diagnosed with COVID-19, 70% were males and the average age was 48.9 ± 14.5 years. In a study conducted by Guan *et al.*, the median age was 47 and 52.1% of the patients were male [31]. Another study by Li *et al.* revealed that 56% of all patients were male and the median age was 59 [32]. Furthermore, another study conducted by Xu *et al.* showed a median age of 41 and 56% of the patients were male [33]. Thus, it can be said that COVID-19 is seen more frequently in males and in middle-aged patients.

In the results of this study, which are also consistent with previous research, low thrombocyte, leukocyte and granulocyte counts were revealed in COVID-19 positive patients. Thus, it can be said that thrombocytopenia, leucopenia and neutropenia may be indicative of COVID-19 disease. Likewise, thrombocytopenia and leukopenia were noted in Guan *et al.*'s study [31]. The thrombocyte count was also found to be low in the study by Assiri *et al.* [34] and leukopenia was noted in another study conducted by Xu *et al.* [33]. In general, while the leukocyte count was lower than 10,000 in viral pneumonias, leukocytosis was seen in bacterial pneumonias with a leukocyte count of more than 50,000 [35]. Additionally, Xu *et al.* revealed in their study that thrombocyte counts are significantly low in pneumonia patients and that this decrease is directly proportional to the patients' clinical status [36]. In a study by Fan *et al.* mild thrombocytopenia and leukopenia was observed in some patients at first admission who were COVID-19 positive [37].

Also, hemoglobin levels in COVID-19 positive patients were found to be significantly higher than in COVID-19negative patients. While no significant difference was observed among females regarding hemoglobin, higher hemoglobin levels were seen in COVID-19 positive male patients. It is possible that these results are also affected by other reasons, such as the presence of comorbidities or anemia, and habits such as cigarette smoking. The patient files used for this study did not include a detailed patient history, and thus, their effect on hemoglobin levels were not accounted for. Also, the normal hemoglobin level in the female population is lower than that of males [38]. Since around 70% of the positive patient group is comprised of males in this study, this is likely to also have an effect on the results.

The small sample size, retrospective data collection, and limited access to clinical baseline characteristics such as pre-existing conditions, medications, and treatments are the main limitations in this study. Our study demonstrates that these routine clinical hematology parameters can identify the patients at risk of developing severe COVID-19 disease. The advent of effective vaccines and other novel therapeutics will almost certainly lead to reduced COVID-19 related mortality over the coming months. However, until widespread immunity has been achieved on a global scale, it is likely that we will continue to be challenged by the significant burden of disease and healthcare-resource utilization associated with this infection. The availability of

prediction models utilizing inexpensive, routine clinical laboratory testing would likely be of significant value to clinicians who continue to be challenged by this disease, particularly in developing countries where healthcare resources are more limited and where access to vaccines may be impeded by the ongoing global demand.

Conclusion

The definitive diagnosis of COVID-19 was made by RT-PCR analysis, but this was a time-consuming and less accessible test. With this test, the time it takes to diagnose and treat patients can be delayed. In our study, low values of leukocytes, neutrophils, platelets and high values of hemoglobin found with a CBC test which is easily available in lab were found to be valuable in terms of the initial diagnosis of COVID-19. In addition, low values of NLR were also indicative of COVID-19.

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