



HEMATOLOGICAL PROFILE OF COVID-19 POSITIVE PATIENTS IN QUETTA, PAKISTAN

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Abstract

In this study, the clinical symptoms and hematological variations of COVID-19 patients were assessed on the first day of examination. The patients were grouped on the basis of their admission to the Intensive Care Units (ICU) "Severe," High Dependency Units (HDU) "Moderate," or General Ward (Mild) of Fatima Jinnah Hospital, Quetta, Balochistan. The levels of leucocytes, neutrophils, lymphocytes, erythrocytes, hemoglobin, hematocrit, mean cell volume and MCHC in the blood upon their first medical examination day were retrieved from medical records of first day laboratory tests. These parameters are good indicators to gauge the course of the disease, protection against further body deterioration, reducing morbidity and mortality. The results of hematological profile revealed that there was an increase in neutrophils in moderate ($76.58 \pm 1.78\%$), severe ($76.07 \pm 2.52\%$) and critical ($82.35 \pm 1.39\%$) groups while there was a decrease in lymphocytes in moderate ($16.31 \pm 1.43\%$), severe ($17.21 \pm 2.11\%$) and critical ($12.74 \pm 1.25\%$) groups. There was an elevation in WBCs level of severe ($11.38 \pm 0.88/L$) and critical class ($12.00 \pm 0.79/L$). However, there was decrease in the hemoglobin (12.50 ± 0.34 g/dL), hematocrit ($34.10 \pm 0.97\%$), MCH (26.03 ± 0.61 pg) and MCHC (29.58 ± 0.73 g/dL) level of critical class. All the above results were showing significant difference ($p < 0.05$) with non-COVID group.

Key words: COVID 19; clinical symptoms; hematological; SARS-CoV-2; critical

• Introduction

In January 2020, the World Health Organization (WHO) designated the coronavirus disease (Covid-19) to be a pandemic. More than 216 countries were affected globally. China was predominantly found to had the initial burden of COVID-19 illness (Hundt, Deng *et al.* 2020). The novel virus that causes coronavirus disease (COVID 19), known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Illg, Muller *et al.* 2021). Coronaviruses belong to the class Coronaviridae that are a group of non-diverging positive-sense RNA viruses (Pourfridoni, Abbasnia *et al.* 2021). Coronaviruses are a family of viruses that have been linked to both intestinal and respiratory illnesses in both humans and numerous animal species. These viruses typically affect the upper

respiratory tract, where they can cause mild to severe infections like the common cold or, in more severe situations, pneumonia (Cai, Huang *et al.* 2020). Fever, dry cough, fatigue, shortness of breath, myalgia, arthralgia, sore throat, and headache are some of the early signs of a virus infection. These symptoms can progress to other conditions, such as respiratory, enteric, neurological, and hepatic diseases, such as acute respiratory distress syndrome (ARDS), acute cardiac injury, or secondary infections. Analysis of individuals exhibiting influenza-like symptoms in the early stages of COVID-19 revealed that the frequency of fever, ageusia, anosmia, headache, and myalgia/arthralgia was considerably greater in COVID-19 patients than in non-COVID-19 patients. Patients with underlying medical issues, as well as older patients, may develop a severe respiratory disease that is fatal (Hundt, Deng *et al.* 2020, Nakanishi, Suzuki *et al.* 2020, Dubey, Mishra *et al.* 2021, Pourfridoni, Abbasnia *et al.* 2021). A simple and direct blood test may be crucial in the diagnosis and follow-up of disease conditions because it can reveal details about the inflammatory process, including the leucocyte count and other characteristics like neutrophil or lymphocyte predominance, the neutrophil-lymphocyte ratio (N/L ratio), C-reactive protein (CRP) as an inflammation marker, collateral organ damage (acute renal and liver failure), and the severity of the disease. The type of pneumonia may be revealed by analysing the results of a blood test, allowing the doctor to ascertain the cause of the illness (Dubey, Mishra *et al.* 2021). Furthermore, it is yet unknown if COVID-19 may be identified and confirmed on the first day of a clinical examination using laboratory results on several clinical indicators (Nakanishi, Suzuki *et al.* 2020).

In this study, the detailed hematological profile in a peripheral blood sample of COVID-19 patients were assessed on the first day of examination, who were admitted to the Intensive Care Units (ICU) “Critical”, High Dependency Units (HDU) “Severe” or General Ward “Moderate” of Fatima Jinnah Hospital, Quetta, Balochistan. These characteristics may be utilized to forecast and gauge the course of the disease, allowing for the patient's protection before their clinical state deteriorates significantly and perhaps reducing morbidity and death.

• Materials and Methods

2.1 Study setting and study population

This study comprises analysis of patients of all age groups, ethnic groups and sex who were mainly diagnosed with SARS-CoV-2 and confirmed the viral nucleic acid on nasopharyngeal swabs by RT-PCR method upon their first medical examination based on WHO Guidelines. The study population of 100 patients was included and this study was approved by the Research Ethics Committee of Fatima Jinnah Hospital, Quetta and Institutional Review Board. Detailed data of patients for hematological parameters, serum biochemistry parameters, and inflammatory biomarkers of patients with confirmed positive COVID-19 status were recorded, between March 2020–December 2020, from electronic medical records of Laboratory Information Centre, Fatima Jinnah Chest Hospital, Quetta.

2.2 Clinical and laboratory data extraction

Clinical and laboratory data were collected retrospectively, plus demographic data, consisting of age, sex and patient outcome. The vital signs on admission, inclusive of blood pressure (BP), respiratory rate (RR), heart rate (HR) and pulse oximeter oxygen saturation were also gathered. The patient discharged from ICU and hospital alive was determined as survivor.

2.3 Laboratory findings in blood

The levels of leucocytes, neutrophils, lymphocytes, erythrocytes, hemoglobin, hematocrit, mean cell volume, MCHC, CRP, d-dimer, serum ferritin, urea, creatinine, bilirubin total, SGPT and alkaline phosphate in the blood upon their first medical examination day were retrieved from medical records of first day laboratory tests.

2.4 Study population grouping criteria

The COVID-19 patient's dataset were analyzed based on their admission to ICU (Critical COVID-19), HDU (Severe COVID-19), or General Ward (Moderate COVID-19). The critical COVID-19, which corresponded to 34 patients samples, severe COVID-19, which also corresponded to 34 patients samples and moderate COVID-19, which corresponded to 32 patients samples. The understudy cases were categorized as **(a) Moderate COVID-19:** Patients with painless upper respiratory tract disease may have mild symptoms such as fever, dry cough or cough with sputum, sore throat, nasal obstruction, anxiety, headache, or hypoxia (normal saturation) were admitted in general wards. **(b) Severe COVID-19:** Pneumonia with no signs of critical disease. Juvenile or adult with the presence of clinical attributes of dyspnea and/or hypoxia, fever, cough, inclusive of $SpO_2 < 94\%$ (range 90–94%) on room air, respiratory rate more or equal to 24 breaths/min were admitted in High Dependency Units. **(c) Critical COVID-19:** Juvenile or adult with clinical features of severe pneumonia together with one of the following; respiratory rate >30 breaths per minute, severe respiratory distress, $SpO_2 < 90\%$ on room air or ARDS or Sepsis/Septic shock and symptoms of unstable alveolar gas exchange in ABG parameters were admitted in Intensive Care Units.

2.5 Statistical analysis

Data statistics was analysed with the SPSS statistics, version 23.0, software. Mean \pm SD (range) was used to represent age while frequency and percentage for gender. The estimated variables of blood and serum parameters were calculated as mean \pm standard deviation. Statistically significant value of P below 0.05 was considered in all statistical analyses.

• Results

3.1 Participant characteristics

In total, 100 patients (72 men and 28 women; 19-97 years; mean age, 52.42 ± 1.61 years) comprised the three COVID 19 (ICU (Critical COVID-19), HDU (Severe COVID-19), or General Ward (Moderate COVID-19) groups, as judged by PCR-positive results while 34 patients (26 men and 8 women) were included in non-COVID 19 group, as judged by PCR negative results. The mean body temperatures of the COVID-19 (PCR-positive) groups were $99.35^\circ F \pm 0.12$.

3.2 Clinical Symptoms on Admission Day

On admission, most patients had fever or dry cough and a third of patients had shortness of breath (SOB). Other symptoms observed were muscle ache, sore throat, nasal congestion, malaise headache, confusion, chest pain, loss of taste and/or smell, vomiting and diarrhea. Additionally, 39 % patients had chronic diseases, including cardiovascular, digestive system, respiratory system, nervous system and renal system diseases. All patients admitted had pneumonia and many presented with impaired organ function consisting of 17 (17%) with ARDS, 08 (8% with acute respiratory injury, 03 (3%) with acute renal injury, 04 (4%) with septic shock and one (1%) with ventilator-associated pneumonia.

3.3 White Blood Cells (WBCs)

The results of hemotological investigation revealed that there was an increase in leucocytes (WBCs) in moderate COVID +ve class ($9.11 \pm 0.74/L$) but these were near to upper limit of the reference range ($9.5 \times 10^9/L$) showing a significant difference ($p < 0.05$) between moderate and non-COVID patients. The WBCs level of severe ($11.38 \pm 0.88/L$) and critical class ($12.00 \pm 0.79/L$) exceeded the upper reference range along with significant difference ($p < 0.05$) with non-COVID patients (Table 1).

3.4 Neutrophils

Interestingly, there was also an increase in neutrophils in moderate COVID +ve class ($76.58 \pm 1.78\%$) and severe class ($76.07 \pm 2.52\%$) but these were near to upper limit of the reference

range (75%) and both showing a significant difference ($p<0.05$) with non-COVID patients. The neutrophils level of critical class ($82.35\pm 1.39\%$) exceeded the upper reference range along with significant difference ($p<0.05$) with non-COVID patients (Table 1).

3.5 Lymphocytes

The current study of hematological profile showed there was a decrease in lymphocytes in moderate ($16.31\pm 1.43\%$), severe ($17.21\pm 2.11\%$) and critical class ($12.74\pm 1.25\%$) but moderate and severe class were near to lower limit of the reference range (20%) and all showing a significant difference ($p<0.05$) with non-COVID patients (Table 1).

3.6 Red Blood Cells (RBCs)

The analyzed data of current findings revealed that the Red Blood Cells (RBCs) in moderate COVID +ve class ($5.31\pm 0.09/L$) and severe class ($5.03\pm 0.19/L$) but these were near to upper limit ($5.8 \times 10^{12}/L$) of the reference range while there was only significant difference ($p<0.05$) showed by moderate COVID +ve and non-COVID patients. The RBCs level of critical class ($3.99\pm 0.13/L$) was near the lower reference range ($3.8 \times 10^{12}/L$) along with significant difference ($p<0.05$) with non-COVID patients (Table 1).

3.7 Hemoglobin (HGB)

The study also recorded that the hemoglobin (HGB) in moderate COVID +ve class (14.6 ± 0.41 g/dL) and severe class (13.69 ± 0.35 g/dL) were in the reference range (11.5-17.5 g/dL). The HGB level of critical class (12.50 ± 0.34 g/dL) was near the lower reference range along with significant difference ($p<0.05$) with non-COVID patients (Table 1).

3.8 Hematocrit (HCT)

We also found in the study that the hematocrit (HCT) in moderate COVID +ve class ($41.58\pm 1.45\%$) and the severe class ($39.83\pm 1.17\%$) were in reference range (35-50 %) while the mean of critical class was near to lower limit of the reference range (35%) showing a significant difference ($p<0.05$) with non-COVID patients. The HCT level of critical class ($34.10\pm 0.97\%$) was below the lower reference range along with significant difference ($p<0.05$) with non-COVID patients (Table 1).

3.9 Mean Corpuscular Volume (MCV)

The current results revealed that the Mean Corpuscular Volume (MCV) in moderate COVID +ve class (78.48 ± 2.55 fL) and severe class (79.58 ± 2.36 fL) were below the reference range (82-100 fL) and both showing a significant difference ($p<0.05$) with non-COVID patients whereas the MCV level of critical class (86.72 ± 1.98 fL) was in the reference range (Table 1).

3.10 Mean Corpuscular Hemoglobin (MCH)

Further results of current study revealed that there was a decrease in MCH in moderate (27.61 ± 0.69 pg), severe (27.64 ± 0.96 pg) and critical class (26.03 ± 0.61 pg) but moderate and severe class were near to lower limit of the reference range (27 pg) and all showing a significant difference ($p<0.05$) with non-COVID patients (Table 1).

3.11 Mean Corpuscular Hemoglobin Concentration (MCHC)

The results of following study also showed that the MCHC in moderate COVID +ve class (34.73 ± 0.33 g/dL) and severe class (33.49 ± 0.56 g/dL) were in the reference range (31.6-35.4 g/dL). The MCHC level of critical class (29.58 ± 0.73 g/dL) was below the lower reference range along with significant difference ($p<0.05$) with non-COVID patients (Table 1).

Table 1. The Hematological Profile of Moderate, Severe and Critical COVID-19 patients with Non-COVID patients

Hematological Profile	Moderate (n=32)	Non-COVID (n=32)	Severe (n=34)	Non-COVID (n=34)	Critical (n=34)	Non COVID (n=34)	Reference Range
WBC	9.11±0.74 ^a	6.42±0.31 ^b	11.38±0.88 ^a	6.31±0.30 ^b	12.00±0.79 ^a	6.31±0.30 ^b	3.5-9.5 10 ⁹ /L
Neutrophils	76.58±1.78 ^a	62.87±1.58 ^b	76.07±2.52 ^a	62.36±1.53 ^b	82.35±1.39 ^a	62.36±1.53 ^b	40-75%
Lymphocytes	16.31±1.43 ^b	28.23±1.20 ^a	17.21±2.11 ^b	27.8±1.17 ^a	12.74±1.25 ^b	27.80±1.17 ^a	20-45%
RBC	5.31±0.09 ^a	4.98±0.08 ^b	5.03±0.19	4.97±0.07	3.99±0.13 ^b	4.97±0.07 ^a	3.8-5.8 10 ¹² /L
HGB	14.6±0.41	14.39±0.17	13.69±0.35	14.32±0.17	12.50±0.34 ^b	14.32±0.17 ^a	11.5-17.5 g/dL
HCT	41.58±1.45	43.34±0.49	39.83±1.17 ^b	43.08±0.51 ^a	34.10±0.97 ^b	43.08±0.51 ^a	35-50 %
MCV	78.48±2.55 ^b	87.43±0.68 ^a	79.58±2.36 ^b	87.41±0.66 ^a	86.72±1.98	87.41±0.66	82-100 fL
MCH	27.61±0.69 ^b	29.76±0.30 ^a	27.64±0.96 ^b	29.68±0.29 ^a	26.03±0.61 ^b	29.68±0.29 ^a	27-34 pg
MCHC	34.73±0.33	34.03±0.17	33.49±0.56	33.98±0.16	29.58±0.73 ^b	33.98±0.16 ^a	31.6-35.4 g/dL

• Discussion

COVID 19 is an acute respiratory infectious disease caused by the coronavirus SARS-CoV-2 and comprehensive studies have found the origin, pathogenesis, diagnosis and treatment of the disease over the past few years. The risk of death increases with concurrent multiple organ failure as the severity of disease progresses rapidly (Liang, Wei *et al.* 2024). Many studies have been published to emphasize the significance of hematological abnormalities with a wide spectrum of analyses to predict the severity of COVID 19 disease. In this context, it is of great importance to have accurate, right and timely prognostic information to optimize patient management and monitoring. According to the described results of our study, the findings showed that the leucocyte count was significantly higher in severe and critical COVID 19 patients compared to moderate COVID 19 patients (Table 1). Similarly, elevated neutrophil count was found in critical patients compared to severe and moderate COVID 19 patients (Table 1). This finding was in line with the analyzed data of some previous studies (Huang, Wang *et al.* 2020, Yang, Liu *et al.* 2020, Sharafi, Jafarzadeh Esfehani *et al.* 2023). These results might be linked to the cytokine storm in ICU-admitted (critical) COVID 19 patients (Huang, Wang *et al.* 2020, QinC 2020, Ikram, Bukhari *et al.* 2022, Sharafi, Jafarzadeh Esfehani *et al.* 2023). On the contrary, a study in Iran reported that leucopenia and leukocytosis were not correlated with COVID 19 severity criterion (Esfahanian, SeyedAlinaghi *et al.* 2021).

The SARS-CoV-2 virus tends to attack the cells through angiotensin-converting enzyme 2 (ACE 2) receptor, which is mostly present on lymphocytes (Raj, Mou *et al.* 2013) and can cause a cytokine storm and lymphocytic infiltration to organs (Lechuga, Morel *et al.* 2023). Hence, this might be the reason for the observed lymphopenia in critical patients. Many studies have found the higher prevalence of lymphopenia in COVID 19 severity (Yun, Sun *et al.* 2020, Rahman, Niloofa *et al.* 2021), which is similar to the analyzed data of our three (moderate, severe and critical) classes of COVID 19 patients on the basis of severity (Table 1). In a previous study, data collected for pediatric COVID 19 patients showed no significant leukopenia and lymphopenia at the time of admission (Bari, Ch *et al.* 2021). Interestingly, a study found the lymphocyte count increased with the increased severity of COVID 19 disease with the prevalence of fever, dyspnea, arthralgia and leukocytosis (Sharafi, Jafarzadeh Esfehani *et al.* 2023).

Red blood cells (RBCs) are the key cellular constituents of the blood. For this reason, they play an essential role to ensure the transfer of oxygen to the tissues and accompanied excretion of carbon dioxide (Russo, Tellone *et al.* 2022). Additionally, decreased red blood cell count was another factor

found in critical (intensive care unit-admitted) patients compared to moderate and severe COVID 19 patients (Table 1). Despite some previous literature have been indicated similar results (Al-Kuraishy, Al-Gareeb *et al.* 2022, Kronstein-Wiedemann, Stadtmüller *et al.* 2022, Lechuga, Morel *et al.* 2023), still, there are differences to confirm the major COVID 19 severity factor. The significant changes in the size and rigidity of RBCs, reduction in hematocrit level and increased RDW (red blood cell distribution width) has been recorded in COVID 19 patients (Russo, Tellone *et al.* 2022).

Reduced hemoglobin concentrations of our analyzed date have been shown in ICU-admitted (critical) COVID 19 patients (Table 1) which is consistent to meta analysis of four studies indicating hemoglobin levels to be lower in critical patients than in mild disease (Palladino 2021, Lechuga, Morel *et al.* 2023). However, few studies found no changes in hemoglobin levels in COVID 19 positive patients (Wan, Xiang *et al.* 2020, Wang, Yang *et al.* 2020). Researches have described drop in levels of hemoglobin, red blood cells and hematocrit (HCT) while raise in mean corpuscular volume (MCV) and reduction in mean cell hemoglobin concentration (MCHC) levels (Mao, Dai *et al.* 2021, Liang, Wei *et al.* 2024). However, the findings of the current study show that the critical COVID 19 patients have decreased MCV levels and increase in HCT and MCHC levels (Table 1). A significantly higher MCHC have been reported in COVID 19 related symptoms (Alfadda, Rafiullah *et al.* 2022), which can have multiple causes, consisting autoimmune hemolytic anemia and rare situations have been recorded in COVID 19 (Lazarian, Quinquenel *et al.* 2020).

To have a comprehensive view of the hematological abnormalities of COVID 19, our results indicated that among the study parameters, fever, dyspnea, lymphopenia and leukocytosis were the highlighted risk factors for severity criterion of COVID 19 disease. We have observed an association among the hematocrit and hemoglobin levels tend to progressively decrease with the aggravation of the COVID 19 disease.

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