Evaluation of Immuno-Hematological Parameters of Severe and Mild COVID-19 Cases in Babylon Province, Iraq

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KEYWORDS
COVID-19, Platelets, Red Blood Cells, Haemoglobin, And Mean Platelet Volume.

ABSTRACT
The hematopoietic system plays a very important role in contracting the corona virus infection. Hematology indicators are among the factors related to the clinical results of patients with covid-19 due to their cost-effectiveness, availability, speed and convenience of testing. The aim of this study was comparing hematological parameters including the number of Red Blood Cells (RBC), hemoglobin, hematocrit, and platelet count among mild and severe COVID-19 patients. Methods: The study was conducted on 100 Iraqi patients COVID-19 patients. Subjects were classified into two groups with mild (n= 50) and severe (n=50) COVID-19 infection symptoms based on the clinical criteria. The hematological parameters measurement included Red Blood Cell (RBC) count, Hemoglobin (Hb) levels, White Blood Cell (WBC) count, Platelet count (PLT), Hematocrit (HCT) levels, Platelet Distribution Width (PDW), and Mean Platelet Volume (MPV). An independent sample T-test was used to compare the means of hematological parameters between two groups. Results: The RBC count was significantly lower in severe group compared to mild group ($P \leq 0.05$). HCT levels were significantly reduced in the severe group compared to mild group ($P \leq 0.05$). The severe patients had a significantly lower PLT than mild patients ($P \leq 0.05$). No significant difference in Hb levels was observed between severe and mild patients. The severe patients had a significantly higher PDW than mild patients ($P \leq 0.05$). Additionally, the severe patients had a significantly higher MPV than mild patients ($P \leq 0.05$). Conclusion: The findings of this study indicate that complete blood count measurements can be used as useful biomarkers to assess the severity of Covid-19. Early identification of severe COVID-19 patients using these markers can help to better manage and accelerate the treatment process for COVID-19 patients.

1. Introduction

In the Wuhan region of China, a novel coronavirus began manifesting in people in December 2019. It was referred to as COVID-19, which is short for “coronavirus disease of 2019." The SARS-CoV-2 virus is the source of the COVID-19 illness. It primarily resides in bats and wild birds but can infect people and other animals. It spreads rapidly among people because the human immune system is not familiar with this new virus (Schwartz and Graham, 2020; Jebril, 2020; Jeffrey *et al*., 2020).

COVID-19 has been a significant health concern since the start of the new year, 2020, and it may be catastrophic, especially for the elderly. Although the clinical disease’s mortality is well understood, its pathophysiology is far less well understood (Mason, 2020).

The COVID-19 virus can infect anyone who has not been exposed to SARS-CoV-2. Nearly half of the 8,866 patients with COVID-19 confirmation were above 50 (47.7%). The average incubation period was 5.2 days, and male to female ratio was close to 2.7:1. In contrast, severe COVID-19 cases and fatalities have mainly affected middle aged individuals and the elderly with a history of smoking or other basic diseases like hypertension and heart disease. The COVID-19 patient death rate was 2.1% during this research (Xu *et al*., 2020).

The hematopoietic system has a key role in the 2019 coronavirus infection. In COVID-19 patients, many haematological abnormalities have been found. Haemoglobin, eosinophils, and basophils have all significantly decreased from the disease's early stages, and this decline is correlated with the disease's severity and medical results. Monocytes dynamics of in COVID-19 are yet unclear since SARS-CoV-2 infection of monocytes seems to have a direct influence on the antiviral adaptive immune systems (Palladino, 2021).

In many haematological laboratory tests, lymphocytes, peripheral eosinophils, and neutrophils were dramatically altered in COVID-19 patients, suggesting that they may serve as a marker for disease progression and medication efficacy (Huang et al., 2020b). Furthermore, numerous studies point to a link between COVID-19 infection and lower haemoglobin (Hb) levels (Lippi and Mattiuzzi, 2020).

Therefore, this study was conducted to compare mild and severe COVID-19 patients in CBC parameters, including red blood cell count, haemoglobin, hematocrit, and platelet count, in Babylon Province, Iraq.

2. Materials and methods

Specimens collection and subjects

This study was carried out from July 2021 to March 2024 in one of the central hospitals of Babylon province, Iraq. The criteria for inclusion in the study were patients who had been diagnosed with Covid-19 and had not been vaccinated and pregnant women and people with blood diseases were excluded from the study. 50 patients were selected for each group of mild and severe COVID-19 infected and healthy personals (150 patients in total). Subjects were classified into three groups with mild and severe COVID-19 infection symptoms based on the clinical criteria set by the World Health Organization (WHO) and healthy personals. Severe COVID-19 infected subjects were included with: Respiratory rate >30 breaths /minute, Oxygen Saturation < 93% on room air, PaO2/FiO2 Ratio < 300 mmHg, clinical signs, and chest X-ray or CT scan. The mild COVID-19 infection subjects were included case who did not meet the criteria for severe disease.

The Scientific and Ethics Committee of Babylon/Hammurabi college of medicine approved the research protocol, research instrument, and participants informed constant. Informed consent was obtained from all patients.

Hematological parameters measurement

According to the treatment protocol of the hospital, blood samples were taken from all patients and healthy individuals. Ethylenediamine tetraacetic acid (EDTA) vacuum tubes were used to collect blood samples. An Automatic hematology analyzer (MS4s) was used to analyze the complete blood count (CBC) of the patients. The hematological parameters measurement included Red Blood Cell (RBC) count, Hemoglobin (Hb) levels, White Blood Cell (WBC) count, Platelet count (PLT), Hematocrit (HCT) levels, Platelet Distribution Width (PDW), and Mean Platelet Volume (MPV).

Statistical Analysis

Data analysis was performed using the IBM SPSS Statistics, version 25.

Descriptive statistics were cased for all variables. An independent sample T-test was used to compare the means of hematological parameters between the groups.

3. Results and discussion

The hematological parameters reported significant differences between the severe and mild COVID-19 patients. Detailed results related to RBC levels, HCT levels, PLT, Hb levels, PDW, and MPV are presented in Figures 1 to 6, respectively. The RBC count was significantly lower in severe group compared to mild group (Mean ± SE: Mild = 5.08 ± 0.07, Severe = 4.6 ± 0.09, $P \leq 0.05$). HCT levels were significantly reduced in the severe group compared to mild group (Mean ± SE: Mild = 41.2 ± 0.60, Severe = 37.5 ± 0.95, $P \leq 0.05$). The severe patients had a significantly lower PLT than mild

patients (Mean ± SE: Mild = 284.3 ± 10.5, Severe = 241.3 ± 16.8, P ≤ 0.05). No significant difference in Hb levels was observed between severe and mild patients (Mean ± SE: Mild = 13.4 ± 0.02 g/dL, Severe = 13.6 ± 0.02). On the other hand, the severe patients had a significantly higher PDW than mild patients (Mean ± SE: Severe = 14.11 ± 0.59, Mild = 9.04 ± 0.86, P ≤ 0.05). Additionally, the severe patients had a significantly higher MPV than mild patients (Mean ± SE: Severe = 10.64 ± 0.18, Mild = 8.35 ± 0.05, P ≤ 0.05).

Table 1. dimorphic data

Covid-19 cases				
Groups **Parameters**	**Severe** **N=50**		**Mild** **N=50**	
Gender	**Male 31 (62%)** **Female 19 (38%)**		**Male 23 (46%)** **Female 27 (54%)**	
Age	**Male**	**Female**	**Male**	**Female**
14-30	**16%**	**%8**	**%25**	**%26**
31-47	**27%**	**14%**	**%52**	**%48**
48-64	**57%**	**78%**	**%23**	**%28**

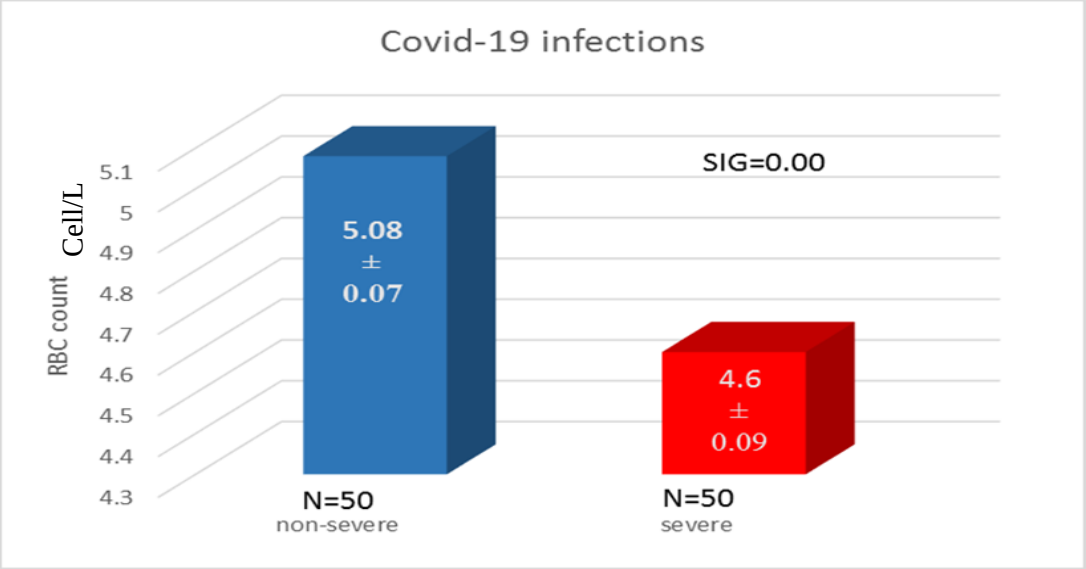

Figure 1. RBC levels significant variations (P ≤ 0.05) of severe & mild COVID-19 viral infection (mean ± SE).

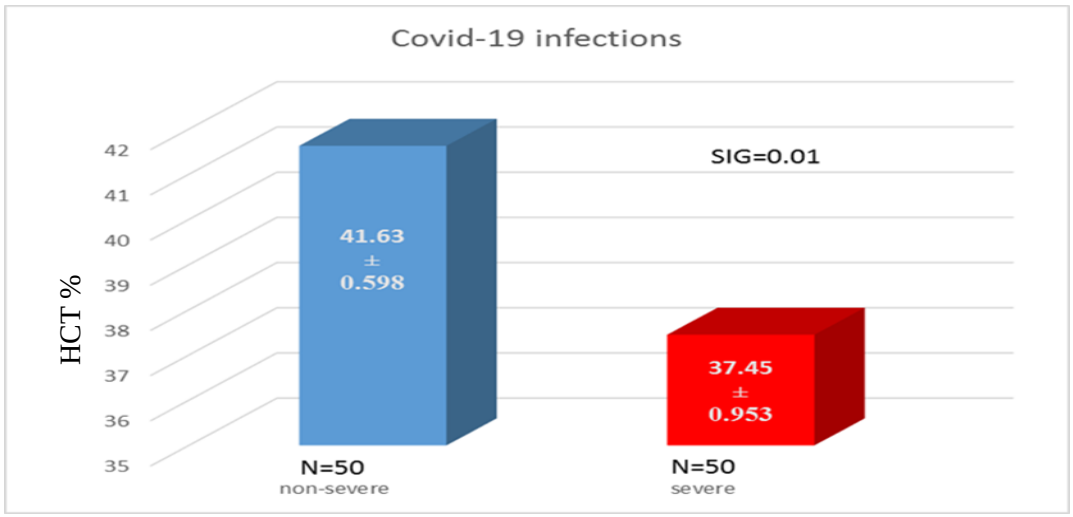

Figure 2. Hematocrit levels significant variation ($P \leq 0.05$) of severe & mild COVID-19 viral infection (mean ± SE).

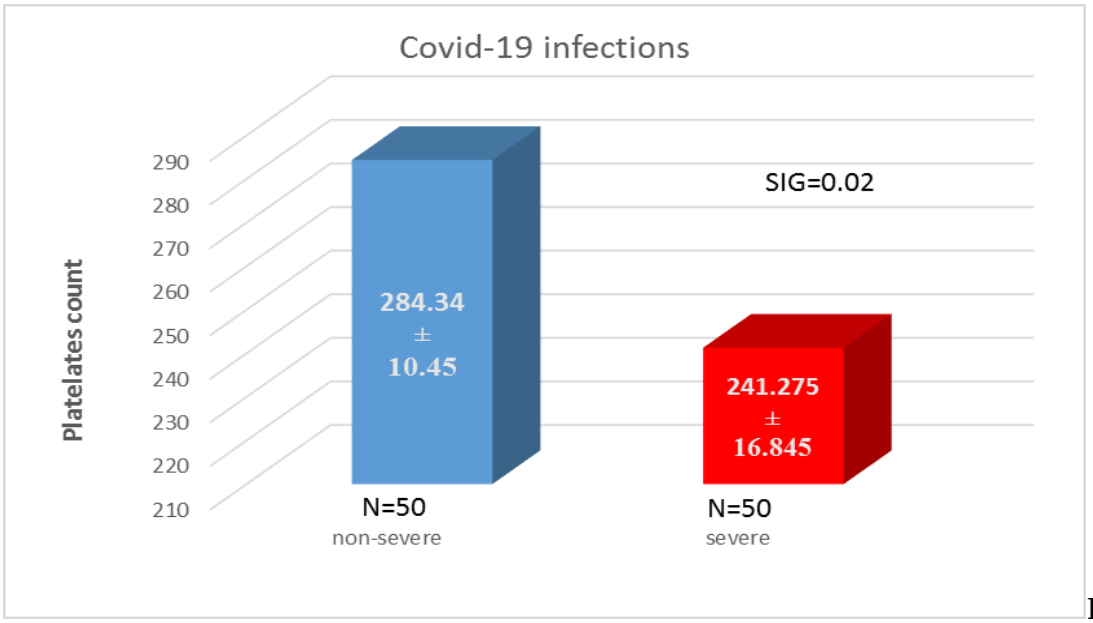

Figure 3. Platelet count significant variation ($P \leq 0.05$) of severe & mild COVID-19 viral infection (mean ± SE).

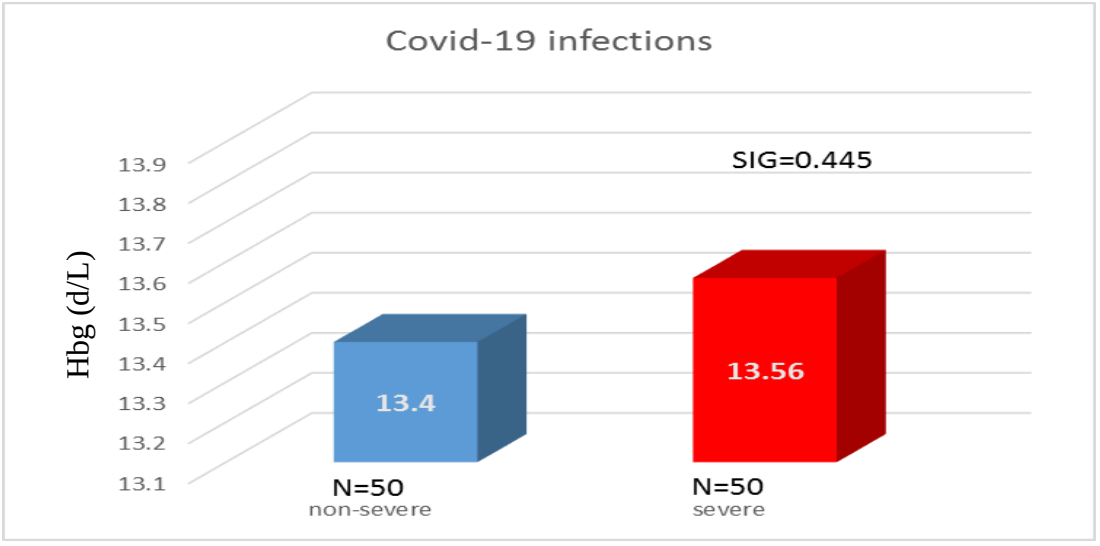

Figure 4. Hb levels significant variation ($P \leq 0.05$) of severe & mild COVID-19 viral infection (mean ± SE).

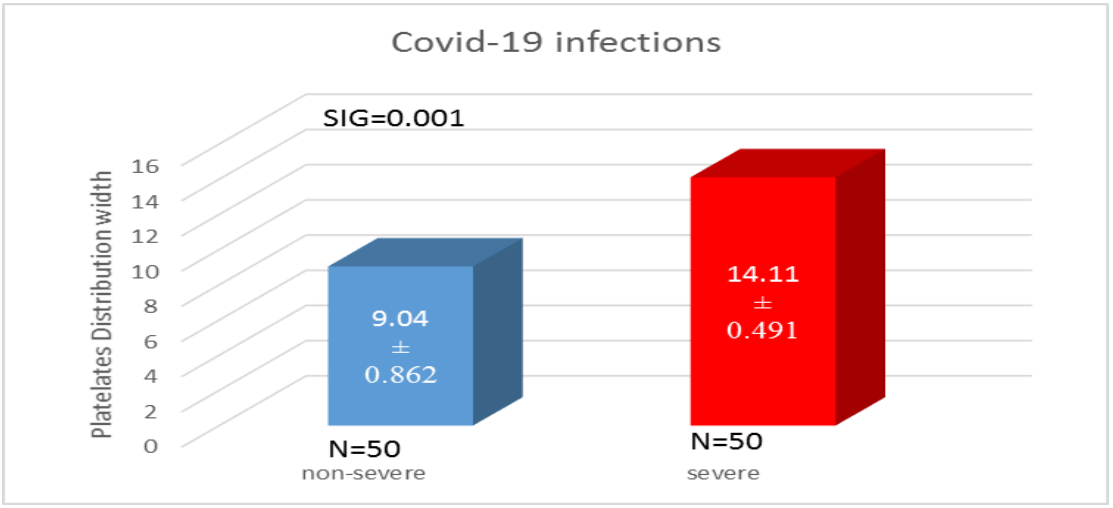

Figure 5. Distribution of platelet width (PDW) significant variation ($P \leq 0.05$) of severe & mild COVID-19 viral infection (mean ± SE).

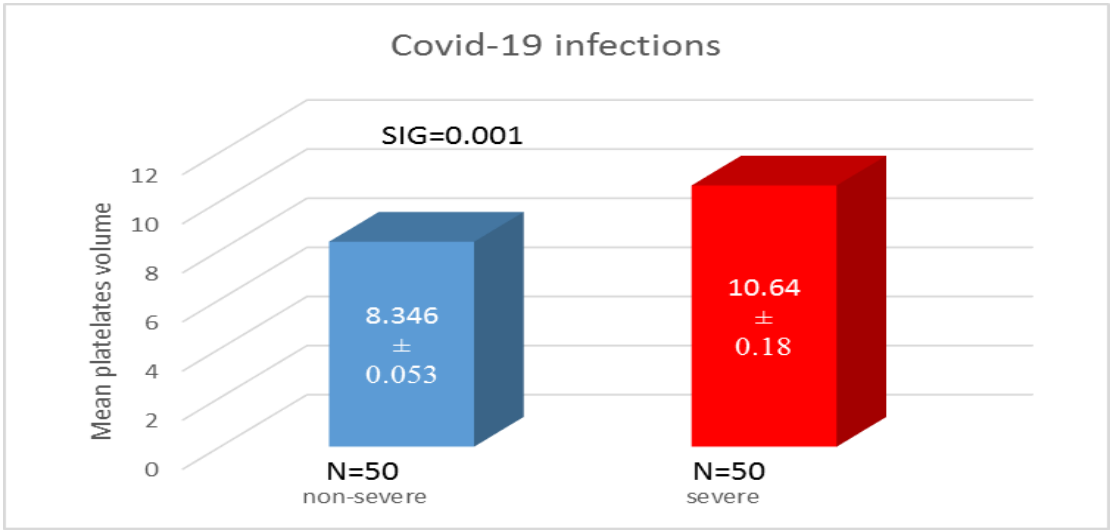

Figure 6. Mean platelet volume (MPV) significant variation ($P \leq 0.05$) of severe & mild COVID-19 viral infection (mean ± SE).

Table 1 shows percentage increase of severe COVID-19 infected male patients. Mildly infected patients had an inverse status, with female patients showing a higher percentage of infections compared to males. This variation may be attributed to high mobility, work in different places, and travel among several provinces. Also, a high percentage of males are uncommitted to health prevention measures compared to females. However, other research found that females are more conscious than males about dealing with a new health issue and the limitations and measures that accompany it. Because they have a worse capacity to handle a crisis, females are more vulnerable to mental health issues, which eventually results in a greater prevalence of anxiety, depression, and sleep difficulties (Giudice et al., 2022).

Females experience a greater psychological strain as a result of the emergency. Because they typically provide care and serve as the family's focal point, they are more cooperative and less likely to spread the virus. On the other hand, males were less inclined to adhere rigidly to restriction procedures and were more likely to frame the pandemic situation favorably, returning to "normal life" fast (Qi et al., 2021). However, regardless of age, males with COVID-19 are more at risk for poor outcomes and mortality than women, according to previous research, even though both genders have the same prevalence (Jin et al., 2020).

As shown in Figure 1, the results demonstrated that the red blood cell count was considerably lower in COVID-19-severely infected patients ($P \leq 0.05$) than in mild ones.

We might use the fall in bone marrow production to describe this trend. According to Elderdery et al. (2022), anemia was substantially more prevalent in COVID-19. Anemia in individuals with severe or serious COVID-19 may be associated with iron homeostasis dysmetabolism (Russo et al., 2022).

Another study suggests that the SARS-CoV-2 infection may impact red blood cells. RBC indicators and the severity of patients' diseases seem related (Bouchla et al., 2022). Researchers hypothesize that COVID-19 prevents erythropoiesis in patients' bone marrow, although the precise mechanism by which it induces anemia remains unclear (Berzuini et al., 2022).

According to Bouchla et al. (2022), the virus may cause RBC oxidative stress by raising intracellular Ca2 levels and cellular susceptibility to mechanical stress. On the other hand, sepsis may be caused by increased RBC-ROS because it makes red blood cells less flexible. This makes the cells shrink and the membranes scramble, which is a process called eryptosis (Pretorius, 2018).

Also, the results demonstrate a substantial decrease ($P \leq 0.05$) in COVID-19-severely infected patients to mild ones in the hematocrit levels, as shown in Figure 2. Anemia and an insufficient supply of healthy red blood cells may cause this decrease in hematocrit levels. Russo et al. (2022) reported decreased hematocrit levels in COVID-19 infection. Other studies concluded that severe COVID patients have hematocrit and RDW (Red Cell Distribution Width) depression (Henry et al., 2020).

Several hypotheses explain how anemia with severe COVID-19 infections results in lower HCT and RDW (Dhinata, 2021). The innate immune system will respond by turning on signaling pathways that cause the liver to create more hepcidin hormone. The digestive system would absorb less iron from food due to the transporter ferroportin's inability to move iron out of cells (Taneri et al., 2020). Long-term infection may result in less iron being available for erythropoiesis, which lowers hemoglobin concentrations. Additionally, SARS-CoV-2 infection might directly harm bone marrow, further interfering with the erythropoiesis process (Henry et al., 2020).

Figure 3 demonstrated a substantial drop in platelet count ($P \leq 0.05$) of COVID-19 severely infected compared to mild ones. Viruses, which could interact with megakaryocytes and inhibit platelet formation, are responsible for this drop. In severe cases of COVID-19 infection, 58–95% of patients have mild thrombocytopenia (Thachil, 2020). In patients with severe infection, only 23x109 to 31x109/L or less of platelets are present, compared to mild infection (Lipp et al., 2020).

A normal count of platelets remains in infected individuals with systemic immunological and coagulation activity maintain a normal count of platelets, indicating a significant compensatory platelet production response. Reports of COVID-19-infected individuals with severe thrombocytopenia were rare (Wool and Miller, 2021). Barrett et al. (2021) found a correlation between an increase in critical illness and all-cause mortality among hospitalised COVID-19 individuals' platelet size, count, and maturity.

Figure 4 illustrates the findings, which revealed no statistically significant variations in haemoglobin levels for severe and mild COVID-19 infections ($P \leq 0.05$). Anaemia is an infection that affects haemoglobin levels and may occur with both severe and mild COVID infections. 38.2% of COVID-19 patients exhibited lower haemoglobin levels, according to Huang et al. (2020a). Age, comorbidities, and illness severity all contributed to a decline.

Another study discovered that the hemoglobin level in severe COVID-19 cases that require admission to the ICU was significantly lower than in mild and moderate cases without the requirement of ICU admission (Henry et al., 2020).

Hypoxia caused by SARS-CoV-2 viral activity in the lung tissue may be linked to anemia caused by COVID-19. The body may experience inflammation due to its gas exchange-related structures, which could impact iron metabolism (Dhinata, 2021). The innate immune system's efforts to stop virus reproduction may impact iron metabolism in addition to causing an inflammatory state. For the virus to reproduce within the human body, it needs a faster metabolism and more iron (Habib et al., 2021).

Figure 5 shows a significant elevation ($P \leq 0.05$) of COVID-19 severely infected compared to mild ones in the platelet distribution width (PDW). It may refer to several problems for those patients. People with cancer, diabetes, respiratory, and cardiovascular diseases have higher PDW levels (Tzur et al., 2019).

Since there is still much to learn about the natural history of COVID-19, the majority of earlier investigations concentrated on the clinical correlations and prognosis linked to PDW in certain illnesses (Gowda et al., 2021).

PDW is a promising indication for diagnosing the mild form of COVID-19, according to Wang et al. (2020). When the result is less than 12.7 fL, a standard peripheral blood test's PDW may alert physicians to SARS-CoV-2 infections. No reports mention PDW and COVID-19, however. PDW modifications are also observed in COVID-19 individuals. They could show a connection between COVID-19 infections and PDW. Another study, however, came to the opposite conclusion, finding a significant predictor at admission for patients' eventual development of acute respiratory distress syndrome (ARDS), with greater relevance when combined with the level of D-dimer rise. (Yovchevska et al., 2022).

In contrast to mild groups, Figure 6 showed a significant increase ($P \leq 0.05$) in mean platelet volume (MPV) in severe COVID-19 patients. Other illnesses linked to high MPV, including cardiovascular disease, diabetes, immune thrombocytopenia, cancer, and others, might also be characterised by bone marrow producing a lot of new platelets.

Turkish research discovered a correlation between MPV and COVID-19 severity (Ozder, 2020). Another study refers to the COVID-19 severity predictor. Despite the lack of clear evidence, Quispe-Pari et al. (2022) have linked an increased or growing MPV to mortality.

A clinical trial demonstrated a correlation between an elevation in pro-inflammatory cytokines and MPV. According to Gao et al.'s research, IL-6 levels rose in COVID-19 patients in direct proportion to the disease's severity. According to these MPV data, rising MPV may result in high levels of IL-6 in COVID-19 (Gumus et al., 2021).

Conclusion & recommendation for futuristic studies

The current study concluded that the haematological parameters related to RBC, haemoglobin, and platelets make a biomarker for severe COVID-19 and that infections do not depend on age, but sex affects the severity of infections.

1- The study conducted a comparative analysis of COVID-19 mild and severe infections in white blood cells and other CBC parameters.

2- We conducted a genetic study to compare COVID-19 mild and severe infections.

This study examines the effect of several COVID-19 vaccines on disease severity.

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