



Hematological Variations Among SARS-COV-2 Patients Attending Zhyan Hospital at Ranya District, Iraq

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Abstract

Millions of people throughout the world have been impacted by the global pandemic virus SARS-COV-2. There is a paucity of information on the impact of SARS-COV-2 on hematological parameters in Kurdistan. To assess the effect of several physiological and pathological factors on the severity of the disease, this study looks at the hematological parameters among SARS-COV-2 patients hospitalized at Zhyan Hospital in Ranya, Kurdistan Region, Iraq. 200 cases were recruited for this study between 28th of September and 31st of December 2021. 50 negative people made up the control group, while 150 SARS-COV-2 patients mild, severe, and critical cases formed the study's three main study groups. The patients in the three groups were compared in terms of their hematological characteristics. The study revealed that compared to controls, SARS-COV-2 patients had significantly increased levels of white blood cells, granulocytes, platelet-large cell ratio, monocyte, red distribution width, platelet distribution width, platelet and decreased lymphocytes. WBC count, granulocyte, platelet-large cell ratio, monocyte, red distribution width, and platelet distribution width were all considerably higher in the critical group of SARS-COV-2 patients than in the severe and mild groups. Additionally, critical patients had considerably higher levels of lymphocytopenia and thrombocytopenia than severe and mild patient groups. Additionally, the critical group contained the highest proportion of SARS-COV-2 patients with concomitant conditions such as hypertension, diabetes and cardiovascular disease. The illness severity of SARS-COV-2 infection is nearly correlated with age, comorbidity, and levels of WBC, Lymphocyte, Granulocyte, Platelets, and P-LCR. Additionally, our results based on basic laboratory data may be useful in early illness severity prediction, and to improve the SARS-COV-2 patient survival rate.

Introduction

Since SARS-COV-2 was found in December 2019, in Wuhan, China, important doubts have been raised about the possibility of a connection between its progression and numerous clinical and laboratory results [1]. Severe instances can result in secondary infections, respiratory distress, arrhythmia, abrupt cardiac damage, kidney failure, shock, and even death [2, 3]. Given the high mortality rate and rapid onset of acute respiratory distress syndrome (ARDS), a prompt diagnosis is essential right away [4]. However, for patients who have a mild illness, all aforementioned outcomes might be possible [5]. In addition, illness procedure begins while that virus attaches to the host cell via its spike protein and invades [6]. Once within a human body, the virus attaches that ACE-2 receptor found in alveoli with the different cells then begins to replicate. So damages type-2 pneumocytes, causing them to release particular inflammatory mediators that attract macrophages [7].

Although SARS-COV-2 is largely of respiratory infection, newer indications suggest might be evaluate that systemic illness, causing several systems, such as gastrointestinal, hematopoietic, cardiovascular, pulmonary, immunological, and neurological systems [8, 9, 10]. To predict the outcomes, including death,

hematological markers related to SARS-COV-2 that are currently being used which are variables taken from multiple sources. Complete blood count (CBC) testing is simple and affordable, counts of leukocytes (neutrophils and lymphocytes) and thrombocytes, and other measurements are all included in the complete blood count (CBC) test [11]. Also, lymphocytopenia, thrombocytopenia, and leukocytosis in complete blood count (CBC), it is likely linked to the requirement for intensive care unit (ICU) care, acute respiratory distress syndrome, and a prolonged hospital stay [12].

With regard to age, comorbidities and gender might affect the mortality rate. They may also be considered as predictors of poor outcomes [13]. On the hematological results of patients in Kurdistan/Iraq who tested positive for SARS-COV-2, little information has been published. The aim of this study to evaluate the variations of hematological parameters among SARS-COV-2 patients at Ranya District's Zhyan Hospital and to assess their correlation with the disease severity.

Materials and methods

A. Study approval and sample design

The ethical statement of the study was approved by the Research Ethics Committee (No. 80), of the University of Sulaimani, College of Medicine (Sulaimaniyah, Kurdistan Region, Iraq). The study was carried out in Zhyan Hospital, Ranya, Al-Sulaimaniyah, KRG, Iraq- the sole corona center in the city, between 28th of September and 31st of December 2021. The study design was retrospective, cross-sectional with one-time sampling after the disease confirmation. SARS-COV-2 disease was diagnosed with the reverse transcriptase polymerase chain reaction (RT-PCR) test of the nasopharyngeal/oropharyngeal swab specimens. The assignment of the patients to the Mild, Severe, and Critical groups, based on WHO guidelines of the diagnosis and treatment criteria of the disease, for which the features were as the following: (1) Mild, minor symptoms, no signs of pneumonia or hypoxia. (2) Moderate, with fever, respiratory tract symptoms, and imaging shows pneumonia. (3) Severe, patients with fever, cough, dyspnea with severe pneumonia or severe acute respiratory infection: RR > 30 breaths/minute, SpO₂ < 92% on room air. (4) Critical, patients with respiratory failure and mechanical ventilation required; shock; Combining other organ failure, intensive care unit is needed.

The study inclusion criteria were: definitive diagnosis of SARS-COV-2 (except for the control group); age range (20 - 90) years, both sexes (male/female), vaccinated and un-vaccinated, smokers and non-smokers, comorbidity and non-comorbidity, and comorbidity type. We obtained the clinical characteristics of SARS-COV-2 patients, including demographic information, clinical symptoms and clinical laboratory investigation including the whole blood count.

B. Blood collection and laboratory diagnosis

Approximately 3 ml of peripheral blood was collected in the EDTA collection tube from the subjects of each group. The test was completed in the clinical laboratory of SMART health tower in Ranya, Al-Sulaimaniyah, KRG, Iraq. Complete cell count was performed via a standardized complete blood cell counter (CBC) automated hematology analyzer (Coulter swelab alfa hematology analyzer/Boule Medical AB/Philippine). The measured parameters were WBC, LYM, GRA, MID, HGB, MCH, MCHC, RBC, MCV, HCT, RDW, PLT, MPV, PDW, PCT, and P-LCR (Figure 1).

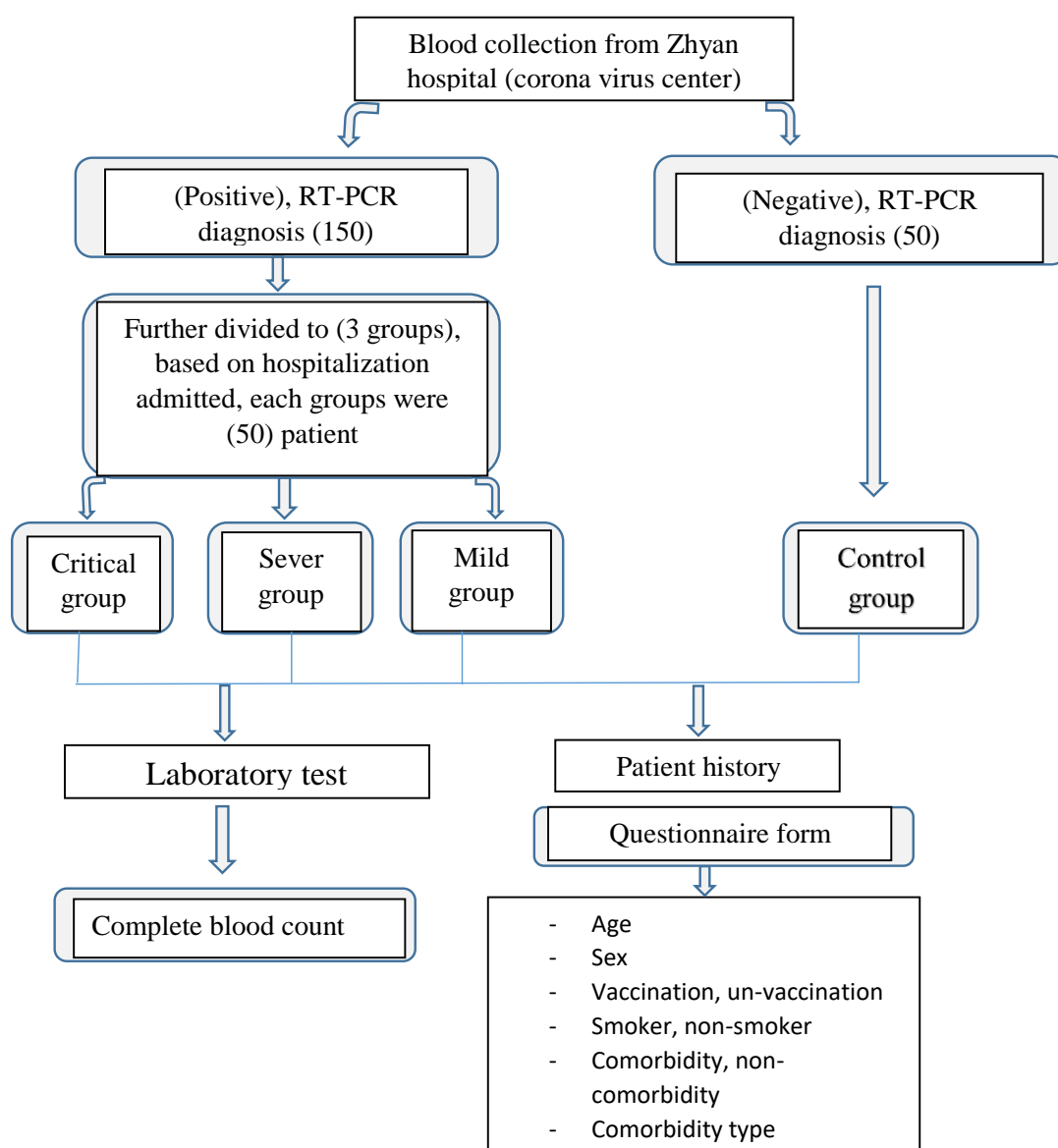


Figure-1: The flow chart shows the overall procedure of blood sample collection, patient history and experimental design.

C. Statistical analyses

The statistical analyses were performed in GraphPad Prism software (version 9.3.1). Regarding the medical history and demographic data, for the qualitative data, the differences between groups were assessed for significance using Pearson chi-square test, whereas, the age data (quantitative) were analyzed with one-way ANOVA followed by Tukey’s multiple comparison test. Furthermore, the age of each group was presented in mean ± SD format utilizing descriptive statistics. Then, the results of the CBC measurements were compared for statistical significance by one-way ANOVA and then multiple comparison by Tukey’s test. The results of multiple comparison analysis were exported in graphical format as well.

Results

The average age of the included subjects (200) was 53.17±16.10 years. With respect to gender, 55% patients were male and the rest were female. Regarding the other parameters, 63% had one or more comorbidity type. Amongst these, hypertension (43%), diabetes (25%) and cardiovascular disease (11.5%) were the most

coexisting conditions. Less common conditions were heart stroke (1%), kidney failure (3%), and liver disease (3%). Furthermore, (95.5%) of the subjects were un-vaccinated and (25.5%) of them were smoking (Table 1).

The mean age of control group (47.64±14.46 years) and mild group (47.34±14.68 years) were similar to each other ($P = 0.9996$), but significantly different from that of severe patients ($P = 0.6082$) (56.98±16.28 years) and critical patients (60.70±14.98 years), and there was no significant difference among severe versus critical patients. Control group versus critical groups and mild versus critical similar to each other ($P = 0.0001$) significantly difference from that of control versus severe ($P = 0.0122$), mild versus severe ($P = 0.0090$).

Table-1: Demographics and baseline characteristics of control, mild, severe and critical groups are shown in terms of number (no.) and percentages (%), along with P -values.

Variable	Control group (n=50)	Mild group (n=50)	Severe group (n=50)	Critical group (n=50)	Total (n=200)	p -value
Age in years (mean ± SD)	47.64±14.46	47.34±14.68	56.98±16.28	60.70±14.98	53.17±16.10	<0.0001
Male Sex no. (%)	(52%)	(58%)	(56%)	(54%)	(55%)	0.9394
Female Sex no. (%)	(48%)	(42%)	(44%)	(46%)	(45%)	
Vaccinated no. (%)	(16%)	(2%)	(0%)	(0%)	(4.5%)	0.0001
Un-vaccinated no. (%)	(84%)	(98%)	(100%)	(100%)	(95.5%)	
Smoking no. (%)	(16%)	(24%)	(28%)	(34%)	(25.5%)	0.2122
Non-smoking no. (%)	(84%)	(76%)	(72%)	(66%)	(74.5%)	
Comorbidities no. (%)	(50%)	(52%)	(72%)	(78%)	(63%)	0.0051
Hypertension no. (%)	(36%)	(34%)	(50%)	(52%)	(43%)	
Diabetes no. (%)	(20%)	(22%)	(16%)	(42%)	(25%)	
Cardiovascular disease no. (%)	(8%)	(10%)	(10%)	(18%)	(11.5%)	
Heart stroke no. (%)	(0%)	(0%)	(2%)	(2%)	(1%)	
Kidney failure no. (%)	(0%)	(2%)	(4%)	(6%)	(3%)	
Liver disease no. (%)	(0%)	(2%)	(2%)	(4%)	(3%)	

For routine blood tests, some included CBC test parameters (WBC, LYM, MID, GRA, MCHC, RDW, PDW, PLT, and P-LCR) showed the significant difference among all groups as shown in (Figure 2), who also showed increased WBCs, GRA, P-LCR, MID, RDW in critical patients than mild patients. Conversely, critical patients had fewer LYM and PLT. Also, according to (Figures 2B and I), except for LYM ($P = 0.0002$) and PLT ($P = 0.0367$), none of the other parameters showed a significant difference among the control and mild group. Furthermore, for most parameters, both groups were significantly different in severe and critical group which were statistically different from each other as well. Moreover, all aforementioned significant CBC parameters except PLT ($P = 0.9398$), showed no significant difference between control and critical group. Apart from the other included CBC test parameters (HGB, RBC, HCT, MCV, MCH, MPV and PCT) showed no significant difference between all four groups (Figure 3).

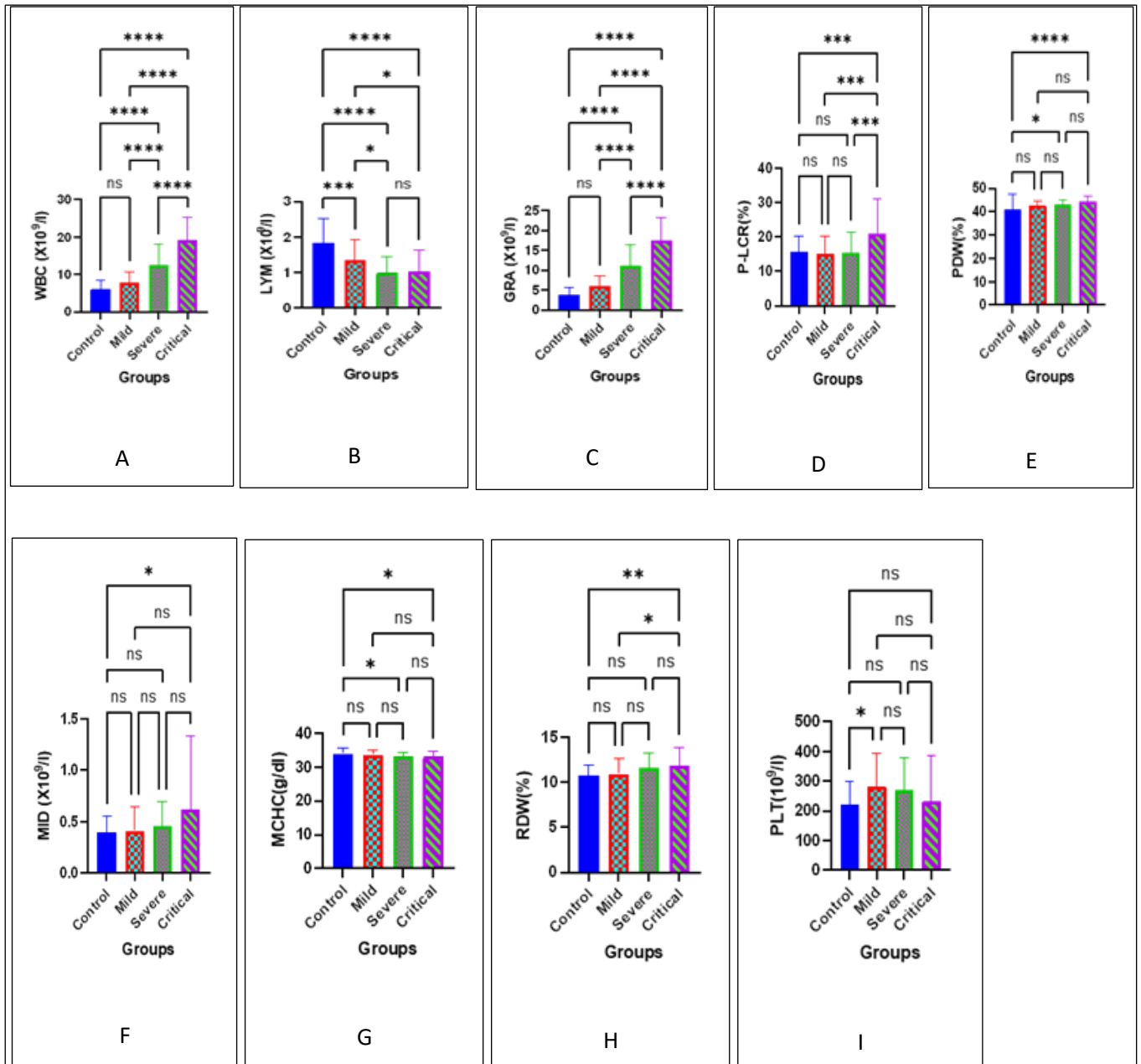


Figure-2: Comparison of blood cell count among control, mild, severe and critical patients with SARS-COV-2 infection. A: WBC (white blood cell count), B: LYM (lymphocyte), C: GRA (granulocytes), D: P-LCR (platelet-large cell ratio), E: PDW (platelet distribution width), F: MID (less frequently occurring WBCs), G: MCHC (mean cell hemoglobin concentration), H: RDW (red cell distribution width), I: PLT (platelet count). Data are presented as mean \pm standard deviation, * = $P < 0.05$, ** = $P < 0.01$, *** = $P < 0.001$, **** = $P < 0.0001$, ns = no significant

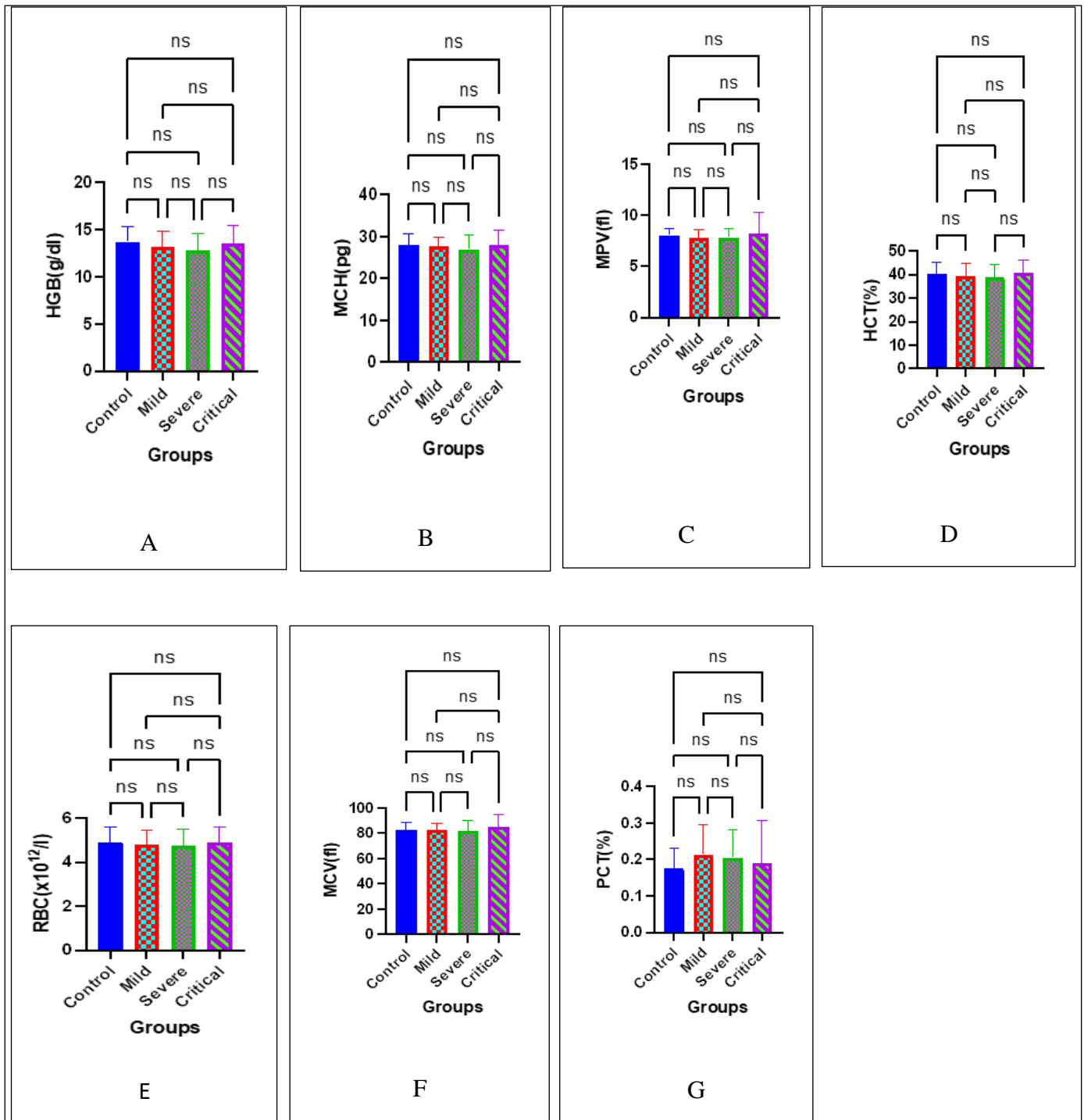


Figure-3: Comparison of blood cell count among control, mild, severe and critical patients with SARS-COV-2 infection. A: HGB (hemoglobin), B: MCH (mean corpuscular hemoglobin), C: MPV (mean platelet volume), D: HCT (hematocrite), E: RBC (red blood cell count), F: MCV (mean corpuscular volume), G: PCT (plateletcrit). Data are presented as mean \pm standard deviation, ns = no significant

Discussion

Recently, numerous studies have focused on potential factors for detecting the disease severity among SARS COV-2 patients [14], as the mortality rate is significantly greater in patients who progress into severe

or critical levels [3]. Thus, it is crucial to identify severe and critical patients in earlier stages, with the aim of improving recovery and reducing mortality rates.

In the present study, the majority of critical and severe ill patients were older and had more comorbidity illnesses than those with mild illness [15]. This was in accordance with previous studies [3], the elderly SARS-COV-2 patients develop to severe disease more often compared to young and middle-aged individuals. This might be explained by a decrease in cell-mediated immune activity and humoral immunological function with age [16].

Furthermore, our study demonstrates a statistically insignificant difference between genders, however, according to [17], the morbidities seem to be more common in males than in women [18]. In addition, the study of [19, 20], in line with our study observations, showed that the coronavirus vaccination was extremely successful in preventing severe illness and death.

In the present study, among the comorbidities associated with disease severity, hypertension, diabetes and cardiovascular disease were the most common ones. These findings were in accordance with [21] Study, additionally proinflammatory cytokine reduction, which results in weakened immune function, may be the cause of this illness. It consistent with study [22], pre-existing conditions have been identified as risk factors for SARS-COV-2 disease severity.

With regard to the contribution of smoking on the spread, severity, and bad outcomes in SARS-COV-2, former studies show its association with an increased severity [23, 24]. Through increasing ACE2 expression (SARS-COV-2 receptor) [25]. However, with respect of smoking, our data indicated no significant differences with worsening the disease outcomes.

In the present study, we analyzed the hematological indices of the included SARS-COV-2 patients and revealed significantly higher mean values of WBC count but lower lymphocytic counts among critically infected patients in comparison to the mild group. Moreover, as a result of high WBC count, multiple infections may arise, which may be induced by glucocorticoids [26]. According to [27], lymphocytes display the coronavirus receptor ACE2 and might be a straight purpose virus. Also, neutrophilia is an indicator of venous thrombosis, and it may play a role in the development of thrombosis by inducing a necroinflammatory response [28]. Furthermore, neutrophils defend us not only through phagocytosis but also through the development of neutrophil extracellular traps (NETs) [29]. Additionally, according to [30] increased granulocytes reported among those who died, in agreement with our outcomes.

Regarding the platelets, a recent meta-analysis has inferred that a lower platelet count predicts serious bleeding [31]. It is uncertain how SARS-COV-2 causes platelet consumption, particularly in cases of severe illness. More theory says that lung injury causes platelet activation and aggregation, eventually leading to thrombocytopenia [32] which is in line with our findings, although, a number of researchers hypothesized that thrombocytopenia may be a poor predictor for platelet levels.

Moreover, RDW was a prognostic value in the setting of SARS-COV-2 critical group which might be due to the influence of respiratory failure and systemic inflammation on erythropoiesis [33]. Higher Red Blood Cell Distribution Width (RDW) in hospitalized patients is related with a significantly increased risk of death and septic shock [34]. The link between increasing RDW and disease severity may be consistent with prior findings in non-SARS-COV-2 infection, suggesting that RDW might rise when RBC production is slow in the presence of increased WBC [35].

The previous studies, reported that patients with SARS-COV-2 have lower hemoglobin levels [36]. However, mean corpuscular hemoglobin concentration (MCHC) have been linked to illness severity [37]. Platelet large cell ratio (P-LCR) increases significantly, but PDW fall significantly [38]. Findings appear in line with our results. On the other hand, survivors exhibited much greater hemoglobin concentrations, mean corpuscular hemoglobin (MCH), and mean corpuscular volume (MCV), according to [30]. There are reports of higher level of red blood cells (RBC) [39] but decreased mean platelet volume (MPV) in SARS-COV-2 patients [38]. Findings inconsistent with our outcomes, which show no significant difference of HGB, MCH, MCV, RBC, MPV, HCT, and PCT parameters among patients.

Conclusion

This study suggests a relationship between disease severity of SARS-COV-2 patients, hematological and clinical manifestations. The study reveals that individuals with higher age and comorbidities are more vulnerable for worsening the disease outcomes. Also, it demonstrates a potential effect of vaccination on decreasing the disease risk. Additionally, elevated WBC count, GRA, P-LCR and lymphocytopenia significantly was more occurred with critical than severe to mild SARS-COV-2 patients. However, with regard to smoking or gender, our results imply a non-significant difference. We suggest the inclusion of other blood measurements such as inflammatory and coagulation parameters and to perform more rigorous statistical analysis in order to determine the best indicator for predicting the disease severity.

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