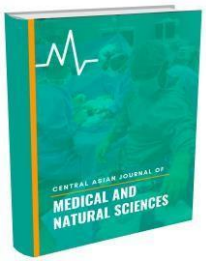

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Article

COVID 19 Severely Disrupts Blood Markers and Renal Function

Muntadher Mohammed Jaber[1,2*], Falah Herez Madhloom Alrabea[1], Samer Kareem Hanoon[1], Ali Ghaleb Ammar[1]

1. Iraqi Ministry of Health, Thi Qar Health Office, Thi Qar, Iraq
2. College of Health and Medical Technologies, National University for Science and Technology, Thi Qar, Iraq

* Correspondence: muntadher099@gmail.com

Abstract: Since the emergence of COVID-19 in Wuhan, extensive research has explored its immediate and long-term effects. This study investigated the relationship between COVID-19 and blood disorders, liver proteins, and biochemical factors. We analyzed 150 samples divided into two groups: 75 COVID-19 patients and 75 healthy, recovered individuals aged 25-75 years. The study examined various hematological and biochemical markers, including WBC, lymphocytes, platelet count, NLR, RBC, CRP, BUN, creatinine, D-dimer, and ferritin. Significant differences were found in hemoglobin levels, WBC count, RBC, blood urea, and serum creatinine, with COVID-19 patients showing increased levels of these markers except for hemoglobin, which decreased. The results indicate that COVID-19 adversely affects hematological markers, renal function, and induces abnormal immune responses. Moreover, the severity of illness is positively associated with blood hemolysis and D-dimer levels, leading to hyperglycemia and pancreatic effects by inhibiting insulin synthesis. These findings underscore the impact of COVID-19 on blood parameters and organ function.

Keywords: Covid 19, WBC, RFT, D. dimer, Ferritin

1. Introduction

In December 2019, for the first time, it was announced that the first confirmed case of the new coronavirus, Previously identified as (coronavirus for severe acute respiratory syndrome), had been recorded in China and then spread to all parts of the world. After the rapid, massive and widespread spread of the Coronavirus 2019 (Covid-19), it became a pandemic on March 11, 2020, and according to what the World Health Organization announced, before that, reports were coming from Wuhan, in Hubei Province, where the epidemic originated in China [1,2] .

The virus was named SARS-CoV-2, or severe acute respiratory syndrome, by the International Committee on Taxonomy of Viruses after its genome was sequenced. It was genetically related to the 2003 coronavirus epidemic that caused the SARS pandemic.Up until July 30, 2022, COVID-19, a disease brought on by the SARS-CoV-2 virus, constituted a serious threat to public health over the world, with 581,182,629 cases and 6,418,043 recorded deaths [3,4].

The SARS-CoV-2 virus belongs to the Nidovirales order, the suborder Cornidovirineae, the family Coronaviridae, and the subfamily Orthocoronavirinae (Fig 1). Because of protrusion on its membrane that resemble spikes, SARS-CoV-2 is an enclosed, symmetrical virus that resembles a crown. Its single-stranded RNA genome has a positive sense [5].

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The pathophysiology of COVID-19 is comprised of multiple mechanisms, such as ACE2-expressing cells being infected by the virus, ACE2 downregulating the RAAS, immune system dysregulation, endothelial cell damage and thromboinflammation, and tissue fibrosis (Fig 2).The majority of COVID-19 individuals have mild, self-limiting symptoms, however the condition can progress in different ways. According to Liang et al and Khan et al, the viral infection typically starts with flu-like symptoms and may either progress from mild to severe or be asymptomatic. In spite of this, up to 30% of patients need to be admitted to the hospital, and up to 17% of them need critical care assistance due to multiorgan failure, hyperinflammation, and acute respiratory distress syndrome (ARDS) [6] .

Significantly higher levels of liver and renal function markers, including blood urea, s.creatinine, C-reactive protein, lactate dehydrogenase, D-dimer, and interleukin-6, have been associated with severe or fatal cases of SARS-CoV-2 [7] . Furthermore, in comparison to milder cases in which patients survived, they are associated with lower levels of albumin, platelet counts, and lymphocytes [8]. The NLR, or neutrophil-to-lymphocyte ratio is a specific indicator of inflammation in a few diseases, including Hashimoto's disease, irritable bowel syndrome, thyroid disorders, SARS-CoV-2 infections, and cardiac ailments. An infection with SARS-CoV-2 also generates significant inflammation [9,10] .

Gaining insight into the association between these biomarkers and COVID20 outcomes could aid in the development of a risk-adapted treatment plan for patients suffering from this illness. This article's goal is to examine the roles that inflammatory, biochemical, and hematological biomarkers play in the pathophysiology of COVID20 disease, as well as how the severity of the disease affects each biomarker's level.

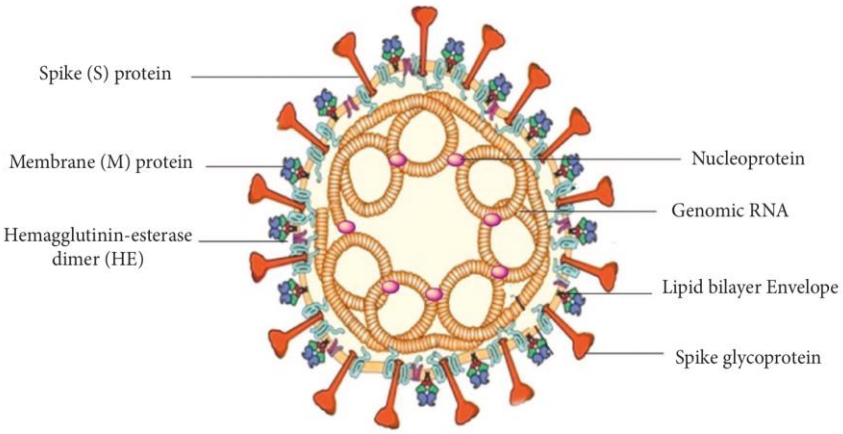

Figure 1. The single-stranded positive-sense (+sense) RNA that makes up the enveloped virus SARS-CoV-2 is depicted in the diagram. Four essential proteins are needed by the virus: envelope, spike, membrane, and nucleocapsid [11].

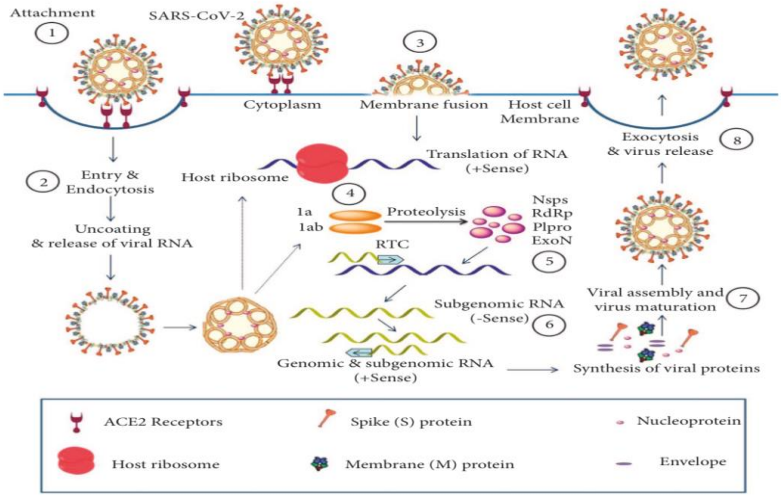

Figure 2. Once inside the host, SARS-CoV-2 has an infectious life cycle. (a) When the S-protein connects to the angiotensin-converting enzyme (ACE2) receptor, the virus attaches. 2) endocytosis or (c) fusion of the viral membrane. (d) Proteins 1a and 1ab are produced by translating the viral RNA. (e) The replicase-transcriptase complex (RTC) and nonstructural proteins are produced via protein proteolysis. (f) Produce fresh viral proteins and RNA (sense). (g) Connectivity to the viral particle. (h) Viral discharge through exocytosis [11].

2. Materials and Methods

This study includes 150 samples that were separated into two groups: 75 patients who were infected with the Corona virus, and the results were taken from the patient records in the isolation unit in Dhi Qar Governorate after obtaining approvals, and 75 samples from healthy people who were exposed to a previous infection and completely recovered, and their ages were between 25. To 75 years.

The blood was centrifuged and utilized to calculate physiological parameters. The Mindray BC-21S Hematology Analyzer measured whole blood counts, and serum chemical assays were performed quantitatively using a FUJIFILM DRI-CHEM NX500Dry Chemistry Analyzer according to the manufacturer's instructions. Serum immunoassays were performed using Cobas e411 Immunoassay Analyzers with Assay Technology Electrophoretic Immunohistochemistry ("ECLIA") according to the manufacturer's recommendations.

3. Results

Characteristics of the study population

The present study enrolled 75 patients with COVID-19 and 75 healthy control subjects. The demographic characteristics of patients and control subjects are shown in table (1). According to age, the mean age of patients with COVID-19 was 55.58 ± 5.85 years old and that of control subjects was 50.32 ± 11.05 years old and there was non-significant difference between different groups (P = 0.065). Regarding to gender, in overall, 79 (52.7%) male and 71 (47.3%) female were included. Patients with COVID-19 included 38 (50.7%) cases were male gender and 37 (49.3%) cases were female, while control subjects included 41 (54.7%) subjects were male gender and 34 (45.3%) subjects were female and there was non-significant difference in the frequency distribution of patients and control subjects

according to gender (P = 0.689). Statistically, significant differences appeared between studying groups for hemoglobin level, WBC count, RBS, B.Urea and S.Creatinine. All these hematological and biochemical parameters showed significant increase in COVID-19 patients as a comparison with control group, except hemoglobin level show significant decrease in COVID-19 patients as a compared with the control group. Regarding Age, gender, lymphocyte count and platelets counts show non-significant differences appeared between studying groups.

In this study, 75 COVID-19 patients and 75 healthy control participants were enlisted. Table 1 displays the demographic details of both patients and control subjects. The mean age of COVID-19 patients was 55.58 ± 5.85 years, while the control participants' mean age was 50.32 ± 11.05 years. P = 0.065 indicates that there was no discernible difference between the groups.

Table 1. Characteristics of patients with COVID-19and healthy control

Characteristic	Patients (n=75)	Healthy Control (n=75)	P
Age (years)	55.58 ± 5.85	50.32 ± 11.05	0.065
Gender			
Male	38 (50.7%)	41 (54.7%)	0.689
Female	37 (49.3%)	34 (45.3%)	
Hemoglobin (Hb)	11.17 ± 1.99	13.55 ± 1.32	< 0.001
White Blood Count (WBC)	12.52 ± 2.42	7.11± 1.64	< 0.001
Lymphocyte Count	2.02 ± 0.62	2.67 ± 0.801	0.286
Platelets counts	237.88 ± 78.94	237.68 ± 63.86	0.989
Random Blood Sugar (RBS) mg/dl	179.30 ± 18.28	103.12 ± 12.52	< 0.001
Blood Urea mg/dl	59.08 ± 7.87	28.10 ± 6.08	< 0.001
S. Creatinine mg/dl	1.70 ± 0.60	0.72 ± 0.28	< 0.001

Measurements of inflammatory parameter

The comparison of inflammatory parameter such as C-reactive protein (CRP) levels between patients with COVID-19 and healthy control subjects has been carried out and the results were demonstrated in figure (3). Mean levels of CRP were (98.02± 12.99 mg/dl vs 3.16 ± 0.76 mg/dl), The level was substantially higher in patients with COVID-19 than in healthy control patients (P<0.001), after comparing the two groups of patients, respectively.

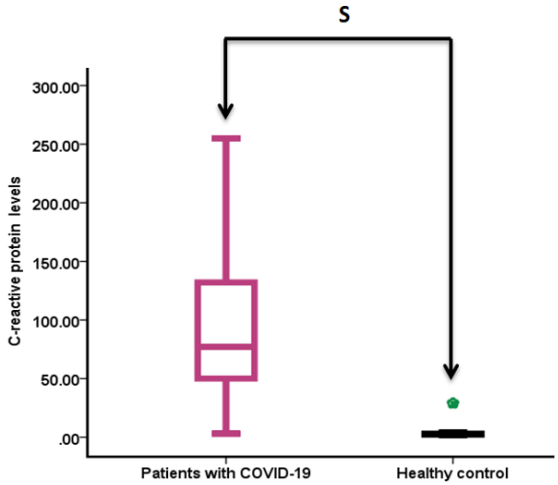

Figure 3. C-reactive protein (CRP) concentrations in patients with COVID-19 and healthy control subjects. S: statistically significant P < 0.05.

Measurements of serum ferritin parameters

The comparison of serum ferritin levels between patients with COVID-19and healthy control subjects has been carried out and the results were demonstrated in figure (4). Mean levels of serum ferritin were (664.64± 67.51 mg/dl vs 69.24 ± 6.23 mg/dl), in patients with COVID-19and healthy control respectively; the level was significantly higher than in patients with COVID-19in comparison with healthy control (P< 0.001).

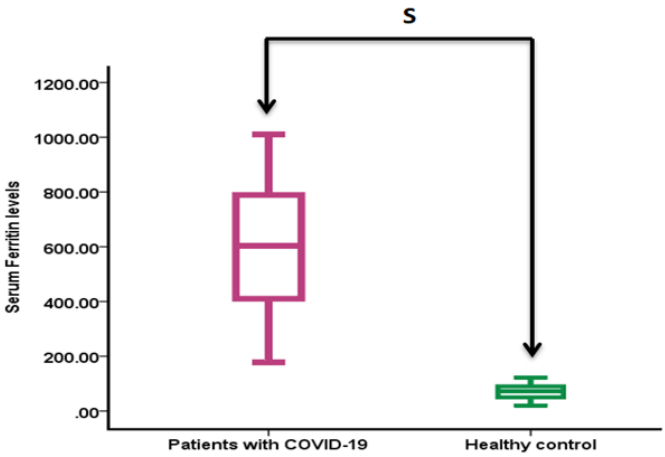

Figure 4. Serum C-reactive protein (CRP) concentrations in patients with COVID-19 and healthy control subjects. S: statistically significant P < 0.05.

Measurements of D. dimer

The comparison of D. dimer levels between patients with COVID-19and healthy control subjects has been carried out and the results were demonstrated in figure (5). Mean levels of D. dimer were (1423.32± 225.22 vs 147.38 ± 15.19), in patients with COVID-19and healthy control respectively; the level was significantly higher than in patients with COVID-19in comparison with healthy control (P< 0.001).

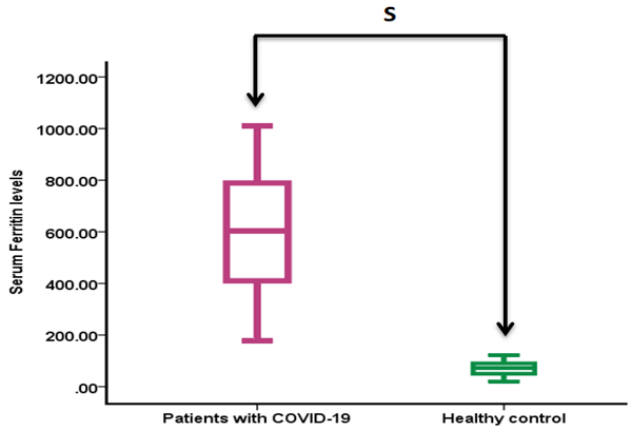

Figure 5. D. dimer concentrations in patients with COVID-19and healthy control subjects. S: statistically significant P < 0.05.

Diagnostic accuracy of different parameters

The diagnostic accuracy of separating COVID-19 patients from healthy control subjects using CRP level was investigated using receiver operating characteristic (ROC) analysis. An AUC value of 0.994 (95% confidence interval [CI], 0.983-1.000, P <

0.001), sensitivity of 98.7%, specificity of 98.7%, PPV of 98.7%, and NPV of 98.7% were obtained with an ideal CRP cut-off value of 11.50 mg/dl.

Furthermore, it is possible to differentiate COVID-19 patients from healthy control people with a sensitivity of 100.0%, specificity of 100.0%, PPV of 100.0%, and NPV of 100.0% by using an ideal ferritin cut-off value of 150 mg/dl.

Receiver operating characteristic (ROC) analysis was done in relation to D-dimer to determine the diagnostic accuracy of employing D. dimer level to differentiate COVID-19 patients from participants in good health. An AUC value of 0.982 (95% confidence interval [CI], 0.960-1.000, P < 0.001), sensitivity of 97.3%, specificity of 97.3%, PPV of 97.3%, and NPV of 97.3% were obtained with an ideal D-dimer cut-off value of 435.0.

Table 2. Roc curve of different parameters

Characteristic	**CRP**	**Ferritin**	**D. dimer**
Cutoff value	> 11.5	> 150.00	> 435.0
P value	**< 0.001**	**< 0.001**	**< 0.001**
Sensitivity %	98.7 %	100.0 %	97.3 %
Specificity %	98.7%	100.0%	97.3%
PPV %	98.7 %	100.0 %	97.3 %
NPV %	98.7%	100.0%	97.3%
AUC (95% CI)	0.994 (0.983-1.000)	1.000 (1.000-1.000)	0.982 (0.960-1.00)

AUC= Area under the curve.
CI= Confidence interval.

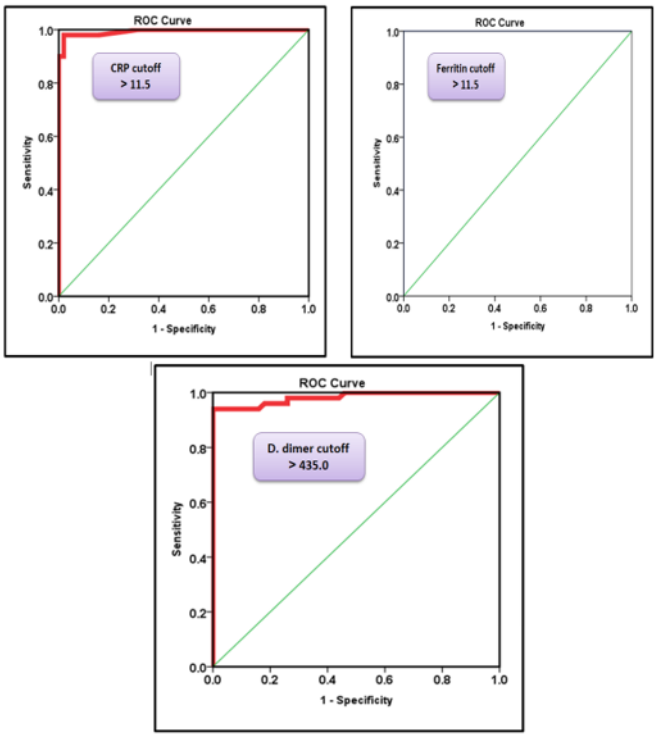

Figure 6. Analysis of the receiver operator characteristic curve using several parameters to determine a potential diagnostic cutoff value

Correlation between different parameters.

The correlations between different parameters in patients with COVID-19were shown in tables(3). The present results show significant positive correlation between CRP level and WBC count (r=0.306, p= 0.031), between D. dimer and WBC count (r= 0.334, p= 0.018) in patients with COVID-20. But the present results show non-significant correlation between all other parameters.

Table 3. Correlation between Different parameters.

Characteristic	Different parameters					
	CRP		Ferritin		D. dimer	
	r	*P*	*r*	*P*	*r*	*P*
HB	0.217	0.131	0.101	0.483	0.104	0.474
WBC	0.306	0.031*	0.249	0.081	0.334	0.018*
lymphocyte	0.047	0.744	0.190	0.186	0.123	0.393
platelets	0.169	0.241	0.031	0.832	0.238	0.097
RBS mg/dl	0.223	0.120	0.073	0.614	0.153	0.289
Urea mg/dl	0.038	0.795	0.004	0.977	0.102	0.480
S.Creatinine mg/dl	0.105	0.470	0.142	0.324	0.032	0.827

r: correlation coefficient.

Logestic regression correlations between different parameters.

The Logestic regression model show that the correlation of inflammatory markers such as CRP in which have directly correlate with ferritin among COVID-19patients as in figure (5), this result might be refer to that COVID-19condition enhances production of CRP in relation to ferritin. Also show there was that the D dimer directly correlate with CRP and ferritin among COVID-19 patients as in figure (5), this result might be refer to that COVID-19condition enhances production of D dimer in relation to CRP and ferritin.

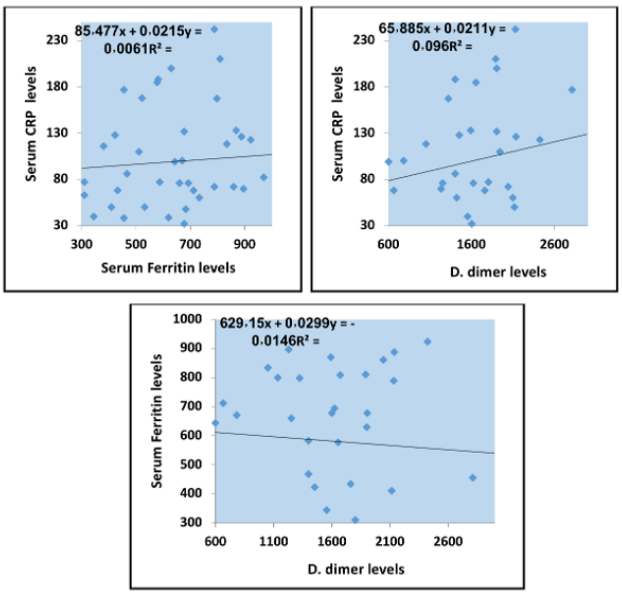

Figure 7. Logestic regression correlations between Different parameters

4. Discussion

According to the current study, the sick group's white blood cell count was much larger than the control group's, but its hemoglobin, lymphocyte percentage, and platelet count were all significantly lower. The male group showed a significant increase in hemoglobin, white blood cell and platelet counts, as well as a rise in the percentage of lymphocytes. The hematological parameters did not differ significantly between the age groups.

The results of the current study were in agreement with those of Asghar et al [12] they discovered that the patient's group had significantly lower levels of hemoglobin, lymphocytes, and platelets, and that these levels were inversely correlated with the severity of the illness. Additionally, it was discovered that there were more white blood cells in the group than in the control. Their analysis revealed that the patient's critical care unit ward had greater white blood cell counts but lower hemoglobin, platelet, and lymphocyte counts. Usul et al [13] obtained results that differed from our study; they discovered that the control groups had significantly higher levels of hemoglobin, platelets, and lymphocytes than the SARS-2 patients did. However, their study concurred with ours in that the SARS-2 patients had higher white blood cell counts.

According to Anurag et al [14], in their study found that the amount of lymphocytes showed a positive association with disease severity, and that a high neutrophil-to-lymphocyte ratio had a negative significance for people with SARS-CoV-2 infection.According to Lagunas-Rangel et al [15], individuals with COVID-19 have a worse prognosis when their neutrophil-lymphocyte ratio is larger.According to Peñaloza et al [16], myeloid cells, such as macrophages and monocytes, are essential for both the uncontrolled pro-inflammatory profile linked to severe COVID-19 and SARS-CoV-2 immunity.

In critical situations that correspond with other disorders, It has been demonstrated that the platelet to lymphocyte ratio is an independent determinant of prognosis and death. This resulted from the identification of lymphocytopenia, or a reduction in lymphocytes, in individuals who were in the critical stage. According to Aktar et al [17], as a result, the platelet to lymphocyte ratio increased in patients receiving treatment in intensive care units or who had passed away than in patients who were either admitted or in isolation wards during the early stages of infection. Low hemoglobin levels can be caused by anemia, coexisting conditions, and lifestyle choices including smoking cigarettes. Since the patient files used in this investigation lacked a thorough medical history, their impact on hemoglobin levels was not taken into consideration. Compared to men, women have a lower average hemoglobin level.

The present findings showed that the patient group's B.urea, S.creatinine, and Random blood sugar level were significantly higher than those of the control group. Patients' B.urea increased significantly in the female group, while Random blood sugar increased dramatically in the male group. S.creatinine did not significantly differ between the genders of the groups. Patients over 70 years of age showed a substantial increase in urea level according to age groups, however there were no significant variations in creatinine or Random blood sugar levels.

This study's findings were in line with those of Ok et al [18], who examined the B.urea nitrogen / creatinine ratio values and their relationship to the severity of the disease. They found that patients' concentrations of both parameters increased significantly when compared to the control group, and that patients with critical status had higher levels of both parameters than those with moderate or severe status. The Cheng [19], study. Their investigation focused on how COVID-19 disease affected individuals with kidney issues, and they came to the conclusion that kidney involvement was associated with a worse prognosis for COVID-19 patients. It appears that kidney illness at admission constituted a higher risk of worsening since patients with raised baseline serum creatinine had higher odds of being hospitalized to the critical care unit and requiring mechanical ventilation.

According to reports, patients with SARS and the influenza A virus subtype H1N1 had a higher chance of dying if they had kidney damage[20] .

The research In line with a recent study. revealed that the amounts of urea and creatinine were noticeably higher in COVID-19 patients, which were linked to an increase in D. Dimer. They also observed that the concentrations of these substances were higher in deceased patients than in patients receiving intensive care unit treatment and in patients in more than moderate status. D-dimer levels are important in the diagnostic algorithms used to rule out venous thromboembolism; in adult CAP, elevated plasma D-dimer levels are a prognostic factor and are linked to an enhanced inflammatory response [21]. The severity of COVID-19 is significantly correlated with D-dimer, according to current studies. D.dimer is a common lab test that is examined on hospitalized patients. However, there is no record of the diagnosis use of D.dimer levels in Covid-19 patients A study by Qiu et al [22] found that there is a combined effect linked to an increase in D. dimer and angiotensin gene expression, and that the degree of kidney effect severity may be related to the amount of virus that enters the lungs as a result of angiotensin-2 receptor overexpression and its effect on the kidneys.

Angiotensin 2 is an enzyme that functions as a receptor for SARS viruses and physiologically resists RAAS activation. Though it is found in the kidney, stomach, lung, and heart, the type I membrane protein ACE-2 is mostly linked to cardiovascular illness [23]. Based on RNA sequencing data from contemporary human tissues, it was found that the expression of ACE-2 in the kidney was roughly 100 times higher than in the lung. This suggests that kidney injury could arise from the coronavirus entering renal cells via an ACE2-dependent mechanism. Moreover, individuals with chronic renal impairment have higher levels of RAAS activity, which causes an increase in ACE2 receptors throughout the body. According to Jiang et al [23], this rise may result in simpler access to SARS-CoV-2 cells for infection.

The results of the Bhandari et al, study and the current investigation were in agreement that patients with COVID-19 have greater levels of RBS, even in those without pre-diabetes [24], and that RBS rises with the progression of the disease. A recent study discovered that pancreatic islets contain ACE2 receptors and that SARS-CoV-1 infection causes hyperglycemia in people who are not diabetics. RBS is a major predictor of mortality risk [25].Three years following SARS recovery, persistent hyperglycemia was noted, indicating damage to the pancreatic beta cells. SARS-CoV-2 may have comparable effects, leading to elevated blood sugar levels [26].

5. Conclusion

This study elucidates the significant impact of COVID-19 on various hematological and biochemical markers, demonstrating marked alterations in hemoglobin levels, WBC count, RBC, blood urea, and serum creatinine among infected patients. The findings reveal that COVID-19 patients exhibit elevated levels of these markers, with the exception of hemoglobin, which shows a decrease. These alterations indicate adverse effects on hematological markers and renal function, alongside abnormal immune responses. Additionally, the severity of COVID-19 is positively correlated with increased blood hemolysis and D-dimer levels, which contribute to hyperglycemia and impaired pancreatic function due to inhibited insulin synthesis. The study underscores the profound impact of COVID-19 on blood parameters and organ function, highlighting the need for ongoing monitoring and management of these markers in affected individuals. Further research is warranted to explore the long-term consequences of these alterations and to develop targeted interventions that can mitigate the adverse effects on hematological and biochemical health in COVID-19 patients.

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