ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Role of biomedical measurements on severity and outcomes of patients with COVID-19 infection: A retrospective follow-up study

Deldar Morad Abdulah[1], Hemin Khalid Saber[2]

[1]*Lecturer, Community and Maternity Nursing Unit, College of Nursing, University of Duhok, Iraqi Kurdistan, Duhok,*
[2]*Lecturer and Physician, Department of Medicine, College of Medicine, Hawler Medical University, Erbil, Iraqi Kurdistan*

Submission: 05-03-2022 Revision: 29-05-2022 Publication: 01-07-2022

ABSTRACT

Background: The clinical manifestations and laboratory biomarkers in the 1st week of the disease course may impact the patient's final clinical outcome. **Aims and Objectives**: In this study, we aimed whether biomedical measurements at the early stage can predict the severity and outcomes of patients with COVID-19. The patients aged 18 years and older who were diagnosed with COVID-19 by the internist met the initial eligibility criterion. The patients with medical records of the laboratory indicators and clinical outcomes were included in this study. **Materials and Methods:** In this retrospective follow-up study, 155 clinically ill patients with COVID-19 were followed up until recovery and death from the disease. **Results**: The average age of the COVID-19 patients was 49.7 (Sta. deviation: 16.6) aged between 18 and 90 years. The patients had mild severity of disease (67.10%) followed by moderate (19.36%), severe (7.74%), and critical (5.81%). The study found that 6.45% (n = 10) of the patients died and 93.55% (n = 145) were recovered from the disease. The concentrations of C-reactive protein (CRP), D-dimer, ferritin, lactate dehydrogenase (LDH), lymphocytes, and white blood cell were increased with increasing severities and in dead patients. D-dimer and CRP were the main contributing factors to the higher severity of disease and mortality among COVID-19 patients. The contributed symptoms to disease severity were diarrhea, epigastric pain, shortness of breath, headache, and fever. The higher LDH and being male were contributed to higher disease severity. **Conclusion**: This study showed that CRP and D-dimer are the main factors contributing to the severity and mortality among COVID-19 patients.

Key words: COVID-19; Inflammation; Mortality; Severity; Thrombosis

Access this article online

Website:
http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v13i7.43640

E-ISSN: 2091-0576
P-ISSN: 2467-9100

INTRODUCTION

The novel coronavirus called COVID-19 discovered in China, in December 2019 was spread to other countries.[1] Since declared by the World Health Organization (WHO), the disease has spread to most countries. Globally by June 24, 2021, there have been 179,065,823 confirmed cases of COVID-19, including 3,886,347 deaths, reported to the WHO.[2] Several studies have reported that the novel virus is extremely infectious. The outbreaks have been reported in clusters in individuals in close contact. The main issues of this disease are nosocomial infections and family transmission.[3,4]

The COVID-19 disease has a different clinical course compared to the previously known diseases.[5] The most common clinical symptoms of the COVID-19 disease are fever, shortness of breath (SOB), and dry cough, and the less common symptoms are headache, diarrhea, productive cough, runny nose, and hemoptysis.[6] These symptoms are different from mild to severe illnesses. Individuals who are aged 65 years and older, smokers, and those with comorbid diseases have significantly more likely to develop severe diseases.[7] The disease has a median incubation period of 5–6 days, but it may take up to 24 days.[8] In addition, the disease may have an unclear infectivity period.[9] The patients are presented with different levels of laboratory

Address for Correspondence:
Deldar Morad Abdulah, Community and Maternity Nursing Unit, College of Nursing, University of Duhok, Nakhoshkhana Road, Duhok - 42001, Iraqi Kurdistan, Iraq. **Mobile:** +9647507443319. **E-mail:** deldarmorad@uod.ac

abnormalities, such as leukopenia, leukocytosis, and lymphopenia.[10]

COVID-19 has similar clinical symptoms to ordinary upper respiratory tract infections in the 1st week. However, the medical condition of the patients may be escalated at any time within the 2nd week of the disease course. The patients may progress to serious disease between 8 and 18 days of the disease onset.[11] The final clinical outcomes of the patients may be controlled or predicted by the clinical manifestations, laboratory indicators, and radiological findings during the 1st week of the disease course. The investigation of the role of biomedical measurements of COVID-19 assists clinicians in establishing a rational and effective therapy for this viral infection.[11]

There are some reports on the role of biomedical measurements on the severity and outcomes in patients with COVID-19 in the literature. However, it has not been examined in the context of this region among the Kurdish population. The clinical course and laboratory indicators may differ between geographic areas.

Aims and objectives

In this study, we aimed whether biomedical measurements at the early stage can predict the severity and outcomes of patients with COVID-19.

MATERIALS AND METHODS

Design and patients

In this retrospective follow-up study, we included the patients who were diagnosed with COVID-19 disease. The patients who attended the private clinic in Erbil city in Iraqi Kurdistan were consecutively screened for the eligibility criteria. The patients were diagnosed by the internist of the study (second author). These patients were followed up until recovery and mortality from the disease.

Inclusion and exclusion criteria

The patients aged 18 years and older were included in the study regardless of sociodemographic aspects. The pediatric patients and those with missing information of laboratory measures and clinical examinations or pregnant at diagnosis were not included in this study.

Diagnosis and measures

The characteristics of the COVID-19 patients were recorded in a pre-designed questionnaire. The symptoms of the COVID-19 patients were documented in the pre-designed questionnaire. The required information of the patients was drawn from the medical records. The diagnosis of the COVID-19 disease was performed using reverse transcription polymerase chain reaction. The severity of the disease COVID-19 was rated as mild, moderate, severe, or critical. The patients who were included in this study were diagnosed at a private clinic in Erbil city in Iraqi Kurdistan between August 15, and October 20, 2020.

The diagnosis of the COVID-19 disease was approved by clinical examinations of the patients through signs and symptoms. The diagnosis of the disease was performed based on the guidelines and the severity of the disease was rated as mild, moderate, severe, or critical.[12] The patients were diagnosed at the private clinic in Erbil city in Iraqi Kurdistan between August 15, and October 20, 2020. The pulmonologist diagnosed the COVID-19 cases based on the WHO *interim guidance* for COVID-19[13] and local guidelines of the Ministry of Health.[12] The severity of the disease was determined based on the guidelines of the Ministry of Health in this region.[12] The category of the disease severity was mild, moderate, severe, and critical. The mild cases were determined if there was no sign of pneumonia on imaging. The moderate cases were determined in the case of the presence of fever and respiratory symptoms together with radiological findings of pneumonia. The severe cases were determined in the case of presence of respiratory distress ≥30 breaths/min; oxygen saturation ≤93% at rest; and arterial partial pressure of oxygen (PaO_2)/fraction of inspired oxygen (FiO_2) ≤300 mmHg (1 mmHg = 0.133 kPa). The severe cases were determined as clear lesion progression on imaging within 24–48 h >50%. The patients with failure and requiring mechanical ventilation, shock, with other organ failures (need intensive care unit care) were considered the critical cases.[12]

Management of COVID-19 disease

The patients with SARS-CoV-2 infection may have an asymptomatic or pre-symptomatic infection. The therapeutic management of non-hospitalized adult patients is based on the National Interim Guidelines for Clinical Management of COVID-19. The guide has information about patients who do not need hospitalization or supplemental oxygen. In addition, it has therapeutic information for those patients who have been discharged from an emergency hospital based on the disease severity and oxygen requirements.[14] We provided supportive care to non-hospitalized patients with acute COVID-19 to decrease the risk of the infection. Furthermore, we advised them when they have to contact a health-care provider and seek an in-person evaluation.[14]

Statistical analysis

The general characteristics of the patients were presented in number (%) or mean (SD). The prevalence rates of the patients were determined in number (percentage). The outcomes of the patients and their clinical features were determined in number (%). The comparisons of C-reactive protein (CRP) and D-dimer in patients with different severities and outcomes

were examined in a median test and Mann–Whitney U-test, respectively. The role of thrombosis and inflammation in the severity of disease and mortality of patients with COVID-19 was examined in nominal logistic regression analysis. The statistical calculations were performed using JMP pro-14.3.

Ethical considerations

The ethical permission for this investigation was received from the College of Medicine, Hawler Medical University. We did not apply any intervention to patients in this study. The authors protected the personal information of the patients throughout the study step.

RESULTS

A total of 155 patients diagnosed with COVID-19 of different severities were included in this investigation. The mean age of the patients was 49.7 (SD: 16.6) aged between 18 and 90 years of both males (75, 48.4%) and females (80, 51.6%). The study found that fatigue (77.4%), myalgia (71.0%), cough (68.4%), fever (67.7%), and sweating (64.5%) were the most prevalent symptoms in COVID-19 patients (Figure 1).

This study showed that most of the patients had mild severity of disease (67.10%) followed by moderate (19.36%), severe (7.74%), and critical (5.81%). The study found that 6.45% (n=10) of the patients died and 93.55% (n=145) were recovered from the disease (Table 1).

The study found that the concentrations of CRP, D-dimer, ferritin, lactate dehydrogenase (LDH), and white blood cell (WBC) were increased with increasing severities. In addition, these indicators were significantly higher in dead compared to recovered patients. The lymphocytes numbers were significantly decreased with increasing disease severity and in dead patients (Table 2 and Figure 2).

Our study showed that D-dimer and CRP were the main factors that contributed to the higher severity of disease in patients with COVID-19. The symptoms were contributed to the disease severity were diarrhea, epigastric pain, SOB, headache, and fever. The higher LDH and being male were contributed to higher disease severity (Table 3).

The study showed that high mortality was associated with an increasing count of WBC, levels of D-dimer, CRP, and LDH (Table 4).

DISCUSSION

We showed that the severity of the COVID-19 disease and mortality was increased with increasing levels of CRP and D-dimer. In similarity with this study, some studies have reported that hyperinflammatory response induced by SARS-CoV-2 is considered to be a significant cause of disease severity and death in COVID-19 infected patients.

The factors associated with severe illness in COVID-19 disease have not been completely understood yet. It seems that severe disease is not only associated with viral load.[15] The excessive inflammatory response to the COVID-19 disease is considered to have a crucial role in disease

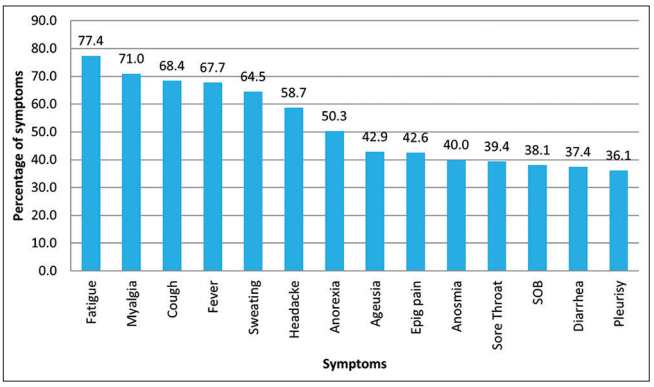

Figure 1: Prevalence rates of symptoms in patients with COVID-19 at the early stage of disease

Table 1: Prevalence rates of disease severity and case fatality rate of COVID-19 Patients

Outcomes and indicators (n=155)	Frequency distribution	
	Number	Percentage
Disease Severity		
Mild	104	67.10
Moderate	30	19.36
Severe	12	7.74
Critical	9	5.81
Disease Outcomes		
Death	10	6.45
Recovered	145	93.55
D-dimer		
Normal	97	62.58
Elevated	58	37.42
CRP		
Normal	100	64.52
Elevated	55	35.48
LDH (IU/L)		
Lowered	18	11.61
Normal	47	30.32
Elevated	90	58.06
Ferritin		
Lowered	12	7.74
Normal	106	68.39
Elevated	37	23.87
Lymphocyte (%)		
Lowered	31	20.00
Normal	117	75.48
Elevated	7	4.52
WBC (10^9/L)		
Lowered	14	9.03
Normal	115	74.19
Elevated	26	16.77

CRP: C-reactive protein, LDH: Lactate dehydrogenase, WBC: White blood cell

Table 2: Comparisons of laboratory indicators in patients with different severities and outcomes in patients with COVID-19

Indicators (n=155)	Severity and outcomes of COVID-19 patients (median (interquartile range)					
	Severity of COVID-19 disease				Outcomes of COVID-19 patients	
	Mild	Moderate	Severe	Critical	Recovered	Dead
CRP (Mg/L)	2.1 (3.1)	21.4 (60.1)	61.0 (79.75)	148 (132.0)	3 (6.3)	197.5 (89.8)
D-dimer (ug/ml)	0.3 (0.3)	1.0 (1.5)	2.0 (1.7525)	6.0 (9.4)	0.3 (0.7)	8.45 (5.2)
Ferritin (ng/ml)	62 (92)	365 (413.3)	941.5 (839.3)	1950 (1120)	98 (273.5)	1845 (1202.5)
LDH (U/L)	200 (224.5)	626.5 (545.5)	899.5 (378)	1450 (600)	279 (474)	1283.5 (517.5)
Lymphocyte	27.2 (13.8)	15.0 (21)	15.3 (17)	11 (22.0)	25 (15)	11 (3.6)
WBC	5500 (2200)	7900 (7975)	13050 (16700)	21500 (24350)	5690 (3300)	9750 (23800)

Median test was performed for statistical analyses (P<0.001). The numbers are in median (interquartile range). CRP: C-reactive protein, LDH: Lactate dehydrogenase, WBC: White blood cell

Table 3: Role of thrombosis and inflammation in severity of disease in patients with COVID-19

Controlling factors (n=155)	Severity of COVID-19 disease		
	Log Worth		P-value
Log [D dimer (ug/ml)]	184.067		0.00000
Log [CRP (Mg/L)]	28.852		0.00000
Diarrhea	8.740		0.00000
Sex	8.289		0.00000
Epigastric pain	7.477		0.00000
SOB	3.955		0.00011
Headache	3.012		0.00097
Log [LDH (U/L)]	2.800		0.00158
Fever	2.253		0.00559
Log [WBC]	1.249		0.05635
Fatigue	0.776		0.16746
Anorexia	0.718		0.19144
Sweating	0.519		0.30237
Pleurisy	0.249		0.56315
Log [ferritin (ng/ml)]	0.239		0.57721
Ageusia	0.231		0.58701
Age	0.162		0.68895
Sore Throat	0.111		0.77448
Anosmia	0.013		0.96984
Myalgia	0.011		0.97567
Cough	0.000		0.99985

The nominal logistic regression was performed for statistical analysis. CRP: C-reactive protein, LDH: Lactate dehydrogenase, WBC: White blood cell

Table 4: Role of thrombosis and inflammation in mortality of patients with COVID-19

Controlling factors (n=155)	Outcome: Mortality		
	Log Worth		P-value
Log [WBC]	21.027		0.00000
Log [D dimer (ug/ml)]	20.565		0.00000
Log [CRP (Mg/L)]	17.849		0.00000
Log [LDH (U/L)]	8.555		0.00000
Age	0.051		0.88913
Severity	0.000		0.99923
Sex	0.000		0.99955
Log [ferritin (ng/ml)]	0.000		0.99977

Nominal logistic regression was performed for statistical analysis. CRP: C-reactive protein, LDH: Lactate dehydrogenase, WBC: White blood cell

severity and mortality.[16] It is related to high concentrations of circulating cytokines, lymphopenia, and significant mononuclear cell infiltration in the lungs, heart,[17] spleen lymph nodes, and kidney.[18]

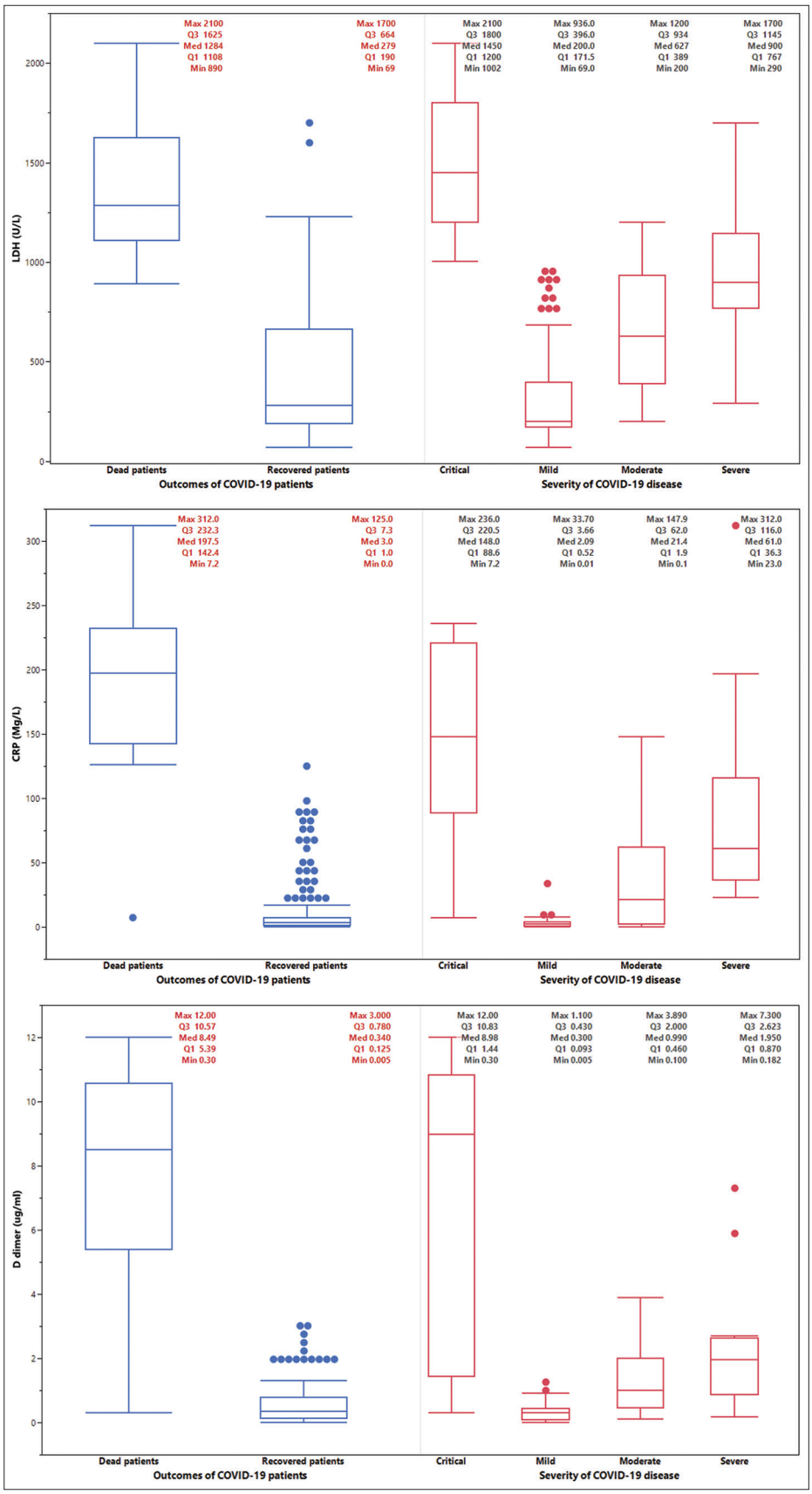

Figure 2: Comparisons of D-dimer, C-reactive protein, and lactate dehydrogenase in patients with different severities and outcomes

Older age and comorbidities are contributing factors to disease severity in COVID-19 patients as reported by the observational investigations. However, the recent investigations on the disease declare that the severe disease develops in younger age groups with no pre-existing medical and clinical conditions. In similarity with the findings reported in this study, high levels of inflammatory biomarkers; including CRP, ferritin, and D-dimers, a higher neutrophil-to-lymphocyte ratio,[19,20] increased serum levels of inflammatory cytokines and chemokines[21-23] are reported to contribute to disease severity and mortality.

Higher rates of venous thromboemboli (VTE) are found in patients with severe COVID-19 compared to their matched groups with acute respiratory distress syndrome. This finding suggests that the high rate is due to mechanisms and VTE risk factors in admitted patients; such as mortality and severe illness.[24] However, it is unclear whether COVID-19-related thrombotic events are due to conventional VTE, immunothrombosis, or a combination of these factors. COVID-19 patients with mild thrombocytopenia, mild prolonged prothrombin time, and increased fibrinogen and raised D-dimer are more pronounced as disease severity increases.[25,26]

The hypercoagulable states in COVID-19 patients have been reported to contribute strongly to mortality.[27] A study reviewed the hypercoagulability mechanisms in sepsis to find out this kind of association. The thrombogenic mechanisms that are highly implicated in the thrombosis of the COVID-19 disease are thrombosis triggered by cytokine storm, macrophage activation syndrome, antiphospholipid antibody syndrome, the complement cascade, and dysregulation of renin-angiotensin system.[28]

D-dimer, as a fibrin degradation product is a sensitive product for detecting fibrinolysis of intravascular thrombus. However, it has no specificity due to the rising of inflammation and other diseases.[29] In similarity with the literature, our study showed that the D-dimer levels were raised with increasing levels of inflammation (CRP0 in patients with COVID-19 (data not shown in the tables). An elevated level of D-dimer in COVID-19 is contributed to mortality.[30,31] In addition, increased D-dimer could be associated with acute lung injury in patients with COVID-19 and are made by the breakdown of intra-alveolar fibrin, which is deposited in ARDS.[32]

SARS-CoV-2 virus mutation may increase the severity of the COVID-19 disease. The clinical and pseudovirus experimental investigations have confirmed that spike protein D614G mutation changes the virus phenotype. However, the effects of the mutation on the following factors are not clear yet; transmission rate between people, disease severity, and the vaccine and therapeutic development.[33]

Limitations of the study

The findings reported in this study must be analyzed with caution as the data were collected from one geographic area facing difficulty to generalize the results to other regions across the country and globe.

CONCLUSION

The results of the study showed that CRP and D-dimer in the 1st week are contributed to disease severity and mortality in the studied group of patients with COVID-19.

ACKNOWLEDGMENT

Not applicable.

REFERENCES

1. Abdulah, DM and AA Mohammed. The consequences of the COVID-19 pandemic on perceived stress in clinical practice: Experience of doctors in Iraqi Kurdistan. Rom J Intern Med. 2020;58(4):219-227.
   https://doi.org/10.2478/rjim-2020-0020
2. World Health Organization. WHO Coronavirus Disease (COVID-19) Dashboard. Geneva: World Health Organization; 2021. Available from: https://covid19.who.int [Last accessed on 2021 Jun 24].
3. Sohrabi C, Alsafi Z, O'Neill N, Khan M, Kerwan A, Al-Jabir A, et al. World Health Organization declares global emergency: A review of the 2019 novel coronavirus (COVID-19). Int J Surg. 2020;76:71-76.
   https://doi.org/10.1016/j.ijsu.2020.02.034
4. Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: A study of a family cluster. Lancet. 2020;395(10223):514–523.
   https://doi.org/10.1016/s0140-6736(20)30154-9
5. Cucinotta D and Vanelli M. WHO declares COVID-19 a pandemic. Acta Biomed. 2020;91(1):157-160.
6. Adhikari SP, Meng S, Wu YJ, Mao YP, Ye RX, Wang QZ, et al. Epidemiology, causes, clinical manifestation and diagnosis, prevention and control of coronavirus disease (COVID-19) during the early outbreak period: A scoping review. Infect Dis Poverty. 2020;9(1):1-12.
   https://doi.org/10.1186/s40249-020-00646-x
7. Centers for Disease Control Prevention. United States COVID-19 Cases, Deaths, and Laboratory Testing (NAATs) by State, Territory, and Jurisdiction. Available from: https://covid.cdc.gov/covid-data-tracker/#datatracker-home [Last accessed on 2021 Jun 23].
8. Kolifarhood G, Aghaali M, Saadati HM, Taherpour N, Rahimi S, Izadi N, et al., Epidemiological and clinical aspects of COVID-19; a narrative review. Arch Acad Emerg Med. 2020;8(1):e41.
9. Zou L, Ruan F, Huang M, Liang L, Huang H, Hong Z, et al. SARS-CoV-2 viral load in upper respiratory specimens of infected patients. N Engl J Med. 2020;382(12):1177-1779.
   https://doi.org/10.1056/nejmc2001737
10. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study. Lancet. 2020;395(10223):507-513.

https://doi.org/10.1016/s0140-6736(20)30211-7

11. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020;323(11):1061-1069.
https://doi.org/10.1001/jama.2020.1585
12. Merza MA, Al Mezori AA, Mohammed HM, Abdulah DM. COVID-19 outbreak in Iraqi Kurdistan: The first report characterizing epidemiological, clinical, laboratory, and radiological findings of the disease. Diabetes Metab Syndr. 2020;14(4):547-554.
https://doi.org/10.1016/j.dsx.2020.04.047
13. World Health Organization. Global Surveillance for COVID-19 Disease Caused by Human Infection with the 2019 Novel Coronavirus, Interim Guidance, 27 February 2020. Geneva: World Health Organization; 2020.
14. World Health Organization. COVID-19 Clinical Management: Living Guidance, 25 January 2021. Geneva: World Health Organization; 2021.
15. Hadjadj J, Yatim N, Barnabei L, Corneau A, Boussier J, Smith N, et al. Impaired type I interferon activity and inflammatory responses in severe COVID-19 patients. Science. 2020;369(6504):718-724.
https://doi.org/10.1126/science.abc6027
16. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS and Manson JJ. COVID-19: Consider cytokine storm syndromes and immunosuppression. Lancet. 2020;395(10229):1033-1034.
https://doi.org/10.1016/s0140-6736(20)30628-0
17. Xu Z, Shi L, Wang L, Zhang J, Huang L, Zhang C, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med. 2020;8(4):420-422.
https://doi.org/10.1016/s2213-2600(20)30076-x
18. Feng Z, Diao B, Wang R, Wang G, Wang C, Tan Y, et al. The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) directly decimates human spleens and lymph nodes. MedRxiv. 2020;2020:20045427.
https://doi.org/10.1101/2020.03.27.20045427
19. Ruan Q, Yang K, Wang W, Jiang L and Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intens Care Med. 2020;46(5):846-848.
https://doi.org/10.1007/s00134-020-05991-x
20. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. Lancet. 2020;395(10229):1054-1062.
https://doi.org/10.1016/s0140-6736(20)30566-3
21. Chen G, Wu D, Guo W, Cao Y, Huang D, Wang H, et al. Clinical and immunological features of severe and moderate coronavirus disease 2019. J Clin Investig. 2020;130(5):2620-2629.
https://doi.org/10.1172/jci137244
22. Qin C, Zhou L, Hu Z, Zhang S, Yang S, Tao Y, et al. Dysregulation of immune response in patients with coronavirus 2019 (COVID-19) in Wuhan, China. Clin Infect Dis. 2020;71(15):762-768.
https://doi.org/10.1093/cid/ciaa248
23. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497-506.
https://doi.org/10.1016/s0140-6736(20)30183-5
24. Helms J, Tacquard C, Severac F, Leonard-Lorant I, Ohana M, Delabranche X, et al. High risk of thrombosis in patients with severe SARS-CoV-2 infection: A multicenter prospective cohort study. Intens Care Med. 2020;46(6):1089-1098.
https://doi.org/10.1007/s00134-020-06062-x
25. Wright FL, Vogler TO, Moore EE, Moore HB, Wohlauer MV, Urban S, et al. Fibrinolysis shutdown correlation with thromboembolic events in severe COVID-19 infection. J Am Coll Surg. 2020;231(2):193-203.e1.
https://doi.org/10.1016/j.jamcollsurg.2020.05.007
26. Bao J, Li C, Zhang K, Kang H, Chen W and Gu B. Comparative analysis of laboratory indexes of severe and non-severe patients infected with COVID-19. Clin Chim Acta. 2020;509:180-194.
https://doi.org/10.1016/j.cca.2020.06.009
27. Tang N, Li D, Wang X and Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost. 2020;18(4):844-847.
https://doi.org/10.1111/jth.14768
28. Hanff TC, Mohareb AM, Giri J, Cohen JB and Chirinos JA. Thrombosis in COVID-19. Am J Hematol. 2020;95(12):1578-1589.
https://doi.org/10.1002/ajh.25982
29. Iba T, Levy JH, Connors JM, Warkentin TE, Thachil J and Levi M. The unique characteristics of COVID-19 coagulopathy. Crit Care. 2020;24(1):1-8.
https://doi.org/10.1186/s13054-020-03077-0
30. Tang N, Bai H, Chen X, Gong J, Li D, Sun Z. Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy. J Thromb Haemost. 2020;18(5):1094-1099.
https://doi.org/10.1111/jth.14817
31. Cummings MJ, Baldwin MR, Abrams D, Jacobson SD, Meyer BJ, Balough EM, et al. Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York city: A prospective cohort study. Lancet. 2020;395(10239):1763-1770.
https://doi.org/10.1016/s0140-6736(20)31189-2
32. Ackermann M, Verleden SE, Kuehnel M, Haverich A, Welte T, Laenger F, et al. Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in Covid-19. N Engl J Med. 2020;383(2):120-128.
https://doi.org/10.1056/nejmoa2015432
33. Akkiz H. Implications of the novel mutations in the SARS-CoV-2 genome for transmission, disease severity, and the vaccine development. Front Med. 2021;8:636532.
https://doi.org/10.3389/fmed.2021.636532

Authors Contribution:
DMA- Concept and design of the study, performed the review for the study and statistical calculations, did the first draft of the manuscript and interpreted the results; **HKS-** Concept of the study, collected the data, followed-up the patients, did the clinical assessment, interpreted the results and final analysis.

Work attributed to:
Private clinic in Iraqi Kurian, Erbil, Iraqi Kurdistan.
Orcid ID:
Dr. Deldar Morad Abdulah - https://orcid.org/0000-0002-8986-5793
Dr. Hemin Khalid Saber - https://orcid.org/0000-0001-6038-0963

Source of Support: Nil, **Conflict of Interest:** None declared.