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RESEARCH ARTICLE OPEN ACCESS

A Cross-sectional Study of Clinical Characteristics and Outcomes among Adults with Laboratory-confirmed SARS-CoV-2 Infection with Omicron Variant

Nawfal R. Hussein[1], Majeed T. Ahmed[1], Brisik H. Rashad[1], Majeed H. Mustafa[2], Narin A. Rasheed[3], Ibrahim A. Naqid[1]*, Zana Sidiq M. Saleem[4], Nashwan M.R. Ibrahim[5] and Dildar H. Musa[5]

[1]Department of Biomedical Sciences, College of Medicine, University of Zakho, Zakho, Kurdistan region, Iraq.
[2]Department of Anaesthesia College of Medical Health Sciences, University of Duhok, Duhok, Kurdistan region, Iraq.
[3]Department of Medical Laboratory Technology, College of Health and Medical Technology Shekhan, Duhok Polytechnic University, Duhok, Kurdistan Region, Iraq.
[4]Department of Medicine, College of Medicine, University of Duhok, Duhok, Kurdistan region, Iraq.
[5]Department of Surgery, College of Medicine, University of Duhok, Duhok, Kurdistan region, Iraq.

***Correspondence:** ibrahim.naqid@uoz.edu.krd

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Abstract

The emergence of the SARS-CoV-2 Omicron variant has raised concerns due to its increased transmissibility and potential implications on clinical characteristics and outcomes in infected individuals. The aims of this report were to study the profile of SARS-CoV-2 infection with omicron variant, investigate the infection outcome, reinfection rates with associated factors, antibody levels, and explore the associations between biochemical markers and disease severity. This prospective cohort study was conducted in Duhok city in the Northern of Iraq. All volunteers with confirmed SARS-CoV-2 RT–PCR and confirmed Omicron infection who were older than 18 years old and agreed to participate were recruited for this study. The study was carried out from January to April 2022. There were 234 cases of confirmed SARS-CoV-2 RT–PCR Omicron infection. The mean age was 48.12±17.3 years, 43.2% were vaccinated, and 40.2% were male. Among the recruited patients, 99.1% recovered and did not need hospitalization. In this study, (38.9%) had a history of previously confirmed COVID-19 infection. Reinfection was significantly higher in females than males (p=0.04; OR= 0.56). It was found that the IgG antibody levels were higher in patients who received Pfizer-BioNTech than in those who received other vaccines (p=0.001). The levels of IgG were also significantly higher in patients with mild infection (p=0.046), whereas the levels of D-dimer were significantly higher in patients with severe cases of the infection compared to those with mild or moderate cases (p=0.001). Additionally, the levels of C-reactive protein (CRP) were observed to be higher in individuals with moderate cases of infection than in mild and severe cases (0.001). Individuals who contracted the Omicron strain generally had positive outcomes. Reinfection with the Omicron variant was relatively high. IgG levels were higher in patients with mild disease, implying that they were associated with decreased disease severity. We found significant associations between D-dimer levels and the severity of the disease. Additional research is required to investigate the long-term effects of Omicron infection.

Keywords: Infection Outcome, Reinfection, SARS-CoV-2 Antibody, Omicron Variant, RT-PCR

INTRODUCTION

SARS-CoV-2, also known as severe acute respiratory syndrome coronavirus 2, is a virus that causes the disease known as COVID-19 (coronavirus disease 2019). It is a member of the coronavirus family, which includes other viruses like the common cold, MERS-CoV (Middle East Respiratory Syndrome coronavirus), and SARS-CoV (severe acute respiratory syndrome coronavirus). SARS-CoV-2 virus was first discovered in Wuhan, China, in December 2020. Since then, the virus has spread throughout the globe, causing an unprecedented pandemic.[1] The virus causes COVID-19, which primarily affects the respiratory system and has a case fatality rate of approximately 2%. The first cases in the Northern of Iraq were discovered in March 2020.[2,3] Since then, the region has experienced three severe outbreaks, with a case fatality rate of 2%. With wave after wave of SARS-CoV-2 variants, hospitals in this low-resource country were overwhelmed with patients.[4,5] In early January 2022, the initial occurrences of the B.1.1.529 (Omicron) variant of SARS-CoV-2 were identified in the same area. The new variant became more widespread than the B.1.617.2 (Delta) variant in the region. Preliminary data from South Africa suggested that the B.1.1.529 variant was more transmissible but caused milder disease than the delta variant.[6] Compared to previous variants, patients infected with the Omicron variant were characterized by fewer admissions to the Intensive Care Unit (ICU), a reduced need for mechanical ventilation, and a lower number of deaths resulting from the infection.[7,8] Additionally, initial reports showed that Omicron is resistant to vaccine neutralization and may cause a high rate of reinfection than was found in previous variants.[6,9] The objectives of the present report were to study the infection profile, investigate the infection outcome, reinfection rates with associated factors, and SARS-CoV-2 antibody levels, and explore the associations between biochemical markers and disease severity.

METHODOLOGY

Study design and settings

This prospective cohort study was carried out in the city of Duhok, located in the Kurdistan region of Iraq. The Ministry of Health protocol for treating COVID-19 patients was followed for the treatment of our patients.[10] All patients (234) with confirmed cases of SARS-CoV-2 RT–PCR and an Omicron infection who were ≥18 years old and agreed to participate were recruited for this study. In March 2020, after the diagnosis of the first cases in the region, COVID-19 centers were established in the city to diagnose and treat patients with COVID-19. In this study, all patients were recruited in COVID-19 centers in Duhok city, Kurdistan Region of Iraq. The study was conducted between January and April 2022. All examinations and laboratory analyses were conducted at inclusion. The exclusion criteria were patients who did not agree to participate, patients with other SARS-CoV-2 variants that were detected by RT-PCR (n=53) and participants younger than 18 years old. The study is reported according to the STROBE statements.[11] All patients were followed up with for one month and their examinations were repeated during this time. Three types of vaccines are used in Iraq: Pfizer; Oxford/AstraZeneca AZD1222 (AstraZeneca) and Sinopharm BBIBP-CorV (Sinopharm).

Definitions

The volunteers who participated in our study were grouped into categories based on the severity of their condition. Those who had no symptoms or signs of pneumonia and no radiological evidence of pneumonia were classified as mild cases. Those who had symptoms and signs of pneumonia as well as radiographic evidence of pneumonia but had normal breathing rates and oxygen saturation levels of 93-95% while at rest were classified as moderate cases. Severe cases were defined as individuals who had radiological evidence of pneumonia, were experiencing breathing difficulties, had oxygen saturation levels of less than 93% while at rest, or had an arterial partial pressure of oxygen (PaO2)/ fraction of inspired oxygen (FiO2) ratio of less than or equal to 300 mmHg (1 mmHg is equivalent to 0.133 kPa). Vaccinated participants were defined in this report as those who received two doses of a vaccine one month before contracting the infection and no later than three months after the second dose. Two outcomes were recorded. First, recovery was defined as afebrile for more than three days, improved respiratory symptoms and negative SARS-CoV-2 RT–PCR results. Second, death of the patients was also recorded. The case fatality rate was determined as the proportion of participants who died from SARS-CoV-2 infection out of all cases diagnosed and confirmed with RT-PCR test. Comorbidity was defined as patients who have a chronic disease. Such patients have chronic disease identification card (ID). Hence, any patient with chronic diseases ID was considered to have comorbidities. Reinfection with the virus that causes COVID-19 refers in which an individual has previously contracted the virus, recovered, and then subsequently contracted the virus again.[12]

IgG, CRP and D-dimer

Vidas SARS-CoV-2 IgG (bioMerieux, France) was used to detect the specific immune response and quantify the level of anti-SARS-CoV-2 IgG antibodies in correlation with the World Health Organization (WHO) International Standard. The assay seeks to identify antibodies that bind specifically to the viral spike (S) protein receptor binding domain. The results are shown as index values. The levels of CRP and D-dimer were assessed using immunoturbidimetry on a Cobas c501 chemistry analyzer (Roche).

SARS-CoV-2 RT-PCR test

The RT-PCR testing for SARS-CoV-2 was conducted using a two-step reaction process that amplifies two distinct genes. The first reaction targeted 75 base pairs of the conserved region of the E gene. The second reaction was targeted a 100 base pair fragment from a conserved region of the RNA-dependent RNA polymerase (RdRP) gene. A positive result of the test was determined when both reactions were positive, a negative result was determined if both reactions were negative and an undetermined result was obtained if one reaction was positive and the other was negative. Then, the Omicron variant was detected using the geneMAP™ 2019-nCoV/Omicron multiplex RTPCR detection Kit. The reaction detected Orf1ab, N gene and N gene Δ31-33 mutations.

Statistics

Statistical analysis of the data was performed by using Minitab 17. We used binary linear regression to study the relationship between continuous variables and outcomes. In addition, we analyzed the categorical data using the chi-square test. The Kruskal–Wallis test was utilized to study the significance of differences in groups with continuous data. In order to establish an association, a chi-square test was employed and results were deemed statistically significant when the p-value was below 0.05.

RESULTS

Participants

There were 234 cases with SARS-CoV-2 RT–PCR confirmed Omicron infection (Table 1). The mean age was 48.12±17.3 years (mean± STDeV), 101 (43.2%) were vaccinated, and 94 (40.2%) were male. In this study, 105 (44.9%) of the patients had one or more chronic comorbidities. The three most common presenting symptoms were fever (100%), myalgia (76.9%), and cough (66.7%). The average time between the onset of symptoms and the start of treatment was 4.77±2.3 days (mean±STDeV). There was no history of recent travel abroad. Among the recruited patients, 232 (99.1%) recovered and did not need hospitalization. In our study, 200 (85.5%) and 21 (9%) patients with mild and moderate infection received vaccine, respectively, whereas 13 (5.6%) of the severe cases received vaccine.

Variables associated with reinfection

In this study, 91 (38.9%) individuals had a confirmed history of COVID-19 infection. We explored the factors that may be associated with reinfection. Females were significantly more likely to be re-infected than males (P=0.04; OR= 0.56) (Table 2). The presence of comorbidities, history of vaccination, age, and IgG levels did not show any association with reinfection.

Variables associated with IgG levels

Among recruited subjects, 101 (43.2%) received two doses of vaccines within three months prior to the study. The IgG levels were not associated with sex, previous history of infection, or comorbidities (Table 3). According to the Iraqi vaccination program, three vaccines were available: Pfizer, AstraZeneca, and Sinopharm. It was found that the IgG levels were higher in patients who received Pfizer than in those who received the other two vaccines (Table 4) (Figure 1).

Severity of COVID-19 and biochemical markers

In our study, 200 (85.47%) of the infections were mild, while 13 (5.55%) of the infections were severe (Table 4). We studied the association between the severity of the infection and biochemical markers. We found that IgG levels were significantly higher in patients who had mild infection (P=0.046) (Figure 2), whereas D-dimer levels were significantly higher in severe cases compared to mild and moderate cases (P=0.001)

Table 1. Characteristics of Recruited Patients

Variable	No.	%
Male	94	40.2
Comorbidity	105	44.9
Vaccinated	101	43.2
Reinfection	91	38.9
Severity		
Mild	200	85.5
Moderate	21	9.0
Severe	13	5.6
Outcome		
Recovery	232	99.1
Death	2	0.9
Clinical Feature		
Fever	234	100.0
Myalgia	180	76.9
Sore	40	17.1
headache	12	5.1
cough	156	66.7
Running nose	17	7.3
sneezing	1	0.4
Diarrhea	3	1.3
vomiting	1	0.4
SOB	29	12.4
loss of appetite	27	11.5
Age (mean± STDeV)	48.12±17.3	
Duration of symptoms (mean± STDeV)	4.77±2.3	

STDeV= standard deviation

(Figure 3). The levels of CRP were higher in cases with moderate infection than in mild and severe cases (0.001) (Figure 4).

DISCUSSION

In this region, the first case of COVID-19 caused by the Omicron variant was diagnosed in January 2022. Despite the large number of reported cases, it was reported that patients seeking medical attention and hospital admission decreased significantly in comparison to patients who were infected with Delta variants.[13] In this report, we followed up with patients who were diagnosed with COVID-19 omicron variants. A total of 234 volunteers were recruited for this study. In a study conducted in City of Tshwane, the first Omicron global epicentre, the severity of COVID-19 disease was reduced in the Omicron-driven wave, with low case fatality rates.[14] In agreement with this, the vast majority of the patients (85.5%) presented mild symptoms, whereas 5.6% presented severe infection. The case fatality rate of the patients recruited in

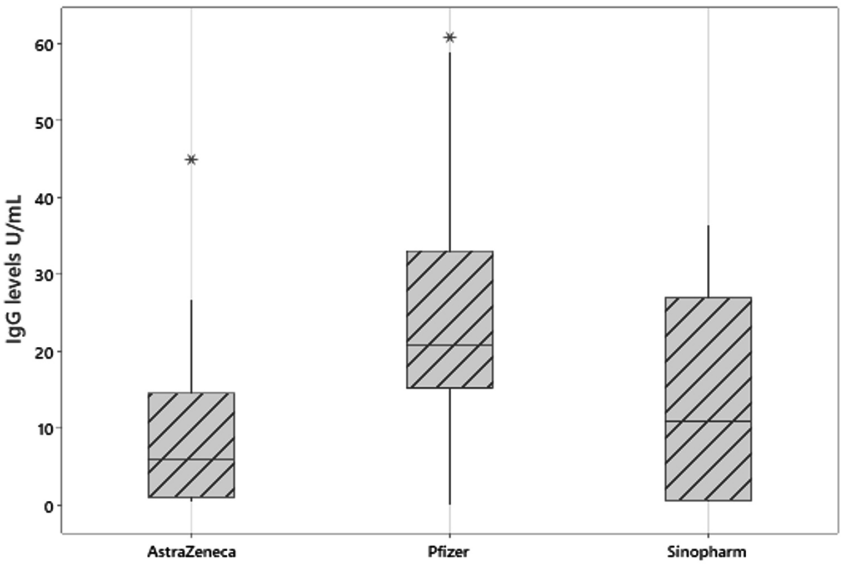

Figure 1. Boxplot Showing IgG Levels in Participants Who Received Different Types of Vaccines. The Kruskal–Wallis statistical test was utilized, and significant differences were found. * Outlier

Table 2. Variables Associated with Reinfection

Variable		First infection	Reinfection	test	OR	CI	P value
Sex	Male	65	29	X^2	0.56	0.323-0.973	0.04
	Female	78	62				
CoMo	Yes	65	40	X^2	0.94	0.555-1.597	0.8
	No	78	51				
Vaccine	Yes	64	37	X^2	0.85	0.497-1.441	0.53
	No	79	54				
Variables	Mean	STDeV		OR	CI	P value	
Age	First	48.98	18.02	BLR	0.99	0.977-1.008	0.34
	Reinfection	46.78	16.1				
IgG	First	10.34	35.84	BLR	1.01	0.994-1.027	0.19
	Reinfection	16.72	15.46				

X^2= Chi squared test; BLR=Binary Logistic Regression; CoMo= Comorbidity

this study was 0.9%, which was lower than that reported with previous variants in the city.[10,15] The case fatality rate may be attributed to the nature of the Omicron variant causing mild disease and good vaccination coverage within the population. It was previously reported that pre-existing immunity, both from vaccination and previous infection, reduces the risk of hospitalization in COVID-19 infection substantially.[16-18] In agreement with this, we found that both vaccination and previous COVID-19 infection offers a protection from severe disease as we found that 88.67% and 40% of patients with mild and moderate infection had been vaccinated, respectively, whereas 8.33% of those who presented severe cases had been vaccinated. This implies that the current vaccines and previous infection do not offer sterile immunity against infection but are associated

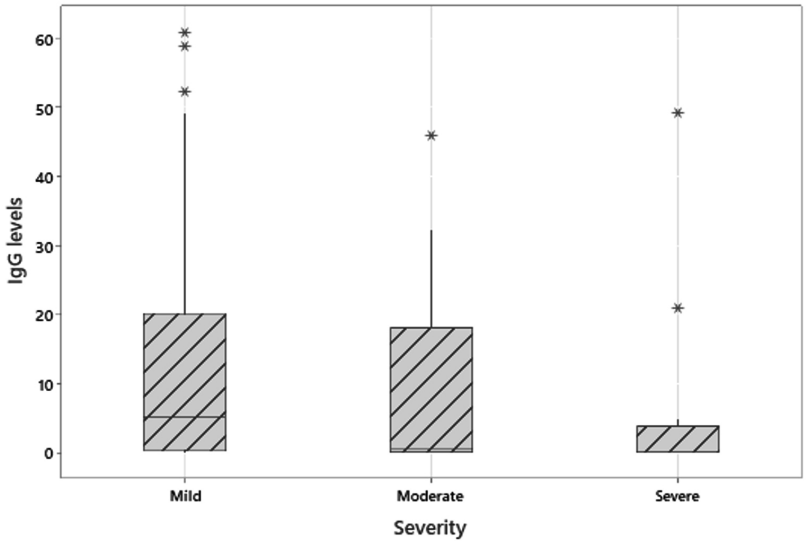

Figure 2. Boxplot Showing IgG Levels in Participants with Different Severities of COVID-19. The Kruskal–Wallis statistical test was utilized, and significant differences were found (P=0.046). * Outlier

Table 3. Variables Associated with IgG Levels.

Variables		Mean	STDeV	test	OR	CI	P value
Gender	Female	20.63	15.59	BLR	1.01	0.992-1.014	0.56
	Male	25.67	57.45				
Previous infection	No	20.99	51.22	BRL	1.01	0.993-1.013	0.53
	Yes	26.82	15.34				
CoMo	No	27.13	55.94	BRL	0.99	0.974-1.011	0.4
	Yes	18.7	14.58				

BLR=Binary Logistic Regression

Table 4. IgG Levels According to the Type of Vaccines

	No.	Median	Mean	Z Rank	DF Value	H-value	P value
AstraZeneca	21	5.9	29.1	-3.85	2	19.94	0.001
Pfizer	68	20.75	59.9	4.37			
Sinopharm	12	10.93	39	-1.51			

with decreased disease severity. Additionally, we found a significant association between age and severity of the disease. It was previously shown that the hazard rate in high in children and patients older than 80 years old.[14] In agreement with this, in our study, the vast majority of patients who were having severe infection were older than 80 years. Because the number of patients who died was very small, we could not investigate the factors associated with fatality. Previously, the reinfection rate was studied in our region, and it was very low.[19] In the current study, the reinfection rate was 38.9%. Such a high reinfection rate may be because Omicron has substantial changes in the spike protein, which is the main driver of the immune response leading to escape from the immune reaction of the previous variants. Then, we investigated the variables associated with reinfection. In contrast to a previous report from the region,[19] we found that reinfection

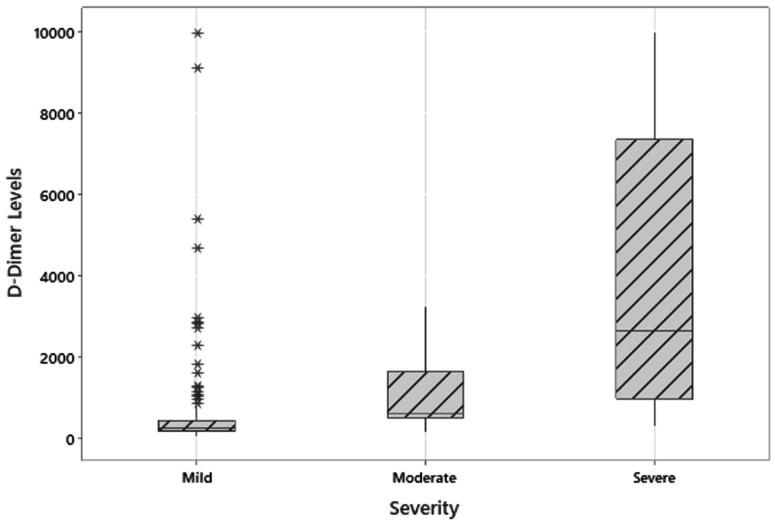

Figure 3. Boxplot Showing D-Dimer Levels in Participants with Different Severities of COVID-19. The Kruskal–Wallis statistical test was utilized, and significant differences were found (P=0.001). * Outlier

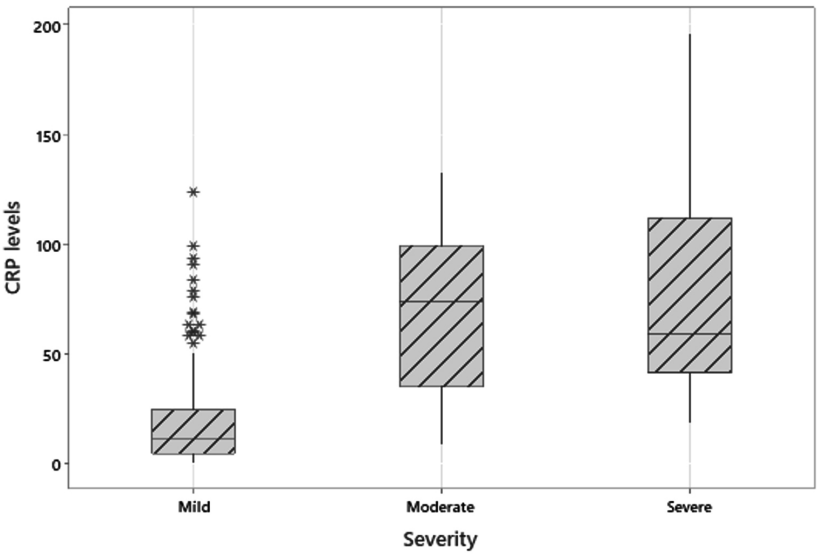

Figure 4. Boxplot Showing CRP Levels in Participants with Different Severities of COVID-19. The Kruskal–Wallis statistical test was utilized, and significant differences were found (P=0.001). * Outlier

was significantly higher in females than males. The association between sex and reinfection is difficult to explain, and more research is needed to investigate the relationship between sex and immune response and reinfection in patients infected with COVID-19. It was previously reported that the reinfection rate was significantly higher in older patients.[20] In contrast, in our study, however, age did not show any association with reinfection. Little is known about immunity against SARS-CoV-2 and the reinfection phenomenon in the context of COVID-19, and more studies are needed to investigate this issue. Besides, we found that a history of vaccination and IgG levels were not associated with a lower rate of reinfection. However, reinfection is still vaccinated persons may be attributed to Omicron's ability to evade the immune system.[21] Then, we studied the impact of vaccination on the severity of infection. It was found that 88.67% and 40% of patients with mild and moderate infection had been vaccinated, respectively, whereas 8.33% of those who presented severe cases had been vaccinated. This implies that the current vaccines and previous infection do not offer sterile immunity against infection but are not associated with decreased disease severity. In support of this, we found the highest levels of IgG in patients with mild infection. Furthermore, we investigated variables that may be associated with IgG levels. According to the Iraqi vaccination program, three vaccines were available: Pfizer, AstraZeneca and Sinopharm. We found that the patients who received Pfizer had IgG levels higher than in those who received the other two vaccines. This is similar to a previous study that found Pfizer vaccine offers the highest levels of IgG than other vaccines,[22] however, in contrast to our study, that same study found that the AstraZeneca vaccine induced higher levels of IgG than Sinopharm.[22] IgG levels were not correlated with sex, previous history of infection, or comorbidities.

According to the local protocol of the management of COVID-19 patients, D-dimer, and CRP levels should be measured for all patients. We studied the associations between these two markers and the severity of COVID-19. We found significant associations between D-dimer levels and the severity of the disease. Our findings are in agreement with a previous study that found that D-dimer levels were associated with the severity of the infection and were reliable prognostic factors for patients with severe infection.[23,24] In addition, we investigated the association between levels of CRP and the severity of infection. In our study, we classified our patients based on their severity into three groups: mild, moderate, and severe diseases. The highest levels of CRP were found in patients with moderate disease. This is in contrast with other studies where CRP levels were associated with severe infection.[24-26] It is important to mention that in previous studies, patients were classified into two groups: patients with mild disease and patients with severe disease.[24-26] Hence, the discrepancy between our results and previous studies may be attributed to the difference in grouping patients.

Our results are useful because they provide insight into the course of the disease caused by the Omicron variant in our region. In addition, factors that may impact the production of antibodies in patients with COVID-19 were studied. Our results can be used to predict the severity of infection by initial biochemical markers. Our study has limitations. First, our sample was not random, and we recruited all the patients with inclusion criteria who visited our clinics in the study period. Second, the sample size was small. However, we could not recruit more patients because the disease was mild, and few patients sought medical attention.

CONCLUSION

To conclude, reinfection seemed high with the Omicron variant, probably because of the nature of the strain. IgG levels were higher in patients with mild disease, implying that they were associated with decreased disease severity. We found significant associations between D-dimer levels and the severity of the disease. Further studies are required to explore the long-term effect of Omicron infection.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTION

DHM, MHM, ZSMS and NMRI conceptualized the study. NRH performed data curation and project administration. MTA, IAN, ZSMS and NMRI designed the study. MTA, NRH, BHR, NAR and IAN applied methodology. MHM, NRH and DHM performed formal analysis. DHM, IAN, MHM, MTA, ZSMS, BHR and NMRI performed investigation. BHR and NRH wrote the manuscript. NAR and NRH reviewed and edited the manuscript. All authors read and approved the final manuscript for publication.

FUNDING

None.

DATA AVAILABILITY

All datasets generated or analyzed during this study are included in the manuscript.

ETHICS STATEMENT

This study was approved by Ethics and Scientific Committee of the College of Medicine at the University of Zakho, Kurdistan, Iraq, wide letter number 2021/163, dated 20th December 2021.

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