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THE ROLE OF FERRITIN LEVEL AND D-DIMER IN SEVERITY OF SARS-COVID-2-INFECTED PATIENTS IN AL-NAJAF AL-ASHRAF GOVERNORATE

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ABSTRACT

Background: *The pandemic results of Coronavirus 2019 (COVID-19) range from moderate to serious, necessitating the rapid assessment and association of diagnostic markers. Patients suffer from infection with SARS-Covid-2 had measurements of ferritin, LDH, and D-dimer. In addition to being a problem for healthcare institutions, the SARS-Covid-2 additionally represents a major financial burden.* ***Aim:*** *To assess the predictive importance of serum ferritin & D-dimer levels as predictors for individuals at risk of serious and fatal infection with SARS-Covid-2.* ***Methods:*** *This study designs as Case-control study was done at AL-Amal Specialized Hospital for Communicable Diseases in Al-Najaf, Iraq, during the period of June to August of 2023. Prior to their enrollment in the clinical study, every individual participant provided written consent. 44 samples which included 22 patients (8 men and 14 women) and 20 control (8 men and 14 women) and varying age groups from 28 to 76 years old—were reported to have symptoms of SARS-Covid-2 infection.* ***Results:*** *The present investigation reveals significant differences between the patient and control groups, as well as between the patient and control groups' age groups and sexes. Patients who are older have a higher age-related prevalence of severe SARS-Covid-2 infection. In total, 22 COVID-19 patients were incorporated into this research; 8 (36.4%) were male and 14 (63.6%) were female. In comparison, there were 8 (36.4%) male and 14 (63.6%) female among 22 healthy control individuals. According to the statistical analysis, there were statistically significant differences between the female and male patients. There wasn't a noticeable difference in the mean serum level of ferritin between the SARS-Covid-2 infected patients' group and the control group (µg/l). Conversely, it was highly significant difference in mean serum level of D-Dimer between the COVID-19 patient group and the control group (µg/l).* ***Conclusion:*** *The age-specific prevalence of severe SARS-Covid-2 infections increases in older adults age of patients: Females showed higher rates of infection than males. Higher level Serum of D-dimer and ferritin are linked with outcomes in patientsCovid-19. Significantly elevated ferritin and D-dimer levels in infection with SARS-Covid-2 recovered individuals, which may serve as SARS-Covid-2 diagnostic biomarkers.*

INTRODUCTION

The novel ß-coronavirus virus, which is part of the Coronaviridae family, is the cause of COVID-19, an infectious disease that was initially identified in Wuhan, China, in December 2019 and transmit throughout the world. The World Health Organization (WHO) continues to classify the SARS CoV2 virus as a pandemic, yet this hasn't made the epidemic any less severe. Over 2,500,000 cases and more than 170,000 mortalities have been recorded globally as of April 22,

2020 (Huyut et al., 2022). According to Liu et al. (2020), a coronavirus is a single-stranded, positive-experience RNA genome that return to Coronavirinae subfamily of the Coronavirdiae group of viruses in the order of Nidovirales. There are three glycoproteins (Spike, Envelope and Membrane) are found on envelope of SARS-CoV-2. Although genome of this virus is RNA, it making more modification and keep proteins on surface layer that help to entry host cell and causing infection (Tian et al., 2020).

There are three types of coronaviruses that infect respiratory system including; Middle East Respiratory Syndrome (MERS), SARS, and COVID-19. The transmission of SARS-CoV-2 is powerful and having no specific medication for its treatment, the emergence (WHO, 2021). Based on several studies, it found approximately 193 million infections and 2.9 million deaths caused by SARS-CoV-2 (Cascella et al., 2022). According to Palich et al., (2021), epidemiological studies reported that a numerous risk variables involve age and several medical illnesses; diabetes mellitus and hypertension, that appear correlate with severity of illness and death. Both humans and animals can become infected with corona viruses, with human corona viruses (HCoVs) responsible for fifteen to thirty percent of common cold cases. compared to human corona viruses (HCoVs), animal reservoir corona viruses may affect humans and result in epidemics in individuals. These zoonotic virus infections cause severe respiratory diseases such as pneumonia and acute respiratory distress syndrome (ARDS), which can be fatal (Dae-Gyun Ahn et al., 2020).

Numerous researches proposed that COVID-19 illness might be mild, asymptomatic, or severe (simply spread by respiratory aerosols). Fever, cough, diarrhea, dyspnea, anosmia, myalgia, vomiting, anorexia, exhaustion, pneumonia, lack of smell or flavor, chills, headache, pain in the throat, and difficulties in breath are among the clinical indications and symptoms of COVID-19. Frequently, the illness worsens and necessitates admittance to the hospital or perhaps a unit for intensive care (Li et al., 2020). When enters the alveoli in the respiratory tract, the virus multiplies and disrupts cells, triggering the body's immune response and cytokines that accelerate the inflammatory process. The exacerbated inflammatory process causes macrophages to become more active and absorb more iron, which increases the production of ferritin in the liver, a protein that is thought to be a sign of organ dysfunction in COVID-19 (Ramos et al., 2020).

A number of laboratory indicators which revealed to be important in investigating of Covid-19 incidence. High COVID-19 infection has been linked to elevated levels of inflammatory biomarkers, such as ferritin, procalcitonin, lactate dehydrogenase (LDH), C-reactive protein (CRP), D-dimer, and interleukin-6 (El Homsi et al., 2020). Blood proteins containing iron are called ferritin. Elevations in ferritin levels in the blood during viral infection may be a sign of viral replication (Cheng et al., 2020). Ferritin, also referred to as the important intracellular iron storage protein, is a positive acute stage reactant that is elevated in various inflammatory situations. It is found in most human tissues as a cytoplasmic protein in cells, as well as in blood and bodily fluids, especially serum and plasma. Moreover, extremely elevated ferritin levels have been linked to illnesses like septic shock syndrome and macrophage activation **(**Feld et al.,2020).

D-dimer is blood diagnostic marker that return to fibrin degradation products. Usually, patients with Covid-19 have higher blood clots and fibrinolysis (Düz et al., 2020). Also, D-dimer is marker for thrombotic illness, which is product of fibrin breakdown. Coagulation of blood cascades was induced by Covid-19 illness that initial causing to viremia or cytokine storm and consequence result of thrombotic problems and coagulopathies in Covid-19 patients (Wool and Miller, 2021).

Recognition of COVID-19 infection can be confirmed by polymerase chain reaction positive results, ground-glass opacities on computed tomography (CT) scans, and symptoms of disease (Li et al., 2020b).

METHODOLOGY

Case-control study was done at AL-Amal Specialized Hospital for Communicable Diseases in Al-Najaf, Iraq, during the period of June to August of 2023. Prior to their enrollment in the clinical study, each individual participant provided written consent. 44 samples which included 22 patient (8 men and 14 women) and 20 control (8 men and 14 women) and varying age groups from 28 to 76 years old—were reported to have symptoms of SARS-Covid-2 infection. **D-dimer** (Up-converting Phosphor Technology): According to the manufacturer, Beijing Hotgen Biotech Co., Ltd. (China). A sample of approximately 2 cc of blood was taken from every patient in a sodium citrate tube, centrifuged, and the D dimer value was determined via a d-dimer kit. D dimer had a normal range of 200–500 ng/ml. A 500 or higher result is regarded as positive (raised). **Ferritin**: The manufacturer's company operations (VIDAS /BIOMEUX) states that this test is automated. Two milliliters of blood samples were centrifuged. Samples of serum were immediately analyzed to determine the serum ferritin level.

RESULTS AND DISCUSSION

In (60) During the period from June to August of 2023, 44 samples which included 22 patients (8 men and 14 women) and 20 control (8 men and 14 women) and varying age groups from 28 to 76 years old—were reported to have symptoms of SARS-Covid-2 infection. The present investigation reveals significant differences between the patient and control groups, as well as between the patient and control groups' age groups and sexes. Patients who are older have a higher age-related prevalence of severe SARS-Covid-2 infection. In total, 22 SARS-Covid-2 patients were incorporated into this research; 8 (36.4%) were male and 14 (63.6%) were female. In comparison, there were 8 (36.4%) male and 14 (63.6%) female among 22 healthy control individuals. According to the statistical analysis, there were statistically significant differences between the female and male patients. There was no significant difference in the mean serum level of ferritin between the SARS-Covid-2 patient group and the control groups (µg/l). Conversely, there was a highly significant difference in the mean serum level of D-Dimer between the SARS-Covid-2 patient group and the control group (µg/l).

Table 1, 2, and 3, displays the descriptive criteria for different biochemical parameters. Ferritin and D-dimer parameters showed a positive correlation. Statistically significant correlation.

Table (1): Descriptive criteria for both Ferritin and D-dimer tests in severe SARS-Covid-2 infected patient.

Test	N	Mean	Std. Deviation	Std. Error
Ferrtin	22	421.3005	309.27604	65.93787
	22	44.4050	23.87522	5.09021
	44	232.8527	288.67007	43.51865
D-dimer	22	1014.6745	1486.59445	316.94300
	22	118.0836	70.92887	15.12209
	44	566.3791	1134.62934	171.05181

Table (2): ANOVA criteria for both Ferrtin and D-dimer tests in severe Covid-19 patients

	Groups	Sum of Squares	df	Mean Square	F-test	Sig.
Ferrtin	Between Groups	1562552.020	1	1562552.020	32.478	.000

	Within Groups	2020655.573	42	48110.847		
	Total	3583207.593	43			
D-dimer	Between Groups	8842627.841	1	8842627.841	7.984	.007
	Within Groups	46514873.328	42	1107496.984		
	Total	55357501.169	43			

Table (3): Correlations criteria for both Ferrtin and D-dimer tests in severe Covid-19 patients

		Sex	**Age**	**Ferrtin**	**D-dimer**
Ferrtin	Pearson Correlation	-.124	.030	1	.388**
	Sig. (2-tailed)	.422	.848		.009
	N	44	44	44	44
D-dimer	Pearson Correlation	-.062	.046	.388**	1
	Sig. (2-tailed)	.691	.766	.009	
	N	44	44	44	44

**. Correlation is significant at the 0.01 level (2-tailed).

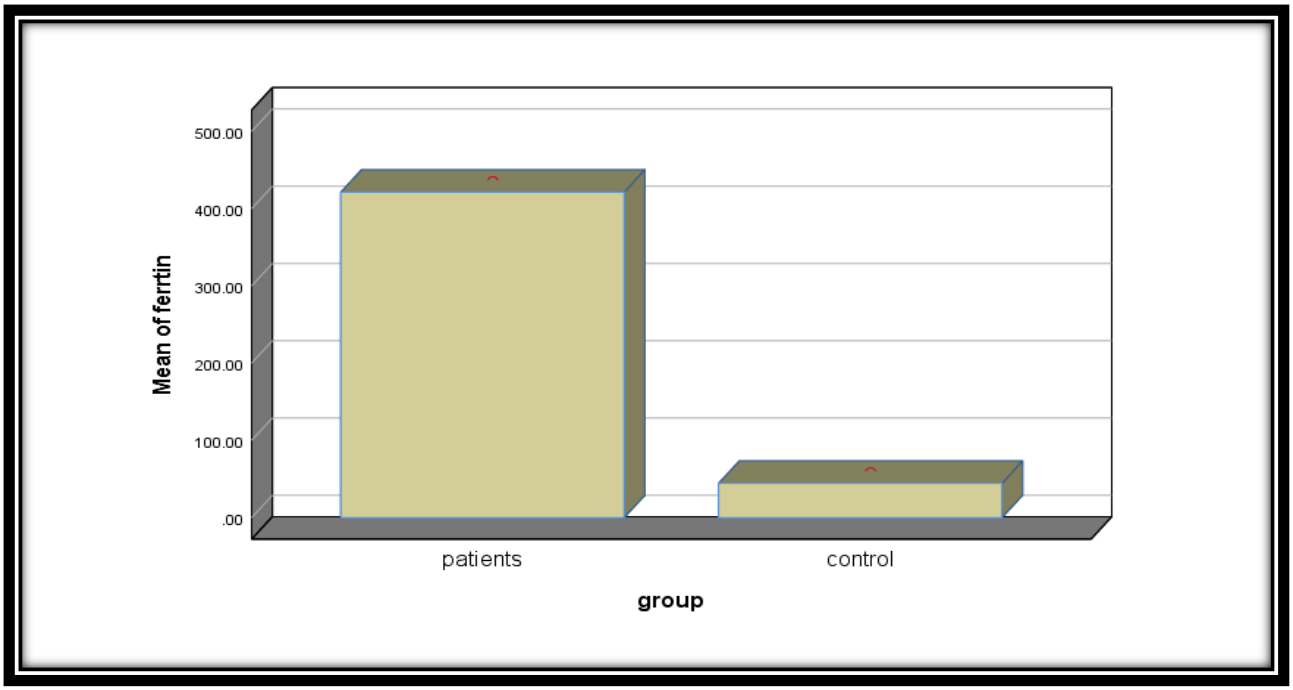

Fig 1: The mean level of Ferrtin test for severe infected patients' illness in Patients and Control.

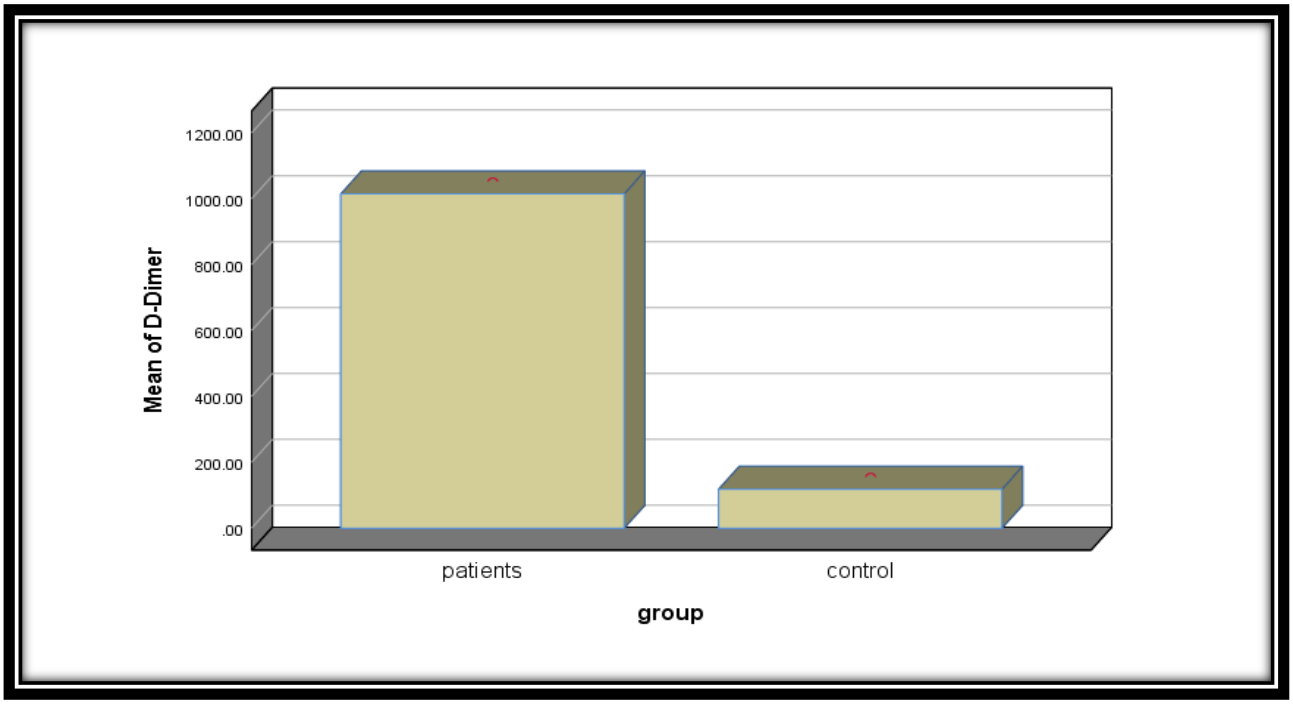

Fig 2: The mean level of D-Dimer test in plasma of severe SARS-Covid-2 infection in patients and Control.

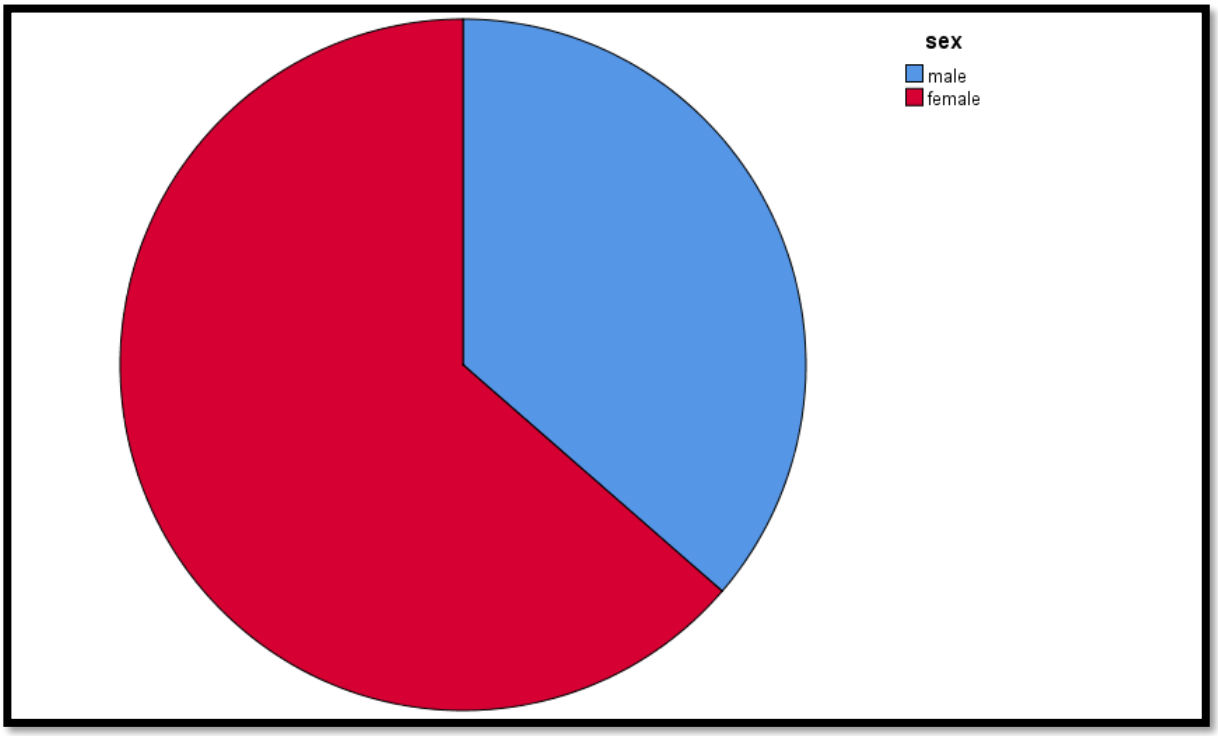

Fig 3: SARS-Covid-2-Infection prevalence according sexes

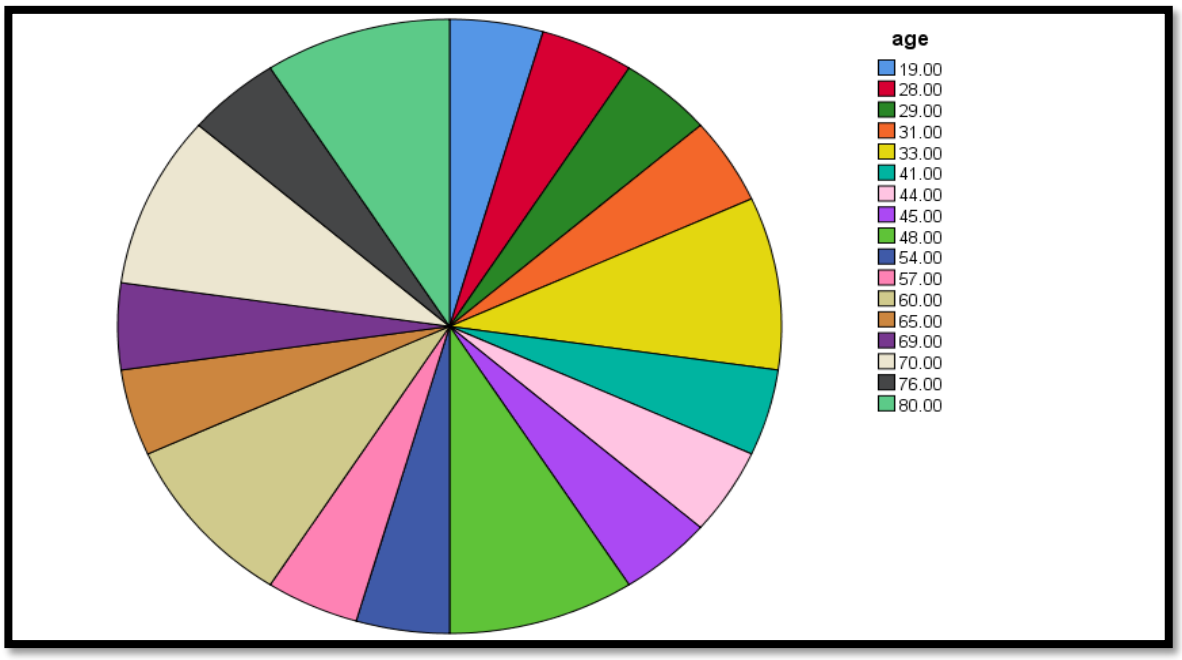

Fig 4: Age groups-related SARS-Covid-2-Infection

The viral genome of SARS-CoV-2 has undergone various modifications as it spreads over the world, and these alterations have certain geographic characteristics. Despite the fact that the virus has been linked to some genetic changes, these do not alter the virulence or transparency. The identification of biological markers linked to prognosis can aid medical professionals in the diagnosis and treatment of patients **(**Korber *et al.*, 2020, Nasser *et al.*, 2021, Al-Himadawy *et al.* 2022).

Older individuals appear to be associated with a more severe clinical picture. According to Verity *et al.* (2019), the average age range is between 50 and 60 years old. In accordance with Chen *et al.* (2020) and Al-Himadawy *et al.* (2023) patients who are older than 60 have a higher risk of lung disease. According to Dotganay *et al.* (2021), the literature is consistent with the rise in illness severity and mortality associated with advanced age and male gender. According to Schurz *et al.* (2019), the X chromosome has the highest concentration of immune-related genes in the human genome, which may similarly account for women's higher immunological responses and predominance in autoimmune disorders.

In COVID-19 patients, ferritin has been proposed as a valuable diagnostic for prognosticating patient outcomes. In accordance with Mehta et al. (2020), higher markers of inflammation, involving ferritin, have been shown to be suspected of serious and life-threatening illnesses. A higher ferritin level was regarded as a predictor of infection and used to estimation the dangerous and fatalities due to SARS-COV-2 infection. Increased serum ferritin levels have been correlated with fatality and serious effects in SARS-COV-2 diseases. The additional research that realized variations in ferritin levels between the patients with mild and severe illnesses proposed that a number of causes, such as the volume of samples utilized during the study, the duration of the patients' infection, and supplementary bacterial infection, might have been responsible for these modifications. Taneri et al. (2020) mention anemia, hypertension, advancing years of age, and other factors as possible reasons of pathologically increased blood ferritin contents.

Another study by Burugu *et al.* (2020) found the patients with severe COVID-19 disease has discovered that ferritin levels of those patients were much greater. The results of this study were in agreement with investigation by Iba *et al.* (2020) who reported that D-dimer was the biomarker with a linear connection with mortality. This study used multivariate analysis to assess whether

biomarker D-dimer, was predictors of death in patients with sepsis. Sepsis-like coagulopathy can be caused by COVID-19. In contrast, COVID-19 is less likely to cause prothrombin and partial thromboplastin times to be extended, reduced antithrombin action, and thrombocytopenia than sepsis. Also, Mukhopadhyay *et al.*, (2022), revealed that D-dimer may suggest elevated danger of thrombosis in severe COVID-19 patients. Furthermore, it was noted that men were more likely than women to experience an exacerbation of COVID-19 symptoms when their D-dimer levels were elevated. These results clearly show a gender difference in the correlation between COVID-19 severity and D-dimer levels. The results coincide with earlier research by Tang *et al.* (2020), were discovered that aberrant coagulation function, include: increased D-dimer, was shown to be connected to the advancement of COVID-19 disease. Advanced D-dimer levels was linked in several studies to a higher danger of death in the COVID-19 patient group (Hayıroğlu *et al.*, 2020). Furthermore, there was highly important association between D-dimer and serum ferritin in SARS-Covid-2 patients.

CONCLUSION

Elevated levels of the blood D-dimer and serum ferritin are critical in determining the degree of severity of SARS-Covid-2 infection in the patients**.**

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