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Article Detection of biochemical markers levels among COVID-19 patients, recovered and vaccinated groups of people

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Abstract: The new virus first appeared in the Chinese city of Wuhan in 2019 and spread around the world, like the outbreak of the Coronavirus (COVID-19), causing severe acute respiratory syndrome in humans, which can be fatal to individuals at risk. The primary purposes of this study are to assess the diagnostic power of the following biochemical (D dimer, CRP, LDH and serum ferritin) markers in identifying the diagnosis and severity of COVID-19 and to find out the differences in these hematological and biochemical markers among COVID 19 patients and recovered. The study included (50) patients diagnosed with COVID-19 (25 males and 25 females) who visited Al-Hussein Teaching Hospital in ThiQar province, (50) Patients recovering from COVID-19 infection, (50) People who have received COVID-19 vaccines and (50: 25 people were vaccinated with Sinopharm and 25 people were vaccinated with Pfizer) healthy subjects as a control group. The study population age ranged from (20-70 years) old. Specialist physicians diagnosed all patients with COVID-19 in this study, which was confirmed by clinical and laboratory tests, especially polymerase chain reaction PCR. The results of the current study have shown that there is a significant difference(P-Value < 0.05) between the study groups according to the age group in each of the levels (D dimer, LDH, serum ferritin). The current study also revealed a significant difference between the study groups according to gender in each of (D. dimer, LDH), and there is no significant difference in each of (CRP, serum ferritin). A significant difference is expected where the difference between the two averages is between the patients' COVID-19 group and the control group, the recovered group, or the vaccinated group(LSD of D. dimer >95.10, LSD of CRP>11.86, S. ferritin >120.61, LSD of LDH>75.45) and no significant between control and recovered. An increase in the levels of the following vital signs for patients with COVID-19: D dimer, CRP, LDH, and serum ferritin. In the recovered groups, the levels were normal.

Keywords: biochemical markers, COVID19, recovered and vaccinated group of people

Introduction

In December 2019, Wuhan, China, became the epicenter of unexplained pneumonia cases. Chinese scientists identified this as a new coronavirus in January 2020, dubbed SARS coronavirus 2 at the time (SARS-CoV-2)¹. COVID-19 is a highly contagious disease that spreads quickly worldwide, prompting the World Health Organization to declare it a pandemic on March 12, 2020². SARS-CoV and Middle East respiratory syndrome coronavirus-2 (MERS-CoV) have generated epidemics in the previous two decades, with mortality rates

of roughly 9.5 percent and 34.4 percent, respectively. COVID-19 was the third highly epidemic disease to be discovered, with a lower mortality rate than SARS and MERS, albeit the mortality rate varied by country. According to WHO figures, the high transmission capability of SARS-CoV-2 has resulted in 45,678,440 confirmed cases in 219 countries as of November 2020. As a result, to describe the acute infection in humans caused by the SARS-CoV, scientists and governments have taken swift and decisive action to track the outbreak and conduct etiological research ³. Laboratory tests validated for SARS-CoV-2 are crucial for the timely management of COVID-19 because they support the clinical decision-making process for controlling infections and detecting asymptomatic cases. This expedites speedy isolation and adequate treatment and consequently reduces contagion rates ⁴. Laboratory findings are among the most critical steps in the diagnosis and follow-up of patients with Covid-19. Many studies have been done to investigate the biomarkers for Covid-19. The primary routine assays requested for COVID-19 clients include complete blood count, Ddimers, and inflammation-related parameters (CRP, ferritin and Lactate dehydrogenase). Because of the potential capability of the virus to greatly hinder several vital organs, such as kidneys and the heart, analyzing the biochemical markers is a suitable way for clinicians to determine the functional processes of these organs ⁵. The main objectives of this study were to assess the diagnostic power of the following biochemicals (D dimer, CRP, LDH, and serum ferritin) in identifying the diagnosis and severity of COVID-19. To find out the differences in these biochemicals among COVID-19 patients and recovered.

Materials and methods

Biochemical factors related to COVID-19 infection

1. D-dimer

D-dimer originates from the lysis of cross-related fibrin with rising ranges indicating the activation of coagulation and fibrinolysis ⁶. D-dimer is the very last made of fibrin degradation. It includes the remnants of all 3 chains (α , β and γ chains) of fibrinogen related via disulfide bonds. The dimeric shape of D-dimer is held via way of means of covalent, intermolecular isopeptide bonds among the γ -chains ⁷.

Early studies have related COVID-19 with hemostatic abnormalities, with one study looking at increased ranges of D-dimer, the measure of coagulation, in non-survivors in comparison to survivors ⁸.

2. C. Reactive Protein

CRP is a plasma protein produced through the liver and precipitated through numerous inflammatory mediators, which include IL-6. Despite being non-specific, this acute segment reactant is used clinically as a biomarker for numerous inflammatory conditions; an upward thrust in CRP stages is associated with a boom in disorder severity ⁹.

3. Ferritin

Ferritin, a main iron storage protein, is essential to iron homeostasis and is concerned with an extensive range of physiologic and pathologic processes. In medical medicine, ferritin is predominantly applied as a serum marker of overall frame iron stores. In iron deficiency and overload, serum ferritin is vital in each analysis and management. Elevated serum and tissue ferritin are related to coronary artery disease, malignancy, and adverse effects following stem molecular transplantation. Ferritin is, without delay, implicated in less common, however probably devastating, human sicknesses, which include sideroblastic anemias and neurodegenerative disorders ¹⁰. Ferritin modulates cytokine

production and release, which is responsible for the cytokine (proinflammatory) storm and limits iron availability to the pathogen ¹¹. In COVID-19-infected patients, elevated ferritin serum levels have been reported to correlate strongly with disease severity ¹².

4. LDH

Lactate is produced inside the cytosol through the fermentative department of the glycolytic pathway through the reduction of pyruvate with the concomitant oxidation of NADH to NAD^{+,} a response catalyzed by lactate dehydrogenase (LDH). This enzyme consists of 4 subunits of distinct kinds named H and M due to their essential expression in the heart and muscle, respectively. In glucose metabolism, the enzyme LDH converts pyruvate to Lactate. Induced LDH secretion is prompted by necrosis of the cell membrane, hinting at viral infection or lung damage, along with the pneumonia induced by SARS-CoV-2¹³.

Study Design and data collection

A case-control study The study included 50 patients diagnosed with COVID-19 (25 males and 25 females) who visited Al-Hussein Teaching Hospital in Nasiriyah City, 50 patients recovering from COVID-19 infection, and 50 healthy subjects as a control group. The study population's ages ranged from 20–70 years old. Specialist physicians diagnosed all patients with COVID-19 in this study, confirmed by clinical and laboratory tests, especially polymerase chain reaction PCR, from September 2021 to April 2022. The practical part of the study was carried out in the Al-Hussein Teaching Hospital Laboratory.

Collection of sample

Five milliliters of human blood were obtained from each subject (patients recovered and controls); 1.8 mL of blood was put in anticoagulant tubes (containing sodium citrate). The sample was separated by centrifugation at 2000 rpm for 20 minutes, and the serum was then isolated and deposited at (-20 0C) until analyzed. The remaining were transferred to EDTA and gel tubes and allowed to coagulate at room temperature for 30 minutes. The sample was separated by centrifugation at 4000 rpm for 5 minutes, and the serum was then isolated and deposited at (-20 0C) until analyzed.

Statistical analysis

Statistical analysis was done using the software SPSS version 2020; the results were expressed as mean \pm standard deviations (mean \pm SD). Oway ANOVA-test and Chi-square were used to compare parameters in different studied groups. P-values (P \leq 0.05) were considered statistically significant.

Results

Table 1 shows significant differences in D.dimer levels between groups according to age group (P 0.05) and significant differences between groups according to age group. Table 2 and Figure 1 show a significant difference between males and females between groups according to gender (P-value 0.05). The difference between the two averages is that the Patients' COVID-19 group and the control group, the recovered group, or the vaccinated group appear to be superior when comparing the groups, as shown in Table 3 and Figure 2, where the difference between the two averages A significant difference is expected between the patients' COVID-19 group and the control group, if the LSD is more significant than 95.10).

Table 1 shows no significant differences in CRP levels between groups according to age group (P- value > 0.05). Table 2 and Figure 1 show no significant difference between males and females between groups according to gender (P-value > 0.05). The difference between the two averages is that the Patients' COVID-19 group and the control group or the recovered group appear to be superior when comparing the groups, as shown in Table 3 and Figure 2, where the difference between the two averages of the Patients' COVID-19 group and the control group, a significant difference is expected (LSD is more excellent than 11.86). There is no significant difference between the recovered and control groups (LSD is less than 11.86).

Table 1 shows significant differences in ferritin levels between groups according to age group and significant differences between groups according to age group (P- value < 0.05). Table 2 and Figure 1 show no significant difference between males and females between groups according to gender (P-value > 0.05). The difference between the two average ferritin Patients in the COVID-19 group and the control group, or the recovered group, appears to be superior when comparing the groups, as shown in Table 3 and Figure 2, where the difference between the two average Patients in COVID-19 group and the control group, or the recovered group and the control group, or the recovered (LSD is more remarkable than 120.61). No significant difference exists between the recovered and control groups (LSD is less than 120.61). There was a considerable rise in serum ferritin in COVID-19 patients, which agrees with Zhou et al. and Kappert et al., who found that serum ferritin is considerably raised in COVID-19 patients compared to healthy controls.

Table 1 shows significant differences in LDH levels between groups according to age group and significant differences between groups according to age group (P-value < 0.05). Table 2 and Figure 1 show a significant difference between males and females between groups according to gender (P-value < 0.05). The difference between the two average LDH Patients in the COVID-19 group and the control group, the recovered group, or the vaccinated group appears to be superior when comparing the groups, as shown in Table 3 and Figure 2, where the difference between the two average Patients COVID-19 group and the control group, or the recovered group, a significant difference is expected (LSD is greater than 75.45).

Categories	Case	No.	D. dimer µg /L	CRP mg/L	S. Ferritin ng/ml	I/II HDH
	Control	11	175	1.7	79	189
(21-30) Year	Patients	5	1136	95	736	885
	Recovered	7	183	2	59	206
	Control	15	163	1.3	100	174
(31-40)Year	Patients	7	630	55	588	745
	Recovered	10	163	1.5	137	156
	Control	15	181	1.8	67	164
(41-50)Year	Patients	9	874	52	629	680

	Recovered	17	171	2.5	122	176
(51-60)Year	Control	8	150	1.6	98	167
	Patients	17	875	62.1	664	558
	Recovered	11	181	1.8	121	194
(61-70)Year	Control	1	150	0.7	45	136
	Patients	12	1039	87.3	894	741
	Recovered	5	184	2.2	111	167
P Value			.000	.941	.000	.000
df =4						

Table 1. It shows the mean of biochemical parameters for each group according to the age group.

	Case	No.	Mean				
Gender			D. dimer µg/L	C.R.P mg/L	S . Ferrritin ng/ml	T/NI HOT	
Male	Control	28	165	1.83	87	173	
	Patients	25	1005	79.5	794	778	
	Recovered	27	163	1.99	129	183	
Female	Control	22	173	1.26	80.03	168	
	Patients	25	807	57.77	577.74	586	
	Recovered	23	183	2.82	98.39	176	
P. Value			.003	.689	.360	.281	
df =2							

Table 2. It shows the mean of biochemical parameters for each group according to the gender.



Figure 1. Show mean of levels biochemical parameters according to gender.

	Mean						
Case	D. dimer μg /L	C.R.P. mg / L	S.Ferritin ng/ml	LDH IU / L			
Control	168.40 b	1.58 b	83.86 b	175.32 b			
Patients	906.02 a	68.64 a	709.38 a	681.04 a			
Recovered	174.80 b	2.04 b	114.96 b	179.90 b			
LSD	95.10	11.86	120.61	75.45			

If the difference between two averages exceeds the LSD value, it indicates a significant difference and vice versa.

Different English letters mean significant differences within the same column below the 0.05 probability level.





Figure 2. The mean levels of biochemical parameters.

Discussion

No significant difference exists between the recovered and control groups (LSD is less than 95.10). Regarding D-dimer, the current study concurred with ¹⁴, who conducted a case-control study with 44 COVID-19 patients and 22 healthy people and discovered that patients with COVID-19 had higher D-dimer levels than controls¹⁴.

The level of C-reactive protein is linked to the severity of inflammation. In COVID-19 patients, it increased in lockstep with the diameter of the biggest pneumonia lesion¹⁵. Serum ferritin levels should Serum ferritin can be used as a predictive and stratifying biomarker for COVID-19 patients and a tool for therapeutic decision-making ^{16,17}. Moreover, no significant difference exists between the recovered and control groups (LSD is less than 75.45). Regarding LDH, the findings were consistent with those of Liu et al. and ²³, who found that LDH was higher in COVID-19 patients compared to healthy controls ^{18,33}.

Conclusions

There was an increase in the serum levels of the following vital signs for patients with COVID-19: D dimer, CRP, LDH, and serum ferritin, while in the recovered, the levels were normal.

Male patients demonstrated higher levels of the following biomarkers: D. dimer, C. reactive protein, serum ferritin, and LDH if compared to females.

Recommendation

To obtain more accurate results, it is necessary to increase the sample size for each of the three groups of patients and recover.

Studying other parameters to compare between groups, for example, following up the level of immunity specific to antibodies, some types of Interleukins, and specialized immune cells in all studied groups.

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