

## Article

### The study of some biochemical parameters in the serum of infected and recovered patients with COVID-19

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#### ABSTRACT

Few biochemical and immunological studies have been conducted on Iraqis infected with novel coronaviruses, and also Patients' post-recovery condition is unknown. Therefore, we aimed to study the impact of COVID-19 on some biochemical compounds in the serum of the infected subjects and to follow up the impact after 6-7 months. The research was conducted in Baghdad-Iraq from October to December 2021, and the study included four groups (each group consisted of 20 subjects): Group (A) Infected subjects without vaccination; group (B) Recovered subjects without vaccination; group (C) Recovered subjects after vaccination; and group (D) Non-infected subjects after vaccination. Subjects with COVID-19 infection confirmed by PCR and vaccinated individuals received the same type of vaccine. The authors measured some positive acute phase reactants (ferritin, C-reactive protein, and D-dimer), antibodies (IgM and IgG), and enzymes (LDH, AST, and ALT) in the subjects' serum. The study result showed an Increase in ferritin, CRP, D-dimer and LDH levels in the serum of infected subjects (group A). The antibody levels in the four groups were elevated, while the liver enzymes (ALT and AST) were in the normal values. Elevation of LDH level also in the serum of recovered subjects (groups B and C). Elevated ferritin, CRP, and D-dimer levels may not remain in infected patients after recovery from COVID-19 except for LDH, which is still elevated in some Iraqi subjects in Baghdad.

**Keywords:** Iraq, COVID-19, Vaccine, Acute Phase Reactants, Antibodies, Liver enzymes

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#### INTRODUCTION

In Wuhan City, Hubei Province, China, Chinese physicians discovered a patient with pneumonia symptoms of unclear etiology in December 2019 and reported it to the World Health Organization (WHO)<sup>1</sup>. In January 2020, the virus was recognized as a coronavirus. The SARS-CoV-2 virus and sickness were eventually dubbed COVID-19 by the WHO, the coronavirus family's third RNA virus<sup>2</sup>.

The continuing COVID-19 epidemic has a significant impact on Iraq. On February 24, 2020, the first COVID-19 patient was reported in Iraq<sup>3</sup>. On March 11, 2020, the World Health Organization (WHO) proclaimed the new coronavirus (COVID-19) outbreak a worldwide pandemic<sup>4</sup>. From December 2020 until now, five variants of COVID-19 have appeared: Alpha, Beta, Gamma, Delta, and finally Omicron in the United Kingdom, South Africa, Brazil, India and Multiple Countries respectively<sup>5,6</sup>.

In order to protect humans from this disease, several COVID-19 vaccines have been developed by many companies using different technologies, and the first virus variant (SARS-CoV-2) appeared in China. In Iraq, three types of vaccines were used: Sinopharm, AstraZeneca-Oxford and Pfizer-BioNTech vaccines<sup>7</sup>. Sinopharm used inactivated whole virus COVID-19 vaccine, while AstraZeneca and Pfizer used RNA technology to stimulate the immune response. The vaccine comprises either self-replicating RNA or messenger RNA (mRNA), which induces cells to produce the SARS-CoV-2 spike protein when injected into human tissue<sup>8,9</sup>.

The inactivated whole virus and the spike protein SARS-CoV-2 are antigens that stimulate the immune system to produce antibodies (Immunoglobulins, Ig)<sup>10</sup>.

SARS-CoV uses angiotensin-converting enzyme 2 (ACE2) as a receptor<sup>11</sup>.

These receptors (ACE2) are present in many cells of the organs, so the coronavirus infects the digestive system, liver, kidneys, and testis, in addition to the respiratory system<sup>12,13</sup>.

During the past two years (2020-2021), many studies and research were conducted that included all aspects of the novel coronaviruses (COVID-19), including clinical biochemical research.

The D-dimer is a fibrin breakdown product (Fibrinolysis) that circulates in healthy blood plasma at low levels, and its level is one of the tests used to diagnose thrombosis in patients. Measuring the amount of D-dimer and coagulation parameters from the onset of COVID-19 illness can also help regulate and manage the condition. Patients with severe COVID-19 have considerably greater blood D-dimer concentrations than those with less severe variants<sup>14,15</sup>.

C-reactive protein (CRP) levels were strongly linked with lung lesions in the early stages of COVID-19 and might represent disease severity, and CRP levels remained high in individuals who died from COVID-19 infection, suggesting that it might be a useful diagnostic for determining disease severity<sup>16,17</sup>. Patients with high CRP, or LDH (Lactate Dehydrogenase), need to be managed carefully and, if required, transferred to an intensive care unit, and elevated LDH was seen in 44% of the infected individuals<sup>18,19</sup>.

In people with COVID-19, digestive system problems and liver damage are prevalent. The care of this special group of patients should be given more attention. COVID-19 patients frequently have abnormal liver biochemical testing. COVID-19 patient's severity and prognosis are linked by biochemical markers in the liver<sup>20,21</sup>. Biochemical markers of liver damage include alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase, and bilirubin<sup>22</sup>.

Only 10.8% of all participants in the study of Kamal et al., 2021<sup>23</sup> had no symptoms after recovering from COVID-19, even though a high majority of them had several symptoms and disorders.

A literature review was performed within the database of PubMed, Google Scholar and Iraqi Academic Scientific Journals; we found few or rare biochemical and immunological studies on Iraqi COVID-19 patients. Analyses

for biochemical substances in the patient's blood are required to follow up on COVID-19 patients, so we aimed to know the effect of this disease on some biochemical and immune parameters of vaccinated and unvaccinated patients and compare it with the results of others' research in order to participate in scientific knowledge of the nature of the new disease, protection, prevention and control of its spread.

## MATERIALS AND METHODS

This study was conducted in a private Al-Harithiya / Baghdad - Iraq laboratory. It was conducted from October to December 2021.

Eighty subjects were included in this study, and the ages of all subjects ranged from 20 to 50 years. They were divided into four groups; each group involved 20 people (10 men and 10 women): Group (A) Infected subjects without vaccination; group (B) Recovered subjects without vaccination; group (C) Recovered subjects after vaccination, and group (D) Non-infected subjects after vaccination. Blood samples were taken from group (A) participants two weeks after infection without vaccination. In contrast, it was taken from the three groups (B, C and D) after 6-7 months of recovery or vaccination.

A questionnaire was conducted for all subjects, including age, gender, type of vaccination, symptoms, location and duration of infection.

All study subjects do not suffer from chronic diseases like diabetes or hypertension. It was confirmed that they were infected with COVID-19 through a PCR examination. The vaccinated subjects were selected from the same type of vaccine.

About 5 mL of blood was taken from all subjects who participated in this study.

This study used different equipment, devices, and apparatuses: MINI VIDAS (bioMérieux, France) for IgM and IgG and Tosoh AIA-360 Automated Immunoassay Analyzer for Ferritin. Roche cobas c111 for CRP, LDH, AST, and ALT, where all Kits used are from Roche company (Germany).

However, the normal value of ferritin (100-300 ng/mL), CRP (0-10 mg/L), (D-dimer (0-500 mg/L), IgM and IgG (0-1), LDH (120-220 U/L), AST and ALT (5-35 U/L).

The mean and standard deviation (SD) were computed for each parameter. The Statistical Package for the Social Sciences (SPSS, Windows version 25) software was used for the statistical analysis.

## RESULTS

Our study included eighty participants. Twenty persons (10 men and 10 women) were studied in each of the four groups (A, B, C, and D).

Data for age (ranging from 20 to 50 years) and acute phase reactant compounds are expressed as mean  $\pm$  standard deviation (SD) for the four groups in Table 1.

The results of Group (A), infected subjects without vaccination, showed a rise in acute phase reactant compounds (ferritin, CRP, and D-dimer) in the serum of 20 participants at a mean age of  $44.25 \pm 7.78$  years. The blood samples were taken from this group (A) two weeks after infection without vaccination. The mean and SD of ferritin, CRP and D-dimer were  $533.45 \pm 161.43$  ng/mL,  $24.64 \pm 8.19$  mg/L, and  $668.55 \pm 1.23$  mg/L respectively.

The mean and SD of age for the three groups B, C, and D, were  $29.25 \pm 5.97$ ,  $29.9 \pm 5.46$ , and  $27.9 \pm 6.16$ , respectively.

As for the results of the other three groups (B, C, and D) in which blood was drawn from the participants after 6 to 7 months, they were as follows: The results of acute phase reactant compounds in the blood of group B (recovered subjects without vaccination), were within the normal ranges: Ferritin ( $238 \pm 70.54$  ng/dl), CRP ( $6.015 \pm 3.23$  mg/L), and D-dimer ( $372.6 \pm 245.44$  mg/L).

Also for group C (recovered subjects after vaccination): Ferritin ( $277.7 \pm 88.1$  ng/mL), CRP ( $10.11 \pm 3.21$  mg/L), D-dimer ( $486.35 \pm 290.51$  mg/L), and for the group D (Non-infected subjects after vaccination): Ferritin ( $205.35 \pm 44.46$  ng/mL), CRP ( $7.04 \pm 2.42$  mg/L), D-dimer ( $265.3 \pm 96.13$  mg/L) were within the normal ranges.

The results of antibodies and enzymes were presented in Table 2 as mean  $\pm$ SD for the four groups.

The results of group A for antibodies (IgM and IgG) were raised, as they were IgM ( $2.525 \pm 1.23$ ) and IgG ( $33.3 \pm 8.42$ ). The lactate dehydrogenase (LDH) also was raised ( $494.45 \pm 222.14$  U/L), while the other enzymes AST and ALT were in the normal values ( $35.4 \pm 18.25$  and  $33.1 \pm 17.31$  U/L respectively).

The antibody IgM in the blood of the three groups B, C, and D, were within the normal values: Group B IgM ( $0.51 \pm 0.43$ ), Group C IgM ( $0.55 \pm 0.51$ ), and Group D IgM ( $0.53 \pm 0.24$ ). Elevation of IgG in the blood of the three groups: Group B IgG ( $19.31 \pm 7.18$ ), Group C IgG ( $44.91 \pm 10.13$ ), and Group D IgG ( $25.21 \pm 7.04$ ).

Our study on some enzymes shows that the results of LDH in the blood of recovered participants (group B and C) were raised ( $265.55 \pm 119.27$  and  $289.5 \pm 123.72$  U/L respectively), While it was in the group D ( $289.5 \pm 123.72$  U/L) within the normal range. The level of AST in the three groups (B, C, and D) was in the normal values ( $23.78 \pm 9.83$ ,  $27.58 \pm 5.81$  and  $26.57 \pm 6.79$  U/L respectively). Also, ALT was in the normal values ( $24.75 \pm 13.46$ ,  $20.45 \pm 6.62$ , and  $13.42 \pm 5.1$  U/L, respectively).

Groups	Age (Years)	Acute Phase Reactants		
		Ferritin (ng/mL)	CRP (mg/L)	D-dimer (mg/L)
<b>A</b>	44.25 $\pm$ 7.78	533.45 $\pm$ 161.43	24.645 $\pm$ 8.19	668.55 $\pm$ 1.23
<b>B</b>	29.25 $\pm$ 5.97	238 $\pm$ 70.54	6.015 $\pm$ 3.23	372.6 $\pm$ 245.44
<b>C</b>	29.9 $\pm$ 5.46	277.7 $\pm$ 88.1	10.11 $\pm$ 3.21	486.35 $\pm$ 290.51
<b>D</b>	27.9 $\pm$ 6.16	205.35 $\pm$ 44.46	7.04 $\pm$ 2.42	265.3 $\pm$ 96.13

**Table 1. The participants ' ages and the impact of COVID-19 on acute phase reactant compounds.**

Groups	Antibodies		Enzymes		
	IgM	IgG	LDH (U/L)	AST (U/L)	ALT (U/L)
<b>A</b>	2.52±51.23	33.3±8.42	494.45±222.14	35.4±18.25	33.1±17.31
<b>B</b>	0.51±0.43	19.31±7.18	265.55±119.27	23.78±9.83	24.75±13.46
<b>C</b>	0.55±0.51	44.91±10.13	289.5±123.72	27.58±5.81	20.45±6.62
<b>D</b>	0.53±0.24	25.20±7.04	167.95±17.52	26.57±6.79	13.42±5.1

*Table 2. The description of antibodies and enzymes in the four groups.*

## DISCUSSION

To our knowledge, this is the rare study to investigate the impact of COVID-19 on some clinical parameters in the serum of recovered Patients.

The SARS-CoV-2 virus (COVID-19) has spread all over the world in the last two years (2020-2021) and infected all ethnicities, ages and genders with different rates of infection, as well as infecting the rest of the body's systems in addition to the respiratory system (4, 12,13,24). We studied 80 subjects (40 males and 40 females) of Iraqi Arabs in Baghdad, ranging in age from 20 to 50 years. The prevalence of COVID-19 infection is influenced by factors such as age and gender<sup>25</sup>. However, our study showed that age and gender did not affect the results.

The results of infected subjects without vaccination (group A) showed a rise in the level of studied acute phase reactant compounds in the serum of participants. Acute phase reactants can be classified as positive or negative, depending on their serum concentrations during inflammation<sup>26</sup>. Positive acute phase reactants (Ferritin, CRP, D-dimer) increase their concentrations during COVID-19 infection<sup>14,18</sup>. Before proceeding to conclusive diagnosis by RT-PCR, a combination of regular laboratory indicators (CRP, LDH, and ferritin D dimer) can be utilized to predict the diagnosis of COVID-19 with acceptable sensitivity and specificity<sup>27</sup>.

The results of post-COVID-19 acute phase reactant compounds in the blood of group B (recovered subjects without vaccination) and group C (recovered subjects after vaccination) were within the normal ranges, and also for group (D) Non-infected subjects after vaccination. This result proves that they were cured of the infections caused by COVID-19 and do not have the etiology of elevation of the positive acute phase reactants.

Antibodies increase in the blood due to the immune response to infection or vaccination. Immune system responses differ significantly between males and females, with females triggering higher immune responses to infections. This disparity in immune responses might substantially influence viral load, illness severity, and death; the male sex is an important risk factor for COVID-19, where the men's infection was more than women's<sup>25, 26, 28</sup>.

The normal levels of ALT and AST in the subjects' serum of the four groups (A, B, C, D) are evidence of non-liver infection, as<sup>29</sup> recorded liver injury in some Iraqis infected with COVID-19, as well as in other countries of the world<sup>20,21</sup>. The LDH level was at the normal value in the non-infected subjects (group D),

while it was elevated in the infected and recovered subjects (groups A, B and C). LDH levels are elevated in many injuries and multiple organ failure<sup>18,30</sup>.

A study in Iraq showed that in individuals with a history of severe COVID-19, elevated ESR and CRP levels and hypoalbuminemia may remain after recovery<sup>31</sup>.

Fatigue was the most prevalent post-COVID-19 symptom reported (72.8 %). In contrast, more serious symptoms such as stroke, renal failure, myocarditis, diabetes and pulmonary fibrosis were recorded by just a few percent of the participants<sup>23</sup>.

Small sample sizes and selection bias limit our study as it was conducted in a single location in Baghdad and did not include large numbers in the governorate or in Iraq as a whole. Further study is needed on the predictive significance of vital signs to increase reliability.

## CONCLUSION

Elevation of all biochemical parameters studied in the subjects' serum with COVID-19 (group A), except liver enzymes (ALT and AST); and increased antibodies against COVID-19 in the four groups due to infection and/or vaccine. The normal level of the parameters studied in the groups (B and C) indicates no post-COVID-19 effect except for a rise of LDH after recovery.

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