

Assessment of Some Physiological Parameters and Trace Elements in Covid 19 Patients, Iraq

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Abstract

The current study aims to estimate the number of physiological parameters including (LDH, D-dimer, and ferritin statuses and a some of trace elements (zinc and magnesium), as well as demographic criteria such as (age, employment status, and habitation) that are believed to be directly and indirectly related to infection with prognosis in Iraqi COVID-19 patients. In the current study, a significant increase in LDH, D-dimer and ferritin (613.34 ± 203.62 , 666.76 ± 157.36 , 596.81 ± 146.66) was observed in patients with Covid-19 compared to healthy people (150.10 ± 27.42 , 191.45 ± 58.82 , 198.92 ± 63.85). In addition to a significant decrease in the percentage of oxygen (86.64 ± 3.42) for patients with Covid 19. As for the trace elements, a significant decrease in zinc and magnesium (65.39 ± 6.04 , 1.53 ± 0.10) was observed for patients with Covid-19 compared to healthy people (94.42 ± 12.73 , 2.09 ± 0.23).

As for age, it was noted in this study that the 40-69 age group is the most affected (59 %), as well as the employment status it was noted that employees are the most vulnerable to the disease, and that those who live in cities are the most affected by Covid 19, as conclusion that age, functional status, and area of residence are risk factors affecting infection with Covid-19, and that measuring oxygen saturation, LDH, D-dimer and ferritin are good specific parameters for determining infection and for knowing the severity of the disease in addition to measuring the trace elements that have a direct and indirect role in infection with covid 19 and the deterioration of the patient's health condition

Keywords: Trace Elements, Zinc, Zn, Magnesium, Mg, Covid 19, D.dimer, Ferritin.

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INTRODUCTION

COVID-19 initially surfaced in Wuhan, China, in December 2019 and is currently deemed an international community health crisis. The SARS-CoV-2 genome is made up of a single-stranded positive-sense RNA virus connected to a nucleoprotein inside a capsid that also contains medium protein in addition to containing of coronavirus to hemagglutinin-esterase (HE) protein (Jiang et al., 2020, Khaerunnisa et al., 2020).

Coronaviruses have produced three significant epidemics in humans: Severe Acute Respiratory Syndrome (SARS-2003), Middle East Respiratory Syndrome (MERS-2012), and Middle East Respiratory Syndrome (MERS-2013). In addition to Acute Respiratory Syndrome (SARS-CoV 2) ((Morfeld et al., 2021).

High temperature, head pain, cough, gastrointestinal signs such as diarrhea, nausea, and abdominal discomfort, and dyspnea are common clinical manifestations of the illness. There are many physiological and biochemical factors that are considered evidence of infection with the Corona virus, even if symptoms are not present, and the most important of

them are Lactate dehydrogenase (LDH) is a kind of enzyme that breaks down. Because its increase has previously been connected to the worst instances of other viral infection (C. Y. Chen et al., 2005) substantial variations in LDH have been recommended among COVID-19 patients with and without cruel symptoms (B. M. Henry et al., 2020).

D-Dimer is another significant physiological marker, increase of D-dimer concentration has been recommended in patients with COVID-19 because it is one of the approaches to assess the thrombotic status, as various researches have demonstrated coagulation in cruel cases of COVID-19 patients (N. Tang et al., 2020)

Ferritin blood problems show to be of limited indicative value in both SARS and MERS, where no change in ferritin levels have been recorded or not examined or not recorded and, While serum ferritin, on the other hand, has been proposed as an important key indicative markers in COVID-19 (K. Kappert et al., 2020)

In severe forms of COVID19, pneumonia, lymphocytopenia, lymphocyte exhaustion, and cytokine storm syndrome are characterized by increased plasma levels of cytokines (IL2, IL7, and IL10), granulocyte

colony-stimulating factor (GSCF), 10 kD interferon-gamma-induced protein (IP10), monocyte chemoattractant protein-1, and monocyte chemoattractant protein-2 (MCP1), macrophage inflammatory protein 1- α (MIP1A), and interferon-alpha (TNF- α) (Dietz and SantosBurgoa, 2020, Kong et al., 2020).

To keep cells from oxidative stress, numerous micronutrients, include vitamins and trace minerals, are essential for appropriate immune system role (Lee et al., 2019). The principal trace elements that have immunomodulatory impact, such as zinc (Zn), manganese (Mn), are cofactors of antioxidant enzymes that can limit viral replication in host cells and so have antiviral action (Jayawardena et al., 2020).

maintain a healthy trace nutrients stability can help the host's immune system respond more effectively and keep him or her in opposition to viral infections (Razzaque, 2020). So the current study aimed to evaluate some physiological parameters that are believed to be direct markers of the disease assessment and to note its development and severity of infection, in addition to measuring some trace elements that are believed to be risk factors for infection with Covid-19 directly and indirectly, in addition to evaluating some Demographic criteria that may be risk factors for contracting COVID-19.

MATERIALS AND METHODS

A total of 200 people took part in this research (100 COVID-19 patients and 100 healthy people). These patients were chosen at random several hospitals in Thi-Qar, Iraq,, which was validated by a reverse transcription polymerase chain reaction test on a nasopharyngeal swab (admitted from january 10, 2021 to august 10, 2021), and patients who taking dietary supplements, multivitamins, or trace elements in any form and pregnant women were eliminated from this study, while healthy persons were chosen at random from Thi-Qar University students and staff, Both genders were between

the ages of 18 and 70 years old, The study was performed according to the ethical forms commended by the human ethics committee guidelines of our institution (no. 22/2020).

A disposable syringe was used to assemble 8 mL of blood from each individual's antecubital vein in a sanitized test tube. After centrifuging the blood sample for 5 minutes at 5000 rpm, the serum was divided and utilized to measures some physiological parameters and trace elements by:

1. Roche Diagnostics GmbH, USA, cobas ® using for measuring D-Diimer, LDH, and Ferritin.
2. Pluse oximeter (CMS50D) equipment from contecTM, China, for measuring O2 and plus rate.
3. BioSystems, español kits for Zink, Iron and magnesium.

The data were analyzed using the SPSS program to get the chi-square value (X²) [28]. (version 25 statistical software). Other data using mean standard deviation (MSD), When the resultant P-value was less than 0.05, the results were considered statistically significant [29].

RESULTS

There were 200 participant in this study (100 as a covid 19 patients and 100 as a healthy people), Table 1 shows their age, work status, and environment type. According to the covid 19 participants' ages, 52 percent of the 100 participants are between the ages of 40 and 69, 32 percent are between the ages of 20 and 39, 12 % are above of 69, and just 4 percent are under 20, Thus, the highest percentage was for the category (40 – 69 age). The bulk of them 100, are employed (46%) or unemployed (39%), in terms of work status, while the minority, 15 % students, However, compared between rural and urban the percent of rural is (39 % from 100 participant and 61 % for urban).

Table 1. Distribution of COVID-19 patients according to age, employment state, and habitation

Parameters		N	%	X ²	P. value
Age	Age interval	< 20	4	4	55.5 < 0.01
		20-39	32	32	
		40-69	52	52	
		> 69	12	12	
Employment state	Employed	46	46	15.8 < 0.01	
	Un-employed	39	39		
	Students	15	15		
Habitation	Rural	39	39	4.84 0.028	
	Urban	61	61		

This experiment examined a variety of physiological markers, which are presented in table 2, and this results show there were a significant deference ($p \leq 0.05$) between

patients and healthy people in O₂ concentration and plus (86.64 ± 3.42 and 96.57 ± 1.88 , 83.59 ± 14.71 and 89.53 ± 4.48), while there were a significant increase in LDH, D. dimer and S. ferritin concentration in patients compared

with healthy people (613.34 ± 203.62 and 150.10 ± 27.42 , 198.92 ± 63.85 successively), 666.76 ± 157.36 and 191.45 ± 58.82 , 596.81 ± 146.66 and

Table 2. Physiological parameters in COVID-19 patients and healthy people

Parameters	Groups	N	Mean & Std.	P. value
O ₂ %	Patients	100	86.64 ± 3.42	$\leq 0.001^{**}$
	Healthy people	100	96.57 ± 1.88	
Plus (bpm)	Patients	100	83.59 ± 14.71	$\leq 0.001^{**}$
	Healthy people	100	89.53 ± 4.48	
LDH (u/l)	Patients	100	613.34 ± 203.62	$\leq 0.001^{**}$
	Healthy people	100	150.10 ± 27.42	
D. dimer (ng/ml)	Patients	100	666.76 ± 157.36	$\leq 0.001^{**}$
	Healthy people	100	191.45 ± 58.82	
S. ferritin (ng/ml)	Patients	100	596.81 ± 146.66	$\leq 0.001^{**}$
	Healthy people	100	198.92 ± 63.85	

Table 3 shows the concentration of trace elements in both patients and healthy people, that appear a significant differences were found in zinc (ze), iron (fe) and magnesium (mg) as there is a decrease in covid 19 patients ($65.39 \pm$

6.04), (4.89 ± 1.19), and (1.53 ± 0.10) comparative with healthy people (94.42 ± 12.73), (16.39 ± 4.51), and (2.09 ± 0.23).

Table 3: The concentration of zink, and magnesium in covid 19 patients and healthy people

Trace elements	Groups	N	Mean & Std.	P. value
Zn $\mu\text{g/dl}$	Patients	100	65.39 ± 6.04	≤ 0.001
	Healthy people	100	94.42 ± 12.73	
Mg mg/ml	Patients	100	1.53 ± 0.10	≤ 0.001
	Healthy people	100	2.09 ± 0.23	

DISCUSSION

The current study dealt with some of the demographic criteria, age, employment state, and habitation, which is believed to be one of the risk factors associated with infection with COVID-19, as current study showed that the highest percentage was for the category (40 – 69 age) as 52 percent This study was similar to previous studies, as infection with Covid-19 is more common in older adults compared to younger ages as this study is similar to (Jamela et al., 2022, and D. Santesmasses et al 2020), And the study differed with (Janice C et al., 2021) As it found that the age group above 75 is the most vulnerable to infection, The reason for the infect of this age group in our current study may be that these people are the most out of the house to practice the profession, which is in direct contact with the external environment with a lack of interest in health and prevention measures against Covid 19 in addition to the advanced age and the lack of healthy nutrition leads to a decrease in immunity, which may be a direct risk factor for infection (A. L. Mueller et al., 2020), Our bodies contain two lines of defense in the immune system against pathogens, the first line called white blood cells, which attack foreign bodies within minutes to hours through direct

ingestion with a process called phagocytes, and the second line through the formation of antibodies, as well as T lymphocytes, which are formed by Thymus gland however, T cells produce chemicals that attack viruses. With age, T cells dwindle, as the thymus produces 10 times fewer T cells in adulthood compared to childhood, so older people produce much less T cells and T cells function is to identify new viruses and other pathogens, and this is one of the reasons for low immunity with age (Márquez et al., 2020).

Among the demographic criteria that were also studied in this research is the employment status, as it was noted that the most affected groups are employees, and this may be due to the lack of commitment to preventive and safety measures: wearing masks, paws, sterilization, maintaining a safe distance, as well as being in Crowded places, which increases the risk of infection with a virus, and our study differed with the (jamela et al., 2022) which found that non-employees are more susceptible to infection, and it coincided with (Ariadna et al., 2022), which reached the same conclusion in our current study.

Another demographic criteria is Habitation as current study found that the population living in urban areas is more infected, as the percentage 61 % while 39 % for rural The reason for this may be due to the fact that urban areas are

more crowded with people than rural areas, in addition to the green and spacious areas that are few compared to rural areas, in addition to the possibility of direct contact between people in urban areas, which leads to a high risk of infection with Covid-19. and it coincided with (Rajib et al., 2021), which found that the death rate from infection with Covid 19 in urban areas more than in rural areas.

Many biochemical parameters have been measured in many previous studies, which are believed to be directly related to infection with Covid-19, or that their increase or decrease causes other diseases that lead to death. One of the most important of these factors that was studied in this research is ((O₂, plus, LDH, D-Dimer, and ferritin), The percentage of oxygen saturation is one of the most important factors that were adopted to determine the severity of the disease in infection with Covid-19, and the percentage of oxygen that determines whether the patient needs to enter the pulmonary resuscitation unit or not, in this study, a significant decrease in the percentage of oxygen (86.64 ± 3.42) was observed for patients compared to healthy people (96.57 ± 1.88). Corona virus is considered one of the viruses that infect the respiratory system, as this virus has receptors angiotensin converting enzyme 2 (ACE2)³⁶⁷ which are largely present in the alveolar epithelial type II cells in lung and type II transmembrane serine protease (TSP2), which facilitates viral attachment to ACE2 and cell entry, so the severe infection is in the lung, As a result there is a decrease in oxygen saturation (Shang J et al 2020, Letko M et al., 2020, Wan Y et al., 2020).

LDH is an intracellular enzyme, and there are five different forms of it that are found in practically all cells throughout the body: LDH-1 in cardiac muscles, LDH-2 in the reticuloendothelial systems, LDH-3 in lung cell, LDH-4 in the pancreas and kidney, and LDH-5 in the skeletal muscles and liver. LDH has been used as one of the key indicators of heart injury since the 1960s, but it is also recognized that its aberrant readings can be caused by hypoxia and harm to many other organs, Significant tissue damage and infection trigger metallic proteases and encourage macrophage-mediated angiogenesis, which raises lactate levels in the extracellular acidic pH. This might result in the release of LDH when tissues are damaged by cytokines (U. E. Martinez-Outschoorn et al., 2011), our current study found a significant increase in LDH enzyme in patients compared to healthy people and the study matched with (B. M. Henry et al., 2020, A. Assiri et al., 2013), LDH (isozyme 3), which is present in lungs tissue, can be released into the blood from lungs tissue damage in COVID-19 patients and can rise with disease severity since LDH has been linked to bad outcome for hospitalized patients in several studies (C. Y. Chen et al., 2005).

Another of the biochemical parameters that was studied in this research is D. Dimer, and the study found a significant increase for patients with Covid 19 compared to healthy people, and this study matched with a (G. Lippi and E. J.

Favaloro., 2020, G. Lippi et al., 2020, Y. Zou et al., 2020), Increased D-dimer levels and thrombocyte counts have also been linked to increase blood clotting states, which may be influencing the cruelty and death of COVID-19 patients' condition, That indicates that an increase in D-dimer is linked to the cruelty of respiratory illness and, consequently, death (F. Zhou et al., 2020), Measuring the concentration of LDH enzyme for infected patients is useful in knowing the development of the disease on the one hand, and the effect of the virus on the various cells of the body on the other, because blood clots may occur in different parts of the body, which may lead to failure in those organs (M. Rostami and H. Mansouritorghabeh., 2020).

The last biochemical parameter that was studied in this research is ferritin, and it was observed in this study that a significant increase in patients infected with Covid 19 compared with healthy people, and this study coincided with (Karanvir et al., 2022, Katia et al., 2021) When infected with the Corona virus, many biochemical and immune changes occur, and therefore they lead to changes in the number of cell proteins and thus plasma proteins, which is called "acute phase proteins" and one of the most important of these proteins is ferritin, which is a protein found in the cytosol and works to store iron, which contributes Mainly in transporting oxygen to cells and an increase and decrease it causes anemia, and some studies believe that ferritin is one of the determinants of the immune system, which is considered a proinflammatory, When covid-19 occurs, the body shows a very strong immune reaction called a cytokine storm, which happens that immune cells attack the cells of the body and even holes occur in the blood vessels, which leads to the leakage of vascular fluids to the surrounding cells, and also changes occur in blood clotting proteins, thus increasing clotting and thus failure in many organs. The body's immune system thus the ferritin is one of the necessary criteria that gives a picture of the state of the disease by interfering with the body's immune system (Vargas-Vargas and Cortés-Rojo., 2020, Ahmed. 2021, Enas et al., 2020).

The trace elements were studied in this research for patients with Covid 19, which is considered the first study in Iraq because of these elements of great importance to the body which their interaction with the immune system, which will be explained later. Two important elements were studied, (zinc and magnesium), and a significant decrease was observed for patients with Covid 19 (zinc 65.39 ± 6.04 , Mg 1.53 ± 0.10) compared to healthy people (zn 94.42 ± 12.73 , Mg 2.09 ± 0.23) and the study agreed with (Ozra et al., 2021, (Oliver et al., 2020) and were substantially linked with patient death, demonstrating that Zn may play a role in COVID-9 etiology, Zinc is an immune system enhancer and is essential for immunocompetence (Chandra RK and Dayton DH., 1982) It has a role in immune cell formation and maturation, as well as the inflammation reaction. Zinc is a cofactor in the cellular machinery of replicative and

transcriptional enzyme system including DNA and RNA polymerases, Zinc is a divalent transitive metal that is required for the antioxidant enzyme SOD to function. Superoxide (O₂) is converted to hydrogen peroxide by SOD (H₂O₂), Redox imbalance and oxidative stress are influenced by SARS-CoV-2 viral pathogenic mechanisms, This syndrome causes an excess of reactive oxygen species (ROS) to be produced, as well as a lack of antioxidant defense systems. Because of the significant link between oxidative stress indicators and the cruelty of viral infections, viral replication and its consequences play a critical role (Delgado-Roche and Mesta. 2020).

Dietary Zn supplementation have been shown to improve health and alleviate the effects of the SARS-CoV-2 virus. On viral infection, trace elements operate as a non specific activators of antioxidant metallo enzymes. Antioxidants raised the amount of T-cell subset, produced more interleukin-2, improved lymphocyte reactivity to mitogens, and potentiated natural killer cells(Ibs KH and Rink., 2003), On the other hand, magnesium is an important element in maintaining the normal breathing process, as it has a key role in the relaxation of bronchial smooth muscles and broncho dilatation, anti cholinergic, anti histaminic, and anti-inflammatory effects as well as mucociliary approval (Ni H et al., 2020, Bhaumik et al., 2019), One of the most important injury caused by Covid 19 is damage to the endothelial of blood vessels, and there are many studies that have found that magnesium has an important role in maintaining the endothelial of blood vessels, as well as the expansion and constriction of these vessels, and that its decrease leads to a poor patient's condition (Varga et al., 2020, Maier., 2012), In addition, several experimental studies have shown that magnesium deficiency leads to an increase in inflammatory determinants such us leukocytes and macrophage activations, pro-inflammatory molecule like interleukin-1, interleukin-6, tumor necrosis factors, vascular cell adhesion molecule-1, plasminogen activator inhibitor-1, and excessive production of free radicals (Kostov and Halacheva., 2018) Thus, its deficiency is considered a risk factor for many diseases, including: cardiovascular disease, hypertension, and diabetes (Nielsen., 2018) From these studies, we conclude that magnesium deficiency is a risk factor for infection with COVID-19, directly and indirectly (Oliver et al., 2020).

CONCLUSION

We conclude from the current study that age, functional status, and area of residence are risk factors affecting infection with Covid-19, and that measuring oxygen saturation, LDH, D- dimer and ferritin are good specific parameters for determining infection and for knowing the severity of the disease in addition to measuring the trace elements that have a direct and indirect role in infection with covid 19 and the deterioration of the patient's health condition. Finally, we recommend conducting studies for

other trace elements that may be related to infection and the body's immune system.

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