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DETECTION OF BIOCHEMICAL VARIATION AMONG COVID-19 INFECTED PATIENTS

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HUSSEIN ALI MOHAMMED AL-BADRI

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By Hussein Ali Mohammed AL-BADRI

November 2022

We certify that we have read this thesis and that in our opinion it is fully adequate, in scope and in quality, as a thesis for the degree of Master of Science

Advisor : Assoc. Prof. Dr. Şevki ADEM
Co-Advisor : Asst. Prof. Dr. Khaled Shalan SAHAB

Examining Committee Members:

Chairman : Assoc Prof. Dr. Hakan ÇOLAK
Chemistry
Çankırı Karatekin University

Member : Asst. Prof. Dr. Ümit YIRTICI
Medical Laboratory
Kırıkkale University

Member : Assoc. Prof. Dr. Şevki ADEM
Chemistry
Çankırı Karatekin University

Approved for the Graduate School of Natural and Applied Sciences

Prof. Dr. İbrahim ÇİFTÇİ
Director of Graduate School

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Hussein Ali Mohammed AL-BADRI

ABSTRACT

DETECTION OF BIOCHEMICAL VARIATIONS AMONG COVID-19 INFECTED PATIENTS

Hussein Ali Mohammed AL-BADRI

Master of Science in Chemistry

Advisor: Assoc. Prof. Dr. Şevki ADEM

Co-Advisor: Asst. Prof. Dr. Khaled Shalan SAHAB

November 2022

The aim of the current thesis is to study the biochemical changes in patients with coronavirus and an attempt to identify in the future the most successful ways to follow up with patients and as a result, treat them with the best drugs in a short period of time. Age had a significant effect on the disease in association with the period of infection. There were no clear signs or significant differences in body mass. IL6, NRL, LYM, and WBC were clear significant differences that could be used in early diagnosis of the disease or to follow up the patient's condition by linking with the rest of the blood parameters that had clear significant differences. Serum creatinine and urea did not have any significant statistically significant differences that could benefit in the follow-up of Covid-19 disease. In our study and by describing the pathway of ESR, CRP, RBS, D-Dimer, and Ferritin, it is possible to understand the mechanism that affects the change in the levels of these parameters in patients with Covid-19 and thus contribute to the early detection of the disease, as the results of these tests indicate the presence of significant differences High and statistically significant in patients when compared with the controls group. Whereas, D-dimer with ferritin is one of the most important diagnostic parameters for Covid-19 disease. There is a need for more studies on viruses, their mechanism of origin, and how they affect the physiology of the human body.

2022, 60 pages

Keywords: Corona virus 2019, SARS, MERS, Liver enzymes, D-dimer, Platelets

ÖZET

COVİD-19 İLE ENFEKTE HASTALAR ARASINDA BİYOKİMYASAL VARYASYONLARIN TESPİTİ

Hussein Ali Mohammed AL-BADRI

Kimya, Yüksek Lisans

Tez Danışmanı: Doç. Dr. Şevki ADEM

Eş Danışman: Dr. Öğr. Üyesi Khaled Shalan SAHAB

Kasim 2022

Mevcut tezin amacı, koronavirüs hastalarındaki biyokimyasal değişiklikleri incelemek ve gelecekte hastaları takip etmenin en başarılı yollarını belirlemeye çalışmak ve sonuç olarak kısa sürede en iyi ilaçlarla tedavi etmektir. Yaş, enfeksiyon dönemi ile ilişkili olarak hastalık üzerinde önemli bir etkiye sahipti. Vücut kütlesinde net belirtiler veya önemli farklılıklar yoktu. IL6, NRL, LYM ve WBC, hastalığın erken teşhisinde veya belirgin anlamlı farklılıkları olan diğer kan parametreleriyle bağlantı kurarak hastanın durumunu takip etmede kullanılabilecek açık anlamlı farklılıklardı. Serum kreatinin ve üre, Covid-19 hastalığının takibinde fayda sağlayabilecek istatistiksel olarak anlamlı bir farklılığa sahip değildi. Çalışmamızda ve ESR, CRP, RBS, D-Dimer ve Ferritin'in izlediği yol anlatılarak, Covid-19 hastalarında bu parametrelerin düzeylerindeki değişimi etkileyen mekanizmayı anlamak ve böylece erken evreye katkıda bulunmak mümkündür. hastalığın saptanması, bu testlerin sonuçlarında anlamlı farkların varlığını gösterdiğinden, hastalarda kontrol grubu ile karşılaştırıldığında yüksek ve istatistiksel olarak anlamlıdır. Ferritinli D-dimer ise Covid-19 hastalığı için en önemli tanı parametrelerinden biridir. Virüsler, köken mekanizmaları ve insan vücudunun fizyolojisini nasıl etkiledikleri hakkında daha fazla çalışmaya ihtiyaç vardır.

2022, 60 sayfa

Anahtar Kelimeler: Corona virüs 2019, SARS, MERS, Karaciğer enzimleri, D-dimer, Trombositler

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Hussain Ali Muhammad AL-BADRI

Çankırı-2022

CONTENTS

LIST OF SYMBOLS

-	Minus
%	Percent
**	Significant
/	Divide
+	Plus
<	Greater than
=	Equal
>	Less than
±	Plus – minus
≤	Greater or equal to
≥	Less or equal to
Ca	Calsium
Cu	Copper
dL	Deciliter
g	Gram
gm	Gram
kg	Kilogram
L	Liter
m^2	Square meter
mcg	Microgram
Mg	Magnesium
mg	Microgram
mIU	Milli-international units
min	Minute
mL	Milliliter
mmol	Milli mole
mol	Mole
ng	Nanogram
nm	Nanometer
NS	Non-significant
rpm	Revolutions per minute
Se	Selenium
Zn	Zinc

LIST OF ABBREVIATIONS

BA	Bronchial asthma
BUN	Blood urea nitrogen
CBC	Complete blood count
C-RP	C-reactive protein
D-DI	D-dimer
ESR	Erythrocyte sedimentation rate
FFD	Free from disease
GGT	Gamma-glutamyl transferase
GOT	Glutamic Oxaloacetic Transaminase
GPT	Glutamic Pyruvic Transaminase
IL – 6	Interleukin - 6
LDH	Lactate dehydrogenase
LYM	Lymphocytes
NRL	Neutrophil
PL	Platelets
PPT	Partial prothrombin time
PT	Prothrombin time
RBC	Read blood cell
RBS	Random blood sugar
RNA	Ribonucleic acid
WBC	White blood cell

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1. INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first described when it appeared among humans in December 2019 in Wuhan, China (McMichael *et al*. 2020). This is the third virus that has kills humans in the past twenty years, in 2002 Severe acute respiratory syndrome coronavirus 1 (SARS-Cov-1) appeared and in 2012 Middle East respiratory syndrome coronavirus (MERS), and this virus (SARS-CoV-2) in 2019 (Munster *et al*. 2020). The number of infected people since the outbreak of the epidemic until May 25 reached 5,370,375 cases, while the number of people who died from the virus was 344,454 cases, and this was distributed over 216 countries, regions or territories (Vilibic-Cavlek *et al*. 2020). The World Health Organization declared (SARS-Cove-2) a pandemic on March 11, 2020 (McMichael *et al*. 2020).

The SARS-Cove-2 virus spreads very quickly among people all over the world. Few countries have not reported cases of infection within their borders. There is evidence of the rapid spread of the virus, as one patient can transmit it to two or three patients with no symptoms (Gates 2020, Hoehl *et al*. 2020). The percentage of infected people without showing symptoms is still unknown (Velavan and Meyer 2020). The transmission of the virus is through direct exposure to the secretions of the patient, especially the secretions of the respiratory tract, as well as through contact with surfaces exposed to the secretions of the patient (Jin *et al*. 2020). The period of survival of the virus in the atmosphere for more than three hours does not reduce its possibility of infection, and in some surfaces such as stainless steel and plastic, the survival period reaches 72 hours (Apollo *et al.* 2020, Phua *et al*. 2020).

Currently, prevention methods must be followed due to the lack of effective treatment to avoid aggravating the situation, and one of the most important prevention methods is infection prevention and control (IPC), and this was considered a practical, evidence-based approach to avoid infection of workers in the medical and nursing field in particular, through documented statistics showing that Infection prevention and control (IPC) has led to a 30% reduction in infection rate in medical clinics and health care centers (Hearn *et al*. 2017).

Scientists named the virus by this name based on their perception of its circular shape surrounded by spike proteins (Weston and Frieman 2020). Divide the virus into four families; α, β, χ and δ Coronavirus; (SARS-Cove–2) is a beta virus and is also called a coronavirus, and in this way, it is similar to its predecessor (SARS-Cove-1) (Weston and Frieman 2020). The pre-identified strains that are similar to the current strain are closely related to it and thus facilitated for epidemiologists to track the evolution of the virus. Approximately 96% of the genetic material (genome) is present in bats (Ra13-TG-2013) (The Covid-19 epidemic 2020). It was later believed that a jump in the virus took place between the host species of bats or another intermediate animal before it was transmitted to humans (The Covid-19 epidemic 2020).

Symptoms of Covid-19 infection appear on most patients 2-14 days after exposure, these symptoms vary from one patient to another and in general, are fatigue, difficulty breathing, dry cough in addition to fever (Glover and Bowen 2004, Cheng *et al*. 2020). Death rate is 6.4% of those infected (Vilibic-Cavlek *et al.* 2020, Zhou *et al.* 2020). The infection of Covid-19 to the lungs and causing acute respiratory distress does not mean that other organs such as the liver, digestive system, heart and central nervous system are not at risk, so all health institutions entered a state of alert, including institutions specialized in kidney diseases (Chen *et al.* 2020, Dawei Wang *et al.* 2020, Huang *et al.* 2020). The increase in coagulation activity often appears in people with Covid-19, especially in acute cases. These in turn, leads to the consumption of clotting factors and as a result diffuse microvascular thrombosis. On hypoxia, this process also helps blood clotting (Tang *et al.* 2020).

While the world is waiting for appropriate anti-coronavirus treatment, Lopinavir / Ritonavir was approved for use as a protease inhibitor in the treatment of HIV (Dong and Gao 2020). It was also used during outbreaks of MERS virus infection as an inhibitor in laboratory and animal models (De Wilde *et al.* 2014). Lopinavir is given in combination with Ritonavir, as the latter increases the half-life of Lopinavir in plasma. P450 (Lu 2020) However, Chinese experiences did not support that there is an improvement in the clinical condition of the patient or saved from death (Chan *et al.* 2015).

1.1 Objectives of the Study

Clinical laboratories have the most prominent role in detecting the Covid-19 virus and continuous follow-up and epidemiological monitoring of patients by determining the values of their serum markers (Sandberg *et al.* 2015). The importance of knowing the values of these signs and ensuring their validity lies in supporting the doctor's decision-making at the right time to control the infection and detect cases that do not show symptoms of infection, and therefore it is easy to isolate infected cases and take the decision to treat them as soon as possible to reduce infection and disease outbreaks (Kubina and Dziedzic 2020).

The values of many laboratory markers have a distinctive role in evaluating the disease and knowing the severity of the infection. They predict the progression of the patient's condition towards more serious diseases, for example, the condition in Covid-19 infections may develop into acute respiratory distress (SRDS), disseminated intravascular coagulation (DIC) (Lippi *et al.* 2020).

There are signs by which a non-fatal course of the disease can be described such as hypoalbuminemia, thrombocytopenia, elevated liver enzymes, absolute neutrophils, creatinine and nonspecific inflammatory markers such as interleukin 6 (IL6). And C-reactive protein (CRP) (Ramírez-Truque and Herrera-Morice 2021). With all the previous parameters, hyper (D-dimer), lymphopenia, and hyperlipidemia should not be neglected, and LDH levels should be monitored in the list of markers (Letelier *et al.* 2021).

2. LITERATURE REVIEW

2.1 Coronavirus Definition

Coronavirus can be defined as one of the RNA viruses, and these viruses are very diverse and closed, and they are also single chained (Zumla *et al.* 2016). One of the most striking things is the decrease in the annual respiratory infection rate after the outbreak of the pandemic. The SARS virus, which infected 8000 people in the world, caused the death of 800 of them, at a rate of 10%. Also, the MERS virus infected 857 officially registered cases, and caused the death of 334 of those infected, meaning that the death rate was 35% (Gretebeck and Subbarao 2015, Drosten *et al.* 2003). Covid-19 is the seventh in the family of coronaviruses. Among the main symptoms that appeared on Covid-19 patients are fatigue, fever and cough, which are common symptoms between SARS, MARS and Covid-19 (Jia Liu *et al.* 2020).

2.2 Structure of Coronavirus

The shape of the Coronavirus is circular, and its surface contains protrusions of glycoproteins that help the virus to adhere to cells of the human body (Hofmann and Pöhlmann 2004), viral assembly (Vennema *et al.* 1996), morphology and release of virus particles and the envelope are what facilitate viral replication and transcription (Gao *et al.* 2020, Snijder *et al.* 2016). Membrane (M), the envelope (E) and glycoprotein (S), all together form structural proteins, which are attached to the envelope. Protein (S) is a membrane protein that resembles cloves, type-1. The S protein has three parts, a large outer part, a central part that is a single-pass transmission membrane, and a tail inside the viral cell. The first and most important step in viral infection is the recognition of host cell receptors by RBDs, where binding interactions occur between the coronavirus and its host receptor (Wentworth and Holmes 2001). For a more accurate look at the shape of the virus, see Figure 2.1.

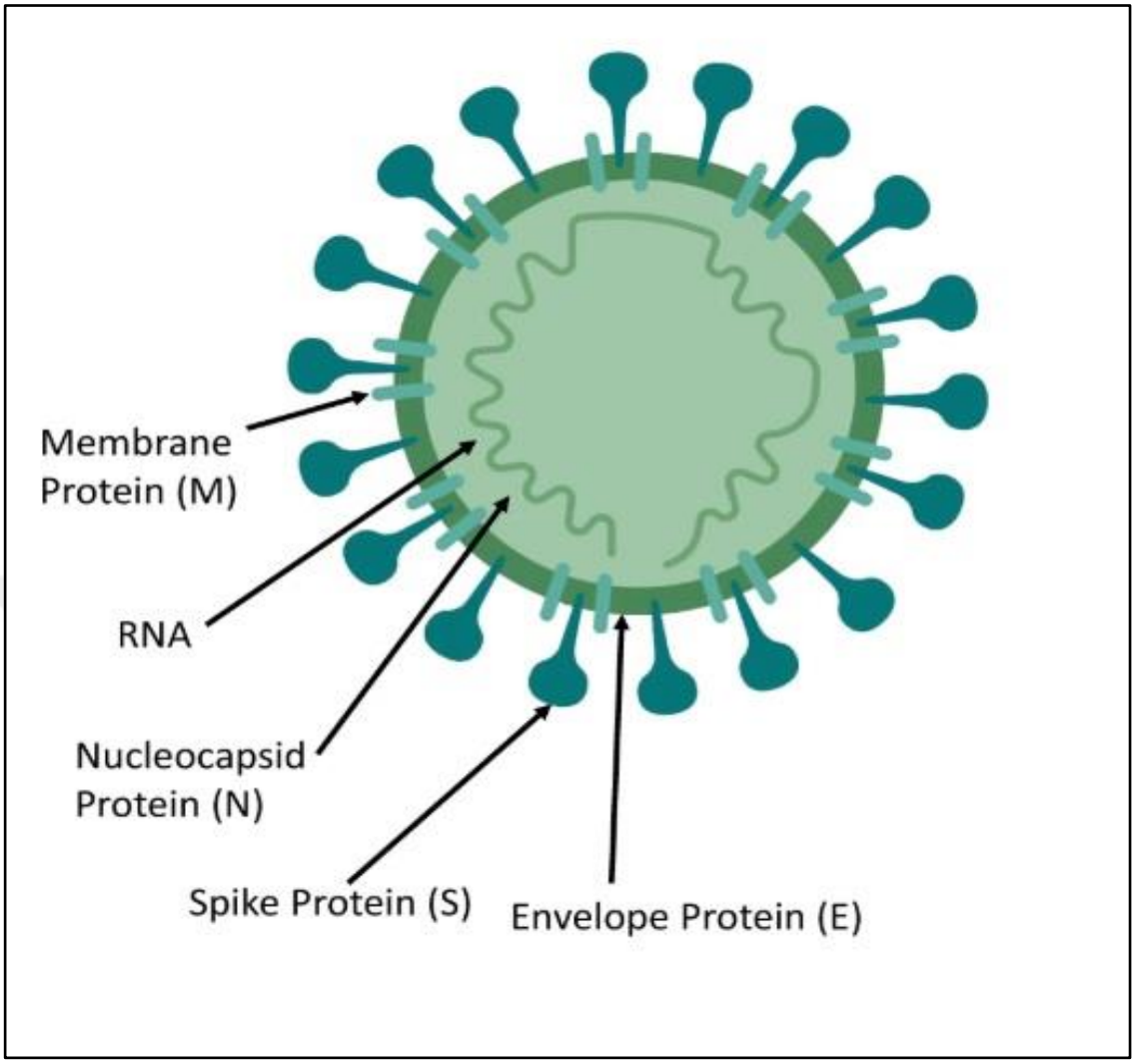

Figure 2.1 The approximate shape of the Corona virus (Seah *et al.* 2020)

To know the mechanism of entry of the Coronavirus into the human cell, it is necessary to identify the receptors that are one of the most important determinants of infection with the coronavirus, and it is also one of the most important targets of the immune surveillance of the host and the body's defense mechanisms. SARS-COV-2 RBD has a higher binding affinity for hACE2 compared to SARS-COV. These conclusions have been substantiated by mutagenesis and skeletal analyzes (Shang *et al.* 2020). To understand the mechanism of entry of the Coronavirus into the human cell, see Figure 2.2.

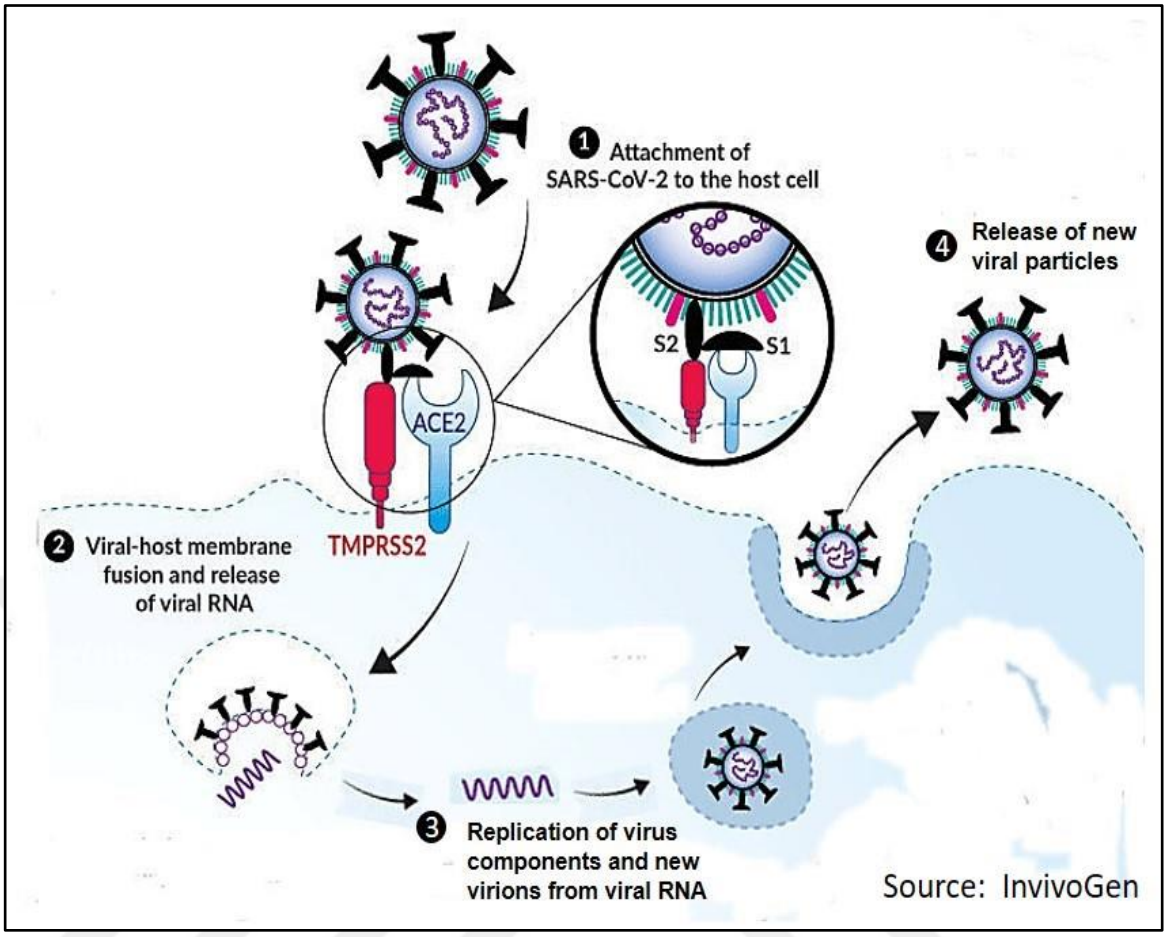

Figure 2.2 The mechanism of entry of the virus into the cell (Muriana *et al.* 2020)

2.3 Epidemiological

Covid-19 is the most important disease that occupied all over the world since 2019 until this moment and before that the SARS virus disease. The main routine tests of interest to patients with Covid-19 are the complete blood count (CBC), and coagulation. Assays (PT, APPT, creatinine, blood urea, LDH, ferritin, and D-dimers), and parameters related to inflammation (ESR, CRP). Due to the virus's ability to cause severe damage to many vital organs such as the heart, liver, and kidneys, analysis of biochemical parameters is one of the most effective means for physicians to assess the functional activity of these organs. Lymphopenia occurs in 70 to 83 %of infected patients upon admission to the hospital ward (Zhou *et al.* 2020, Guan *et al.* 2020).

Disease, lymphatic deterioration, and elevated plasma inflammatory cytokine levels are associated with disease severity and eventual death (Dawei *et al.* 2020, Qin *et al.* 2020). Suggesting a pro-inflammatory response or a condition called in the literature, the cytokine cyclone, this may also play a role in disease progression and severity, as shown in SARS and MERS (Channappanavar and Perlman 2017). Therefore, it is important to know the details of what happens when infected. Presence of SARS-CoV-2 viral RNA in the patient's blood, together with acutely elevated plasma interleukin 6 (IL6) levels as well as other biomarkers along with D-related coagulopathy and disseminated intravascular coagulation DIC, have a strong association with medical severity and mortality (Chen *et al.* 2020, Henry *et al.* 2020).

The most prominent challenge, and perhaps considered the main one, is the lack of awareness of positive cases (Cheng *et al.* 2007). Similar studies concluded that C-reactive protein was associated with disease progression and predicted early acute Covid-19 disease because the viral infection was accompanied by inflammation that led to protein secretion (Zhang *et al.* 2020, Bohn *et al.* 2020, Xu *et al.* 2020). Another important indicator is ferritin, which was higher in the severe group than in the other groups. Given the mounting evidence in the literature about ferritin as an early marker of severity in Covid-19 patients (Huang *et al.* 2015, Van den Brand *et al.* 2014).

2.4 Transmission

Droplets can carry the Coronavirus from an infected person to a healthy person, as many studies have proven this, and that flying droplets through exhalation, speech, coughing and sneezing can transmit the virus for a distance of more than a meter and a half (Morawska *et al.* 2009, Lindsley *et al.* 2015), and that is at indoor airspeeds (Matthews *et al.* 1989). Where a drop of 5 μm can move for several meters, may exceed ten meters, and settle from a height of 1.4 meters to the ground, and this has been proven in epidemic diseases SARS-COV- 1 (Yu *et al.* 2004). Studies have also shown that the MARS-CoV-1 virus is also transmissible in the same way through exhalation and others (Yan *et al.* 2018). What was revealed is that the small droplets of 5 μm size bind the viral RNA while they are in the air after being released through exhalation and

coughing (Liu *et al.* 2020). Among the most important guidelines that international studies and bodies focus on is social distancing, washing hands well, and not being exposed to the droplets and coughs of patients (Organization 2020). These prevention methods are good, but they are not sufficient, especially in enclosed spaces where there is little ventilation (Somsen *et al.* 2020), as shown in Figure 2.3.

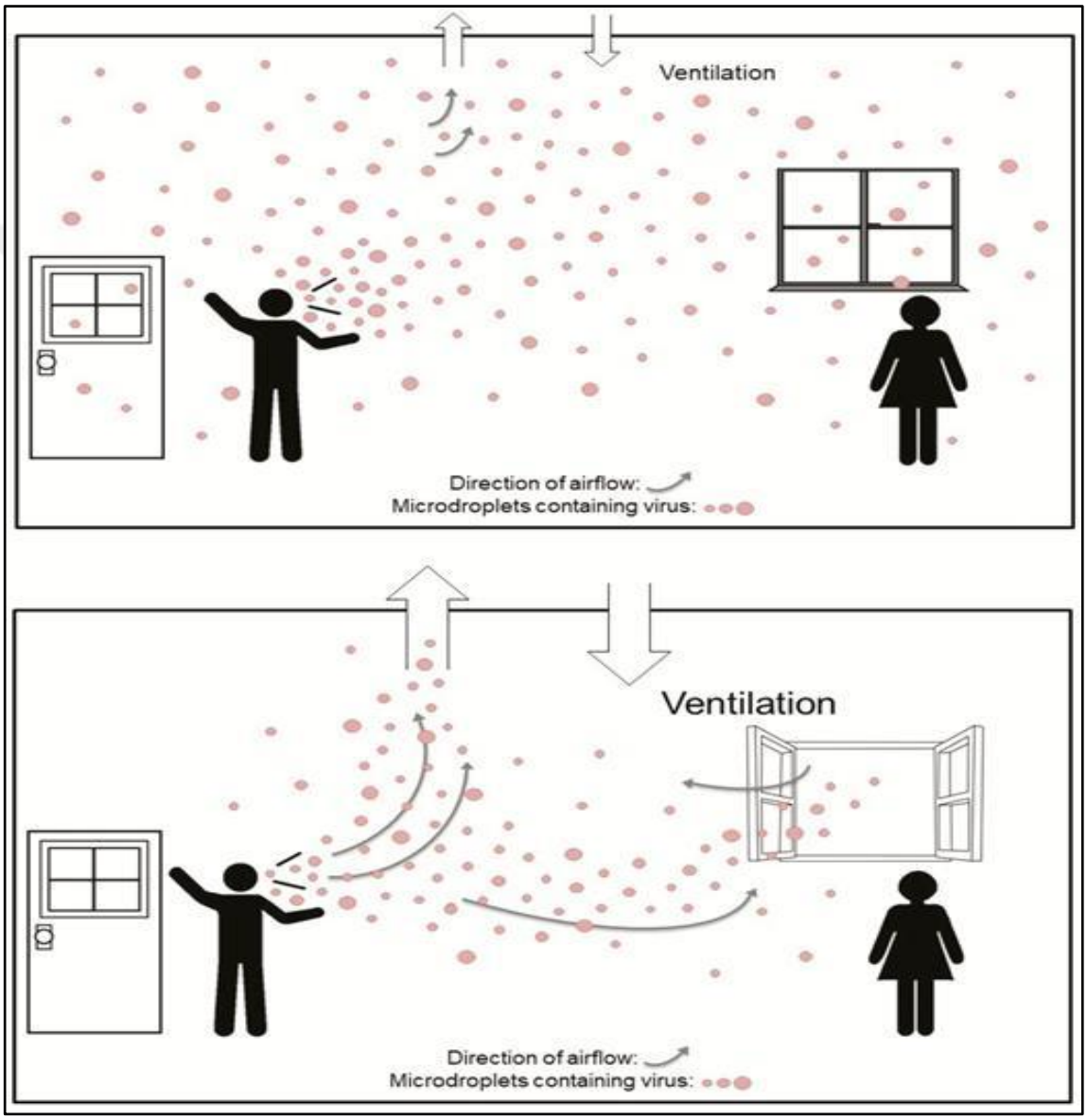

Figure 2.3 Distribution of respiratory microdroplets in an indoor environment with (A) inadequate ventilation and (B) adequate ventilation (Lidia *et al.* 2020)

2.5 Symptoms of Infection

One of the most significant symptoms seen in patients with Covid-19 is bilateral vitreous opacity on computed tomography. The most prominent symptoms associated with the disease are cough (76%), muscle pain (44%), fever more than (95%), and headache (8%), shortness of breath (55%), diarrhoea (3%), and hemoptysis (5%). There is also a case of one patient who did not have a fever at the beginning of the infection (Chen *et al.* 2020). Studies have also confirmed the presence of chest pain, pain in the pharynx, swollen tonsils, enlarged lymph nodes, loss of appetite, heart palpitations, runny nose, sore throat and dizziness (Chen *et al.* 2020, Liu *et al.* 2020). About children's injuries, the detection of disease factors improved with the increase in diagnosed cases, so reports of their infection began to rise (Duan Wang *et al*. 2020, Sun *et al*. 2020, Dong *et al*. 2020, Xia *et al*. 2020, Li *et al*. 2020).

2.6 Treatment

There is no effective treatment for Covid-19 patients, but there are measures that can be taken to support the infected, including treatment of fluid deficiency, hypoxia and mechanical ventilation (Jin *et al*. 2020). The immune response to the virus lies in the accompanying viral infection with fatal pneumonia, so one of the most important measures to be taken is to treat the infection The concomitant infection is taken from the experiments conducted on SARS patients (Sibila 2008). Corticosteroid treatment did not improve the condition of patients in SARS and MERS, so the recommendations of the WHO were not to give systemic Corticosteroid to patients with Covid-19 (Organization 2020). Despite the recommendations of the WHO Association, the association of chest diseases in China recommended the use of Corticosteroid (Zhao *et al*. 2020).

Also, Lopinavir/ritonavir (protein enzyme inhibitors) and interferon alfa (an antiviral agent) were also used in all patients with Covid-19 by inhalation, this method was used in the treatment of patients with MERS previously, has also been used umifenovir, which inhibits viral endocytosis and viral replication, has been used, and this treatment

is licensed in Russia and China for the treatment and prevention of influenza (Haviernik *et al*. 2018). After the outbreak of the pandemic, the US Food and Drug Administration approved the treatment of people with Covid-19 with plasma from those who recovered from the disease (the convalescent period) (Joyner *et al*. 2020).

2.7 Prevention and Control

Corona Virus 2019 is a new disease, studies indicate that it was previously transmitted between animals, but it is currently transmitted from animals to humans. The outbreak of this disease among humans is the latest epidemic that has developed into a pandemic, so the necessary measures must be taken to prevent infection. An outbreak of the disease among hospital staff, as some hospitals became receiving patients from their employees, as is the case in hospitals in Wuhan, China, to prevent transmission of infection to the medical staff, hospital entrances were divided into special places for patients and other places for the medical staff. Full of protective gloves and filter masks. The ability to organize patients according to priorities and direct them to specific places and according to specialization also had a role in limiting the spread of disease among the medical staff as patients with fever were directed to the fever hall, and others were directed to other departments for diagnosis and treatment. The wearing of gloves by staff working in hospitals when touching body fluids, secretions, excreta, blood, vomit and things that may be contaminated by patients, and washing hands well after removing gloves. One of the important things taken in hospitals is to reduce aerosols by isolating the air and wearing protective masks and medical glasses (Cai *et al*. 2020).

Complete closure and social isolation had the greatest role in preventing the spread and reducing the number of infections. Avoiding exposure to the patient's secretions, coughing and sneezing are some of the most important means of control and prevention (staying away from patients or those we suspect of being infected, a distance of not less than a meter as a safety distance) (Tomar and Gupta 2020).

2.8 Vaccination

To limit the spread of the Coronavirus infection, the vaccine must be taken according to the recommended doses, especially after authorizing its use by the World Health Organization (Organization 2020) and the US Food and Drug Administration (Krause *et al*. 2020). Among the most important groups in society and those who have priority in vaccination are medical and health personnel, especially workers in health isolation halls, because of the high probability of injury. It is necessary to start with the advanced age groups 65 and over and those who suffer from previous diseases such as high blood pressure and diabetes because they are two to four times more likely to be infected than healthy people (Wang *et al*. 2020). Exposure of elderly people to infection can expose them to death (Stokes *et al*. 2020, Kim *et al*. 2021).

Several studies have been published showing the effectiveness of the vaccine in Italy and others (Fabiani *et al*. 2021), where these studies confirmed that the recipients of the vaccine for the first dose from 14-21 days and seven days for the second dose, the safety rate from infection with Covid-19 were 84% and 95%, respectively (Fabiani *et al*. 2021). The effect of vaccination with the Pfizer and AstraZeneca vaccines for the first dose is 80% protection from hospitalization, and the Pfizer vaccine prevented patients from deteriorating their condition and reaching death by 85%, this was confirmed by Lopez-Bernal *et al* (Bernal *et al*. 2021).

2.9 Determination Du to Covid-19 Infection

2.9.1 Hematological determination

Coagulation system determination: Changes in coagulation parameters have also been observed. Following the publication of Tang that suggested a vascular component for SARS-CoV-2 patients, we examined the parameters of hemostasis. Classic signs of DIC (disseminated intravascular coagulation) are platelet count, fibrinogen concentration, D-dimer concentration, prothrombin time and activated partial

thromboplastin time (Cui et al. 2020). As a consequence, not a small fraction of stable patients with sudden death, we should consider acute organs, embolism and infarction. Although the incidence of thrombosis has not been determined in Covid-19 patients (Park et al. 2020).

Blood clot formation has been found in histopathological studies based on autopsy or biopsies, which are very similar to those seen in SARS infection and MERS (Jin et al. 2020). However, conventional anticoagulants must be carefully considered, as the risk of bleeding may be increased in patients with Covid-19 (Mao et al. 2020). Biomarkers, which can identify clot formation in its early stages, can be used to assess formation and response to treatment. D-dimers are fibrinolytic products that are useful in the clinical decision base for the prevention of pulmonary embolism (Simon et al. 2006). In a number of studies comparing D-dimer levels of Covid-19 patients with levels of bacterial pneumonia and using consecutive D-dimer levels after hospitalization and demonstrating their association with markers of inflammation, this explains why Covid-19 patient parameters such as fibrinogen are elevated (Han et al. 2020).

WBC determination: The patient's white blood cells are measured with a blood test called a complete blood count (CBC). If the patient's white blood cell count is higher than normal, this may be an indication of infection or inflammation. A low white blood cell count also indicates a problem with the patient's immune system. This is a common problem in people who have cancer or who take certain medications that suppress the immune system.

Typical reference ranges for a WBC number are (UCSF Health WBC count).

- Low: Less than 4,500 WBCs/μ L.
- Normal: 4,500 to 11,000 WBCs per microliter.
- High: more than 11,000 white blood cells per microliter.

A high white blood cell count, also called an elevated white blood cell count, is usually a significant sign of the body's resistance to infection, and this same rule applies to Covid-19. Research has shown that people with Covid-19 who do not develop symptoms often have a significantly elevated number of white blood cells (Han et al. 2020).

Lymphocytes: Lymphocytes are scattered throughout the human body, and they produce antibodies, and proteins that are released to fight the causes and pathogens of diseases, and thus they help the immune system, which plays its role in fighting infection. The role of B cells is to attack invading viruses and bacteria, while T cells destroy cells damaged by things like viruses or cancer (Jingyuan et al. 2020). The elevated lymphocyte level observed in asymptomatic people with Covid-19 makes sense. This is clear evidence that their immune systems are doing a good job of keeping the coronavirus in check by creating antibodies and thus destroying damaged cells (Han et al. 2020).

Neutrophils: Neutrophils are immune cells available in large numbers in human blood, as they account for 50-70% of white blood cells. The first to respond in case the body is exposed to infection are neutrophils, in addition to their participation in any chronic infections (Soehnlein et al. 2017). In the case of viral infection, although it has a protective role in fungal and bacterial infections (Tomar et al. 2020, Galani and Andreakos 2015). There is no clear evidence for the action of these cells, but it has been suggested that they enhance antiviral defences and this is done through their interaction with other immune cells,this interaction leads to the release of cytokines, and their degradation, assimilating the attacking virus and triggering the oxidative explosion (Galani and Andreakos 2015, Naumenko et al. 2018).

There is a close association between lung diseases associated with acute psychological distress and neutropenia, as these cases were also reported in the SARS infection (Camp and Jonsson 2017). When infected with Covid-19, mobilization was observed. Polymorphic nuclei (PMN) of the immune response when infected with Covid-19, in

addition, neutrophils were among the most prominent indicators of a person's symptoms of Covid-19 infection (Wang et al. 2020, Singh et al. 2021, Guan et al. 2020).

RBC determination: Red blood cells are one of the types of blood cells, and they are the most numerous in the blood. Red cells are the main means for vertebrates to carry oxygen (O2) to all tissues of the body through blood flow in the circulatory system. Red blood cells take oxygen from the lungs through breathing and release it into the body's tissues during the passage of blood in the capillaries. It produces approximately 2.4 million new blood cells per second in adult humans (Sackmann 1995). The cells are produced in the bone marrow and continue to circulate for about 100-120 days in the body after which they are regenerated and their components circulated by macrophages (Li and Lykotrafitis 2014). The cycle takes approximately 60 seconds (1 minute). Red blood cells make up about 84% of the cells in the human body, numbering between 20 and 30 trillion red blood cells (Sender et al. 2016, Pierigè et al. 2008).

Silent hypoxia must have mechanisms and we must understand them to find out why some people with Covid-19 can lead their lives normally despite the lack of oxygen (Doctor et al. 2005). Some theories have been discussed to explain this silent hypoxia. To name a few, he suggested a reason for the silent hypoxia because the differential effect of O2 and CO2 on gas exchange might lead to the relative preservation of the ability of the lungs to excrete carbon dioxide despite the decrease in O2 levels. Because the body is better able to detect changes in carbon dioxide than O2, which leads to an increase in patients' breathing rate despite the presence of low levels of oxygen and as a result, the feeling of shortness of breath does not appear. The mechanism (s) that underlie the generation of NO within RBCs are not well clear. However, acidosis, hypoxia, and tissue hypoxia cause NO generation by RBCs (Singel and Stamler 2005, Ulker et al. 2013).

Platelets determination: One of the most important things that people with Covid-19 are exposed to is the complications that result from thrombosis, and it was found that there is a link between the decrease in the number of platelets and the progression of the disease (Amgalan and Othman 2020, Yang et al. 2020). Severe Covid-19 is also

associated with upregulation by antibodies to apoptosis in platelets, found a link between platelets and levels of D-dimers in plasma, which leads to thromboembolism and its complications, in people with Covid-19, especially severe cases. Apoptosis of platelets is an important factor in the persistence of inflammation and the increased risk of thrombosis, and this could be a potential therapeutic target. The programmed cell death that occurs due to infection with Covid-19 has not yet been identified (Uhlén et al. 2015). The SARS-CoV1 virus that caused the epidemic in 2003 was inducing apoptosis in Vero cells and this is a method that depends on the replication of the virus (Ren et al. 2005).

Severe cases of Covid-19 are associated with hypercoagulability and there is an inflammatory response that leads to thrombosis in Covid-19 patients and as a consequence to the micro thrombotic events (Bikdeli *et al*. 2020, Gu *et al*. 2020). This coordinated stimulation of the inflammatory and thrombotic response is termed coagulates, acute phase thrombotic levels including D-dimer and fibrinogen are elevated in Covid-19 patients (Libby and Lüscher 2020, Lowenstein and Solomon 2020).

2.10 Deterioration of Liver Enzyme

Abnormalities in liver function were frequently observed in Covid-19 patients, the most common abnormalities were hypoalbuminemia followed by elevations of gamma-glutamyl transferase, aminotransferase, bilirubin, and alkaline phosphatase. Furthermore, when comparing severe and non-severe Covid-19 cases, liver abnormalities such as hypoalbuminemia, GGT, transaminase elevation, and bilirubin were more likely in those with severe disease. However, the elevations of alkaline phosphatase in the blood of the sufferers were not significantly higher in the severe group. The pooled frequency of GOT and GPT elevations was similar in the overall Covid-19 cases, and interestingly the prevalence of GOT elevations was more than that of GPT in severe Covid disease. The most important finding in our meta-analysis is hypoalbuminemia. This is likely related to the fact that albumin is an acute phase negative reactant and is not indicative of hepatic dysfunction. A meta-analysis confirms that liver enzyme elevations in Covid-19, even in the severe Covid-19 category, are

mild to moderate in most cases. This does not mean that there have been few, reports of extremely elevated transaminases (>10 times the upper limit), as this phenomenon is uncommon (Nishikawara *et al*. 2006, O'Brien-Simpson *et al*. 2015).

Hepatic failure is extremely rare although there is only one case report available in a patient with severe Covid associated with his use of multiple drugs and the development of hepatic impairment after acceptance that the effect of the drugs is the effective factor in this case (Nishikawara *et al*. 2006). Most of the studies included in our analysis reported the use of several drugs such as antibiotics, antivirals (ritonavir, aribidol, remdesivir, hydroxychloroquine) and steroids. Several of these medications may have contributed to liver impairment after hospitalization. The increase that appeared to us is 6 times the risk of severe disease, and the increase that leads to the possibility of death was 16 times in patients who have been proven to have an increase in LDH in most of the cases. Studies reporting the death as an outcome have demonstrated elevated LDH levels in >95% of the deceased and <60% of the survivors. Severe infection causes tissue damage by cytokine leading to LDH release (Martinez-Outschoorn *et al*. 2011).

2.11 Effect Renal Function

Covid-19 has a history in people with chronic kidney disease. These patients have an inflammatory condition with some functional defects in innate and adaptive immune cells, (Betjes 2013) and have a higher risk of developing upper respiratory tract infection (Cohen-Hagai *et al*. 2016) and pneumonia (Sibbel *et al*. 2016). The patients with elevated serum creatinine levels were more likely to be admitted to the ICU and were admitted to mechanical ventilation, indicating that CKD on admission presents a greater risk of deterioration. Renal injury has previously been reported to be associated with an increased risk of death in patients with subtype A H1N1 and SARS (Chu *et al*. 2005, Jung *et al*. 2011). Therefore, renal function monitoring should be emphasized even in patients with mild respiratory symptoms, and special attention should be paid to altering renal function after they enter clinical practice to obtain an accurate and early diagnosis of the condition. This includes adequate circulatory support and avoidance of highly toxic drugs to the kidneys, thus improving the vital diagnosis of Covid-19. Acute

renal failure results from the sudden loss of renal function and is strongly associated with increased mortality and morbidity (Vanmassenhove *et al*. 2017).

The improve early detection in case of kidney injury, frequent measurements of serum creatinine should be performed in Covid-19 patients. The possibility that the aetiology of kidney disease in patients with Covid-19 is multiple. First, the novel coronavirus is likely to have direct cytopathic effects on the kidney tissue (through a direct effect on the tissue of this vital organ). This is supported by the detection of coronavirus fragments in the blood and urine in both SARS patients (Peiris *et al*. 2003), and recently Covid-19 patients (Huang *et al*. 2020). with SARS-COV receptors, as reported in the 2003 literature (Zhou *et al*. 2020).

RNA sequencing data taken from modern human tissues showed that the expression of ES2 in urinary organs (kidneys) was 100 times higher than in respiratory organs (lungs) (Wang *et al*. 2020). Therefore, the cause of kidney disease may be the entry of MERS-COV into kidney cells via an ACE2-dependent pathway. Second, the deposition of virus-antigen immune complexes or virus-induced specific immune mechanisms (lymphocyte or specific antibody) (T cell) to kidney damage. However, microscopic samples of kidneys from SARS patients have been reported to show the normal aspect of the glomeruli and the absence of electron-dense deposits (Chu *et al*. 2005).

2.12 Blood Urea and Creatinine

Several studies have shown that (BUN, Scar) are one of the most important risk factors that lead to the development of the disease in patients with Covid-19 (Cheng *et al*. 2020). Rated these indicators in patients with Covid-19 because they are useful for clinicians to monitor kidney function. Currently, most doctors have relied on the definition of acute renal failure by the recommendations issued by the Kidney Disease Diagnosis Improvement Organization around the world (KDIGO) on the following, that is, if one of the following conditions is met:

(1) The increase in creatinine is greater than or equal to 0. 3 mg/dL within 48 hours.
(2) The increase in creatinine by an amount greater than or equal to 1.5 times the baseline during the previous seven days.
(3) The volume of urine if it is 0.5 mL/ kg/ hour and for 6 hours (Khwaja 2012).

2.13 Inflammatory Markers determination

2.13.1 ESR

The indicators used routinely to detect inflammation, including ESR, show a moderate increase in their rates during viral infection, it has been proven that the host inflammatory response in the event of infection with COVID-19 is very broad, as this response leads to a cellular storm that disrupts a large number of body organs (Ng *et al*. 2020). The ESR test is considered the least specific test for the inflammatory state because it is affected by other pathophysiological conditions, meaning that it is not useful for a specific clinical case (Xu *et al*. 2020). ESR is closely related to the shape, size, and concentration of red blood cells in addition to the characteristics of the plasma (Ramsay and Lerman 2015). High ESR continuously causes joint damage, and this damage causes joint diseases and as a result, leads to osteoporosis (Hanada *et al*. 2016, Atzeni *et al*. 2017).

2.13.2 C-RP

One of the most important tests for distinguishing inflammation if it is a bacteria or a virus is the C-reactive protein test, which is more useful and sensitive than the erythrocyte sedimentation rate, as the C-reactive protein test is a typical test that is increasingly expressed in cases of infection and associated inflammation (Pepys and Hirschfield 2003, Yao 2019). The CRP test is called acute-phase protein, and its elevation, in addition to inflammation, indicates tissue damage (Pepys and Hirschfield 2003). Studies by Lee and others on COVID-19 patients have confirmed that elevated CRP is an indicator of COVID-19 infection (Li *et al*. 2020). CRP enhances

phagocytosis by specific CRP receptors and this process removes disease-causing microorganisms in pneumonia caused by infection with COVID-19 as it does not rule out the initiation of a process called cytokine storm (CRS) and this process is directly related to the mortality rate of COVID-19 patients (Azar *et al*. 2020). Studies have shown that C-reactive protein is continuously increased in non-survivors until their death while it stabilizes and declines in survivors (Chen *et al*. 2020).

2.13.3 IL - 6

Cases of COVID-19 infection were divided into several sections, some of them are mild, and those with whom do not show any symptoms, including moderate ones, which are characterized by dry cough, fever, muscular weakness and fatigue, including moderate ones. As for severe cases, acute respiratory distress appears, and their condition may deteriorate to the failure of some organs (Bai *et al*. 2020, Xu *et al*. 2020). Their critical injury is closely related to the so-called inflammatory cytokine storm (Chen *et al*. 2020, Zumla *et al*. 2020). This cytokine storm is characterized by a high plasma concentration of the level of interleukin 6 (IL-6). A careful study of the patients showed that the groups classified as severe cases had a higher level of (IL-6) than the average group (Chen *et al*. 2020, Cai 2020, Wan *et al*. 2020). What characterizes the cytokine storm and what has considered a driving force for it is the excessive rise of (IL-6). This rise is very dangerous for those infected with COVID-19 and has serious diseases that are difficult to treat (Zumla *et al*. 2020).

3. MATERIALS AND METHODS

3.1 Materials

3.1.1 Design of study

(150) patients whose ages ranged between (25-101 years) were selected after obtaining their consent. These cases range from mild, moderate, and critical injuries, and (50)samples from people without the disease for the purpose of comparison, as described in the section below. This study was conducted in Jalawla General Hospital, specifically in the epidemiological hall for the tests available in the hospital, and laboratory work was conducted in its laboratories in the clinical biochemistry department, and the rest of the advanced tests were conducted in a specialized laboratory after samples were withdrawn from patients, separated, frozen and transported refrigerated to the laboratory in Diyala - Iraq. The study lasted for 3 months, from March 1, 2022 to June 1, 2022.

3.1.2 Hardware and tools

1. CBC ERBA.
2. Mini vidas.
3. Cobas.
4. Centrifuge.
5. Micropipette.
6. Tips.
7. Syringe 10 cc.
8. Gel tube.
9. EDTA tube.
10. Sodium citrate tube.

3.1.3 Sample collection

Based on the reports of the pulmonologist, the patients were diagnosed and the types of samples were determined, 10 ml of venous blood was drawn for each patient in several types of tubes (Gel tube, EDTE tube, Sodium citrate tube). Blood samples were allowed to coagulate relative to samples in Gel Tube for 15 min on a rack at room temperature before centrifuged for 10 minutes 3500 rpm. Then the serum was isolated from the rest of the cells. The serum was withdrawn using a small pipette and then frozen on a plain tube inside the freezer.

3.2 Methods

3.2.1 ESR

Clinical laboratories play the most prominent role in detecting many diseases, including the Covid-19 virus, continuous follow-up and epidemiological monitoring of infected patients, or assisting in early detection of infection by determining the values of their serum markers. The importance of knowing the values of chemical parameters and verifying their validity and whether they are within the normal level or within the level of the control group lies in supporting the doctor's decision-making in a timely manner to control the infection and discover cases in sick people who do not show symptoms of infection, and therefore as a result of these procedures it is easy to isolate infected cases and their treatment and effective contribution to the early treatment of the disease.

3.2.2 Random blood sugar (RBS) test

The test that determines the amount of sugar in blood samples is the random blood sugar assay, this test detects the quantity of glucose in samples, the blood sugar chart provides descriptions of blood sugar values in terms of mg/dL, it has been collected about 3-5 mL blood in a red top tube at any time of the day, then it were centrifuged in the tube for 2 minutes and use the serum for test and finally record the result.

3.2.3 Complete blood count (CBC)

Complete blood count was checked to assess hemoglobin (Hb) levels and white blood cells (WBC) and blood count platelets. Blood samples were analyzed within a few minutes using (ERBA560)

Add the blood sample to a vial containing EDTA. Put the vial in the rotate shaker for 3-5 minutes. After the rotate time is finished take the blood sample and entered in a complete blood count machine(ERBA560) The machine will read the blood sample through a few minutes, the results of Hb and WBC were appeared in a machine.

3.2.4 Chronic diseases

Diseases that old for a long time are called a chronic diseases, it included heart disease, diabetes, high blood pressure, cancer and asthma. In this study, it has been chosen a sample of a patients and then, ask them if they have a chronic disease, record the information about the history of the disease and another information such as patient age, sex and the patient's condition.

3.2.5 Body mass index (BMI) (kg/m^2)

To measure the body mass index should be calculated body fat based on the weight in kilogram and height in cm of the adult male or female and calculate the body mass index (BMI) using Equation (3.1).

$$\text{Body mass index } (kg/m^2) = \text{Weight in kilogram/ Height in } cm^2 \quad (3.1)$$

3.2.6 CRP test

Reagent composition; R1: Diluent / Tris buffer 20 mmol / L; R2: Latex / Latex particles coated with goat anti – human CRP; CAL: Calibrator / Human serum.

Procedure: Prewarm the cuvette holder of the photometer and the reagent to 37 °C, utilizing distilled water zero the machine at 540 nm. Pipette into a cuvette 15 µL of sample or calibrator or blank and 1 mL of reagent, mix and insert the cuvette into the instrument and record the absorbance after five minutes of calibrator or sample addition.

Calculation: Calculate the absorbance difference of each point of the calibration curve and select the values obtained against the CRP concentration of each calibrator dilution. Calculate the CRP concentration in the sample by application its absorbance differences (A5-Ablank) in the calibration curve.

3.2.7 Ferritin test

Procedure: Install the photometer at 650 nm by using distilled water then pipette into the a cuvette 0.8 mL of R1 diluent, 100 µL of the sample or blank and 0.2 mL of R2 latex, mix well and read the absorbance (A1) and after 8 minutes of the reagent addition.

Reagent composition

R1: Diluent / Glycine buffer 20 mmol/ L; **R2:** Latex/ latex particles coated with polyclonal anti-human ferritin antibodies; **CAL:** Calibrator / Human ferritin.

3.2.8 D-Dimer test

Principle: Agglutination the particles of the latex coated with monoclonal anti D-Dimer antibody when they react with plasma sample that contain D-Dimer. The particles of latex agglutination is proportional to the D-Dimer concentration in the sample.

Reagent composition

R1: Diluent / Borate buffer 0.1 mol / L; **R2:** Latex / Latex particles coated with monoclonal antibody anti D-Dimer; **CAL:** Calibrator / Lyophilized solution of highly purified human D-Dimer contains bovine, albumin, stabilizers, and preservative.

Procedure: Install the instrument to 405 nm then pipette into the cuvette, 800 µL of R1 diluent, 25 µL of sample or calibrator or blank and 100 µL of R2 latex, mix well and read the absorbance (A1) and after 2 minutes.

3.2.9 Partial thromboplastin time (PTT) test

Principle: The blood capacity for formation the fibrin clot by hemostatic pathway included coagulation the factors: I, II, V, VIII, IX, X, XI, and XII, calcium and platelet lipids. The examination is accomplished by the addition of a suspension in the sample of rabbit brain cephaline with a surface activator, the PTT has evidenced to be a simple measurement of the coagulation mechanism.

Reagent composition

PTT: Rabbit brain cephaline and ellagic acid activator with buffer. Stabilizers and preservatives.

Procedure: Incubate calcium chloride to 37 °C for 10 minutes. Pipette 50 µL of sample or control plasma into a cuvette then incubate for 3 minutes at 37°C. Add 50 µL of PTT reagent to the cuvette, incubate at 37 °C for 3 minutes. Add 50 µL of calcium chloride and then record the clotting time in seconds.

Calculations: Calculate the mean of clotting time of duplicate, samples, controls, and observed the clotting time in seconds. PTT = PTT of the patient in seconds/ PTT of the normal plasma in seconds

3.2.10 GTT test

Principle: Gamma-glutamyltransferase catalyzed the transfer of glutamyl group from Y-glutamyl-3-carboxy-4-nitroanilide to glycylglycine to form L- Y- glutamyl-glycylglycine and 5-amino-2-nitro-benzole. The 5-amino-2-nitro-benzole amount formed, observed kinetically at 405 nm is proportional to the enzyme activity present in the sample.

Reagent composition

R1: Buffer / Glycylglycine. Tris 133 mmol / L. Glycylglycine 138 mmol / L; **R2:** Substrate / Glupa- C, L-Y- Glutamyl-3-carboxy-4- nitroanilide.

Procedure: Incubate all the reagent, sample and controls to 2-8 °C, install the instrument to zero absorbance with distilled water. Pipette into the cuvette 1 mL of the reagent with 100 µL of the sample, mix then insert the cuvette into the cell holder. Incubate for 60 seconds and record the initial absorbance reading, this step after 1, 2, and 3 minutes, calculate. The differences between absorbance, Calculate the results mean to compute the absorbance average per minutes. For the calculations, it can use the Equation (3.2) and Equation (3.3).

$$U / L = \Delta A / Min \times 1111 \quad (3.2)$$

$$U / L \times 16.67 = n\ Kat / L \quad (3.3)$$

3.2.11 Interleukin -6 (IL-6) test

We use the Interleukin -6 (IL-6) determination kit to calculation the IL-6 concentration as below.

Insert the IC card into analyzer machine and read the card, add 50 µL of sample to the buffer tube and mix well. Get 80 µL of sample and add to the cassette and then insert that into the incubator for 15 minutes. Insert the cassette into the analyzer and click

"Test", the results will display on screen and the results will printed automatically, then print the results.

3.2.12 Urea test

The enzyme urea is hydrolyzed urea to form ammonia and carbon dioxide, the ammonia is transformed to glutamate by glutamate dehydrogenase. For determine the urea levels, it can use Equation (3.4) and Equation (3.5).

$$\text{Urea} + H_2O \xrightarrow{\text{Urease}} 2\,NH_4^+ + CO_2 \qquad (3.4)$$

$$2\text{- Oxoglutamate} + NH_4^+ + 2\,\text{NADH} \xrightarrow{\text{Glutamate dehydrogenase}} \text{Glutamate} + 2\text{NAD} + 2H_2O \qquad (3.5)$$

Reagent compositions

R1: Buffered urease /* Tris buffer 125 mmol / L, 2- oxoglutarate 10 mmol / L, urease > 140 U /L, glutamate dehydrogenase > 120 U / L; **R2:** Coenzyme / NADH 1.5 mmol / L.

Procedure: Mix 1 mL of reagent with 10 µL of sample or standard then insert the cuvette into the holder, record the absorbance at 340 nm after 30 seconds (A1) and after 90 seconds (A2). For the calculations urea levels, Equation (3.6) can be apply.

$$\text{Urea (mg/dL)} = (A1\text{-}A2)_{\text{sample}} / (A1\text{-}A2)_{\text{standard}} \times C_{\text{standard}} \qquad (3.6)$$

3.2.13 Low density lipoprotein (LDL) cholesterol test

Principle: This technique based on precipitation of low density lipoproteins by polyvinyl sulfate in serum, centrifuge the precipitant and test as residual cholesterol of the rest of VLDL and HDL remaining in the supernatant.

Reagent compositions

R1: Precipitation reagent / polyvinyl sulfate 170 g / L; **CAL:** LDL cholesterol standard / Cholesterol 50 mg / L.

Procedure: Put all the reagents and samples at room temperature, add to labelled tube 0.2 mL of sample or standard with 0.1 mL of R1 reagent and vortex for 10 minutes at 25 °C then centrifuge for 2 minutes at 12000 rpm then remove an aliquot of supernatant and measure the total cholesterol of the sample by prepare two series of tests and measured the remaining cholesterol in the supernatant. Putinto the R1 tube 1 mL of each labelled blank, sample and standard supernat then add50 µL of the sample supernat to the supernat tube, also put 50 µL of the standard supernat into the standard tube then read the absurbance at 500 nm. For the calculations LDL levels, it can be use Equation (3.7) and Equation (3.8).

$$\text{Cholesterol}_{\text{supernat}}\ (\text{mg/ dL}) = (A_{\text{supernatant}} / A_{\text{standard}}) \times C_{\text{standard}} \quad (3.7)$$

$$\text{LDL cholesterol (mg / dL)} = \text{Total cholesterol} - \text{cholesterol}_{\text{supernatant}} \quad (3.8)$$

3.2.14 Creatinine test

Principle: Under alkaline conditions, creatinine reacts with picrate ions to form reddish complex. The increase of absorbance can be measured through the complex formation in a prefixed interval of time is proportional to the creatinine concentration in the sample, it can use Equation (3.9) to determine creatinine levels.

$$\text{Creatinine} + \text{Picric acid} \xrightarrow{\text{pH} > 12/37^{\circ}\text{C}} \text{Red addition complex} \quad (3.9)$$

Reagent composition

R1: Picric acid 25 mmol / L; **R2:** Alkaline buffer / Phosphate buffer 300 mmol / L, SDS 2 g/L; **CAL:** Creatinine standard / Creatinine 2 mg / dL, organic matrix based primary standard.

Procedure: Set the spectrophotometer to zero absorbance then pipette into the cuvette 1 mL of working reagent and 100 µL of sample standard. Mix and insert the cuvette and record the absorbance at 510 nm after 30 second (A1) and after 90 second (A2) of the sample or standard addition, it can be use Equation (3.10) to determine the levels of creatinine in (mg/dL)

$$\text{Creatinine concentration (mg/ dL)} = \{(A1\text{-}A2)_{\text{sample}} / (A1\text{-}A2)_{\text{standard}}\} \times C_{\text{standard}} \quad (3.10)$$

3.2.15 GOT and GPT test

Principle: The transfer of the amino group from L-aspartate to oxoglutarate to form glutarate and oxaloacetate by the aspartate aminotransferase. Also the alanine aminotransferase catalyzes the moving of amino group from L- alanine to oxaglutarate to form glutarate and pyruvate. For the calculation GOT and GPT, it can use Equation (3.11) and Equation (3.12).

$$\text{L- Aspartate + 2-oxoglutarate} \xrightarrow{\text{GOT /pH 7.4}} \text{L- Glutarate + oxalacetate} \quad (3.11)$$

$$\text{L- Alanine + 2-oxoglutarate} \xrightarrow{\text{GPT / PH 7.4}} \text{Glutarate + pyruvate} \quad (3.12)$$

Reagent composition

R1a: GOT substrate / Phosphate buffer 100 mmol / L, L- aspartate 200 mmol / L, ketoglutarate 2 mmol / L; **R1b:** GPT substrate / Phosphate buffer 150 mmol / L, L-alanine 200 mmol / L, ketoglutarate 2mmol / L; **R2:** DNPH / 2,4-Dinitrophenyl hydrazine 1 mmol / L; **R3:** 4N NaOH / Sodium hydroxide 4 mol / L; **CAL:** Pyruvic acid 1.8 mmol / L, secondary standard.

Procedure: Pipette into the labeled tubes, 0.5 mL of blank and 0.5 mL of GOT into the GOT substrate tube, 0.5 mL of GPT into the GPT substrate tube, warm the tubes to 37 °C for 5 minutes into the bath then add 100 µL of GOT and 100 µL of GPT into the

serum tube, mix and return the tube to bath at 37 °C for 1 hour. Add 0.5 ml of blank, 0.5 mL of GOT and 0.5 mL of GPT into the DNPH tube, then mix and stand the tube at 25 °C for 20 minutes, add 5 mL of blank, 5 mL of GOT and 5 mL of GPT into the NaOH (0.4N) tube then mix and stand the tube for 5 minutes at 25 °C. Read the absorbance of the sample against the water blank. Read the GOT or GPT units from the corresponding curves of the absorbance.

4. RESULTS

4.1 The Results of Age and other Parameters

The results were in the study of the parameters mentioned in Table 4.1 and Figure 4.1 with the Covid-19 virus, Chronic Diseases (group A = 1.0000; group B = 1.5570), age (group A = 57.6400; group B = 64.5369), the patient´s condition (group A = 0.9200; group B = 1.8993), Infection (group A = 45.6692; group B = 2.0000), the results of these parameters indicated that there were significant statistically significant differences, which indicated that they were affected by Covid 19 at P = < 0.05. These results confirm its clinical usefulness in diagnosing the disease, especially at these ages.

While the rest of the parameters mentioned in Table 4.1 and Figure 4.1 indicate that there are no significant statistically significant differences for patients infected with Covid 19, and these results explain it that excess obesity has no strong relationship in infection or the development of patients.

Table 4.1 The mean of WCM, age, sex and other in patients with COVID-19

Group Statistics						
Test	**Groups**	**N**	**Mean**	**Std. Deviation**	**Std. Error Mean**	**P**
Chronic Diseases	Group A	50	1.0000	0.00000	0.00000	0.000
	Group B	149	1.5570	0.88059	0.07214	0.000
WCM	Group A	50	93.3800	7.49936	1.0605	0.821
	Group B	149	93.6107	5.74069	0.47030	0.843
BMI	Group A	50	26.5176	2.81328	0.39786	0.586
	Group B	149	26.2281	3.38270	0.27712	0.552
Age	Group A	50	57.6400	18.57995	2.6276	0.017
	Group B	149	64.5369	17.06527	1.3980	0.023
Sex	Group A	50	1.3200	0.47121	0.06664	0.235
	Group B	149	1.2349	0.42537	0.03485	0.261
SPO_2	Group A	50	70.0600	14.26629	2.0175	0.273
	Group B	149	67.4564	14.58455	1.1948	0.270
The patient´s condition	Group A	50	0.9200	0.14515	0.02053	0.000
	Group B	149	1.8993	0.30191	0.02473	0.000
Infection	Group A	50	45.6692	51.60338	7.2978	0.000
	Group B	149	2.0000	0.82199	0.06734	0.000

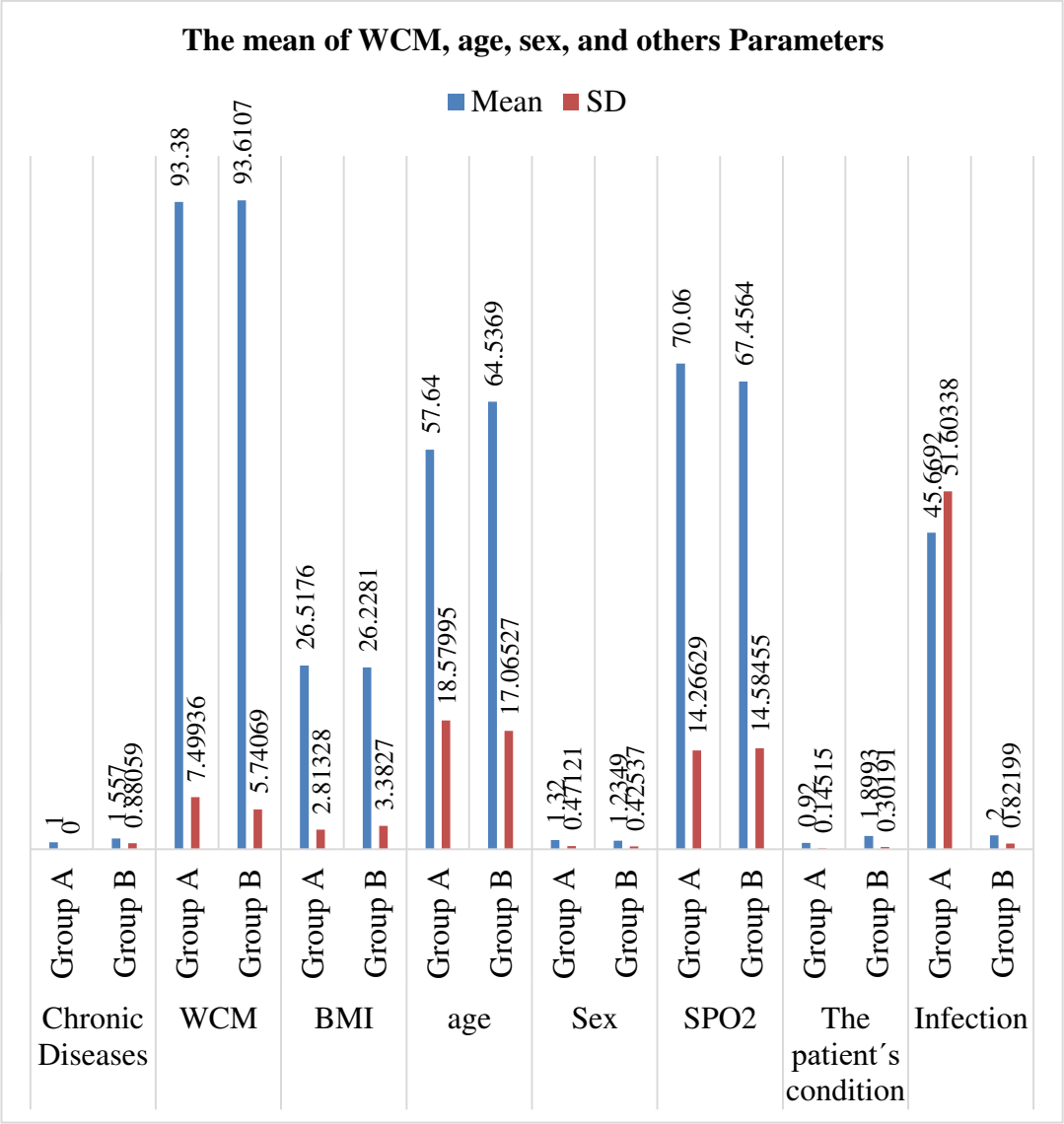

Figure 4.1 The mean of WCM, age, sex and other in patients with COVID-19

In the improved independent t-test for CD, WCM, BMI, age, Sex, SpO_2, PC and Infection, the results showed that the sample effect size was as shown in Table 4.2, where the Levene Test tells us the effect level of the studied sample.

Table 4.2 The independent t-test for CD, WCM, BMI, age, Sex, SPO_2, PC, and Infection

Indep Test									
		Levene Test		t-test for Equality					
		F	Significance	t	df	MD	SED	95% Confidence Interval of the Difference	
								Lower	Upper
CD	**EV**	122.0	0.000	-4.466	197	-0.55705	0.12474	-.80305	-0.31104
	Not- EV			-7.722	148.0	-0.55705	0.07214	-.69961	-0.41449
WCM	**E**	4.629	.033	-.227	197	-.23074	1.01735	-2.23703	1.77555
	Not- EV			-0.199	69.27	-.23074	1.16017	-2.54504	2.08356
BMI	**EV**	.000	.991	.545	197	.28948	.53123	-0.75815	1.33711
	Not- EV			.597	100.2	.28948	.48486	-0.67243	1.25139
Age	**EV**	1.239	.267	-2.418	197	-6.89691	2.85267	-12.5225	-1.27123
	Not- EV			-2.317	78.58	-6.89691	2.97638	-12.8217	-0.97210
Sex	**EV**	4.736	.031	1.191	197	0.08510	0.07146	-0.05582	0.22602
	Not- EV			1.132	77.54	0.08510	0.07520	-0.06463	0.23483
SPO_2	**EV**	.210	.647	1.098	197	2.60362	2.37081	-2.07181	7.27906
	Not- EV			1.110	85.89	2.60362	2.34481	-2.05778	7.26502
PC	**EV**	2.356	.126	-22.07	197	-.97933	.04437	-1.06684	-.89182
	Not- EV			-30.46	173.4	-.97933	.03214	-1.04277	-.91589
Infection	**EV**	11.23	.001	10.37	197	43.6692	4.20783	35.3710	51.9673
	Not- EV			5.984	49.00	43.6692	7.29813	29.0031	58.3352

EV = Equal variances; SED = Standard Error Difference; Not-EV = Not Equal variances; MD = Mean Difference

4.2 The Results of Serum Creatinine, Blood Urea, and others Parameters

In the same study, the averages of IL-6, NRL, LYM, and WBC, respectively, were clinically significant and statistically significant when performing the statistical analysis at P = < 0.05, while the results of serum creatinine and urea levels indicated that there were no significant differences with statistical significance and could be affected by Covid -19 disease as shown in Table 4.3 and Figure 4.2.

Table 4.3 The mean of serum creatinine, urea, IL-6, and other in patients with COVID-19

Test	Groups	N	Mean	Std. Deviation	Std. Error Mean	P
Creatinine	Group A	50	1.3722	.23221	.03284	.137
	Group B	149	1.7782	1.91287	.15671	.012
Urea	Group A	50	58.226	6.05090	.85573	.193
	Group B	149	72.930	79.3321	6.49914	.026
IL-6	Group A	50	32.861	5.41968	.76646	.000
	Group B	149	2.9645	5.57981	.45712	.000
NRL	Group A	50	7.0270	1.21568	.17192	.000
	Group B	149	83.414	1.79565	.14711	.000
LYM	Group A	50	5.4970	2.40290	.33982	.000
	Group B	149	7.7589	1.39717	.11446	.000
WBC	Group A	50	3.8566	.62491	.08838	.000
	Group B	149	7.9314	4.56128	.37367	.000

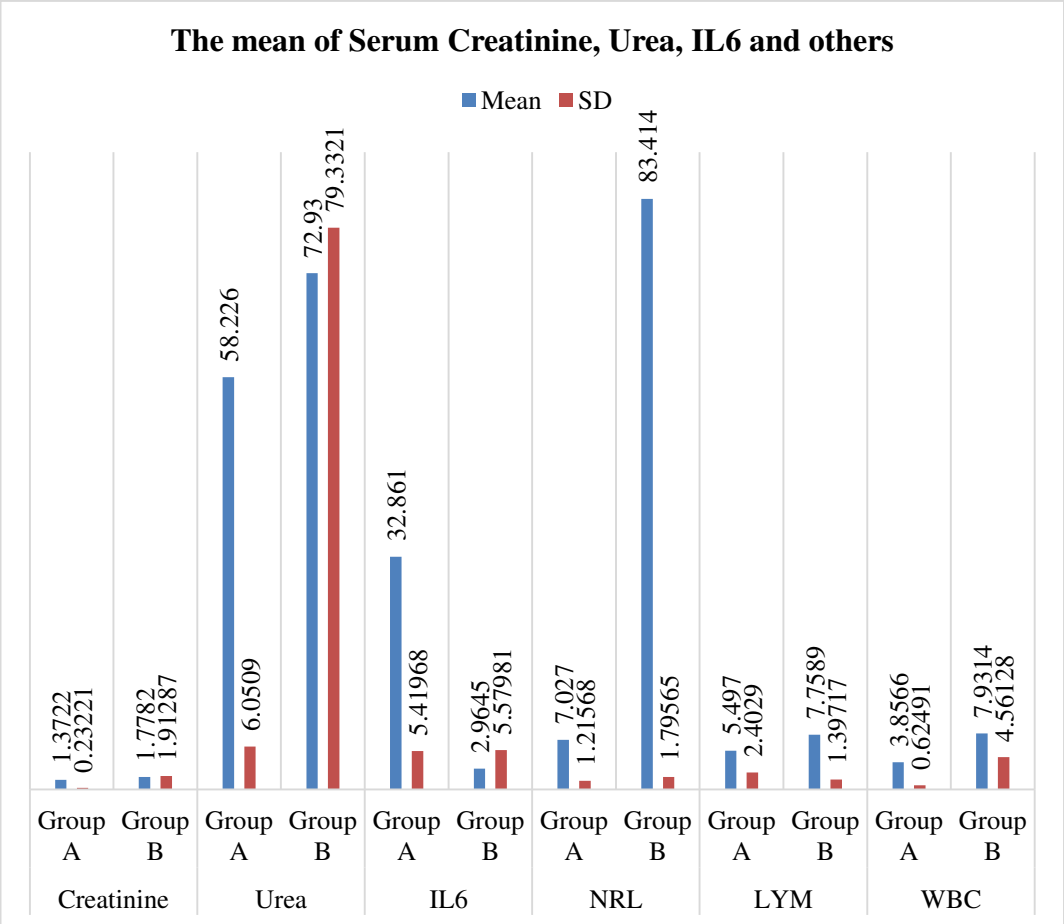

Figure 4.2 The mean of serum creatinine, urea, IL-6, and others in patients with COVID-19

In the improved independent t-test for serum creatinine, blood urea, IL-6, NRL, LYM, and WBC, the results showed that the sample effect size was as shown in Table 4.4, where the Levene Test tells us the effect level of the studied sample.

Table 4.4 Independent t-test for serum creatinine, blood urea, IL-6, NRL, LYM, and WBC

		Levene Test		t-test for Equality					
		F	Significance	t	df	MD	SED	95% Confidence Interval of the Difference	
								Lower	Upper
Creatinine	**EV**	18.16	0.000	-1.495	197	-0.40599	0.27164	-.94168	.12970
	Not- EV			-2.536	160.3	-0.40599	0.16011	-.72219	-.08979
Urea	**EV**	21.06	0.000	-1.307	197	-14.7046	11.2489	-36.8884	7.47928
	Not- EV			-2.243	153.0	-14.7046	6.55524	-27.6550	-1.75417
IL-6	**EV**	2.551	0.112	33.01	197	29.8973	0.90550	28.1115	31.6830
	Not- EV			33.50	86.43	29.8973	0.89242	28.1233	31.6712
NRL	**EV**	9.744	0.002	-279.8	197	-76.3877	0.27299	-76.9260	-75.8493
	Not- EV			-337.5	124.8	-76.3877	0.22627	-76.8355	-75.9398
LYM	**EV**	45.26	0.000	-8.123	197	-2.26193	0.27845	-2.81105	-1.71280
	Not- EV			-6.308	60.49	-2.26193	0.35858	-2.97907	-1.54478
WBC	**EV**	30.27	0.000	-6.287	197	-4.07481	0.64815	-5.35302	-2.79660
	Not- EV			-10.61	163.4	-4.07481	0.38398	-4.83302	-3.31660

EV = Equal variances; Not-EV = Not Equal variances

4.3 The Results of ESR, CRP, and Others Parameters

Because blood parameters are directly affected in Covid 19 patients, our study confirmed that the change in the mean levels of ESR, CRP, RBS, D-Dimer, and Ferritin respectively, is of high clinical importance, with high moral differences, and more statistically significant when conducting the statistical analysis at P = < 0.05, while the results indicated that these parameters are diagnostic and can be used as markers to follow up the patient's condition during the period of infection and treatment due to the presence of significant statistically significant differences when comparing the disease group with the control group in the same study as shown in Table 4.5 and Figure 4.3.

Table 4.5 The mean of ESR, CRP, RBS, and others in patients with COVID-19

Test	Groups	N	Mean	Std. Deviation	Std. Error Mean	P
ESR	Group A	50	4.6724	0.45974	0.06502	0.000
	Group B	149	59.9262	22.89845	1.87591	0.000
CRP	Group A	50	244.780	44.99990	6.36395	0.000
	Group B	149	44.2754	42.56187	3.48680	0.000
RBS	Group A	50	55.8800	7.12466	1.00758	0.000
	Group B	149	4.4344	0.88078	0.07216	0.000
D-Dimer	Group A	50	223.280	32.32806	4.57188	0.000
	Group B	149	2778.02	3437.224	281.5883	0.000
Ferritin	Group A	50	13.0140	0.65528	0.09267	0.000
	Group B	149	205.214	145.1854	11.89405	0.000

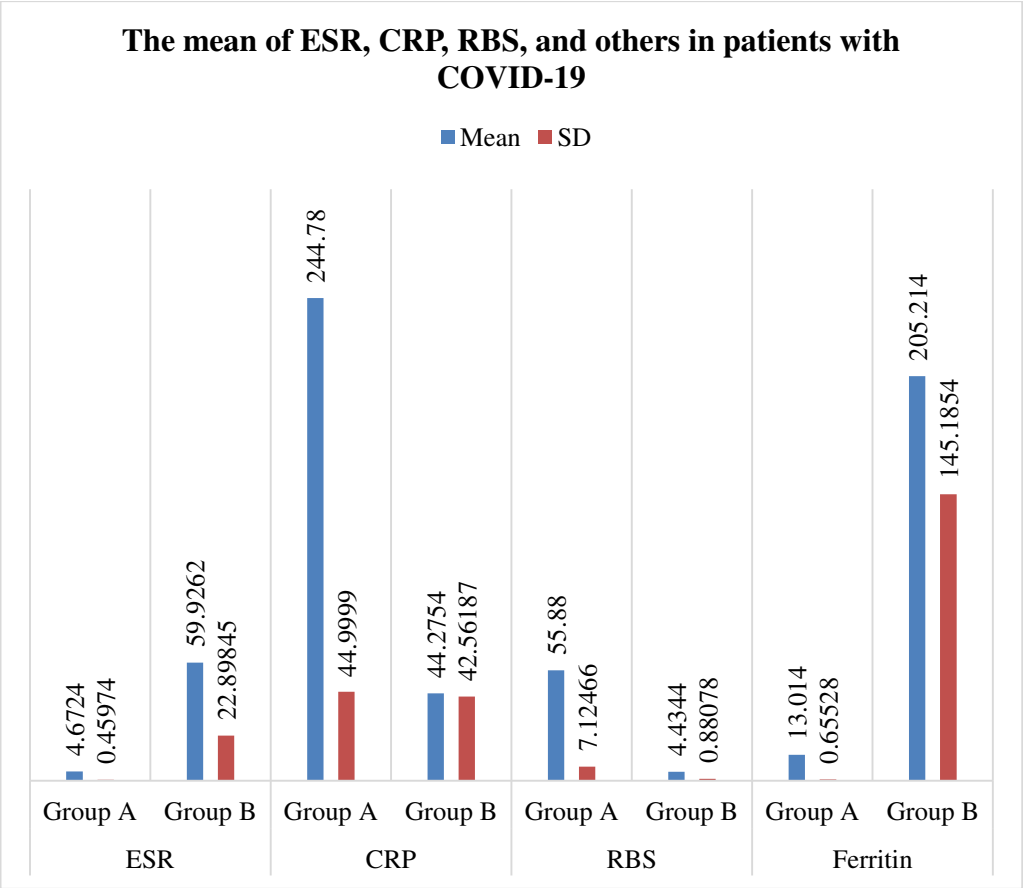

Figure 4.3 The mean of ESR, CRP, RBS, and others in patients with COVID-19

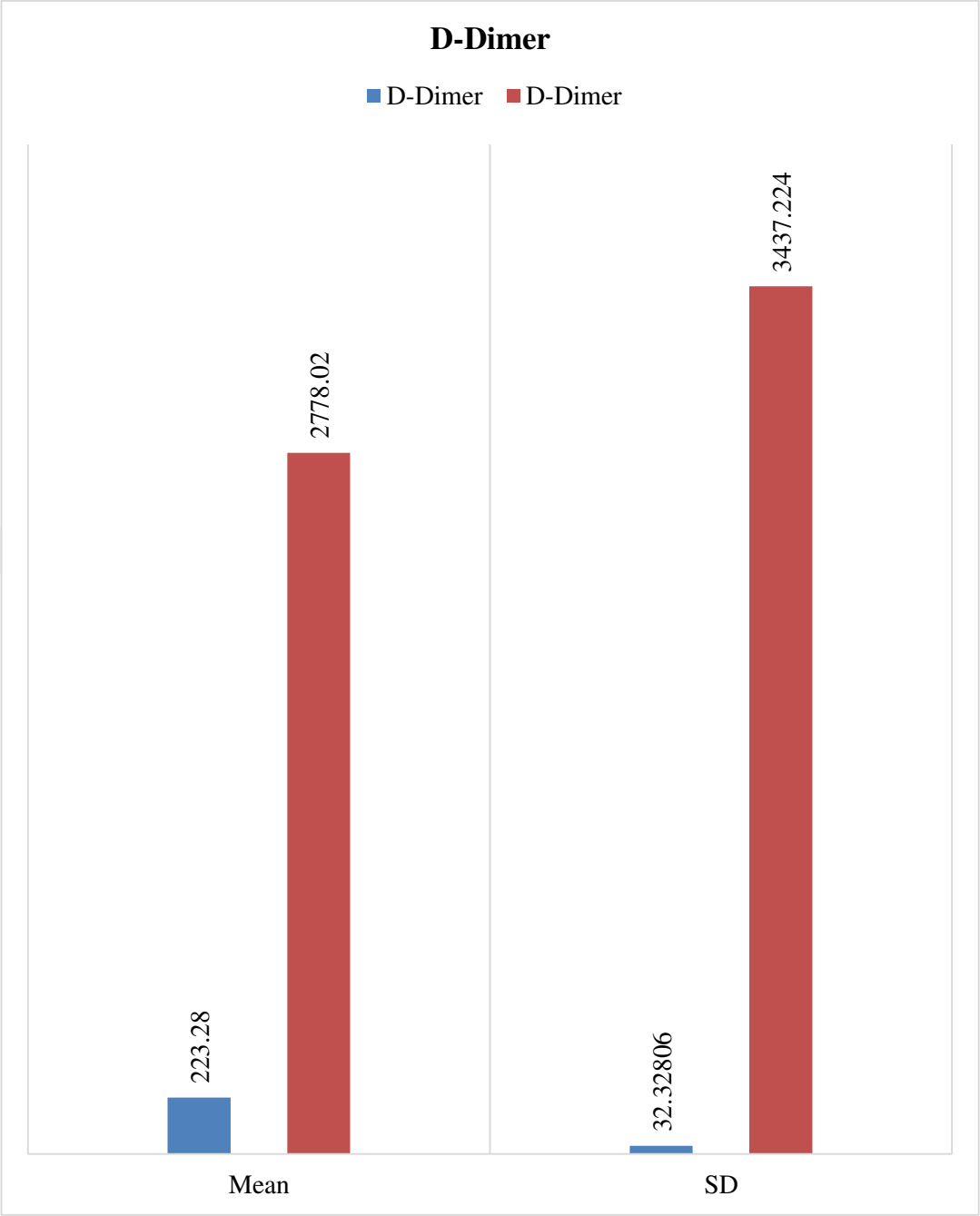

Figure 4.4 The mean of D-Dimer in patients with COVID-19

In the improved independent t-test for ESR, CRP, RBS, D-Dimer and Ferritin, the results showed that the sample effect size was as shown in Table 4.6, where the Levene test tells us the effect level of the studied sample.

Table 4.6 The independent t-test for ESR, CRP, RBS, D-Dimer, and Ferritin

		Levene Test		t-test for Equality					
		F	Signifi cance	t	df	MD	SED	95% Confidence Interval of the Difference	
								Lower	Upper
ESR	**EV**	64.40	.000	-17.03	197	-55.253	3.24400	-61.6512	-48.8563
	Not- EV			-29.43	148.3	-55.253	1.87704	-58.9629	-51.5445
CRP	**EV**	.411	.522	28.41	197	200.504	7.05736	186.586	214.422
	Not- EV			27.63	80.43	200.504	7.25656	186.064	214.944
RBS	**EV**	147.4	.000	86.61	197	51.4455	.59399	50.2741	52.6169
	Not- EV			50.92	49.50	51.4455	1.01016	49.4161	53.4750
D-dimer	**EV**	62.51	.000	-5.247	197	-2554.7	486.923	-3514.99	-1594.49
	Not- EV			-9.071	148.0	-2554.7	281.625	-3111.27	-1998.22
Ferritin	**EV**	60.00	.000	-9.345	197	-192.20	20.5669	-232.760	-151.641
	Not- EV			-16.15	148.0	-192.20	11.8944	-215.705	-168.695

EV = Equal variances; Not-EV = Not Equal variances

4.4 The Results of Platelet, PT, and others Parameters

Because liver and blood parameters are directly affected in covid-19 patients, our study also confirmed that the change in the mean levels of IL6, NRL, LYM, and WBC, respectively, is of clinical importance and has statistical significance when performing the statistical analysis at P = < 0.05, while the results indicated that these parameters are diagnostic and can be used as markers to follow up the patient's condition during the period of injury and treatment because there are significant statistically significant differences when comparing the disease group with the control group in the same study as shown in Table 4.7 and Figure 4.4.

Table 4.7 The mean of PLT, PT, PTT, and others in patients with COVID-19

Test	Groups	N	Mean	Std. Deviation	Std. Error Mean	P
PLT	Group A	50	30.0640	3.29035	.46533	.000
	Group B	149	168.489	128.236	10.50551	.000
PT	Group A	50	223.540	27.9841	3.95755	.000
	Group B	149	16.7114	5.27525	.43217	.000
PTT	Group A	50	19.4880	4.37277	.61840	.000
	Group B	149	35.4295	5.41925	.44396	.000
LDH	Group A	50	38.2080	13.0743	1.84899	.000
	Group B	149	185.496	55.4670	4.54403	.000
GPT	Group A	50	19.0320	6.56834	.92890	.001
	Group B	149	24.0872	10.1368	.83044	.000
GGT	Group A	50	38.208	11.6348	1.7583	.000
	Group B	149	60.5973	15.9229	1.30446	.000
GOT	Group A	50	19.032	5.74792	0.8593	.720
	Group B	149	20.2282	14.3978	1.17952	.720

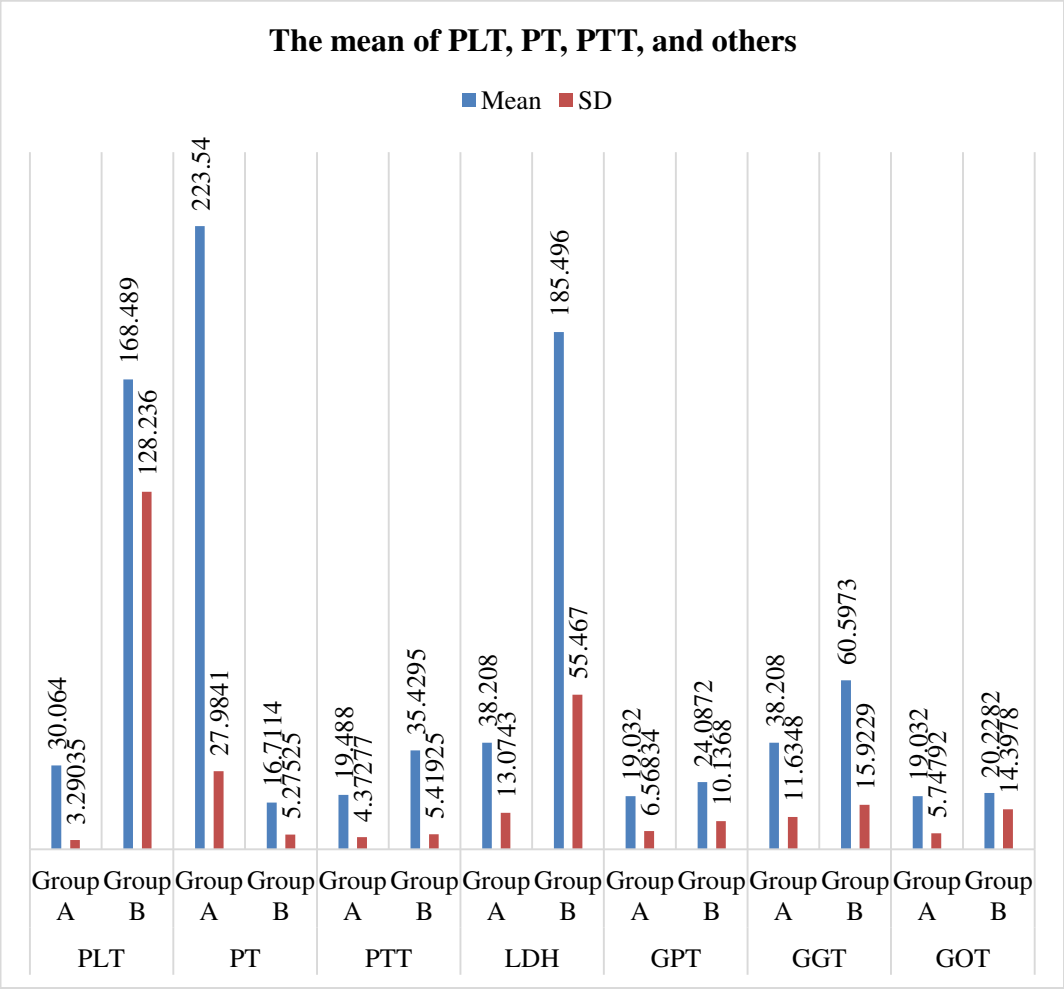

Figure 4.5 The mean of PLT, PT, PTT, and others in patients with COVID-19

In the improved independent t-test for platelet, PT, PTT, LDH, GPT, GGT and GOT, the results showed that the sample effect size was as shown in Table 4.8, where the Levene test tells us the effect level of the studied sample.

Table 4.8 The independent t-test for platelet, PT, PTT, LDH, GPT, GGT and GOT

T		Levene Test		t-test for Equality					
		F	Significance	t	df	MD	SED	95% Confidence Interval of the Difference	
								Lower	Upper
PLT	EV	37.77	.000	-7.619	197	-138.425	18.1678	-174.254	-102.597
	Not- EV			-13.1	148.5	-138.425	10.5158	-159.205	-117.646
PT	EV	422.	.000	86.16	197	206.828	2.40029	202.095	211.562
	Not- EV			51.95	50.17	206.828	3.98108	198.833	214.824
PTT	EV	.370	.544	-18.83	197	-15.9415	.84640	-17.6106	-14.2723
	Not- EV			-20.94	103.4	-15.9415	.76126	-17.4512	-14.4318
LDH	EV	32.39	.000	-18.57	197	-147.288	7.92938	-162.926	-131.651
	Not- EV			-30.02	185.6	-147.288	4.90582	-156.966	-137.610
GPT	EV	1.845	.176	-3.299	197	-5.05525	1.53254	-8.07754	-2.03295
	Not- EV			-4.057	130.9	-5.05525	1.24599	-7.52013	-2.59037
EV = Equal variances; Not-EV = Not Equal variances									

4.5 The Correlation Tests

The Pearson test was conducted to find out the correlations between interleukin 6, ferritin and the rest of the chemical parameters with Covid 19 patients, and the results were as in Table 4.9, Table 4.10, and Table 4.11.

Table 4.9 The correlation test between IL-6 and ferritin with other parameters in patient with COVID-19

Correlations																							
	CD	WCM	BMI	age	Sex	SPO2	PC	Infection	Creatnnn	Urea	IL6	NRL	ESR	WBC	LYM	CRP	RBS	DDaimer	Firrrtin	PLT			
CD-Pearson Correlation	1	.033	.051	.150*	.025	-.046	.210**	-.183**	.150*	.157*	-.239**	.302**	.276**	.177*	.175*	-.239**	-.303**	.202**	.251**	.206**			
Significance (2-tailed)		.647	.474	.034	.726	.517	.003	.010	.035	.027	.001	.000	.000	.012	.013	.001	.000	.004	.000	.003			
WCM Pearson Correlation	.033	1	.379**	.100	.061	-.077	-.018	-.055	.094	.114	.002	.019	.037	.093	-.100	.017	-.016	.107	.103	.099			
Significance (2-tailed)	.647		.000	.162	.392	.282	.801	.442	.186	.109	.979	.787	.603	.190	.162	.810	.818	.133	.147	.164			
BMI- Pearson Correlation	.051	.379**	1	-.001	.076	-.145*	.028	-.009	-.096	-.114	.016	-.047	-.131	-.121	.017	-.007	.034	-.110	-.084	-.121			
Significance (2-tailed)	.474	.000		.987	.287	.040	.698	.903	.176	.108	.827	.507	.065	.089	.815	.921	.629	.122	.236	.087			
Age- Pearson Correlation	.150*	.100	-.001	1	.286**	-.142*	.046	-.181*	.159*	.172*	-.120	.168*	.142*	.136	.146*	-.074	-.165*	.242**	.231**	.185**			
Significance (2-tailed)	.034	.162	.987		.000	.045	.521	.011	.025	.015	.091	.018	.046	.055	.039	.296	.020	.001	.001	.009			
Sex- Pearson Correlation	.025	.061	.076	.286**	1	-.061	-.143*	-.004	.090	.093	.112	-.086	.029	.081	.002	.152*	.103	.075	.057	.045			
Significance (2-tailed)	.726	.392	.287	.000		.393	.045	.951	.206	.190	.116	.230	.685	.252	.982	.033	.149	.290	.424	.532			
SPO2- Pearson Correlation	-.046	-.077	-.076	.000	-.061	1	-.061	.048	-.023	-.022	.079	-.075	.011	.014	-.036	.080	.088	-.052	-.038	.014			
Significance (2-tailed)	.517	.282	.040	.045	.393		.395	.505	.743	.758	.269	.289	.872	.841	.612	.262	.216	.466	.590	.840			
PC- Pearson Correlation	.210**	-.018	.028	.046	-.143*	-.061	1	-.484**	-.412**	-.424**	-.948**	.840**	.429**	-.058	.388**	-.917**	-.819**	-.122	.115	-.004			
Significance (2-tailed)	.003	.801	.698	.521	.045	.395		.000	.000	.000	.000	.000	.000	.414	.000	.000	.000	.087	.107	.954			
Infection- Pearson Correlation	-.183**	-.055	-.009	-.181*	-.004	.048	-.484**	1	-.078	-.067	.552**	-.592**	-.468**	-.234**	-.231**	.446**	.543**	-.225**	-.343**	-.290**			
Significance (2-tailed)	.010	.442	.903	.011	.951	.505	.000		.276	.347	.000	.000	.000	.001	.001	.000	.000	.001	.000	.000			
Creatinine- Pearson Correlation	.150*	.094	-.096	.159*	.081	.014	-.917**	-.078	1	.991**	.239**	.113	.511**	.797**	.067	.211**	-.131	.865**	.759**	.823**			
Significance (2-tailed)	.035	.186	.176	.025	.252	.841	.429**	.276		.000	.001	.111	.000	.000	.347	.003	.066	.000	.000	.000			

Table 4.10 The correlation test between IL-6 and ferritin with other parameters in patient with COVID-19

	PLT	Ferriti	DDai	RBS	CRP	ESR	WBC	LYM	NRL	IL-6	Urea	Creati	Infecti	PC	SPO2	Sex	age	BMI	WCM	CD
Urea-Pearson Correlation	.817**	.753**	.851**	-.116	.223**	.503**	.790**	.053	.101	.245**	1	.991**	-.067	.424**	-.022	.093	.172**	-.114	.114	.157**
Significance (2-tailed)	.00	.00	.00	.10	.00	.00	.00	.45	.15	.00		.00	.34	.00	.75	.19	.01	.10	.10	.02
IL6-Pearson Correlation	-.172*	-.274**	-.045	.901**	.935**	-.564**	-.107	-.459**	-.916**	1	.245**	.239**	.552**	-.948**	.079	.112	-.120	.016	.002	-.239**
Significance (2-tailed)	.015	.000	.524	.000	.000	.000	.133	.000	.000		.000	.001	.000	.000	.269	.116	.091	.827	.979	.001
NRL-Pearson Correlation	.483**	.561**	.360**	.986**	.891**	.777**	.414**	.471**	1	.916**	.101	.113	.592**	.840**	-.075	-.086	.168**	-.047	.019	.302**
Significance (2-tailed)	.000	.000	.000	.000	.000	.000	.000	.000		.000	.157	.111	.000	.000	.289	.230	.018	.507	.787	.000
LYM-Pearson Correlation	.230**	.304**	.181*	-.502**	-.457**	.355**	.201**	1	.471**	-.459**	.053	.067	-.231**	.388**	-.036	.002	.146*	.017	-.100	.175**
Significance (2-tailed)	.001	.000	.010	.000	.000	.000	.004		.000	.000	.459	.347	.001	.000	.612	.982	.039	.815	.162	.013
WBC-Pearson Correlation	.964**	.747**	.761**	-.420**	-.136	.756**	1	.201**	.414**	-.107	.790**	.797**	-.234**	-.058	.014	.081	.136	-.121	.093	.177*
Significance (2-tailed)	.000	.000	.000	.000	.056	.000		.004	.000	.133	.000	.000	.001	.414	.841	.252	.055	.089	.190	.012
ESR-Pearson Correlation	.793**	.803**	.688**	-.773**	-.521**	1	.756**	.355**	.777**	-.564**	.503**	.511**	-.468**	.429**	.011	.029	.142*	-.131	.037	.276**
Significance (2-tailed)	.000	.000	.000	.000	.000		.000	.000	.000	.000	.000	.000	.000	.000	.872	.685	.046	.065	.603	.000
CRP-Pearson Correlation	-.171*	-.213**	.027	.899**	1	-.521**	-.136	-.457**	-.891**	.935**	.223**	.211**	.446**	-.917**	.080	.152*	-.074	-.007	.017	-.239**
Significance (2-tailed)	.016	.002	.703	.000		.000	.056	.000	.000	.000	.002	.003	.000	.000	.262	.033	.296	.921	.810	.001
RBS-Pearson Correlation	-.491**	-.567**	-.369**	1	.899**	-.773**	-.420**	-.502**	-.986**	.901**	-.116	-.131	.543**	-.819**	.088	.103	-.165*	.034	-.016	-.303**
Significance (2-tailed)	.000	.000	.000		.000	.000	.000	.000	.000	.000	.104	.066	.000	.000	.216	.149	.020	.629	.818	.000
D-Dimer-Pearson Correlation	.836**	.901**	1	-.369**	.027	.688**	.790**	.181*	.360**	-.045	.851**	.865**	-.543**	-.122	-.052	.075	.242**	-.110	.107	.202**
Significance (2-tailed)	.000	.000		.000	.703	.000	.000	.010	.000	.524	.000	.000	.001	.087	.466	.290	.001	.122	.133	.004

Table 4.11 The correlation test between IL-6 and ferritin with other parameters in patient with COVID-19

	PLT	Fırrıtın DDanm	RBS	CRP	ESR	WBC	LYM	NRL	IL6	Urea	Creatin	Infectio	PC	SPO2	Sex	age	BMI	WCM	CD
Fırrıtın Pearson Correlation	.840**	1	-.567**	-.213**	.803**	.747**	.304**	.561**	-.274**	.753**	.759**	-.343**	.115	-.038	.057	.231**	-.084	.103	.251**
Significance (2-tailed)	.000		.000	.002	.000	.000	.000	.000	.000	.000	.000	.000	.107	.590	.424	.001	.236	.147	.000
PLT-Pearson Correlation	1	.840**	-.491**	-.171*	.793**	.964**	.230**	.483**	-.172*	.817**	.823**	-.290**	-.004	.014	.045	.185**	-.121	.099	.206**
Significance (2-tailed)		.000	.000	.016	.000	.000	.001	.000	.015	.000	.000	.000	.954	.840	.532	.009	.087	.164	.003
PT-Pearson Correlation	-.436**	-.518**	.971**	.896**	-.743**	-.369**	-.496**	-.986**	.924**	-.053	-.065	.609**	-.856**	.070	.087	-.161*	.051	-.008	-.296**
Significance (2-tailed)	.000	.000	.000	.000	.000	.000	.000	.000	.000	.455	.362	.000	.000	.328	.224	.023	.478	.908	.000
PTT-Pearson Correlation	.590**	.636**	-.800**	-.629**	.756**	.531**	.411**	.801**	-.645**	.330**	.341**	-.456**	.532**	-.031	-.041	.151*	-.009	.020	.234**
Significance (2-tailed)	.000	.000	.000	.000	.000	.000	.000	.000	.000	.000	.000	.000	.000	.665	.566	.034	.905	.782	.001
LDH-Pearson Correlation	.780**	.830**	-.801**	-.524**	.871**	.694**	.403**	.802**	-.574**	.544**	.556**	-.476**	.429**	-.070	.007	.223**	-.083	.089	.299**
Significance (2-tailed)	.000	.000	.000	.000	.000	.000	.000	.000	.000	.000	.000	.000	.000	.324	.925	.002	.245	.213	.000
GPT-Pearson Correlation	.688**	.737**	-.823**	.097	.537**	.618**	.109	.238**	.031	.726**	.729**	-.120	-.170*	-.043	.088	.207**	-.068	.134	.111
Significance (2-tailed)	.000	.000	.000	.171	.000	.000	.125	.001	.662	.000	.000	.093	.016	.542	.219	.003	.343	.059	.118
GGT-Pearson Correlation	.689**	.814**	-.676**	.885**	.622**	.584**	-.062	.297**	.733**	.757**	.760**	-.781**	-.724**	-.027	.105	.190*	-.100	.144	.068
Significance (2-tailed)	.000	.000	.000	.000	.000	.000	.449	.000	.000	.000	.000	.000	.000	.744	.203	.020	.223	.081	.412
GOT-Pearson Correlation	.766**	.853**	-.710**	.920**	.668**	.672**	-.038	.278**	.801**	.820**	.824**	-.755**	-.797**	-.028	.099	.202*	-.102	.167*	.078
Significance (2-tailed)	.000	.000	.000	.000	.000	.000	.650	.001	.000	.000	.000	.000	.000	.733	.228	.013	.215	.042	.342

5. DISCUSSION AND CONCLUSION

5.1 Discussion

The study concluded that clinical laboratories play the most prominent and clear role in the detection of many, including the Covid-19 virus, continuous follow-up and epidemiological monitoring of infected patients, or help in early detection of infection by determining the values of their serological markers. The importance of knowing and validating chemical parameter values and whether they are within the normal level or within the level of the control group is to support the clinician's timely decision to control infection and detect pathological conditions.

Age had a significant effect on the disease in association with the period of infection. There were no clear signs or significant differences for body mass. IL-6, NRL, LYM, and WBC were clear significant differences that could be used in early diagnosis of the disease or to follow up the patient's condition by linking with the rest of the blood parameters that had clear significant differences. Serum creatinine and urea did not have any significant statistically significant differences that could benefit in the follow-up of Covid -19 disease.

In our study, through which we describe the ESR, CRP, RBS, D-Dimer and Ferritin pathway, it is possible to understand the mechanism that influences the change in the levels of these parameters in patients with Covid -19 and thus contribute to the early detection of the disease, as the results of these tests indicate the presence of high significant differences. And it was statistically significant in patients when compared with the controls group. Whereas, D-Dimer with Ferritin is one of the most important diagnostic parameters for COVID-19 disease.

5.2 Conclusion

An overall random effects meta-analysis showed significantly higher serum levels of IL-6 in the severe group than in the non-severe group with a mean difference of +23.1 pg/mL (95% CI: 12.42-33.79) and the overall effect of 4.24 (P-value < 0.001). Meta-regressions showed that neither age nor sex significantly influenced the mean difference of IL-6 between the groups. Meta-analysis and meta-regression reveal a reliable relationship between IL6 and COVID-19 severity, independent of age and sex. Future research is, however, required to assess the effect of BMI on the pattern of IL-6 production in patients with COVID-19. Also, there might be confounding factors that influence the relationship between IL-6 and COVID-19 severity and remain as yet unknown (Mojtabavi *et al*. 2020).

Coronaviruses may activate dysregulated host immune responses. As exploratory studies have suggested that interleukin-6 (IL-6) levels are elevated in cases of complicated Covid-19, Consistent results were found in sensitivity analyses exclusively restricted to studies comparing patients requiring ICU admission vs no ICU admission (two studies; n = 540; ratio of means = 3.24; 95%CI, 2.54-4.14; P < 0.001; I2 = 87%). Nine of ten studies were assessed to have at least moderate risk of bias. In patients with Covid-19, IL-6 levels are significantly elevated and associated with adverse clinical outcomes. Inhibition of IL-6 may be a novel target for therapeutics for the management of dysregulated host responses in patients with Covid-19 and high-quality studies of intervention in this field are urgently required (Coomes and Haghbayan 2020).

Age and age-related comorbidities, such as dyslipidaemia, hypertension or diabetes, determined more frequent severe forms of the disease in this study than in previous literature cohorts. Our cases are older than those so far reported and the clinical course of the disease is found to be impaired by age. Immunosenescence might be therefore a suitable explanation for the hampering of immune system effectors. The adaptive immunity would become exhausted and a strong but ineffective and almost deleterious innate response would account for COVID-19 severity. Angiotensin-converting enzyme inhibitors used by hypertensive patients have a protective effect in regards to COVID19

severity in our series. Conversely, patients on angiotensin II receptor blockers showed a severer disease (Jurado *et al*. 2020).

Hospitalized patients with COVID-19 should undergo a comprehensive daily CBC with manual WBC differential to monitor for numerical and morphologic changes predictive of poor outcome and signs of disease progression (Pozdnyakova *et al*. 2021).

Identifying clinical-features or a scoring-system to predict a benefit from hospital admission for patients with COVID-19 can be of great value for the decision-makers in the health sector. This includes the elder age group, male gender, and presence of comorbidities like diabetes and history of hypertension. ROC and Precision-Recall curves showed that among all variables, D dimers (>1.5 mg/dL), Urea (>6.5 mmol/L), and Troponin (>13.5 ng/mL) could positively predict the admission to ICU in patients with COVID-19. Using these three predictors with their cut of values can identify patients who are at risk of developing critical COVID-19 and might need aggressive intervention earlier in the course of the disease (Hachim *et al*. 2020).

WBC count at admission is significantly correlated with death in COVID-19 patients. Higher level of WBC count should be given more attention in the treatment of COVID-19 (Zhu *et al*. 2021).

SN-CAP showed more inflammatory reaction than COVID-19. Old people with chronic diseases are more susceptible to COVID-19 and have a high likelihood of developing severe and critically severe infection. Levels of WBC, lymphocytes, neutrophils, CRP, NLR, PLR, troponin-I, creatinine, and BUN are important indicators for severity grading in COVID-19 (Zhou *et al*. 2020).

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CURRICULUM VITAE

Personal Information

Name and Surname : Hussein Ali Mohammed AL-BADRI

Education

MSc	Çankırı Karatekin University Graduate School of Natural and Applied Sciences Department of Chemical Engineering	2020-Present
Undergraduate	Diyala University College of Science Department of Chemistry	2013-2017