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EVALUATION OF THE ACTIVITY OF LIVER ENZYMES AND SOME BIOCHEMICAL VARIABLES IN PREGNANT WOMEN INFECTED WITN COVID-19 IN KIRKUK GOVERNORATE

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WALEED IBRAHIM HAMEED HAMEED

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By Waleed Ibrahim Hameed HAMEED

June 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. Nadia Ahmed SALEH

Examining Committee Members:

Chairman **:** Prof. Dr. Volkan EYÜPOĞLU
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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Waleed Ibrahim Hameed HAMEED

ABSTRACT

EVALUATION OF THE ACTIVITY OF LIVER ENZYMES AND SOME BIOCHEMICAL VARIABLES IN PREGNANT WOMEN INFECTED WITN COVID-19 IN KIRKUK GOVERNORATE

Waleed Ibrahim Hameed HAMEED

Master of Science in Chemistry

Advisor: Assoc. Prof. Dr. Şevki ADEM

Co-Advisor: Asst. Prof. Dr. Nadia Ahmed SALEH

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Some hematological and biochemical markers were measured in COVID19 patients (pregnant women) as part of the research. 60 pregnant women with COVID-19 infection and 30 control subjects were included in this study. Research was carried out at Kirkuk's hospitals between January 2022 and April 2022. The following is a breakdown of the participants: Pregnant women in the first group: 30 healthy women. In the second group, 30 samples were taken from infected pregnant women aged 18 to 30 years old. Pregnant women between the ages of 30 and 40 are in the third group, which includes 30 samples. RBC count, Hb concentration, PCV/MCV ratio, and percentage of MCV decreased significantly (P 0.05) in patients compared to control group. Patients' WBC and neutrophil and lymphocyte percentages rose significantly (P 0.05), whereas their lymphocyte and neutrophil percentages decreased significantly (P 0.05). Otherwise, the proportion of eosinophils, monocytes, and basophils in patients (15.71±2.18) compared to the control group indicates no significant differences (P 0.05). Patients' levels of liver enzymes were found to be significantly (P 0.05) elevated. Finally, the findings revealed that patients' levels of total protein, albumin, and vitamin D3 were significantly decreased (P 0.05).

2022, 53 pages

Keywords: COVID19, Liver enzymes, Vitamin D3, Total protein, Albumin

ÖZET

KIRKÜK VALİLİĞİNDE KOVİD-19'A GÖRÜLEN HAMİLELERDE KARACİĞER ENZİMLERİ VE BAZI BİYOKİMYASAL DEĞİŞKENLERİN ETKİNLİKLERİNİN DEĞERLENDİRİLMESİ

Waleed Ibrahim Hameed HAMEED
Kimya, Yüksek Lisans
Tez Danışmanı: Doç. Dr. Şevki ADEM
Eş Danışman: Dr. Öğr. Üyesi Nadia Ahmed SALEH
Haziran 2022

Araştırmanın bir parçası olarak COVID19 hastalarında (hamileler) bazı hematolojik ve biyokimyasal belirteçler ölçüldü. Bu çalışmaya COVID-19 enfeksiyonu olan 60 hamile kadın ve 30 kontrol deneği dahil edildi. Araştırma Kerkük hastanelerinde Ocak 2022 ile Nisan 2022 arasında gerçekleştirildi. Katılımcıların dağılımı aşağıdadır: Birinci gruptaki hamile kadınlar: 30 sağlıklı kadın. İkinci grupta ise 18-30 yaşları arasındaki enfekte gebelerden 30 örnek alındı. 30 örneklemden oluşan üçüncü grupta ise 30-40 yaş arası gebeler yer almaktadır. Kontrol grubuna kıyasla hastalarda eritrosit sayısı, Hb konsantrasyonu, PCV/MCV oranı ve MCV yüzdesi önemli ölçüde azaldı (P 0,05). Hastaların WBC ve nötrofil ve lenfosit yüzdeleri önemli ölçüde yükselirken (P 0,05), lenfosit ve nötrofil yüzdeleri önemli ölçüde azaldı (P 0,05). Aksi takdirde, hastalarda (15,71±2.18) kontrol grubuna kıyasla eozinofil, monosit ve bazofil oranı anlamlı bir farklılık göstermez (P 0,05). Hastaların karaciğer enzim düzeylerinin önemli ölçüde (P 0,05) yükseldiği bulundu. Son olarak, bulgular hastaların toplam protein, albümin ve D3 vitamini düzeylerinin önemli ölçüde azaldığını ortaya koydu (P 0,05).

2022, 53 sayfa

Anahtar Kelimeler: COVID 19, Karaciğer enzimleri, Vitamin D3, Toplam protein, Albümin

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Waleed Ibrahim Hameed HAMEED

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LIST OF SYMBOLS

μL	Microliter
g	Gram
mg/dL	Milligrams per decilitre
mL	Milliliter
mM	Millimeter
nm	Nanometer

LIST OF ABBREVIATIONS

ACE	Angiotensin-converting enzyme-2
ACE2	Angiotensin-converting enzyme 2
ALP	Alkaline phosphatase
ALT	Alanine aminotransferase
ARDS	Acute Respiratory Stress Syndrome
ARDS	Acute respiratory distress syndrome
AST	Aspartate Aminotransferase
AT2	Alveolar type 2
BAS	Basophil
CMV	Cytomegalovirus
CRP	C-reactive protein
CT	Computed tomography
E	Envelope
EDTA	Ethylenediaminetetraacetic acid
FDA	Food and Drug Administration
GCSF	Granulocyte colonystimulating factor
HIV	Human immunodeficiency virus
ICU	Intensive care unit
IFN	Interferon
IgM	Immunoglobulin M
IP10	IFN-induced protein 10
ISGs	IFN-stimulated genes
LYM	Lymphocytes
M	Membrane
MI	Myocardial infarction
MIP1A	Macrophage inflammatory proteins 1A
MON	Monocytes
N	Nucleocapsid
NEU	Neutrophil
NIR	Neutrophil to lymphocyte ratio
SST	Serum separator tubes
TNF-α	Tumor Necrosis Factor-Alpha
WBC	White blood cells

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1. INTRODUCTION

SARSCoV-2, a new coronavirus illness, was discovered in September of this year. WHO said that the new coronavirus, also known as COVID-19, has quickly spread to various countries and killed many people (Cook *et al.* 2020). Coronavirus infection produces acute respiratory syndrome and affects the lungs. The virus is thought to have originated in some animals, such as bats. The new coronavirus was discovered in a seafood market in Wuhan, China (Wu and McGoogan 2020). This disease has the potential to spread from person to person. The coronavirus is known for its high rate of infection, which has resulted in a global epidemic (Zhu *et al.* 2020).

There are antibodies that may be discovered and used to establish how long an infection has been active, including IgM and IgG. SARSCoV-2 infection raised IgM and IgG antibody levels after 6 and 15 days, respectively. Some individuals with COVID 19 had multiple organ failure and even death as a consequence of the disease's rapid progression (Xiao *et al.* 2020). As a result, specific antibody detection is required for SARS-2 infection confirmation in patients suspected of infection (GONHC 2020).

SARS-Cov-2 infection induces clusters of severe and potentially deadly pneumonia, according to the clinical and pathological features of COVID-19 patients recently described. the (Guan *et al.* 2020) There is anorexia, myalgia and respiratory dyspnea in addition to the normal symptoms of high fever, tiredness and a dry cough with this pneumonia (Chen *et al.* 2020) specialists agree that SARS-Cov-2 also affected the three most critical organs: hearing, kidney, and liver in addition to lung damage (Henry et al. 2020). Findings based on (Wang *et al.* 2020). These results are most often obtained by laboratory testing rather than through surgery or autopsy.

Although COVID-19 was once thought to be solely responsible for cases of pneumonia, more research has shown that individuals with severe infection are more likely to develop intravascular coagulation and coagulopathy, both of which increase the risk of death (Levi and Iba 2021, Asakura and Ogawa 2021). These findings suggested that in

COVID-19-infected people, the coagulation pathway is particularly active (Zuo *et al.* 2020, Zamboni 2020).

Multiple hematological laboratory investigations of lymphocytes revealed significant changes in peripheral eosinophils and neutrophils in COVID-19 patients, indicating that these cells might be employed as a biomarker for both disease progression and drug efficacy. Furthermore, some research suggests a link between COVID19 infection and a drop in hemoglobin (Hb) levels (Lippi and Mattiuzzi 2020). This possible link had already been noted with other forms of pneumonia (Rahimi-Levene et al. 2018).

1.1 Aims of Study

- Pregnant women who have been exposed to COVID-19 should have their RBC and WBC levels analyzed.

- Pregnant women infected with COVID-19 should have their Hb, PCV, and MCV levels assessed.

- Pregnant women infected with COVID-19 should have their total protein and albumin levels tested.

- Pregnant women with COVID-19 infection should have their ALT, AST, and ALP levels examined.

2. LITERATURE REVIEW

2.1 COVID-19

Viruses are little parasitic particles that are unable to multiply on their own. They can infect and multiply in the host cell if they enter it. The recognized components of a viral structure are genetic material, a capsid protein coat, and an outer sheath of lipids. The nucleic acid and protein shell of a virus' infectious virion make up the virion's fundamental building blocks (Khaykelson and Raviv 2020). Since the 1960s, researchers have documented cases of virus-caused respiratory illnesses in both adults and children (Gardner 1968).

Coronaviruses are one of the fundamental viruses that cause respiratory disorders. Coronaviridae is the name of this family. The coronavirus, which causes diseases including pneumonia and bronchitis, infects many people at least once in their lives. Alpha, Gamma, Beta, and Delta are four types of single-stranded RNA viruses known as Coronaviruses (Pal *et al.* 2020). four coronaviruses that cause minor respiratory sickness (Su *et al.* 2016). Despite this, two coronaviruses, SARS-CoV and MERS-CoV, were responsible for two devastating epidemics (Cui *et al.* 2019).

After the SARS-CoV outbreak in southern China was declared an emergency in 2003, extensive research was carried out to control and cure the illness. Over 8,000 people were afflicted, and 774 people died as a result, according to the WHO (Zhu *et al.* 2020). MERS-COV was shown to be the cause of a second case of acute respiratory illness in Saudi Arabia in 2012 as well. According to published accounts, the fatality rate was over 35% (Zhang *et al.* 2020).

2.1.1 Virology

Coronaviruses are virions with envelopes that contain viral particles. These virion particles have a diameter of 120 nanometers. Cloverleaf features on the virus's surface, such as glycoproteins and proteins, have generated a crown-like structure. Because of their crown structure, these viruses are also known as coronaviruses. In these viruses, a nucleocapsid portion comprised of capsid-coated proteins is introduced into the virus's genetic material (Figure 2.1). (Mittal *et al.* 2020).

The coronavirus is part of the RNA genomic genus. The virus's nucleocapsid may have spiraling or circular genomic sequences. Only one nucleotide sequence in the coronavirus genome is responsible for the virus's genetic code (ribonucleic acid). Virus genomic RNA has an abundance of adenine nucleotides around the '3' end in the 50 area of the methylation warhead. These enzymes are responsible for transcribing the genome of Coronaviruses and creating new copies of themselves by using the host cell's resources to do so, which is contained in the genome (Neerukonda et al. 2020). SARS-CoV-2 is a member of the beta-corona virus genus, according to study. The SARS-CoV-2 virus consists of three structural proteins: the nucleocapsid (N), spike (S), and membrane/envelope (Figure 2.1). Protein M aids in the formation of viral envelopes once the virus has been introduced into the host (Kim *et al.* 2020).

Viral replication and dissemination are dependent on protein E's ability to support viral development and germination (Schoeman and Fielding 2019). Multifunctional N protein is credited with boosting viral transcription and assembly, as it performs a variety of tasks (Kang *et al.* 2020). Host cells are attached to viruses via the protein Spike (S). The pharmaceutical and vaccine industries can't ignore it. Proteins N, M, and E are not considered therapeutic targets since they do not respond to neutralizing or immunological antibodies (Walls *et al.* 2020).

The recently found SARS-CoV-2 glycoprotein has two subunits, S1 and S2, which are typically shown as a sword-like spike. On the other hand, crystallography may reveal the protein's true structure. Using the Protein Data Bank (PDB) model of this

glycoprotein, it is possible to see how the infection process is assisted in a number of ways. A polybasic amino acid bridge connects S1 and S2, which might be useful for viral targeting research (Andersen *et al.* 2020). To attach to and enter the host cell, the virus utilizes an S-protein. Infected cells undergo transcribing, which continues until the host cell is dead and the virus has completely taken over (McIntosh *et al.* 2020).

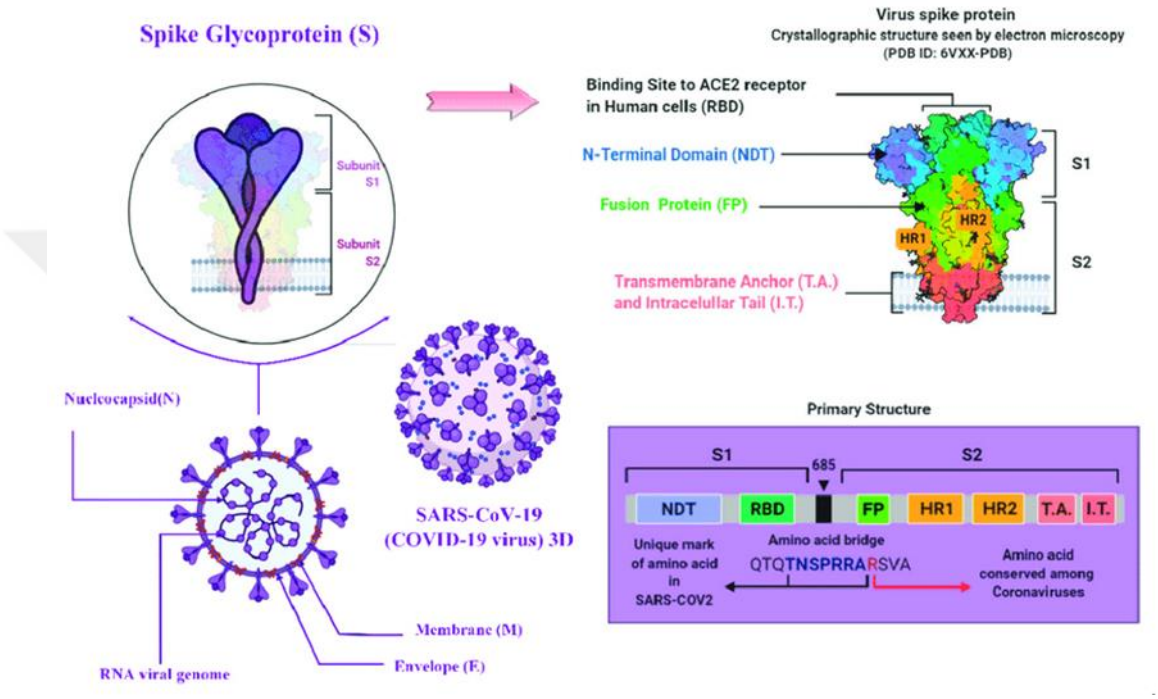

Figure 2.1 Analysis of the spike glycoprotein of the SARS-CoV-2 virus (McIntosh *et al.* 2020)

2.1.2 Transmission

Uncertainty surrounds the Huanan Seafood Wholesale Market's involvement in the spread of illness. This market was associated to a number of the early COVID-19 cases, showing that SARS-CoV-2 was spread by animals (Li *et al.* 2020). However, genetic research has shown that the virus was put on the market from an unknown source, where it propagated more fast despite people-to-people transmission having happened earlier (Yu *et al.* 2020) Take a look at this (Figure 2.2).

Individual transmission has been proven by clusters of afflicted families and healthcare staff (Chan *et al.* 2020). Most participants had no exposure to the market after January 1, and just ten percent had any exposure prior to the start of the new year (Li *et al.* 2020). When a person coughs or sneezes, respiratory droplets are dispersed among those with whom they have a close social circle. There is evidence that SARS-CoV and other coronaviruses can persist on materials for up to 96 hours (Kramer *et al.* 2006) and that fomites might be a major source of transmission.

Sickness may spread asymptomatically, however this is up for debate. Asymptomatic transmission was described in a paper published on January 30; however, it was subsequently discovered that the authors did not interview the patient personally, who had complained before the sickness was spread (KupferschmidtK *et al.* 2020). It was recently shown that transmission may occur without symptoms (Bai et al. 2020), although this research might be undermined by inaccurate self-reporting of symptoms or interactions with other patients and fomites. Findings concerning illness features might change often due to selection bias. An incubation period of 5.2 days (95 percent confidence interval: 4.1-4.7) was observed in one experiment (Li *et al.* 2020).

A 14-day incubation time is common, however incubation has been known to last as long as 19 or even 24 days (Huang *et al.* 2020). The most basic reproductive number may be calculated using a variety of approaches and results (R0). In a completely susceptible population, one sick individual may infect an average of R0 others (Bauch and Oraby 2013). When compared to the 2009 global H1N1 influenza, SARS had a R0 of 2.7. (Yang and colleagues 2009). An R0 of 2.2 was found in one research with a 95% confidence range of 1.4–3.9. According to Li and colleagues (Li *et al.* 2020).

R0 was determined to be 3.28 in a second research that included 12 trials. For example, it's important to understand the role of super spreaders, which may be a substantial source of outbreak in large clusters but have minimal effect on R0's value, as well (Kucharski and Althaus 2015). Pre-pandemic stage or acute phase of epidemic may have an unstable R0 (Bauch and Oraby 2013).

Nine pregnant women who contracted COVID-19 late in their pregnancies did not have significantly worse symptoms than non-pregnant women, and there was no evidence of intrauterine sickness caused by vertical transmission (Chen 2020). Among 138 COVID-19 patients in a healthcare setting, 41% had SARS-CoV-2 transmitted to them by the hospital, according to a research (Wang *et al.* 2020). Studying 425 patients, researchers discovered that the number of instances among health-care employees rose with time (Li *et al.* 2020).

People who have had close contact with viruses in higher concentrations are more at risk of contracting the disease. There were 441 confirmed cases of COVID-19 outside of China as of February 12, 2020, according to data gathered by WHO, with the first export case being documented in Thailand in January 2020. In 11 nations, local transmission has been documented, with Singapore reporting the most (Sookaromdee *et al.* 2020).

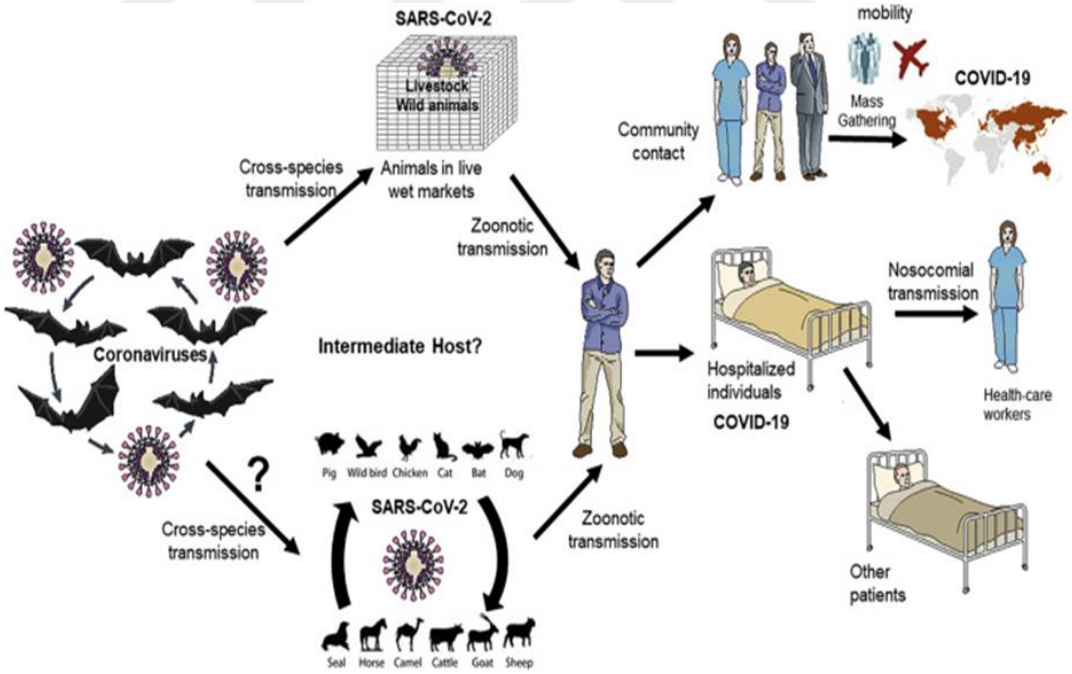

Figure 2.2 Transmission of COVID-19 (Sookaromdee *et al.* 2020)

2.1.3 Nosocomial-related infections

Secondary SARS-CoV-2 transmission may occur in hospitals due to the large number of ill persons they house (Drosten *et al.* 2014). Patients with COVID-19 have been found to get the virus while being treated in the hospital, which has been suggested as a second way the virus is spread. When SARS-CoV-2 positive patients' ward surfaces were tested for viral RNA in surface samples, washroom services and air samples were found to be positive for the virus.

Patients receiving oxygen via a nasal canula had the highest levels of airborne viral concentrations in this study, with virus copies per liter of air measuring 19.17 and 48.22, respectively. In order to avoid transmission within nosocomial settings, healthcare practitioners must carefully consider approaches to implement into practice in order to prevent SARS-CoV-2 dissemination via droplets and fomites. Preventive measures may be employed during medical procedures in addition to decontaminating common surfaces and equipment and protecting oneself. Due to the fact that SARS-CoV-2 may be identified in coughing or sneezing, oral therapies such as dental care and endoscopy should take this into consideration (Ather *et al.* 2020).

Ather *et al.* (2020) established a step-by-step inference approach for the management and screening of patients before dental treatments. Infection with SARS-CoV-2 may be spread by the fecal–oral route in the stool of infected patients, according to new findings (Zhang *et al.* 2020).

Vero E6 cells infected with fecal contents from sick people demonstrate a cytopathic effect two days after a second-round passage, according to a study by (Xiao *et al.* 2020). After a second passage of cells, electron imaging revealed globular viral proteins with distinctive surface spike projections once again.

A recent study in Hong Kong found that 17.6 percent of COVID-19 patients had digestive problems. Even though the lung samples were negative, 48.1% of patient stool

samples were positive for viral RNA. Taking excrement samples from patients and performing other medical procedures should be done cautiously, according to this study's findings (Cheung *et al.* 2020). Because patient feces samples may be present during medical procedures like colonoscopies, more caution must be used (Soetikno *et al.* 2020).

The spread of the COVID-19 pandemic has harmed critical care units in hospitals (ICUs). Another problem has been preventing the transmission of the virus from COVID-19 ICU patients to other patients and hospital personnel, as well as managing the growing demand for healthcare. Capacity and infrastructure for infection prevention have been included in ICU regulations to address this problem. Critically ill patients should be protected from the dangers of fomite transmission. For COVID-19 patients, it's critical to disinfect non-disposable medical equipment including ventilators and ICU beds (Phua *et al.* 2020).

2.1.4 Risk factors

Direct contact with SARS-CoV-2 is the most common method of transmission for most patients infected with the virus, especially males aged 34 to 59. (Bai *et al.* 2020, Wang *et al.* 2020). SARS-CoV-2 infection is more likely to strike those with diabetes, heart disease, or a stroke (Chen et al. 2020). Elderly people as well as those with underlying health conditions such as cardiovascular disease (CVD), cerebrovascular disease (CVA), and diabetes are more likely to have severe cases (Bai *et al.* 2020, Wang *et al.* 2020).

Microbial ailments, such as bacteria and fungi, may also produce severe symptoms (Chen *et al.* 2020). In children under the age of 15, there have been fewer recorded cases of COVID-19 (Bai *et al.* 2020, Wang *et al.* 2020). No cases were discovered in children under the age of 15 according to a study of 425 COVID-19 participants published on January 29 in Wuhan. Both (Liu *et al.* 2020 and Li *et al.* 2020) have cited this study. 28 pediatric cases have been reported as of January 2020. There is a broad variety of clinical symptoms among infected youngsters, but the most majority have just

minor side effects with no fever, making their prognosis favorable (Shen and Yang 2020).

Another examination revealed that a youngster had radiographic ground-glass lung opacities, although he or she had no symptoms (Chan *et al.* 2020). The bottom line is that kids may be less susceptible to illness or, if they are, they may show fewer symptoms than adults, thus their families may not obtain treatment, leading to an underestimating of COVID-19 incidence in this age range.

2.1.5 Pathogenesis

Small genetic alterations may have a big influence on the chemotaxis and host range of betacoronavirus, despite the fact that it exhibits a high degree of species specificity like all other COVID19. The fact that SARS-CoV and MERS-emergence CoV have become two of the most lethal zoonotic illnesses in human history shows how adaptable these viruses are (Zaki *et al.* 2012). They served as intermediate hosts for SARS-CoV in palm civets and camels. Both viruses originated in bats, and humans served as their last hosts. (Guan *et al.* 2003).

Intermediate hosts are necessary for cross-species transmission because they allow for more direct interaction between a virus and its new host and the adaption needed for optimal viral replication in that organism. (Brennan *et al.* 2014). SARSCoV-2 should be examined thoroughly in terms of host adaptability, viral evolution, infectivity, and transmission mechanisms since it has the potential to spread globally. The host range of a virus is influenced by several molecular interactions, such as receptor contact. An atp-binding domain (S) of the envelope spike (S) protein of SARS-CoV-2 has been found structurally comparable to that of SARS-CoV. (Lu *et al.* 2020).

COVID19 and AT2 pneumocytes, both of which generate lung surfactant, may be infected by SARS-CoV-2 via the same receptor, ACE2, according to later structural investigations (Wan *et al.* 2020). Both the S1 and S2 domains found in coronavirus

spike proteins are essential for receptor binding and cell membrane fusion, respectively. There are around 50 amino acids in the S1 domains of SARS and SARSCoV-2 that are shared by other bat-derived viruses (Lu *et al.* 2020).

SARS' potential to transmit from person to person has been bolstered by the finding of residues that alter the SARS receptor binding domain's interaction with ACE2 (Wan *et al.* 2020). Despite the fact that the receptor binding SARS-CoV-2 spike gene sequence is more similar to that of SARSCoV, SARS is more closely connected with bat-SL-CoVZC45 at the complete chromosomal level than (Lu *et al.* 2020).

Species specificity, on the other hand, is created by a procedure that goes beyond just recognizing receptors. Immediately after the SARS virus binds to its receptor, the host's immune system begins to respond. In order to successfully infect a new host, SARS must be able to dodge or overcome innate immune signals. Although the process by which SARS evades the immune system and proceeds to illness is still largely unknown. CoV-2 may have a same pathogenic mechanism, considering the similarity between COVID-19 symptoms and SARS symptoms. An increase in ISGs is induced by SARS-CoV infection, and this increases the production of type IFN. SARSCoV encodes at least eight viral antagonists that impede IFN induction in order to avoid the antiviral effects of IFN and cytokines (Totura *et al.* 2012).

Antiviral and immune system responses to viral infection need to be controlled in order to restrict viral growth and dissemination. Pathogenesis occurs as a consequence of the virus' lytic effects on host cells and the overreaction of the immune system. Patients with severe pneumonia have been observed in study, with fever and a dry cough being the most prevalent early signs. Patients with ARDS and septic shock advanced fast, resulting to multiorgan failure and death in around 10 percent of patients (Chen et al. 2020.

SARS-CoV-2 may have entered the human body via the airway ciliated epithelium and alveolar type II (pulmonary cells that create pulmonary surfactant) because of the presence of ACE2 on these cells in humans (Hamming *et al.* 2004). A similar

inflammatory destruction pattern is documented in SARS and COVID-19 patients Serum from SARS patients exhibited increased levels of cytokines. Lung inflammation and significant injury are connected with these cytokines (Wong *et al.* 2004). SARS-CoV-2-infected patients have been shown to have elevated blood cytokines (Huang *et al.* 2020).

Because the GSCF and TNF levels in ICU patients are so much higher than in the general population, this suggests that a cytokine storm may be to blame for the severity of the illness. Anti-inflammatory cytokines were also found to be strong in these people, which was unexpected for someone with a viral infection. There are just a few reports of SARS-CoV-2 infection among children, and the virus mostly affects older men (Huang *et al.* 2020). A recent study shows that SARS-CoV is more likely to infect elderly Cynomolgus macaques than young ones in monkey models of the virus (Smits *et al.* 2010).

2.1.6 Diagnosis

In accordance with the China National Health Commission, the diagnosis of COVID-19 sickness is made based on the disease's epidemiological history, clinical symptoms, and confirmed SARS infection using one of the following methods: Analyzing IgM and IgG antibodies using RT-PCR, high-throughput genotyping, and serological testing (Shen and Yang 2020, Zu *et al.* 2020). Diagnosis in COVID-19 Suspected Cases.

All demographic and clinical criteria for SARS-CoV-2 infection should be satisfied before a diagnosis can be made.

Close relatives of COVID-19 cases; neonates born to definite COVID-19 mothers; and anybody who has a fever or respiratory difficulties who has had contact with the epidemic city cases related to a group outbreak. Chronic cough, fatigue, and a low granulocyte or lymphocyte count are all common in the early stages of infection with COVID-19. If no other infectious agents are found, the symptoms of infection with

COVID-19 can be explained by the presence of I fever (reduced fever or normal temperature in some cases), chronic cough, and fatigue (Singhal *et al.* 2020, Shen and Yang 2020).

- COVID-19 has been confirmed

Diagnosis People should be on the lookout for if any of the following apply: Airway or serum genetic sequencing is extremely comparable to the known SARS-CoV-2 genome, as validated by RT-PCR in both samples. SARS-CoV-2 was found in both samples (Shen and Yang 2020).

- Evaluation in a laboratory

SARS-CoV-2 RNA may be detected using RT-PCR. SARS-CoV-2 ribonucleic acids were found in throat swabs, sputum, lower airway secretions, stool, and blood samples. " There is no difference in viral load between symptomatic and asymptomatic individuals, according to studies, between the nasal cavity and the throat (Zou *et al.* 2020). If an oropharyngeal swab is taken, it should be preserved in the same container as nasopharyngeal swab samples; if not, it should be discarded. Despite CT findings suggestive of viral pneumonia and negative RT-PCR results from oropharyngeal swabs in numerous cases, SARS-CoV-2 was subsequently found to be positive in other cases. Swabs from the nasopharynx should be taken to test for SARS-CoV-2, according to the CDC (IGC 2019).

Sputum should only be collected from people who have a productive cough, not from those who have been forced to cough up sputum. If initial testing is negative but COVID-19 concerns linger, the WHO suggests collecting and reviewing samples from several airway locations for further testing. A serological test for SARS-CoV-2 should be used instead of a ribonucleic acid test since ribonucleic acid testing might provide false negative findings (Tang *et al.* 2020). Radiographic lung abnormalities were found

in a patient with typical clinical symptoms and IgG and IgM antibodies to SARS-CoV-2 but negative four-time RT-PCR testing for the disease (Dong *et al.* 2020).

2.1.7 Treatment

COVID-19 patients get individualized treatment that is based on their unique set of symptoms; there is no one-size-fits-all cure for this disease. Researchers and doctors treating COVID19 patients correctly (Zumla *et al.* 2020). Researchers are testing antiviral drugs, immunosuppressants, monoclonal antibodies, and vaccines (Bhavana *et al.* 2020).

To limit SARS-CoV-2 viral replication, the patient's immune system is challenged early on; nonetheless, tissue damage due to severe immunological/inflammatory responses may occur in the acute phases of the illness (Tufan *et al.* 2020). According to clinical data, antiviral drugs are most effective in the early stages of the illness. In contrast, it is expected that immunosuppressive/anti-inflammatory medication will be most effective in COVID-19's most severe stages. It is more effective in the early stages of SARS-CoV-2 infection to use anti-SARS-CoV-2 antibody-based treatment. SARS-CoV-2 monoclonal antibodies are recommended as a consequence (Mansourabadi *et al.* 2020).

The US Food and Drug Administration has given the green light to the use of Dexamethasone and Remdesivir (FDA). Additionally, it's recommended for those people in the hospital who are in need of extra oxygen (Chorin *et al.* 2020). Remdesivir is an intravenous nucleotide medicine produced from adenosine analogues. Remdesivir's route of action against the SARS-CoV-2 virus is shown in (Figure 2.3). An antiviral compound known as Remdesivir inhibits viral replication by prematurely stopping the transcription of the viral genome, as shown in the case of HIV (Figure 2.3). Corticosteroid Dexamethasone has a significant influence on the recovery of patients during the acute phase of illness, when they are dependent on mechanical ventilation (Pasin *et al.* 2021).

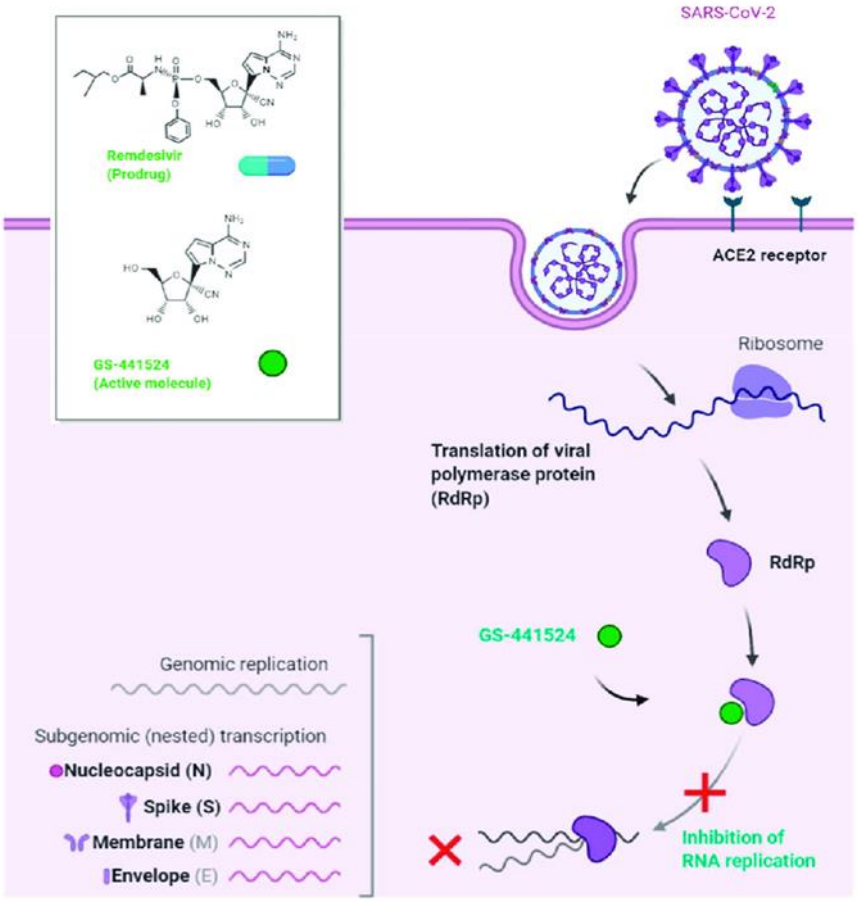

Figure 2.3 Remdesivir's putative method of action against coronavirus replication (Pasin *et al.* 2021)

3. MATERIALS AND METHODS

An instrumentation Table 3.1 is provided below for your reference.

Table 3.1 Instruments utilized in this study are listed in the table below

Instruments and glasses	Company	Country
ELISA	Labon	China
Spectrophotometer	Biobase	India
Centrifuge	Memmert	Germany
Light microscope	Olympus	Japan
Oven	Memmert	Germany
Water bath	Memmert	Germany
Shaking water bath	Memmert	Germany
Sysmex device	Sysmax	Japan
Pipette	BioSan	Germany
Different glasses	-----	China
Refrigerator	BEKO	Turkey

3.1 Patients

60 subjects (pregnant female) patients suffering from COVID-19 infection and 30 pregnant female (as control) were used in this study. The study was done in different hospitals in Kirkuk city, in the period from January 2022 to April 2022. The subjects were dividing as follow:

- First group: 30 sample as healthy pregnant female.
- Second group: 30 sample of infected pregnant female with age 18 to 30 years.
- Third group: 30 sample of infected pregnant female with age 30 to 40 years.

3.2 Blood Samplings

After 10-12 hours of fasting, specimens were tested from participants in this study (pregnant female). Before centrifugation, serum samples were preserved in Gold-top SST and EDTA tubes. Since being centrifuged at 3500 rpm for 10 minutes, the serum samples were extracted and kept in Eppendorf tubes. All samples were dissolved once the specimen collection procedures were completed in preparing them for bioassay.

3.3 Hematological Analysis

The impedance approach was used to measure the concentrations of leukocytes (WBC), erythrocytes (RBC), and platelets (PLT) using a hematological analyzer. Photometric measurement technology is used to determine the hemoglobin (HGB) concentration of red blood cells. Using optical laser-based flow cytometric technology, a five-part leukocyte difference (LYM percent, MON percent, NEU percent, EOS percent, BAS percent) is achieved.

3.4 Biochemical Analysis

3.4.1 Liver enzymes

- Estimate ALT

As stated in Table 3.2 spectrophotometry was used to measure alanine aminotransferase.

Table 3.2 Steps of ALT procedure

Sample	50 µL
Reagent R	1000 µL
After mixing, incubate for two minutes. The fluctuation in absorbance (at 340 nm) was recorded every minute for a period of three minutes at a temperature of 37 degrees Celsius. Absorbance fluctuation per minute (ΔA/min) may be calculated	

The activity of ALT is computed using the following Equation 3.1:

$$(\Delta A/min)\ x\ Factor \tag{3.1}$$

- Estimate AST

As stated in Table 3.3 spectrophotometry was used to measure aspartate aminotransferase.

Table 3.3 Steps of AST procedure

Sample	50 µL
Reagent R	1000 µL
After mixing, incubate for two minutes. The fluctuation in absorbance (at 340 nm) was recorded every minute for a period of three minutes at a temperature of 37 degrees Celsius. Absorbance fluctuation per minute (ΔA/min) may be calculated	

The activity of AST is computed using the following Equation 3.2:

$$(\Delta A/min)\ x\ Factor \tag{3.2}$$

- Estimate ALP

As stated in Table 3.4 spectrophotometry was used to measure Alkaline phosphatase.

Table 3.4 Steps of ALP procedure

Sample	50 µL
Reagent R	1000 µL
After mixing, incubate for two minutes. The fluctuation in absorbance (at 340 nm) was recorded every minute for a period of three minutes at a temperature of 37 degrees Celsius. Absorbance fluctuation per minute (ΔA/min) may be calculated	

The activity of ALP is computed using the following Equation 3.3:

$$(\Delta A/min)\ x\ Factor \tag{3.3}$$

3.4.2 Total protein

The reaction reagent, specimens were all incubated at 37°C under reaction conditions. Following that, the additions were made in line with the Table 3.5.

Table 3.5 Steps for making albumin

Working reagent	1 mL
Sample or standard	20 µL
After 5 minutes of mixing the serum with the test agent, the absorbance was measured at 550 nm	

The concentration of total protein is calculated according to the Equation 3.4:

$$Results = sample / standard \; x \; C \; Standard = mg/dL \quad (3.4)$$

3.4.3 Albumin

The reaction reagent, specimens were all incubated at 37°C under reaction conditions. Following that, the additions were made in line with the Table 3.6.

Table 3.6 Steps for making albumin

Working reagent	1 mL
Sample or standard	5 µL
After 5 minutes of mixing the serum with the test agent, the absorbance was measured at 630 nm	

The concentration of albumin is calculated according to the Equation 3.5:

$$Results = sample / standard \; x \; C \; Standard = mg/dL \quad (3.5)$$

3.4.4 Vitamin D3

Solid phase enzyme-linked immunoassay (ELISA) based on the competitive binding principle, the 25(OH) Vitamin D ELISA kit.

Procedure:

- Using 10 mL of 25(OH) D Standards, and specimens, fill each well as needed.

- Using 200 mL of 1x biotinylated 25 (OH) D reagent, fill each well.
- Using a plate shaker set to 200–400 rpm, carefully mix the solution in wells for 20 seconds.
- Incubate plate for 90 min at 18–26 °C.
- Using 300 mL of 1x Wash Buffer, fill each well and discard the contents.
- 200 mL of Enzyme Conjugate into each well and incubate for 30 min at 18–26 °C.
- The materials of wells should be deleted.

Results:

The standard curve given by the kit manufacturer is used to extract the vitamin D3 level in each of the trial samples Figure 3.1.

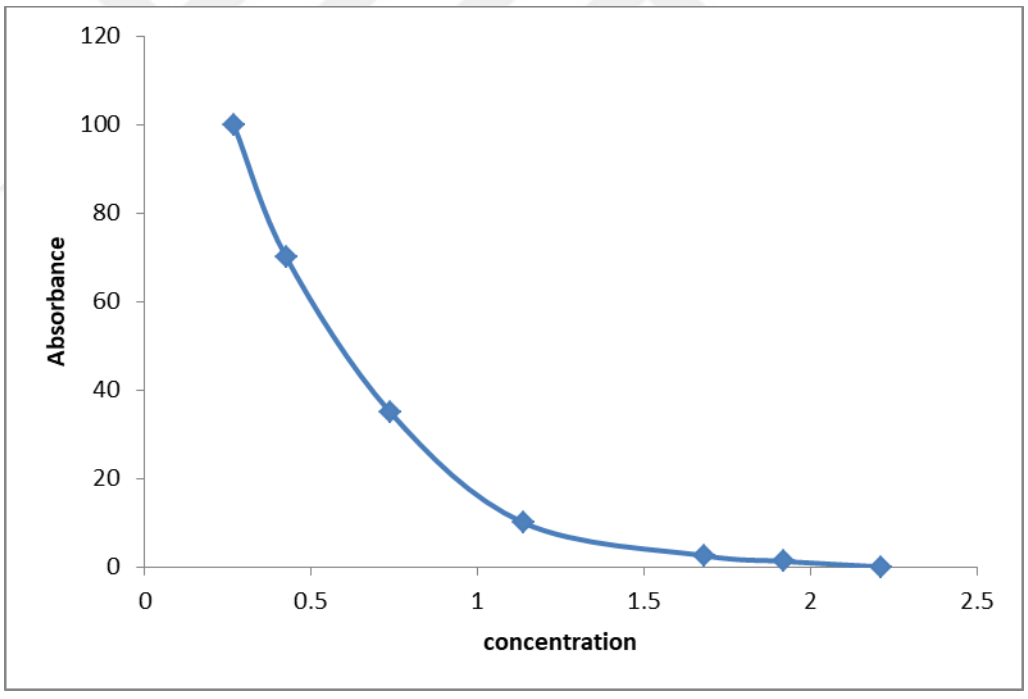

Figure 3.1 Standard curve for vitamin D3 concentration determination

3.5 Statistical Analysis

Minitab, a statistical analysis program, and Excel, a spreadsheet program, were used to statistically analyze the data. The information was presented as a mean standard deviation. The current study's findings were statistically investigated using the ANOVA test and the Dunkin' multiple test to detect significant differences between test group by comparing their arithmetic averages.

The impedance approach was used to measure the concentrations of WBC, and RBC, using a hematological analyzer. Photometric measurement technology is used to determine the hemoglobin (HGB) concentration of red blood cells. Using optical laser-based flow cytometric technology, a five-part leukocyte difference (LYM percent, MON percent, NEU percent, EOS percent, BAS percent) is achieved.

4. RESULTS AND DISCUSSION

4.1 Hematological Study

Table 4.1 exhibited a significant (P <0.05) reduce in the count of RBC in patients compared to control group, as the count of RBC in COVID individuals was (4.16±0.172; 4.09±0.078), while its concentration in the control group was (5.398±0.36) Figure 4.1 and Figure 4.2. The results shows a significant (P <0.05) reduce in Hb concentration in patients (12.033±0.261; 12.15±0.32) compared to control group (14.592±0.78).The results shows a significant (P <0.05) reduce in percentage of PCV in patients (36.472±2.361; 35.017±1.74) compared to control group (43.271±3.461). The results shows a significant (P <0.05) reduce in percent of MCV in patients (62.285±5.891; 64.45±4.86) compared to control group (81.394±9.773) Figure 4.3 and Figure 4.4.

Table 4.1 Hematological parameters in studied groups

Parameter	First group	Second group	Third group	P-Value
RBC	5.398±0.36	4.16±0.172*	4.09±0.078*	0.0001
Hb	14.592±0.78	12.033±0.261*	12.15±0.32*	0.0319
PCV	43.271±3.461	36.472±2.361*	35.017±1.74*	0.017
MCV	81.394±9.773	62.285±5.891*	64.45±4.86*	0.001

Table 4.2 exhibited a significant (P <0.05) increased in the count of WBC in patients (11.515±0.99; 11.417±2.34) compared to control group (7.574±0.395).the percentage of neutrophil shows a significant (P <0.05) increased in patients (83.51±4.81; 81.84±3.67) compared to control group (64.01±6.79).the percent of lymphocytes shows a significant (P <0.05) reduced in patients (15.71±2.18; 14.65±2.05) compared to control group (28.05±2.36). Whereas, the percent of eosinophil shows non-significant (P <0.05) changes in patients (2.5±1.73; 2.42±1.93) compared to control group (3.2±1.92).the percent of basophil shows non-significant (P <0.05) changes in patients (0.286±0.488; 0.385±0.265) compared to control group (0.571±0.535).the percent of monocytes shows non-significant (P <0.05) changes in patients (3.6±2.074; 3.52±2.154) compared to

control group (4.167±1.941) Figure 4.5, Figure 4.6, Figure 4.7, Figure 4.8, Figure 4.9 and Figure 4.10.

Table 4.2 WBC count and differentiation in studied groups

Parameter	First group	Second group	Third group	P-Value
WBC	7.574±0.395	11.515±0.99*	11.417±2.34*	0.0001
Neutrophil	64.01±6.79	83.51±4.81*	81.84±3.67*	0.0001
Lymphocytes	28.05±2.36	15.71±2.18*	14.65±2.05*	0.001
Eosinophil	3.2±1.92	2.5±1.73*	2.42±1.93*	0.589
Basophil	0.571±0.535	0.286±0.488*	0.385±0.265*	0.317
Monocytes	4.167±1.941	3.6±2.074*	3.52±2.154*	0.651

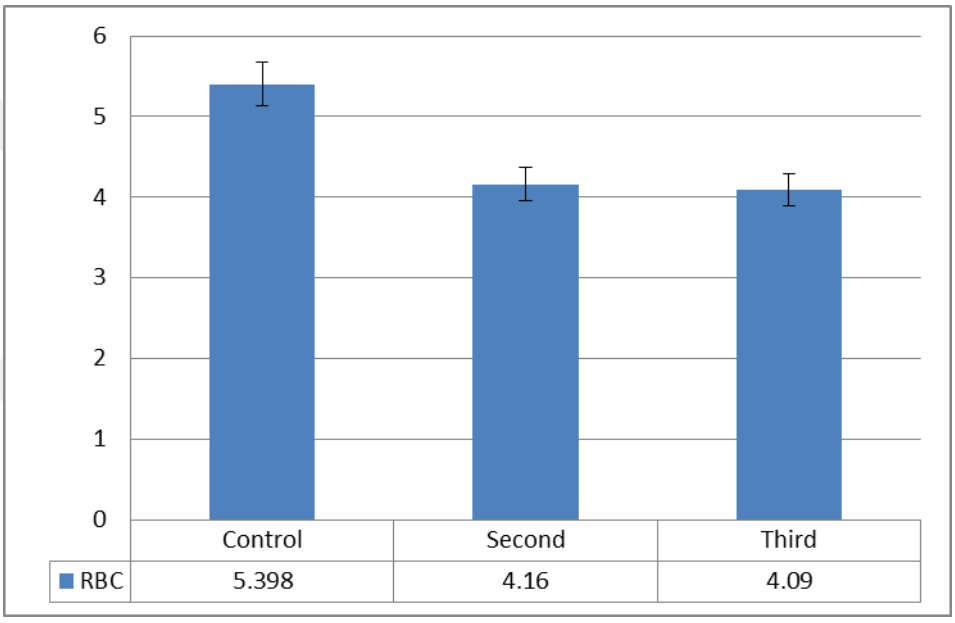

Figure 4.1 RBC count in both groups

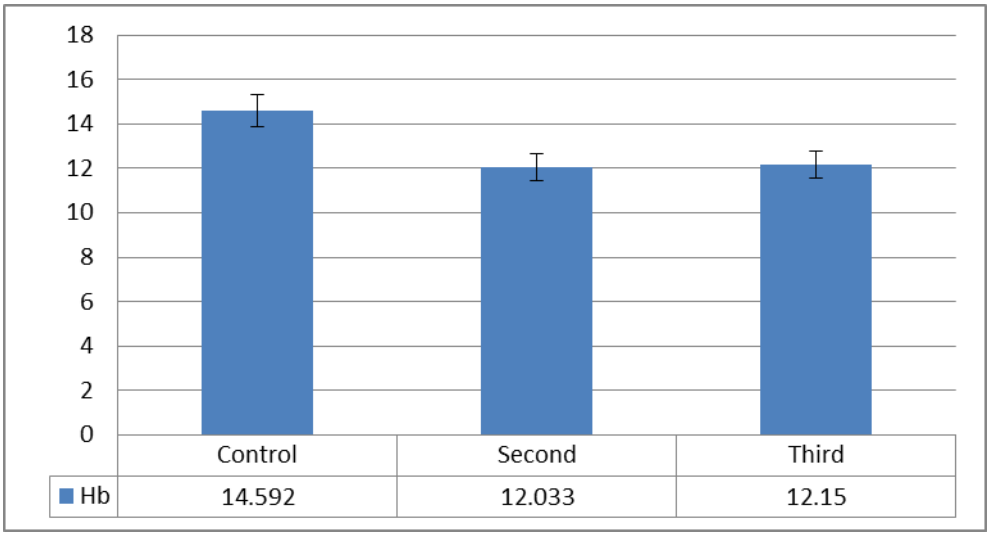

Figure 4.2 Hemoglobin in both groups

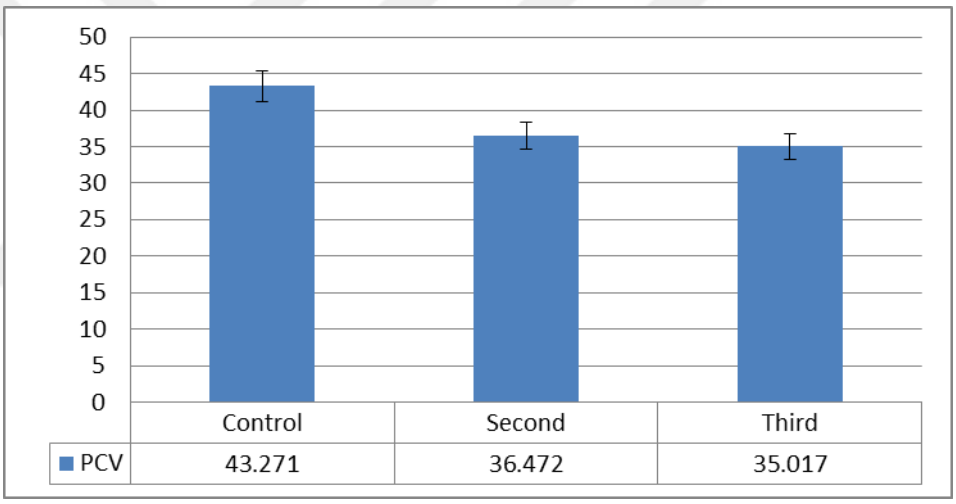

Figure 4.3 PCV percent counts in both groups

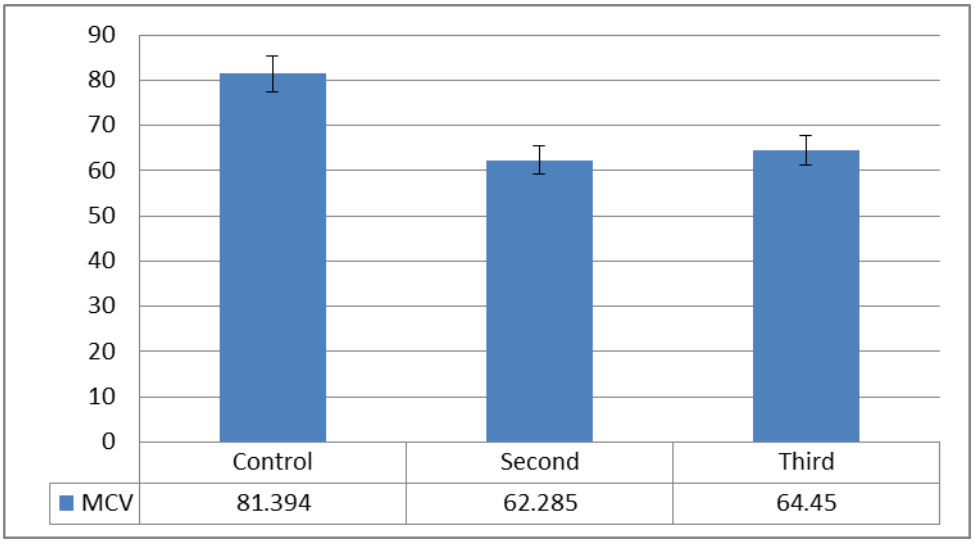

Figure 4.4 MCV percentages in both groups

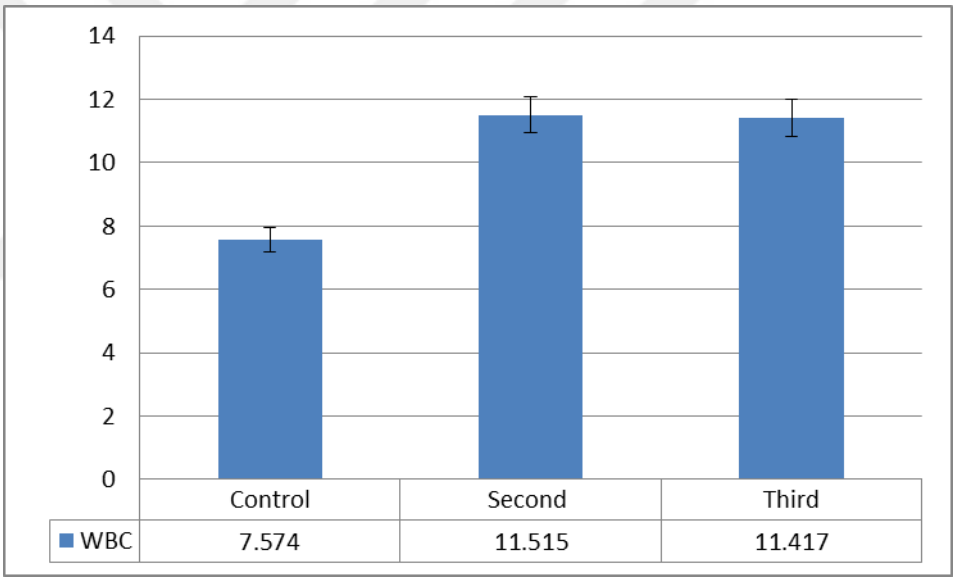

Figure 4.5 WBC counts in both groups

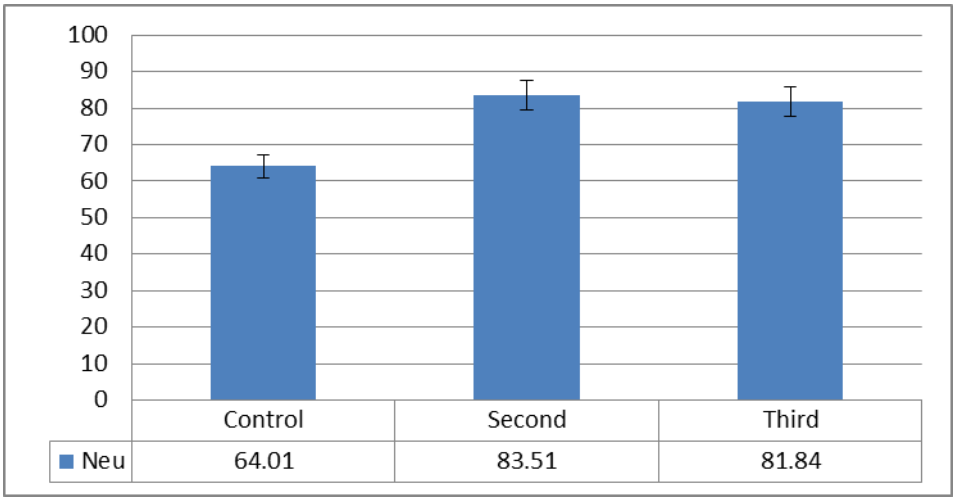

Figure 4.6 Neutrophil percentages in both groups

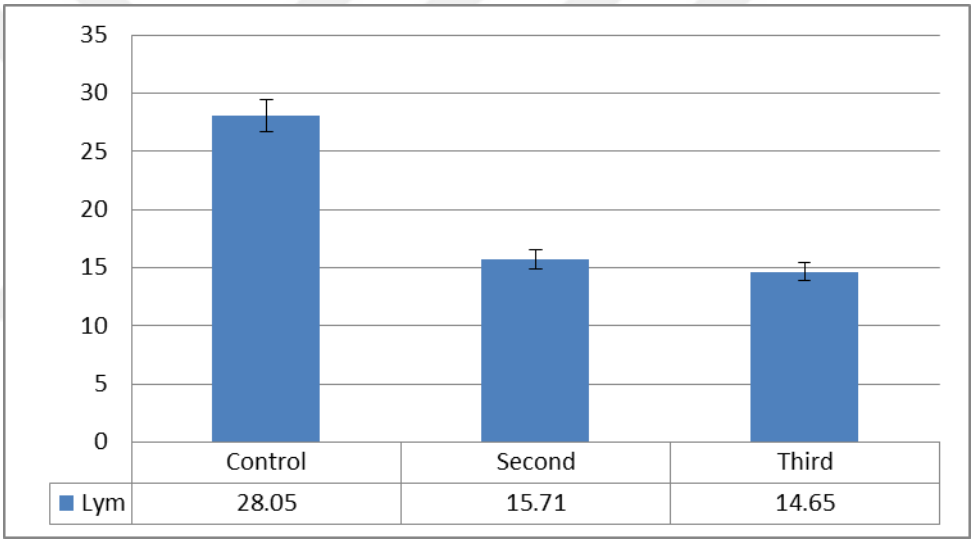

Figure 4.7 Lymphocytes percentage in both groups

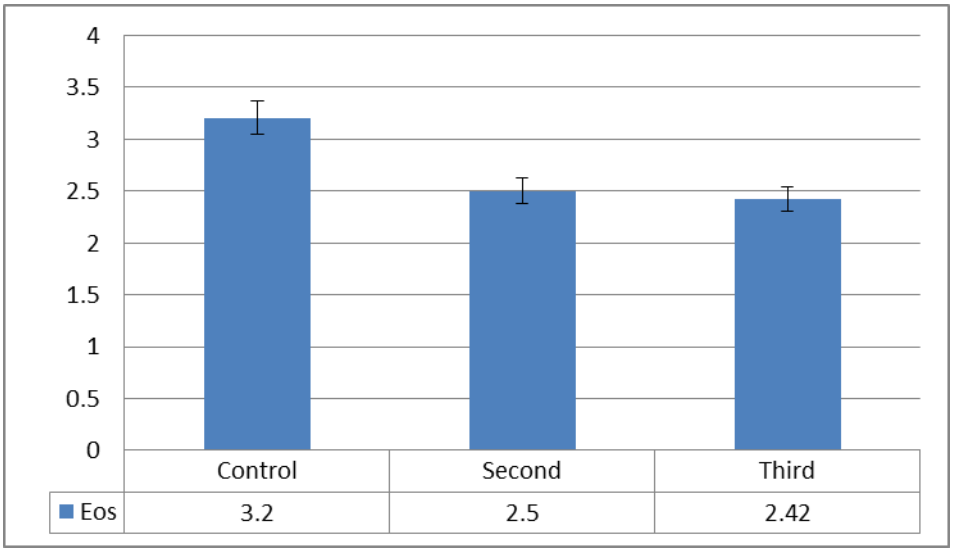

Figure 4.8 Eosinophil percentages in both groups

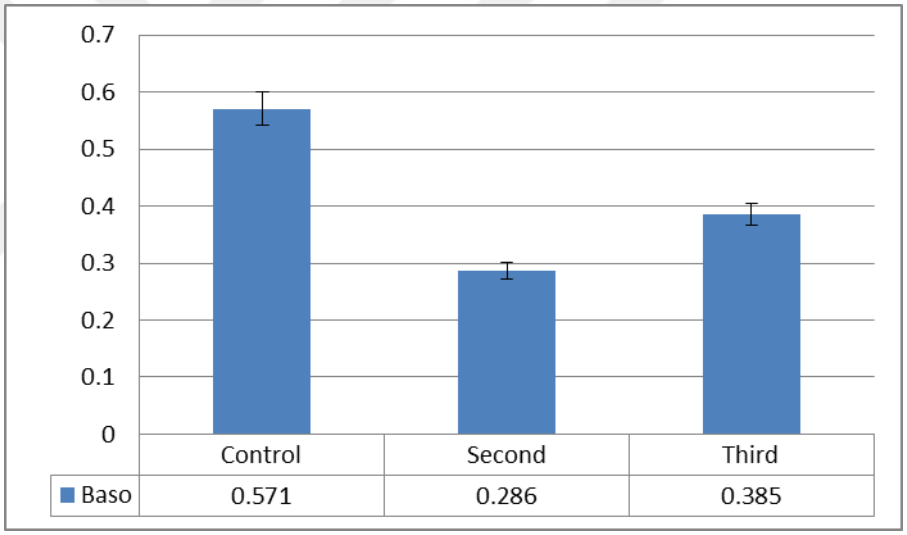

Figure 4.9 Lymphocytes percentage in both groups

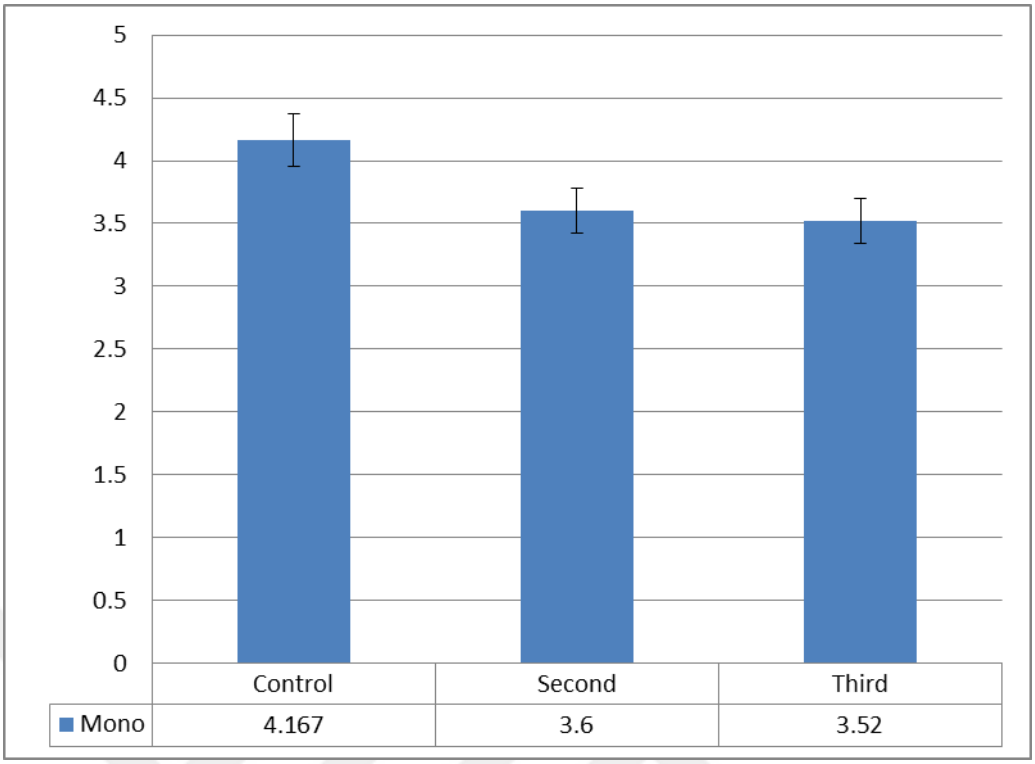

Figure 4.10 Eosinophil percentages in both groups

According to the present research, COVID-19 participants' hematological values were all significantly lower than those of controls. Another research found that COVID-19 patients had considerably reduced RBC and Hb, as well as a quick reduction in Hb and RBC in COVID-19 patients. This result is consistent with these data" (Berzuini *et al.* 2021). Patients with severe COVID-19 were shown to have considerably reduced red blood cell parameters (Mei *et al.* 2020). When COVID-19 causes anemia, it isn't clear exactly how. However, it's widely believed that the disease inhibits the bone marrow's ability to produce blood cells.

Hb levels were higher in COVID-19-positive patients compared to COVID-19-negative individuals, according to the study (Usul *et al.* 2020). If our findings vary from those of other researchers, it might be because of variations in the study population, such the prevalence of underlying chronic health disorders and smoking. Such issues were not subject to any exclusionary criterion (Rossato and Vincenzo 2020).

Many of the COVID-19 patients who were admitted to the hospital had normal CBCs when they arrived, according to (Fan 2020). (normal Hb, and WBC). Individuals in the COVID-19 study exhibited considerably higher RDW levels than those in the control group.

Type 2 pneumocytes, renal epithelial cells, lymphocytes, and other cells with ACE receptors may all be found throughout the body. It is possible that the virus is responsible for the elevated levels of cytokines such as IFN-induced protein 10, monocyte chemoattractant protein 1, macrophage inflammatory protein 1, and tumor necrosis factor. It results in ARDS and the failure of several organs. It's been reported that this has happened (Rothan and Byrareddy 2020, Li *et al.* 2020, Huang *et al.* 2020).

The presence of neutrophilia and/or lymphocytopenia in COVID-19 pneumonia has been linked to poor results in several investigations. In the early stages of the SARS CoV-2 infection, the neutrophil to lymphocyte ratio (NLR) predicts disease severity. Patients with severe illness had considerably fewer granulocytes than healthy individuals (Khartabil *et al.* 2020).

As infections and tissue damage increase, the blood's neutrophil population rises. Forty-nine COVID-19 patients had higher neutrophil counts on the first day, although these levels dropped before or shortly after therapy in most cases. There were dark-like toxic granules in the cytoplasm and light blue agranular areas on the cells' periphery in neutrophils from COVID-19 patients. Some of the patients in this condition had low neutrophil counts. It is common to see neutrophil depletion in nuclear smears as well as granular changes in peripheral blood smears.

When Covid-19 patients arrived at the hospital, they had immature granulocytes and metamyelocytes. There were also two cases when neutrophil peroxidase activity was significantly reduced. In 5-7 days of treatment with antivirals, the aforementioned alterations were completely reversed. A substantial number of apoptotic cells were found in blood smears from COVID-19 patients.

Researchers Sadigh et al. (2020) found that the number of smeared neutrophils was considerably higher in COVID-19 patients than in healthy controls in a study of 78 peripheral blood smears. COVID-19 individuals were also shown to have granulocytic responses that were immature and dysmorphic. Leukocytosis was shown to be associated with an increased risk of respiratory syndrome, mortality, and an elevated troponin in a review research (Terpos 2020). Another study found that NLR ratios were greater in COVID-19 patients than in healthy controls (Kong *et al.* 2020).

WBC levels are normal or much lower in the early stages of COVID-19 when there are no symptoms, but these indications may alter as the illness progresses, according to study (Fan *et al.* 2020, Zhang *et al.* 2020). The wbc count was within normal ranges in 68.1 percent of patients and raised in 12.3 percent of the patient population in a study of 140 hospitalized patients identified with COVID-19 using CT scan results, researchers discovered. Although leukopenia has been reported to range between 28.1% and 68.1% in various studies, this shows that there may be a correlation between leukopenia and the result of COVID-19 (Wang *et al.* 2020, Abdo-Cuza *et al.* 2020, Khaled and Hafez 2020).

In the COVID-19 experiment, which was conducted in Wuhan, China, patients with ischemia had a higher wbc count than those without ischemia. In COVID-19 individuals with higher troponin levels, researchers found a connection between the disease and the percentage of white blood cells (WBCs) (Zheng *et al.* 2020).

RT-PCR-positive individuals exhibited lower absolute WBC counts than RT-PCR-negative individuals, according to the results of (Mardani *et al.* 2020). Non-survivors had higher white blood cell counts than survivors in a study by Javanian et al. Researchers found a link between a higher CRP and a higher mortality risk for those with lymphoma and a low WBC count (Javanian *et al.* 2020). Henry et almeta-analysis .'s claims that There was a substantial difference in the WBC count between non-survivors of COVID-19 and survivors. According to their meta-analysis, the WBC count increases somewhat in patients with severe COVID-19, but a considerable rise may indicate a bad clinical prognosis.

According to a research by (Fan *et al.* 2020), reactive lymphocytes were discovered in 69 percent of individuals who had lymphocytes redaction, as well as in 69 percent of those who were infected with COVID-19 (Lymphopl-asmacytoid). ICU patients had lower CD45+, 19+, 8+, 4+, and 16/56+ levels than non-ICU patients, according to the study. The CD4+/8+ ratio was unaffected in any of the patients, as it was with other viral diseases including HIV and CMV. The fact that patients with COVID-19 had decreased amounts of total lymphocytes, T and B lymphocytes, and NK lymphocytes compared to healthy persons is also noteworthy (Chan *et al.* 2020). This suggests that SARS-CoV-2 pathogenesis and lymphocyte modification are likely to be linked.

Additionally, the COVID-19 ICU patients had significantly less lymphocytes, CD4+ T cells, and B cells than the control group (Chan *et al.* 2020). More research is needed to determine if lymphopenia is a risk factor for sickness severity or mortality. Results showed that there was a correlation between the degree of lymphocyte redaction and the need for ICU stays (Zhang *et al.* 2020, Huang *et al.* 2020).

While in the hospital, patients who have significant lymphopenia are more likely to die. At the time of admission or while in the hospital, the severity of COVID-19 may be linked to a drop in the Lymphocyte/WBC ratio An investigation by Zhao et al. 2020 found that individuals with lymphopenia were three times more likely to have severe COVID-19. In addition, researchers found that COVID-19 patients had a decreased amount of suppressor T cells. They also discovered a correlation between the severity of COVID-19 and a reduction in T helper concentrations. Those with COVID-19 had higher T helper percentages, whereas those with severe instances had lower memory T helper percentages. In addition, there were significantly less regulatory T cells in COVID-19 patients.

Although the reduction in circulating T lymphocytes during inflammatory responses or the use of steroids might explain lymphopenia linked with COVID-19, other theories have been presented. Lymphocyte lysis and lymphopenia may be caused by SARS-CoV-2 infection, which has the capacity to infect lymphocytes directly. Because ACE2 and CD147 are expressed on the cell membranes (Watanabe *et al.* 2010). A new set of

clinical symptoms emerges 7-14 days after the initial signs show, and they are connected to rising levels of pro-inflammatory mediators (Liu *et al.* 2020).

Another idea proposes that increased cytokine activity causes secondary lymphoid organs like the spleen to shrink and cell renewal to be disrupted, leading to leukopenia. This, in turn, increases FAS expression and apoptosis. IL-6, TNF-alpha, and IFN-alpha levels in the circulation have a negative connection with lymphoma count (Giamarellos-Bourboulis *et al.* 2020).

4.2 Liver Enzymes

Table 4.1 shows a significant (P <0.05) increase in the activity of ALT in patients compared to control group, as the concentration in the serum of patients was (63.49±4.21; 68.14±5.08), while its concentration in the control group was (25.17±2.14) (fig: 4-1). The results shows a significant (P <0.05) increase in the activity of AST in patients (58.31±5.58; 63.47±7.89) compared to control group (21.85±9.05).The results shows a significant (P <0.05) increase in the activity of ALP in patients (105.48±15.58; 119.37±11.9) compared to control group (51.37±6.47).

Table 4.3 Liver enzymes in studied groups

Parameter	First group	Second group	Third group	P-Value
ALT	25.17±2.14	63.49±4.21*	68.14±5.08*	0.0001
AST	21.85±9.05	58.31±5.58*	63.47±7.89*	0.0001
ALP	51.37±6.47	105.48±15.58*	119.37±11.9*	0.0001

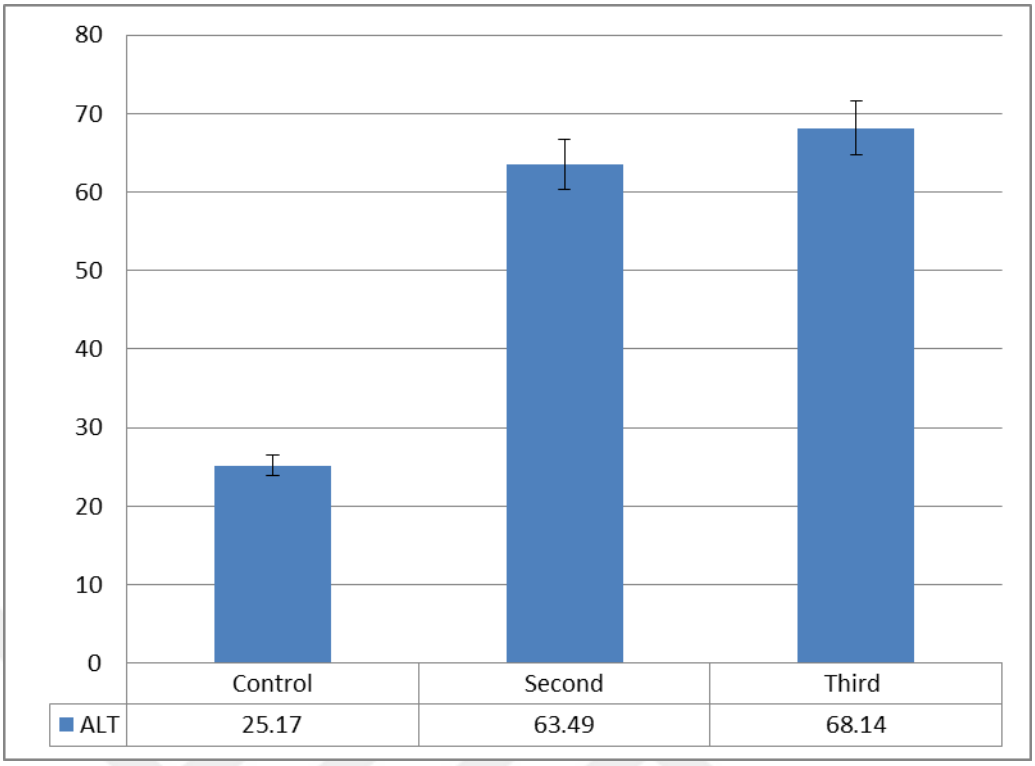

Figure 4.11 ALT activities in both groups

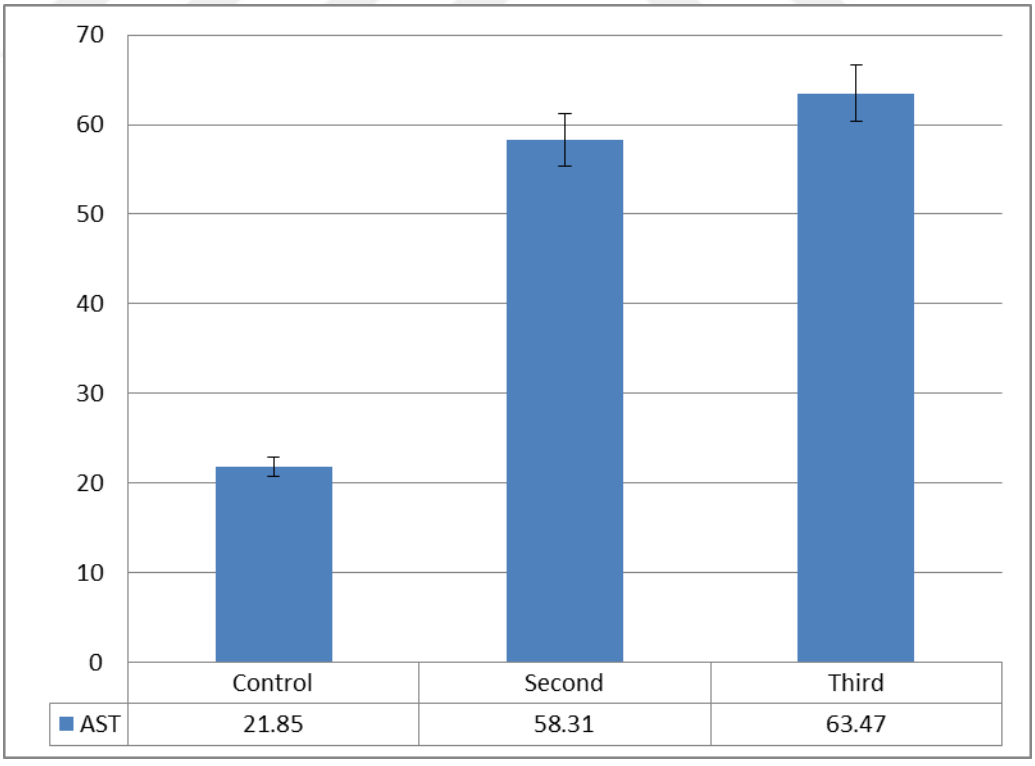

Figure 4.12 AST activity in both groups

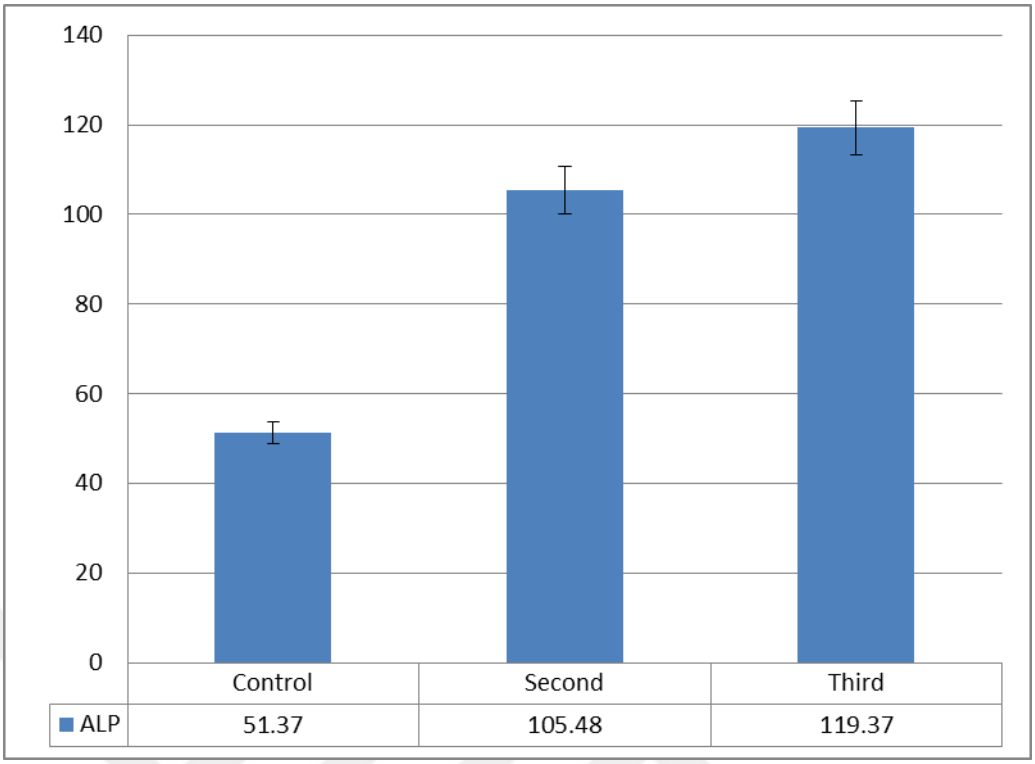

Figure 4.13 ALP activity in both groups

The current findings revealed that pregnant women infected with COVID19 had higher levels of liver enzymes. According to (Chen *et al.* 2020), the mean rate of ALT was 39.0, and the appropriate level of AST was 34.0 in 99 subjects with infection of COVID-19 in the Wuhan area. Total bilirubin was 15.1 on average, and liver parameters were only slightly elevated, which is consistent with the current study.

Zhang *et al.* (2020) Only one of the 115 COVID-19 patients evaluated in Wuhan had ALT levels over 150 u/L, and only one had ALT levels above 100 u/L. In 17 instances, AST levels rose to 40–120 U/L; TBIL levels rose to 21–31.5 mol/L in seven cases; ALP levels rose to 120–300 U/L in six cases; and GGT levels rose to 142.5 U/L in three cases. Wang et al. found that ICU patients had higher ALT and AST values than non-ICU patients (35 vs 23, P=0.007 and 52 vs 29, P0.001, respectively) (Wang *et al.* 2020).

Filipe S. Cardoso detailed the state of liver damage in people who were seriously ill. A 10-day stay in the ICU resulted in a rise in ALT and AST values, however the highest was never more than twice the upper limit. Although the rise in GGT was gradual, it

finally reached three times the upper limit of what is considered normal. After being admitted to the ICU, the median GGT peak occurred eight days later. Late cholestasis was a prevalent complication of liver disease in the general population (Cardoso *et al.* 2020).

Similar results were found by (Cai *et al.* 2020). In Shenzhen, 417 COVID-19 suspects were questioned. Abnormal liver test results more than two standard deviations over the upper normal limit were seen in a small percentage of individuals (4%). One-to-two times the normal upper limit level was found in 12.71 percent of cases, two-to-three times the normal top limit level was found in 1.2 percent of cases, and three-to-four times the normal upper limit value was found in 10 instances in 2.4% of cases.

There were 25 fatalities among individuals infected with COVID-19 (Li *et al.* 2020). The average ALT and AST values in these individuals were 24 and 37 U/L, respectively, and liver function was only mildly reduced, despite the fact that almost all patients had decreased albumin 32.8 mol/L in the bloodstream. For 60 COVID-19 individuals, (Bloom *et al.* 2020) examined the ALT and AST change patterns over time and found that the change trends were almost equal. It may slightly increase over time, peaking on the ninth day of admission and then progressively decreasing, with an expanding range of no more than 40 U/L over the course of longer time.

4.3 Total Protein and Albumin

Table 4.4 demonstrated a significant ($P < 0.05$) reduce in levels of ALT in patients compared to control group, as levels in the serum of patients was (6.21±0.14; 6.16±0.18), while its concentration in the control group was (7.04±0.38) (fig: 4-1). The results shows a significant ($P < 0.05$) reduced in levels of AST in patients (2.38±0.17; 2.32±0.11) compared to control group (3.14 ±0.25).

Table 4.4 Total protein and albumin in studied groups

Parameter	First group	Second group	Third group	P-Value
Total protein mg/dL	7.04±0.38	6.21±0.14*	6.16±0.18*	0.014
Albumin mg/dL	3.14 ±0.25	2.38±0.17*	2.32±0.11*	0.009

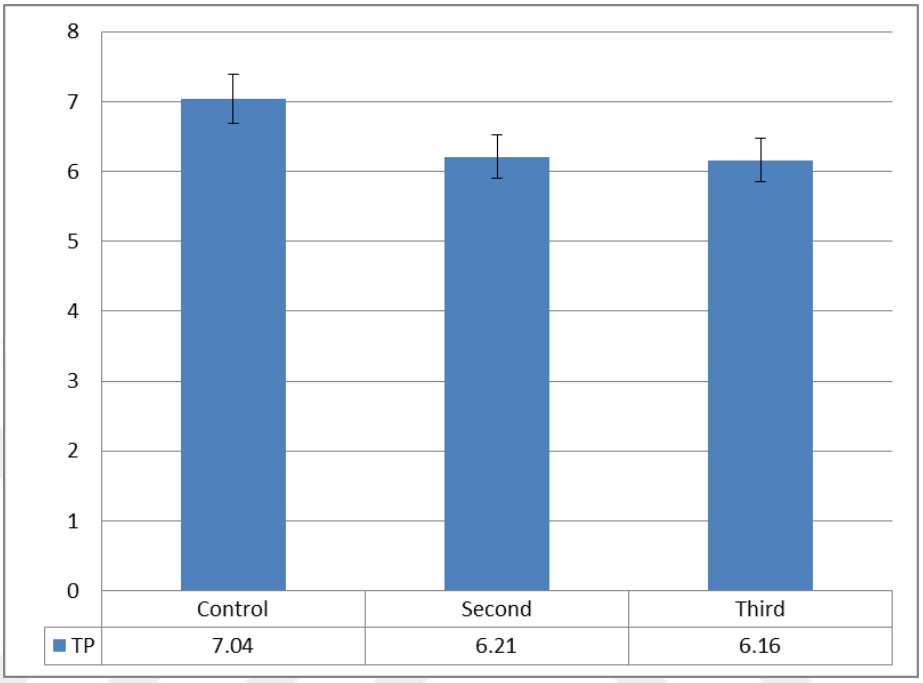

Figure 4.14 Total protein levels in both groups

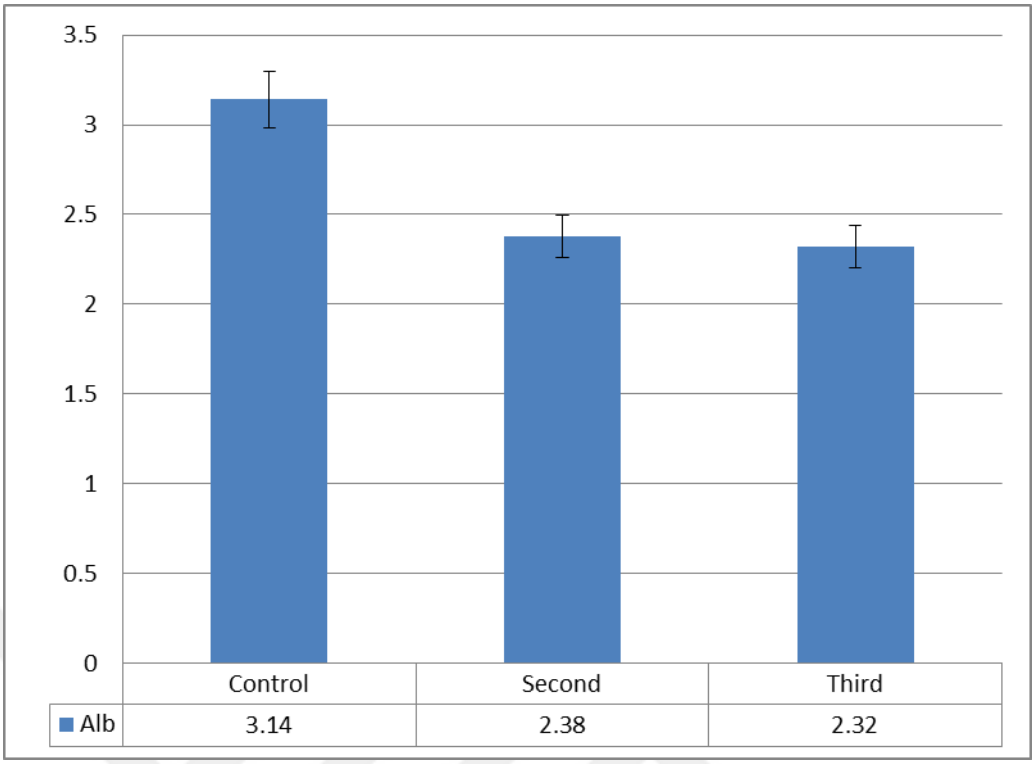

Figure 4.15 Albumin levels in both groups

Recent investigations have shown lower levels of total protein and albumin in pregnant women who were infected with COVID19. Compared to patients with normal liver enzyme levels, those who had liver damage and abnormally low levels of liver enzymes had significantly lower amounts of albumin and total protein (p00001). After the onset of COVID-19, the 'cytokine storm' released large acute-phase cytokines, which may be linked to decreased nutritional intake and the 'cytokine storm's involvement in lowering hepatic albumin production' (Ramadori 2020, Qian *et al.* 2019).

Hypoalbuminemia and severe COVID-19 infection are well-known to be associated (Aziz *et al.* 2020, Huang *et al.* 2020). Hypoalbuminemia exacerbates the dangers of infection with COVID-19 (Huang *et al.* 2020). As soon as an infection becomes severe, albumin breakdown in cells rises significantly (Bahar 2002). COVID19-induced hypoalbuminemia is a frequent problem (Huang *et al.* 2020). Serious COVID-19 patients had lower levels of serum albumin compared to mild cases (Danwang *et al.* 2020).

Other papers, on the other hand, suggested that albumin transfusion for COVID-19 treatment be used with caution until the exact mechanism of hypoalbuminemia was determined. The underlying role of albumin in individuals with infections of COVID-19 was investigated in a review of nine papers. Albumin transfusion therapy for COVID-19 people may have a modest benefit based on available evidence focused on ARDS and sepsis. According to a pilot study, albumin intake reduces hypercoagulability in COVID-19 subjects and avoids ischemic events (Violi *et al.* 2021).

The four patients' total protein levels were initially normal. It's worth noting that the average score was much lower than that of healthy people, which might be seen as another more indication that SARSCov-2 is affecting liver function. Total protein concentration decreased in three-quarters of COVID-19 patients in this study as a hepatocyte-produced protein. This modification added to the data that living lesion was a fairly typical occurrence in SARS-Cov-2 patients. (Jiang *et al.* 2008) discovered that the quantities of numerous proteins decreased in a SARS investigation. Such a consistent observation suggested that the pathogenic coronavirus might be responsible for protein metabolic problem.

4.4 Vitamin D3

Table 4.5 demonstrated a significant reduce in the concentration of D3 in the infected patients (10.31±2.17; 10.27±4.08 ng/ml) compared to the healthy persons (25.05±2.49 ng/ml).

Table 4.5 Concentration of Vit. D3 in studied groups

Parameter	First group	Second group	Third group	P-Value
Vit. D3	25.05±2.49	10.31±2.17*	10.27±4.08	0.0001

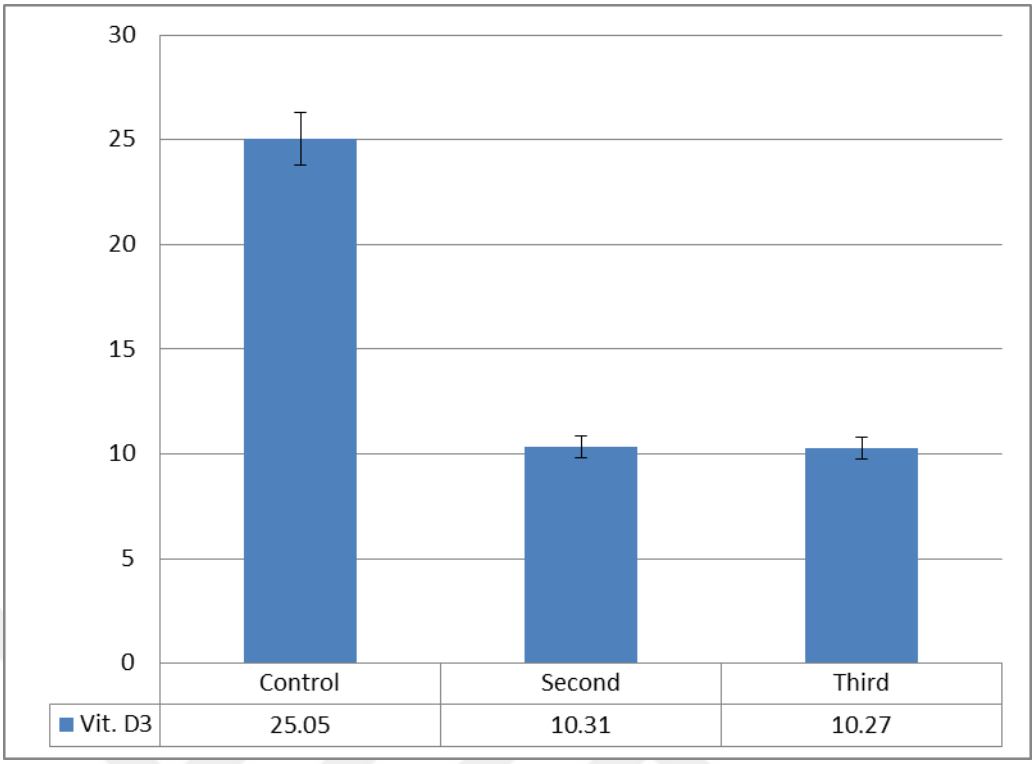

Figure 4.16 Vitamin D3 levels in both groups

Vitamin D is a lipophilic hormone that may be obtained from both food and sunlight. Vitamin D is not only involved in bone homeostasis but also in immune system response (White 2008). The respiratory alveolar epithelium serves as the first line of defense against inhaled pathogens. With alveolar macrophages and dendritic cells, it is one of the most significant players in innate immunity. They trigger intracellular signaling pathways that lead to antimicrobial defenses, generation of inflammatory mediators, and adaptive immunological responses in the organism (Basu and Fenton 2004).

According to a new study, low 25-OH-D3 concentrations are associated to cytokines and respiratory illnesses (Lu *et al.* 2020, D'Avolio *et al.* 2020) in 1377 control subjects with high C reactive protein levels, serum 25(OH)D3 concentrations were 30 ng/mL lower. COVID-19 patients had greater blood 25(OH)D3 concentrations than non-COVID-19 patients, but there were no differences between these groups and COVID-19 persons in this regard.

COVID-19 and vitamin D levels have been examined in a number of research investigations (Bilezikian *et al.* 2020, Murai *et al.* 2021, Hariyanto *et al.* 2021). In these research, vitamin D concentration and infection risk are examined in connection to COVID-19 severity and vitamin D concentrations. It has been shown that those who lack vitamin D are more likely to have elevated levels of interleukin-6 (IL-6) (Baeke *et al*. 2010).

While vitamin D insufficiency is more common in severe instances, no link has been identified between it and an increased risk of infection, according to recent research. This study found that vitamin D insufficiency is linked to a higher risk of hospitalization and mortality (Hariyanto *et al.* 2021). Studies have revealed that vitamin D may protect the body in many ways, including by increasing its natural defenses such as its immune system and its physical defenses against sickness (Evans *et al.* 2020).

By inhibiting B cell proliferation, maturation, and antibody production, vitamin D may also affect T cell phenotype and COVID-19-induced response. DHA (Docosahexaenoic It's due to this change in adaptive immune response that Th2 cytokines are more prevalent than Th1 cytokines (Th2). This may lessen the number of cytokines generated if the condition is severe (Evans *et al.* 2020).

5. CONCLUSIONS AND RECOMMENDATION

5.1 Conclusions

- RBC count, Hb concentration, PCV percentage, and MCV percentage decreased significantly (P 0.05) among pregnant women with COVID-19 infection.
- There was a significant (P 0.05) increase in the number of WBC and the percentage of neutrophils in pregnant women with COVID-19 infection.
- In addition, pregnant women with COVID-19 infection had considerably higher levels of liver enzymes, according to the study results (P 0.05).
- Total protein and albumin D3 were considerably reduced in pregnant women with COVID-19 infection (P 0.05), according to the data.
- There was a significant difference in vitamin D3 levels between pregnant women who had COVID-19 infection and those who did not (P 0.05).

5.2 Recommendation

- Infected pregnant women should have their cytokine levels checked.
- Pregnant women infected with COVID-19 should have their hormone levels tested.
- If pregnant women infected with COVID-19 exhibit high levels of antioxidant enzymes, they should be investigated further.
- There should be testing for oxidative stress in pregnant women infected with the COVID-19 virus.

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CURRICULUM VITAE

Personal Information

Name and Surname : Waleed Ibrahim Hameed HAMEED

Education

MSc	Çankırı Karatekin University Graduate School of Natural and Applied Sciences Department of Chemistry	2020-Present
Undergraduate	Mosul University Faculty of Education for Pure Sciences Department of Chemistry	2009-2013