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EVALUATION OF ANGIOTENSIN CONVERTING ENZYME (ACE), INTERLEUKIN-6, UREA, CREATININE, LACTATE DEHYDROGENASE (LDH), AND OTHER PARAMETERS IN COVID-19 PATIENTS

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NOORULDEEN NAJIM ABDULLAH AL-MAGSOOSI

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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

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ABSTRACT

EVALUATION OF ANGIOTENSIN CONVERTING ENZYME (ACE), INTERLEUKIN-6, UREA, CREATININE, LACTATE DEHYDROGENASE (LDH), AND OTHER PARAMETERS IN COVID-19 PATIENTS

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Angiotensin-converting enzyme (ACE) Angiotensin (Ang) II pathway plays important regulatory effects on both the hemostasis of the circulatory system and the immunological responses. The purpose of this research was to analyze the relationship between illness severity and ACE activity, as well as to evaluate the level of ACE activity present in COVID-19 by comparing them to healthy persons. It is essential to the effective care of COVID-19 patients that risk factors for early development toward severe illness and/or death be identified. In this study, 90 subjects (45 women and 45 men) with varying degrees of disease activity and a control group consisting of 90 healthy individuals matched for age, gender, and body mass index will be evaluate (ACE), IL6, urea, creatinine, lactate dehydrogenase and other parameters in patients with covid-19). The study found clinical significance age, weight and body mass ($P<0.05$). They were also of great importance to ACE and LDH ($P<0.05$), and their impact was evident in Covid 19 patients. While there was no clear importance for fats. The study concluded that the factors of age, weight, ACE and LDH have the greatest role in the development and severity of Covid-19 disease.

2022, 48 pages

Keywords: Angiotension converting enzyme, IL6, Urea, LDH, COVLD-19

ÖZET

COVID-19 HASTALARINDA ANJİYOTENSİN DÖNÜŞTÜRÜCÜ ENZİM (ACE), İNTERLEUKIN-6, ÜRE, KREATİNİN, LAKTAT DEHİDROJENAZ (LDH) VE DİĞER PARAMETRELERİN DEĞERLENDİRİLMESİ

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Anjiyotensin dönüştürücü enzim (ACE) Anjiyotensin (Ang) II yolu, hem dolaşım sisteminin hemostazı hem de immünolojik yanıtlar üzerinde önemli düzenleyici etkilere sahiptir. Bu araştırmanın amacı, hastalık şiddeti ile ACE aktivitesi arasındaki ilişkiyi analiz etmenin yanı sıra COVID-19'da bulunan ACE aktivitesi seviyesini sağlıklı kişilerle karşılaştırarak değerlendirmekti. COVID-19 hastalarının etkili bakımı için, ciddi hastalık ve/veya ölüme doğru erken gelişim için risk faktörlerinin tanımlanması çok önemlidir. Bu çalışmada, farklı derecelerde hastalık aktivitesine sahip 90 kişi (45 kadın ve 45 erkek) ile yaş, cinsiyet ve vücut kitle indeksi açısından eşleştirilmiş 90 sağlıklı bireyden oluşan kontrol grubu (ACE), IL6, üre, kreatinin değerlendirilecektir. , laktat dehidrogenaz ve covid-19 hastalarında diğer parametreler). Çalışma yaş, ağırlık ve vücut kitlesinin klinik olarak anlamlı olduğunu buldu ($P<0,05$). ACE ve LDH için de büyük önem taşıyorlardı ($P<0,05$) ve etkileri Covid 19 hastalarında belirgindi. Yağlar için net bir önemi yokken. Çalışma, yaş, kilo, ACE ve LDH faktörlerinin Covid-19 hastalığının gelişiminde ve şiddetinde en büyük role sahip olduğu sonucuna vardı.

2022, 48 sayfa

Anahtar Kelimeler: Anjiyotensin dönüştürücü enzim, IL6, Üre, LDH, COVİD-19

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Nooruldeen Najm Abdullah AL-MAGSOOSI

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CONTENTS

LIST OF SYMBOLS

-	Minus
%	Percent
**	Significant
/	Divide
+	Plus
<	Greater than
=	Equal
>	Less than
±	Plus minus
≤	Greater or equal to
≥	Less or equal to
µg	Microgram
µL	Micro liter
dL	Deciliter
g	Gram
kg	Kilogram
L	Liter
m^2	Square meter
mIU	Milli-international units
min	Minute
mL	Milliliter
mmol	Milli mole
mol	Mole
ng	Nanogram
nm	Nanometer
NS	Non-significant
rpm	Revolutions per minute

LIST OF ABBREVIATIONS

ACE	Angiotensin-converting enzyme
ANG	Angiotensin
ARDS	Acute respiratory distress syndrome
HDL	High-density lipoprotein-cholesterol
LDH	Lactate dehydrogenase
LDL	Lipoprotein cholesterol
RBC	Red blood cells
VLDL	Low-density lipoprotein cholesterol

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1. INTRODUCTION

Angiotensin-converting enzyme (ACE) is responsible for the transformation of angiotensin into other compounds, while The angiotensin (Ang) II pathway is responsible for exerting significant regulatory effects on coagulation in the circulatory system as well as immunological responses. This route is critically important in the development of acute lung injury as well as acute respiratory distress syndrome (ARDS), both of which are incapacitating consequences that may result after an infection with SARS-CoV-2. The objective of this study is to investigate the serum ACE activity in COVID-19 patients in order to ascertain whether or not there is a correlation between this activity and the clinical manifestations and degree of severity of the disease (Vandenberg *et al*. 2021). The role that various biomarkers play in the process of assessing the prognosis for persons who have COVID-19 is now the subject of investigation, and many distinct biomarkers are currently being explored. One of these biomarkers of interest is termed lactate dehydrogenase (LDH), and this is especially true considering that greater levels of LDH have in the past been related to poorer outcomes in persons who were suffering from various viral infections. Other biomarkers of interest include: Initial research conducted on individuals diagnosed with COVID-19 has shown that there may be significant differences in LDH levels between patients and others who do not have a serious disease. As a consequence of this, we decided to conduct a combined analysis of the research that had been previously published in order to evaluate the likelihood of a relationship between increased LDH levels and greater probabilities of disease severity and mortality in COVID-19 patients (Pfefferbaum and North 2020).

1.1 Aim of Study

The current study's objectives were to determine the levels of ACE and interleukin-6, in addition to a number of other parameters, in patients who had been diagnosed with COVID-19; to evaluate the level of ACE activity in COVID-19 by contrasting patients

with healthy individuals; and to investigate the relationship between the severity of the disease and ACE activity.

2. LITERATURE REVIEW

Angiotensin-converting enzyme (ACE) that converts angiotensin to other substances is important regulatory and effects on circulatory hemostasis and immunological responses are exerted by the angiotensin (Ang) II pathway. This pathway plays a significant part in the progression of acute lung damage and acute respiratory distress syndrome (ARDS), both of which are debilitating complications that may arise after an infection with SARS-CoV-2. The purpose of this research is to explore the serum ACE activity in patients with COVID-19 and to determine whether or not there is an association between this activity and the clinical aspects and severity of the illness (Lone and Ahmad 2020).

It has been established that pro-inflammatory cytokines play an important role in the pathophysiology of lung injury in individuals who are plagued with coronavirus disease 2019 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus, according to the evidence (SARS-CoV-2). As a result, we read the recent paper that was published in a Journal by Ye and colleagues, who explain the "cytokine storm" that occurs in COVID patients, with a great deal of interest. 1 A significant number of individuals who are afflicted with COVID-19 will go on to have a severe immunological response that is maintained by cytokines and will ultimately result in alveolar infiltration by macrophages and monocytes (Becker 2020).

Patients who are at risk of developing serious COVID-19 and who may need aggressive management early on in the course of the illness may be identified by the use of these three predictors together with their respective cut of values. There is a correlation between having a higher level of blood urea nitrogen at 24 hours and having worse outcomes in COVID-19 pneumonia (Graham 2020).

Several different biomarkers are now being investigated to determine the function that they play in the process of determining the prognosis for people who have COVID-19. One of these biomarkers of interest is called lactate dehydrogenase (LDH), and this is particularly true given that higher levels of LDH have in the past been linked to worse

outcomes in individuals who were suffering from other viral infections. Initial findings in patients with COVID-19 have shown that there may be substantial disparities in LDH levels between patients and those who do not have severe illness. As a result, we carried out a combined analysis of the previously published research in order to investigate the possibility of a connection between elevated LDH levels and higher probabilities of illness severity and death in COVID-19 patients (Jeyanathan *et al*. 2020).

In this research, there will be a total of 90 participants, 45 of whom will be male and 45 of whom will be female. There will also be a control group consisting of 90 healthy persons, all of whom will be matched for age, gender, and body mass index. Analyze patients with covid-19 for levels of Angiotension enzyme (ACE), Interleukin-6, urea, creatinine, lactate dehydrogenase, and any other relevant indicators.

2.1 Interleukin 6

It is possible for the soluble mediator known as IL6 to have an effect that is pleiotropic, which means that it may have an effect on inflammation as well as the immune response and hematopoiesis. In the beginning, there were many different functions of IL6 that were examined, and their distinct designations were determined from the particular biological activities that they carried out (Šenolt *et al*. 2017). Because of its influence on the acute phase of protein synthesis in hepatocytes, this protein was given the term hepatocyte-stimulating factor, or HSF for short (Meng *et al*. 2020).

Interleukin 6 (IL6) is produced almost instantaneously and only for a short period of time in response to infections and injury to tissue. This cytokine provides a contribution to the defense of the host by activating acute phase responses, hematopoiesis, and immunological reactions (Khodakheir *et al*. 2017).

2.1.1 Role

IL6 has the potential to increase the proliferation of murine pluripotent stem cells by cooperating in a synergistic manner with the action of IL3. IL3 is essential for ensuring that the advancement of the cell cycle is maintained, whereas IL6 is important for triggering the entrance of dormant progenitor cells into the cell cycle. Additionally, IL6, in combination with stem cell factor and thrombopoietin, has the potential to induce megakaryopoiesis. Interleukin 6 was first identified as a lymphokine that is generated by T cells and is accountable for triggering the last maturation stage of B cells, which ultimately culminates in the generation of antibodies (Jeyanathan *et al*. 2020).

This discovery was made possible by the fact that interleukin 6 is a lymphokine. The synthesis of immunoglobulin M (IgM), immunoglobulin G (IgG), and immunoglobulin A (IgA) is only boosted by recombinant human IL6 in B cells that had previously been stimulated by Staphylococcus aureus Cowan I or pokeweed mitogen (PWM). In B cells that are in a resting state, this is not the case. Anti-IL6 antibody was demonstrated to decrease PWM-induced Ig production, which shows that IL6 is one of the important factors in PWM-induced Ig production (Keller *et al*. 2019).

PWM-induced Ig production was shown to be blocked by anti-IL6 antibody. In addition, it was shown that an increase in the production of primary and secondary anti-SRBC (sheep red blood cell) antibodies in mice in vivo occurred when IL6 was present. These antibodies target sheep red blood cells. In addition, IL-6 had the potential to increase the creation of IgA in murine Peyer's patch B cells, which were already committed to the manufacture of IgA. This was one of the functions that these cells were already doing (Hofmann *et al*. 2016).

In addition to this, it is in charge of regulating the production of proteins that play a role in the control of how genes are expressed. It is likely that the high number of genes that are regulated by the activity of IL6 may provide an explanation for the pleiotropic nature of this interleukin. As a consequence of this, the biological consequences of IL6

production have been related to its effects, which underscores the significant role it is essential in the activation and regulation of the immune response (Hussien *et al*. 2022).

There have been two distinct mechanisms identified as being responsible for the facilitation of IL6's effect of inhibiting Th1 polarization. The following summarizes each of these mechanisms: (2) Interleukin 6 (IL6) has an influence on the release of the interferon interferon-gamma (IFN) by CD4 T cells. IFN is an essential interferon for the promotion of the polarization of Th1 cells. (1) IL6 causes CD4 T cells to produce more IL4 and directs the immune response toward Th2, and (2) IL6 has an effect on the amount of IFN that is produced by CD4 T cells. It has been shown that inhibiting the generation of IFN- in Th1 cells has the same effect on the activation of CD8 T cells as the effect that is caused by these cells (Šenolt *et al*. 2015).

In addition to this, it was shown that anti-Ig or dextran sulfate could activate murine B cells, and that mouse IL6 could still function on these cells. Synergistically, an increase in murine B cell proliferation and differentiation may be brought about by the coordinated actions of IL6 and IL1. In addition to its capacity to promote the development and differentiation of T cells, interleukin 6 may also boost the proliferation of mitogen-stimulated thymocytes and peripheral T cells. This is in addition to its ability to drive the growth of T cells. When IL2 is present in the culture media, it was also shown that it has the potential to stimulate the differentiation of cytotoxic T cells in murine and splenic cells (Hsu *et al*. 2017).

2.1.2 Influence

After being produced in a local lesion during the first stage of inflammation, IL6 then makes its way to the liver by way of the circulation. After this, there is a rapid induction of a large number of clinical stage enzymes, including C-reactive protein (CRP), haptoglobin, and 1-antichymotrypsin.. Other acute phase proteins include haptoglobin and fibrinogen. However, IL6 prevents the body from producing fibronectin, albumin, and transferrin by blocking their production. At first, these biological effects on

hepatocytes were explored on the presumption that they were HSF's responsibility (Jeyanathan *et al*. 2020).

A substantial complication of a variety of chronic inflammatory illnesses is brought about by the formation of amyloid A amyloidosis, which takes place when high-level concentrations of SAA are permitted to exist for a protracted length of time (Liu *et al*. 2021).

The accumulation of amyloid fibrils is the outcome of this process; this accumulation, in turn, causes progressive damage in a number of organs. In addition, as IL6 is the factor responsible for modulating the transporters of iron and zinc in the serum, it plays a role in the regulation of the levels of iron and zinc (Tolulope and Deborah 2015). Hypozincemia is connected with inflammation, which is produced by IL6 because it raises the the zinc importer on hepatocytes. Hypozincemia is associated with inflammation (Caparrós *et al*. 2018).

It is ultimately due to the delivery of IL6 to the bone marrow since it encourages the maturation of megakaryocytes, which leads to the generation of platelets. For the goal of assessing the amount of inflammatory activity, the fluctuations in acute phase protein levels, as well as the changes in red blood cell and platelet counts, are analyzed in routine clinical laboratory examinations (Niess *et al.* 2018).

In addition, IL6 is the factor that is responsible for promoting the differentiation of naïve CD4+ T cells into more specialized cells. In the process of transitioning from the innate immune response to the acquired immunological response, this provides an important function that is vital to the process. Although it has been demonstrated that IL6, in conjunction with transforming growth factor (TGF)-, is necessary for the development of Th17 cells from naive CD4+ T cells (Hofmann *et al*. 2016).

In addition, it has been shown that in addition to being responsible for the synthesis of IL21, IL6 is also important for encouraging the growth of T-follicular helper cells. Ig

synthesis, and more especially IgG4 creation, are both under the control of IL21, which is responsible for their regulation. IL6 is also important for the differentiation of CD8+ T cells into cytotoxic T cells (Patel *et al*. 2017).

This process takes place in the body. Both hypergammaglobulinemia and the generation of autoantibodies are symptoms it. This is the reason why IL6 has the ability to induce the differentiation of activated B cells into plasma cells that produce antibodies (Khodakheir *et al*. 2017).

IL6 is responsible for a range of other effects, many of which are observed to be present in chronic inflammatory illnesses. These effects include, but are not limited to, those on hepatocytes and lymphocytes, as previously mentioned. The production of IL6 in the stromal cells of the bone marrow has a number of effects, one of which is that it stimulates RANKL (Mora-Bau *et al*. 2015).

This is only one of many effects. This, in turn, leads to the breakdown of bone and the condition known as osteoporosis. Inflammatory lesions are characterized by a number of pathogenic characteristics, including increased vascular permeability and enhanced angiogenesis. IL6 is also responsible for inducing an excessive production of VEGF, which results in increased vascularization and improved angiogenesis. In conclusion, it has been demonstrated that IL6 promotes either the proliferation of keratinocytes or the production of collagen in dermal fibroblasts (Delanaye *et al*. 2017).

Both of these processes, which may be responsible for the alterations seen in the skin of systemic sclerosis patients, have been shown to be induced by IL6 (Šenolt *et al*. 2017).

2.2 Blood Urea

Urea is a nitrogen-containing molecule that is produced in the liver as a byproduct of protein metabolism and the urea cycle, among other processes, in the human body. Urea is also known as BUN, which stands for blood urea nitrogen. The kidneys are

responsible for the removal of about 85 percent of urea, while the gastrointestinal (GI) tract is responsible for the elimination of the remaining 15 percent. When renal clearance is decreased, as it is in conditions such as acute and chronic renal failure or compromised function, there is a greater likelihood that serum urea levels may increase (Okojie and Omorokpe 2018).

It is possible for there to be an increase in the synthesis of urea under a number of different conditions that are not associated to renal sickness. It is possible for individuals to produce less pee when they are fasting, consuming a diet low in protein, or if they are suffering from a severe form of liver disease (Stapleton 2017).

By testing the ratio of BUN to creatinine in a patient with a high BUN, a physician is able to differentiate between pre-renal and renal causes of the condition. Individuals who have pre-renal disease have a ratio that is close to 20:1, while patients who have intrinsic renal disease have a ratio that is closer to 10:1. It is conceivable that bleeding in the upper gastrointestinal tract is accompanied by a ratio of BUN to creatinine that is particularly high (Dadzie *et al*. 2019).

2.2.1 Creatinine

Creatinine is one of the important NPN waste products formed. Transamination of the amino acids arginine, glycine, and methionine produces it in some organs. It moves in body until reaches the brain to become phosphocreatine (Tseng *et al*. 2018, Delanaye *et al*. 2017). The muscles create the bulk of creatinine. As a result, the patient's muscle mass influences the concentration of plasma creatinine. Because it is less affected by diet, creatinine is a better indicator of renal function than BUN. When you eat a lot of meat, your serum creatinine level rises (Zhao *et al*. 2015).

Patient who with fluid overload has a less serum creatinine because dilution of blood. Because of greater muscular mass, the masculine sex and African race will produce

more creatinine as adults. Every day, about 2% of the creatine in the body is converted to creatinine (Juturu and Wu 2016).

Clinical diseases that cause greater muscle breakdown can raise blood creatinine levels by up to 5 mg per day. Creatinine is excreted outside of the kidneys (mostly through the intestine), especially in advanced renal failure (Delanaye *et al*. 2017).

2.3 Corona Virus

2.3.1 Overview

It has been given the name Coronavirus Illness 2019 (COVID-19), and it is an infectious condition that is brought on by Coronavirus-2. When the illness was found and reported for the first time in December 2019 in the city of Wuhan (China), it soon spread to other cities and nations, resulting in a pandemic that is still ongoing and has expanded to more than 200 countries around the world. Because it has become the single most significant threat to the health of people all around the world, COVID-19 is the focus of the efforts of a large number of researchers who are looking for medications that are both curative and preventive in nature (Kaur and Gupta 2020).

People who have diabetes have an increased likelihood of passing away, despite the fact that it is anticipated that the overall mortality rate among patients with COVID-19 condition would be less than 6 %. According to the findings of recent studies, diabetic patients who have glycemia levels that are not well controlled have a mortality risk that is roughly four times greater and a hospitalization term that is approximately four times longer than patients who do not have diabetes (DM) (Juturu and Wu 2016).

However, further study is necessary to substantiate these findings. Nevertheless, it has been shown that diabetes raises the risk of COVID-19 complications in people (Guner *et al*. 2020). On the other hand, no information whatsoever is available on the specific molecular interactions that take place between DM and COVID-19. Concerning

COVID-19 and diabetes, we will investigate a variety of molecular interactions in an effort to perhaps create some novel preventive and therapeutic drugs against COVID-19 in diabetic patients (Mathieu *et al*. 2021).

2.3.2 Classification

Both humans and birds are potential hosts for these RNA viruses, which are closely linked to one another. They have the potential to cause a range of respiratory problems in birds and people, from moderate to severe, depending on the severity of the exposure. There have been cases of SARS, MERS, and COVID-19 in humans, and all of them have been linked to more severe strains of this virus. However, some of the cases are quite mild. Cows and pigs get afflicted with diarrhoea as a direct result of their consumption, while mice develop hepatitis and encephalomyelitis as a result of their consumption (Zaim *et al*. 2020).

When someone has SARS-CoV-2 infection, they almost always have it in their lungs. The cardiovascular system, the central nervous system, and the gastrointestinal tract are a few examples of other organs that are susceptible to infection with *E. coli (*Kaur and Gupta 2020). This virus is thought to infect host cells by forming a link with angiotensin-converting enzyme type 2, which then allows the virus to attach itself to the host cell (ACE2) (Juturu and Wu 2016).

The ACE2 enzyme is what catalyzes the hydrolysis of angiotensin II (Ang II), which leads to the production of angiotensin-1-7 (a vasodilator) (DeRoo *et al.* 2020). A virus is responsible for causing severe acute respiratory syndrome, often known as SARS-CoV-2 (SARS) (Figure 2.1). This enzyme is produced almost exclusively by alveolar type II cells in the pulmonary tissues; nevertheless, it is possible to find it in other kinds of cells, such neurons and myocardial cells, in the same tissues (Vaira *et al*. 2020).

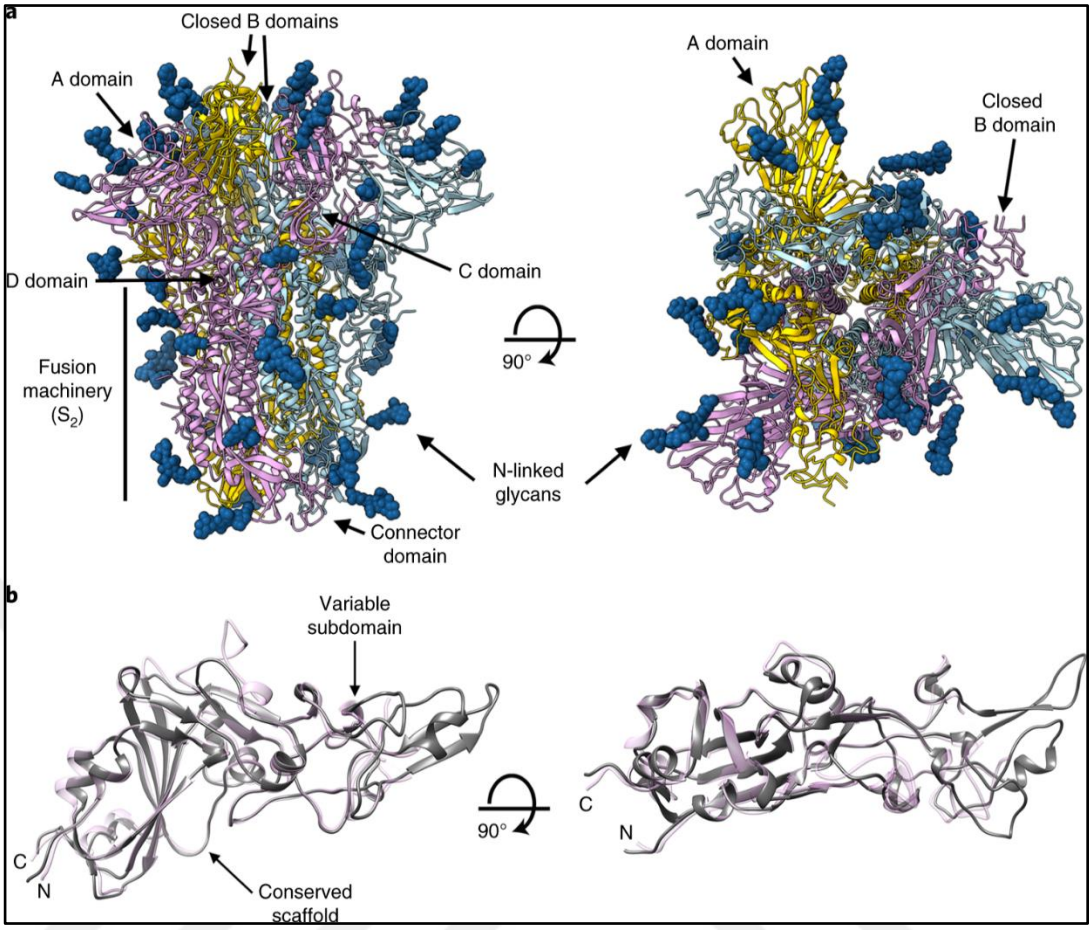

Figure 2.1 Anatomical foundation for human coronavirus attachment to glycosaminoglycan (Roo *et al.* 2020)

2.4 Lactate Dehydrogenase (LDH)

LDH is an enzyme that may be found in the majority of the body's tissues. In general, this enzyme is found throughout the body. It plays a vital role in a process called as cellular respiration, which is the conversion of glucose (sugar) acquired from meals into energy. This process is also known as glycolysis (Vlachostergios *et al.* 2015).

Even though LDH is found in significant quantities inside the cells and tissues of the body, the levels of this enzyme that are typically found in blood are rather low (Figure 2.2). On the other hand, tissues that have been harmed as a result of either an accident or a disease may release elevated quantities of LDH into the circulation. This can happen for a number of reasons, as explained later (Pohanka 2020).

In spite of an LDH test is useful in establishing a diagnosis of tissue damage, further tests are usually necessary in order to determine the precise location where the damage has occurred. Even though an LDH test is helpful in making a diagnosis, One example of this kind of evaluation is the LDH isoenzymes test. There are five unique versions of the LDH enzyme, and these various forms are referred to as LDH isoenzymes (Mazzio *et al.* 2021).

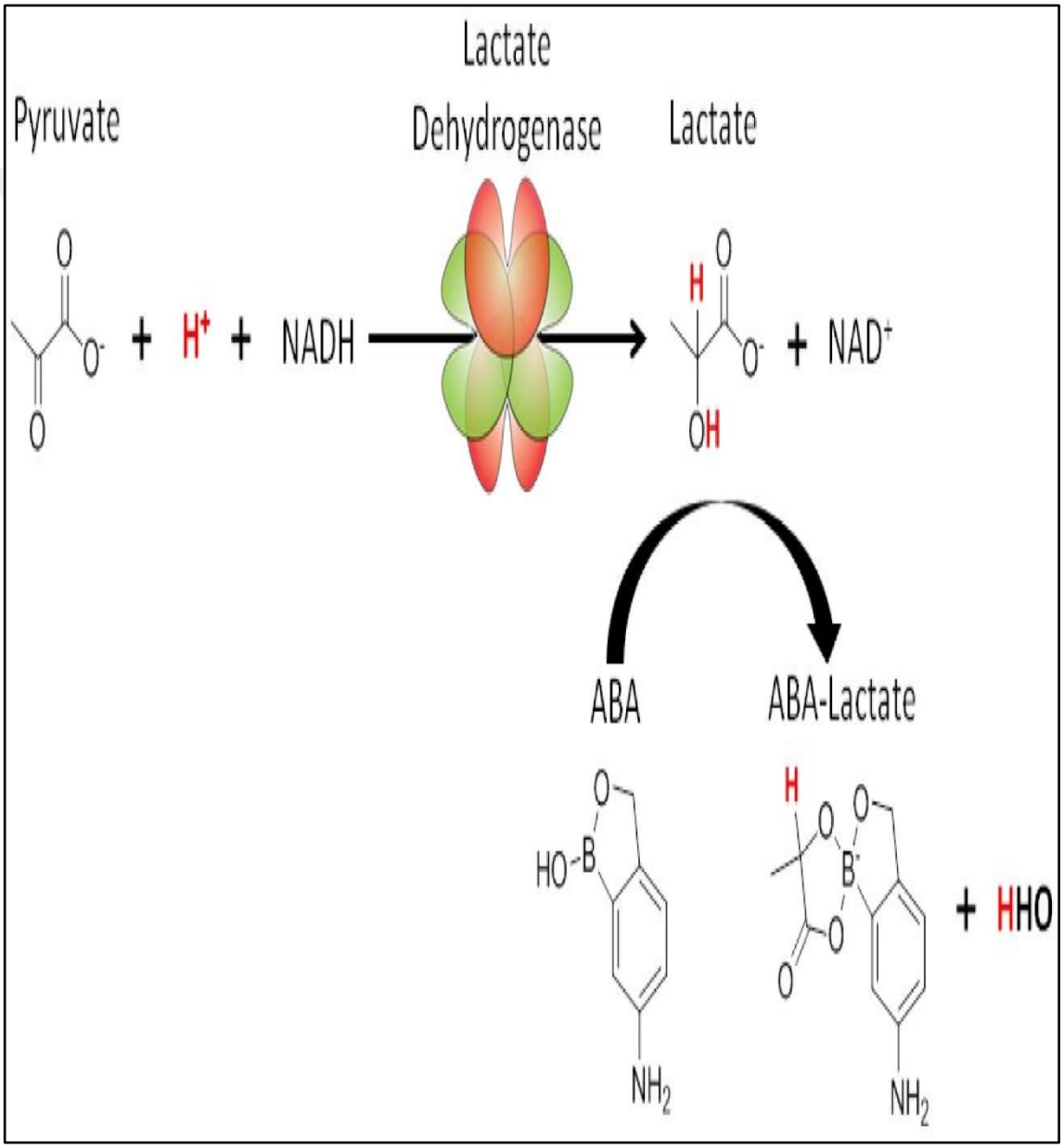

Figure 2.2 LDH isoenzymes (Miyamoto *et al.* 2018)

These isoenzymes may be found in variable amounts and locations throughout the body's organs and tissues. Medical experts are able to acquire a better idea of the nature of the cellular damage, as well as its location and severity, by calculating the amounts of these isoenzymes that are present in the blood of the patient. LDH is present in the blood cells, the liver, the heart, the kidneys, the pancreas, and the brain. It is also found in the pancreas. In addition to muscles and pancreas, LDH may be found in liver, kidneys, pancreas, and the brain (Jung *et al.* 2019).

The major goal of the LDH test is to provide assistance in assessing the degree of damaged tissue in the body as well as its placement throughout the body. This may be accomplished via the use of the test. With the help of this test, the quantity of this enzyme, which is also known as lactic acid dehydrogenase in certain instances, that is present in the blood or, on occasion, in other physiological fluids can be figured out using different techniques (Zhang *et al.* 2017).

LDH is a kind of enzyme, which is a form of protein. Enzymes are very important in the body. LDH has a significant amount of effect on the process through which the body generates energy. It can be found in almost all of the tissues in the body, such as those in the blood, kidneys, brain, and lungs, to name a few of the organs in which it may be found (Ozaki *et al.* 2017).

When these tissues are damaged, they let out the enzyme LDH, which may then be found in the circulation or other physiological fluids. It is probable that certain tissues in the body have been damaged as a consequence of a disease or injury if the level of LDH in the blood or other fluids is high. LDH may be found in the blood and other fluids. Whenever there is a breakdown or loss of cellular structure, this enzyme is released into the fluid component of the blood. This may happen for a number of reasons. This substance is referred to as "serum" or "plasma" in the medical world (Juturu and Wu 2016).

2.4.1 Cellular

There are five possible isomeric forms of LDH, and they may be found structured in tetramers of either of the two types of subunits, which are labeled as muscle (M) or heart, respectively (H). Isoforms LDH-1 through LDH-5, which are also known as isozymes, have been given the designations LDH-1 through LDH-5. Every isoform exhibits its gene in a completely different way depending on whatever organ it is found in (Vlachostergios *et al.* 2015). The capacity of LDH to manifest in a variety of different ways is one factor that contributes to the usefulness of this protein as a clinical diagnostic marker (Mazzoli *et al.* 2020).

Isozyme LDH-1 is the most common isozyme that can be discovered in the tissue of the heart, and it is made up of four different subunits that are heart-specific (4H). Isozyme LDH-2 is the predominant form of the enzyme that may be found in red blood cells as well as the reticuloendothelial system. It is comprised of three subunits of the heart and one component of the muscle (3H1M). The LDH-3 isozyme is the predominant form of the LDH enzyme that may be detected in the lungs. It has a chemical formula of 2H2M and is composed of two subunits of the heart and two subunits of the muscle (Vargas *et al.* 2016).

Isozyme LDH-4 is the primary isozyme that may be discovered in the kidneys of an individual. In spite of the fact that all five of these isoforms are responsible for catalyzing the identical process from start to finish, they may be distinguished from one another thanks to variations in their affinity for the substrate, inhibitory concentration, isoelectric point, and electrophoretic mobility. The technique of LDH zymography enables the viewing of these five isoforms when they are functioning normally (Jia *et al.* 2018).

In spite of the fact that LDH is found mostly in the cytoplasm, evidence of its presence in mitochondria has been discovered as a result of a number of different examinations. It has been shown that yeast, plants, and mammals each possess their own unique form of mitochondrial L-lactate dehydrogenase (mL-LDH). After then, the mL-LDH in the

mitochondrial matrix performs the role of a catalyst, helping to accelerate the process of converting L-lactate to pyruvate. Numerous cancer cells have altered the processes of their mitochondria in order to meet the much higher need for energy that they have. Because of this unusually high degree of glycolysis seen in cancer cells, mL-LDH may be a contributor to the elevated rate of oxidative phosphorylation (Gallo *et al.* 2015).

It is the L-isomers that are responsible for both the intake of and the manufacture of L-lactate, which is the enantiomeric form of lactate that is most prevalent in vertebrates. A gene that may be discovered on chromosome 11p15.4 is responsible for encoding the LDHA variant of the enzyme. A protein containing 332 amino acids is produced when this gene is translated into a protein. The LDHB gene, which can be located on the 12p12.1 region of chromosome 12, is the one that is in charge of the manufacture of a protein that is 334 amino acids long (Vlachostergios *et al.* 2015).

The generation of the isozyme forms of lactate dehydrogenase enzymes, which range from LDH-1 through LDH-5, is the responsibility of both the LDHA gene and the LDHB gene. The enzyme lactate dehydrogenase is made up of three different subunits, which are designated as lactate dehydrogenase-A, lactate dehydrogenase-B, and lactate dehydrogenase-C, respectively. These three subunits are constructed according to the instructions provided by the two genes. There are five various varieties of LDH, and each one has a total of four subunits that make it up (Sauer *et al.* 2017).

Additional two subunits, denoted LDHC and LDHBx, are needed in mammalian cells in order to finish the creation of an LDH tetramer. These subunits are necessary for the development of an LDH tetramer. The LDHC gene is responsible for the encoding of the LDHC protein, which is exclusive to the testes. On the other hand, the LDHBx gene is responsible for the encoding of the LDHBx protein, which is exclusive to the peroxisome. The LDHB gene's readthrough variant is represented by the sign LDHBx in genetic notation (König and Fröhlich 2017).

In order to make LDHBx, it is necessary to first translate the LDHB mRNA, at which time the stop codon has to be read as encoding an amino acid in order for the translation

to continue. As a direct result of this, translation continues until it reaches the following stop codon, which adds seven amino acid residues to the normal LDH-H protein. This occurs because of the fact that translation continues until it reaches the subsequent stop codon. These residues are responsible for encoding the peroxisomal targeting signal, which is what allows LDHBx to be delivered into the peroxisome in the first place (Liaud *et al.* 2015).

The M subunit and the H subunit of LDH are the two separate subunits that make up LDH. Both of these subunits have the identical active site structure, which means that the amino acids that are engaged in the process are also the same in both of these subunits. The alanine that is located in the M-chain is replaced with glutamine that is located in the H-chain when looking at the tertiary structure. The two subunits end up with unique sets of biological features as a result of the chemical events that took place. As a consequence of this, the H subunit is able to bind at a faster pace, despite the fact that its catalytic activity is five times lower than that of the M subunit. Pyruvate is transformed into lactate by the action of the LDHA subunit, which has a stronger affinity for pyruvate and carries a net charge of IL-6. In the process, NADH is turned into NAD+ (Elshaghabee *et al.* 2016).

LDH is an enzyme that is essential to the process of maintaining homeostasis when there is a limited supply of oxygen. When a person engages in strenuous exercise, there is a precipitous drop in the quantity of oxygen that is present in their muscle tissues. When oxygen is no longer available, the electron transport chain (ETC) as well as the ATP synthase enzyme both come to a halt. This is because oxygen is often the chain's very last electron acceptor (Lee *et al.* 2017).

Despite this, muscle cells are still able to carry out their functions since NAD+ may be used to produce ATP, which in turn allows for the maintenance of their functioning. Lactic acid is the final product that is produced as a direct consequence of the fermentation process that LDH goes through. Throughout the process, NADH will be used as a source of electrons for LDH, which will then create NAD+. After that, the glycolysis pathway will be taken in order to make ATP using this NAD+ that has been

passed via it. This route leads to a reduced quantity of ATP generation in compared to the ETC; yet, it permits the cell to continue carrying out its physiological and biochemical operations even when oxygen is not present (Singhvi *et al.* 2017).

2.4.2 Role

The conversion from pyruvate to lactate is catalyzed in a direction that may be switched around thanks to lactate dehydrogenase, which is one of the H transfer enzymes, also known as oxidoreductases. This is accomplished by the use of NADH. The enzyme, in its most fundamental form, plays a part in the process of anaerobic glucose metabolism, which takes place under conditions in which oxygen is either absent or present in extremely low quantities.

On the other hand, the lactate that is produced as a byproduct of the anaerobic conversion of glucose does not go farther down the metabolic route. The liver is the sole organ that has the capability of carrying out any extra metabolic processes on it (Vlachostergios *et al.* 2015). As a direct result of this, lactate is released into the circulation and transported to the liver in order to be processed. LDH is the enzyme that is responsible for carrying out the opposite reaction of the Cori cycle in the liver, this process turns lactate into pyruvate (Zhang *et al.* 2016).

The enzyme lactate dehydrogenase causes the muscles to use up all of the oxygen that is available to them so that it may convert pyruvate into lactic acid when the body is engaged in some kind of physical exercise. Pyruvate does not undergo any further digestion in erythrocytes since these cells do not include mitochondria. Instead, pyruvate is retained in the cytoplasm where it awaits transformation into lactate at some point in the future. During this process, NADH is changed into NAD+. This is an important step in the metabolic pathway (Lee *et al.* 2017).

It is essential to have access to substantial concentrations of NAD inside the cell in order to properly carry out the early phase of glycolysis. This phase is the first step in

the glycolysis process. Anaerobic glycolysis creates just 2 molecules of ATP per molecule of glucose, while oxidative phosphorylation generates 36 molecules of ATP per molecule of glucose. Oxidative phosphorylation is a more efficient way of producing energy from glucose (Tsuge *et al.* 2019).

It's possible that the H and M subunits that make up the LDH enzyme have a different composition in certain tissues than they do in others, but this only applies to those tissues (this was covered in the "cellular" section above). This difference is due to the fact that the tissues have differing metabolic rates, energy needs, and roles, all of which are reflected in the ratio of LDHA to LDHB that they possess. LDHA is a long-chain omega-3 fatty acid, while LDHB is a short-chain omega-3 fatty acid The release of around forty percent of the lactate that is present in circulation is attributable to the skeletal muscle tissue. This lactate is absorbed further, mostly by the liver and kidneys, where it then undergoes the process of oxidation in order to make glucose. Glucose is the end product of this process (Papadimitriou *et al.* 2016).

In conditions of rest, about 10 percent of the lactate is oxidized in the brain to feed 8 percent of the cerebral energy needs, and the remaining lactate is released into circulation. This occurs when the brain is in a state of relative inactivity. When these circumstances are present, the brain's needs for energy are satisfied. On the other hand, hyperlactatemia and physical exercise may both lead to the intake of lactate. Although lactate is required for the upkeep of sixty percent of the metabolic activities that occur in the brain, cerebral lactate oxidation only contributes up to thirty-three percent of the total (Zhang *et al.* 2016).

A function of LDH, particularly LDHA, is changed in cancer cells as compared to normal cells. This difference is most pronounced in cancer cells. This issue is not present in normal cell function. Even in the presence of oxygen, cancer cells continue to make use of the enzyme lactate dehydrogenase, also known as LDH, in order to accelerate their aerobic metabolism and increase glycolysis, ATP synthesis, and lactate generation (Vlachostergios *et al.* 2015).

The Warburg effect is the term given to this particular sort of process. Beneficial to the cells, aberrant cancer cells are able to avoid the creation of oxidative stress brought on by the ETC when they switch to a metabolic phenotype that is anaerobic (Blaya *et al.* 2018).

2.4.3 Diagnosis

The LDH diagnosis is able to identify the amount of LDH that is already present in the serum as a consequence of damaged tissues leaking LDH. This may be done because LDH is a protein that is released into the bloodstream. The catalytic characteristic of LDH that leads to the reversible oxidation of L-lactate to pyruvate, which is mediated by the hydrogen acceptor, NAD+, is employed as the basis for the measurement of the LDH activity. This ensures that the most accurate results are obtained. Evaluation of the rate of NADH production that causes a change in the sample's optical density as measured spectrophotometrically at 340 nm is performed in clinical diagnostic laboratories (Rodrigues *et al.* 2017).

Spectrophotometric analysis makes it possible to monitor either the forward process of oxidation of L-lactate to pyruvate or the reverse reaction of pyruvate synthesis from pyruvate. Both of these reactions may be traced back to their respective starting points. For the purpose of conducting research, the activity of LDH may be assessed in a wide range of materials, such as plasma, serum, tissue, and cells, in addition to the media used for cultivating the cells in a culture dish. When working with serum and plasma samples, extreme caution is essential because hemolysis, which causes the release of enzymes from ruptured erythrocytes, has the potential to induce an artificial elevation in those levels. This can occur because of the release of enzymes from hemolyzed erythrocytes (Pundir *et al.* 2016).

In order for LDH levels to be deemed normal, they need to fall somewhere between the range of 140 to 280 U/L. On the other hand, the clinical interpretation is dependent on the signs and symptoms that are shown by the patient. Because LDH is generated during the process of blood clotting, the serum will nearly always contain a higher

concentration of the enzyme than would be seen in the plasma. Intense physical activity is associated with an increase in LDH activity, which is one of the factors that contributes to the production of lactic acid in normal physiological circumstances (Mushegian 2016).

It is possible for a drug or prescription to have an effect on an LDH test, which might lead to an inaccurate reading being produced as a result. It is conceivable that a falsely low LDH result might be created by the presence of significant levels of vitamin C. This is because vitamin C is a powerful antioxidant (Jung *et al.* 2019).

On the other hand, there is a possibility that some anesthetics, aspirin, alcohols, opioids, and procainamide might cause an incorrectly high level of LDH. It is possible that the LDH test will not indicate any abnormalities other than an unusually high concentration of one or more types of isozymes (Zheng *et al.* 2015).

An rise in blood LDH levels might be the consequence of a wide variety of various medical conditions, such as cancer, anemia, some viral diseases, pancreatitis, liver disease, renal disease, muscle injury, trauma, a heart attack, and certain infectious infections. When compared to older children and adults, infants and younger children often have significantly elevated normal levels of LDH levels. This is in contrast to older children and adults. The reason for this is that LDH levels tend to go up and down as people become older. The normal range for newborns is 135 to 750 U/L (units/L), the normal range for children up to the age of 12 months is 180 to 435 U/L, and the normal range for people who are more than 18 years old is 122 to 222 U/L (Jackson *et al.* 2016).

The LDH isozyme test, in addition to measuring the quantity of LDH that is present in the samples, offers information on the kind of tissue damage, its location, and its severity. H and M subunits are what make up the tetrameric enzyme known as LDH. The tissue specificity that results from the tissue-specific synthesis of subunits is what allows the enzymes to assemble in a predetermined ratio (Vlachostergios *et al.* 2015).

This is what is meant by the phrase "specified ratio." For instance, the LDH that is particular to the heart (LDH-1) preferentially synthesizes all four H subunits, while the LDH that is specific to the liver (LDH-5) is solely formed of all M-subunits. In the testing of LDH isozymes, the electrophoretic mobility shift is the method that is used to place the isozymes into one of the five groups that are numbered 1 through 5. When put in an electric field, the subunits exhibit a different movement because of the varied composition of the subunits themselves, which causes a variance in the total charges. This variation in total charges is what causes the variation in total charges. An good separation pattern of LDH isozymes may be accomplished in a buffer with a pH of 8.6 (Kong *et al.* 2019).

3. MATERIALS AND METHODS

3.1 Materials

3.1.1 Laboratory devices and some tools

In Table 3.1, the discribtion of some tools and laboratory devices during the current study to arrive to aim of study.

Table 3.1 the discribtion of Some tools and laboratory devices

No.	Devices and tools	Origins
1	ELISA system	USA
2	Centrifuge	Korea
3	UV-VIS Spectrophotometer	USA
4	Water bath	Memmert, Germany
5	Incubator	Korea
6	Hot plate	UK
7	Vortex maxi-mix III	UK
8	pH meter	Inlop –Korea
9	Balance	Switzerland
10	Oven	UK
11	Automatic micropipettes, to deliver 10 to 1000 µL, and pipette tips	China

To arrive to the goal, is have been evaluated the the angiotensin converting enzyme (ACE), interleukin 6, urea, creatinine anfd lipid profile and other parameters in patients with covid-19 in Iraq. The purpose of this research was to determine the level of ACE activity present in COVID-19 by comparing them to healthy persons and to evaluate the relationship between illness severity and ACE activity.

3.1.2 Studied groups

Figure 3.1 shows the groups related to the current study, the number of patients group and control group are included.

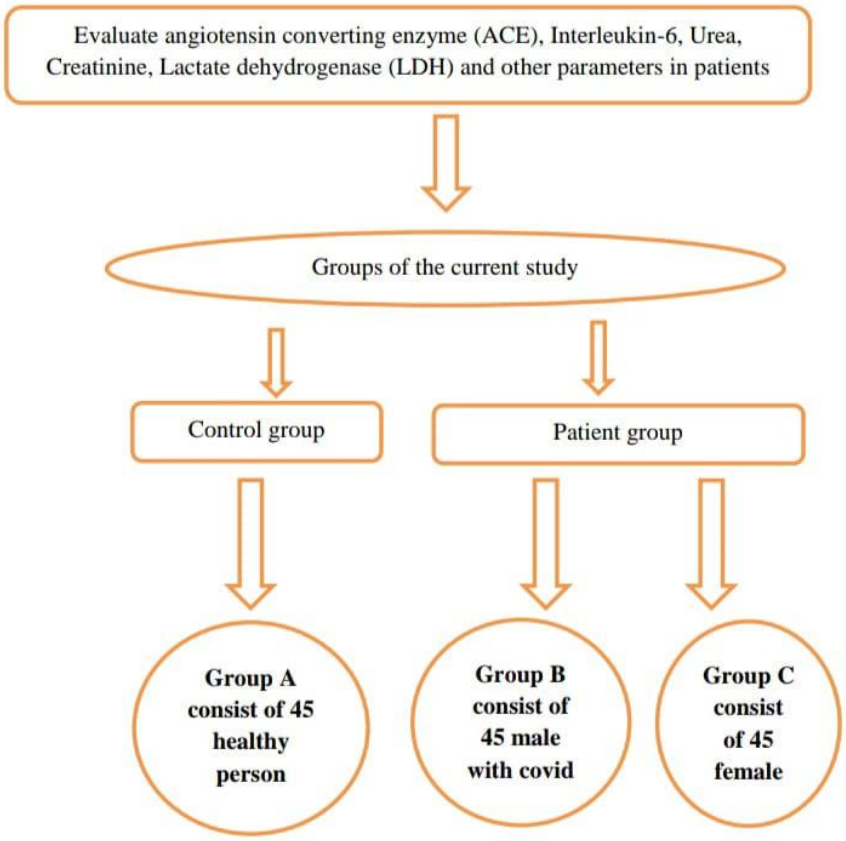

Figure 3.1 Studied groups

3.1.3 Blood samples

The blood samples of this study were obtained from patient 5 mL of blood by using of sterile medical syringes from brachial vein , and placed in plain tubes, then left in the tube at room temperature for half an hour in order to coagulate the blood and centrifuge the samples at (3000 rpm / min) for 5 minutes to separate serum from other components of blood, the serum will be separated and withdrawn serum by micropipette then place in other plain tubes for conduct biochemical markers.

3.2 Methods

3.2.1 Measurement

Sample collection:

The blood samples for lipid profile should be collected after 10-12 hours of fasting, add 5 mL of blood in a tube and centrifuge for 3 minutes and use the serum for test. Calculate the total cholesterol, HDL, LDL, VLDL and triglycerides.

The test result is obtained in two specific steps: First, through this step, LDL cholesterol, LDL cholesterol and LDL cholesterol are both eliminated before being degraded by enzymatic processes. LDL cholesterol is removed first. In the second phase of the process, well-defined enzymatic processes are performed in the presence of HDL-specific surfactants in order to assess the amount of cholesterol that is still present in the HDL fraction.

3.2.2 Blood urea test

Procedure

1. Mix 1 mL of each blank, sample and Cal standard in a reagent tube, put 10 µL of sample in a sample tube, 10 µL of CAL standard in CAL standard tube.
2. Incubate all the tubes for 10 minutes at 25 ºC, then add 1 mL of R3 reagent to the blank, sample and CAL standard tube and read the absorbance at 600 nm against the reagent blank, the calculation can be done using the Equation 3.1.

$$(A\ sample\ /\ A\ standard)\ \times\ C\ standard\ =\ mg/dL\ urea \qquad (3.1)$$

Reagent compositions

R1: Enzyme reagent urease at a concentration of 500 U/L; R2: Buffered chromogen at a concentration of 20 mmol of phosphate buffer per liter at a pH of 6.9; EDTA at a concentration of 2 mmol per liter; sodium salicylate at a concentration of 60 mmol per liter; sodium nitroprusside at a concentration of 3.4 mmol per liter.

3.2.3 Procedure of angiotensin converting enzyme (ACE) test

Inoculate 10 µL of blood serum with100 µL of buffered ACE substrate solution in conical centrifuge tube at 37 ºC for 30 minutes, then add 850 µL of GGCN solution to stop the reaction, add 50 µL of GGT solution to the tube and put the tube in a microcuvet and record the absorbance changes above a two minutes duration. The blank treated the same as the sample, blank buffered inoculated instead of buffer ACE substrate, record the changes in absorbance over two minutes duration.

Take 100 µL of blank buffer and 10 µL of saline buffer and put them in centrifuge tube containing 850 µL of GGCN solution, then add 50 µL of GGT solution, moveresize the mixture to the microcuvet and enroll the absorbance changes over two minutes, then add 50 µL of GGT solution, transfer the mixture to the microcuvet and read the changes in absorbance, the calculations can be done by Equation 3.2.

$$\text{ACE (U/L)} = \{\Delta A/2\ \text{min}_{\text{Sample}} - \Delta A/2\ \text{min}_{\text{Substrate}}\} / \{\Delta A/2\ \text{min}_{\text{standard}} - \Delta A/2\ \text{min}_{\text{AT}}\} \quad (3.2)$$

Reagents

Buffer ACE Substrate : 0.238 g of HEPES, 0.35 g of NACL, 1.136 g of Na_2SO_4, 0.179 g of Hip- Gly dissolved in 15 mL of distilled water, then add 50 µL of NaOH, PH 8; Serum Blank Buffer: Prepared as buffer ACE substrate; HEPES : NaCl 150 mmol/L pH 7.9.

3.2.4 Interleukin 6 test

Put the IC card into the analyzer instrument, push the start button, the instrument read the card, put 50 µL of sample in buffer tube, add 80 µL of sample to the cassette and incubate for 15 minutes, fit in the cassette into the analyzer instrument and push the test button, the instrument will displayed and printed the results.

3.2.5 Procedure of serum creatinine test

Inoculate the reagent, standard and sample at 37ºC, set the photometer of spectrophotometer to zero nm with distilled water. Add 1mL of reagent and 100µL of standard or sample into a cuvette and insert the cuvette into the instrument, then read the absorbance of the specimens at 510 nm after 30 minutes (A1) , and after 90 minutes (A2) of the standard or sample addition, the calculation can be done using Equation 3.3.

$$(A2 - A1_{sample}) / (A2\text{-}A1_{standard}) \} \times C_{standard} = mg / dL \text{ S. creatinine} \quad (3.3)$$

Principle

This approach is based on the picrate reaction (Equation 3.4), in which creatinine combines with picrate ions to create a complex when exposed to an alkaline environment. The rate of production may be determined by observing the increase in absorbance over a period of time, which is proportional to the amount of creatinine present in the sample.

$$\text{Creatinine} + \text{Picric acid} \xrightarrow{\text{pH12/ 37}^{o}\text{c}} \text{Red complex} \quad (3.4)$$

Composition of the reagents: R1: picric acid at a concentration of 25 mmol/L; R2: alkaline buffer and phosphate buffer at a concentration of 300 mmol/L with a pH of 12.7; Sds at a concentration of 2 g/L; CAL: The standard for creatinine, with creatine at 2 mg/L.

3.2.6 Total cholesterol test

Fisrt, cholesterol esterase transforms to cholesterol and fatty acids, then the cholesterol is oxidase to cholestenone and hydrogen peroxide and finally the jumble of phenol and 4- aminoantipyrine are condensed by hydrogen peroxide to form quinonemine dye and

H_2O, the quinonemine dye to the concentration of cholesterol in the sample, the calculation of total cholesterol can be done by using Equation 3.5 and Equation 3.6.

$$Cholesterol + O2 \xrightarrow{Cholesterol\ oxidase} Cholestenonemine + H2O2 \quad (3.5)$$

$$4 - AA - Phenol \xrightarrow{Peroxidase} Quinonemine + 4H2O \quad (3.6)$$

Reagent composition

Cholesterol esterase (250 U) 250 U/L, peroxidase (1 Ku) 1 Ku/L, 4- aminoantipyrine (0.33 mg/L), and phenol (4 mg/L) are the monoreagents. CAL: Cholesterol standard / cholesterol 200 mg / dL.

Procedure: Mix 1mL of each from blank, sample and cal standard, then put it in R1 monoreagent tube, 10µL of sample in sample tube and 10 µL of cal standard in CAL standard tube. Incubate all the tubes at 25 ºC for 10 minutes, read the absorbance at 500 nm against the blank.

3.2.7 Triglyceride test

Hydrolysis of serum triglyceride is performed by evaluating lipoprotein lipase, then the glycerol in phosphor glyceride is hydrolyzed by ATP and glycerol kinase to produce glycerol-3-phosphate and ADP. Glycerol -3- phosphate is oxidized to form DHAP and hydrogen by glycerol phosphate oxidase.

By assessing the peroxidase 4- amino antipyrine and phenol are catalyzed to form quinoemine and water, proportional to concentration of triglyceride in the sample, the reaction of calculation can be done using the Equation 3.8, Equation 3.9 and Equation 3.10.

$$\text{Glycerol} + \text{ATP} \xrightarrow{\text{Glycero kinase}} \text{Glycerol-3- P} + \text{ADP} \quad (3.8)$$

$$\text{Glycerol-3- P} + O_2 \xrightarrow{\text{Glycerophosphate oxidase}} \text{DHAP} + H_2O_2 \quad (3.9)$$

$$\text{4-AA} + 4\ \text{Phenol} \xrightarrow{H_2O_2 \text{ / peroxidase}} \text{Quinnonemine} + H_2O \quad (3.10)$$

Procedure

Add 1 mL of blank, sample and CAL standard each one in R1 monoreagent tube and mix well, then put 10 µL of sample in sample tube, also 10 µL of CAL standard in CAL standard tube. The computation of Triglycerides can be done depending on Equation 3.11.

$$\{A_{\text{samples}} - A_{\text{standard}}\} \times C_{\text{Standard}} = \text{mg /dL Triglycerides} \quad (3.11)$$

4. RESULTS AND DISCUSSION

4.1 Results

The purpose of this study included: determine ACE and interleukin-6 and other parameter in patients with Covid-19. The purpose of this research was to analyze the relationship between illness severity and ACE activity, as well as to evaluate the level of ACE activity present in COVID-19 by comparing them to healthy persons. The actual care of COVID-19 patients requires first and foremost the identification of risk factors for early development toward severe illness and/or fatality. An increase in blood urea nitrogen at 24 hours has been associated with worse outcomes in COVID-19 pneumonia.

4.1.1 Age, weight and BMI

Regarding age, weight and BMI, it was discovered that they were a high significantly men (39.658 ± 9.457, 87.011 ± 31.775 and 29.166 ± 13.679 respectivly) and women (42.057 ± 17.47, 78 ± 19.594 and 26.446 ± 12.684 respectivly) in groups in patients with COVID-19 Table 4.1 and Figure 4.1 at P = < 0.05 when compared to control group (31.546 ± 7.849, 78 ± 19.594 and 26.446 ± 12.684 respectivly). When doing Pearson test was the correlation between ACE with age, weight and BMI r = 0.637**, 0.352* and 0.047 respectively at P = < 0.05 as a shown in Table 4.4.

Table 4.1 The following is a sample of the qualities

Variables	**Group AC**	**Group BP**	Group CP	**Total**	**P-value**
	Mean ± SD N = 45	Mean ± SD N = 45	Mean ± SD N= 45	Mean ± SD N = 135	
Age	31.546 ± 7.849	39.658 ± 9.457	42.057 ± 17.47	37.68 ± 11.95	0.035
Weight	76.068 ± 21.684	87.011 ± 31.775	78 ± 19.594	80.23 ± 25.757	0.042
BMI	23.584 ± 7.584	29.166 ± 13.679	26.446 ± 12.684	26.75 ± 10.5346	0.027

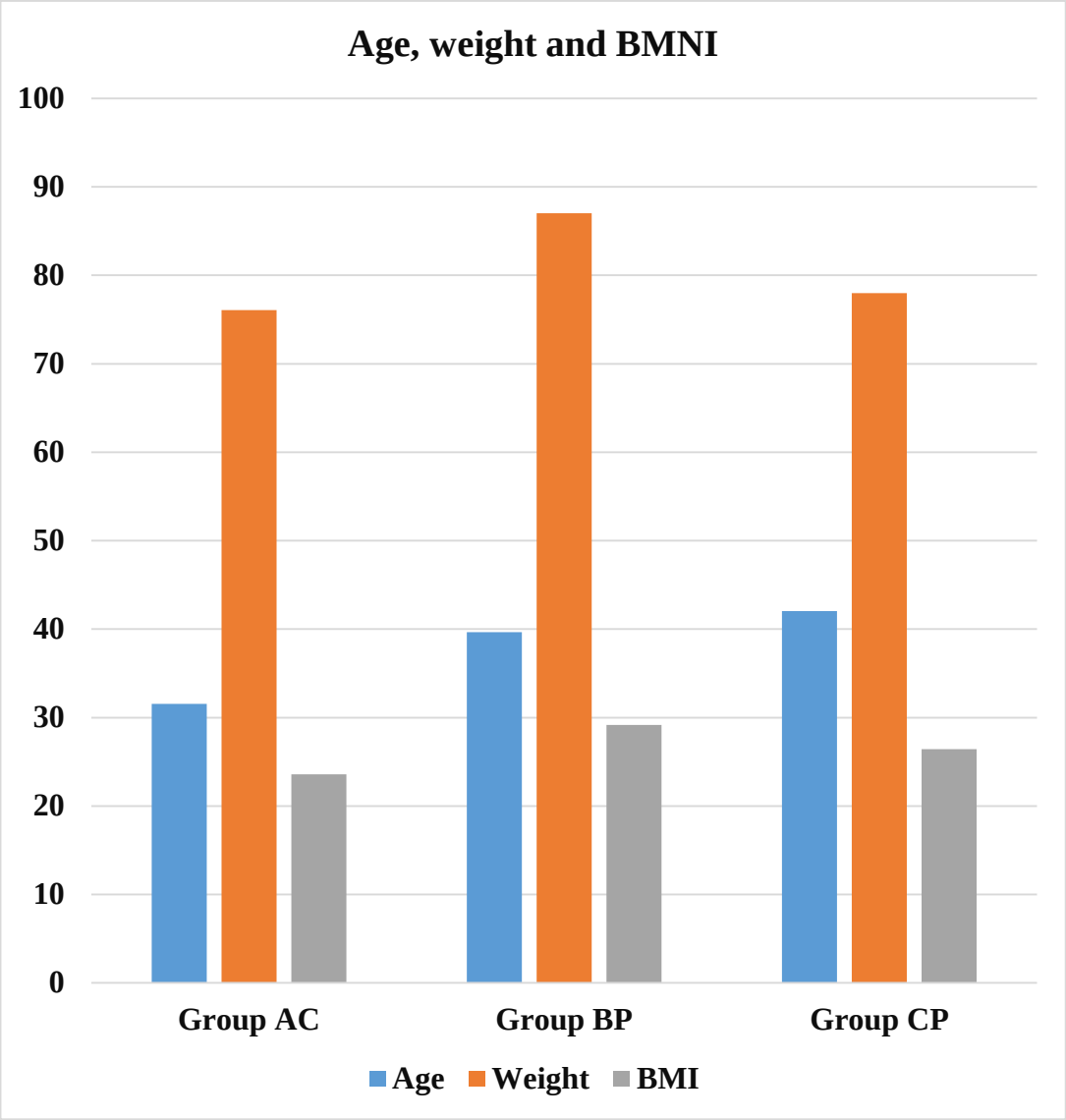

Figure 4.1 The mean of age, weight, and BMI for all studied groups

4.2 Examining Normal Levels for ACE, IL6, Bl.urea, Creatinine and LDH

Regarding ACE, blood urea and LDH, it was discovered that they were a high significantly for ACE and LDH but a non-significant difference for men (37.743 ± 9.5447, 26.463 ± 11.473 and 329.64 ± 41.467 respectivly) and women (34.758 ± 12.574, 24.578 ± 10.547 and 291.574 ± 39.64 respectivly) in groups in patients with COVID-19 Table 4.2 and Figure 4.2 at P = < 0.05 when compared to control group (25.579 ± 10.64, 23.537± 8.474 and 134.75 ± 21.648 respectivly).

Regarding IL6 and serum creatinine it was discovered that they were a high significantly for IL6, but non a significant serum creatinine for men (3.4631 ± 1.537 and 1.6783 ± 0.6472 respectivly) and women (4.5741 ± 1.086 and 0.9546 ± 0.860 respectivly) in groups in patients with COVID-19 Table 4.2 and Figure 4.3 at P = < 0.05 when compared to control group (0.4953 ± 0.053 and 0.7582 ± 0.1436 respectivly). When doing Pearson test was the correlation between ACE with IL6, blood urea, serum creatinine and LDH r = 0.538*, 0.011, 0.076 and 0.554* respectively at P = < 0.05 as a shown in Table 4.4.

Table 4.2 Evaluation of biochemical nutritional markers according to normal values: comparison between groups

Variables	**Group AC Mean ± SD N = 45**	**Group BP Mean ± SD N = 45**	**Group CP Mean ± SD N= 45**	**Total Mean ± SD N = 135**	**P-value**
ACE	25.579 ± 10.64	37.743 ± 9.5447	34.758 ± 12.574	33.56 ± 11.086	0.048
IL6 (pg/mL)	0.4953 ± 0.053	3.4631 ± 1.537	4.5741 ± 1.086	3.758 ± 0.959	0.001
Bl. urea	23.537± 8.474	26.463 ± 11.473	24.578 ± 10.547	24.75 ± 9.674	0.082
S. Creatinine	0.7582 ± 0.1436	1.6783 ± 0.6472	0.9546 ± 0.860	1.057 ± 0.574	0.067
LDH (U/L)	134.75 ± 21.648	329.64 ± 41.467	291.574 ± 39.64	218.64 ± 33.75	0.036

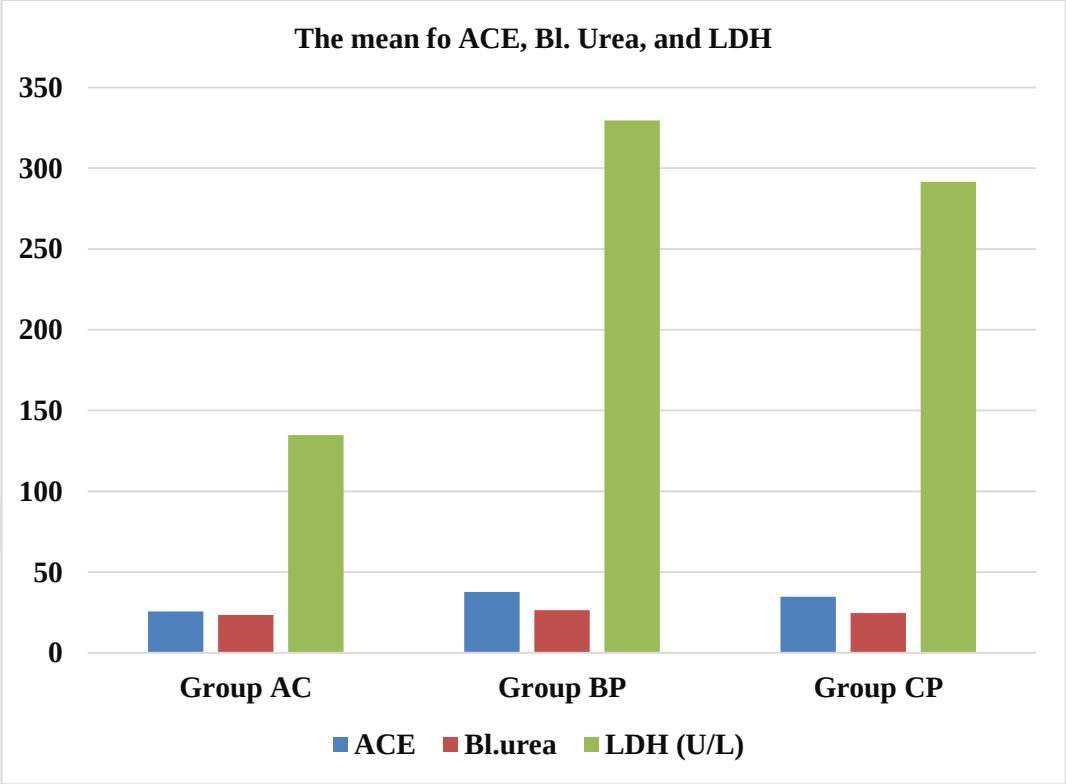

Figure 4.2 Means of ACE, blood urea, and LDH for all studied groups

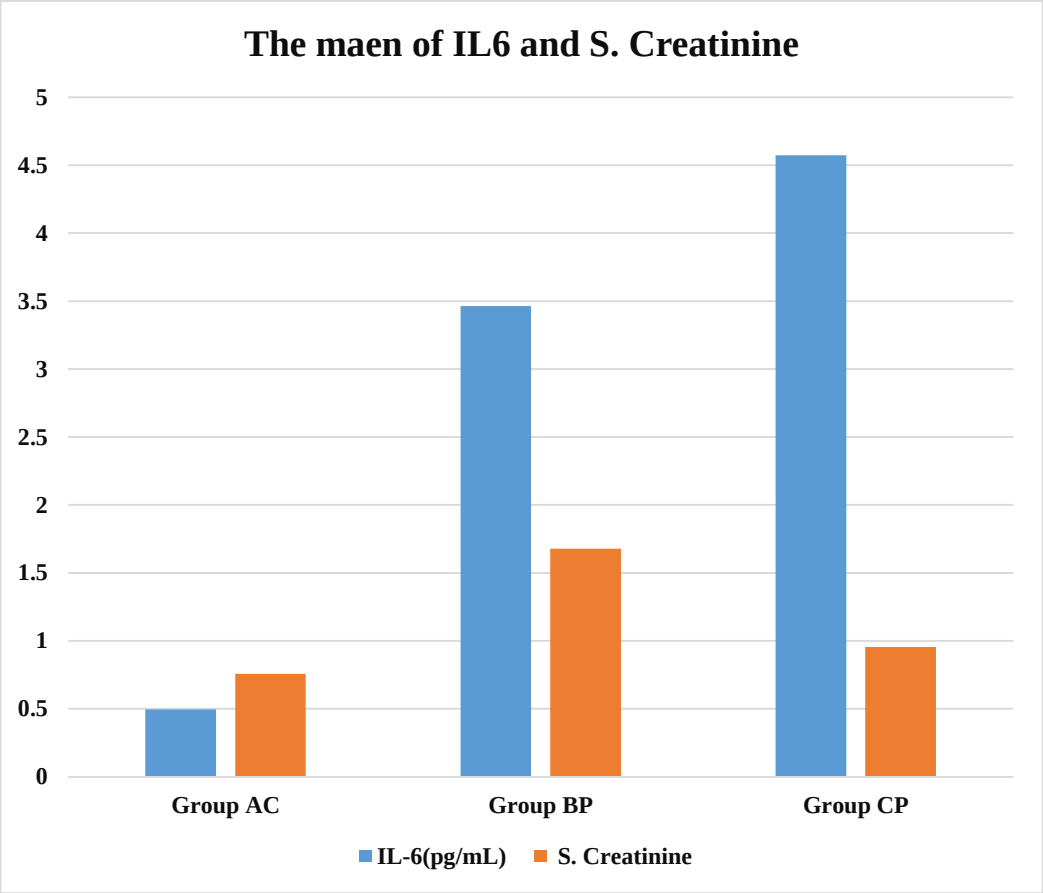

Figure 4.3 Means of IL6 and S. Creatinine for all studied groups

4.3 Lipid Profile and Glucose

Regarding total cholesterol, triglyceride, HDL LDL and VLDL and serum creatinine it was discovered that they were a non-significantly for men (172.4 ± 45.754, 141.647 ± 24.657, 49.564 ± 13.563, 109.32 ± 26.689 and 25.558 ± 15.571 respectivly) and women (169.473± 7.849, 108.573 ± 33.534, 44.6747 ± 17.473, 111.647 ± 38.684 and 23.113 ± 9.578 respectivly) in groups in patients with COVID-19 Table 4.3 and Figure 4.4 at P = < 0.05 when compared to control group (164.68 ± 28.478, 107.6 ± 31.57, 53.647 ± 18.467, 115.47 ± 37.583 and 22.647 ± 11.654 respectivly).

When doing Pearson test was the correlation between ACE with total cholesterol, triglyceride, HDL, LDL and VLDL, r = 0.058, 0.0443, 0.107, 0.066 and 0.048 respectively at P = < 0.05 as a shown in Table 4.4.

The glucose level was discovered that they were a significantly men (133.473 ± 35.658) and women (122.57 ± 33.644) in groups in patients with COVID-19 Table 4.3 and Figure 4.5 at P = < 0.05 when compared to control group (86.583 ± 17.583 respectivly). When doing Pearson test was the correlation between ACE with glucose r = 0.846** at P = < 0.05 as a shown in Table 4.6

Table 4.3 Evaluation of biochemical nutritional markers according to normal values: comparison between groups

Variables	Group AC Mean ± SD N = 45	Group BP Mean ± SD N = 45	Group CP Mean ± SD N= 45	Total Mean ± SD N = 135	P-value
Tc	164.68 ± 28.478	172.4 ± 45.754	169.473± 37.849	168.75 ± 32.741	
Tg	107.6 ± 31.57	141.647 ± 24.657	108.573 ± 33.534	116.86 ± 29.474	0.095
HDL	53.647 ± 18.467	49.564 ± 13.563	44.6747 ± 17.473	48.857 ± 46.745	0.241
LDL	115.47 ± 37.583	109.32 ± 26.689	111.647 ± 38.684	108.53 ± 34.754	0.085
VLDL	22.647 ± 11.654	25.558 ± 15.571	23.113 ± 9.578	33.757 ± 12.647	0.142
RBS	86.583 ± 17.583	133.473 ± 35.658	122.57 ± 33.644	113.75 ± 28.647	0.002

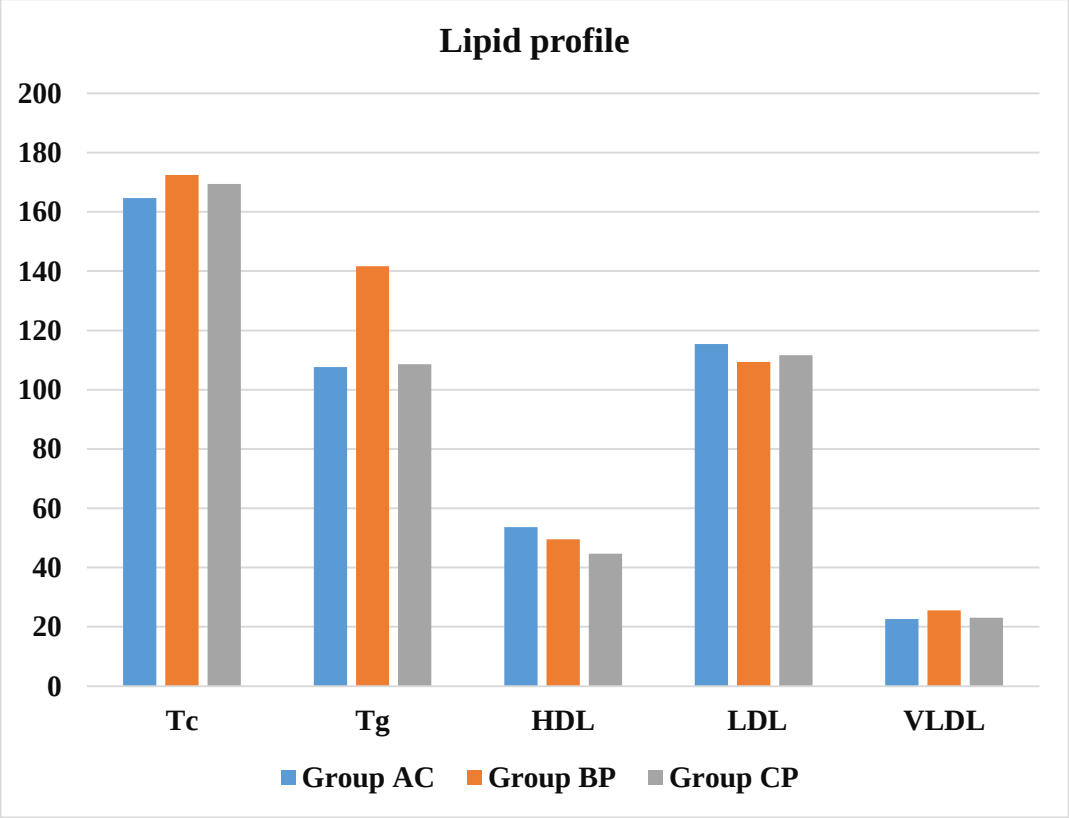

Figure 4.4 Levels for lipid profile

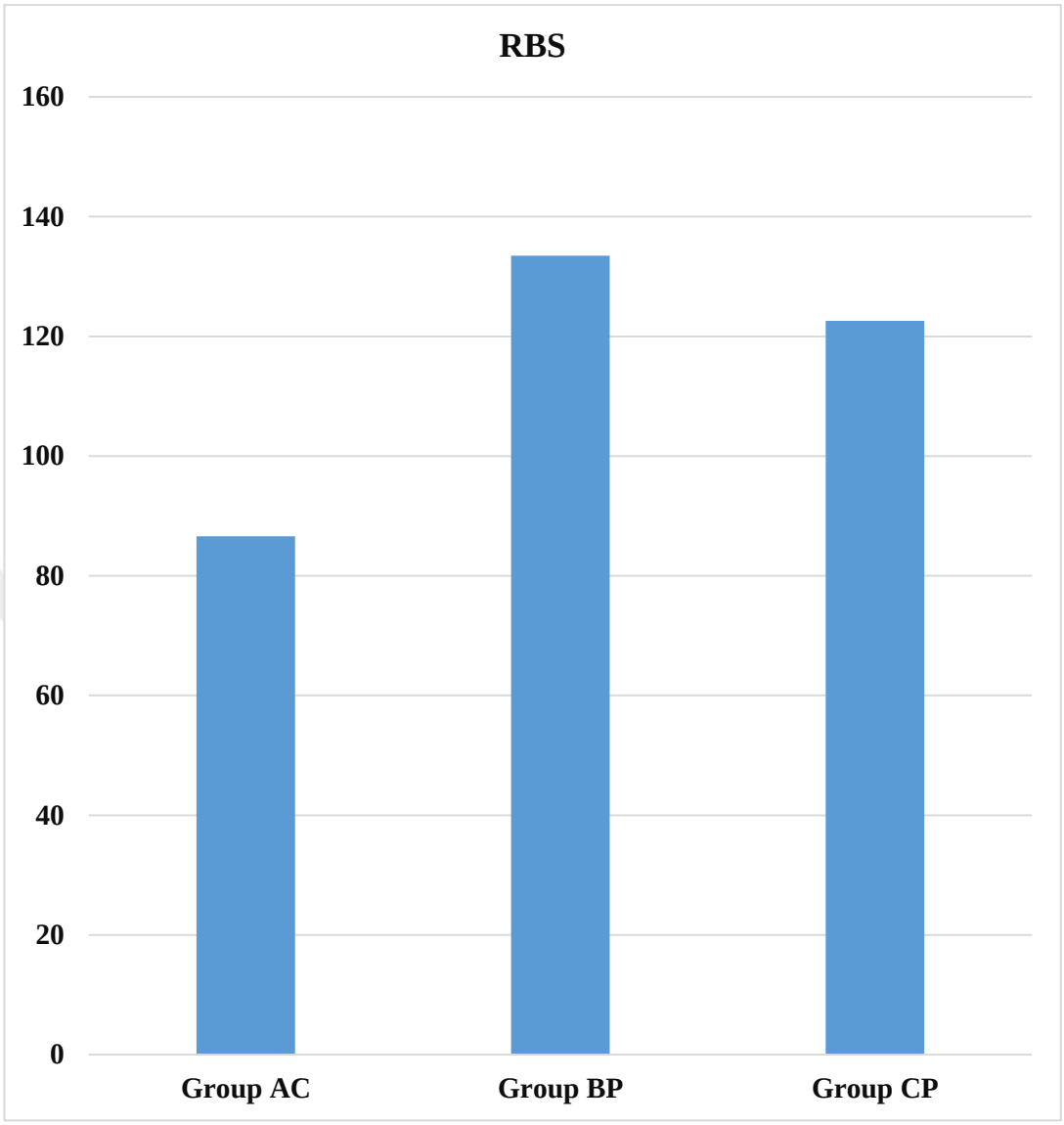

Figure 4.5 Levels for RBS

4.4 Evaluation of Biochemical Markers Based on Mean Correlation with HCV

The evaluation of biochemical markers based on mean correlation with HCV have shown clearly in Table 4.5.

Table 4.4 The correlation between biochemical parameters and HCV disease severity in each study group

Variables	***r***	**P-value**
ACE- Age	0.637**	<0.05
ACE - Weight	0.352*	< 0.05
ACE - BMI	0.047	> 0.05
ACE - IL6	0.538*	< 0.05
ACE - T. cholesterol	0.058	>0.05
ACE - Triglycerides	0.0443	>0.05
ACE - HDL	0.107	> 0.05
ACE - LDL	0.066	> 0.05
ACE - VLDL	0.048	> 0.05
ACE - Blood urea	0.011	> 0.05
ACE - Creatinine	0.076	> 0.05
ACE - LDH	0.554*	< 0.05
ACE - RBS	0.846**	< 0.05

5. CONCLUSION AND DISCUSSION

5.1 Conclusion

The study found clinical significance age, weight and body mass. They were also of great importance to ACE and LDH, and their impact was evident in Covid 19 patients. While there was no clear importance for fats. The study concluded that the factors of age, weight, ACE and LDH have the greatest role in the development and severity of Covid-19 disease.

5.2 Discussion

Coronaviruses have the potential to stimulate host immune responses that are poorly controlled. Because preliminary research revealed that patients with difficult Covid-19 had higher levels of interleukin 6 (IL6), we decided to do a thorough examination and meta-analysis of the relevant research in order to evaluate the state of knowledge in this area. The results of a meta-analysis of mean IL6 concentrations showed that individuals with difficult Covid-19 had 2.9 times greater levels than those with noncomplicated condition (Coomes and Haghbayan 2020).

Cytokines have a critical role in the regulation of immunological as well as systemic inflammation. Among them, interleukin 6 (IL6) is particularly significant because of the pleiotropic effects that it has. In this article, we provided the information that suggests that the severity of COVID-19 infection is directly associated to circulating levels of IL6. An increase in IL6 levels has been found in the past in patients who were suffering from respiratory dysfunction. This finding suggests that COVID-9 infection may contribute to a common mechanism of cytokine-mediated lung injury. In addition, it would seem that the highly pathogenic SARS-CoV-2 is linked to fast viral replication as well as a propensity to invade the lungs.

This results in an increased response of IL6-induced acute respiratory distress. Therefore, based on the findings of this study, it seems that repeated measurements of circulating IL6 levels might be a crucial factor in determining the course of illness in COVID-19-infected individuals. An increased level of IL6 has been shown to be a reliable biomarker for the severity of an infection caused by the hepatitis B virus (HBV), which is in agreement with our results.

Therefore, it is prudent that instant initial assessment of IL6 level be executed upon hospitalization, due to its great benefits to analyze exacerbating clinical characteristics and progression of the disease in COVID-19. This evaluation should be performed as soon as possible after hospitalization of COVID-19 patients (Ulhaq and Soraya 2020).

There was shown to be genetic variation that might explain anywhere from 18% to 37% of the variation in ACE levels. When genetic variations from the ORIGIN study were analyzed, researchers found that a drop in ACE levels, as measured by standard deviation, was also not connected with an increase in COVID-19 susceptibility or severe illness. Making use of different genetic variations from the AGES cohort. There was no correlation between genetically lowered blood ACE levels and either vulnerability to COVID-19 illness or the severity of the disease. According to these findings, those who are currently receiving treatment with Tricyclic antidepressants should continue doing so during the COVID-19 epidemic (Butler-Laporte *et al*. 2021).

The raised levels LDH were related with a 6 times greater likelihood of severe COVID-19 disease. In the early stage of myocardial infarction, as well as in conditions of hemolysis, there is an increase in the amount of it. In the event that cellular damage occurs, lactate dehydrogenase is released from inside the cells, leading to a rise in both its content and function in the plasma. In individuals with this condition, a high serum LDH activity is a marker that indicates a poor prognosis. LDH is a marker that may be used to diagnose a variety of inflammatory conditions, such as infections, cancers, heart attacks, sepsis, or cardio-pulmonary compromise. Lactate dehydrogenase has been shown by Denese and colleagues to be a possible index of vascular permeability in immune-mediated lung damage. Initial findings published in individuals with COVID-

19 have revealed substantial disparities in LDH levels between patients and those who do not have the severe condition (Szarpak *et al*. 2021).

REFERENCES

Becker, R. C. 2020. COVID-19 update: Covid-19-associated coagulopathy. Journal of Thrombosis and Thrombolysis, 501: 54-67.

Blaya, J., Barzideh, Z. and LaPointe, G. 2018. Symposium review: Interaction of starter cultures and nonstarter lactic acid bacteria in the cheese environment. Journal of Dairy Science, 101(4): 3611-3629.

Butler-Laporte, G., Nakanishi, T., Mooser, V., Renieri, A., Amitrano, S., Zhou, S. and Richards, J. B. 2021. The effect of angiotensin-converting enzyme levels on Covid-19 susceptibility and severity a Mendelian randomization study. International Journal of Epidemiology, 50(1): 75-86.

Caparrós, E. and Francés, R. 2018. The interleukin-20 cytokine family in liver disease. Frontiers in Immunology, 9: 1155.

Coomes, E. A. and Haghbayan, H. 2020. Interleukin-6 in COVID-19: a Systematic Review and Meta-Analysis. Reviews in Medical Virology, 30(6): 1-9.

Dadzie, I., Quansah, E., Puopelle Dakorah, M., Abiade, V., Takyi-Amuah, E. and Adusei, R. 2019. The effectiveness of dipstick for the detection of urinary tract infection. Canadian Journal of Infectious Diseases and Medical Microbiology, 2019: 1-6.

Delanaye, P., Cavalier, E. and Pottel, H. 2017. Serum creatinine: not so simple. Nephron, 1364: 302-308.

DeRoo, S. S., Pudalov, N. J. and Fu, L. Y. 2020. Planning for a COVID-19 vaccination program. JAMA, 32324: 2458-2459.

Elshaghabee, F. M., Bockelmann, W., Meske, D., De Vrese, M., Walte, H. G., Schrezenmeir, J. and Heller, K. J. 2016. Ethanol production by selected intestinal microorganisms and lactic acid bacteria growing under different nutritional conditions. Frontiers in Microbiology, 7: 47.

Gallo, M., Sapio, L., Spina, A., Naviglio, D., Calogero, A. and Naviglio, S. 2015. Lactic dehydrogenase and cancer: an overview. Front Biosci Landmark Ed, 2020, 1234-49.

Graham, B. S. 2020. Rapid COVID-19 vaccine development. Science, 3686494: 945-946.

GÜNER, H. R., Hasanoğlu, İ. and Aktaş, F. 2020. COVID-19: Prevention and control measures in community. Turkish Journal of Medical Sciences, 50(SI-1): 571-577.

Hofmann, M. A., Kiecker, F. and Zuberbier, T. 2016. A systematic review of the role of interleukin-17 and the interleukin-20 family in inflammatory allergic skin diseases. Current Opinion in Allergy and Clinical Immunology, 165: 451-457.

Hsu, Y. H., Li, H. H., Sung, J. M., Chen, W. Y., Hou, Y. C., Weng, Y. H. and Chang, M. S. 2017. Interleukin-20 targets podocytes and is upregulated in experimental murine diabetic nephropathy. Experimental and Molecular Medicine, 493: e310-e310.

Hudson, A., Romao, R. L. and MacLellan, D. 2017. Urinary tract infection in children. CMAJ, 18916: E608-E608.

Hussien, D. T., Shabana, A. A., Hassan, A. S. and Elmarghany, E. B. 2022. Assessment of serum interleukin-20 level in rheumatoid arthritis patients: Relation to disease activity and ultrasound measures. The Egyptian Rheumatologist, 442: 181-186.

Jeyanathan, M., Afkhami, S., Smaill, F., Miller, M. S., Lichty, B. D. and Xing, Z. 2020. Immunological considerations for COVID-19 vaccine strategies. Nature Reviews Immunology, 2010: 615-632.

Jia, B., Pu, Z. J., Tang, K., Jia, X., Kim, K. H., Liu, X. and Jeon, C. O. 2018. Catalytic, computational, and evolutionary analysis of the d-lactate dehydrogenases responsible for d-lactic acid production in lactic acid bacteria. Journal of Agricultural and Food Chemistry, 66(31): 8371-8381.

Jung, S., Hwang, H. and Lee, J. H. 2019. Effect of lactic acid bacteria on phenyllactic acid production in kimchi. Food Control, 106: 106701.

Juturu, V. and Wu, J. C. 2016. Microbial production of lactic acid: the latest development. Critical Reviews in Biotechnology, 36(6): 967-977.

Kaur, S. P. and Gupta, V. 2020. COVID-19 Vaccine: A comprehensive status report. Virus Research, 288: 198114.

Keller, K. E., Yang, Y. F., Sun, Y. Y., Walter, M. R. and Wirtz, M. K. 2019. Analysis of interleukin-20 receptor complexes in trabecular meshwork cells and effects of cytokine signaling in anterior segment perfusion culture. Molecular Vision, 25: 266.

Khodakheir, T. N., Pourtalebi-Firoozabadi, A., Sangtarash, M. H. and Nikravesh, A. 2017. Association between interleukin-19 IL-19 and interleukin-20 IL-20 genes polymorphisms with multiple sclerosis in an iranian population. Gene Cell Tissue, 42: e11957.

Kong, X., Zhang, B., Hua, Y., Zhu, Y., Li, W., Wang, D. and Hong, J. 2019. Efficient L-lactic acid production from corncob residue using metabolically engineered thermo-tolerant yeast. Bioresource Technology, 273: 220-230.

König, H. and Fröhlich, J. 2017. Lactic acid bacteria. In Biology of Microorganisms on Grapes, in Must and in Wine, pp. 3-41, Springer, Cham.

Lee, J. W., In, J. H., Park, J. B., Shin, J., Park, J. H., Sung, B. H. and Kweon, D. H. 2017. Co-expression of two heterologous lactate dehydrogenases genes in Kluyveromyces marxianus for l-lactic acid production. Journal of Biotechnology, 241: 81-86.

Liaud, N., Rosso, M. N., Fabre, N., Crapart, S., Herpoël-Gimbert, I., Sigoillot, J. C. and Levasseur, A. 2015. L-lactic acid production by Aspergillus brasiliensis overexpressing the heterologous ldha gene from Rhizopus oryzae. Microbial Cell Factories, 14(1): 1-9.

Liu, R., Yin, H., Sun, X., Liu, S., Wang, A., Wu, Y. and Xing, C. 2021. Interleukin 20 receptor A expression in colorectal cancer and its clinical significance. Peer J., 9, e12467.

Lone, S. A. and Ahmad, A. 2020. COVID-19 pandemic–an African perspective. Emerging Microbes and Infections, 91: 1300-1308.

Mathieu, E., Ritchie, H., Ortiz-Ospina, E., Roser, M., Hasell, J., Appel, C. and Rodés-Guirao, L. 2021. A global database of COVID-19 vaccinations. Nature Human Behaviour, 57: 947-953.

Mazzio, E., Mack, N., Badisa, R. B. and Soliman, K. F. 2021. Triple Isozyme Lactic Acid Dehydrogenase Inhibition in Fully Viable MDA-MB-231 Cells Induces Cytostatic Effects That Are Not Reversed by Exogenous Lactic Acid. Biomolecules, 11(12): 1751.

Mazzoli, R., Olson, D. G. and Lynd, L. R. 2020. Construction of lactic acid overproducing Clostridium thermocellum through enhancement of lactate dehydrogenase expression. Enzyme and Microbial Technology, 141: 109645.

Meng, B., Wu, D., Cheng, Y., Huang, P., Liu, Y., Gan, L. and Cao, Y. 2020. Interleukin-20 differentially regulates bone mesenchymal stem cell activities in RANKL-induced osteoclastogenesis through the OPG/RANKL/RANK axis and the NF-κB, MAPK and AKT signalling pathways. Scandinavian Journal of Immunology, 915: e12874.

Mickiewicz, K. M., Kawai, Y., Drage, L., Gomes, M. C., Davison, F., Pickard, R. and Errington, J. 2019. Possible role of L-form switching in recurrent urinary tract infection. Nature Communications, 101: 1-9.

Miyamoto, T., Oguma, Y., Sato, Y., Kobayashi, T., Ito, E., Tani, M. and Nakamura, M. 2018. Elevated creatine kinase and lactic acid dehydrogenase and decreased osteocalcin and uncarboxylated osteocalcin are associated with bone stress injuries in young female athletes. Scientific Reports, 8(1): 1-10.

Mora-Bau, G., Platt, A. M., van Rooijen, N., Randolph, G. J., Albert, M. L. and Ingersoll, M. A. 2015. Macrophages subvert adaptive immunity to urinary tract infection. PLoS Pathogens, 117: e1005044.

Mushegian, A. A. 2016. Bacteria stop fermentation with lactic acid. Science Signaling, 9(457): ec288-ec288.

Niess, J. H., Hruz, P. and Kaymak, T. 2018. The interleukin-20 cytokines in intestinal diseases. Frontiers in Immunology, 9: 1373.

Okojie, R. O. and Omorokpe, V. O. 2018. A survey on urinary tract infection associated with two most common uropathogenic bacteria. African Journal of Clinical and Experimental Microbiology, 193.

Ozaki, A., Konishi, R., Otomo, C., Kishida, M., Takayama, S., Matsumoto, T. and Kondo, A. 2017. Metabolic engineering of Schizosaccharomyces pombe via CRISPR-Cas9 genome editing for lactic acid production from glucose and cellobiose. Metabolic Engineering Communications, 5: 60-67.

Papadimitriou, K., Alegría, Á., Bron, P. A., De Angelis, M., Gobbetti, M., Kleerebezem, M. and Kok, J. 2016. Stress physiology of lactic acid bacteria. Microbiology and Molecular Biology Reviews, 80(3): 837-890.

Patel, R., Polage, C. R., Dien Bard, J., May, L., Lee, F. M., Fabre, V. and Hanson, K. E. 2022. Envisioning Future Urinary Tract Infection Diagnostics. Clinical Infectious Diseases, 747: 1284-1292.

Pfefferbaum, B. and North, C. S. 2020. Mental health and the Covid-19 pandemic. New England Journal of Medicine, 3836: 510-512.

Pohanka, M. 2020. D-Lactic Acid as a Metabolite: Toxicology, Diagnosis, and Detection. Biomed Research International, 2020: 3419034-3419034.

Pundir, C. S., Narwal, V. and Batra, B. 2016. Determination of lactic acid with special emphasis on biosensing methods: A review. Biosensors and Bioelectronics, 86: 777-790.

Rodrigues, C., Vandenberghe, L. P. S., Woiciechowski, A. L., de Oliveira, J., Letti, L. A. J. and Soccol, C. R. 2017. Production and application of lactic acid. In Current Developments in Biotechnology and Bioengineering, pp. 543-556. Elsevier.

Sauer, M., Russmayer, H., Grabherr, R., Peterbauer, C. K. and Marx, H. 2017. The efficient clade: lactic acid bacteria for industrial chemical production. Trends in Biotechnology, 35(8): 756-769.

Šenolt, L., Leszczynski, P., Dokoupilová, E., Göthberg, M., Valencia, X., Hansen, B. B. and Canete, J. D. 2015. Efficacy and Safety of Anti–Interleukin-20 Monoclonal Antibody in Patients With Rheumatoid Arthritis: A Randomized Phase IIa Trial. Arthritis and Rheumatology, 676: 1438-1448.

Šenolt, L., Prajzlerová, K., Hulejová, H., Šumová, B., Filková, M., Veigl, D. and Vencovský, J. 2017. Interleukin-20 is triggered by TLR ligands and associates with disease activity in patients with rheumatoid arthritis. Cytokine, 97: 187-192.

Singhvi, M., Zendo, T., Iida, H., Gokhale, D. and Sonomoto, K. 2017. Stimulation of d- and l-lactate dehydrogenases transcriptional levels in presence of diammonium hydrogen phosphate resulting to enhanced lactic acid production by Lactobacillus strain. Journal of Bioscience and Bioengineering, 124(6): 674-679.

Stapleton, A. E. 2017. The vaginal microbiota and urinary tract infection. Urinary Tract Infections: Molecular Pathogenesis and Clinical Management, 5: 79-86.

Szarpak, L., Ruetzler, K., Safiejko, K., Hampel, M., Pruc, M., Kanczuga-Koda, L. and Jaguszewski, M. J. 2021. Lactate dehydrogenase level as a COVID-19 severity marker. The American Journal of Emergency Medicine, 45: 638-639.

Tolulope, A. and Deborah, O. 2015. Urinary tract infection amongst pregnant women in Amassoma, Southern Nigeria. African Journal of Microbiology Research, 96: 355-359.

Tseng, C. C., Yang, R. J., Ju, W. J. and Fu, L. M. 2018. Microfluidic paper-based platform for whole blood creatinine detection. Chemical Engineering Journal, 348: 117-124.

Tsuge, Y., Kato, N., Yamamoto, S., Suda, M., Jojima, T. and Inui, M. 2019. Metabolic engineering of Corynebacterium glutamicum for hyperproduction of polymer-grade L-and D-lactic acid. Applied Microbiology and Biotechnology, 103(8): 3381-3391.

Ulhaq, Z. S. and Soraya, G. V. 2020. Interleukin-6 as a potential biomarker of COVID-19 progression. Medecine et Maladies Infectieuses, 50(4): 382.

Vaira, L. A., Salzano, G., Deiana, G. and De Riu, G. 2020. Anosmia and ageusia: common findings in COVID-19 patients. The Laryngoscope, 1307: 1787-1787.

Vandenberg, O., Martiny, D., Rochas, O., van Belkum, A. and Kozlakidis, Z. 2021. Considerations for diagnostic COVID-19 tests. Nature Reviews Microbiology, 193: 171-183.

Vargas, E., Ruiz, M. A., Campuzano, S., de Rivera, G. G., López-Colino, F., Reviejo, A. J. and Pingarrón, J. M. 2016. Implementation of a new integrated d-lactic acid biosensor in a semiautomatic FIA system for the simultaneous determination of lactic acid enantiomers. Application to the analysis of beer samples. Talanta, 152: 147-154.

Vlachostergios, P. J., Oikonomou, K. G., Gibilaro, E. and Apergis, G. 2015. Elevated lactic acid is a negative prognostic factor in metastatic lung cancer. Cancer Biomarkers, 15(6): 725-734.

Zaim, S., Chong, J. H., Sankaranarayanan, V. and Harky, A. 2020. COVID-19 and multiorgan response. Current Problems in Cardiology, 458: 100618.

Zhang, C., Zhou, C., Assavasirijinda, N., Yu, B., Wang, L. and Ma, Y. 2017. Non-sterilized fermentation of high optically pure d-lactic acid by a genetically modified thermophilic Bacillus coagulans strain. Microbial Cell Factories, 16(1): 1-10.

Zhang, L., Li, X., Yong, Q., Yang, S. T., Ouyang, J. and Yu, S. 2016. Impacts of lignocellulose-derived inhibitors on l-lactic acid fermentation by Rhizopus oryzae. Bioresource Technology, 203, 173-180.

Zhao, X., Zeisel, S. H. and Zhang, S. 2015. Rapid LC-MRM-MS assay for simultaneous quantification of choline, betaine, trimethylamine, trimethylamine N-oxide, and creatinine in human plasma and urine. Electrophoresis, 3618: 2207-2214.

Zheng, Z., Zhao, M., Zang, Y., Zhou, Y. and Ouyang, J. 2015. Production of optically pure L-phenyllactic acid by using engineered Escherichia coli coexpressing L-lactate dehydrogenase and formate dehydrogenase. Journal of Biotechnology, 207: 47-51.

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