

An overview of COVID 19 effects On Some human Body Function Bio Markers

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Abstract: Despite the emergence of COVID 19 since 2019 and despite the many studies that researchers have raced to uncover the truth about this virus, there is still great ambiguity in everything related to this virus, especially its behavior inside the human body and the body's reaction to it. The body reaction to COVID 19 differ greatly from one individual to another in terms of its type and severity. Hence the importance of this review, as if we understand the changes that this virus causes in the human body and are able to measure its bioindicators, this gives us the ability to understand the behavior of this virus inside the body and thus enables us to overcome it. The investigation of different biomarkers induced by COVID 19 infection will open the door to the researchers to understand the molecular mechanism of viral infection gives new diagnostic tools for the viral infection and gives the researcher a chance for discovering new strategies for COVID 19 treatment and prevention, and invention of new pharmaceutical products for viral treatment.

Keywords: COVID 19, liver, kidney, heart, function, biomarkers

1. Introduction

COVID- 19 or coronavirus is a contagious respiratory disease that is caused by severe acute respiratory syndrome coronavirus 2 or the SARS-CoV-2 . The disease was first observed in the Wuhan, in China, December 2019 and has emerged in a form of a global pandemic condition since it has affected worldwide (Alam et al., 2020). The World Health Organisation on January 30, 2020 has declared the outbreak of COVID-19 as a public health emergency that leads to the current pandemic situation at international concern (Sohrabi et al., 2020). The corona virus (or COVID-19) belongs to bigger family of viruses, that is causing common flu and the critical respiratory diseases like the Middle East respiratory syndrome MERS and Severe acute respiratory syndrome SARS (Chathappady House et al., 2021).

There are five types of the corona virus (or COVID-19), which are the mutant form of the virus that has been discovered few years back which has increased the mortality rate of the viral infection all over the world. These five types are the gamma, delta, beta, alpha and the omicron being the new variant that has been discovered (Karim & Karim, 2021).

COVID-19 virus enters the host cells through an enzyme called angiotensin-converting enzyme-2 (ACE2). The presence of this enzyme on the cell membrane allows the virus to enter the cell, as it works to bind to some proteins on the surface of the virus, such as Spike S protein (Kuhn et al.,

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2004). ACE2 is normally present in many different parts of the body such as ectopic cells, pulmonary alveolar cells, external small intestine, vascular endothelium, and smooth muscle cells (Gheblawi et al., 2020). ACE2 is primarily a transmembrane glycoprotein type 1 (Lambert et al., 2005), and it regulates the angiotensin system by inhibiting the action of ACE, as well as preventing acute respiratory distress syndrome (ARDS) (Ni et al., 2020).

There are three stages of infection of COVID-19, in the first stage infiltration of corona virus takes place, second phase marks with the pulmonary phase which marks with the inflammation in the lungs, and in the last and final stage of infection of COVID-19, systemic inflammation in lungs, cytokine storm and severe infection in the lungs take place (Aguilar et al., 2020). Presence of increased levels of many inflammatory biomarkers such as c-reactive proteins CRP which have been observed in the patients diagnosed with COVID-19 infection and these increased levels are associated or considered as indicator of increased risk of another severe disease that is cytokine storm. Another example of biochemical biomarker's alteration in case of COVID-19 infection is Lymphopenia, which is identified as a hallmark for this viral disease and it can be detected in the early stages of COVID-19 infection (Yuki et al., 2020). COVID-19 can affect the patient in the mild, moderate and severe scenario. It is a harmful viral infection which can be fatal if not treated with time. Several biochemical indicators are developed with the emergence of new symptomatic change which reflect the main pathophysiology of disease have been introduced or identified are considered as potential indicator which are associated with developing risk of many other severe diseases (Tjendra et al., 2020). Increase in the severity and inflammation markers and various acute phase reactants has been associated with the systemic processes and cytokine storms occur in the body after the exposure of the virus. In addition of this a number of other body infections are also associated with the infection of COVID-19 virus, which includes, diffuse alveolar damage, acute kidney injury, acute respiratory failure, multiple organ failure, irregular cardiac functions, irregular pattern in the level of oxygen (Zaim et al., 2020). Hematological alterations like White blood cells WBC and Platelets PLT are also detected in the blood samples of corona patients (Duarte et al., 2020). The emergence of new symptoms in different patients and their dynamic changes have led to the development of many biochemical indicators in the laboratory that helps to reflect on the important pathophysiology of the COVID-19 like heart enzymes, liver functions, completed blood counts, kidney functions, C-reactive protein CRP, D-dimer and blood gases (Leulseged et al., 2021). These biochemical indicators have been identified as the potential indicator that is associated with the development of risk factors of other diseases that can cause severe health issues.

1.1. Human Coronaviruses

The main origin of human coronaviruses is bats. An intermediate host such as Camels transfers MERS-CoV from bats to humans. MERS-CoV, is related to different bat coronavirus species, that appeared several centuries ago. The most closely related bat coronavirus and SARS-CoV deviated in 1986 (Pal et al., 2020). Seven human coronaviruses (HCoVs) have been identified Up-to-date. In humans, four of them are known to be less harmful and classically cause only mild respiratory diseases in healthy human adults. But, they could be the reason for common cold infections, while it can lead to long term, life-threatening diseases in people with weak immune systems. (Taylor et al., 2021) Human coronaviruses that cause MERS, SARS and COVID-19, are considered harmful and could lead to severe illness such as shortness of breath and even death. COVID-19 disease tends to be milder than SARS and MERS, but less harmful than previously mentioned four human coronaviruses (Taylor et al., 2021)

1.2. Coronavirus disease 2019 (COVID-19)

It is an infectious disease, the virus that cause this disease is severe acute respiratory syndrome coronavirus 2 which is known as (SARS-CoV-2). The World Health Organization (WHO) recommended 2019-nCoV as the name of COVID-19 in 2020 (World Health Organization, 2020a). The first case known with COVID-19 was diagnosed in December 2019 in Wuhan, China, Firstly, the virus and disease in Wuhan were generally named as "coronavirus" and "Wuhan coronavirus", also, it was known as "Wuhan pneumonia". After that the disease has spread worldwide, leading to an continuing pandemic. (Zimmer, 2021) In 11 February 2020, WHO issued the names of COVID 19 and SARS-CoV-2, where, CO stands for corona, VI for virus, D for disease, and 19 for 2019, the year of the outbreak. In public communications, the name of the virus is known as "the COVID 19 virus" (Gover et al., 2020)

1.3. Structure of Covid-19

The new COVID-19, is most closely related to a group of SARS-CoVs found in humans, bats, pangolins and civets, and as other coronaviruses it has a relatively simple structures (fig. 1), and their design helps us to know how they work (Hu et al., 2021) .The new COVID-19 and the SARS virus are very similar in structure, but there are also differences due to their genomes changes. Such as the way they are transmitted from one individual to another, and the different symptoms of coronaviruses (Das et al., 2021). Corona has a distinctive appearance, when seen under a powerful microscope, they have a spherical pleomorphic shape that is coated with spikes of protein, to fascilate access into host, these spikes uses an N-terminal signal sequence to bind and infect new healthy people (Santos-Sánchez & Salas-Coronado, 2020). Under these spikes there is a membrane layer. This membrane can be interrupted by cleansers and alcohols, and this is why soap and water, or alcohol sanitizer are used effectively against COVID-19 (Das et al., 2021). COVID-19 virion is an RNA enveloped, with positive-sense beta-Coronavirus that is belong to the family Coronaviridae. Inside a helix capsid, the genome is packed by the nucleocapsid protein (N). There are another three structural proteins linked to the viral envelope: envelope (E), membrane (M), and glycoprotein spike (S) (Ghafoor et al., 2021). The average diameter of Virions in diameters are about 80 to 120 nanometers. Protein S (150 kilodalton) and its project about 17 to 20 nanometers from the surface of virion, at the distal end, it swells up to 10 nanometers (Santos-Sánchez & Salas-Coronado, 2020). S protein binding to angiotensin converting enzyme (ACE2) is the first step in facilitating cellular entry of COVID-19 on precise cellular receptor sited on the surface of the host cell. (ACE2) is a common receptor for SARS-CoV as well; zoonotic transmission also is facilitated by this receptor because these viruses can attached ACE2 from various animal species (Cuervo & Grandvaux, 2020). Protein M is a three transmembrane domain glycoprotein that is located on the virion envelope membrane and fasciitate virus entry to host cell, it is relatively small (from 25 to 30 kilodalton) (Ghafoor et al., 2021). Protein E is presented inside the virions in small amounts, it is very small (8 to 12 kilodalton), variable and it is important in infection process. Protein N is the main component in nucleocapsid that is constituted by two different domains, an N-terminal domain, and a C-terminal domain, and they can bind to ribonucleic acid with different mechanisms (Santos-Sánchez & Salas-Coronado, 2020).

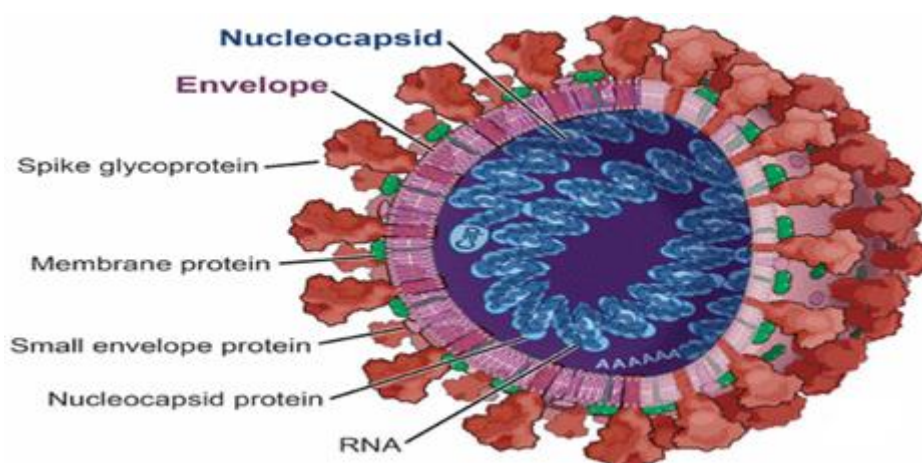


Figure 1. Structure of coronaviruses. (Bergmann & Silverman, 2020)

RNA viruses have small genomes which are subject to constant change, these changes, called mutations that help the virus adaptation and to infect other host species. COVID-19 is thought to be originated from bats, but jumping of mutations from animals to humans is not yet well understood (Andersen et al., 2020). Novel coronavirus particles are gathered in the Golgi complex and the endoplasmic reticulum. Budding of membrane between these partitions was stated in association with N protein and genomic RNA along with E, M, and S proteins. The whole virions are transported to the extracellular environment after a predictable secretory pathway (Santos-Sánchez & Salas-Coronado, 2020). Researchers have studied the virus to well understand the genetic structure of the virus to realize how to effectively treat it (Udugama et al., 2020). Also, it is important interactions to produce vaccines, and to diagnose the disease. Most microscopic studies of COVID-19 were made using transmission electron microscopy. Also, high resolution scanning electron microscopy (SEM) is used to study inner cellular structures of the virus. Evidence of infection-induced cellular remodeling was found, and the development of a specific region for viral morphogenesis. SEM also distinguished viral cell surfing between intercellular extensions (Caldas et al., 2020).

1.4. Replication cycle of COVID-19 and Cell entry

Infection starts by the attachment of viral spike protein to its matching host cell receptor. After that, a furin-like protease of the host cell cuts and stimulates the receptor-attached spike protein S. this well separate protein S into S1(virus penetration receptor-binding domain) and S2(facilitate fusion) polypeptide (Santos-Sánchez & Salas-Coronado, 2020). Depending on the available host cell protease, cutting and stimulation will allow the virus entrance to the host cell by direct fusion or endocytosis of the viral cover with the host membrane (Jackson et al., 2022). After the entry to the host cell, the virus elements are uncovered, and its genome pass in to the cell cytoplasm. The RNA genome of the coronavirus has a 5 methylated cap and a 3 polyadenylated tail, this lets it to perform like a messenger RNA and then it will be translated directly by the ribosomes of the host cell's (Santos-Sánchez & Salas-Coronado, 2020). Translation result in two large overlapping polypeptides, pp1a and pp1ab that were translated by host ribosomes, and form the initial viral genome overlapping open reading frames ORF1a and ORF1b (Jackson et al., 2022). The polyprotein pp1ab is the larger and results from -1 ribosomal frameshift caused by a slippery sequence (UUUAAAC) and RNA pseudoknot downstream by the end of open reading frame ORF1a. The ribosomal frameshift lets the constant translation of ORF1a tracked by ORF1b (Santos-Sánchez & Salas-Coronado, 2020). Proteases are unique for the polyproteins, PLpro (nsp3) and 3CLpro (nsp5), which cut the

polyproteins at dissimilar precise places. Cutting of polyprotein pp1ab yields in 16 nonstructural proteins (nsp1 to nsp16). Produced proteins contain various replication proteins such as RNA-dependent RNA polymerase (nsp12), exoribonuclease (nsp14) and RNA helicase (nsp13) (Jackson et al., 2022). Many nonstructural proteins combine to form a multi-protein replicase-transcriptase complex (RTC). RNA-dependent RNA polymerase (RdRp) is the main replicase-transcriptase protein. Replication and transcription of RNA from an RNA strand is derived by RdRp. The replication and transcription process are supported by other nonstructural proteins in the complex. For example, the exoribonuclease nonstructural protein, offers extra reliability to replication by giving a proofreading job that is not present in the RNA-dependent RNA polymerase (RdRp) (Santos-Sánchez & Salas-Coronado, 2020). One of the main jobs of the complex is viral genome replication. RdRp directly facilitates the synthesis of negative-sense genomic RNA from the positive-sense genomic RNA. After that the replication of positive-sense genomic RNA from the negative-sense genomic RNA occurs (Jackson et al., 2022). RNA recombination seems to be a main reason in determining genetic changeability in coronavirus species, the ability of a coronavirus species to jump from one host to another, and defining the development of novel coronaviruses. Template shifting during genome replication could be the reason for recombination in coronaviruses (Sheahan et al., 2020).

Cell entry of COVID-19 occurs through the interaction of the receptor-binding domain of the spike protein with angiotensin-converting enzyme (ACE2) receptor, which causes cleavage/activation of the spike protein by cellular proteases. After fusion of the viral envelope with the cellular membrane, the viral positive-strand RNA is translated into a polyprotein and cleaved by viral proteases, forming the replicase-transcriptase complex (RTC) within double-membrane vesicles (Cuervo & Grandvaux, 2020). The RTC that contains error-prone RNA-dependent RNA polymerase then mediates viral RNA replication, which leads to viral protein synthesis and produce more viral RNA. Viral proteins translocate to the endoplasmic reticulum (ER), assembling in the ER-Golgi intermediate compartment (ERGIC), and daughter virions are released by exocytosis, these daughter virions often contain mutations due to the error-prone nature of the replication cycle, and these mutants may alter different aspects of COVID-19 pathophysiology (Otto et al., 2021). There are thousands of COVID-19 variants that are grouped into either clades or lineages variants. The WHO, in association with partners, expert networks, institutions, national authorities, and investigators, found a novel nomenclature systems for identification and following COVID-19 genetic families by GISAID (???), Nextstrain and Pango(not understand). Nowadays, using the Greek Alphabet letters by the experts arranged by WHO has recommended the labeling of variants. For example, Alpha, Beta, Delta, and Gamma, giving the explanation that they "will be easier and more applicable for non-scientific persons. Nextstrain classified the variants into five clades (19A, 19B, 20A, 20B, and 20C), GISAID classified the variants into seven (L, O, V, S, G, GH, and GR). And the Pango tool classified the variants into lineages, with many of them being classed under the B.1 lineage (Backer et al., 2020)

Effect of in COVID-19 on Liver Function biomarkers.

Several studies reported the damage of the liver in COVID-19 patient with increased level of hepatic enzymes like alanine transaminase ALT than the normal level. This indicates the association of liver damage with the viral infection. In recent studies, it has been observed that COVID-19 infection has adverse effects on the liver function (McGrowder et al., 2021). Coronavirus binds with ACE2 on the cholangiocytes, this binding leads to the dysfunction of the cholangiocytes that induce the systematic inflammatory response causing the liver injury in the patient. Because of this, the aspartate aminotransferase AST level is increased in the patient (Alqahtani & Schattenberg, 2020).

Albumin is an important factor of serum proteins and is associated with the systematic inflammation. The decreased level of serum albumin indicates among nutritional status, kidney as well as liver dysfunctions and is seen to be the independent predictor of the survival rate in patients (Keller, 2019; Soeters et al., 2019). The decreased albumin level is found to be an independent factor that is associated with COVID- 19 patients and the reason for their unimprovement during the infection. Therefore, it can be regarded that the low level of albumin can indicate the risk index of positive COVID-19 infection in the individual (Huang et al., 2020). The degradation of body protein is observed in severe and critical cases of COVID-19 patient, decreased serum level of the total protein TP, pre albumin, and albumin, which is related to the mortality in different diseases. The loss of TP indicates the dysfunction of immune system and exacerbates the symptoms of COVID-19 infection. Luo et al., 2020, Li et al., 2020). From clinical characteristics and the laboratory findings that were collected from COVID-19 patients well analyzed which showed abnormal alkaline phosphatase ALP activity in almost 20% patient (Hwaiz et al., 2021). This indicates that the activities of the hepatic enzymes in COVID-19 patients are abnormal which can be a sign of the viral replication in the liver. With the development of COVID-19 infection in patients, the development of different abnormalities in liver is observed (Bertolini et al., 2020). In certain studies, it has been observed that the level of Gamma glutamyl transferase GGT is increased and is frequently present in patients that are affected from COVID-19 virus. it is usually seen that the level of GGT is increased in patient suffering from Severe pulmonary diseases like pneumonia then in the patient with the mild pneumonia (Ma et al., 2021). This increased level of GGT is the reason for a patient to stay under medication for a longer period of time (Liu et al., 2021). The laboratory diagnosis of the COVID -19 patient demonstrate that severity of COVID-19 infection is associated with increased level of bilirubin in the blood (Italia et al., 2021). It is also observed that the patient in the intensive care unit ICU who is affected by the viral infection has increased level of the bilirubin than those patients were admitted in the ICU. In severe patient, the level of liver dysfunction is higher which is indicated by the increased level of bilirubin in the blood (Liu et al., 2020). From different analysis it has been observed that the level of lactate dehydrogenase LDH is almost six-fold times increased in severe COVID-19 viral infection. With the increased level of LDH in patients, the mortality rate is also increased by 16 times. That is why the LDH level should be monitored frequently to diagnose the progression or the decompensation of the disease (Henry et al., 2020). The CRP are acute phase protein, which is an indication of initial marker of the inflammation in the body (Stringer et al., 2021). During the state of inflammatory disease, the CRP level are able to activate the classical complement cascade of immune system although the effect of these proteins on COVID-19 patient is not properly known. However, the level of these proteins can be used to detect the COVID-19 disease in patients. It has been observed that the CRP are higher during the infection and is regarded as early detector of the severity of the infection (Mosquera-Sulbaran et al., 2021). A recent systematic analysis found that the patients and mortality caused by COVID-19 have elevated values of the D-Dimer level (Conte et al., 2021). However, there are no consistent values for the cut off from the level which can be used to predict the adversity of the infection. The mortality rate associated with the level is higher, although the effect of the anticoagulation on the D-Dimer level is not clear and its level is low in the patient who is receiving the anticoagulation (Kermali et al., 2020).

1.5. Effect of COVID-19 on kidney function biomarkers.

Several patient sufferings from severe cases of the COVID-19 virus have shown signs for the damage of the kidneys, even in patients who did not have any history of kidney problems (Askari et al., 2021). Certain laboratory results indicated that the creatinine levels were higher in severe cases of

the viral infection (Pourbagheri-Sigaroodi et al., 2020). The BUN is considered as an important and independent risk factor in the mortality rate of the COVID-19 patient. Although the relationship of the BUN, its dynamic change and the severity of the viral infection is still under study. In certain studies it has been found that the increased level of the BUN is associated with elevated in hospital mortality rate of the patient (Ok et al., 2021). From different studies it has been observed that the patient with COVID-19 virus infection have reported with a lower level of uric acid in the blood than that of the normal level at the time of admission. The lower level of the unique acid is associated with the severity of the disease especially in males. However, the serum uric acid level is not an independent unreliable risk factor for the development of the severe COVID-19 disease (Chen et al., 2021). Although its increased level in the patient might cause other health problems which can add a negative impact on the patient.

1.6. Effect of COVID-19 on cardiac biomarkers

Cardiac troponin is a biomarker for the identification of myocardial injury and myocardial infarction. The clinical use of cardiac troponin is extended beyond the diagnosis, which has an important role in the identification of the risk that is associated with the acute coronary syndrome, cardiovascular diseases and coronavirus diseases. The biomarker indicates the severity of the viral infection, which can be associated with myocardial damage with it being critical if the level is increased in the patient (Chan & Ng, 2010). Studies have recorded that the Troponin T level is increased in patient with COVID-19 infection and significantly related with the fatal outcomes of the infection. This increased level can be caused by several mechanism including microangiopathy, viral myocarditis, cytokine driven myocardial damage along with unmasked coronary artery disease CAD. It can be said that COVID-19 infection being a primary respiratory disease, it involves cardiovascular system by misbalancing the renin-angiotensin- aldosterone system that is mediated by the ACE2 depletion (Tersalvi et al., 2020). Studies provided evidence about the incidence of the increased level of creatinine kinase CK and the mortality rate (Akbar et al., 2021). It has been observed that the level of CK and the poor outcome of the COVID-19 infection in patients dependent on each other. The elevated level is related to almost 50% for the poor outcome, which is not associated with other factors like age, sex as well as other health issues (De Rosa et al., 2021). A previous analysis provides evidence about the increased level of CK-MB and its association with the severity of COVID-19 infection. Another analysis suggests that increase the level of the CK-MB is significantly related with the increased risk of mortality in the patient infected by COVID-19 virus (Shi et al., 2020).. The SARS coronavirus targets the ACE2 and caused different issues in the body like myocardium. The CK-MB found in myocardium is the marker associated with the diagnosis of any kind of damage in the myocardium (Mythili & Malathi, 2015).

1.7. Effect of COVID-19 on lipid profile

Covid-19 is RNA virus that have lipid envelope and so the biosynthesis pathway of Cholesterol plays a vital role in assembly, replication and infectivity of the viral particles (Abu-Farha et al., 2020). That is why it is recommended that patient who is on treatment of cholesterol modifying drugs should continue to take the medicine during COVID-19 infection. It is also recommended that patient who has acquired severe viral infection should be treated with Cholesterol modifying drugs, which would help to prevent the life-threatening complications of the cardiovascular tissues (Garg & Khanna, 2021). Different studies suggested that patient with severe COVID-19 infection are reported to have higher Triglyceride level during admission in the hospital and prior to the infection. The elevated

level of triglycerides is associated with severity of the viral infection and our good detector of the severity of the COVID-19 (Masana et al., 2021). The total lipid profile can be considered as one of the sensitive markers for the inflammation in the body due to COVID-19 virus and therefore should be monitored in the patient with the infection (Mahat et al., 2021). In COVID 19 patient, the high-density lipoprotein cholesterol HDL is found to be lower than the normal level before or during the infection. Some of the clinical data provides evidence, which shows that the significant decrease of the HDL cholesterol level in the body is associated with the severity and mortality rate of the COVID-19 infection (Wang et al., 2020). The HDL cholesterol performs several functions which includes regulation of the immune response, antioxidation, anti-apoptosis and the anti-thrombosis formation (Kaji, 2013), so it has been observed that the composition and the function of these cholesterol are immensely changed during COVID-19 infection. The level of low-density lipoprotein LDL cholesterol in patients suffering from COVID-19 infection. The decrease of the LDL cholesterol is seen to be irreversible, and the level continuously decreased until the time of death (Koçar et al., 2021). It is also seen that Cholesterol has become an important factor in the COVID infection although its molecular mechanism is still unclear (Tang et al., 2021). According to Masana et al. (2021), the entry of COVID virus into the host body is dependent on the cholesterol and so drugs that elevate the influx of Cholesterol can be used for the treatment of COVID-19 patient.

1.8. Effect of COVID-19 pancreatic enzymes

It has been observed that patient affected with COVID-19 virus might incur complications, which are associated with the increased level of pancreatic enzyme in the blood, which includes acidosis, diabetes and renal failure. It is observed that COVID-19 affected the epithelial lining of the duct of the salivary gland, which is also a source of Amylase in the blood (de-Madaria et al., 2021). In recent studies the COVID-19 causes that's true intestinal symptoms like gastroenteritis, which is caused by the elevated levels of pancreatic enzyme (Zippi et al., 2020). Lipase is the key in that helps to digest the triglycerides and is secreted by kidneys. A recent study from different parts worldwide, provide evidence of the pancreatic injury that is defined by the increased level of the light base up to the level of almost 17% in active COVID-19 cases. (de-Madaria et al., 2021).

1.9. COVID-19 and blood glucose levels

In several studies, it has been observed that individual with higher level of glucose in the blood and individual with normal blood sugar level have equal chances of being infected by the COVID-19 virus (Li et al., 2020). However, people with diabetes face severe problems, which can have complications that might worsen if they are infected, although chances of getting affected is not recorded. The chances of getting serious health complications with diabetes are observed during COVID-19 infection as they already have dysfunction of the pancreas (Lim et al., 2021). It is also observed that the viral infection can elevate the inflammation and internal swelling in patient suffering from diabetes, which contributes to the severity of the infections (Alves et al., 2012).

1.10. Effect of COVID-19 on blood electrolytes

The patient with the COVID-19 infection are found to have the Sodium level altered in the blood (Nahkuri et al., 2021). It has been recorded that hospitalised patient with COVID-19 infection that have higher levels of Na in the blood have a risk of dying more three times than the patient with normal level. On the contrary patient who has lower levels of Na in their blood are seen to have necessity for respiratory ventilators and support system. The prognosis of the COVID-19 patient is

seen to be poor with the abnormal levels of the Na and low sodium level in the blood increases the requirement for intubation or some other ways of breathing support for the patient (Tzoulis et al., 2021). Evidence is showed that the K is excessively excreted to urine, which can cause severe health problems in the COVID-19 patient. The electrolytic virus with special reference to K abnormalities is reported as one of the most common clinical manifestations for the COVID-19 infection. The impairing of the activity of the epithelial Na channels that is caused by the virus causes this balance (Mabillard & Sayer, 2020). Several studies provide evidence on the effect of COVID-19 infection on Calcium Ca level in the blood system. It has been observed that moderate and extreme cases of COVID-19 have resulted for the decreased level of Ca during the initial phase of the infection. The level of Ca in the blood is related to the severity of the viral infection and therefore it can be regarded as a biomarker for the clinical severity of the COVID-19 virus in the initial onset of the symptoms (Zhou et al., 2020). Some initial studies have reported about the various abnormalities in the electrolyte level during the admission of the patient and the progress of the severity from mild to extreme form of the disease (Lippi et al., 2020). The electrolytic imbalance affects the patient care along with providing inside in the battle physiology of the COVID-19 disease. Several studies confirmed that the severity of the COVID-19 disease is related to the reduced level of electrolyte in the blood, which needs to be measured in the initial phase of the infection and frequently monitored to avoid complications in the future (Pourfridoni et al., 2021).

1.11.Effect of COVID-19 blood gases

There are few studies about the effect of COVID-19 virus on the blood gases. However, some major studies indicated that the admission of individuals suffering from COVID-19 virus in the intensive care unit is reported to have alkalemia on the arterial blood gas ABG. The higher range of pH and Decreased level of partial pressure of the oxygen PO₂ in the arterial blood is associated with the survival of the patient (Bezuidenhout et al., 2021). In certain studies, it has been observed that positive patient of COVID-19 who have been in the emergency room showed increase levels of PCO₂ and lower of ionized calcium as compared to the systematic to the COVID-19 negative patient. The analysis of blood gas would help for the identification of the COVID-19 virus in the patient and can be regarded as the early sign of the hypoxia (Elezagic et al., 2021). Patient that is affected with COVID-19 exhibit the oxygen level as incompatible with the life without the dyspnea. Judging the severity of hypoxemia on the oxygen supplement is seen to be problematic because prior to intubation the estimation of the condition of the patient is critical (Tobin et al., 2020). The current outbreak of the COVID-19 virus is associated with different respiratory, cardiac, liver as well as issues related to multi organ failure. The symptomatic patient with COVID-19 viral infection high level of the bicarbonate HCO₃ on arterial bloods and can be regarded as a rapid identifying sign of the COVID-19 positive patient (Cobre et al., 2021).

1.12.Effect of COVID-19 iron and ferritin

Evidence is demonstrated that severe COVID-19 infection causes the decrease alteration of the Iron Fe level, which is being handled at the systematic level as the Hyperferritinemia, , Are seem to be relevant proportion of the patient whose infection is on set after two months (Sonnweber et al., 2020). In a recent study about COVID-19 it was observed that the patient with the severe as well as extremely severe COVID-19 infection shows increased level of Ferritin. In extremely severe cases of COVID-19 group which is higher than the severe COVID-19 group (Cheng et al., 2020). The metabolism of Iron and anaemia might play a vital role in the multiple organ dysfunction syndromes

during the coronavirus disease (Sonnweber et al., 2020). The decrease level of unsaturated iron binding capacity UIBC indicates the deficiency of iron and the inability to observe it in the blood, which might affect different organs in the body during the viral infection (Lv et al., 2021).

1.13.Hematological effect of COVID-19

Hypoxia is observed in severe cases of COVID-19 infection which is related to SARS-CoV 2 Mediated band 3 alteration that might decrease the ability of the RBC for reducing the ATP. This would result from the reduced vasodilation and delivery of oxygen to the tissues and the cells. Since the average life span of RBC is almost 120 days, the defect and damaged form of these cells circulate in the patient for almost three months before they are eliminated from the body (Misiti, 2021). COVID-19 is combined with anaemic hypoxia, which leads to decreased level of haemoglobin Hb in the blood. Since the RBC are damaged during COVID-19 infection, they lose their ability to combine and circulate the Hb. Deprivation of oxygen and accumulation of Iron in lungs cause vasoconstriction and pneumonia (Cavezzi et al., 2020). In-patient with COVID-19 infection, the hematocrit Level is seen to be reduced due to the decreased level of RBC in the blood, which can be a sign of anaemia and cause health issues which might be fatal as well (Djakpo et al., 2020). In COVID-19 patient, rapid desaturation of oxygen is one of the common symptom that cause serious respiratory failure. Intubation and mechanical ventilator are required to elevate the oxygen level. However, the effect of COVID-19 virus on the mean cell volume MCV is still unknown, However, some studies have found that there is a slight increase in people with Covid 19 (Lanini et al., 2020). With the reduced Hb and RBCs in the blood, the patient suffering from COVID-19 virus might acquire anaemia. Although the effect of the virus on mean cell haemoglobin MCH is still unknown (Suliman, 2021). Although the oxygen level is seen to be reduced in COVID-19 patient, the effect of the COVID-19 on the mean corpuscular haemoglobin concentration MCHC is not clear. Although the Hb and the RBCs in the patient are significantly reduced, which can cause severe health issues like anaemia. It has been observed that patient suffering from COVID-19 infection, who were diagnosed with higher level of red cell distribution width RDW which was greater than 14.5% during admission had a mortality risk of almost 31%. On the other hand patient with low RDW ranging from lower than 14% had a mortality range of 11% (Higgins et al., 2020). With the oxygen saturation in COVID-19 patient it has been observed that the mean platelet volume MPV has differed between the different days of hospitalisation and can be considered as a significant parameter for the prediction of mortality rate in patients (Güçlü et al., 2020). Different findings have suggested that COVID-19 infection has been associated with elevation of the production of immature and large platelets such as megakaryocytes in response to the elevated consumption of platelets. It has also been observed that go with 19 infection is related to the elevated production of the immature platelets in spite of the fact that the normal platelet counts was in normal range (Wool & Miller, 2021). The platelet distribution width PDW is widely and frequently used for clinical practice. High level of PDW is associated with severe sepsis (Guclu et al., 2013), although the effect of COVID-19 on this parameter is still not clear, However, there is a study indicating that PDW increases its level in acute cases and is associated with an increased mortality rate in covid-19 patients (Aydınyılmaz et al., 2021). Several studies have given evidence that severe infection and death of patients suffering from COVID-19 has a elevated white blood cell count WBCs in their blood (Zhao et al., 2020). Some other studies also suggested that lower levels of WBC or higher levels of WBC in association with the lower level of Lymphocytes has been associated with severe illness as well as death in COVID-19 infection (Elshazli et al., 2020). Several cases have been recorded in which the Neutrophils count is elevated in blood during severe COVID-19 infection, the excessive amount of Neutrophils count

in the blood would be able to explain pathogenesis of COVID-19 virus causing lung injury and pneumonia (Wang et al., 2020). Several studies determined that severity of the disease is associated with abnormal lower count of the Lymphocytes in blood. With this, the mortality rate is high due to lymphopenia associated with COVID-19 infection (Huang & Pranata, 2020). Studies provided evidences about the activated monocytes in the blood that has shown infiltration of the lungs in COVID-19 patient. The average count of the Monocytes was lower in patients that were associated with high mortality rate (Knoll et al., 2021). COVID-19 infection is reported to be associated with eosinopenia in patients suffering from acute respiratory deterioration along with COVID-19. Lung pathology associated with Eosinophil is reported to be associated with viral infections and is a complication for other variants of coronavirus (Djangang et al., 2020). It has been observed that severe COVID-19 infection is associated with reduced range of basophile in the blood. It is also reported that negative association between the basophil percentage and the basophil count of the WBC is also seen in hospitalised as well as severe COVID-19 diseases (Murdaca et al., 2021).

Conclusion

COVID-19 infection induces lots of human body alterations that differs from person to the other. This alteration includes biochemical and hematological ones. The biochemical alterations manifested by disturbance in nearly all body organs functions biomarkers, especially hepatic, renal, cardiac and pancreatic and immunological biomarkers as well as blood electrolytes and minerals. The hematological alterations include disturbance in all blood elements and their function. lots of studies especially the in vivo ones are needed to solve the COVID-19 mystery.

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