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Coronavirus: A Biochemical Approach

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Review

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Abstract

The purpose of this study is; to give information about the biological structure, metabolism and interaction of the Covid-19 agent virus with the defense system; to reveal the relationship between biochemical blood values and the defense system in Covid-19 cases and to update the data on preventing the damage that the virus may cause, in line with scientific developments. Relevant articles found by searching the keywords "SARS-CoV-2" and "Coronavirus" in Pubmed, Web of Science and Google Scholar databases and Google Search Engine were included in the study. This virus, called SARS-CoV-2, which originated in Vuhan, China and caused the disease called Covid-19, spread to almost all countries of the world and caused a high number of deaths in a very short time. Using the virus RNA, the infected cell begins to produce proteins that will keep the immune system at bay and help create new copies of the virus. For this reason, monitoring the disease and sharing information all over the world, epidemiological contact history, clinical features, biochemical tests in all blood and urine and other conditions are important evaluations for the treatments of the patient. It is imperative to follow the global situation and to make correct decisions according to the changes in epidemiology and to update the information of employees.

Keywords: SARS-CoV-2, Covid19, biochemical tests

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Öz

Bu çalışmanın amacı; Covid-19 etkeni virüsün biyolojik yapısı, metabolizması ve savunma sistemiyle etkileşimi hakkında bilgi vermek; Covid-19 vakalarında biyokimyasal kan değerleri ile savunma sistemi ilişkilerini ve virüsün yaratabileceği tahribatları engellemek konusundaki verileri bilimsel gelişmeler doğrultusunda güncelleyerek ortaya koymaktır. Pubmed, Web of Science ve Google Scholar veri tabanlarında ve Google Arama Motorunda "SARS-CoV-2" ve "Coronavirus" anahtar kelimeleri aranarak bulunan ilgili makaleler çalışma kapsamına alınmıştır. Çin'in Wuhan kentinde ortaya çıkmış ve Covid-19 adı verilen hastalığa yol açan SARS-CoV-2 olarak adlandırılan bu virüs, dünyanın neredeyse bütün ülkelerine yayılmış ve çok kısa bir sürede yüksek sayıda ölümlere neden olmuştur. Enfekte olan hücre, virüs RNA'sını kullanarak, bağışıklık sistemini uzak tutacak ve virüsün yeni kopyalarını oluşturmaya yardımcı olacak proteinler üretmeye başlar. Süreç dinamiktir ve yeni keşifler ve değişiklikler her an olabilir. Bu nedenle tüm dünyada hastalığın izlenmesi ve bilginin paylaşılması, epidemiyolojik temas öyküsü, klinik özellikler, tüm kan ve idrarda biyokimyasal testler ve diğer durumlar hastanın tedavisi için önemli değerlendirmelerdir. Küresel durumun izlenmesi ve

epidemiyolojideki değişimlere göre yerinde ve doğru kararlar alınması ve çalışanlarının bilgilerini güncellemeleri zorunludur.

Anahtar Kelimeler: SARS CoV-2, Covid19, biyokimya testleri

Introduction

Sharing experience and information on the new coronavirus as soon as possible is vital, as it is now firmly on the global agenda. We do not have much information on the virus yet, but studies are continuing. Multiple research projects and case studies have been conducted by the Infectious Diseases, Clinical Microbiology, Virology, and Internal Diseases departments in recent years but there is almost no information on the biochemistry of the virus and the biochemical effects in infected patients. Clarification of how a toxic or pathological (viral, bacteriological, carcinogenic) substance taken from the outside affects the metabolic biochemical parameters may be the primary information that makes it possible to decrease the damage or ensure recovery from the agent.

Initially, only two types of HCoV, HCoV229E and HCoV-OC43 are known to cause infections in humans and animals. But in 2002 nearly 4 viruses have been identified since, each one causing people a severe illness.

In 2003, these four viruses, HCoV-229E, HCoV-NL63, HCoV-OC43 and HCoVHKU1, which caused acute respiratory failure, had significant effects on respiratory system pathogenesis [1-6].

SARS-CoV appeared in 2003 as the first international health emergency of the 21st century and caused the deaths of hundreds of people. Approximately ten years later, the MERS-CoV (Middle East Respiratory Syndrome Coronavirus) virus appeared in a hospital in Zarqa, Jordan in April 2012, and was identified in Saudi Arabia in September. This virus had previously never been shown in humans or animals [6-8].

The first MERS-CoV case in Turkey was seen in October 2014 and a laboratoryconfirmed MERS-CoV infection was reported to the WHO's Regional Office for Europe-EURO by the Turkish National Health Legislation Focus Point [9].

At the end of 2019, a new epidemic started in China by the International Virus Taxonomy Committee, which was similar to SARS-CoV and spread all over the world in a short period of three months [1]. The global mortality rates have been reported daily by the Ministry of Health in Turkey and countries around the world since the first day of the pandemic [10-12]. Studies on the subject conducted by the Turkish Ministry of Health, University Research Hospitals, and Medical Laboratories are continuing. In addition, the Pendik Veterinary Control Institute, which operates under the General Directorate of Food Control under the Ministry of Agriculture and Forestry, was included in the vaccine production study organized by The Scientific and Technological Research Council of Turkey (TÜBİTAK) against the virus that causes Covid-19 disease. Studies conducted so far indicate that the transmission after the first case is within 56

days, while the transmission period is 214 days. Considering the information obtained from the cases, the symptoms of the new type of coronavirus are fever, cough, dyspnoea, myalgia, fatigue, and diarrhoea. The first symptoms include loss of smell and taste. The high mortality rates from the disease are thought to be mostly seen in the elderly and immunosuppressed patients. This has resulted in the younger age groups taking the disease less seriously [13, 14]. Most of the fatal cases have been a result of respiratory failure. Myocardial damage/heart failure signs have also been reported and some patients have died because of circulatory failure [15]. The potential complications include septic shock, acute cardiac damage, arrhythmia, cardiovascular collapse (ARDS), and multiple organ failure. Some cases have also been found to be positive for other viruses (coronavirus, influenza A virus, rhinovirus, influenza A H3N2) [12].

The information we have so far about this new virus is inadequate as regards the diagnosis, transmission mode, incubation period (3 to 14 days), accurate prediction of the number of infected cases in the society, and the easy spread that causes the pandemic. In addition, the transmission of the disease to healthcare staff and its easy spread in the society make the disease more complex. Since there is no definite treatment or vaccine for this viral disease, it creates a significant problem for those with a suppressed immune system or a chronic disorder, and the elderly [8, 16, 17].

We present the current knowledge on the biological structure and metabolism of the Covid-19 virus and its interaction with the immune system, together with the data on the relationship between the biochemical blood values and the defense system in Covid-19 cases, in order to prevent the potential damage caused by the virus as updated with scientific developments.

Using the study coronavirus and biochemical test keywords, available data and studies in all search engines were examined.

Results

This virus, which appeared in Wuhan, China, called SARS-CoV-2, which caused the disease called Covid-19, spread to almost all countries of the world and caused a high number of deaths in a very short time. The infected cell, using the virus RNA, begins to produce proteins that will keep the immune system away and help create new copies of the virus.

Biological Structure and Metabolism

Coronaviruses are single-chain, enveloped RNA viruses with positive polarity. This means that they do not contain the RNAdependent RNA polymerase enzyme, but they can encode this enzyme in their genomes. They have rod-like extensions on their surfaces. These viruses are named Coronavirus based on these extensions that appear like a crown, i.e. “corona” in Latin [9, 17, 18]. Zoonotic diseases known as severe acute respiratory syndrome coronavirus (SARS-CoV), Middle East respiratory syndrome corovirus (MERSCoV)

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cause death as well as severe respiratory defects [2, 19].

Coronaviruses are included in the Coronaviridae family and the Orthocoronavirinae subfamily. The Orthocoronavirinae subfamily is separated into four genera (and many sub-genera) as Alpha, Beta, Gamma and Delta coronavirus. Viruses belonging to these genera can be found in humans, bats, pigs, cats, dogs, rodents, and poultry [9, 17]. The disease spectrum caused by Coronavirus in humans can range from simple colds to severe acute respiratory syndrome.

A novel severe acute respiratory syndrome (SARS)-like coronavirus (SARS-CoV-2) recently emerged and is rapidly spreading in humans, causing Covid-19. In a study, the differences between SARS-CoV-2, SARS-CoV and RaTG13 in ACE2 recognition revealed the potential for human-to-human transmission of SARS-CoV-2 [20].

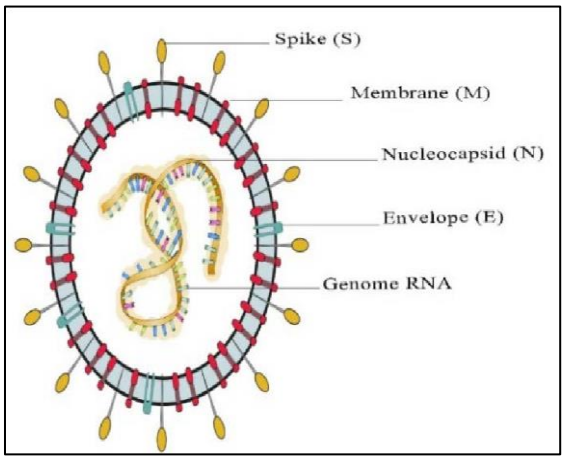

Figure 1. *Structure of the coronavirus*

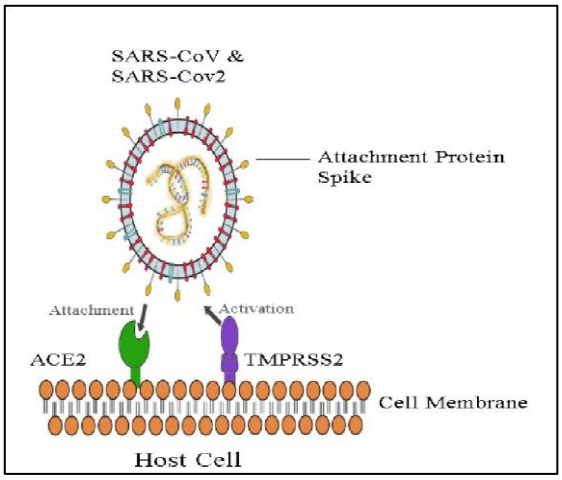

Figure 2. *Mechanisms of coronavirus cell entry*

The virus is currently thought to belong to the beta coronavirus family, which has an envelope and particles that are round or oval and usually polymorphic, with a diameter of 60 to 140 nm. SARS-CoV-2 has four structural proteins, also known as S (spike), E (envelope), M (membrane), and N (nucleocapsid) proteins. N protein holds the RNA genome, and S, E and M proteins together form the viral envelope. Spike protein causes the host to adhere to the cell membrane. Currently, there are 107 protein structures related to Covid-19 in the database where protein structures are collected. It is believed that the protein undergoes a conformational change to bind to the receptor, a protein called ACE2, which is the main target of the spike protein and is common in cells in our respiratory system. In addition, the complex crystalline structure of the RBB portion of the ACE2 and spike protein is predicted to play a role in the interaction with the glycans on ACE2 [21-23].

The nucleocapsid protein is an important structural protein for the coronaviruses. It is

highly abundant in the viruses. Its function involves entering the host cell, binding to the viral RNA genome, and forms the ribonucleoprotein core. The SARS-CoV-2 N protein shares high homology with the SARS-CoV N protein, with a sequence identity of 90.52% [24-26]. Coronaviruses mainly target epithelial cells and are often associated with acute or chronic gastrointestinal and respiratory infections, which can become chronic when the virus is elongated [25]. According to studies, ACE2, which is the entry receptor of SARS-Co viruses into cells, has been detected in lung epithelial cells, kidney, lymph, adrenal glands, small intestine, arterial-venous endothelial cells and colon in humans [26, 27]. In addition, they have been supported by experimental animal infections studies that they are effective on the central nervous system [28].

While the studies have stated that the new virus is 88% similar to SARS-CoV and 50% similar to MERS-CoV [29] another study suggests that it shows sequence similarity with SARS-CoV and MERS-CoV 79% and with MERS-CoV [30].

Interaction with the Immune System

The SARS-CoV-2 coronavirus enters the body by breathing (after someone close to us has coughed), contact with a surface infected by the virus, or through our face. The virus is first positioned in the throat, respiratory tract, and lungs. The genetic material of the virus consists of about 30,000 bases. The infected cells begin to produce proteins by using the virus RNA that will keep the immune system away and help create new copies of the virus. This stage takes about a week. Each infected cell dies by breaking up and releasing millions of copies of the virus. These viruses can then infect nearby cells or scatter with droplets that escape from the lungs [11, 31].

Most people recover at this stage without any symptoms because their immune system defeats the virus. Adequate and balanced nutrition is one of the important elements for a strong immune system and fighting against bacterial, viral, fungal, parasitic, and toxicological diseases. Covid-19 progresses more severely in patients with advanced age and accompanying diseases such as asthma, diabetes, and heart disease. Current data indicate that the disease is severe in 1015% of the cases and results in death in approximately 2-3% [11]. There are several studies showing that the immune system in these age and patient groups is either suppressed or not strong enough, due to reasons such as limited or poor nutrition [31]. Carbohydrates, proteins, fats, vitamins, minerals, and water are indispensable for the functioning of the organism with their different roles in the immune system and should be taken in a balanced manner [32]. While certain nutrients are necessary precursors for the development of immune system cells, some are known to stimulate the production of immune system cells or take part in the inflammatory response, while others with antioxidant properties have a positive effect on the immune system [33, 34].

The blood results of the severe cases reported from various hospitals and various countries have shown a deficiency of the vitamins A, D, E, and C in addition to iron in most of these patients [11, 14].

These vitamins are part of the body's antioxidant defense system and eliminate free radicals. Decreasing and balancing the free radicals in the body is important for healthy metabolic activity. The overproduction of free radicals plays an important role in the development of many chronic diseases. It is very important for the immune system to be strong in order to prevent viral diseases or to survive them with the least amount of damage as in many other diseases. Vitamin A and D have immune system regulatory and anti-inflammatory properties while vitamin E and C have an antioxidant effect [34]. Iron and zinc deficiencies have a negative effect on the immune system. Probiotics and prebiotics are known to be support the immune system. A properly functioning immune system acts as the natural defense system of the body and supports the treatment of many diseases while shortening the recovery period [20, 33].

A limited diet or decreased energy intake has been shown to increase the severity of influenza infection in patients with diabetes, cancer, and high blood pressure. Obese individuals also have a higher prevalence of infection and a lower antibody response [35, 36].

Çapan et al. conducted a study on coronavirus patients with a mean age of 39.8±14.6 years. Two cases were hospital employees and additional disease was present in 4 cases. The most common symptom was shortness of breath (80%), followed by cough (70%), nausea, vomiting, and sputum production (30%).

Leukocytosis and erythrocyte sedimentation rate elevation were present in 3 cases. Pneumonic infiltration on chest x-ray was observed in 8 cases [37].

The Effect on Biochemical Blood Values

Clinical Biochemistry laboratories conduct studies to support the clinicians during the diagnosis, treatment, and follow-up processes through in vitro and in vivo analyses of various biological samples. Their main goal is to conform to the highest quality standards while using the most advanced techniques in all requestrelated processes and delivering the results to the relevant clinics. It is important that all studies on the coronavirus pandemic that currently threatens the world are conducted with the same goal.

The most common hematological finding in these patients is lymphopenia, followed by leukocytosis and leukopenia [14, 38].

Lactate dehydrogenase (LDH), aminotransferase, and C-reactive protein (CRP) values are elevated in almost all Covid-19 patients with no change in procalcitonin levels. Patients with advanced disease may have lymphopenia in addition to increased creatinine phosphokinase (CPK), ferritin, and Ddimer (>1 mcg/ml) levels as well as increased prothrombin time, as a result of kidney damage [10-14]. Some haematological parameters (e.g. WBC, lymphopenia, CRP, LDH, CK and

troponin) were associated with the severity of Covid-19 [12-14]. The results indicate that the differences in BLOOD, PRO, SG and pH are caused by SARS-CoV-2 infection, not bacterial infection [16]. In a study, blood parameters in patients aged 52 years, C-reactive protein>64.79 mg/L, lactate dehydrogenase>245 U/L, Ddimer> 0.96 ug/mL, serum amyloid A>100.02 mg/L or albumin g 36 g/L, and it is stated that the progression of Covid-19 to the critical stage can be a prognostic indicator in these values and lymphocyte count, serum potassium and procalcitonin [12].

Lian et al. reported leukocytopenia in 32.04%, lymphocytopenia in 16.77%, thrombocytopenia in 1.08%, increased international normalized ratio (INR) in 14.84%, and decreased albumin levels in 36.56% of their patients. Increased ALT levels were seen in 10.11% and increased AST levels in 11.18% of the patients. The creatine kinase level had increased by 4.95% and lactate dehydrogenase levels by 25.16%. Some studies have found vitamin D deficiency in Covid 19 patients. Vitamin D is reported to be protective against Covid 19 due to its immunomodulating, anti-inflammatory, antifibrotic, and antioxidant effects [23].

In urine samples taken from Critical Covid-19 patients admitted to Renmin Hospital, latent blood (KAN), proteinuria (PRO), bilirubin, urobilinogen, hydrogen potential (pH), specific gravity (SG), ketone (KET), urine glucose (GLU-U), nitrite and leukocytes (LEU) were examined. The positive rates of BLOOD and PRO were significantly higher in patients with Covid-19 than in healthy controls (P <0.05). The differences in SG and pH values between patients with Covid-19 and healthy controls were statistically significant (P<0.05) [38]. Tükek and Alibeyoğlu reported that laboratory tests revealed a normal or decreased peripheral white blood cell count and increased lymphocyte count in these patients, together with increased liver enzymes, lactate dehydrogenase (LDH), muscle enzymes and myoglobin, as the disease can involve the muscles in some critical patients. Calcium and protein have been found to be increased. While high CRP and ESR levels were found in the majority of the patients, the procalcitonin level was normal. D-dimer is reported to increase and the peripheral blood lymphocytes to decrease in severe cases [12-14]. Leukopenia is seen in the patients and the decrease in lymphocyte count is noteworthy. Lactate dehydrogenase, creatine phosphokinase, and transaminases may be increased. In addition, most patients develop thrombocytopenia in time [39-40]. Increased ALT, AST, BUN, and creatinine have also been reported in addition to DIC and hemolysis [40]. Vitamin D, E, and C deficiency is also seen at high rates in severe cases. Vitamin D, known as a steroid hormone, is classified as vegetable-based ergocalciferol and animal-based cocalciferol (synthesized from 7-dehydrocholesterol with the effect of the sun rays on the skin). Ergocalciferol and cholecalciferol are metabolized with the same metabolic pathways in the body [41].

Coronavirus nucleic acid testing is not the gold standard for detecting or eliminating new corona virus pneumonia mainly because of the lack of confirmation of many nucleic acid detection technologies despite their availability, the uncertain or unknown specificity and sensitivity, and the false negative results at a certain percentage as shown by the positive results on repeated tests in clinically positive patients who were initially negative with the test. All these factors are thought to be directly correlated with the amount of viral load [27, 38].

Treatment Methods

The best available treatment strategy for patients with Covid-19 is fully supportive. Clinicians and intensive care professionals apply most of what they have learned during the SARS outbreak to guide the current treatment of Covid-19. Admission recommendations to critical care units, guidelines for infection control, and procedures for minimizing hospital contamination are being created [42]. As an immune modulatory treatment method in the treatment of SARS-CoV, corticosteroids with anti-inflammatory and immunosuppressive effects ensure early recovery of fever. Ribavirin, which is a nucleoside analogue used in treatment, is the most administered agent with antiviral activity against many DNA and RNA viruses. Ribavirin blocks the viral replicase polyprotein and therefore stops RNA replication. Another method used in the treatment of SARS-CoV is the protease inhibitor. The lopinavir-ritonavir formulation, which is also used in the treatment of HIV infection, can be used in combination with ribavirin in the early stages of the disease and may support the antiviral therapy [2, 11, 14, 20]. However, additional studies are required to develop new treatment methods such as additional antiviral treatments, anti-monoclonal antibody, and anti-viral peptides and vaccines, as well as the use of interferon and steroids in the treatment of immunemediated lung damage [43]. Consensus was reported to be present about administering low dose of corticosteroid and being careful in using antibiotics in the treatment in the studies conducted in China [23].

Conclusion

The new type of coronavirus has caused major concerns worldwide due to its global spread. According to current analyses, patients with hypertension, cardiovascular disease, diabetes, kidney disease, and chronic obstructive pulmonary disease, in addition to smokers are the groups that most commonly require hospitalization. Pregnancy and old age are the other risks that must be monitored [44, 45].

Ultimately, novel coronaviruses are likely to emerge periodically in humans because of frequent cross-species infections and occasional spill over events, given the high prevalence and wide distribution of coronaviruses, the large genetic diversity, and frequent recombination of their genomes, and an increasing level of human-animal interaction. Urine dry chemical tests have the characteristics of being fast, useful, and economical, and can be used for biochemical parameters of urine, co-diagnosis

of urinary tract infections (UTI), diagnosis of kidney diseases and monitoring therapeutic effects. The effect of glycan interactions should not be overlooked in drug and vaccine development. SARS-CoV-2 and Sars-CoV-2 small changes in conformation and sequence can lead to differences in the affinity of spike proteins to the ACE2 protein. These structural and biochemical findings will provide preliminary information in mutation studies, inhibitor design, and vaccine research [27, 46].

In addition, structural information about the conformational change of protein complexes as the virus enters the human cell through membrane fusion will also guide the development of molecular strategies to prevent this [23, 46, 47].

All national scientific institutions, research universities, and hospitals should develop a diagnosis and treatment process based on changes in the status of the epidemic in all areas and the constant updates on the new coronavirus pneumonia. The process is dynamic and new discoveries and changes can occur at any time. It is extremely important for all health care institutions to monitor the disease and share information worldwide. It is also mandatory to follow the global situation and make appropriate and correct decisions according to the changes in the epidemiology, while also updating the information provided to the employees.

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