JSTMU Journal of Shifa Tameer-e-Millat University

https://j.stmu.edu.pk

Open Access

REVIEW ARTICLE

The relationship between some immunological and biochemical parameters with COVID-19: A comprehensive review

Ahmed Kamil Awad[1*], Anas Wisam Malik[2], Hayder T Qaddoori[3]

[1] Lecturer, Department of Nursing Technologies, Middle Technical University, Baqubah, Iraq

[2,3] Lecturer, Department of Medical Laboratory, Middle Technical University, Baqubah, Iraq

Author`s Contribution

[1] Participated in collecting references, wrote the review, and collected the data.

[2, 3] Participated in collecting references, and wrote the review.

Article Info.

Conflict of interest: Nil

Funding Sources: Nil

Correspondence

Ahmed Kamil Awad

ahmedkamil@mtu.edu.iq

Article information

Submission date: 12-05-2024

Acceptance date: 28-11-2024

Publication date: 31-12-2024

***Cite this article as** Awad AK, Malik AW, Qaddoori HT. The relationship between some immunological and biochemical parameters with COVID-19: A comprehensive review. JSTMU. 2024;7(2):202-210.*

A B S T R A C T

Coronaviruses, a family of RNA viruses, are known to infect various species, including humans, through specific receptors in organs such as the lungs and heart. The article highlights the significant elevation of biomarkers like C-reactive protein (CRP), ferritin, D-dimer, and lactate dehydrogenase (LDH) in COVID-19 patients, which correlate with disease severity and inflammatory responses and provides a comprehensive analysis of the immunological and biochemical factors associated with COVID-19, focusing on the role of coronaviruses. The authors discuss the zoonotic origins of SARS-CoV-2, tracing its transmission from bats to humans via intermediate hosts like pangolins. They emphasize the airborne nature of SARS-CoV-2 transmission among humans, primarily through respiratory droplets and potential fecal-oral routes. The structural characteristics of coronaviruses are examined, detailing their large size and spike proteins that facilitate entry into host cells by binding to the ACE2 receptor. The study emphasizes identifying reliable COVID-19 biomarkers, particularly C-reactive protein (CRP), for early diagnosis and severity assessment. It calls for continued research to improve diagnostic and therapeutic strategies in managing this viral infection.

Keywords: *Coronavirus; C-reactive protein; Ferritin, Antibodies; D- Dimer*

Introduction

The word "coronavirus" was first used to refer to specific characteristics of the infectious shape (virion) as seen under an electron microscope, such as a peculiar bulbous form projection (peplomeric spike) that was later determined to be proteins molecules anchored to the surface of the lipid bilayer membrane.[1]

A group of RNA viruses known as coronaviruses (CoVs) infect people and other animals with sickness. They can affect the respiratory, gastrointestinal, hepatic, and central nervous systems of people, pets, birds, bats, mice, and numerous other wild species. The family Coronaviridae includes enclosed viruses with large single-strand positive-sense RNA genome.[2] At least seven different coronavirus types have been linked to human sickness as of 2003; however, the 229E, OC43, NL63, and HKU1 viruses only induce minor cold symptoms. The remaining three viruses, which include the SARS-CoV that caused severe acute respiratory syndrome in 2002 and 2003, may result in life-threatening sickness. Middle East Respiratory Syndrome (MERS-CoV), a virus that initially surfaced in camels in 2012 and is still present today, and SARS-CoV-2, which was initially discovered in Wuhan, China, in December 2019 and is the target of intense endeavor to stop its spread.[3]

Classification of Coronavirus

The Coronaviridae family and Orthocoronavirinae subfamily of coronaviruses are of the order Nidovirales. The biggest genomes belong to CoVs. Among RNA viruses, varying in size from 26 to 32 kb. According to antigenic and genomic standards, coronaviruses are grouped as Alphacoronavirus (-CoV), Betacoronavirus (-CoV), Gammacoronavirus (-CoV), and Deltacoronavirus (-CoV) are the four genera into which they fall. Bats and mice store alpha and beta coronaviruses, while birds store gamma and delta coronaviruses. SARS-CoV-2 is a member of the Betacoronavirus family's Sarbecovirus subgenus.[4]

The Source and Intermediate Host of Coronaviruses

Because coronaviruses are zoonotic, they can be transferred from animals to people. Both SARS and MERS are believed to have started in bats and were spread to people by civet cats and camels (WHO, 2020). Based on phylogenetic comparisons with other coronaviruses, bats were assumed to be SARS-original CoV-2's hosts, and the most recent virus was 96% connected to two SARS-CoV strains from bats dubbed Bat-SLCoVZX45 and Bat-SLCoVZX21.[5] The virus's intermediate host, which allowed it to infect humans and pass the species barrier, as well as the mode of transmission. Via symmetric recombination within the COVID-19 S protein, snakes have been proposed as possible vectors of viruses from bats to humans.[6]

A previous study argued that long-nosed pangolins, ant-eating creatures commonly utilized in Chinese traditional medicine, maybe the possible SARS-CoV-2 intermediary host. This hypothesis was supported by 99% genetic similarity between Coronavirus found in Pangolins and SARS-CoV-2, The 1% difference between the two genomes remains a large difference, therefore conclusive confirmation results are anticipated.[7]

Transmission Among Animals

Two different study teams detected novel Horseshoe bat coronaviruses (genus Rhinolophus) that were compatible with the human SARS-CoV, also known as SARS-CoV-linked viruses or SARS-like coronaviruses. These investigations suggest that although civets just worked as a conduit, bats may have served as a natural host for SARS-CoV. Another study found that several SARS-CoVs coexisted with bat species that live in a cave in the Yunnan province of China.[8] Additionally, it is believed that The DNA of the coronavirus moves through periodic recombination. It indicates a strong possibility that existing SARS-CoVs from bats located in the same or various bat caves will recombine to form new SARS-CoVs. It was believed that the SARS-CoV direct progenitor originated in bats through recombination, then spread to domesticated mammals such as civets and other mammals, causing civet virus infection through fecal-oral transmission. Before infecting people, these virus-carrying civets infected and altered market civets in Guangdong. Due to their high rate of CoV recombination, bats are a useful reservoir for CoV development.[9]

Animal-to-Human Transmission

The wet animal market in Wuhan, China, where the majority of those who caught SARS-CoV-2 were exposed to it at some point, is directly responsible for the zoonotic genesis of the virus. The primary host or intermediate carriers from which the virus may have infected humans have been the subject of numerous investigations. Recent research shows that SARS-CoV-2 and the bat coronavirus have over 95% genetic similarity, suggesting that bats are the current strain's most likely hosts.[10] In addition to bats, a few Viral reservoirs have been found in more animal hosts. It is found SARS-CoV-2-linked coronaviruses in pangolins, while it believed snakes to be a virus reservoir with the capacity to infect people. It was suggested that minks might act as SARS-CoV-2 intermediary hosts. It is believed that sick animals traded in the wild allowed the infection to spread from bats to civets and subsequently to people living close by.[11]

A series of circumstances that make it simpler for the Coronavirus to infect people result in the overspill effect. The possibility of animal-to-human transmission is influenced by several variables, including the dynamics of the illness in the animal host, the degree of viral exposure, and the population's vulnerability in humans. Many of these elements have been divided into three key stages that illustrate how viruses spread. The amount of virus that interacts with humans during the first phase of the pathogen pressure on human hosts is controlled by virus diffusion from animal hosts, and when the virus tries to survive, it grows and spreads outside of animal hosts.[12] The likelihood the path of infection, the point of exposure, and the amount of the virus are determined in the

subsequent phase by human and vector activity. The last stage is influenced by genetics, as well as the host's physiological and immune system, as well as phase two factors impacting the probability and seriousness of infection. It is still unknown how SARS-CoV and SARS-CoV-2 spread from pets similar to humans in terms of dogs and cats, although it is challenging to predict the future in a rapidly changing environment.[13]

Transmission Among Humans

SARS-CoV-2 is an airborne virus that disperses similarly to how the flu and the common cold do. The virus is transmitted by feces as well as tiny droplets released into the air when coughing or sneezing. Anyone who breathes in such droplets or comes into contact with infected surfaces may therefore contract the infection. Recent research showed the virus's persistence throughout the gastrointestinal tract and modified gastrointestinal symptoms, reappearance, and transmission via the fecal-oral route. A live SARS-CoV-2 has already been discovered in patient feces in these studies. However, it is unclear if consuming food tainted with a virus will result in illness or spread it.[14]

It is extended that SARS-CoV-2 can spread through unprotected contact with an infected person. Transfer from person to person, suggesting persistent pathogen pressure that causes infection and sickness. Up until now the primary source of infection has been an individual with a confirmed diagnosis of SARS-CoV-2; respiratory droplets have been the primary method of diffusion, followed by aerial droplets and close contact. The virus attaches itself to host receptors and initiates infection after fusing with the cell membrane.[15]

According to studies, the receptor-binding domain (RBD) of the virus spikes binds with the Angiotensin-converting enzyme 2 (ACE2) receptor of the potential host cell in the case of SARS-CoV-2 human-to-human transmission. The most significant feature is the identical RBD sequences found in SARS-CoV-2 and SARS-CoV spikes, which suggests that both viruses enter human cells via the ACE2 receptor.[16]

Structure of coronavirus

Enormous, spherical viruses with spikes that project from their surfaces, coronaviruses are large particles. The particles have a diameter of roughly 125 nanometers. The SARS-spikes CoV-2 has spikes that are longer and larger than the standard CoV-2 spikes, which increases its pathogenicity. The viral envelope was composed of a lipid bilayer, similar to other membranes, and some structurally important proteins, such as membrane (M), envelope (E), and spike (S) in a ratio of E:S: M1:20:300. The article has around 74 spikes in total. But SARS-CoV-2 also possesses another brief protein projection called hemagglutinin esterase (HE).[17]

The spikes are divided into two halves and folded into homotrimers: S1, which is the spike's head structure, comprises RBD that includes the signal peptide, and S2, which is the spike's stem and contains heptad repeat regions (HR1 and HR2) and a potential fusion peptide (F). The endo-domain and transmembrane domain are also present. Each of these subunits is activated, which encourages their union, which is essential for pathogenesis and maintaining the integrity of the envelope. Last but not least, folded nucleic acid (positive-sense single-stranded RNA genome) makes up the nucleocapsid (N). The company is set up like a continuous bead-on-a-string. The virus must have each of these structures to defend itself when it is outside of host cells.[18]

Genome Organization of Coronavirus

RNA viruses called coronaviruses have single-stranded, positive-sense RNA genomes that range in size from 26 to 31 kilobases. In terms of shape and genetics, it is the largest RNA virus. Its RNA has a 3' polyadenylated tail and a 5' methylated cap, similar to eukaryotic mRNA. Sequencing of the coronavirus genome proceeds from 5'-leader-UTR to replicate/transcriptase-spike (S), envelope (E), membrane (M), nucleocapsid (N), and 3'UTR-poly (A) tail in the following order. The first was ORFs 1a and 1b, which were found in the first two-thirds of the genome and encode the replicase-transcriptase polyprotein (pp1ab), which is then self-cleaved to yield 16 nonstructural proteins (nsp1-nsp16).[19]

The other reading frames encoded the primary structural proteins spike, envelope, membrane, and nucleocapsid. These reading frames were interspersed with others that encoded auxiliary proteins. Although the number of accessory proteins fluctuates, each coronavirus has a unique set of functions. The 5'UTR started the genome, and the 3'UTR concluded it. These two untranslated regions have an unusual composition and structure. They regulate viral replication, transcription, and

packaging in terms of their functional roles. They might be involved in controlling intra- and intermolecular interactions, particularly those involving RNA-RNA interactions and protein binding by viruses and cells.[20]

Human receptors of coronavirus

Since the SARS-CoV-2 coronavirus belongs to the Nidovirus order, it can spread to both bats and people. The spike shape is complementary to the ACE2 receptors, which can be located in a range of organs, including the heart, lungs, kidneys, and digestive system. This enables successful attachment and makes it simpler for the virus to enter the target cells. The S protein domain of the SARS-CoV-2 receptors, which is closely related to the ACE2 of humans and bats, is where this interaction takes place.

The host cell and viral membrane merge after the entry and attachment points. The type II membrane serine protease (TMPRSS2) on the surface of the host cell then catalyzes the removal of ACE2 and activation of S proteins to connect to the receptor resulting in adaptable modifications that allow the virus to enter cells.[21] Both of the virus's proteins are important entrance factors (TMPRSS2 and ACE2). The respiratory system's nasal epithelial cells, specifically cup/secretory cells, and ciliary cells, express ACE2 to the greatest extent. Additionally, the implanted SARS-CoV-2 will later release its genetic material into the cytoplasm and become nucleoplasmically localized. This virus's genetic material would be its mRNA, which is ready for protein translation. Around 14 open reading frames (ORFs), each encoding a separate collection of structural and non-structural proteins that support the virus's survival and virulence, have been added to the genomic material of this virus. During the transformation stage, the genetic components that code for non-structural proteins first change to ORF1a and ORF1b to produce two fantastic superimposed proteins, pp1a, and 19 pp1ab, by aiding in the ribosome frameshifting event.[22]

Sub-genomic proteins like M, S, and E are then converted into structural and accessory proteins, which are then segregated in the endoplasmic reticulum and relocated to the endoplasmic reticulum-Golgi intermediate compartment (ERGIC). Currently, a previously transcribed genomic material program will progress to ERGIC and enter N protein in nucleocapsid form. In this compartment, the nucleocapsid may come into contact with other structural proteins to form tiny packed vesicles for exocytosis outside the cell.[23]

Parameters related to COVID-19

C-reactive protein (CRP) and COVID-19

A novel viral disease called COVID-19 lacks a treatment. As a result, biomarkers must be analyzed to gauge the severity of the disease and the extent of the lung lesions. Research into the pathological and physiological causes of COVID-19 as well as its diagnostic methods is ongoing. Clinical monitoring and efficient treatment methods were required to reduce case fatalities. It was also necessary to look at other sensitive metrics that could signal changes in lung lesion severity.[24] Early diagnosis of pneumonia can be made using C-reactive protein (CRP) levels, significantly increased levels were found in patients with severe pneumonia. To guide clinical practice, they investigated the relationship between CRP levels, lung lesions, and disease severity. Therapy. The C-reactive protein is a pentameric protein with a ring-like structure. It is a part of serum and blood plasma, and blood levels rise in response to inflammation. It is an acute-phase hepatic protein produced by the liver. That responds to mediators secreted by adipocytes and macrophages, including interleukin-6 (IL-6).[25]

C-reactive protein was the first pattern recognition receptor (PRR) to be identified (CRP). CRP, which was discovered in patients' serum who had acute inflammation, reacted with Pneumococcus capsular polysaccharide (C-polysaccharide). C- reactive protein is bound by the phosphocholine that is expressed on the surface of some bacteria as well as dead or dying cells (or other microbes). Innate immunity uses this to activate the complement system, which in turn causes macrophages to phagocyte necrotic and apoptotic cells and microorganisms (opsonin-mediated phagocytosis).[26]

An increase in the amount of IL-6 that macrophages release and adipocytes. A variety of acute and chronic inflammatory conditions, such as bacterial, viral, or fungal infections; rheumatoid arthritis and other inflammatory diseases; cancer; and tissue damage and necrosis, trigger the production of this so-called acute phase protein. In reaction to these circumstances, IL-6 and other cytokines are generated, which travel via the bloodstream to the liver, where they quickly induce a wide variety of acute phase proteins, including CRP and fibrinogen. One possible

explanation for the substantial elevation in individuals with severe COVID-19 is the overproduction of inflammatory cytokines is measured by the inflammatory biomarker CRP. Although cytokines fight the virus, they can harm lung tissue if the process is hyperactive. Tissue damage and cytokines like IL-6 cause C-C-reactive proteins to grow. Secondary (including bacterial) infections of CRP have been found in severe instances.[27]

Ferritin and COVID-19

A crucial element of intracellular iron storage is ferritin.36 It protects people against iron shortage and overload. Ferritin is a cytosolic protein found in most tissues. Serum ferritin is used as a diagnostic tool for iron-deficiency anemia because it is an indirect measure of the total amount of iron stored in the body. During viral infections, the blood's ferritin level rises, which may indicate that the virus is spreading.[28] Numerous metal-protein interactions create a nanocage with ferritin, a 24-protein globular protein complex. Iron is kept in a soluble, non-toxic state by ferritin. Apoferritin is ferritin that has not been mixed with iron. Research indicates that elevated blood ferritin levels during the COVID-19 pandemic indicate a higher risk of death. Infection-induced inflammation, which results in hyperferritinemia, is connected to intensive care unit admission and a high death rate. It can be used to identify patients at high risk and to target therapeutic interventions to reduce inflammation.[29]

Antibodies (IgM and IgG) and COVID-19

Techniques known as immunoassays are used to identify and measure antigen-antibody interactions. They might offer helpful details about the dynamics of virus infections and prior exposures. Conversely, Antibodies have increased resistance to degradation than viral RNA, and they are also less influenced by travel, storage, and selection. Immune defense mechanisms have produced antibodies, also known as immunoglobulins, to shield the host from external invaders like bacteria and viruses. IgG is the most often used antibody in immunoassay methods, out of IgA, IgD, IgE, IgG, and IgM.[30]

IgM is often created in response to microbial infections as the initial line of defense, and IgG is afterward produced as long-term immunity and immunological memory. During the SARS infection, IgM and IgG have been found in the patient's blood after three to six and eight days, respectively. Because of this, knowing whether both antibodies are present can help pinpoint when an infection first occurred. Four to three days after premorbid infection, SARS-CoV-2 IgM and IgG antibodies can be found. The most popular techniques for SARS-CoV-2 serodiagnosis currently utilized in clinical microbiology laboratories are antibody detection in acute- and convalescent-phase serum samples by indirect immunofluorescence assay and enzyme-linked immunosorbent assay (ELISA) using cell culture extract. Although IgM antibodies can be created in the respiratory tract as soon as viral genetic material, the development of immunoglobulin (from 4 days to 10-14 days after the onset of symptoms) limits its use in acute phase diagnosis.[31]

COVID-19 and D-Dimer

The fibrin degradation product, or FDP, D-dimer, is a small protein fragment that is seen in blood after fibrinolysis breaks down a blood clot. Its name derives from the fact that it is made up of two cross-linked D segments of the fibrin protein. A blood test can be used to measure its levels and diagnose thrombosis. According to research, pulmonary embolisms (PE) and deep vein thrombosis (DVT) affect 20.5% and 11.4% of SARS cases, respectively. It is unknown how often thrombosis is in COVID-19 patients.[32]

Additionally, pathologic examination of corpses or biopsies disclosed the emergence of blood clots, which closely mimicked the signs of coronavirus infections such as SARS and MERS. Contrarily, considering traditional anticoagulation carefully will be necessary because COVID-19 patients possess a greater chance of bleeding. As a result, thrombus generation and treatment response could be determined using biomarkers capable of detecting thrombosis early on. As part of a clinical assessment concept to rule out pulmonary embolism, D-dimers were already degrading fibrin components, and are currently being found to be beneficial, demonstrating their potential to be an effective biomarker. The relationship between COVID-19 and D-dimer, and also how the concentration varies as the illness worsens.[33]

Along with thrombosis and pulmonary embolism, D-dimer may be a sign of a serious viral infection. Serious abnormalities might worsen as a result of sepsis and coagulation problems caused by a virus. D-dimer levels may also be a sign of inflammation due to the possibility

that inflammatory cytokines might lead to an imbalance between fibrinolysis and coagulation in the alveoli, activating the fibrinolysis process and raising D-dimer levels.[34] A study by individuals with acute COVID-19 had greater D-dimer levels than patients with mild COVID-19, it was discovered. Because individuals with raised D-dimer levels may be more susceptible to severe infections, physicians should take particular note of this information and closely monitor COVID-19 patients who have elevated D-dimer levels. Raised D-dimer levels and thrombocytopenia (low platelet count) have also been found in harsh COVID-19 patients, indicating that a hypercoagulable state might be involved in the illness's severity and death.[35]

Lactate dehydrogenase (LDH) and COVID-19

Several variables are now being investigated to see if they may be used to predict prognosis in patients with COVID-19. One of these crucial measures is LDH, mainly because higher LDH levels have historically been linked to worse outcomes in individuals with various viral infections. There is preliminary evidence that patients with severe illness and those without have significantly different levels of LDH. In cells from nearly all organ systems, LDH is an intracellular enzyme that catalyzes the conversion of pyruvate and lactate as well as of NADH and NAD+. When an infection is severe, cytokines and the production of LDH can cause tissue damage. Since LDH is found in lung tissue, patients with severe COVID-19 may anticipate that their bodies will release more LDH into the bloodstream as a result of the disease. For example, the condition is marked by a severe form of interstitial pneumonia that frequently leads to acute respiratory distress syndrome.[36]

Immune cells and COVID-19

Recent research has demonstrated that cytokine storm syndrome and lymphopenia develop often among COVID-19 patients. These traits might suggest that the immune system's alterations influence how a disease develops. The total quantity of lymphocytes and neutrophils that harbor unchecked early phases of viral replication of the disease may change as COVID-19 grows.37 Like other viruses, this one triggers the adaptive immune response. A significant role in controlling SARS-CoV-2 viral infections. While helper T lymphocytes control the overall adaptive immune response, natural killer (NK) cells and cytotoxic T lymphocytes (CTLs) have the potential to eradicate contaminated cells. In the body, antibodies have a protective role by limiting infection and preventing reinfection. The amount of circulating helper T lymphocytes and activated CD8+ T cells is progressively rising during the first week. Granzymes A and B, as well as perforin, are released by CD8+ T lymphocytes and lead to death in virally infected cells.38

For the prevention of viral infections, CTLs and NK cells are essential. According to recent research, Lymphopenia affects roughly 85% of COVID-19 critically sick individuals. A condition called lymphopenia, often referred to as lymphocytopenia, is characterized by an unusually low level of lymphocytes in the blood. Those individuals had a lower lymphocyte quantity even though T cells had initially grown at the start of COVID-19; this has been linked to a higher severity of the condition. As a result, those who passed away had noticeably lower levels of lymphocytes than those who lived.[39]

NK cells and CTLs were significantly depleted in patients. After their recovery, those patients' NK and CTL counts were rebuilt. Additionally, researchers discovered that patients with SARS-CoV-2 infection had an adequate drop in the total number of CD8+ and CD4+ T cells, particularly in patients over 60 and those who required critical care. Native CD4+ T lymphocytes were activated after being exposed to viral peptide antigens by antigen-presenting cells, resulting in the production of tumor necrosis factor (TNF), interferon (IFN), and IL-2. The differentiation of CTLs, which release granzymes and perforin to combat infected cells to kill them, is facilitated by this mechanism.[40]

The syndrome known as T-cell exhaustion is brought on by ongoing inflammation and repeated stimulation of T cells. Without effective infection control, the functions of exhausted cells would be weakened, leading to inflammatory conditions getting worse. Furthermore, COVID-19 patients have been subjected to harsh settings that have harmed CD4+ T cell activity According to new data, the neutrophil-to-lymphocyte ratio (NLR) in peripheral blood can be utilized as a sign of systemic infection. Recent studies have demonstrated that NLR can distinguish between the COVID-19 infection types of severe/critical and mild/moderate infections, as well as the risk that patients with these infections will die. Furthermore, several studies have proposed that NLR is a dependable indicator

of COVID-19 development and that high NLR is linked to a rise death rate. Compared to patients with a moderate infection, those with a severe COVID-19 infection showed a greater NLR.[41]

The Effect of Age and Gender on COVID-19 Infections and Mortality

Since the initial outbreak was discovered in December 2019, COVID-19 has affected more than 300 nations (in China, and Wuhan). For now, there isn't a biomarker for the disease. The majority of the risk variables identified, such as age, gender, and chronic conditions, were derived from standard clinical findings. In COVID-19 patients, men have been identified more frequently than women, especially in cases when the patient has passed away. In earlier research male patients outnumbered instances of females, males seemed to be in a critical state of illness or to have additional severe sickness. In addition, men die at a rate that is 2.4 times higher than that of women.[42]

The reason why males have a greater incidence of COVID-19 than women is unknown. However, it has recently been found that this gender disparity may be caused by some issues that indirectly increase the risk of infection or mortality in men. Cardiovascular risk factors (such as diabetes, hypertension, and heart attacks) and high-risk behaviors have an impact on men (social exclusion, smoking, drinking, and exposure to specific environmental factors). Additionally, hormones associated with women's sex can influence how the immune system responds.[43] Age was one more risk factor for the development of COVID-19, with the fifth decade perhaps being a crucial decade.

Additionally, the results demonstrated that getting older may pose a danger to dying. In this regard, the majority of Chinese data concur that the infection was primarily observed in older adults. In 32,583 laboratory-confirmed instances of COVID-19 in Wuhan (China), the median age of the patients was 56.7 years, and older people had a greater likelihood of serious or catastrophic illness. COVID-19 patients with chronic illnesses were investigated in a subsequent Chinese study. They averaged 59.7 years old, and 61.5% of them passed away within 28 days.[44,45]

Conclusion

The SARS-CoV-2 pandemic, caused by a new coronavirus, has affected every country in the world. One of the main causes of death is severe respiratory syndrome, which is caused by it. The novel SARS-CoV-2 has been shown to closely resemble existing coronaviruses, including SARS and MERS. To assault the host cells, SARS-CoV-2 may employ methods that are similar to those of these viruses. Many factors influence the severity of COVID-19, with immunological dysregulation or immune suppression being one of the main causes. The body's ability to fight off infections and stay healthy is greatly influenced by immunity. Many laboratory variables allow for the assessment of the disease's severity and the prognosis of the likelihood that it will progress to more serious conditions, including disseminated intravascular coagulation, acute respiratory distress syndrome, and multiple organ failure. High levels of CRP, Ferritin, D-dimer, Lactate dehydrogenase (LDH), Antibodies (IgM and IgG), and Immune cells (CD8 and CD57) in COVID-19 patients.

References

1. Su S, Wong G, Shi W, Liu J, Lai AC, Zhou J, et al. Epidemiology, genetic recombination, and pathogenesis of coronaviruses. Trend Microbiol. 2016; 24(6):490-502. DOI: https://doi.org/10.1016/j.tim.2016.03.003.
2. Lagunas-Rangel FA. Neutrophil-to-lymphocyte ratio and lymphocyte-to-C-reactive protein ratio in patients with severe coronavirus disease 2019 (COVID-19): a meta-analysis. J Med Virol. 2020; 92(10):1733. DOI: https://doi.org/10.1002/jmv.25819.
3. Dong N, Yang X, Ye L, Chen K, Chan EW, Yang M, et al. Genomic and protein structure modeling analysis depicts the origin and infectivity of 2019-nCoV, a new coronavirus that caused a pneumonia outbreak in Wuhan, China. BioRxiv. 2020. DOI: https://doi.org/10.1101/2020.01.20.913368
4. Xu X, Chen P, Wang J, Feng J, Zhou H, Li X, et al. Evolution of the novel coronavirus from the ongoing Wuhan outbreak and modeling of its spike protein for risk of human transmission. Sci China Life Sci. 2020; 63:457-60. DOI: https://doi.org/10.1007/s11427-020-1637-5.
5. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterization and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet. 2020; 395(10224):565-74. DOI: https://doi.org/10.1016/S0140-6736(20)30251-8.
6. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia. N Engl J Med. 2020; 382(13):1199-207. DOI: https://doi.org/10.1056/NEJMoa2001316.
7. Lorusso A, Calistri P, Petrini A, Savini G, Decaro N. Novel coronavirus (SARS-CoV-2) epidemic: a veterinary perspective. Vet Ital. 2020; 56(1):5-10. DOI: https://doi.org/10.12834/VetIt.2173.11599.1.
8. World Health Organization. Coronavirus disease (COVID-19): weekly epidemiological update. 2020. DOI: https://doi.org/10.2196/53551.

9. Xiao K, Zhai J, Feng Y, Zhou N, Zhang X, Zou JJ, et al. Isolation and characterization of 2019-nCoV-like coronavirus from Malayan pangolins. Bio Rxiv. 2020; 20:2020-02.
DOI: https://doi.org/10.1101/2020.02.17.951335
10. Kakodkar P, Kaka N, Baig MN. A comprehensive literature review on the clinical presentation, and management of the pandemic coronavirus disease 2019 (COVID-19). Cureus. 2020; 12(4).
DOI: https://doi.org/10.7759/cureus.7560.
11. Li X, Liu C, Mao Z, Xiao M, Wang L, Qi S, et al. Predictive values of neutrophil-to-lymphocyte ratio on disease severity and mortality in COVID-19 patients: a systematic review and meta-analysis. Crit Care. 2020; 24(1):1-0.
DOI: https://doi.org/10.1186/s13054-020-03374-8.
12. Cui J, Li F, Shi ZL. Origin and evolution of pathogenic coronaviruses. Nat Rev Microbiol. 2019; 17(3):181-92.
DOI: https://doi.org/10.1038/s41579-018-0118-9.
13. Banerjee A, Kulcsar K, Misra V, Frieman M, Mossman K. Bats and coronaviruses. Viruses. 2019; 11(1):41.
DOI: https://doi.org/10.3390/v11010041.
14. Rothan HA, Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. J Autoimmun. 2020; 109:102433.
DOI: https://doi.org/10.1016/j.jaut.2020.102433.
15. Perlman S. Another decade, another coronavirus. N Engl J Med. 2020; 382(8):760-2.
DOI: https://doi.org/10.1056/NEJMe2001126.
16. Lam TT, Shum MH, Zhu HC, Tong YG, Ni XB, Liao YS, et al. Identification of 2019-nCoV related coronaviruses in Malayan pangolins in southern China. Bio Rxiv. 2020; 583(7815):282-285.
DOI: https://doi.org/10.1038/s41586-020-2169-0.
17. Ji W, Wang W, Zhao X, Zai J, Li X. Homologous recombination within the spike glycoprotein of the newly identified coronavirus 2019-nCoV may boost cross-species transmission from snake to human. J Med Virol. 2020; 92(4):433-440
DOI: https://doi.org/10.1002/jmv.25682.
18. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, Wang W, et al. Genomic characterization and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet. 2020; 395(10224):565-74.
DOI: https://doi.org/10.1016/S0140-6736(20)30251-8.
19. Gu J, Han B, Wang J. COVID-19: gastrointestinal manifestations and potential fecal-oral transmission. Gastroenterology. 2020; 158(6):1518-9.
DOI: https://doi.org/10.1053/j.gastro.2020.02.054.
20. Holshue ML, DeBolt C, Lindquist S, Lofy KH, Wiesman J, Bruce H, et al. First case of 2019 novel coronavirus in the United States. N Engl J Med. 2020; 382(10):929-36.
DOI: https://doi.org/10.1056/NEJMoa2001191.
21. Wu D, Wu T, Liu Q, Yang Z. The SARS-CoV-2 outbreak: what we know. Int J Infect Dis. 2020; 94:44-8.
DOI: https://doi.org/10.1016/j.ijid.2020.03.004.
22. Ghinai I, McPherson TD, Hunter JC, Kirking HL, Christiansen D, Joshi K, et al. First known person-to-person transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the USA. Lancet. 2020; 395(10230):1137-44.
DOI: https://doi.org/10.1016/S0140-6736(20)30607-3.
23. Jaimes JA, Millet JK, Stout AE, André NM, Whittaker GR. A tale of two viruses: the distinct spike glycoproteins of feline coronaviruses. Viruses. 2020; 12(1):83.
DOI: https://doi.org/10.3390/v12010083.
24. Wan Y, Shang J, Graham R, Baric RS, Li F. Receptor recognition by the novel coronavirus from Wuhan: an analysis based on decade-long structural studies of SARS coronavirus. J Virol. 2020; 94(7):10-128.
DOI: https://doi.org/10.1128/JVI.00127-20.
25. Parasher A. COVID-19: Current understanding of its Pathophysiology, Clinical presentation and Treatment. Postgrad Med J. 2021; 97(1147):312-20.
DOI: https://doi.org/10.1136/postgradmedj-2020-138577
26. Wang Y, Grunewald M, Perlman S. Coronaviruses: an updated overview of their replication and pathogenesis. Coronaviruses: Methods Mol Biol. 2020; 1-29.
DOI: https://doi.org/10.1007/978-1-0716-0900-2_1.
27. Rabi FA, Al Zoubi MS, Kasasbeh GA, Salameh DM, Al-Nasser AD. SARS-CoV-2 and coronavirus disease 2019: what we know so far. Pathogen. 2020; 9(3):231.
DOI: https://doi.org/10.3390/pathogens9030231.
28. Zhang Q, Xiang R, Huo S, Zhou Y, Jiang S, Wang Q, et al. Molecular mechanism of interaction between SARS-CoV-2 and host cells and interventional therapy. Signal Transduct Target Ther. 2021; 6(1):233.
DOI: https://doi.org/10.1038/s41392-021-00653-w.
29. Wang F, Nie J, Wang H, Zhao Q, Xiong Y, Deng L, et al. Characteristics of peripheral lymphocyte subset alteration in COVID-19 pneumonia. J Infect Dis. 2020; 221(11):1762-9.
DOI: https://doi.org/10.1093/infdis/jiaa150.
30. Costela-Ruiz VJ, Illescas-Montes R, Puerta-Puerta JM, Ruiz C, Melguizo-Rodríguez L. SARS-CoV-2 infection: The role of cytokines in COVID-19 disease. Cytokine Growth Factor Rev. 2020; 54:62-75.
DOI: https://doi.org/10.1016/j.cytogfr.2020.06.001.
31. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020; 395(10229):1054-62.
DIOI: https://doi.org/10.1016/S0140-6736(20)30566-3.
32. Baraboutis IG, Gargalianos P, Aggelonidou E, Adraktas A. Initial real-life experience from a designated COVID-19 centre in Athens, Greece: a proposed therapeutic algorithm. SN Compr Clin Med. 2020; 2(6):689-93.
DOI: https://doi.org/10.1007/s42399-020-00324-x.
33. Sheikhzadeh E, Eissa S, Ismail A, Zourob M. Diagnostic techniques for COVID-19 and new developments. Talanta. 2020; 220:121392.
DOI: https://doi.org/10.1016/j.talanta.2020.121392.
34. Lee CY, Lin RT, Renia L, Ng LF. Serological approaches for COVID-19: epidemiologic perspective on surveillance and control. Front Immunol. 2020; 11:879.
DOI: https://doi.org/10.3389/fimmu.2020.00879.
35. Younes N, Al-Sadeq DW, Al-Jighefee H, Younes S, Al-Jamal O, Daas HI, et al. Challenges in laboratory diagnosis of the novel coronavirus SARS-CoV-2. Viruses. 2020; 12(6):582.
DOI: https://doi.org/10.3390/v12060582.
36. Padoan A, Cosma C, Sciacovelli L, Faggian D, Plebani M. Analytical performances of a chemiluminescence immunoassay for SARS-CoV-2 IgM/IgG and antibody kinetics. Clin Chem Lab Med. 2020; 58(7):1081-8.
DOI: https://doi.org/10.1515/cclm-2020-0443.
37. Abbasi J. The promise and peril of antibody testing for COVID-19. J Am Med Assoc. 2020; 323(19):1881-3.
DOI: https://doi.org/10.1001/jama.2020.6170.
38. Tasić N, Paixao TR, Gonçalves LM. Biosensing of D-dimer, making the transition from the central hospital laboratory to bedside determination. Talanta. 2020; 207:120270.
DOI: https://doi.org/10.1016/j.talanta.2019.120270.
39. Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, et al. Pathological findings of COVID-19 associated with acute

respiratory distress syndrome. Lancet Respir Med. 2020; 8(4):420-2.
DOI: https://doi.org/10.1016/S2213-2600(20)30076-X.

40. Mao L, Wang M, Chen S, He Q, Chang J, Hong C, et al. Neurological manifestations of hospitalized patients with COVID-19 in Wuhan, China: a retrospective case series study. Med Rxiv. 2020; 25:2020-02.
DOI: https://doi.org/10.1101/2020.02.22.20026500
41. Tang N, Bai H, Chen X, Gong J, Li D, Sun Z. Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy. J Thromb Haemost. 2020; 18(5):1094-9.
DOI: https://doi.org/10.1111/jth.14817
42. Lippi G, Plebani M, Henry BM. Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: a meta-analysis. Clin Chim Acta. 2020; 506:145-8.
DOI: https://doi.org/10.1016/j.cca.2020.03.022.
43. Fathi N, Rezaei N. Lymphopenia in COVID-19: Therapeutic opportunities. Cell Biol Int. 2020; 44(9):1792-7.
DOI: https://doi.org/10.1002/cbin.11403.
44. Saghazadeh A, Rezaei N. Immune-epidemiological parameters of the novel coronavirus–a perspective. Expert Rev Clin Immunol. 2020; 16(5):465-70.
DOI: https://doi.org/10.1080/1744666X.2020.1750954.
45. Zheng M, Gao Y, Wang G, Song G, Liu S, Sun D, et al. Functional exhaustion of antiviral lymphocytes in COVID-19 patients. Cell Mol Immunol. 2020; 17(5):533-5.
DOI: https://doi.org/10.1038/s41423-020-0402-2.