Relationship Between the Severity of SARS-coV-2 Infection and Interleukin-10

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ABSTRACT

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has rapidly spread worldwide, leading to the COVID-19 pandemic. Understanding the host's immunological response to SARS-CoV-2 infection is critical for finding effective treatments. Interleukin-10 is an anti-inflammatory cytokine that control immune responses. However, its exact involvement in the context of SARS-CoV-2 infection severity is unknown.We conducted a systematic review and meta-analysis to understand better the association between SARS-CoV-2 infection severity and IL-10 levels. A comprehensive search was conducted across various databases to identify relevant published research. The studies included analyses of IL-10 levels in COVID-19 patients, stratified by disease severity. The results of our investigations show a positive association between the severity of SARS-CoV-2 infection and IL-10 levels, indicating that IL-10 may play a role in disease etiology. More research is required to comprehend the molecular foundation of this association and to explore the therapeutic prospects of targeting IL-10 in COVID-19 treatment. Having this knowledge could help develop particular treatment plans for COVID-19 patients based on their immune profiles.

Keywords: SARS-coV-2, COVID-19 pandemic , IL-10 levels

Introduction

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), a beta coronavirus, shares similar genetic binds with both Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV). Both severe acute respiratory syndrome (SARS) and

Middle East respiratory syndrome (MERS) are caused by these viruses, respectively. Notably, SARS-CoV-2-caused COVID-19 has garnered global attention.

Both SARS-CoV and MERS-CoV show high deaths rates, commonly leading to inflammatory viral pneumonia that develops into acute respiratory distress syndrome (ARDS). In the context of COVID-19, ARDS was identified in 81% of lethal cases.

A new letter released in The Lancet suggests a comprehensive review of hyperinflammation in all COVID-19 patients. Identifying individuals who might profit from regulation of immunity or suppression of immunity is essential to prevent acute lung injury (ALI). The coronavirus family contain of four "established" human coronaviruses (HCOVs), two of which have been detected since the 1960s: HCOV-OC43 and HCOV-229E. These two viruses cause less severe respiratory diseases and, after rhinoviruses, are the most usual reason (10–30 percent) of the usual (1)(2)(3). Two novel human coronaviruses, HCoV-NL63 and HCoV-HKU1, were discovered as a result of developed coronavirus screening. New studies propose that HCoV-NL63, -229E, and -OC43 are the outcome of zoonotic spread from bats(4).

Considering the crucial role of interleukin 6 (IL-6) in airway disease, initial research using antibodies against the IL-6 Receptor (Tocilizumab) to isolate this cytokine in response to COVID-19 infection have provided positive outcomes, but more studies is needed. (5).

Cytokine Storm in COVID-19 Patients

As of October 24, 2020, severe acute respiratory syndrome coronavirus (SARS-CoV)-2 infection was responsible for over 42 million COVID-19 infections and over 1.1 million deaths worldwide. Severe sick COVID-19 patients develop a clinical condition called cytokine release syndrome (CRS;) that is defined by fast and continuous systemic rise of more than twenty inflammatory cytokines and chemokines (6). CRS triggers acute respiratory distress syndrome (ARDS) and secondary hemophagocytic lymphohistiocytosis, which frequently result in multiple organ failure and death. The major among the more than 20 increased inflammatory cytokines/chemokines is interleukin 6, an important cytokine in CRS-induced fatalities in blood cancer individuals having modified T cell treatment. Initial medical research in treating cellular immunotherapy-induced CRS shows that blocking interleukin 6 activation may lower COVID-19 deaths. Nevertheless, a recent Phase III COVACTA trial (7), which was randomized and double-blind, failed to demonstrate a statistically significant reduction in mortality when evaluating the clinical efficacy of tocilizumab, an anti-IL-6R antibody, in COVID-19 patients(8).

Although CRS in COVID-19 patients is like that previously observed in SARS patients infected with SARS-CoV, a unique characteristic of the COVID-19 cytokine storm is the high elevation of interleukin 10 (IL-10) in severe sick individuals(6)(9)(10)(11)(12)(13). It has become clear how crucial IL-10 is as a potential immunological biomarker for assessing the severity of COVID-19 illness. Like interleukin 6, Increased interleukin 10 production can be sign of bad result in COVID-19 patients (9)(10).

2.1 Aim of the study

1. Understand the Role of IL-10: Explore why IL-10, traditionally considered an anti-inflammatory cytokine, rises dramatically during severe SARS-CoV-2 infection.
2. Evaluate Predictive Value: Investigate whether IL-10 levels can indicate disease result in COVID-19 patients.
3. Consider Novel Mechanisms: Examine alternative mechanisms underlying IL-10 elevation, including potential resistance to its classical anti-inflammatory action.
4. The commercial reasons for selling vaccines.
5. Striving to better control any potential pandemic.
6. Improving human health through a better understanding of germs.

2.2 Epidemiology of sars- covid 19

Human cases of SARS-CoV-2 were first reported in late 2019, and the disease was dubbed Coronavirus-Disease-19 (COVID-19). The ilness quickly spread around the world, and in March 2020, the WHO defined COVID-19 a pandemic disease. Here we present a random review of the state of knowledge on SARS-CoV-2 epidemiological features and parameters in a random review. The number of cases and deaths was updated through the end of March 2020. The first wave of epidemics could be detected in many nations, allowing some countries the chance to calculate first-wave infection rates (15)(16).

Transmission

The primary sites of SARS-CoV-2 colonization are the upper respiratory tract. The virus can also replicate in the the gastrointestinal tract, and RNA of the virus has been detected in the blood of critically ill patients (15). Aerosols and respiratory droplets are the primary modes of spread (16). The mode of transmission has not been definitively determined (17).

SARS-CoV2 replicates in the upper respiratory tract. Unlike SARS, SARS-CoV-2 can also spread from infected people who don't show any symptoms (18)(19).

Age distribution of cases

In the majority of countries, the age group between 20 and 59 years old has the highest number of cases. Different patterns can be seen in the outbreaks in China, Korea, Italy, and Germany (Figure 1). The number of affected young kids (0–9 years) remained small throughout the epidemic (Figure 1)] (20)(21)(22)(23). The specific age trends in the first wave of the epidemic in Germany demonstrate the earliest incidence in age groups over 80 years and an increase in young people in the later stages of the epidemic (20).

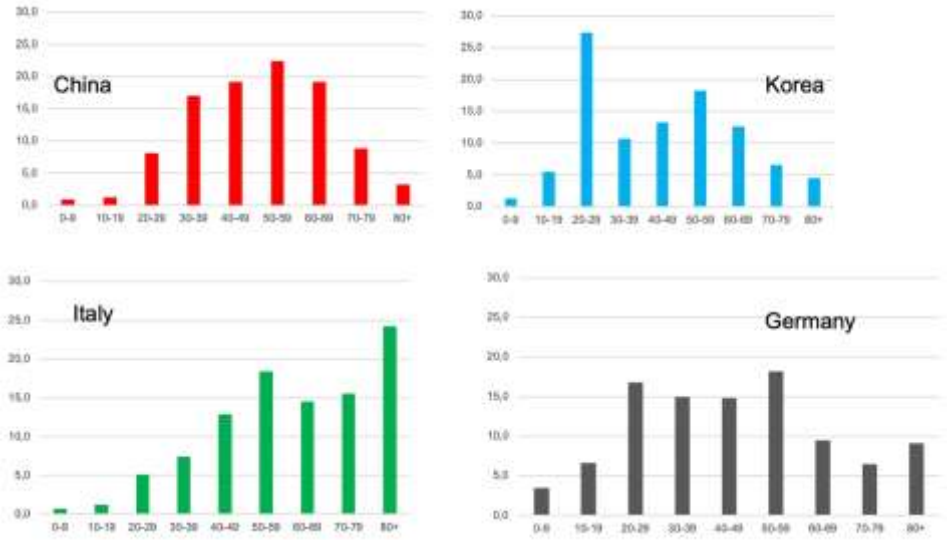

Fig 1(Age distribution of COVID-19 cases in China, Korea, Italy, and Germany)

How deadly is SARS-CoV-2?

One of the most important measures of the degree of an epidemic is the infection fatality rate IFR). Because of the elevated prevalence of simple diseases, the diagnostic data do not reflect the total number of infections. Therefore, the case fatality rate (CFR) will be higher than the IFR. There is considerable variation in CFRs across countries in COVID-19mostly because to test methods and age distribution in the individuals (Tables 1, 2).

Researchers at Imperial College London established the first statistical model to estimate age-dependent mortality (Table 2) Almost all other estimates are based on relative models, cohort analyses, at the national level seroprevalence surveys and outbreak Monitoring has been conducted, e.g., South Korean (Table 1) (22) 24)(25).(26)(

Consensus estimates for IFR have not yet been developed, but most models estimate these parameters between 0.5 and 1. (Table 1) The two examples with the smallest numbers include a group with particularly elevated mortality, individuals over 80 years (25)(26).

COVID-19 CFR (perhaps with the exception of nations where mortality data is not yet complete) All present numbers are greater than CFR for influenza 1918(27). Furthermore, organ transplantation was not available in any of these outbreaks. Assuming twenty-five percent of people with COPD require intensive ventilation, the COPD CFR ought to be increased by a suitable aspect. FR alone does not determine the degree of seriousness of an epidemic. The degree of seriousness also depends on the age distribution in mortality and the type of attack. In sharp contrast to COVID-19, younger patients (ages 20–49) have been reported to have significantly higher mortality than influenza 1918 and attack rates with symptoms ranging from 9 to 40%, exceedingly almost national COVID -19 erupted over all so far (Table 2) (27).

Excessive death rates can also be used to gauge the seriousness of the epidemic. Death toll from COVID-19 has been reported from many sources, such as 185,000 extra fatalities in the opening eighteen weeks of 2020 from 24 European countries (28). There is no excess mortality, but Germany's weekly mortality shows a sign of COVID deaths, a sign of the week for Germany (Figure 2a), a clear sign for the two highest rate countries (Figure 2b) and two countries with very low SARS-CoV-2 prevalence (29).

Age (years)	Case-fatality rates					Infection-fatality rate (IFR) Modell			
	China	Italy	Germany	Spain	Südkorea*	Indiana, USA**	ENE, Spain	International (Imperial College)	France
0–9	0%	0.1%	0.01%	0.3%	0%	n.d	< 0.01%	0.0016%	0.001%
10–19	0.2%	0%	0.01%	0.1%	0%	0.01%	< 0.01%	0.0069%	0.001%
20–29	0.2%	0.1%	0.03%	0.3%	0%	0.01%	0.01%	0.031%	0.005%
30–39	0.2%	0.3%	0.07%	0.3	0.1%	0.01%	0.025%	0.084%	0.02%
40–49	0.4%	0.9%	0.2%	0.6%	0.2%	0.12%	0.07%	0.16%	0.05%
50–59	1.3%	2.7%	0.8%	1.5%	0.5%	0.12%	0.29%	0.59%	0.2%
60–69	3.6%	10.8%	4.0%	5.2%	1.4%	0.12%	1.15%	1.93%	0.7%
70–79	8.0%	26.6%	13.5%	14.6%	6.7%	0.12%	3.38%	4.28%	1.9%
80+	14.8%	34.6%	26.4%	21.8%	21.0%	?**	8.12%	7.8%	8.3%
Overallt	2.3%#	13.8%	3.8%	8.2%	1.6%	0.26%**	0.83%	0.657%	0.5%**

Table 1(Age-specific case fatality rates in different countries and models for infection fatality rates).

Country population	China (only Hubei)	Spain	Italy	Germany	France (only French model appl [25])	United Kingdom
Population (millions)	57.20	46.94	60.36	83.02	66.99	66.65
Seroprevalence						
National	4%	5.4%	2.5%	n.d	n.d	6.0%
Regions	Hubei 4% Hongkong 0%	Madrid 11.5% Barcelona 6.8% Baleares 1.1% Asturia 1.4%	Lombardy 7.5% Piemont 3.0% Tuscany 1.0% Sicily 0.3%	Bad Feilnbach 6% Gangelt 15.5%	n.d	London 13.0% Yorkshire 3.9% South-West 2.8%
Est. Cases and attack rates of SARS-CoV-2						
Cases notified (8/2020)	68,053	250,273	260,307	233,776	223,419	316,371
Overall CFR	5.2%	7.5%	13.7%	4.0%	13.6%	14.3%
Cases—lower bound est	0.19 Mio	0.74 Mio	0.96 Mio	0.34 Mio	2.1 Mio	1.75 Mio
Cases—upper bound est	0.96 Mio	3.18 Mio	4.46 Mio	1.49 Mio	6.0 Mio	8.85 Mio
Attack rate (min–max)	0.33–1.68%	1.57–6.78%	1.51–7.39%	0.42–1,80%	3.3–9.3%	2.6–13.1%

Table 2(SARS-COV-2 infections, seroprevalence and attack rates in different countries).

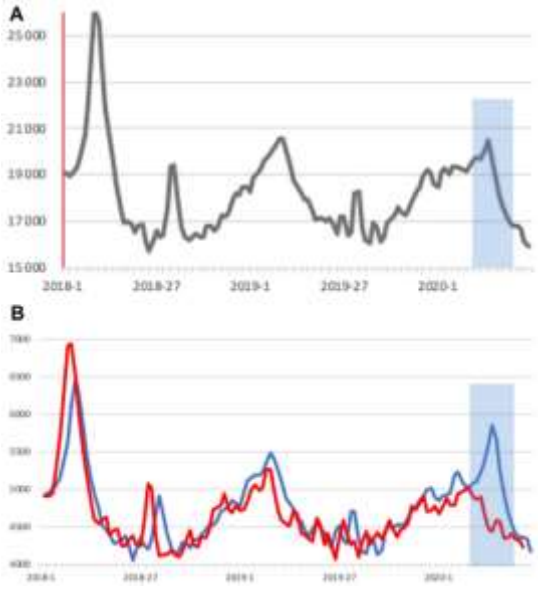

Fig. 2 (A, B Weekly deaths 2018-5/2020 in Germany and two regions, a Bavaria plus Baden-Württemberg (combined, blue line) (b) Mecklenburg-Vorpommern plus Saxonian-Anhalt combined red line), adjusted for population size by factor 4.5 (weekly deaths in means over 2 weeks. Period with deaths due to COVID shaded in gray (weeks 8–20/20,209)

2.2.1 Origin of virus

What does it mean to say a virus mutates or changes?

Viruses can make small changes in their genome by making new copies of themselves. These changes are known as “mutations. Viruses with one or more additional mutations are referred to as “variants” of the original virus.

As more bacteria circulate, they change. Sometimes these changes can cause a virus to adapt to its environment compared to the original virus. This process of successful adaptation and selection is called “virus evolution”.

Some changes may alter the properties of the virus, such as variability of infection (e.g., it can spread more rapidly) or severity (e.g., it can cause more severe disease) (30).

Coronavirus evolutionary relationships (Figure 3) show some reasons for optimism. Coronavirus infection has various effects. Some, like the HKU1 vaccine, only cause fever. These species are so harmless that they do not require any vaccination. However, others, such as the SARS and MERS viruses that appeared in the first years of the 2000s, are more deadly illnesses with elevated mortality rates than COVID-1 SARS was eradicated a couple of years after it began affecting people, but scientists made some steps in making a vaccine while it was still at risk and researchers were still developing MERS vaccines protect people, and they are making promising progress, but not a working vaccine (31).

The rate of evolutionary change is a key factor in growing a vaccine against a new pathogen. Pathogens that alternate slowly (e.g., due to the fact they mutate hardly ever) stay very nearly identical from one disease to other, making them a frequent target for vaccine development, On the other hand germs that exchange speedily can cut up into many unique lineages in a short time, developing a complex evolutionary tree. This makes it hard to create a single vaccine that may come across and combat all the diverse branches of the pathogen’s various phylogenies. HIV, for instance, the quickest rate of mutation of any organic lineage ever studied with the aid of technological know-how and modifications at a first-rate pace. For these reasons, despite over 35 years of research, there is still no HIV vaccine. (32).

By considering COVID-19 as just one strain among many similar coronaviruses, we can also determine the potential duration of immunity acquired through vaccination or infection. Human coronaviruses that generate symptoms similar to a cold promote transient immunity. Although you might become infected with the same virus again in less than a year, immunity to SARS and MERS—viruses more closely linked to COVID-19 and that cause severe illness, like COVID-19—seems to last for several years (though not indefinitely). A reasonable initial estimate is that immunity to COVID-19 would last a few years, and that we might need to get vaccinated after that—though we need more information to be certain. (33)(34).

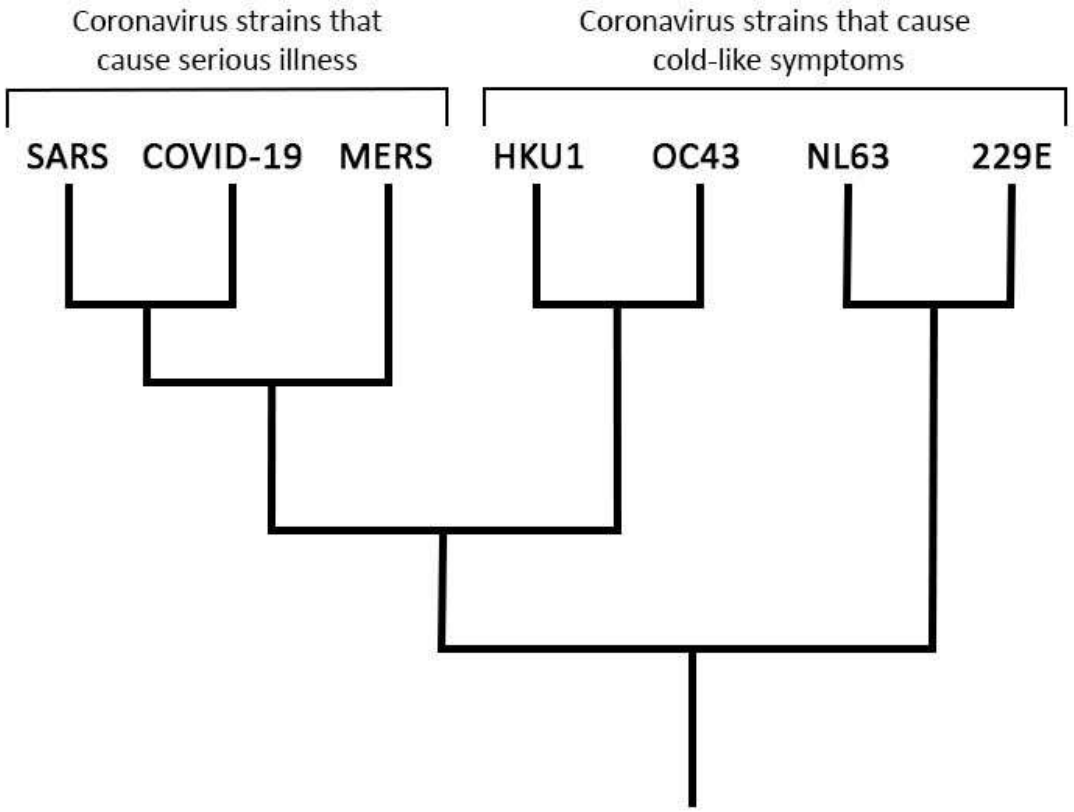

Fig. 3(The evolutionary relationships among coronaviruses)

This tree contain several of the important discoveries. Five of the main clades of coronaviruses (one to five) lineages in the figure, every mainly constrained to a specefic area (as proven via the colored explores grouping inside continents of Asia and Africa). The figureuses symbols to demonstrate the host creature (mostly horseshoe bats) for every virus, with the upper red star representing the virus that caused the previous SARS outbreak and the lower red star representing SARS-CoV-2. (34).

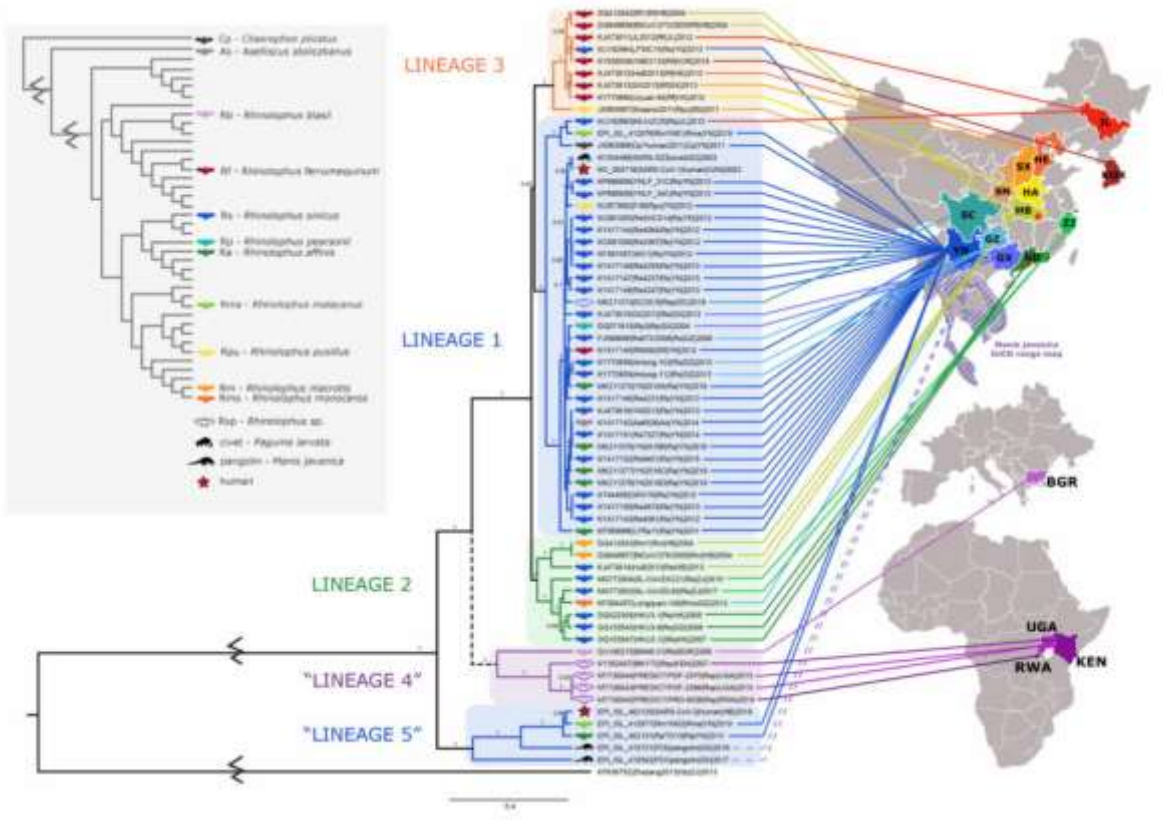

Fig.4(The different lineages of the virus)

2.2.2 Clinical manifestation

COVID-19 can cause different signs and symptoms in different people. Some of them are not very common, but still important to know. For instance:

Thromboembolic events

•The information that is currently available on thrombotic risk in critically ill The small number of COVID-19 patients is based on case series from France, China, and The Netherlands.

These findings might point to a higher risk of thrombotic events, such as stroke and pulmonary embolism, in hospitalized patients.

COVID-19 patients. Skin problems. In one study, out of 88 people who had COVID-19, 18 people (20%) had skin problems like rash and hives4. There are also some reports of purple toe sores in people who might have COVID-19, as shown in (fig. 5) (35).

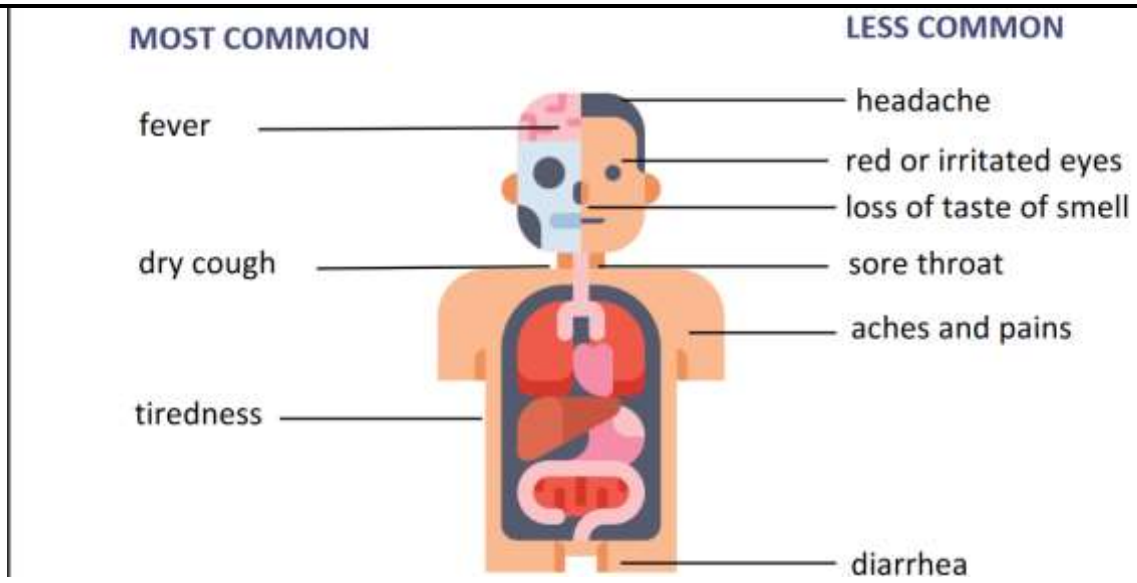

Fig 5(Clinical manifestation linked to COVID-19).

2.2.3 Immunology and pathophysiology

ARS-CoV-2 attaches to ACE 2, the receptor at the host target cell. The virus replicates and releases itself inside the lung cells, causing non-particular signs and symptoms including fever, muscle aches, headache, and breathing troubles (36). In a hamster experiment, the virus damages the cells within the olfactory epithelium briefly, inflicting olfactory issues, which can also account for the fast-term lack of taste and scent frequently visible in COVID-19 (37). The presence of ACE 2 receptors in various tissues can also explain the locations of contamination and patient signs and symptoms. For instance, the ACE 2 receptor is on the epithelium of other organs which includes the intestine and endothelial cells within the kidney and blood vessels, which may additionally account for gastrointestinal symptoms and cardiovascular troubles (38). Lymphocytic endothelin's have been seen in postmortem pathology exams of the lung, coronary heart, kidney, and liver in addition to liver cell loss of life and coronary heart attack in sufferers who died of covid 19 (36)(39). These findings display that the virus without delay influences many organs, as become the case in SARS-CoV-1 and influenzae.

Following viral entrance, the first inflammatory reaction draws T cells specific to the virus to the infection site. Here, the infected cells are destroyed before the virus spreads, resulting in most people's recovery (40). SARS-CoV-2 induces an abnormal host immune response in patients who progress to a severe state of illness (40)(41). For instance, postmortem histology of the lung tissues of COVID-19-related patient deaths has confirmed the inflammatory nature of the injury, exhibiting characteristics like the lung pathology seen in severe Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS) such as bilateral diffuse alveolar damage, hyaline-membrane formation, interstitial mononuclear inflammatory infiltrates, and desquamation. Mucus plugs with fibrinous exudate within the respiratory tract are a characteristic of COVID-19, and they are probably answerable for the infection's severity even in young human beings (44). This can be delivered by using an excess of seasoned-inflammatory cytokines that increase in the lungs and sooner or later cause lung parenchyma harm (40).

Additionally, some humans have multi-organ failure and septic surprise (40). For example, the release of fantastically touchy troponin and natriuretic peptides is a commonplace early signal of cardiovascular contamination in COVID-19(45). Sporadic intra-alveolar bleeding and the development of platelet-fibrin clots in minor artery arteries are also found, which is constant with the medical condition of coagulopathy (43). Cytokines usually control and regulate immunity, inflammation, and blood cell production; but, expanded cytokines build-up in different organs in some patients can also cause numerous tissue damage, or a cytokine release syndrome (cytokine storm), ensuing in capillary leak, clot formation, and organ failure (40)(46).

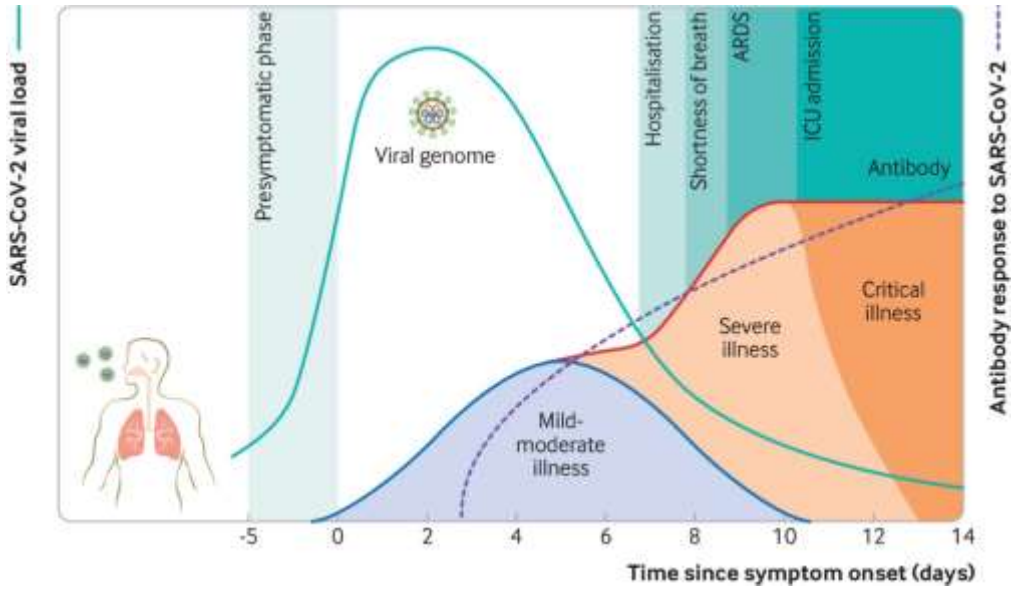

Fig .6(Immune response and disease spectrum).

2.2.4 Variants

When the virus changes, a different, or other version, the cause of COVID-19 becomes apparent. the virus can become more dangerous, spreadable, or infectious.

Once infected, the virus can replicate. In this process, each copy's genetic code may alter at random during this process. We call these changes mutations.

A change does not affect the virus in any way.

Some mutations don't have any effect on the virus but other mutations make:

• Infect a person’s cells and become life-threatening.

• The virus is more adept at evading the body’s defenses.

• Reduce the accuracy of virus testing.

• Drugs used to prevent or treat COVID-19 lose their effectiveness or do not work at all.

• Vaccines become less effective.

Also the new variant is become extra aggressive, more spreadable, vaccine-resistant, capable of purpose extra excessive illnes—or all the above, as compared with the authentic strain of the virus (30)(48).

More detailed information about most widespread variants :

Omicron:

Omicron and its variants have been the most common SARS-CoV-2 lines within the United States for the previous years. The greatest variety of COVID-19 instances inside the USA Is nevertheless because of subvariants of the authentic Omicron strain (BA.1), which has vanished. Omicron was first diagnosed in November 2021 in Botswana and South Africa. Cases soon started showing up and unfolding to different countries. By December of those 12 months, Omicron changed into chargeable for over a million each day instances in the United States. It had given upward thrust to numerous subvariants in 2022. In 2023, the most common Omicron strain inside the United States is EG.5 (also known as "Eris"), even as researchers are keeping an eye on BA.2.86 (also known as "Pirola"), another novel strain.

Contagiousness: Omicron's subvariants are superb at spreading the infection. The original strain of Omicron was more infectious than Delta. One clarification became that greater than 30 of Omicron's mutations are at the virus's spike protein, the element that attaches to human cells, and several of those are believed to boost the opportunity for infection.

Severity: Scientists are still running to research approximately whether the cutting-edge Omicron traces cause extra excessive disorder than their predecessors. Data has advised that the original Omicron stress became less excessive, in popularity, than preceding editions, according to the CDC. But it has additionally been noted that surges in instances may additionally result in an enormous will increase in hospitalizations and deaths as they did when the version changed into spreading at the begin of 2022, while the demise charges have been as high or better than they have been for the duration of the Delta variation peak inside the previous fall (48)(49)(50).

Delta

Delta (B.1.617.2) Was the first recognized in India in late 2020; it quickly unfolded at some stage in the world, turning into what changed into the essential model of the coronavirus—till Omicron took its vicinity in mid-December of 2021.

Contagiousness: Delta was plenty more infectious than the previous editions—it was estimated to cause more than twice as many instances. In Connecticut, it changed into eighty to 90% more transmissible than the Alpha variant. In the U.S., COVID-19 instances and hospitalizations had been dropping till Delta arrived in June 2021 and reversed the fashion. In the autumn of 2021, even the states with excessive vaccination quotes had spikes in cases, and experts recommended human beings get their booster pictures.

Severity: Delta prompted greater extreme disorder than other editions in those who hadn't been vaccinated. Early research from Scotland and Canada, both stated using the CDC, recommended Delta became greater probability to bring about hospitalization in the unvaccinated. A record in the Lancet published that human beings in England had twice the hospitalization hazard with Delta than they did with Alpha, the the former strong variation in that United States of America (50)(51)(52).

Beta :

Beta (B.1.351) was first detected in South Africa in overdue 2020 and then spread to other international locations. It had many mutations that made specialists fear its ability to escape antibodies.

Contagiousness: The CDC said Beta became 50% more infectious than the unique COVID-19 strain.

Severity: There was some evidence that Beta could cause extra hospitalization and loss of life than other different versions (50)(51)(53).

Alpha:

Alpha (B.1.1.7) turned into the first of the publicized variations. Alpha first appeared in Great Britain in November 2020 and infections surged in December of that year. It soon surfaced around the world and became the dominant version in the U.S., where the CDC categorized it as a variation of concern. Then, Alpha diminished away with the rise of the greater aggressive Delta variation.

Contagiousness: It was thought that certain mutations in the spike protein of Alpha would make it more contagious. It is estimated that the B.1.1.7 lineage is 30–50% more contagious than the original SARS-CoV-2 strain. Alpha accounted for 66% of cases in the U.S. in mid-April 2021, prior to Delta becoming the norm, according to a June CDC analysis.

Severity: Research indicates that the B.1.1.7 lineage became more lethal than the original virus and was more likely to infect irritated people inside the hospital. (50)(51)(54).

2.2.5 Diagnosis of virus

Types of Tests

Molecular Tests:

Molecular tests, also known as RT-PCR, are the most accurate approach for COVID-19 diagnosis. To look for the genetic material of the virus, they use samples taken from the nose, throat, or saliva. They achieve this by making a large number of copies of the virus's DNA, the test is very sensitive, and a positive result person invariably indicates COVID-19 infection.

Receiving answers from these tests can be a slow process, lasting anywhere from 2 days to more than a week, depending on the circumstances in your area, since they are usually conducted in specialized labs.

Antigen Tests:

Antigen COVID-19 tests, or rapid tests usually yield outcomes more quickly than a molecular test, but they also run a greater risk of failing to detect an infection that is still active. They can yield results in a matter of minutes, but in contrast to molecular testing, they require a higher concentration of the virus to produce a positive result. Your healthcare professional may occasionally request that you undergo a molecular test to confirm results if an antigen test comes up negative.

Antibody Tests:

An antibody test is used to detect the body's immune reaction to SARS-CoV-2. Although the blood test typically provides quick results, it is only useful for detecting if you have the disease not if you have a current infection. A current infection should not be diagnosed using antibody testing. Experts are still unsure if antibodies protect you from getting the virus again, so you should not use antibody test results to decide if you are immune to the virus (55)(56)(57).

2.2.6 Vaccination

Vaccination is a straightforward, secure, and efficient method for shielding yourself from dangerous diseases before encountering them. It harnesses your body's innate defenses to expand resistance to precise infections, bolstering your immune device.

Also teach your immune system to provide antibodies, just like it does while faced with a disorder. However, given that vaccines simplest include inactivated or weakened kinds of germs—inclusive of viruses or bacteria—they do not induce the illness or expose you to its potential complications (58)(59).

Vaccines can give active immunity against dangerous agents by stimulating the immune system to target those agents. Once triggered by a vaccine, the antibody-producing cells (known as B cells or B lymphocytes) remain primed and ready to react if the agent ever enters the body. Furthermore, vaccines can provide passive immunity by supplying antibodies or lymphocytes already created by an animal or human donor.

Typically, most vaccinations are delivered by injection (parenteral administration), although some can be taken orally or even nasally (flu vaccine). Vaccines administered via mucosal surfaces, such as the lining of the stomach or nasal passages, seem to induce a stronger antibody reaction and might be the most effective route of administration (59). The table below demonstrates the differences between coronavirus vaccines:

2023-2024 Pfizer-BioNTech vaccine/Comirnaty	2023-2024 Moderna vaccine/Spikevax	2023-2024 Novavax COVID-19, adjuvanted vaccine
Type mRNA vaccine	Type mRNA vaccine	Type Protein subunit vaccine
Effectiveness Helps protect people of all ages against COVID-19 severe illness, that requires hospital care or causes death.	Effectiveness Helps protect people of all ages against COVID-19 severe illness, that requires hospital care or causes death.	Effectiveness Helps protect people of all ages against COVID-19 severe illness, that requires hospital care or causes death.

Side effects Pain, swelling, or redness where the shot was given, tiredness, headache, muscle pain, fever, and swollen lymph nodes. uncommon cases of allergic reaction minutes to hours after injection. Rare cases of heart problems in the two weeks after vaccination.	Side effects Pain, swelling, or redness where the shot was given, tiredness, headache, muscle pain, fever, and swollen lymph nodes. uncommon cases of allergic reaction minutes to hours after injection. Rare cases of heart problems in the two weeks after vaccination.	Side effects Pain, swelling, or redness where the shot was given, tiredness, headache, muscle pain, fever, and swollen lymph nodes. uncommon cases of serious allergic reaction minutes to hours after injection. Rare cases of heart problems in the 10 days after vaccination.
Ingredients Messenger RNA, Fats, Sugar and Acidic ingredients (60)(63).	Ingredients Messenger RNA, Fats, Sugar and Acidic ingredients (61)(63).	Ingredients Protein, Fats, Sugar, Herbal fraction, Salt and Acidic ingredients (62)(63).

Table 3. (Comparing the differences between COVID-19 vaccines) (63).

2.3 Interleukin

Interleukins (ILs) are cytokines that are Once thought to be exclusively produced by leukocytes, now produced by a wide variety of other bodily cells. They play an essential role in immune cell activation and differentiation as well as in facilitating the cells' motility, adhesion, maturation, and proliferation. (64).

Interleukin is a type of cytokine that helps maintain the balance of the immune system as shown in Fig. 7. It was initially discovered from leukocytes, but now it is produced by several different parts of body cells. Proteins and signaling molecules that are expressed and secreted by leukocytes, the white blood cells, and certain other bodily cells. More than 50 interleukins and associated proteins are encoded in the human genome. Many cells currently generate interleukins, including lymphocytic cells and macrophages with a solid structure and function (65).

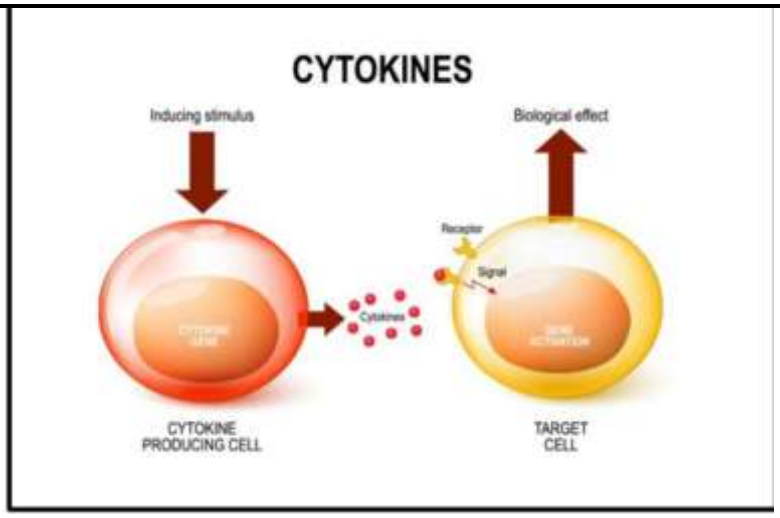

Fig.7 (cytokines).

The term interleukin was coined by Dr. Vern Petkau of the University of Victoria in 1979. The name is derived from the Greek prefix inter-, meaning "as a means of communication", and the suffix -leaking, meaning "derived from leukocytes". At the time, it was believed that interleukins were produced exclusively by leukocytes and acted on leukocytes. However, it has since been discovered that More recently, it has been found that many different types of bodily cells create interleukins. In spite of this, the word "interleukin" is still in use.

As cytokines produced by lymphocytes that mediate immunological responses, certain interleukins are categorized as lymphokines. (66).

2.3.1 Diversity and classification

interleukin _1(IL-1)

The endothelium, fibroblasts, astrocytes, macrophages, big granular lymphocytes, and B cells all release IL-1. T cells, B cells, macrophages, endothelium, and tissue cells are the main targets of IL-1. Increased leukocyte/endothelial adhesion, macrophage stimulation, lymphocyte activation, fever from hypothalamic stimulation, and liver release of acute phase proteins are all brought on by IL-1. It may also result in cachexia and apoptosis in a variety of cell types. (67)(68).

Interleukin-2 (IL-2)

IL-2 produced byukin-2 (IL-2) primarily targets T cells and has several effects on them. It promotes you provided:

IL-2, produced by T cells increasesleukin-2 (IL-2) (69).

Interleukin-3 (IL-3)

IL-3 is a cytokine that is produced by T cells and stem cells 1) It is a multilineage colony-stimulating factor that regulates the concentrations of various blood-cell types (70).

Interleukin-4 (IL-4)

CD4+T cells of the Th2 subtype produce IL-4, which acts on both B and T cells. It is a growth factor for B-cells and causes selection of IgE and IgG1 isotypes. It also causes Th2 differentiation and proliferation and inhibits IFN gamma-mediated activation on macrophages. In addition, it promotes mast cell proliferation in vivo (71).

Interleukin-5 (IL-5)

CD4+T cells (Th2) are responsible for producing IL-5, which targets B cells. This results in the production of B-cell growth factor and differentiation, as well as IgA selection. Additionally, it causes eosinophil activation and increased production of these innate immune cells.

Interleukin-6 (IL-6)

IL-6 is produced by T and B lymphocytes, fibroblasts, and macrophage. Its primary effects include B-cell differentiation and stimulation of acute phase proteins. The principal targets of IL-6 are B lymphocytes and hepatocytes (72)(73).

Interleukin-7 (IL-7)

Pre-B cells and T cells undergo proliferation when exposed to IL-7, which is produced by bone marrow, stromal cells (74).

Interleukin-8 (IL-8)

IL-8 is produced by monocytes and fibroblasts and primarily targets neutrophils, basophils, mast cells, macrophages, and keratinocytes. It induces neutrophil chemotaxis, angiogenesis, superoxide release, and granule release (78).

Interleukin-9 (IL-9)

The cytokine produced by Th9, Th2, Th17, mast cells, NKT cells, and regulatory T cells is IL-9. IL-9 exerts its effects on multiple types of cells and different tissues. It enhances T-cell survival, mast cell activation, and synergy with erythropoietin also known as human cytokine synthesis inhibitory factor (CSIF), is an anti- inflammatory cytokine.

T lymphocytes are the cells that generate IL-10. Th1 cells are its main focus. It results in interferon gamma and IL-2 suppression. It also downregulates pathogenic Th17 cell responses and reduces antigen presentation, MHC class II expression of dendritic cells, and co-stimulatory molecules on macrophages. It suppresses the generation of IL-12 by macrophages. (76).

Interleukin 10 (IL-10)

The anti-inflammatory cytokine Interleukin 10 (IL-10): which is also known as human cytokine synthesis inhibitory factor (CSIF). It is produced by Th2 cells and its primary target is Thl cells.IL-10 has the ability to inhibit both IL-2 and interferon-gamma.It also reduces antigen presentation and MHC class II expression in dendritic cells, co-stimulatory molecules on macrophages, and pathogenic Th17 cell responses. Furthermore, it inhibits IL-12 production by macrophages. (78)(79).

2.3.2 Immune system regulation

Interleukins, a group of cytokines, are produced by various immune system cells. Their primary role is to regulate immunity. Interleukins achieve this by binding to specific receptors on the surface of target cells, like other cytokines (80)."

The immune system relies heavily on interleukins, and rare deficiencies in some of these proteins have been associated with autoimmune diseases or immune deficiencies. Most interleukins are produced by CD4 helper T-lymphocytes, monocytes, macrophages, and endothelial cells. Their role includes fostering the development and differentiation of T and B lymphocytes, as well as hematopoietic cells."

They play a crucial role in activating immune responses, including inflammation (81).

There are many types of cytokines, which affect different parts of the immune system: • Some cytokines can stimulate activity. Certain types of cytokines stimulate leukocytes to become more effective killers, attracting other leukocytes to the confrontation area. While other types of cytokines inhibit the activity, which helps end the immune response. Some cytokines, called interferons, affect the replication (replication) of viruses. Cytokines also contribute to the mechanism of acquired immunity (82).

Conclusion

This study investigated the link between interleukin-10 (IL-10) levels and the severity of SARS-CoV-2 infection.

Our data show that patients with severe COVID-19 had significantly higher IL-10 levels than patients with non-severe instances. These findings indicate that IL-10 may play an important role in the etiology of severe COVID-19

The study found that patients with severe COVID-19 had significantly higher IL-10 levels, suggesting IL-10 may play a role in the disease's severity.

Further research is needed to understand the processes IL-10 contributes to illness severity and the therapeutic benefits of targeting IL-10 in COVID-19 treatment. The study has limitations, including a small sample size, the inability to conclude a causal association, and the need for larger-scale clinical trials to assess the efficacy and safety of targeted treatments.

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