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RESEARCH ARTICLE OPEN ACCESS

PANDEMICITY OF COVID-19 IN HUMANS

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ABSTRACT

Coronaviruses are named after the crown like spikes on their surface. SARS-CoV-2 is the novel coronavirus that causes coronavirus disease 2019 or COVID-19. When the invasion by SARS-CoV-2 is limited or contained at sites of nasal passage and conducting airways around throat by both innate & acquired immune responses, COVID-19 can be mild, or even asymptomatic. But when the infective virions manage to move down and invade the gas exchange units of lungs called alveoli, it will be a serious life threatening damage. Not only that, infective virions can enter bloodstream (sepsis), leading to disseminated COVID-19. Sepsis occurs when infective virions of SARS-CoV-2 reach and spread through carrier bloodstream, causing tissue damage everywhere it goes as far as there are susceptible types of human body cells with welcoming hACE2 receptors on their surfaces. The infection or invasion of a human host for the first time by a pathogenic virus, (also known as a primary exposure to that specific virus) generates acquired immunity against that virus. So that if the same pathogenic virus enters the body of the same person it infected first, the immune response activated by the primary exposure will destroy it promptly. The only reliable approach to fight against viral diseases or infections is vaccination as there is nearly no medicine or chemotherapy to cure viral diseases except managing them. Vaccination of SARS-CoV-2 can be done or occurs in two possible ways, i.e., by natural infection and by health professionals. Thus, those people who have been infected by SARS-CoV-2 and have been recovered from it will not have to take vaccination against COVID-19. The key objective of this paper is to impart the pandemicity and pathogenicity of COVID-19 including susceptible, types of human body cells, to SARS-CoV-2 infection. Nearly and inevitably, when all human populations are vaccinated naturally by infection and by health professionals against SARS-CoV-2 invasion, then it will be the end of pandemic COVID-19 in human populations of the globe. As the consequence of this it is the good of human life that overbalances the pain and evil of COVID-19; we are stepping to that optimistic end!!!!

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INTRODUCTION

Types of Human Coronavirus

Coronaviruses are named after the crown-like spikes on their surface. Four main sub-groups of coronaviruses are recognized:- alpha, beta, gamma, and delta. Human coronaviruses were first identified in the mid-1960s. Seven coronaviruses that can invade people are:- 229E (alpha coronavirus), NL63 (alpha coronavirus), OC43 (beta coronavirus), HKU1 (beta coronavirus), MERS-CoV (the beta coronavirus that causes Middle East Respiratory Syndrome, or MERS), SARS-CoV (the beta coronavirus that causes severe acute respiratory syndrome, or SARS), SARS-CoV-2 (the novel coronavirus that causes coronavirus disease 2019, or COVID-19). People around the world commonly get infected with human coronaviruses 229E, NL63, OC43, and HKU1. Sometimes coronaviruses that infect animals can evolve and make people sick and become a new human coronavirus. Examples of this are 2019-nCoV, SARS-CoV, and MERS-CoV. Like other respiratory illnesses, COVID-19, the disease caused by the new coronavirus, can cause lasting lung damage. As we continue to learn about COVID-19, we are understanding more regarding how it affects the lungs while people are sick and after recovery [1]. COVID-19, the disease caused by the new coronavirus, can cause lung complications such as pneumonia and, in the most severe cases, acute respiratory distress syndrome, or ARDS. Sepsis, another possible complication of COVID-19, can also cause lasting harm to the lungs and other organs [2]. The key

objective of this paper is to impart the pandemicity and pathogenicity of COVID-19 including susceptible, types of human body cells, to SARS-CoV-2 infection.

Review

COVID-19 Pneumonia: In patients with COVID-19 pneumonia, the lungs become filled with fluid and inflamed, leading to breathing difficulties. For some patients, breathing problems can become severe enough, requiring treatment in the health center with oxygen or even a ventilator [3] . The pneumonia caused by COVID-19 tends to damage both lungs. Alveoli/air sacs in the lungs fill with fluid, limiting their ability to take in oxygen and causing shortness of breath, cough and other symptoms. While most patients recover from pneumonia without any lasting lung damage, the pneumonia associated with COVID-19 may be severe. Even after the disease has passed, lung injury may result in breathing difficulties that might take months to improve.

Acute Respiratory Distress Syndrome (ARDS): As COVID-19 pneumonia precedes, more of the alveoli become filled with fluid leaking from the tiny dialated blood capillaries in the lungs. Eventually, shortness of breath sets in, and can lead to acute respiratory distress syndrome (ARDS), a form of lung failure. Patients with ARDS are often unable to breath on their own and may require ventilator support to help circulate oxygen in the body [3]. Whether it occurs at home or at the hospital, ARDS can be fatal [4]. Patients who survive ARDS and recover from COVID-19 may have lasting pulmonary scarring.

Sepsis: The other possible complication of a severe case of COVID-19 is sepsis. Sepsis occurs when an infection reaches and spreads through the bloodstream, causing tissue damage everywhere it goes. The work of lungs, heart and other body systems is tightly interdependent. In sepsis, the cooperation between the organs falls apart. Entire organ systems can start to shut down, one after another, including the lungs and heart. Sepsis, even when survived, can leave a patient with lasting damage to the lungs and other organs [5-7].

Superinfection: If a person has COVID-19, the immune system works actively to fight the pathogenic viral invader. COVID-19 is caused by a coronavirus called SARS-CoV-2. Coronaviruses belong to a group of viruses that infect animals. A coronavirus infection usually targets two body parts: as an infection in the lungs that includes some cases of what people would call the common cold, or as an infection in the gut that causes diarrhea. COVID-19 begins in the lungs like the common cold coronaviruses, but then causes havoc with the immune system that can lead to long-term lung damage or death [8-10]. SARS-CoV-2 is genetically very similar to other human respiratory coronaviruses, including SARS-CoV and MERS-CoV. However, the subtle genetic differences translate to significant differences in how readily a coronavirus infects people and how it makes them sick. SARS-CoV-2 has the same genomic equipment like the original SARS-CoV, which caused a global outbreak in 2003, but with around 6,000 mutations sprinkled around in the usual places where coronaviruses change [11-16].

How the virus infects: Every coronavirus infection with a virus particle, a spherical shell that protects the genome (a single long string of genome with the associated protein material) and inserts it into a human cell. The genome instructs the cell to make around 30 different parts of the virus, allowing the virus to reproduce. The cells that SARS-CoV-2 prefers to infect have a protein called ACE2 on the outside that is important for regulating blood pressure. The infection begins when the long spike proteins that protrude from the virus particle latch on to the cell's ACE2 protein. From that point, the spike transforms, unfolding and refolding itself using coiled spring-like parts that start out from the core of the spike. The reconfigured spike hooks into the cell and crashes the virus particle and cell together. This forms a channel where the viral genome can snake its way into the unsuspecting cell.

How SARS-CoV-2 infects, sickens and kills people: SARS-CoV-2 has a sliding scale of severity. Patients under age 10 seem to clear the virus easily, most people under 40 seem to bounce back quickly, but older people suffer from increasingly severe covid-19. The ACE2 protein that SARS-CoV-2 uses as a door to enter cells is also important for regulating blood pressure, and it does not do its job when the virus gets there first. This is one reason COVID-19 is more severe in people with high blood pressure. SARS-CoV-2 is more severe than seasonal influenza in part because it has many more ways to stop cells from calling out to the immune system for help [4].

Fluid Inflamed, thickened respiratory membrane

A ventilator and mechanical breathing: Ventilators are not a cure for COVID-19 patients, but mechanical breathing assistance that can keep patients alive while they battle the infection. Critical care ventilators are more than just air pumps. They are finely tuned machines with software that must be constantly adjusted by skilled medical workers to ensure that patients receive the right combination of oxygen level, pressure, breath volume and breathing rate [3]. Both SARS-CoV-2 and SARS-CoV gain entry via a receptor called ACE2. More commonly known for their role in controlling blood pressure and electrolytes, these receptors are also present in the lungs, back of the throat, gut, heart muscle, and kidneys. As part of the immune response, white blood cells, such as neutrophils and macrophages, rush into the alveoli. Meanwhile, blood vessels around the air sacs become leaky in response to inflammatory chemicals that the white blood cells release. This fluid puts pressure on the alveoli from outside and, in combination with the lack of surfactant, causes them to collapse. As a result, breathing becomes difficult, and the surface area in the lung where oxygen transfer usually takes place becomes reduced, leading to breathlessness [5].

Symptoms of COVID-19 include:

- Sneezing,
- Fever,
- Chills
- Cough,

Fatigue,

- Shortness of breath or difficulty in breathing,
- Muscle or body aches,
- Headache,
- Sore throat,
- New loss of taste,
- Loss of smell,

- Loss of appetite,
- Nausea or vomiting,
- Congestion or runny nose,
- Persistent pain or pressure in the chest,
- Diarrhea,
- New confusion, and
- Inability to wake, or stay awake.

Common Symptoms of COVID-19: Researchers in China found that the most common symptoms among people who were hospitalized with COVID-19 include:

- Fever: 99%,
- Fatigue: 70%,
- A dry cough: 59%,
- Loss of appetite: 40%,
- Body aches: 35%,
- Shortness of breath: 31%, and
- Mucus or phlegm: 27%.

Emergency Symptoms of COVID-19: It is advised to call a doctor or hospital right away if you have one or more of the following COVID-19 symptoms:

- Trouble breathing,
- Constant pain or pressure in your chest,
- Bluish lips or face, and
- Sudden confusion.

Transmission of COVID-19

- SARS-CoV-2 can be transmitted when a healthy person is in close contact (within 1 meter) with someone who has respiratory symptoms of COVID-19 such as coughing or sneezing. This puts the healthy person at risk of having his/her mucosae infected (in mouth and nose) or conjunctiva of eyes as they are exposed to infective respiratory droplets,
- Transmission of COVID-19 viral disease is possible by direct contact with infected people and indirect contact with surfaces of inanimate objects (**fomites**) in the immediate environment or with objects used on the infected person (e.g., stethoscope or thermometer), and
- It would be a serious misunderstanding for us to rule out/omit airborne mode of transmission of SARS-CoV-2 infection, anchoring/sticking to contagious mode of transmission only!!

Preventive measures against COVID-19

- Avoid mass gatherings,
- Avoid close contact with anyone who is sick and has symptoms, being away from by 2 meters or more,
- Stay home as much as possible and keep distance between yourself and others, especially if you have a higher risk of serious illness,
- Keep in mind that some people may have COVID-19 and spread to others, even if they don't have symptoms or don't know they have COVID-19,
- Wash your hands often with soap and water, or use an alcohol-based hand sanitizer that contains at least 60% alcohol,
- Cover your mouth & nose with a cloth face mask in public spaces, such as grocery store, where it is difficult to avoid close contact with others,
- Cover your mouth and nose with your elbow or a tissue when you cough or sneeze. Throw away the used tissue. Wash your hands right away,
- Avoid touching your eyes, nose and mouth,
- Avoid sharing dishes, glasses, towels, bedding and other household items if you are sick,
- Clean and disinfect high-touch surfaces, such as doorknobs, light switches, electronics and counters, daily,
- Stay home from work, school and public areas if you are sick, unless you are going to get medical care, and
- Avoid public transportation, taxis and ride-sharing if you are sick.

The difference between Flu and COVID-19: Both Flu and COVID-19 are respiratory illnesses but they are caused by different viruses. Flu is caused by infection with influenza viruses whereas COVID-19 is caused by infection with SARS-CoV-2. Because some of the symptoms of Flu and COVID-19 are similar, it can be unreliable to show the difference between them based on symptoms alone. However, there are some key differences (differential diagnosis) between the two.

The following are titles of 3 different videos underlined on COVID-19 & Flu Attack

Now, copy and paste the title of each video (only the blue colored & underlined) on Google search space on your computer desktop screen and then press Enter key of your computer keyboard. Click video. Now, click the slide with the correct Title you pasted.

1) Title of video: **Patient with coronavirus speaks out [via torchbrowser.com]**
2) Title of video: **Flu Attack! How A Virus Invades Your Body – YouTube [via torchbrowser.com]**
3) Title of video: **The TRUTH of How Coronavirus Spreads and How to Prevent Coronavirus - Airborne Transmission**

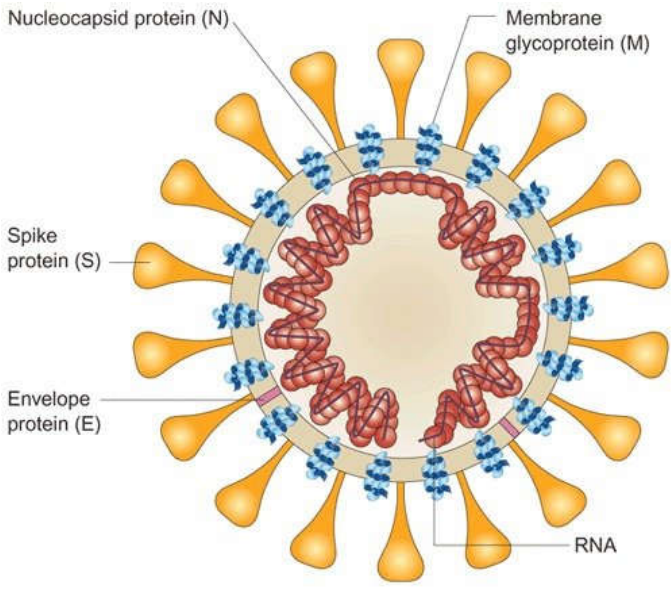

Figure 1. Anatomy of SARS-CoV-2 which causes coronavirus disease 2019 (COVID-19)

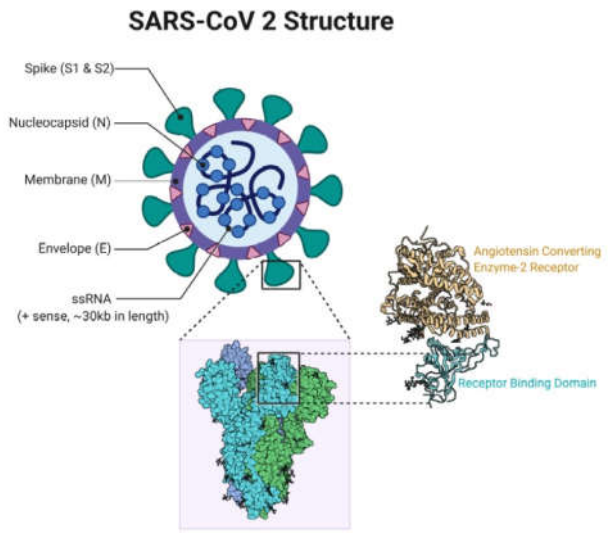

Figure 2. Anatomy of SARS-CoV-2 which causes coronavirus disease 2019 (COVID-19)

Observe the single-stranded RNA Genome that bears 30 kilobyte, meaning having the length of 30 nucleotides with a positive sense. Receptor binding domain used to attach to the welcoming ACE2 receptors on a susceptible host cell surface is also showed. Positive sense viral RNA is similar to messenger RNA (mRNA which is positive in polarity) and thus can directly/immediately be translated in the ribosome into protein.

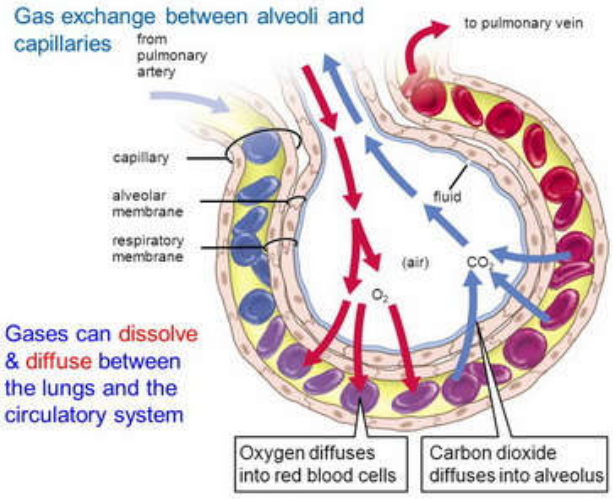

Figure 3. Exchange of O_2 and CO_2 between alveoli and capillaries in a healthy person

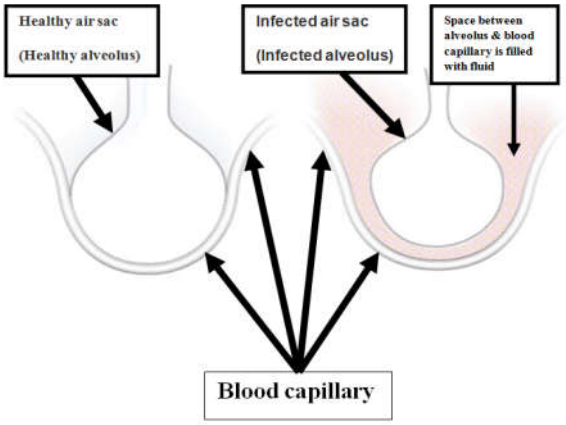

Figure 4. Gas exchange sites in a person diagnosed (tested positive) for SARS-CoV-2 infection

On the other hand, negative-sense viral RNA is complementary to mRNA, being nucleotides with nitrogenous bases that are different from those of the mRNA and thus it must be converted to positive-sense RNA by an RNA polymerase before being translated in ribosome into protein.

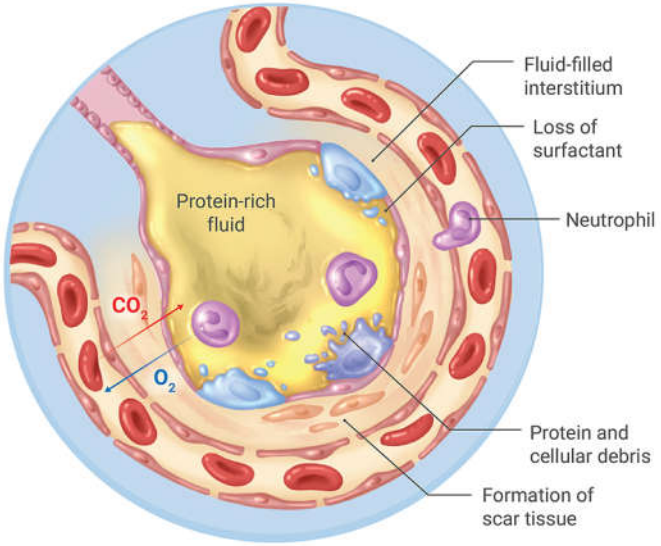

Figure 5. Morphology of a patient's alveolus filled with fluid due to invasion by SARS-CoV-2

Gas exchange sites in the alveolus of Fig.5 had been damaged.

'Silent hypoxia' may be killing COVID-19 patients. But there's hope.

Figure 6. Lungs of a patient infected by SARS-CoV-2

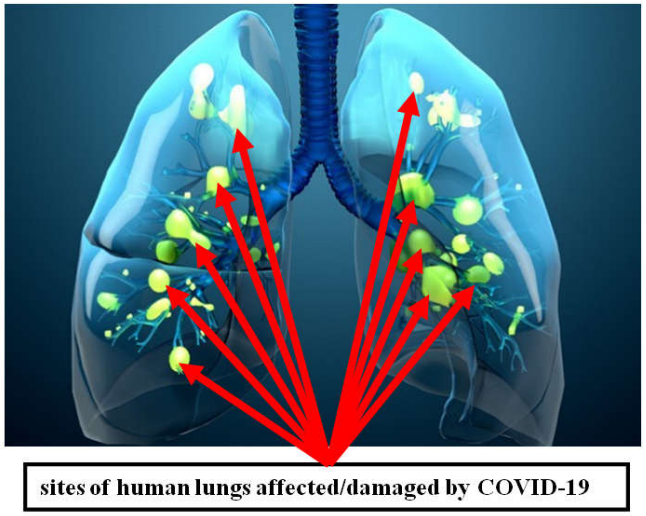

Figure 7. Pathogenesis in human lungs caused by SARS-CoV-2

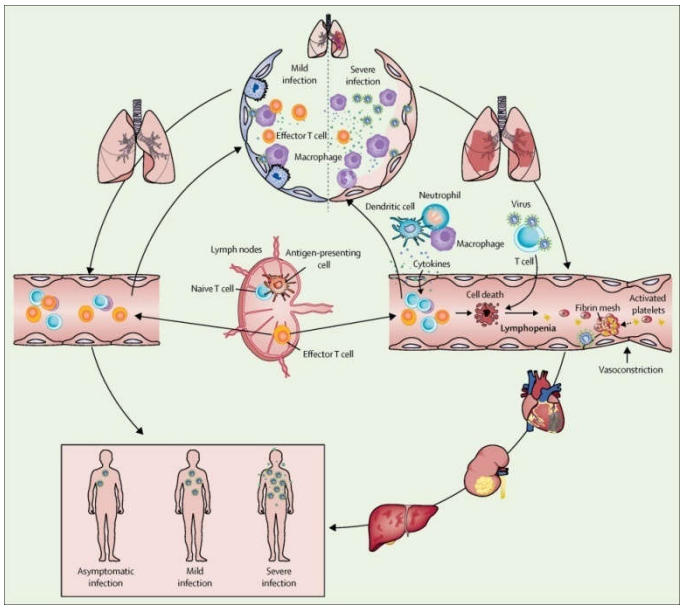

Figure 8. Asymptomatic/presymptomatic to severe infections with SARS-CoV-2 or disseminated COVID-19 among humans [Li H et al, 2020]

DISCUSSION

Global report, on pandemic SARS-CoV-2 invasive infection in human populations of the entire world, to WHO until 30 Jun. 2020 showed that there had been:

10,185,374 confirmed human cases, and

►503,862 confirmed deaths of COVID-19.

Therefore, the cumulative global human death rate due to COVID-19 was $\frac{503862x100}{10,185,374} = \underline{\underline{4.95\%}}$

In the past outbreaks, the case fatality rates i.e., death rates of Ebola virus infection in humans varied from 25% to 90%, being deadlier than that of SARS-CoV-2.

The term pandemic means an epidemic (i.e., a rapid spread) of an infectious disease that has spread across a large region, for instance multiple continents or worldwide, affecting a substantial number of people. With this definition in mind, COVID-19 is a pandemic disease that has rapidly spread throughout the world within a few months, being impossible to contain in the country where it has been the beginning of it. Retrospective investigation by Chinese authorities had identified human cases of SARS-CoV-2 infection, confirming that the onset of COVID-19 symptoms was in early December 2019 [17]. When nerve endings in our respiratory system are irritated by SARS-CoV-2 infection, we generate jets of cloudy droplets full of infective virions driven with very forceful coughing or sneezing that can even spectacularly shake our heads. These jets of respiratory droplets do contain so many infective virions of SARS-CoV-2 that contaminate the air and are inhaled by healthy people around the patient of COVID-19. If the mode of airborne transmission was not involved, COVID-19 could have been contained in China or at least within the continent of Asia. COVID-19 the onset of which was in Wuhan, China managed to spread and occupy the entire world within a few months because it involved both airborne and contagious modes of transmission. As it was verified by researchers in China, the most common symptom in COVID-19 patients is fever being detectable in about 99% of people who are positive for SARS-CoV-2 infection where about only 1% of the patients can be asymptomatic and/or presymptomatic. That is why passengers' or travelers' body temperatures are measured on roads at checkpoints by health professionals. Fever is also known as hyperthermia, pyrexia, or elevated temperature. Fever means a body temperature that is higher than normal. Any virus pathogenic to humans can infect only the types of cell with welcoming receptors (on their surfaces) for that particular virus. SARS-CoV-2 infects human body cells that bear or express human angiotensin-converting enzyme2 (hACE2) on their surfaces. The types of human body cells that express hACE2 receptor on their surfaces include:

- goblet cells in the nasal passage which secrete mucus,
- lung cells called type II pneumocytes in gas exchange units known as alveoli, and
- intestinal cells referred to as enterocytes used for nutrient absorption

Other types of human body cells in different organs are also known to bear hACE2 receptors on their surfaces. In other words, the types of human body cells that are susceptible to infection by SARS-CoV-2 are the ones which bear/express hACE2 on their surfaces [18, 19]. Disseminated COVID-19 by way of sepsis is possible because types of cells that express hACE2 on their surfaces are found in tissues of different types of human body organs (Fig. 8).

Conclusion

- The infection or invasion of a human host for the first time by a pathogenic virus, (also known as a primary exposure to that specific virus) generates acquired, adaptive, or specific immunity against that virus. So that if the same pathogenic virus enters the body of the same person it infected first, the immune response activated by the primary exposure will destroy it promptly. The only reliable approach to fight against viral diseases or infections is vaccination as there is nearly no medicine or chemotherapy to cure viral diseases except managing them. Vaccination of SARS-CoV-2 can be done or occurs in two possible ways, i.e., by natural infection and by health professionals. Thus, those people who have been infected by SARS-CoV-2 and have been recovered from it will not have to take vaccination against COVID-19.
- vaccination naturally by infection with the live pathogenic SARS-CoV-2 is certainly expected as far as the virus is immunogenic enough to induce acquired immunity in the body of human hosts without the need of any adjuvant.
- vaccination by health professionals is the practical application with attenuated immunogenic antigen of SARS-CoV-2 which causes COVID-19.
- natural vaccination by infection with live SARS-CoV-2 is associated with the risk of death (with mortality rate of about 4.95%) because of the nonattenuated virulent status of the pathogenic virus, being able to replicate in the body of the patient whereas the vaccination by health professionals with attenuated immunogenic

vaccine is totally free from the risk of dying for the client.

- Once the immune response caused by immunogenicity of this novel virus in all individuals of the world human populations is acquired via vaccination either by health professionals or by the pandemic natural infection, the antigenicity of SARS-CoV-2 with the immune response will lead to an irreversible elimination of COVID-19!!!!
- Nearly and inevitably, when all human populations are vaccinated naturally by infection and by health professionals against SARS-CoV-2 invasion, then it will be the end of pandemic COVID-19 in human populations of the globe. As the consequence of this it is the good of human life that overbalances the pain and evil of COVID-19; we are stepping to that optimistic end!!!!

Ethical Clearance: I declare that no ethical error is committed in the production of this paper. I also declare that I don't have any conflict of interest with anybody.

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