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(REVIEW ARTICLE)

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Coronavirus: A current update based on evidence

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Abstract

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the severe acute respiratory syndrome (SARS-CoV-2). The infection began in 2019 in Wuhan, China, and has spread worldwide, bringing about a pandemic. Basic indications incorporate fever, cough, and shortness of breath. While most of cases bring about mild indications, some advancement to pneumonia and multiorgan failure. The infection is spread from one individual to others by means of respiratory droplets, often produced during coughing and sneezing. Measures recommended preventing the infection incorporate successive hand washing, use of masks, keeping up a distance from others, and not contacting one's face. Based on current published evidence, the review sum up insights concerning the pathogenesis, the study of disease transmission, diagnosis, and the management methods for the disease prevention. It is trusted that this review will assist general public to recognize and deal with SARS-CoV2, and give reference for future studies.

Keywords: Coronavirus; Infection; Pathogenesis; Prevention; Disease

1. Introduction

COVID-19 is an infectious disease induced through a newly found Coronavirus [1]. Coronaviruses are diverse group of viruses infecting many distinctive animals, and they are able to cause slight to extreme breathing infections in human beings. In 2002 and 2012, respectively, particularly two pathogenic coronaviruses with zoonotic origin, extreme acute breathing syndrome coronavirus (SARS-CoV) and Middle East breathing syndrome coronavirus (MERS-CoV), emerged in people and induced deadly breathing illness, making rising coronaviruses a brand new public health concern in the twenty-first century [2]. At the cease of 2019, a unique coronavirus precised as SARS-CoV-2 (severe acute respiratory syndrome) emerged within side the city of Wuhan, China, and induced an outbreak of uncommon viral pneumonia. On January 9, 2020, Chinese nation media suggested that a team of researchers led by Xu Jianguo had recognized the pathogen behind a mysterious outbreak of pneumonia in Wuhan as a singular coronavirus. Although the virus turned into quickly after named 2019-nCoV, after which renamed SARS-CoV-2, it remains normally recognised actually as the novel coronavirus [3-5].

Being particularly transmissible, this novel coronavirus disease, additionally referred to as coronavirus disease 2019 (COVID-19), has unfold rapidly all over the world. It has overwhelmingly exceeded SARS and MERS in phrases of each the variety of inflamed human beings and the spatial variation of epidemic areas [6]. The ongoing outbreak of COVID-19 has posed an excellent threat to worldwide public health. From 2020 till yet we are struggling from SARS-CoV2. The progressing outbreak of COVID-19 has represented a phenomenal threat to global public health [7]. In this Review, we

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sum up the comprehension of the nature of SARS-CoV-2 and COVID-19. Based on as of late distributed discoveries, this exhaustive review covers the fundamental science of SARS-CoV-2, including the current discoveries of transmission analysis and countermeasures against COVID-19. As of May 22, 2021, the disease has infected in excess of 266,816,884 individuals, with 5,280,397 revealed passings. North and South America are the most noticeably terrible struck areas as far as case check and fatalities, yet Asia isn't a long way behind, due to the mostly surges in India. The worldwide economy has dived, as regulation and moderation endeavors keep on intruding on manufacturing, education, the financial sector, and numerous different strolls of life. But the future course of this infection is unknown. Since knowledge about this virus is rapidly developing, readers are encouraged to update themselves routinely.

2. Pathophysiology

To recognize the pathogenic mechanisms of SARSCoV-2 and to talk about the current therapeutic targets; it is critical to describe the viral structure, genome, and replication cycle. A schematic structure of Coranvirus has been depicted in Figure1. The Covid particles are coordinated with long RNA polymers firmly pressed into the focal point of the molecule, and encompassed by a defensive capsid, which is a cross section of repeated protein molecules referred to as capsid or coat proteins.The proteins in Coronavirus are termed as nucleocapsid [8,9]. CoVs are positive-stranded RNA viruses with a nucleocapsid and envelope. A SARSCoV-2 virion is about 75–160 nm in diameter, having +ssRNA genome of about 26 to 32 kilobases one of largest acknowledged RNA virus with a 5′-cap shape and 3′-poly-A-tail [10]. The Covid core molecule is additionally encircled by an external film envelope made of lipids (fats) with embedded proteins. It consists of 4 structural proteins, referred to as the S (spike), E (envelope), M (membrane), and N (nucleocapsid) proteins; the N protein holds the RNA genome, and the S, E, and M proteins collectively create the viral envelope [9,11]. Similarly to other coronaviruses SARS-CoV, SARS-CoV-2 uses the same receptor, angiotensin-converting enzyme 2 (ACE2) and fuses with the membrane of the host cellular. SARSCoV-2 then makes use of serine proteases TMPRSS2 (transmembrane protease serine 2) for S protein priming, infecting the goal cells. The spike proteins of SARSCoV-2 includes subunits; S1 receptor binding and S2 fusion, to mediate the virion binding to receptor protein and provoke membrane fusion [12]. The S1 and S2 subunits are divided via way of means of the S cleavage site. To facilitate virion attachment to receptor and fuses with cells membrane, the spike protein desires to be cleaved via way of means of mobile proteases from the S1/S2 cleavage site. Interestingly, the molecular evaluation of S proteins identifed an insertion at S1/S2 site, that is absent in different SARS-CoV, though the significance of this insertion remains unknown, evidently this precise insertion is supplying a gain-of-feature benefit for an easy cellular contamination and efficient spreading all through the human host [13, 14]. The viral RNA hijacks the host cellular's equipment to provoke the viral genome replication and polypeptides chain synthesis and shape the replication-transcription complex (RCT) had to synthesize the sub-genomic RNAs in addition to structural proteins (envelope and nucleocapsid). The viral envelope has a critical function with inside the viral assembly, release, and selling viral pathogenesis. However, many studies are required to recognize structural traits of SARS-CoV-2 [10, 12, 15].

The pathogenesis of SARS-CoV-2 contamination in human beings manifests itself as moderate signs and symptoms to severe respiratory failure. On binding to epithelial cells in the respiratory tract, SARS-CoV-2 begins replicating and migrating right all the way down to the airways and enters alveolar epithelial cells with inside the lungs. The fast replication of SARS-CoV-2 with inside the lungs may also cause a robust immune response. Cytokine hurricane syndrome reasons acute respiratory distress syndrome and breathing failure, which is taken into consideration the primary purpose of dying in sufferers with COVID-19 [16]. Older patients above >60 years and with severe pre-current sicknesses have a more risk of growing acute breathing misery syndrome and death. Multiple organ failure has additionally been said in a few COVID-19 case. The various clinical disorders caused by this virus is mentioned in Table 1.

Histopathological adjustments in sufferers with COVID-19 arise in particular with inside the lungs. Histopathology analyses confirmed bilateral subtle alveolar damage, hyaline membrane formation, desquamation of pneumocytes and fibrin deposits in lungs of sufferers with severe COVID-19 [17, 18]. Exudative infection changed into additionally shown in a few cases. Immunohistochemistry assays detected SARS-CoV-2 antigen withinside the higher airway, bronchiolar epithelium and submucosal gland epithelium, as in kind I and kind II pneumocytes, alveolar macrophages and hyaline membranes withinside the lungs [19].

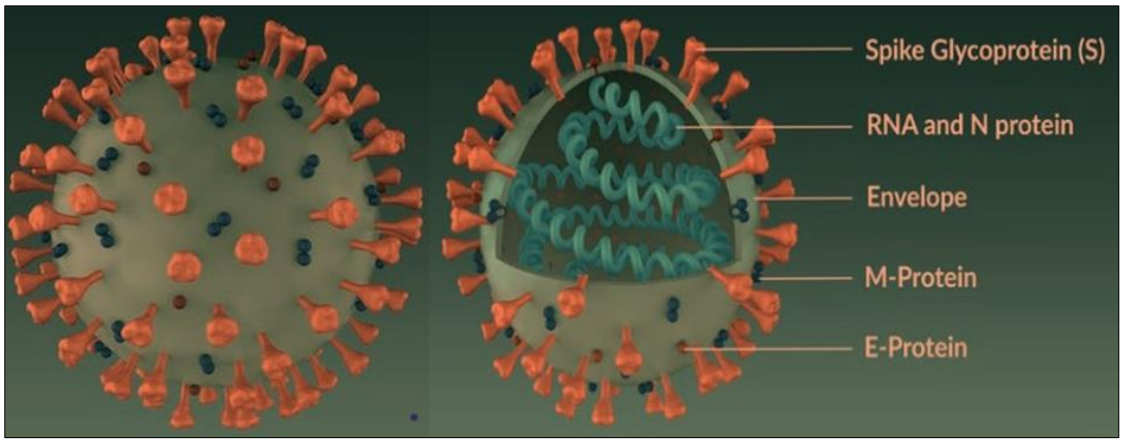

Figure 1 The structure of Coronavirus 2019

Table 1 Clinical Disorders caused by Coronavirus infection

Disorders	Clinical features
Systemic	Fever, Cough, Fatigue, Headache, Haemoptysis, Acute Cardiac Injury, Hypoxemia, Lymphopenia, Dysponea, Diarrhoea [20]
Respiratory	Sputum Production, Sneezing, Throat Pain, Rhinorrhoea, Pneumonia, Ground –Glass Opacities, Rnaaemia, Acute Respiratory Distress Syndrome [21]
Neurological	Meningoencephalitis, Guillain-Barré Syndrome, Acute Disseminated Encephalomyelitis, Stroke, Epilepsy, Chemosensory Disturbances, Nerve And Muscle Affection [22]
Social	Poor mental health outcomes, Isolation, Anxiety , Depression [23]

2.1 Transmission of SARS-CoV-2 Infection

As per the scientist briefs and epidemiologic information, the possible modes of transmission of SARS CoV 2 could include contact, airborne, droplet, faecal-oral, fomite, blood borne, animal-to-human and mother-to-Foetus transmission. The throw out of droplets during face-to face openness during talking, coughing, or wheezing is the most well-known method of transmission [24-26]. Transmission of SARS-CoV-2 can happen through immediate, backhanded, or close contact with contaminated individuals through tainted emissions like spit and respiratory discharges or their respiratory drops, which are ousted when a infected individual coughs, wheezes, talks or sings [12, 27]. Delayed exposure to affected individual with SARS –CoV2 and briefer vulnerability to people who are symptomatic i.e coughing or wheezing are related with higher danger for transmission, while brief vulnerability to asymptomatic contacts are less inclined to bring about transmission. Respiratory drops are >5-10 μm in distance across while drops <5μm in breadth are alluded to as drop cores or aerosols [28].

Airborne transmission is characterized as the spread of an infectious agent brought about by the scattering of droplet nuclei that stay infectious when suspended in air over significant distances and time. As per a report from WHO (World Health Organization), it has been stated SARS-CoV-2 may likewise spread through mist concentrates, especially in indoor areas with poor ventilation. The physics of exhaled air and flow physics have generated hypotheses about probable mechanisms of SARS-CoV-2 transmission via fine droplets [29]. These theories advise that 1) some of respiration droplets generate microscopic aerosols (<five μm) through evaporating, and 2) normal breathing and talking outcomes in exhaled aerosols. Thus, a prone individual ought to inhale droplets, and will end up infected if the aerosols incorporate the virus in enough amount to purpose infection inside the recipient [30]. However, the percentage of exhaled droplet nuclei or of breathing droplets that evaporate to generate fine droplets, and the infectious dose of viable SARS-CoV-2 required to cause infection in some other individual aren't known, however it's been studied for different respiration viruses [31].

Respiratory droplets or secretions expelled via way of means infected people can contaminate surfaces and gadgets, developing fomites, resulting contamination of surfaces [32]. Viable SARS-CoV-2 virus and/or RNA detected via RT-PCR may be found on the surfaces for durations starting from hours to days, relying at the ambient surroundings along with

temperature and humidity and the sort of surface, mainly at excessive concentration in health care centres in which COVID-19 sufferers had been being treated. Therefore, transmission may arise circuitously via touching surfaces withinside the instant surroundings or surfaces infected with virus from an infected person can be a thermometer, stethoscope, syringe, or bed sheets), accompanied via touching the eyes, nose or mouth [33].

As per steady proof, there are no scientific reports regarding surface contamination from SARS-CoV-2 and survival of virus on certain surfaces, directly confirmed via fomite transmission. Individuals who come into contact with possibly irresistible surfaces regularly likewise have close contact with the infected individual, making the differentiation between respiratory droplet and fomite transmission hard to perceive [34]. Nonetheless, fomite transmission is viewed as a probable method of transmission for SARS-CoV-2, given reliable discoveries about ecological contamination in the proximity of infected cases nearby and the way that other Covids and respiratory infections can communicate this way [35].

Pregnant women, their foetuses, and infants are likely going to deal with a high-threat population at some point of the ebb and flow COVID-19. Writing at the outcomes of COVID-19 diseases at some point of being pregnant is steadily developing studied. Salem et al. Pregnant women who emerge as COVID-19-positive are normally both asymptomatic or mild-to-reasonably indicative, like non-pregnant women [36]. Pneumonia is possibly, broadly identified outcomes in pregnant women with COVID-19. Initially, it can't be definitely stated that SARS-CoV-2 infection builds the hazard of and neonatal, fetal and maternal difficulties. Pregnant ladies with COVID-19 with co-morbidities have expanded dangers of difficulties: there are territorial varieties in the paces of unfavorable results detailed [36,37]. In spite of the fact that remarkable, the survey shows that upward transmission is conceivable. Furthermore, the third trimester is by all accounts the most weak time of contamination or infection [38].

Previously, there is no proof for intrauterine transmission of SARS-CoV-2 from infected pregnant ladies to their fetuses, in spite of the fact that information remain limited.WHO has published a logical brief on breastfeeding and COVID-19. But in July, 2020 India registers its first possible case of Covid 19 from mother to new born by vertical transmission. Various reports of mother-to-child infection of the novel Covid (SARS-CoV-2) have driven researchers to test how the infection enters the fetus inside the womb [39]. ICMR-National Institute for Research in Reproductive Health (ICMR-NIRRH) and Indian Institute of Science (IISc), Bengaluru, has examined molecular players in the placenta which may be responsible for allowing the virus to access the developing fetus.They have tracked down that a subset of cells in the placenta might be responsible for permitting SARS-CoV-2 section into the developing fetus.Like certain other infections (for example HIV), SARS-CoV-2 seems, by all accounts, to be capable of crossing this placental barrier [40].

The mRNAs coding for the SARS-CoV-2 binding receptor (ACE2) and the proteases required for viral entry and proteins required for viral multiplication were found to be expressed by certain subtypes of placental cells, which are involved with key placental functions [39, 40]. Also, in view of an systematic review data from 93 pregnant ladies with COVID-19, the researchers could show that within this cohort, almost 12% had placental infection with SARS-CoV-2, proposing a possibility of mother-to-child transmission of the virus [41].

SARS-CoV-2 RNA has likewise been identified in other organic examples, including the urine and feces of some infected patients. To date, however, there have been no distributed reports of transmission of SARS-CoV-2 through defecation or urine [42].

A few examinations have revealed recognition of SARS-CoV-2 RNA, in one or the other plasma or serum, and the virus can replicate in platelets. In any case, the role of bloodborne transmission stays questionable; and low viral concentration in plasma and serum recommend that the danger of transmission through this course might be low.

3. Assessment and diagnosis

Once someone has contracted coronavirus, it may take 2–14 days for signs and symptoms to appear. The common incubation duration seems to be roughly 5–6 days. The maximum common signs and symptoms of COVID-19 are dry cough, fever and tiredness [35]. Some sufferers may also have aches and pains, nasal congestion, runny nose, sore throat or diarrhea. These signs and symptoms are commonly slight and start gradually. As per clinical symptoms, the World Health Organization outlines the following Clinical Syndromes associated with Covid 19, mentioned in Table 2 [43].

Table 2 Clinical Syndromes associated with Covid 19

Mild Illness	Uncomplicated upper respiratory tract viral infection Non-specific symptoms such as fever, fatigue, cough (with or without sputum production), anorexia, malaise, muscle pain, sore throat, dyspnea, nasal congestion, or headache.
Pneumonia	Can show symptoms of pneumonia but no signs of severe pneumonia and no need for supplemental oxygen. Patients can be productive, with an accelerated sputum load however that is a much less common presentation in viral pneumonia.
Severe Pneumonia	Fever or suspected respiratory infection, High Respiratory Rate > 30 breaths/min; Severe Respiratory Distress; or SpO2 ≤ 93% on Room Air. While the analysis is made on medical grounds, chest imaging can also additionally perceive or exclude a few pulmonary complication.
Acute Respiratory Distress Syndrome (ARDS)	Severe difficulty in breathing. i.e., labored, rapid breathing. – Shortness of breath. Tachycardia , Cyanosis (blue skin, lips and nails), Think frothy sputum , Metabolic acidosis, Abnormal breath sounds, like crackles – PaCo2(Partial Pressure of carbon dioxide) with respiratory alkalosis Diagnostic Tools (Radiograph, CT Scan, or Lung Ultrasound): Bilateral Opacities, lobar or lung collapse, or nodules; Respiratory failure not fully explained by cardiac failure or fluid overload. ARDS is defined by the patient's oxygen in arterial blood (PaO2) to the fraction of the oxygen in the inspired air (FiO2). Mild ARDS: 200 mmHg < PaO2/FiO2a ≤ 300 mmHg Moderate ARDS: 100 mmHg < PaO2/FiO2 ≤ 200 mmHg Severe ARDS: PaO2/FiO2 ≤ 100 mmHg
Sepsis	Due to dysregulated host response to suspected or confirmed infection, it can result in Life-threatening organ dysfunction. Low Oxygen Saturation , Difficult or Fast Breathing, Fast Heart Rate, Reduced Urine Output, Altered Mental Status, Weak Pulse, Acidosis, Thrombocytopenia, Hyperbilirubinemia or High Lactate.
Septic Shock	Persisting hypotension despite volume resuscitation, requiring vasopressors to maintain MAP (Mean arterial pressure) ≥ 65 mmHg and serum lactate level > 2 mmol/L. Tachypnoea, Mottled or Cool Skin or Purpuric Rash; Increased Lactate.

Antibody tests have limited diagnostic use: if a person is tested early in the course of infection, when their immune response is still building up, the test might not detect antibodies [44]. Immunoassays have been developed for rapid detection of SARS-CoV-2 antigens or antibodies. Such lateral flow assays have been developed for detecting antigens such as the SARS-CoV-2 virus or for detecting antibodies (IgM and IgG) against COVID-19.Monoclonal antibodies specifically against SARS-CoV-2 have been ysed for several rapid antigen assays [45].

However, IgM responses are notoriously nonspecific, and given the weeks required to develop specific IgG responses, serology detection is not likely to play a role in active case management except to diagnose/confirm late COVID-19 cases or to determine the immunity of health care workers as the outbreak progresses [46].

The desired testing approach to confirm if the person is suffering from Covid 19 is the real-time reverse transcription-PCR (RT-PCR) test much like that developed for the prognosis of SARS-CoV. RT-PCR involves the reverse transcription of SARS-CoV-2 RNA into complementary DNA (cDNA) strands, followed by amplification of specific regions of the cDNA. It labels the viral RNA using matching pieces of sequences (primers), DNA binding enzymes and stock of DNA letters.

RNA isolated from upper and lower respiratory specimens is reverse transcribed to cDNA and subsequently amplified using Applied Biosystems instrument with software version [47] .

During the amplification process, the probe anneals to a specific target sequence located between the forward and reverse primers. During the extension phase of the PCR cycle, the 5' nuclease activity of Taq polymerase degrades the bound probe, causing the reporter dye to separate from the quencher dye, generating a fluorescent signal. Fluorescence intensity is monitored at each PCR cycle [48].

In general, examination of COVID-19 is ordinarily utilized polymerase chain reaction (PCR) test through the nasal swab. The initial, and preffered, technique for testing is the collection of upper respiratory samples by means of nasopharyngeal and oropharyngeal swabs [49, 50]. The utilization of bronchoscopy as an analytic strategy for COVID-19 isn't suggested as the vaporized aerosol that is created represents a considerable danger for the patients and medical care staff.

The affectability of testing with RT-PCR fluctuates with timing of testing comparative with the exposure. SARS-CoV-2 RNA has been withdrawn from upper and lower respiratory tract specimens, and the virus has been isolated in a cell culture of upper respiratory tract discharges and bronchoalveolar lavage. Lower respiratory tract containing bronchoalveolar lavage liquid, are more intutive than upper respiratory examples [51]. Wang et al, performed study where 1070 specimens were gathered from 205 patients with COVID-19 in China. It was noted that bronchoalveolarlavage liquid specimens had the most noteworthy positive rates of SARS-CoV-2, with (93%), accompanied by sputum (72%), nasal swabs (63%), and pharyngeal swabs (32%) [48, 52]. Saliva maybe an alternative specimen source that requires less protective equipment and less swabs, however requires further approval.

Although, presence of SARS-CoV-2 RNA in the lower and upper respiratory tract and in extrapulmonary samples stays uncleared. Viable SARS-CoV 2 has been segregated from respiratory,urine, blood, and feces tests [53]. The particularity of the RT-PCR test is by all accounts high, in spite of the fact that there might be false-positive outcomes because of swab contamination, particularly in asymptomatic patients. The affectability rate isn't clear, yet is assessed to be around 66–80%. Factors adding to false negative test outcomes incorporate time from exposure, specimen source and specimen collection technique [54,55]. A single negative test doesn't prohibit SARS-CoV-2 disease, particularly in highly exposed patients, if the test is performed towards the starting of infection or has been done by nasopharyngeal swab. For this situation, it could be advisable to repeat the test or gather a deeper respiratory tract sample, like BAL. Apart from RTPCR Test, laboratory, clinical, and imaging findings could also be utilized to make a possible investigation against suffering from Covid 19.

It has been seen that health research center investigated confirmation among hospitalized patients with pneumonia included leucopenia (9–25%) or leucocytosis (24–30%), gentle thrombocytopenia (present in roughly 30% of patients) and raised D-dimer esteems (present in 43%-60% of patients) lymphopenia (63%) and raised degrees of alanine aminotransferase and aspartate aminotransferase (37%) [56, 57]. Expanded aggravation records, for the most part including diminished procalcitonin and expanded C-reactive protein (CRP) levels, are related with clinical seriousness, are common. Complete blood check – lymphopenia, eosinopenia, and neutrophil/lymphocyte proportion ≥ 3.13 are identified with more noteworthy seriousness and more awful anticipation. Immunological markers that may likewise address hazard factors for more noteworthy seriousness or potentially more terrible anticipation are: diminished upsides of CD4 + T and CD8+ lymphocytes, NK cells and expanded upsides of IL6, IL-8, IL-10, IFN-γ, TNF-IL-2R, TNF-α, GM-CSF, and IL-1 β [58, 59].

Thrombocytopenia is identified with a higher danger of myocardial harm and a more regrettable prognosis. Xu Panyang, 2020 examined the mechanim of thrombocytopenia in Covid 19 Patients [60]. Viral contamination and inflammation affects lung. In their examination, they tracked down that Direct contamination of bone marrow cells by the infection and inhibition of platelet synthesis. Following infection disease, cytokine storm destroys bone marrow progenitor cells and prompts the abatement of platelet production. Lung injury indirectly results in reduction of platelet synthesis. Platelet agglomeration in the lungs, results in microthrombi and platelet consumption as a potential mechanism of thrombocytopenia in COVID-19 [60, 61].

According to examine led, by Ruan et al. it was noticed expanded troponin levels were accounted for in 7% of patients who therefore died because of fulminant myocarditi. Troponin seems, by all accounts, to be a strong prognostic indicator of mortality. At long last, it was noticed that ferritin and D-dimer levels were typically high in hospitalized patients [62].

3.1 Radiological imaging

Typical chest computed tomographic (chest CT) imaging abnormalities for individuals with COVID-19 are diffuse, ground-glass opacities (Figure 2). Patients referred for CT should undergo non–contrast material–enhanced chest CT unless CT pulmonary angiography is required to detect pulmonary embolism (PE) [63]. Patients of all ages can become infected with SARS-CoV-2 and may need to undergo chest imaging [64]. Low-radiation-dose chest CT performed on the basis of these principles has been shown to be feasible for imaging patients with COVID-19, with noninferior diagnostic quality and a radiation dose reduction of around 90% compared with those of a standard CT acquisition. Therefore, performing low-radiation-dose CT instead of full-radiation-dose CT as standard for the evaluation of the lung parenchyma in COVID-19 can be defended on the basis of the ALARA (As Low As Reasonably Achievable) [65].

The CT of ICU Patients, has significantly depicted ground glass opacities on the lower and peripheral lobes, bilateral multiple lobular and subsegmental areas of consolidation. Involvement of lung segments could predict the severity of disease. These opacities have ill-clarified margins, smooth or irregular interlobular, air bronchograms, or thickening of septal ,and adjacent pleura, with the progression of disease [34,66]. The swift evolution of abnormalities can be seen within two weeks, from onset of infection. Other than, CT imaging conventional . Plain chest X-rays are less sensitive than computed tomography, but may evidence sparse bilateral consolidations accompanied by ground glass opacities, peripheral/subpleural images, predominantly in the lower lobes [67-68]. Chest X ray could also be used, but its sensitivity rate is low (around 59%).

Pulmonary ultrasonography has mild ensitivity for typical findings are B-lines, consolidations and pleural thickening. The advantages of this method are its lower cost, absence of radiation exposure, and the fact that it does not require sedation or transportation of unstable patient. Ultrasound is yet another way as a diagnostic tool in a very limited number of cases [69] . Islam N et al., evaluated the diagnostic accuracy of thoracic imaging using computed tomography (CT), X-ray and ultrasound in people with suspected COVID-19. In light of the discoveries demonstrate that chest CT is sensitive and moderately explicit for the finding of COVID-19. Ultrasound is sensitive however not for the finding of COVID-19. Ultrasound may assume a part in observing the monitoring of sickness through the location of interstitial lung disease features, for example, B lines and subpleural consolidations and pleural thickening [70].

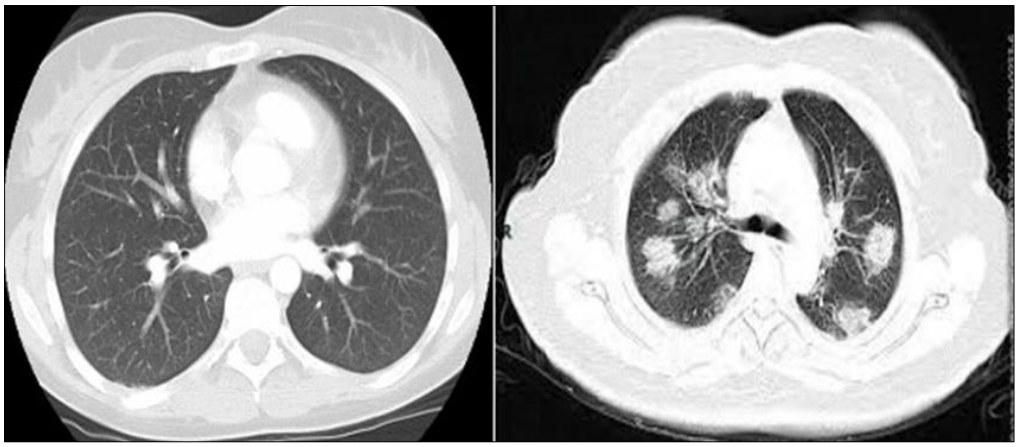

Figure 2 Left side shows CT image of healthy lungs in 40 year woman and Rightside image shows chest CT image of COVID infected person interpretating subpleural curvilinear opacity (arrow) and an area of ground-glass opacity with superimposed septal thickening (arrows) in a 50 year old woman

However, on these imaging features, several retrospective studies have shown that CT scans have a higher sensitivity (86–98%) and improved false negative rates compared to RT-PCR and other imaging technique However, CT appears to be extra unique in detecting apical intraparenchymal lesions [71].

The disadvantage of CT for all sufferers seems to be unreasonable in terms of cost, radiation exposure and time. As per literature, CT scanning ought to be reserved for patients with an undefined clinical picture, in addition to differential diagnosis [72].

3.2 Treatment

Researchers all throughout the world have created medicines and antibodies for the new Covid disease known as COVID-19. A few organizations are dealing with antiviral medications, some of which are now being used against

different diseases, to treat individuals who have COVID-19 [73]. Vaccines extraordinarily decrease risk of infection via preparing the immune system to perceive and fight pathogen, for example, bacteria or viruses. Most exploration on COVID-19 immunizations includes producing reactions to all or part of the spike protein that is remarkable to the infection that causes COVID-19. At the point when an individual gets the immunization, it will trigger a resistant reaction [74].

In the event that the individual is infected by the infection later on, the immune system recognizes the virus and, because it is already prepared to attack the virus, shields the person from COVID-19 [75]. Aside from this, various nations dealing with this crisis, many researchers have considered the impacts of diverse medications on patients with COVID-19, belonging to a group of antivirals, resistant modulators,anti-toxins, and anticoagulants. Some clinical center focuses plasma treatment alongside these drugs.The following classes of medications are being assessed or created for the administration of COVID-19: antivirals (eg, remdesivir, favipiravir), anti inflammatory (dexamethasone, statins), antibodies (eg, healing plasma, hyperimmune immunoglobulins), targeted immunomodulatory treatments (eg, tocilizumab, sarilumab,anakinra, ruxolitinib), antifibrotics (eg, tyrosine kinase inhibitors) andanticoagulants (eg, heparin) [76-78].

Almost certainly, different treatment modalities may have various efficacies at various stages of ailment and in the various manifestations of disease. Inhibition of viral would be relied upon to be best from the beginning of infection, while, in hospitalized patients, immunomodulatory specialists might be valuable to prevent disease, and anticoagulant may be helpful to prevent thromboembolic complications [79]. Most antiviral medications going through clinical testing in patients with Coronavirus are repurposed antiviral specialists initially created against Hepatitis, flu, HIV, Ebola, or SARS/MERS [80].

Convalescent plasma has also been used as a last resort to improve the survival rate of patients with various viral infections, such as SARS, H5N1 avian influenza, pandemic 2009 influenza A H1N1 (H1N1 pdm09), and severe Ebola virus infection. One feasible explanation of the efficacy of convalescent plasma therapy is that the immunoglobulin antibodies withinside the plasma of patients getting better from viral infection would possibly suppress viremia [81,82]. The U.S. Food and Drug Administration (FDA) has given emergency authorization for convalescent plasma remedy with high antibody ranges to treat COVID-19. It can be used for a few hospitalized humans ill with COVID-19 who're both early of their contamination or who've weakened immune systems [83].

Blood donated via way of means of humans who've recovered from COVID-19 has antibodies to the virus that causes it. The donated blood is processed to eliminate blood cells, leaving behind liquid (plasma) and antibodies [84]. These may be given to humans with COVID-19 to reinforce their capacity to combat the virus.Following plasma transfusions, enhancements in medical condition were observed, along with normalization of body temperature, lower in Sequential Organ Failure Assessment score, rise in PaO2/FiO2, resolution of ARDS , a achievement of weaning from mechanical ventilation , and decline in viral loads [85-86].

The ongoing surge in Covid-19 instances has seen a massive upward thrust in the demand for supplemental oxygen. Shortness of breath occurs due to the way Covid-19 affects the patient's respiratory system [87]. The lungs allow the body to absorb oxygen from the air and expel carbon dioxide. When a person inhales, the tiny air sacs withinside the lungs -alveoli- amplify to seize this oxygen, that is then transferred to blood vessels and transported via the rest of the body [88-89]. Respiratory epithelial cells line the respiratory tract. Their primary characteristic is to shield the airway tract from pathogens and infections, and additionally facilitate fueloline exchange. The SARS-CoV-2 can infect those epithelial cells.To combat such infection, the immune system of the body releases cells that cause inflammation [90]. When this inflammatory immune reaction continues, it impedes the normal transfer of oxygen withinside the lungs. Simultaneously, fluids too build up. Both those factors blended make it hard to breathe. Low degrees of oxygen prompted by Covid-19 are inflammatory markers, which include increased white blood cell counts and neutrophil counts [91].

Oxygen treatment in patients with serious COVID-19 saves lives. The accessibility of supplemental oxygen treatment should be the primary focus for management of patients suffering from extreme COVID-19 [92]. Delivery of oxygen in COVID-19 patients with extreme hypoxemia can be increased by utilizing a non-rebreathing mask and inclined positioning. Patients with fatigue and in danger of exhaustion as a result of respiratory depletion do require invasive ventilation [93]. In these patients, lung defensive ventilation is fundamental, for which restricting the PEEP level on the ventilator might be significant. This may decrease casualty fatal risk of over half in intrusively ventilated COVID-19 patients. Over 75% of patients hospitalized with COVID-19 require supplemental oxygen treatment. For patients who are inert to regular oxygen treatment, warmed high-stream nasal canula oxygen might be administered [94-95].For patients requiring obtrusive mechanical ventilation, lung-defensive ventilation with low flowing volumes (4-8 mL/kg,

anticipated body weight) and level pressing factor under 30 mg Hg is suggested. Also, inclined positioning, a higher positive end-expiratory pressure,and transient neuromuscular blockade with cisatracurium or other muscle relaxants may work with oxygenation [96].

Physiotherapy could have a strong function in providing exercise, mobilization and rehabilitation interventions to survivors of critical infection myopathies related to COVID-19 so that it will enable a purposeful return to home [97]. It may be beneficial in the respiratory treatment and physical rehabilitation of patients, not able to clear airway sections independently, or may also be effective for high risk individuals with existing comorbidities that may be associated with hypersecretion or ineffective cough (e.g. neuromuscular disease, respiratory disease, cystic fibrosis etc) [98]. A review of this current treatment has been mentioned in Table 3.

A few patients with COVID 19-related respiratory failure have high lung consent, they are still prone to profit by lung-defensive ventilation [99]. Associates of patients with ARDS have shown comparable heterogeneity in lung consistency, and even patients with more noteworthy consistency have shown advantage from lower tidal volume strategies [100]. The limit for intubation in COVID-19–related respiratory failure is questionable, in light of the fact that numerous patients have typical work of breathing yet serious hypoxemia. In any case, hypoxemia without respiratory trouble is very much endured, and patients may do well without mechanical ventilation [101].

Table 3 Current undergoing treatments for Covid 19

Drugs	Antivirals RNA-dependent RNA polymerase inhibitors	Remdesivir (RDV)	It causes to ambiguous the RNA polymerase, and eventually, prevents its replication. RDV was developed in 2017 to treat Ebola, and has a wide spectrum of antivirus activities [102,103].
		Favipiravir (FPV)	FPV directly inhibits influenza virus transcription, and the drug inhibits the virion M2 ion channel. It is able to inhibit different strains of influenza virus resistance to drugs such as amantadine, zanamivir, and rimantadine [104, 105]
		Ribavirin	It is a synthetic guanosine analogue antiviral drug that has been used to treat Hepatitis C virus, respiratory syncytial virus (RSV), and some viral hemorrhagic fevers. It interferes with duplication of the viral genetic material [106, 107].
	Protease inhibitors	Chloroquine, Hydroxy chloroquine (CQ/ HCQ)	They shown to increase endosomal pH, which prevents virus/cell fusion. Also, interferes with the glycosylation of cellular receptors of SARS-CoV. Active against malaria as well as autoimmune diseases (such as rheumatoid arthritis [RA], lupus erythematosus) [108,109]
		Lopinavir/ritonavir (LPV-RTV)	They inhibits the protease enzyme by forming an inhibitor-enzyme complex thereby preventing cleavage of the gag-pol polyproteins. This results in immature, noninfectious viral particles. The drug has higher activity against HIV-1 [110,111].
		azithromycin	Consequently, the regimen of hydroxychloroquine in combination with azithromycin is probably a promising opportunity to remdesivir in the remedy of patients with SARS-CoV-2 infection in the future. It is used in many bacterial infections [112-113].
		Teicoplanin and other glycopeptides	Teicoplanin specifically inhibits the activities of host cell's cathepsin L and cathepsin B, which are responsible for cleaving the viral glycoprotein allowing exposure of the receptor-binding domain

			of its core genome and subsequent release into the cytoplasm of host cells. Thus, teicoplanin blocks virus entry in the late endosomal pathway. The drug has been used in Ebola Virus infections [114,115].
	Immune modulators	Corticosteroids (CSs)	CSs has antiimflammatory properties bind to their receptors in the cytoplasm of target cells and exert their impacts. These receptors are broadly found in the lungs, and hence, CSs are generally utilized in the control of inflammatory lung diseases.It has been accounted for that ACE2 expression diminishes with the utilization of inhalers corticosteroid [116, 117].
		Baricitinib	The drug can block the infection process and does not appear to allow viruses to spread the infection to the lungs by preventing clathrin-mediated endocytosis. It is a selective inhibitor of Janus kinase (JAK) and disrupts activation of proinflammatory mediators. The drug is effective in combination with other direct-acting drugs, including RDV and LPV-RTV, which reduces viral infections and inflammatory responses [118,119]
		Tocilizumab (TCZ)	TCZ is a human monoclonal antibody and an IL-6 inhibitor. TCZ performs this function through inhibiting the binding of this cytokine to its receptors, thereby inhibiting the proinflammatory activity of IL-6. It became proven that TCZ reduced inflammatory markers and the patients' need for ventilation suffering from Covid 19 [120,121].
	Anticoagulants	Heparin	It has been discovered strange coagulation and presence of dispersed intra vascular coagulation (DIC) were normal in death with novel Covid pneumonia. Infections disrupt the capacity of endothelial cells, bringing about significant degrees of thrombin production, inactivation of fibrinolysis, and conditions causing undeniable level coagulation. Therefore, use of heparin showed thrombosis prevention or thromboprophylaxis in COVID-19 patients, including improved survival, without serious complications such as bleeding [122,123].
		Nafamostat mesylate	The drug is known as an existing treatment used for DIC and was able to effectively inhibit the S protein-mediated cell fusion of MERS-CoV.Also, drug improved clinical conditions in Covid 19 patients taking supplemental oxygen therapy [124,125].
Herbal medications		*Echinacea purpurea*	Shows, immunomodulatory impact and act particularly as an immunostimulator. Increased launch of numerous cytokines, along with IL-1, IL-10, and TNF-α through macrophages. Macrophages may also have a minimum quantity or no ACE2 receptors on their surface. They are taken into consideration to have consistent capability for the phagocytosis of SARS-CoV-2 and

			release TNF-α with different proinflammatory cytokines via the humoral immune response [126, 127]
		Xanthorrhizol	Has anti-inflammatory and antioxidant effect. Act as an immunosuppressant that may be used as a treatment for COVID-19 because of its ability to inhibit proinflammatory cytokines [128,129].
		Cinchona sp	The bark of the Cinchona trees produces quinine alkaloids, which were also an effective treatment of malaria for more than several centuries. It has immunostimulant and immunosuppressant activities against viral infections. When quinine effectively intensifies the production of the well-known cytokine IFN-α, it functions as an immunostimulator to inhibit viruses [130,131].
Convalescent plasma	Transfer of antibody from people who've recovered from Covid infection to help others recover [132].		
Physiotherapy	Use of Positive Pressure Breathing Devices (e.g. IPPB), Mechanical Insufflation-Exsufflation (Cough Assist) Devices, Intra/Extra Pulmonary High Frequency Oscillation Devices (e.g. the Vest / MetaNeb / Percussionaire etc.) Manual Techniques (e.g. Percussion/Manual Assisted Cough) that may lead to coughing and expectoration of sputum Any Mobilisation or Therapy that may result in Coughing and Expectoration of Mucus Positioning, Suctioning, Nebuliation and Humidificationcan be used as non invasive treatment [133, 134].		

3.3 Current scenario

Virus are continually changing, and this incorporates SARS-CoV-2. These genetic varieties occur over the time and can prompt the rise of new variations that may have different characteristics. In March, 2021 another "double mutant" variation of the Covid has been identified from tests gathered in India [135]. Authorities checking if the variation, where two changes meet up in a similar infection, might be more irresistible or less influenced by immunizations [136]. The Indian SARS-CoV-2 Consortium on Genomics (INSACOG), a gathering of 10 public labs under India's wellbeing service, done genomic sequencing on the most recent examples. Genomic sequencing is a testing process to map the entire genetic code of an organism - in this case, the virion [135,137].

The genetic code of the virus works like its instruction manual. Mutation in viruses are basic yet the majority of them are insignificant and don't cause any change in its ability to transmit or cause serious infection [138]. However, some mutation, similar to the ones in the UK or South Africa variation genealogies, can make the infection more irresistible and sometimes much deadlier. The introduction of Double mutant in key areas of the virus spike protein may build these risks and permit the virus to escape from the immune system [139].

The spike protein is the part of the virus that it uses to enter human cells. The double mutant strain was accordingly named B.1.617, with the L452R and E484Q changes meeting up. The E484Q change has qualities of a formerly distinguished variation – the E484K – which was found in the quick spreading Brazilian and South African variations, making it profoundly contagious. The L452R mutation, then again, assists the virus evades the body’s immune response [135,140].

According to the reports from WHO, the huge number of infections in India could also increases chances of new and more hazardous variants emerging and expanded rises in cases also counts not taking necessary precautionary measures and huge social mixing and large gatherings too. Because of new variations, India tallies 3.46 crore complete cases right now, and 4.73 lakh passings. An expanded in Covid patients has been found in year ,2021 in contrast with 2020 [141].

Besides Covid, the incidence of and death toll from black fungus or mucormycosis were steadily on the rise in India. This is a relatively rare but potentially fatal condition [143]. Medical specialists were calling it a ‘pandemic within Covid-19

pandemic'. Some early signs of the condition include "sinus pain or nasal blockage on one side of the face, one-sided headache, swelling or numbness, toothache and loosening of teeth. The disease was being majorly seen in people who have recovered from Covid, or are recovering. Without treatment, it can lead to lethal bloodstream infection [140]. The medical care team are currently using Liposomal Amphotericin B for treating black fungus infections [144].

On 26 November 2021, WHO designated the variant B.1.1.529 a variant of concern, named Omicron, on the advice of WHO's Technical Advisory Group on Virus Evolution (TAG-VE). Preliminary evidence suggests there may be an increased risk of reinfection with Omicron (ie, people who have previously had COVID-19 could become reinfected more easily with Omicron), as compared to other variants of concern, but currently information is limited.

3.4 Current status

India started administration of COVID-19 vaccines on 16 January 2021. Two vaccines got approval for emergency use in India at the beginning of the program, including Covishield (an adaptation of the Oxford–AstraZeneca antibody made by the Serum Institute of India), and Covaxin (created by Bharat Biotech) [145]. In April 2021, Sputnik V was supported as a third antibody, with deployment expected to start by late May 2021.Russia's Sputnik V has been considered to be protected, and works in a way similar to Oxford-AstraZeneca jab which is being made in India as Covishield [146]. Sputnik V gives around 92% security against Covid-19, as per late stage trial outcomes, published in The Lancet [147]. India has so far given in excess of 100 million doses of two approved vaccines - Covishield and Covaxin. With the complete case count of more than 13.5 million cases, India is presently just behind the United States which has detailed in excess of 31 million cases. With 13.4 million cases, Brazil is currently at number three [148,149]. India administered more than 180 million doses in August as it continues to ramp up its vaccination drive to stave off a third wave of Covid. This was more doses than all the Group of Seven (G7) countries - Canada, the UK, the US, Italy, Germany, France and Japan - put together, according to an official statement. The WHO Country Office for India (WCO India) has been working closely with the Government of India (GoI) to step-up preparedness and response measures for COVID-19, including surveillance and contact tracing, laboratory testing, risk communications and community engagement, hospital preparedness, infection prevention and control, and implementation of containment plan at all three levels of the health system – national, state and district. The government aims to vaccinate all eligible Indians by the end of 2021.It has so far given more than 700 million doses of three approved jabs. More than half of India's eligible population - some 126 crore - have received at least one dose of a Covid vaccine, official data says. [150]. At current vaccinate rate, 41% of population will be vaccinated by 2021. Yet, specialists say that the speed of immunization has been moderate and except if the drive is increased, the objective could be missed. As Omicron has been designated a Variant of Concern, there are several actions WHO recommends countries to undertake, including enhancing surveillance and sequencing of cases; sharing genome sequences on publicly available databases, such as GISAID; reporting initial cases or clusters to WHO; performing field investigations and laboratory assessments to better understand if Omicron has different transmission or disease characteristics, or impacts effectiveness of vaccines, therapeutics, diagnostics or public health and social measures

The most effective steps individuals can take to reduce the spread of the COVID-19 virus is to keep a physical distance of at least 1 metre from others; wear a well-fitting mask; open windows to improve ventilation; avoid poorly ventilated or crowded spaces; keep hands clean; cough or sneeze into a bent elbow or tissue; and get vaccinated when it's their turn**.**

4. Conclusion

The world is struggling from the Covid 19, till now. Extensive measures could be taken to reduce person to person transmission. Special concerns and endeavors should be implemented to or decrease transmission of virus in susceptible populations including kids, health care workers, and geriatric. Different nations including India have implemented significant control measures including travel screenings to control additionally spread of the infection. Much development has been done inview of diagnosis and treatment of infected persons suffering from mild to severe Covid 19. Vaccines have developed and the drive plan to vaccinate people are still in progress. The mutant Covid strain is a word for concern as the transmission and infective rate is likely to rise in compare to previous strain. This can be controlled by maintain suitable distancing, avoid crowded public gatherings and to take appropriate measures updated by World Health Organization. The only hope is that we will overcome from this present situation and things will be fine in future.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare that they have no conflicts of interest.

Statement of informed consent

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