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A Review article on a Coronavirus Disease 2019 (COVID-19)

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ABSTRACT

Coronaviruses (CoVs) have become major challenges to global public health in the last two decades, including serious outbreaks like SARS in 2002, MERS in 2012, and the COVID-19 pandemic caused by SARS-CoV-2.[6] SARS-CoV-2 was first detected in Wuhan, China, in December 2019, and quickly became a worldwide health emergency, causing the World Health Organisation (WHO) to proclaim a pandemic on March 11, 2020.[3,25] This beta-coronavirus from the Coronaviridae family is very contagious, with clinical manifestations ranging from asymptomatic to severe respiratory distress, multi-organ failure, and death.[19] SARS-CoV-2's zoonotic origin and rapid human-to- human transmission have sparked global worry.[6] The present investigation talks about the epidemiology, pathophysiology, and clinical manifestations of COVID-19, with a focus on the virus's fast propagation, diagnostic problems, and the involvement of inflammatory responses such as cytokine storms in illness development.[31] Early diagnostic tools, including as RT-PCR and serology, were critical in detecting cases, but the dearth of effective therapies originally necessitated dependence on preventative measures such as lockdowns, quarantine, and mask regulations.[34,41] The pandemic has contributed to remarkable scientific progress, including the invention of mRNA vaccines and targeted therapeutics like monoclonal antibodies and antiviral medicines.[38,9] These advances have resulted in considerable reductions in global case counts and fatality rates.[25] However, obstacles persist, such as vaccination reluctance, unequal distribution, and the management of long-term consequences.[43] COVID-19 highlights the critical need for global collaboration, strong healthcare systems, and preparedness plans to combat future pandemics.[25] This assessment sheds light on the pandemic's effect and offers lessons for future pandemic management and response efforts.[41]

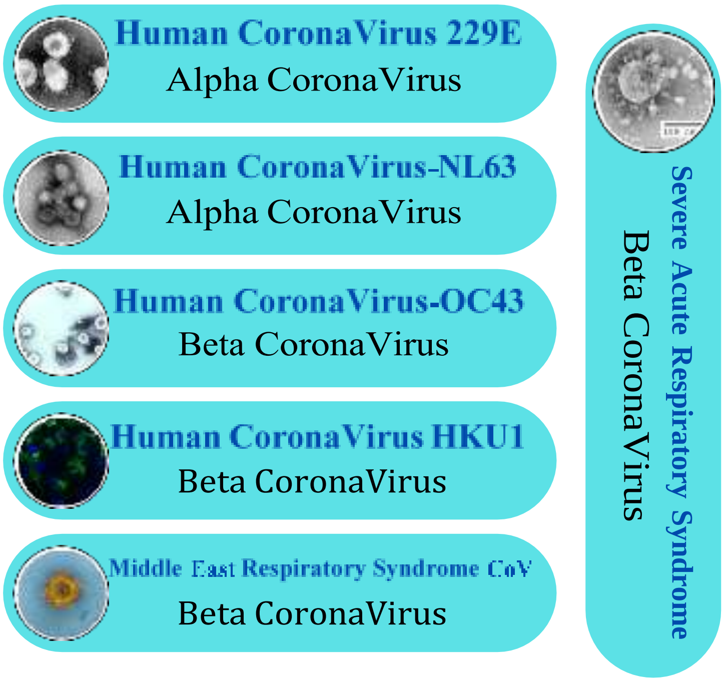
Keywords: COVID-19, SARS-CoV-2, Coronavirus, Pandemic, Vaccination, RT-PCR, Pathophysiology

Introduction:

Coronaviruses (CoVs) have been linked to major illness outbreaks in East Asia and the Middle East within the last 20 years. In 2002 and 2012, respectively, the Middle East respiratory disease (MERS) and severe acute respiratory disease (SARS) appeared.**[6]** A new coronavirus known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that causes coronavirus disease 2019 (COVID-19) surfaced in late 2019 and has since spread over numerous nations and territories, posing a threat to world health.**[3]**

Health professionals across the world are working to contain additional illness outbreaks

brought on by the new CoV, formerly known as 2019-nCoV, which was discovered for the first time on December 12, 2019, in Wuhan City, Hubei Province, China.[3] The World Health Organisation (WHO) declared on February 11, 2020, that COVID-19, which is caused by SARS-CoV-2, is the official designation for the current CoV-associated illness.[25] The Huanan South China Seafood Market in Wuhan was identified as the main patient cluster.[23] Members of the Coronaviridae (subfamily Coronavirinae) family, which includes CoVs, infect a wide variety of hosts and cause symptoms and illnesses that vary from the common cold to serious and ultimately lethal conditions like SARS, MERS, and, now, COVID-19.**[17]** While SARS-CoV-2 is a member of the same lineage of CoVs that cause SARS, it is genetically different from the other seven members of the CoV family that infect humans.**[16]** Before 2020, human CoV 229E (HCoV-229E), HCoV-NL63, HCoV-OC43, HCoV-HKU1, SARS-CoV, and MERS-CoV were the six CoVs known to infect humans.**[17]**



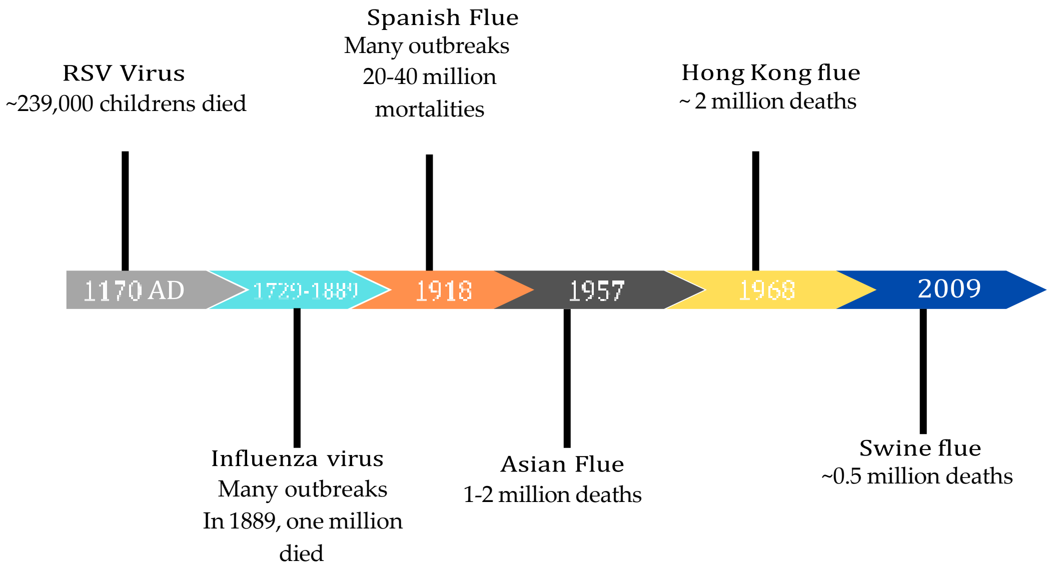
The public health of the world is being threatened by newly evolving CoVs.**[6]** The current COVID-19 pandemic is the third human CoV outbreak in the previous 20 years.**[3]** Fan et al.'s prediction of possible CoV epidemics in China that resemble SARS or MERS after virus transmission from bats is not coincidental.**[6]** After first appearing in China, COVID-19 quickly expanded throughout the nation before reaching other nations.**[3]** On January 31, 2020, the WHO declared a global health emergency due to the severity of the epidemic and its potential for worldwide transmission.**[25]** On March 11, 2020, they designated it a pandemic crisis. We are now unable to treat COVID-19 successfully since there are currently no licensed vaccinations or particular antiviral medications.**[7]** Therefore most nations are making efforts to prevent the further spreading of this potentially deadly virus by implementing preventive measures and control strategies.**[25]**

Now, we will learn about the history of Coronavirus.

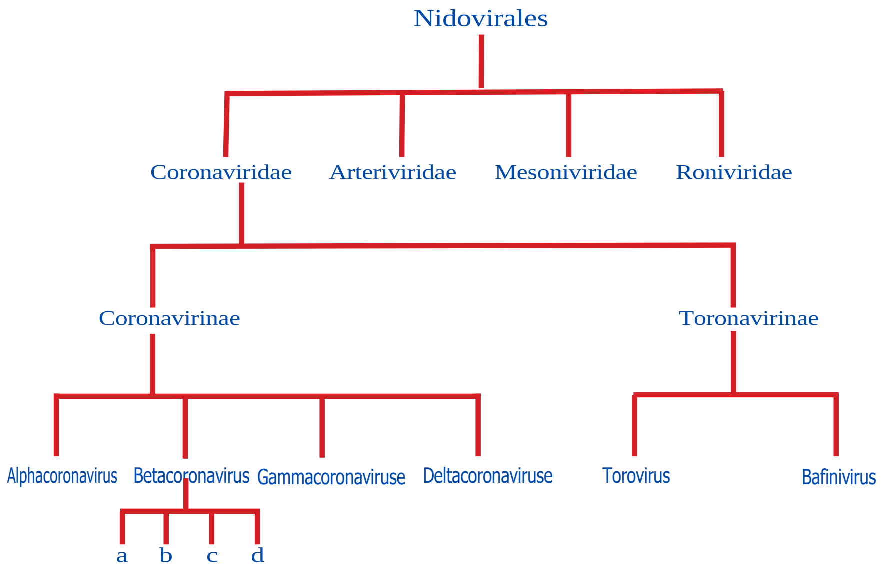
History of Coronavirus :

Acute respiratory tract infections (ARTIs) are among the most common illnesses, affecting people of all ages and genders.**[19]** These infections are caused by a variety of microorganisms, including bacteria and viruses like Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis, as well as viruses such as Influenza A and B, respiratory syncytial virus (RSV), parainfluenza, adenovirus, and coronaviruses.**[19]** However, when it comes to contagiousness and medical urgency, RSV, Influenza A or B, and coronaviruses are typically the most concerning, as they have been responsible for several large-scale epidemics and pandemics.**[21]**

In particular, coronaviruses and influenza viruses are known to cause more severe symptoms, often leading to significant outbreaks that especially affect older adults.**[19]** The term "pandemic" comes from Greek, meaning "all the people," and refers to the spread of a disease across large regions or globally.**[41]** In contrast, a localized outbreak is called an epidemic, which is often linked to seasonal virus strains.**[19]** Pandemics can arise when new virus strains emerge, enabling human-to-human transmission before people have had time to build immunity.**[3]** These pandemics can occur due to different genetic mechanisms, have unpredictable death rates across all age groups, and vary greatly in how and when they arise and resurface.**[19]** Pandemics caused by some of the viruses associated with respiratory tract are shown below



This was the history of respiratory viruses outbreaks, Now let's move forward to the our main topic that is Coronavirus.**[19]** Coronavirus has been known to cause human infection since 1960s, but it has only been in the last 20 years that its potential to cause fatal epidemics has come to light. COVID-19 is the third significant coronavirus-related respiratory disease outbreak in 20 years,**[6]** COVID-19, has seriously upset the global socioeconomic equilibrium.**[31]** SARS-CoV-2 (Severe Accute Respiratory Syndrome Coronavirus-2) is the strain of the Coronavorus that is causes respiratory illness that is responsible for the COVID-19 pandemic.**[3]** SARS-CoV-2 belongs to the family Coronaviridae, which belongs to the order Nidovirales. The family has two subfamilies, Coronavirinae and Torovirinae.**[16]** Alphacoronavirus, Betacoronavirus, Gammacoronavirus, and Deltacoronavirus these are the four genera into which coronavirinae are divided. Earlier, the genus Betacoronavirus was subdivided into lineages A, B, C, and D.**[17]** Now, these lineages have been classified as subgenera of Betacoronavirus—as Embecovirus (lineage A), Sarbecovirus (lineage B), Merbecovirus (lineage C), and Nobecovirus (lineage D) SARS-CoV-2 belongs to the genus Betacoronavirus and subgenus Sarbecovirus.**[16]**



Coronaviruses are spherical, encapsulated viruses with a diameter of 80–120 nm. They can occasionally be pleiomorphic. The club-shaped spike projections that emerge from the virus's surface are what define the virus. It is called a coronavirus because of these spikes, which give it a characteristic look like a solar corona. Although coronaviruses are sensitive to heat and UV light, they may be kept for many years at a temperature of -80 °C. However, researchers frequently inactivate these viruses by heating them to 56 °C for 30 minutes. Coronaviruses can also be made inactive by peracetic acid, disinfectants which contain chlorine, and 75% ethanol.**[17]**

Although the previous outbreaks of Coronaviruses didn't affect the humanity much, but it also has affected on people's and Researcher's mind as deadly as SARS-CoV-2.

SARS (Severe Acute Respiratory Syndrome) is a previously unidentified animal CoV that first appeared in southern China's wet markets and then evolved within the human host to allow for human-to-human transmission.**[6]** There were 8,098 confirmed cases and 774 deaths in total (9.6%) from the SARS outbreak that was reported in 2002–2003. The Asia-Pacific area was particularly impacted by the pandemic, specifically mainland China.**[3]** The epidemiological resemblance of SARS-CoV-2 (COVID-19) to influenza viruses raises serious concerns about this epidemic, despite the fact that its case fatality rate (CFR) is lower than that of SARS-CoV**[19]**. A pandemic might ensue from this failure of the public health system.**[31]**

Now let's head towards the epidemiology of Coronavirus

Epidemiology of Coronavirus :

Due to poor adaptation for human maintenance of SARS-CoV, MERS-CoV, and SARS-CoV- 2, they are anticipated to propagate primarily through other zoonotic reservoirs, with sporadic outbreaks in the vulnerable human population, maybe through an intermediary host animal. In particular, the new coronavirus has a very high rate of human-to-human transmission, resulting in a wide range of clinical symptoms in infected patients. For example, within a month of the disease's onset, Guan et al. conducted a detailed examination of the clinical features of afflicted patients from 552 hospitals throughout 30 provinces in China. Approximately 48% of the 1099 patients with laboratory-confirmed COVID-19 cases were men. Because there were so many different symptoms, it was first challenging to diagnose the sickness. Fever was present in 43.8% of the patients who were evaluated at the time of presentation; however, it rose to 88.7% following hospitalisation. After being admitted to the hospital, approximately 15.7% of the patients experienced severe symptoms. When compared to SARS-CoV or MERS-CoV, SARS- CoV-2 seems to have a lower mortality rate, despite the enormous number of deaths linked to COVID-19. Due to the disease's fast spread, government agencies and public health officials have implemented previously unheard-of measures, including travel bans, widespread curfews, the isolation and quarantine of affected people, etc.

Since the December COVID-19 outbreak in Wuhan, China, the virus has quickly moved to other countries, and the increasing number of cases indicates that the disease is still spreading.**[3]** A seafood market in the Wuhan province was first implicated in a number of COVID-19-related acute pneumonia cases (>50 persons) that were recorded in China.**[23]** Since then, there have been around ten million infected people, yet this figure may still be underestimated because asymptomatic individuals and untraced exposures are quite likely to occur.**[21]** The causal agent has been identified as a unique kind of coronavirus based on sequence-based analysis of patient isolates.**[4]** Additionally, the accurate detection of the viral infection has been greatly aided by sequencing technology and other methods.**[34]** Originally, SARS-CoV-2 was thought to infect people who had gone to the fish market or eaten food made with the infected animals.**[23]** Many people who had no prior history of visiting the seafood market also tested positive for COVID- 19, according to subsequent research and contact tracing of COVID-19-positive patients.**[24]**

These findings have raised the prospect of the virus spreading from person to person, which has now been documented in more than 200 nations worldwide.**[25]**

An epidemiological examination of patients in a family cluster, where some family members travelled to Wuhan but one did not, indicated the potential for human-to-human transmission of SARS-CoV-2.**[23]** Liu et al. documented in a different investigation that SARS-CoV-2 infection has spread to an epidemic level in Shenzhen, China. According to this extensive investigation, the primary causes of SARS-CoV-2's urban expansion may be intra-family and communal transmission.**[24]** SARS-CoV-2 is mostly spread from person to person when an infected person is nearby and they are exposed to respiratory droplets, aerosols, cough, or sneeze. These aerosols can reach lungs via inhalation through the nasal passage.**[25]** Droplets of different sizes are how SARS-CoV-2 is spread, just as previous respiratory illnesses like SARS- CoV and MERS-CoV. Generally, respiratory droplets are defined as droplets with a particle diameter greater than 5 to 10 μm, whereas nuclei are defined as droplets with a diameter smaller than 5 μm. Airborne transmission is the term used to describe the spread of illnesses by virus- containing nucleus droplets that remained after big droplets evaporated. These airborne droplets may spread from person to person across a metre in distance and stay in the atmosphere for a very long period. On the other hand, SARS-CoV-2, is mostly spread via contact and respiratory droplets. In fact, in an extensive analysis of more than 75,000 people with COVID in china, indication of airborne transmission was not reported.**[25]**

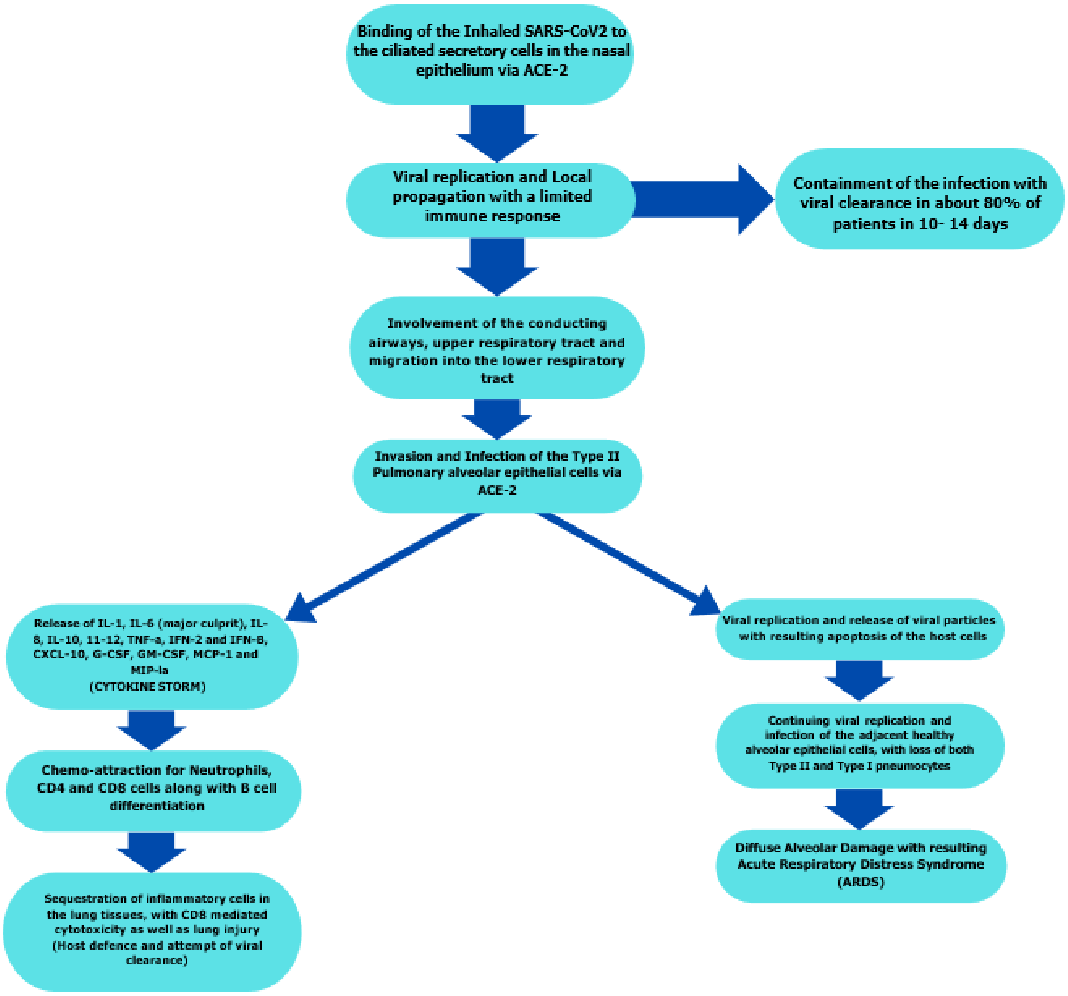
When two people are within one meter of one another and the other person has respiratory symptoms like coughing or sneezing, droplet transmission of SARS-CoV-2 occurs.**[27]** The virus may be spread by the infected person's conjunctiva (eyes) or mucosae (mouth and nose) through contaminated droplets. The virus is most frequently transmitted through mucosae, while it is comparatively less frequently transmitted through the conjunctiva. Furthermore, like the other coronaviruses, SARS-CoV-2 may perhaps cause nosocomial outbreaks by contaminating the environment for transmission. Investigations on the kind and degree of environmental contamination are still necessary, though. Ong et al. have recently investigated a variety of samples, including swabs, PPE samples, and surface samples of items used on sick people. Ong et al. have recently examined a variety of samples from patients housed in a well-protected isolation room (12 air exchanges per hour), including swabs, PPE samples, and surface samples of items used on infected persons. According to the study, respiratory droplets and faecal shedding from SARS-CoV-2-positive patients may provide a risk of disease transmission by contaminating the environment.**[28]**

As we have seen epidemiology of coronavirus as how it spread and transmitted let's head towards the Pathophysiology of COVID-19.

Pathophysiology of Coronavirus :

As we have seen today we know so much about the coronavirus but not too much about its pathogenesis. In simple terms, While the transmission and presentation of COVID-19 have been extensively studied, the pathogenesis remains mostly unknown.**[30]** Let's try to draw a flow chart regarding the pathogenesis of coronavirus.

Following flow chart presents an outline of illness pathogenesis.



SARS-CoV-2 spreads through respiratory aerosols and attaches to ACE-2 receptors, which are abundant in the nasal cells of adults. Once inside, the virus replicates in the nasal lining and begins infecting ciliated cells in the airways.**[30]** This process takes a few days and triggers only a mild immune response. However, even at this early stage with low levels of the virus, people are highly contagious, and the infection can be detected using nasal swabs.**[31]**

Clinical manifestations:

The symptoms of infections, including those caused by COVID-19, often overlap and may present as fatigue, muscle pain, sneezing, sore throat, dry cough, high fever, and respiratory issues.**[22]** In more severe cases, complications such as pneumonia, acute respiratory distress syndrome, kidney failure, and even death can occur.**[31]** Older adults, children, and individuals with preexisting health conditions—such as lung or heart diseases, diabetes, and cancer—are particularly at higher risk of severe outcomes from COVID-19.**[31]** However, it is crucial to note that the presence of these symptoms does not definitively indicate a COVID-19 infection, as similar manifestations are observed in other viral illnesses. Distinguishing features, such as shortness of breath and gastrointestinal symptoms like diarrhea, alongside recent exposure to a confirmed COVID-19 case or travel to areas with known outbreaks, may increase the likelihood of the disease.**[22]** In such instances, diagnostic testing for COVID-19 is essential to confirm the infection.

Pathophysiologically, COVID-19 is characterized by elevated levels of chemokines, cytokines, leukocytes, and pro-inflammatory markers such as C-reactive protein (CRP). These immune responses contribute to the systemic inflammation observed in infected patients.**[30]** Recovery from the disease varies significantly among individuals, with some recovering quickly, while others, especially older adults or those with underlying health conditions, may take longer.**[31]**

The World Health Organization (WHO) has classified the COVID-19 virus as a beta- coronavirus (β-CoV) belonging to the 2B group.**[25]** Genomic analyses reveal that the virus shares approximately 80% similarity with severe acute respiratory syndrome coronavirus (SARS-CoV) and 50% similarity with the Middle East respiratory syndrome coronavirus (MERS-CoV).**[19]** Both SARS-CoV and MERS-CoV are known to have originated in bats, a trait shared by COVID-19, underscoring the zoonotic nature of these pathogens.**[6]**

The understanding of COVID-19's clinical, pathological, and genetic characteristics is essential for developing effective diagnostic, therapeutic, and preventive strategies.**[19]** Despite the challenges posed by the disease, significant progress has been made in identifying its transmission dynamics, risk factors, and molecular mechanisms, which will inform future responses to similar pandemics.**[31]**

Diagnosis:

Molecular test (RT-PCR)

Molecular testing (RT-PCR). Upper respiratory tract samples are taken using nasopharyngeal and oropharyngeal swabs, whereas lower respiratory tract samples are collected using expectorated sputum and bronchoalveolar lavage (only for mechanically ventilated patients).**[34]** The samples are refrigerated at 4°C before being delivered to the laboratory for amplification of the viral genetic material via a reverse-transcription method.**[32]** This entails creating a double-stranded DNA molecule from the current viral RNA using either reverse transcription PCR (RT-PCR) or real-time RT-PCR. Finally, the amplified genetic material is analysed to identify conserved sections of the SARS-CoV-2 genetic code. The test should be repeated for verification in cases of a positive result and to confirm viral clearance in COVID-19 positive patients. The specificity of these tests is low; roughly 53.3% of COVID-19-confirmed patients had positive oropharyngeal swabs, and approximately 71% of patients tested positive for RT-PCR using sputum samples. RT-PCR findings often reveal positive within 2-8 days.**[35]**

Serology

Till date, no effective antibody test has been developed. A centers for disease control and prevention (CDC) research on test developed by US Vaccine Research Centre at the National Institute of Health is on going, which seems to have a specificity higher than 99% with a sensitivity of 96%**[39]**

Blood tests

- A normal or reduced white blood cell count (and lymphopenia) can be seen in many instances, which is thought to indicate a poor prognosis.
- Lactate dehydrogenase, C reactive protein, creatine kinase (CK MB and CK MM), aspartate amino transferase, and alanine aminotransferase levels have all increased.
- Some individuals have higher D-dimer levels as well as a high neutrophil-to lymphocyte ratio.
- Coagulation anomalies can be seen in severe instances, as evidenced by an increase in prothrombin time and internal normalised ratio.

Coagulation abnormalities can be observed in severe cases, as indicated by increase in prothrombin.**[47]**

Chest X-ray

Chest X-rays are frequently inconclusive in the early stages of illness and may not reveal any major changes. As the infection advances, bilateral multifocal alveolar opacities develop, which may be accompanied by pleural effusion.**[36]**

Treatment:

Supportive Care and Respiratory Support

Currently, best practices for managing acute hypoxic respiratory failure and ARDS should be followed. Many countries and professional bodies have created evidence-based guidelines, including the National Institutes of Health's regular updates.

Over 75% of COVID-19 patients in hospitals require supplementary oxygen treatment.**[36]** Patients who do not respond to standard oxygen therapy may benefit from heated high-flow nasal cannula oxygen. For patients requiring invasive mechanical ventilation, lung-protective ventilation with modest tidal volumes (4-8 mL/kg, projected body weight) and plateau pressure below 30 mg Hg is advised. Prone posture, increased positive end-expiratory pressure, and short- term neuromuscular inhibition using cisatracurium or other muscle relaxants can improve oxygenation.**[29]** Despite good lung compliance, individuals with COVID-19 respiratory failure may still benefit from lung-protective ventilation. Lower tidal volume techniques have been demonstrated to benefit patients with ARDS, despite varying levels of lung compliance among cohorts.

The threshold for intubation in COVID-19-related respiratory failure is debatable, as many patients have normal breathing but severe hypoxia.**[31]** "Earlier" intubation allows for a more controlled intubation process, which is crucial given the logistical hurdles of transferring patients to an airborne isolation chamber and putting on personal protection equipment before intubation. In the absence of respiratory distress, hypoxaemia can be easily tolerated and patients may not require mechanical ventilation. Using earlier intubation thresholds may lead to unnecessary mechanical breathing and difficulties for certain patients. There is inadequate information to provide recommendations on whether to intubate earlier or later.

Observational studies show that 8% of hospitalised COVID-19 patients had bacterial or fungal co-infections, whereas up to 72% get broad-spectrum antibiotics. Withholding antibacterial medications in COVID-19 patients may be sensible until more results. They should be reserved for individuals with radiological abnormalities and/or inflammatory markers compatible with co-infection, as well as those who are immunocompromised or severely unwell.**[31]**

Targeting the virus and the host response:

COVID-19 management entails evaluating or developing a variety of medication classes, including antivirals, antibodies, anti-inflammatory drugs, targeted immunomodulatory treatments, anticoagulants, and antifibrotics. Different therapy approaches are thought to be beneficial at different phases of the illness. Remdesivir, for example, has showed promise in decreasing recovery durations in hospitalised patients, although lopinavir-ritonavir and hydroxychloroquine have not proven apparent advantages in clinical studies.**[6]** Antibody-based therapies, such as convalescent plasma, have had mixed success; although early case reports indicated some improvement, later investigations demonstrated no substantial advantage over normal therapy. Anti-inflammatory medications such as dexamethasone have been shown to reduce mortality in critically sick patients requiring oxygen or ventilation, but immunomodulatory treatments such as tocilizumab and sarilumab target excessive inflammatory responses that can cause organ damage.**[29]** Anticoagulants, particularly low molecular weight heparin, are commonly used in hospitals to lower the risk of thromboembolic problems, and research is underway to investigate the advantages of greater dosages in persons with increased D-dimer levels. Because the efficacy of these medicines varies with illness stage and severity, personalised methods are critical for improving patient outcomes.**[30]**

Prevention and development of vaccine:

COVID-19 is a possibly avoidable condition. The epidemiology of infection throughout the world clearly demonstrates the association between the intensity of public health activity and transmission control.**[25]** However, because most nations have implemented several infection control techniques, it is difficult to determine their respective benefits.**[42]** This is an increasingly significant subject since ongoing interventions will be necessary until viable vaccinations or therapies are developed.**[25]** In general, these interventions can be divided into those consisting of personal actions case (eg, physical distancing, personal hygiene, and use of protective equipment) and contact identification (e.g., test-trace-track-isolate, reactive school or workplace closure), regulatory actions (e.g., governmental limits on sizes of gatherings or business capacity; stay-at-home orders; proactive school, workplace, and public transport closure or restriction; cordon sanitaire or internal border closures), and international border measures (e.g., border closure).**[41]** A top aim is to find a combination of interventions that minimises societal and economic disruption while effectively managing illness. Optimal measures may differ between countries due to resource constraints, geography (e.g., island nations and international border measures), population, and political issues.**[42]**

The evidence for public health initiatives remains unchanged since the 1918 flu epidemic.**[41]** Mathematical modelling and empirical data show that public health interventions such as home quarantine, mass gathering limitations, travel restrictions, and social distance lower transmission rates. When therapies are removed, the risk of reappearance increases.**[42]**

There is presently no human vaccination for SARS-CoV-2, however approximately candidates are being developed.**[39]** Nucleic acids (DNA or RNA), inactivated or live attenuated viruses, viral vectors, and recombinant proteins or virus particles are some of the approaches used.**[38]** Technical barriers to developing an effective vaccine include whether S or receptor-binding domain proteins stimulate more protective antibodies, prior exposure to adenovirus serotype [which impairs immunogenicity in the viral vector vaccine], the need for adjuvant, the feasibility of large-scale production and regulation (e.g., ensuring safety and effectiveness), and legal barriers (e.g., technology transfer and licensure agreements).**[39]** The SARS-CoV-2 S protein looks to be a viable immunogen for protection, however whether targeting the whole protein or only the receptor-binding region is sufficient to prevent transmission remains unclear.**[38]** Considerations include the possible length of protection and the number of vaccine doses required to achieve immunity. Over a dozen vaccines for SARS-CoV-2 are now in phase 1-3 studies.**[39]** Future preventative strategies may include monoclonal antibodies, hyperimmune globulin, and convalescent titer.**[9]** If effective, these measures might benefit high-risk populations such as health care professionals, vital workers, and older folks (especially in nursing homes or long-term care institutions).**[39]**

Current condition and future perspective:

Current Condition

As at the end of the year 2024, it can be observed that the number of coronavirus cases and deaths have reduced on a global scale. According to WHO statistics, over a period of 28 days, new cases decreased by 58 percent, while deaths dropped by 31 percent. Such fluctuations can be still seen in areas like Europe and Americas, but the situation is significantly better now.**[25]** Several factors contributed to this decrease such as increased vaccination rate, better treatment options and increased natural immunity.**[39]** But some countries continue to have the challenges caused by unfair distribution of vaccines and lack of healthcare resources.**[43]** Worldwide, infectious diseases are not common except in vaccine-untreated or high-risk populations.**[9]** Other health policies such as wearing of masks and more ventilation of the affected areas remain very important in managing these cases.**[25]** Even hospitalization cases and ICU cases have significantly decreased in comparison to the last rounds.**[31]**

Future perspective

1. Combatting potential pandemics: The professional community stresses the certainty of new pandemics emerging.**[41]** We have learned from COVID-19 that we need to invest in public health systems, ensure fair access to vaccines, and provide aid at best for the targeted countries. The developments in mRNA vaccine and predictive modeling technologies look good for the future reliefs.**[43]**

2. Novel therapeutic approaches: The emergence of nanoparticle therapy, bioflavonoids, and different antiviral drugs continues to be researched, which will help in the management of both acute COVID-19 and the long terms effects of it. The requirement of funding in these areas remains appreciated.**[9]**
3. Addressing public health issues: Countries are beginning to move to practices of more sustainable pandemic management, which involves getting more granular with data, more advanced home testing and clinical interventions. Addressing vaccine hesitancy and misinformation is crucial related to future prevention of health crises.**[25]**
4. So what have these events highlighted?: Impact of Covid on accessibility to and mitigation of risks in different countries, what role inequities played. Reducing these disparities is important in order to limit the consequences of further pandemic outbreaks. International co-operation is required to achieve improved health equity throughout the world.**[43]**

Lockdowns are not the preferred course of action but in endocrine scenarios their implementation can be attempted and this becomes part of the new normal contingency plan.

[41] A global tightening is now evergreen policies are complemented by strengthening of prevention detection and response system.**[42]**

Such an integrated approach allows not only to overcome an ongoing pandemic but also to better counter future risks.**[41]**

Conclusion:

The COVID-19 Pandemic was one of the catastrophic events that have affected the world in the last century.**[31]** This has shown the challenges that need to be overcome when addressing international public health.**[25]** While there have been strides in the fight against the virus, including vaccination drives, access to healthcare resources is still daunting.**[43]** Even with most areas recording a decline in the number of infections and deaths from the virus, the pandemic highlights how important global health is.**[25]**

The impact of continued inequitable health care cannot be downplayed as COVID-19 has been left unchecked in some areas due to failing to build an effective health infrastructure.**[43]** Also, the combination of anti-vaccine sentiment and in some cases, scientifically inaccurate news accounts has made achieving critical mass immunization efforts more difficult than it could potentially have been, meaning that further efforts in educational campaigns are needed.**[25]**

Developmental strides in novel therapeutic strategies like mRNA vaccines, genetically modified nanoparticles and novel antivirals prove useful in treating COVID-19 while at the same time can be used as a preparation for any possible pandemic in the future.**[38]** However, if these strategies are to be used fully, Iraq needs to undertake long-term funding of research, systems, and public health to improve their utilization.**[43]**

Also, the policy of containment of the viral outbreaks in the last decades has clearly shown that the integrated approach to the problem resolves it significantly more efficiently.**[41]**

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