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COVID-19: A Comprehensive review of the Pandemic and its impact

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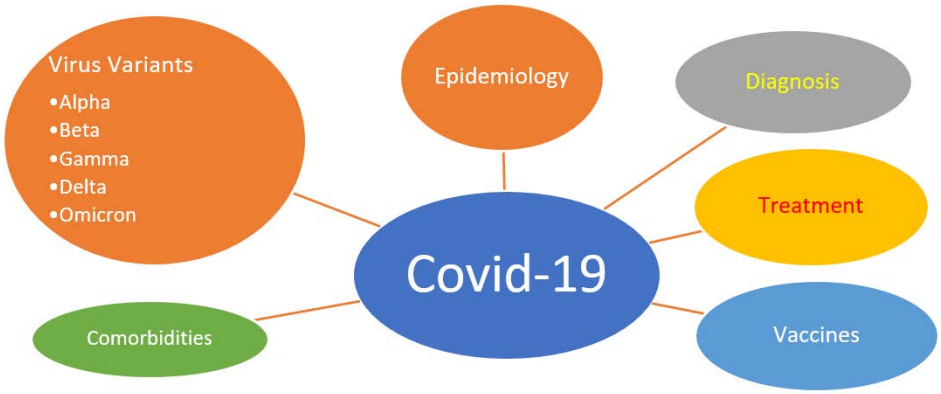
ABSTRACT



The World recently witnessed a pandemic of COVID-19 disease. The cause of the disease is a novel coronavirus, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) virus. Despite having a low case fatality rate than other diseases caused by different viruses of the Coronaviridae family, the COVID-19 disease caused nationwide lockdowns and worldwide havoc. The present review provides consolidated information regarding the epidemiology, viral morphology and its variants, clinical symptoms, diagnosis, complications, vaccines, and treatment for the COVID - 19 disease. It is an attempt to chart the course of the pandemic with insights from prevalent literature detailing how the world emerged from the pandemic and the steps imperative to prevent future outbreaks.

Keywords: *SARS-CoV-2, Pandemic, Coronaviridae, SARS-CoV-2 strains, Vaccines*

INTRODUCTION

The World has witnessed many pandemics, from the earliest known pandemic, “the plague of Justinian" in the year 541-543,[1] to the most severe Spanish flu pandemic with 500 million deaths worldwide in 1918, and the most recent COVID-19 pandemic. The COVID-19 disease is caused by a novel coronavirus SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2). The pandemic originated in Wuhan, Hubei province, Central China, where the first case of pneumonia of unknown origin was reported on 8 December 2019.[2] Subsequently, cases were reported in operating dealers and vendors in the Wuhan Huanan Seafood Wholesale Market, which closed on 1 January 2020 for sanitization and disinfection.[3] The SARS-CoV-2 virus gets transmitted via respiratory droplets and aerosols spread by coughing and sneezing, which land on the nose, mouth, or eyes[3] of an uninfected individual spreading the disease. Preventive measures for controlling the disease transmission include hand-washing for at least 20 seconds with soap and water or using hand sanitizer (at least 60% alcohol content). Refraining from group activities involving large crowds or going to crowded places, and maintaining at least 6 feet of distance between two people, especially if they are coughing or sneezing (social distancing), are also some more preventive measures.[4] Despite having a lower fatality rate (approx. 2% - 3%) as compared to SARS (approx. 10%) and MERS (approx. 40%), the COVID-19 disease spread across the World at an alarming rate and, as of 10 July 2022 around 553 million confirmed cases and over 6.3 million deaths have been reported globally,[5] spanning more than 220 countries and territories.

EPIDEMIOLOGY

The spread of COVID-19 started from an epidemic pneumonia outbreak on 12 December 2019 in Wuhan, China. The disease outbreak began at a local seafood market where six initial patients

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with severe pneumonia were sellers or delivery men from the seafood market.[6,7] By 13 January 2020, a case of COVID-19 in Thailand was recorded, the first case outside of China. The USA reported the first case of COVID-19 in North America on 23 January and France reported Europe's first case on 24 January 2020. By 27 January 2020, the virus had reached India as well.

With the number of cases on the rise reaching 1 million worldwide, WHO declared COVID-19 as a pandemic on 11 March 2020 while on 12 March India reported its first fatality due to COVID-19. As of 10 February 2023, India has reported 44,683,862 confirmed cases and a total of 530,750 deaths.[8]

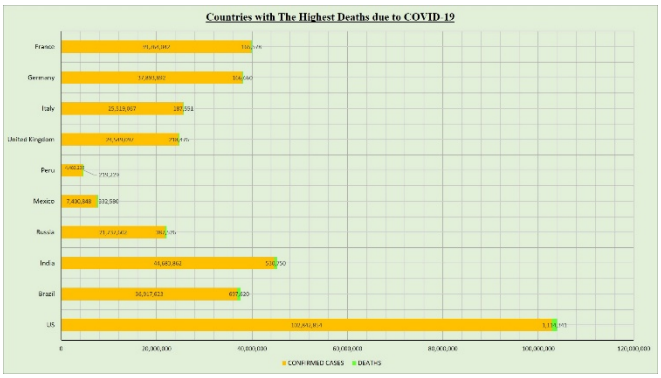

Figure 1: The graph shows the 10 countries with the highest deaths due to COVID-19[9,10]

The evolution of the COVID-19 outbreak varied amongst regions and nations. African nations were predicted to have catastrophic impacts early on in the pandemic. However, these predictions did not turn into a reality. At first, the seemingly low African case count was primarily attributed to the low testing rates and case reporting; however, recent data from seroprevalence studies point to a more extensive virus circulation in the community. Despite that, a continuing low COVID-19 burden hints at the involvement of other factors. One such factor significantly affecting the decreased COVID-19 load is the demographic pyramid. It is well established that the mortality rates are prominently higher among older populations, with the age of 65–74 years at 35 times higher risk of being hospitalized due to SARS-CoV-2 infection and at 1100 times higher risk of dying from COVID-19.[11]

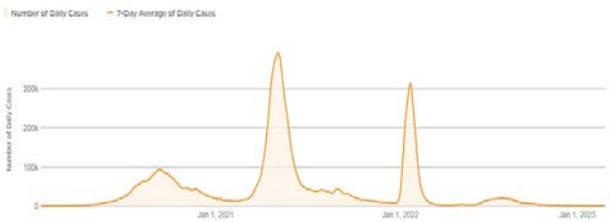

Figure 2: Evolution of COVID-19 outbreak in India. The 7-day moving average is calculated for each day by averaging the new cases of that day, the three days before, and the three next days[9,12].

On the other hand, Africa has the youngest population among all global regions, with a median age of 19.7 years, contributing to a low COVID-19 burden.[13] Another factor is the prevalence of comorbidities. According to WHO reports, high-income or upper-middle-income countries and those in the South African Development Community have double the mortality rates as compared to lower-income and lower-middle-income countries in other economic regions of Africa.[14] This variation in the number of deaths was primarily due to comorbidities such as hypertension, diabetes, chronic obstructive pulmonary disease, HIV, and obesity, increasing the severity and risk of mortality in COVID-19 patients. The prevalence of such comorbidities was higher in high-income countries, thus, raising the death toll in these nations.[14] Higher mortality in European nations like Italy can be explained using demographic characteristics. According to the Italian National Institute of Health, the CFR in Italy was 7.2% among 22,512 cases up to March 17, 2020.[13] This CFR in Italy (7.2%) was significantly higher than that reported in China (2.3%). The high CFR in Italy was probably due to the higher rate of infections among the elderly, as the age-specific CFR was similar between China and Italy in the age groups below 70 years.[15]

Viral Morphology

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is a beta-coronavirus belonging to a group of SARS-CoV and SARS-like bat-derived viruses[16]. Coronaviruses belong to a group of viruses containing short single-strand ribonucleic acid (ssRNA) as genetic material.[17] Coronaviruses are divided into four different genera alpha, beta, gamma, and delta. The Alpha- and Beta-coronaviruses originate from mammals, particularly bats. The Gamma- and Delta viruses originate from pigs and birds.[18] The length of the RNA strands in coronaviruses ranges from 26 to 32 kb.[17] The SARS-CoV-2 virus has a genome size of approximately 29.9 kb and shares 79% genome sequence identity with SARS-CoV and 50% with MERS-CoV.[19] The SARS-CoV-2 virus contains four structural proteins (S, E, M, and N) and sixteen non-structural proteins (nsp1−16).[20] The nucleocapsid protein (N) forms the capsid outside the genome while the three other structural proteins: membrane protein (M), spike protein (S), and envelope protein (E) are associated with the envelope that packs the genome. The M protein and E protein are responsible for the membrane structure of the coronavirus and glycoprotein spikes (S) on the outer surface are responsible for the attachment and mediate entry of the virus to host cells.[17,21]

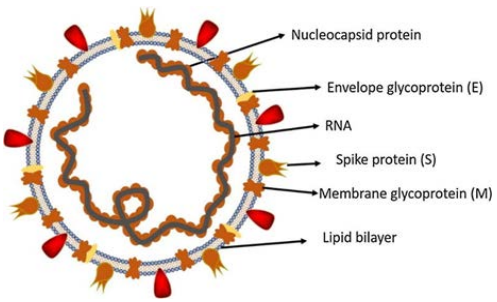

Figure 3: Structure of SARS-CoV-2.[19]

SARS-CoV-2 infects lung alveolar epithelial cells using receptor-mediated endocytosis via the angiotensin-converting enzyme II (ACE2) as an entry receptor and this heralds the beginning of the life cycle of SARS-CoV-2 in the host cells[18]. The S protein gets cleaved into S1 and S2 subunits and the receptor-binding domain (RBD) in the S1 subunit binds to the host receptor (ACE2), followed by the fusion of the S2 subunit to the cell membrane[22].

VIRAL VARIANTS

Variants of the SARS-CoV-2 emerged due to rapid mutations in its single-stranded RNA genome[23]. It is suspected that a mutation in a single amino acid (T372A) in the viral genome could have helped the SARS-CoV-2 virus to spread from bats to humans, thereby acting like a zoonotic disease[23,24]. Many factors are responsible for generating viral mutations including the intervention of the human immune system. The immune system machinery in humans can cause interference in the viral genome resulting in the introduction of viral mutations[25]. A variant of concern is a viral variant known to spread more quickly, cause more severe disease, escape the body's immune response, change the clinical presentation, or decrease the effectiveness of available tools like public health measures, diagnostics, treatments, and vaccines[26,27]. The current variant of concern is the Omicron variant of B.1.1.529 Pango lineage, which includes BA.1, BA.2, BA.3, BA.4, BA.5, and descendent lineages. It also includes BA.1/BA.2 circulating recombinant forms such as XE. As of August 2022, there have been a total of five variants of concern identified by the WHO. The variants include the Alpha variant of B.1.1.7 Pango lineage, the Beta variant of B.1.351 Pango lineage, the Gamma variant of P.1 Pango lineage, the Delta variant of B.1.617.2 Pango lineage and the Omicron variant of B.1.1.529 Pango lineage[26].

SYMPTOMS

About 80% of the people affected with COVID-19 develop mild to moderate disease, while only 5% develop critical illness[28]. Two categories of COVID symptoms exist. Acute COVID, which are symptoms that develop 4-5 days post-infection, and long COVID, symptoms that persist even after weeks or months post-infection. A cohort study from acute care hospitals in England, Scotland, and Wales identified the median duration of symptoms before admission as 4 days, with the most common being cough (68.9%), fever (71.6%), and shortness of breath (71.2%)[29]. Typical symptoms of the disease include: Fever (87.9%), dry cough (67.7%), fatigue (38.1%), sputum production (33.4%), shortness of breath (18.6%), sore throat (13.9%), headache (13.6%), myalgia or arthralgia (14.8%), chills (11.4%), nausea or vomiting (5.0%), nasal congestion (4.8%), diarrhea (3.7%), and hemoptysis (0.9%), and conjunctival congestion (0.8%)[30].

Table 1: Variants of concern of the SARS-CoV-2 virus[26,31]

WHO label	Pango lineage	Earliest documented samples	Mutation
Alpha	B.1.1.7	The United Kingdom, Sep-2020	Includes 17 mutations in the viral genome out of which eight mutations (Δ69-70 deletion, Δ144 deletion, N501Y, A570D, P681H, T716I, S982A, D1118H) are in the spike (S) protein
Beta	B.1.351	South Africa, May-2020	Includes 9 mutations (L18F, D80A, D215G, R246I, K417N, E484K, N501Y, D614G, and A701V) in the spike protein, of which 3 mutations (K417N, E484K, and N501Y) are located in the RBD and increase the binding affinity for the ACE receptors
Gamma	P.1	Brazil, Nov-2020	Includes 10 mutations in the spike protein (L18F, T20N, P26S, D138Y, R190S, H655Y, T1027I V1176, K417T, E484K, and N501Y) out of which 3 mutations (L18F, K417N, E484K) are located in the RBD, similar to the beta variant
Delta	B.1.617.2	India, Oct-2020	Includes 10 mutations (T19R, (G142D*), 156del, 157del, R158G, L452R, T478K, D614G, P681R, D950N) in the spike protein
***Omicron**	B.1.1.529	Multiple countries, Nov-2021	Includes more than 30 mutations in the spike protein and in T91 in the envelope, P13L, E31del, R32del, S33del, R203K, G204R in the nucleocapsid protein, D3G, Q19E, A63T in the matrix, N211del/L212I, Y145del, Y144del, Y143del, G142D, T95I, V70del, H69del, A67V in the N-terminal domain of the spike, Y505H, N501Y, Q498R, G496S, Q493R, E484A, T478K, S477N, G446S, N440K, K417N, S375F, S373P, S371L, G339D in the receptor-binding domain of the spike, D796Y in the fusion

			peptide of the spike, L981F, N969K, Q954H in the heptad repeat 1 of the spike as well as multiple other mutations in the non-structural proteins and spike protein.

***Includes BA.1, BA.2, BA.3, BA.4, BA.5 and descendent lineages**

Acute COVID

Infection with COVID-19 results in the appearance of symptoms 4-5 days post-infection. A study conducted by the COVID symptom group identified six types of cluster symptoms that appeared 5 days post-infection[32,33]. These are:

Cluster 1: Symptoms without fever ("flu-like"): Headache, loss of smell, muscle pains, cough, sore throat, chest pain, no fever,
Cluster 2: Symptoms with fever: Headache, loss of smell, cough, sore throat, hoarseness, fever, loss of appetite,
Cluster 3: Gastrointestinal symptoms: Headache, loss of smell, loss of appetite, diarrhea, sore throat, chest pain, no cough,
Cluster 4: Severe level 1 symptom (fatigue): Headache, loss of smell, cough, fever, hoarseness, chest pain, fatigue,
Cluster 5: Severe level two symptoms (confusion)—Headache, loss of smell, loss of appetite, cough, fever, hoarseness, sore throat, chest pain, fatigue, confusion, muscle pain,
Cluster 6: Severe level three symptoms (abdominal and respiratory)—Headache, loss of smell, loss of appetite, cough, fever, hoarseness, sore throat, chest pain, fatigue, confusion, muscle pain, shortness of breath, diarrhea, abdominal pain.

Long COVID:

The term "Long COVID" was coined by Elisa Perego, an archaeologist at University College London, in a clinical context to describe the persistence of symptoms weeks or months post-infection. The two stages of Long COVID, depending upon the duration of symptoms, include post-acute COVID (more than 3 weeks but less than 12 weeks) and chronic COVID (more than 12 weeks) as shown in Figure 4[34].

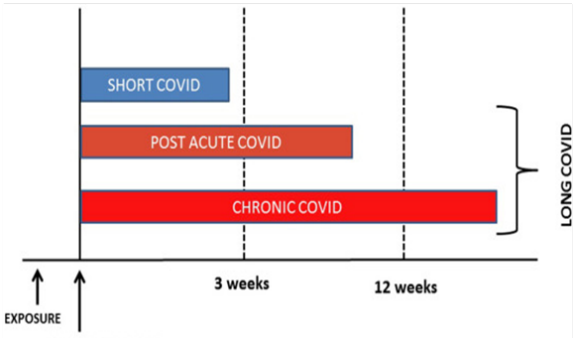

Figure 4: Long COVID classification[32]

Long COVID can be relapsing in nature and is also known as "post-COVID syndrome." People with long COVID symptoms test negative (PCR) for the disease, which indicates microbial recovery. Thus, the time lag between microbial recovery and complete clinical recovery can be termed as post-COVIID syndrome. A study that monitored people for 12 months after the onset of COVID-19 symptoms found that in the 12th month, 22.9% were completely devoid of any residual syndrome. It identified the most common symptoms of long COVID as, Reduced exercise capacity (56.3%), Fatigue (53.1%), Dyspnea (37.5%), Problems with concentration (39.6%), Problems with finding words (32.3%), Sleeping (26.0%).[32,35]

Neurocognitive symptoms were more pronounced in females.[36] Depending upon the most dominant cluster of syndromes, long COVID can be divided into different categories which are discussed further in Table 2.

DIAGNOSIS

Detection of SARS-CoV-2 RNA using real-time reverse-transcription polymerase chain reaction (RT-PCR) is the preferred method for COVID-19 diagnosis.

Table 2: Categories of Post-COVID syndrome[28,30,32,35]

Post-COVID syndrome	Predominant clinical features	Remarks
Post-COVID fatigue syndrome	Profound fatigue	Rule out causes like anaemia, hypothyroidism, electrolyte imbalance
Post-COVID cardio-respiratory syndrome	Cough, low-grade fever, shortness of breath, chest pain,	Sudden increase in dyspnoea can be due to tension pneumothorax, pulmonary embolism, coronary artery disease or heart failure in patients recovered from COVID-19
Post-COVID neuro-psychiatric syndrome	Headaches, anosmia, neurocognitive difficulties, insomnia, depression, and other mental health conditions	In patients with acute onset, neurological symptoms consider vasculitis, thrombosis, or demyelination. Post-COVID psychological issues have to be addressed properly.
Post-COVID gastro-intestinal syndrome	Abdominal discomfort, diarrhoea, constipation, vomiting,	GI symptoms can be sequelae of the disease. Various drugs used during acute COVID, especially lopinavir/ritonavir produces GI symptoms
Post-COVID hepato-biliary syndrome	Nausea, jaundice, deranged LFT	Drugs used in the treatment of COVID-19 like remdesivir, favipiravir, lopinavir/ritonavir, and tocilizumab can cause hepatic impairment.

Post-COVID musculoskeletal syndrome	Muscle pains and weakness, arthralgia	May be due to disease, prolonged ICU care, neurological problems, myopathy, or electrolyte imbalance. Usually subside during follow-up. Inflammatory arthralgia has to be differentiated from other causes like RA, SLE
Post-COVID thromboembolic syndrome	Depending upon the vascular territory of involvement breathlessness in PE, chest pain in CAD, and limb weakness and neurological deficit in CVA	Early diagnosis and treatment are lifesaving. Follow the standard treatment protocol.
Post-COVID multisystem inflammatory syndrome/post-COVID autoimmune syndrome	Fever, gastrointestinal symptoms, rash, chest pain, palpitations	Elevated levels of markers of inflammation.
Post-COVID genito-urinary symptoms	Proteinuria, haematuria, development of kidney injury	Endothelial dysfunction, coagulopathy, complement activation, direct effect of the virus on the kidney, sepsis, and multi-organ dysfunction contribute to the development
Post-COVID dermatological syndrome	Vesicular, maculopapular, urticarial, or chilblain-like lesions on the extremities (COVID toe)	NA

Upper respiratory samples, mainly nasopharyngeal swabs, are the primary specimens used and the viral genes targeted include the N, E, S, and RNA-dependent RNA polymerase (RdRP) genes[37]. The basis of Real-time RT-PCR assays is the detection and quantification of a fluorescent signal generated during the PCR amplification step, providing faster results than conventional RT-PCR. The test's sensitivity depends on various factors like viral load, time from viral exposure, and specimen source. RT-PCR testing can have instances of false negatives due to insufficient viral load. It also has other limitations like sample storage problems, low-quality nucleic acid purification, and high cost, but still, it remains the standard diagnostic test.

Rapid antigen tests have been accepted worldwide as a method for the COVID-19 diagnosis. These tests detect the presence of viral proteins in the sample with the help of immunochromatography methods. The test checks for the nucleocapsid protein of SARS-CoV-2, the most abundant protein the virus expresses. These are valid for only acute infections and are to be used within the first 5-12 days after symptom onset. Rapid antigen tests have the advantage of not requiring hospital or laboratory facilities and are easy to use and interpret. They have a turnaround time of 15 - 20 minutes and are compatible with the samples collected from anterior nares rather than the nasopharynx. These tests have lower sensitivity in comparison to the RT-PCR method and bear a risk of giving false negative results in asymptomatic patients with low viral load, who might be at an early stage of the infection.

Serological testing is another method for COVID-19 diagnosis by detecting antibodies against SARS-CoV-2 in the blood. Antibodies against the spike (S) protein are used for detection, but other viral proteins can be used as well. The presence of the viral antigen in the blood itself can also be used for detection. Serology testing is valuable to identify past infections since the development of antibodies can take several weeks post-exposure. Antibodies are detected by enzyme-linked immunosorbent assay using a qualitative detection of IgG or IgM antibodies. A study done in Wuhan using colloidal gold-based immunochromatographic strip and comparing it with real-time RT-PCR found the sensitivity of immunochromatographic assay with IgM and IgG combinatorial detection in real-time RT-PCR confirmed cases to be 11.1% at the early stage (1–7 days after onset), 92.9% at the intermediate stage (8–14 days after onset), and 96.8% at the late stage (more than 15 days)[38].

RISK FACTORS: COMORBIDITIES

COVID-19 is equally transmissible in all age groups. Many studies have shown that older adults and people with underlying comorbidities such as hypertension, obesity, and cardiovascular diseases are at higher risk of contracting severe illness and death from COVID-19 infection. According to the CDC, older adults are at a higher risk of getting severely sick from COVID-19, with the number of deaths among people over age 65 being 97 times higher than the number of deaths among people between the ages of 18-29 years[39]. A study comprising 27,670 samples showed that the most common pre-existing comorbidities in COVID-19 patients were hypertension (39.5%), cardiovascular disease (12.4%), and diabetes (25.2%).[40,41] Another study comprising 22,573 patients found that hypertension is the most prevalent comorbidity in 55.4% of the deceased COVID-19 patients, followed by cardiovascular disease in 30.7% patients, cerebrovascular disease in 13.4% patients, and chronic kidney disease in 9.05% patients. The mortality rate was significantly higher for patients with these comorbidities, the most prominent risk factor being chronic kidney disease, followed by cardiovascular disease, hypertension, and cerebrovascular disease[42]. A study done using clinical data of 417 patients found that class II obese patients had more comorbidities in comparison to the other groups. Patients with BMI above the average BMI (29 kg/m2) and the presence of underlying comorbidities showed a significant increase in admission to ICU, development of Acute Respiratory Distress Syndrome, need for ventilation, and

mortality compared to patients below BMI of 29 kg/m2 and underlying comorbidities[43].

TREATMENT

In the initial wake of the pandemic, no registered medicine for treatment of COVID-19 was available and hence a majority of the treatment was being done using experimental therapies and drug repurposing.

Hydroxychloroquine/ Chloroquine are anti-malarial and autoimmune drugs. Chloroquine is also known to show antiviral activity possibly by increasing the endosomal pH required for virus/cell fusion, as well as interfering with the glycosylation of cellular receptors (ACE2) of SARS-CoV[44]. Hydroxychloroquine and chloroquine both were shown to be effective in the control of COVID-19 infection in vitro and hydroxychloroquine was found to be more potent[45,46]. However, a randomized, controlled, open-label platform trial found that patients who received hydroxychloroquine did not have a lower incidence of death at 28 days than those who received usual care[47]. Another observational study compared outcomes in terms of time to recovery, worsening, and death in patients who received chloroquine/ hydroxychloroquine + Azithromycin and those who did not and found no significant differences in associated time to recovery for patients receiving any chloroquine/ hydroxychloroquine + Azithromycin.[48]

Remdesivir is an antiviral agent. It is an adenosine analogue, which incorporates into nascent viral RNA chains and results in pre-mature termination of viral replication. Remdesivir was also shown to be highly effective against COVID-19 infection in vitro.[47] The US Food and Drug Administration (FDA) approves the use of Intravenous remdesivir for the treatment of COVID-19 in adults and pediatric patients aged ≥28 days and weighing ≥3 kg. A randomized, double-blind, placebo-controlled trial involving non-hospitalized patients with COVID-19 found that a 3-day course of remdesivir resulted in an 87% lower risk of hospitalization or death than placebo.[49] Earlier in 2020 WHO recommended against the use of remdesivir in COVID-19 patients though now in 2022 based on clinical trial data WHO also suggests the use of remdesivir in mild or moderate COVID-19 patients who are at high risk of hospitalization.[50]

Ivermectin is an anti-parasitic drug that was shown to be an inhibitor of SARS-CoV-2 in vitro. However, Ivermectin is currently not recommended for the treatment of COVID-19 in any form of disease severity by WHO.[51,52]

Lopinavir-ritonavir is a protease inhibitor combo therapy used to treat HIV. It was proposed as antiviral therapy against COVID-19 during the early onset of the pandemic however a randomized, controlled, open-label trial found there to be no benefit of lopinavir-ritonavir treatment in hospitalized adult patients with severe COVID-19.[53] The WHO currently strongly recommends against the use of lopinavir-ritonavir.[52]

Molnupiravir is an oral antiviral drug that targets the RNA-dependent RNA-polymerase enzyme of the virus and induces mutations in the viral RNA. A meta-analysis of phase 1-3 trials found Molnupiravir to significantly reduce the risk of hospitalization or death in patients with mild-to-moderate COVID-19.[54]

Dexamethasone is a corticosteroid drug used for its anti-inflammatory and immunosuppressive effects. In a controlled, open-label RECOVERY trial dexamethasone was observed to decrease 28-day mortality in patients who were mechanically ventilated or required oxygen support; in contrast, no benefit was seen in patients not receiving any respiratory support[55]. The WHO guidelines strongly recommend the use of dexamethasone only for patients with severe or critical COVID-19[52].

Convalescent Plasma (CP) therapy is used as a strategy of passive immunization in the management of the disease. It targets to neutralize the SARS-CoV-2 virus by serving as a source of antiviral antibodies. CP appeared to be promising early on but multiple studies found CP therapy not effective. An open-label, parallel arm, phase II, multicenter, randomized controlled trial concluded that Convalescent plasma therapy was not associated with a reduction in progression to severe COVID-19 or mortality.[56] Another randomized placebo-controlled trial found that treatment with convalescent plasma did not improve clinical outcomes in adults with COVID-19.[57] The WHO currently recommends against treatment with Convalescent plasma therapy in patients with non-severe, severe and critical COVID-19.[52]

Alongside the administration of drugs, a larger part of COVID-19 recovery includes providing supportive care to relieve patients of varying symptoms. Supportive care can range from simply keeping a check on other health conditions a patient may suffer from, to providing supplemental oxygen to maintain oxygen saturation levels or even mechanical ventilation in critically ill patients.[57–59]

VACCINES FOR COVID-19

Vaccines are biological preparations conferring active acquired immunity against a particular disease. They have played a vital role throughout history in curbing the spread of deadly diseases like smallpox[60]. The genomic sequence of the SARS-CoV-2 virus was released on 11th January 2020, which led to a fast-paced vaccine development environment worldwide.[61]

By February 2021, 64 types of vaccines were prepared using different technologies (RNA, replication-defective viral vector, virus-like particle, inactivated virus, and protein subunit) that entered phase III clinical trials.[62] The vaccine development speed for COVID-19 was record-breaking in the entire vaccine development history, with vaccine candidate development within six months of the pandemic and conditional approval for usage within ten months.[63] As of 26 August 2022, 12,449,443,718 vaccine doses have been administered worldwide.[64]

Different vaccines have different mode of action depending upon the method used to induce immunity in the host against the virus. All the available vaccines for the SARS-CoV-2 virus were made using different techniques.[65]

Viral vector type of vaccine (AstraZeneca/AZD1222, Janssen/Ad26.COV 2.S) uses a nonrelated viral vector to deliver the SARS-CoV-2 genetic material producing a particular viral protein recognized by the immune system.

Table 3: List of COVID-19 vaccines which obtained Emergency Use List by WHO.[63,65]

Name of the Vaccine	Type	Manufacturer	Date of release/ approval	Number of doses
Pfizer/BioNTech Comirnaty vaccine	mRNA vaccine	BioNTech	31 December 2020	Three-dose primary series for individuals of 6 months to 4 years of age. Two-dose primary series for individuals 5 years of age and older. Third primary series dose for individuals 5 years of age and older deemed as immunocompromised.
ChAdOx1 nCoV-19 Corona Virus Vaccine/ SII/COVISHIELD	mRNA vaccine	Serum Institute of India Pvt. Ltd. (SIIPL)	16 February 2021	Two doses of 0.5 ml each with the second dose administered between 4 to 12 weeks after the first dose
AstraZeneca/AZD1222	Recombinant vaccine	University of Oxford, Vaccitech	16 February 2021	Two doses of 0.5 ml each with the second dose administered between 8 to 12 weeks after the first dose
Janssen/ Ad26.COV 2.S	Viral vector vaccine	Johnson & Johnson	12 March 2021	Single dose regimen
Moderna COVID-19 vaccine (Spikevax)	mRNA vaccine	ModernaTX, Inc.	30 April 2021	Two doses (100 µg, 0.5 ml each) 8 weeks apart for adults aged 17 and above Two doses (100 µg, 0.5 ml each), given intramuscularly, 4 weeks apart for adolescents aged 12 to 17 years Two doses (50µg in 0.25 ml each), 4 weeks apart for children aged 6 to 11 years
				Two doses (25 µg [0.25 ml each), 4 weeks apart for children aged 6 months to 5 years
Sinopharm COVID-19 vaccine	Inactivated vaccine	Beijing Institute of Biological Products Co., Ltd	7 May 2021	Two doses (0.5 mL each) at an interval of 3 to 4 weeks Third additional dose recommended for persons aged 60 and above
Sinovac-Corona Vac vaccine	Inactivated vaccine	Sinovac	1 June 2021	Two doses (0.5mL) with a preferred interval of 14–28 days between the doses Third additional dose recommended for persons aged 60 and above
Bharat Biotech BBV152 COVAXIN vaccine	Inactivated vaccine	Bharat Biotech's BSL-3 (Bio-Safety Level 3) high containment facility	3 November 2021	Two doses (0.5 ml) administered at an interval of 4 weeks
Novavax COVID-19	Protein subunit vaccine	Novavax, Inc.	20 December 2021	Two doses in the primary series with an interval of 3–8 weeks

The mRNA vaccines (SII/COVISHIELD, Pfizer/BioNTech, Moderna) contain viral mRNA that produces a specific viral protein recognized by the immune system. Inactivated vaccines (Sinopharm, Sinovac-CoronaVac, Bharat Biotech BBV152 COVAXIN) contain a killed or inactivated form of the SARS-CoV-2 virus recognized by the immune system. Protein vaccines (Nuvaxovid (NVX-CoV2373, Covovax (NVX-CoV2373)) contain a protein of the SARS-CoV-2 virus recognizable by the immune system.[65] A total of nine vaccines have obtained EUL (Emergency use listing) by WHO as of 12th January 2022. (Table 3). On 31st August, 2022 the U.S. Food and Drug Administration authorized the usage of the Moderna COVID-19 Vaccine and the Pfizer-BioNTech COVID-19 Vaccine bivalent formulations for

use as a single booster dose at least two months following primary or booster vaccination.

The bivalent vaccines contain two messenger RNA (mRNA) components of the SARS-CoV-2 virus, one of the original strains of SARS-CoV-2 and the other one in common between the BA.4 and BA.5 lineages of the omicron variant of SARS-CoV-2. This bivalent booster dose is expected to provide immunity against the current circulating omicron variant in the US. [FDA]

PREVENTION

The COVID-19 pandemic functioned as a wake-up call for the world. It highlighted the lack of preparedness to manage highly infectious diseases. The challenges faced during the pandemic led to a considerable improvement worldwide in the healthcare sector. Despite state-of-the-art hospitals and medical facilities, developed countries suffered more losses than developing countries due to delayed action. In the year 6 CE, the city of Rome was devastated by fire. As a result, the first fire brigade was established, known as the "Cohortes Vigilum." Similarly, creating a conglomerate from nations across the world can help check potential disease outbreaks in the future. Allocating proper funds for research and innovation, including pandemic prevention, is another measure that can be taken. As was done with vaccines during the pandemic, finding ways to develop treatments quickly will help reduce mortality due to a novel disease. Better guidelines and correct resources should be made available to the public to ensure their safety during health emergencies. Such practices may help prevent outbreaks from evolving into epidemics and subsequently into pandemics.

CONCLUSION

WHO officially declared COVID-19 disease as a Public Health Emergency of International Concern (PHEIC) on 30 January 2020, with an official death toll of 171. As of 30th August 2022, the number of deaths due to the COVID- 19 disease worldwide is 6,467,023.[66] The number of excess deaths, that is, indirect deaths caused due to the pandemic worldwide, lies in the range of 16.5 to 18 million.[67] Despite having relatively simple preventive measures like wearing an appropriate face mask, maintaining a distance of 1 meter, and avoiding crowded places, the disease spread rapidly worldwide due to people not adhering to existing protocols and delaying seeking medical attention once infected. Despite the mass panic, a joint effort was made globally for fast-paced vaccine development and production against the disease. Vaccine development was expedited at an unprecedented speed, marking it the first time in history wherein a vaccine was approved for usage in such a short duration. The first vaccine candidate was approved for public administration within ten months of the pandemic. The importance and attention paid to vaccine development during the pandemic should chart the course for speedy drug development as well. The worst bout of the pandemic may seem to be over, but there is a strong need to remain vigilant and follow appropriate protocols. We should learn from the COVID-19 pandemic and create a full-fledged international body dedicated to pandemic prevention in the future.[67,68] The course of the pandemic should be carefully scrutinized to avoid future pandemics. The pandemic has paved the way for expedited methods for treatment and prevention of the infection.

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AUTHORS CONTRIBUTION

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CONFLICT OF INTEREST

Authors have no conflict of interest to declare.

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