Review Article

COVID-19 Pandemic - Acute Health Challenges for the Human Beings: A Systematic Review

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ABSTRACT

The COVID-19 outbreak is vindicating to be an unprecedented disaster and critical health issue to humanity in all aspects, including economic, social and psychological, not seen since the 1918 influenza pandemic. It has a too early and hare-brained catastrophic impact on the world. Not only underdeveloped countries but also the countries having high income and said to be well developed are also affected very severely by the outbreak. Since it's coming out in Asia late last year 2019, the virus has spread to every continent except Antarctica. A total of 35,25,116 peoples are infected, and 2,43,540 peoples were died worldwide due to COVID-19 epidemic, and till now, no specific treatment and vaccine against coronavirus have been discovered. The pandemic is moving like a wave - one that may yet crash on those least able to cope. COVID-19 is much more than a health menace as by stressing every one of the countries it plosive; it has the potential to create devastating crises that will leave deep scars. In this article, we performed a review to describe existing literature about COVID-19 epidemiology, pathophysiology, diagnosis and management along with its emotional impact on medical staff and common people and an effort has also been made to light the long-term effects on COVID-19 survivors. Web of Science, Scopus, SciFinder, Pubmed, Medline and EMBASE databases have been searched for relevant articles. During the current scenario, it is not possible to evaluate the full health, social and economic impact of this worldwide disaster; this review represents a picture of the current state of the art and the global implications of this new and yet uncertain pandemic.

Keywords: COVID-19, Emotional aspects, Coronavirus, SARS-CoV-2, Pneumonia, Pandemic-2019.

INTRODUCTION

World Health Organization (WHO) states that emerging viral diseases are the causes of severe health issues and hazardous incidents for humans. During the last two decades, several devastating viral infections have ensued and tried to extermination to humanity. In the year 2002-2003, a viral epidemic arose as severe acute respiratory syndrome coronavirus (SARS-CoV) in China, and twenty-five other countries are also swayed which leads to approximately 8000 infection cases and nearby 800 graves, and in 2009[1, 2], another viral epidemic H1N1 influenza[3, 4] had been recorded. While recently, a newer viral plague named as Middle East Respiratory Syndrome Corona Virus (MERS-CoV) was emerged and firstly identified in Saudi Arabia in 2012 which infected approximately 2500 and caused 800 graves and still having some sporadic cases in the same region[5, 6]. At present, WHO China country office, on December 31, 2019; reported an epidemics of instances in which patients were suffered from lower respiratory tract infections in Wuhan city of China's Hubei Province[7, 8]. The very firstly reported cases of this disease were classified and treated as "Pneumonia"[9]. After intensive investigation, the Chinese Centre for disease control (CDC, China) finds out that the epidemic is due to a novel virus which belongs to the coronavirus (CoV) family[10]. In this view, on February 11, 2020, Dr Tedros Adhanom Ghebreyesus, the WHO Director-General, announced this disease as "Coronavirus disease 2019 (COVID-19)" as caused by a new coronavirus (nCoV).

This nCoV is highly contagious, and we have seen that it has been spread globally very pronto due to which on January 30, 2020, WHO declared this disease as a Public Health Emergency of International Concern (PHEIC). A group of microbiologist explained that coronaviruses (CoVs) are the major pathogens in the emergence of severe respiratory diseases at Wuhan city of China in last 2019. These CoVs are found in different animal species and belong to the single-stranded RNA viruses (ssRNA) family, which is a vast virus family[11]. They can cross "species-barriers" and may cause crankiness in humans which may range from the common cold to harsh and more severe illness. The acuteness and severity of "Severe Acute Respiratory Syndrome coronavirus (SARS)" and the "Middle East Respiratory Syndrome coronavirus (MERS)" we have seen scrupulously in the past[12]. One more remarkable and fascinating information about these viruses is that most probably they are originated from the bats and then moved into the mammalian hosts[13-17]. The dynamics of SARS-Cov-2 are currently undiscovered, but there is speculation that it also has an animal origin[18]. The surreptitious potential for these viruses to evolve to become a pandemic worldwide seems to be a sedate and severe public health risk. Concerning to COVID-19, the WHO raised the fulmination to the nCoV epidemic to the "extremely soaring level", on February 28, 2020[19]. Probably, the effects of the epidemic caused by the nCoV

have yet to emerge as the situation is quickly evolving. On March 11, as the number of COVID-19 cases outside China has increased 13 times and the number of countries involved has tripled with more than 118,000 cases in 114 countries and over 4,000 deaths, WHO declared the COVID-19 a pandemic[20].

World Governments are continuously on work to establish the countermeasures to stem possible devastating effects of the pandemic-health organizations working with coordinating the information flow and outstripping directives and guidelines to mitigate the impact of the threat best. At the same time, scientists throughout the world are working tirelessly to collect the information about transmission mechanisms, the clinical spectrum of disease and developing rapidly new diagnostic techniques, prevention and therapeutic strategies. It is not possible to say about the time when the pandemic will reach to its peak because both the virus-host interactions and the mechanism of evolution of the epidemic have many uncertainties. In this consequence, the therapeutic strategies to deal with the disease are only supportive, and prevention expected at reducing transmission in the community is regarded as the best weapon. In China, lofty isolation measures led to a progressive diminution of cases in the last few days. In Italy, and the northern hemisphere, initially, and subsequently throughout the peninsula, political and health establishment are making implausible efforts to contain a shock wave that is rigorously testing the health system[18]. In the midst of the crisis, the author has chosen to use the scientific databases such as Pubmed, Scopus, Web of Science, SciFinder and springer materials etc. to access the scientific information on COVID-19. The prime aim, therefore, is to collect data and scientific evidence and to provide a comprehensive review of the topic of COVID-19 that will be continuously updated.

AETIOLOGY

CoVs are positive-sense-single-stranded RNA viruses[21, 22], appeared as a crown-like structure under an electron microscope[23] due to presence of glycoproteins spike (S) on the envelope (E).

Table 1: Classification of coronavirus

Order	*Nidovirales*	
Family	*Coronaviridae*	
Subfamily	*Orthocoronavirinae*	
Genera		α-*CoVs*
		β-*CoVs*
		δ-*CoVs*
		γ-*CoVs*

Text Box No. 1
Common Human Coronavirus
Common HCoVs, in immune-competent individuals, can cause common colds and self-limiting upper respiratory infections, but in immune-compromised and elderly populations may also cause lower respiratory tract infections.

CoVs can be grouped into four genera and named accordingly α, β, δ, and γ-CoVs. The classification of coronavirus can be given as in table No. 1. Probably, rodents and bats are the gene sources of α and β CoVs while avian species are the gene sources of δ and γ CoVs. The beta CoVs genus can be divided into five sub-genera[24]. These viruses can cause neurological, hepatic, respiratory, and enteric diseases in different animal species, including camels, cattle, cats, and bats. To date, seven human CoVs (HCoVs) have been identified which are capable of infecting humans. Disease-causing coronavirus to human can be grouped into two categories, i.e. common human coronavirus and other human coronaviruses (see table No. 2). Common human coronavirus can cause common ailments such as cold and related infection (Supplementary information: text box no. 1). In contrast, other human coronavirus is epidemic in nature and cause severe diseases (Supplementary information: text box no. 2). General, estimation suggest that 2% of the population are healthy carriers of a CoVs and that these viruses are to blame for about 5% to 10% of acute respiratory infections[25].

Table 2: Human coronavirus

Common human CoVs		Other human CoVs	
1.	229E (α corona virus)	1.	SARS-CoV
2.	NL63 (α corona virus)	2.	MERS-CoV
3.	OC43 (β corona virus)	3.	SARS-CoV-2
4.	HKU1 (β corona virus)		

Text Box No. 2
Other Human Coronavirus
Other HCoVs cause epidemics with variable clinical severity featuring respiratory and extra-respiratory manifestations. Concerning SARS-CoV, MERS-CoV, the mortality rates are up to 10% and 35%, respectively.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): SARS-CoV-2 belongs to the β-CoVs category. Its shape is round or elliptic and often pleomorphic for with a diameter of approximately 60-140 nm[26]. The genome of nCoVs has 89% nucleotide identity with bat SARS-like-CoVZXC21 and 82 % with human SARS-CoVs[27]. That's why the newly found virus was called SARS-CoV-2. Its genome contains 29891 nucleotides, encoding for 9860 amino acids. Based on genomic analyses scientists concluded that SARS-CoV-2 probably evolved from a strain found in bats. It is heat and ultraviolet rays sensitive. It can be inactivated effectively by the use of several antiseptics and disinfectants such as sodium hypochlorite (6%), hydrogen peroxides, Chloroform, ethanol (75%), isopropanol, monochloramine and peroxyacetic acid etc.[28, 29].

TRANSMISSION

The first case of the COVID-19 disease was linked to direct exposure to the Huanan Seafood Wholesale Market of Jianghan District, Wuhan, Hubei, China[30], therefore, the

animal-to-human transmission was presumed as the primary mechanism for the mode of transmission in patient zero of COVID-19[24]. Nevertheless, subsequent cases were not associated with the above transmission mechanism. Therefore, the virus could also be transmitted from human-to-human, and symptomatic infected people are the most frequent source of COVID-19 spread, it may also be concluded. The possibility of spread before symptoms develop seems to be intermittent, although it cannot be debarred, that's why it is also suggested that individuals who remain asymptomatic could also transmit the virus. This indicates that the use of isolation is the best way to contain this epidemic in close proximities.

The transmission of COVID-19, primarily, occurs through respiratory droplets from coughing and sneezing, same as other respiratory pathogens and through contact routes[20, 25]. In closed spaces, aerosol transmission is also possible. Data related to the spreading of SARS-CoV-2 from China suggested that close contact is necessary for its transmission among individuals. The spread, in fact, is principally limited to family members, healthcare professionals, and other close contacts[18]. Investigation reports suggest the incubation time could be within 3 to 7 days commonly and in exceptional cases may be up to 2 weeks, as the longest time from infection to symptoms was calculated as 12.5 days, while WHO reported it between 2 to 10 days[31, 32]. Data also concludes that this new epidemic can be doubled about every seven days, and on average, each patient can transmit the infection to an additional 2.2 individuals[32]. However, in the exceptional case where the incubation period is longer than two weeks- reflects double exposure[32]. The duration from the incipience of COVID-19 symptoms to death ranges from 6 to 41 days, with a median of 14 days[31]. This term is dependent on the age of the patient and the status of the patient's immune system. It was smaller among patients > 70-years old contrasted with those under the age of 70 years[33]. The severity of the clinical picture seems to be correlated with age (>70 years), co-morbidities such as diabetes, chronic obstructive pulmonary disease (COPD), hypertension, obesity and male sex but currently no scientifically valid explanations have been developed[31, 34, 35].

EPIDEMIOLOGY

Data displayed on the WHO Health Emergency Dashboard (May 06, 2020, 07.00 pm CEST) report 35,25,116 confirmed cases worldwide since the beginning of the epidemic and 2,43,540 (6.90%) cases have been deceased[36]. Initially, the disease was evolved in China, but today (May 06, 2020) it had been spread worldwide. There are 212 countries and territories around the world, and two international conveyances are affected by the outbreak of COVID-19[37]. In the current time, the Europe continent is profoundly suffering from highest cases as of now confirmed 14,94,073 and deceased 1,44,114; after Europe, North America is also having 2nd high infected cases as of now confirmed 13,48,588, and deceased 79,700; while in China, all COVID-19, patients were recovered[37]. No death and no new case of COVID-19 has been reported since last week in China. The most up-to-date information on the epidemiology of this emerging pandemic can be obtained from the following sources:

1. WHO Health Emergency Dashboard: Coronavirus (COVID-19)

(https://covid19.who.int/)

2. Worldometer: COVID-19 coronavirus pandemic

(https://www.worldometers.info/coronavirus/)

3. Johns Hopkins University and Medicine: Coronavirus resource centre: COVID-19 Dashboard by the Center for Systems Science and Engineering

(https://coronavirus.jhu.edu/map.html)

GENOME STRUCTURE AND PATHOPHYSIOLOGY

CoVs are enveloped having positive-sense-single-stranded RNA (+ssRNA) viruses with nucleocapsid. To define the pathogenetic mechanisms of SARS-CoV-2, its viral and genome structure must be considered as necessary. In SARS-CoV-2, the genomic structure is organized in a +ssRNA of approximately 30-32 kb with a 5'-cap structure and 3'-poly-A tail. This +ssRNA is known as genomic RNA (gRNA). The genomic RNA (gRNA) is used as a template to directly translate polyprotein 1a/1ab (pp1a/pp1ab)[38], which encodes non-structural proteins (nsps) to form the replication-transcription complex (RTC)[39]. The transcription work occurs through RCT, which organized in a double-membrane vesicle and transcription termination occurs at transcription regulatory sequences located between open reading frames (ORFs). ORFs work as templates for the production of subgenomic-mRNAs (sgmRNAs). RTC synthesizes a nested set of subgenomic RNAs (sgRNAs). These sgRNAs possess common 5'-leader and 3'-terminal sequences. Minus strand gsRNA serves as the templates for the production of sgRNA[40].

In an atypical CoVs genome, at least six ORFs can be present. The 1st ORFs (ORF1a/b), about 2/3rd of the whole genome length can encode 16 non-structural proteins (nsps). Among these ORFs, a frameshift between ORF1a and ORF1b has been found. This frameshift guides the production of polypeptides (both pp1a and pp1ab). These polypeptides are processed by virally encoded protease. Apart from ORF1a and ORF1b, other ORFs which are the 1/3rd of the genome near the 3'-terminus encode certainly for structural proteins, including spike (S), membrane (M), envelope (E), and nucleocapsid (N) proteins and accessory protein chains [11]. Accessory and special structural proteins such as HE protein, 3a/b protein and 4a/b protein, translated from the dedicated sgRNAs are present on different types of CoVs. There is an absolute correlation between the pathophysiology and virulence of CoVs, which clearly links the function of nsps and structural proteins. Various research underlined that nsps could block the host immune responses[38, 41].

Structural proteins play a crucial and significant role in pathogenicity and virulence mechanism. Among the structural proteins, the envelope (E) has a pivotal role in virus pathogenicity as it promotes viral assembly and release. Spike (S) are glycoproteins composed of two subunits (S1 and S2). Spikes (S) on the viral surface contains homotrimers of S proteins acts as guiding link to the host receptors[42]. A spike mutation probably occurred in late November 2019, triggered jumping to humans, seen in recent research reports[43]. Viral mutations are the key to explaining probable disease relapses. To determine the structural characteristics of SARS-CoV-2 in pathogenetic mechanisms, an intensive research will be needed.

The clinical spectrum of COVID-19 is highly diversified from asymptomatic forms to clinical infirmities characterized by severe respiratory failure that requires mechanical ventilation and assistance in an intensive care unit (ICU), to multi-organ and various other systemic manifestations in terms of sepsis, septic shock, and multiple organ dysfunction syndromes (MODS)[44], along with occasional asymptomatic infections. The main symptoms of COVID-19 are reported in table 3 (Supplementary information: text box no. 3).

Table 3: Common Symptoms Associated with COVID-19

Telltale Symptoms Associated with COVID-19
Fever
Dry cough
Dyspnea
Headache
Sore Throat
Rhinorrhea

Text Box No. 3
Symptoms of COVID -19

The most common symptoms at the onset of COVID-19 illness are fever, cough, and fatigue, while other symptoms include sputum production, headache, haemoptysis, diarrhoea, dyspnoea, and lymphopenia.

Several research reports observe that SARS-CoV-2 can cause severe acute respiratory syndrome which can be classified and treated as pneumonia[13, 45-48]. It is a very complex mechanism by which SARS-CoV-2 produces pneumonia[18, 38, 41]. Clinical and preclinical researches indicate that the viral infection is capable of producing an excessive immune reaction in the host. In some cases, a "cytokine storm" type reaction takes place, which causes extensive tissue damage[49]. The virus may pass through the nasal and larynx mucous membrane and then entered into the lungs through the respiratory tract. Then virus would attack to the targeting organs which express angiotensin-converting enzyme 2 (ACE2) such as lungs, kidney, heart and GIT[50-52]. From this stage, the 2nd attack of disease is started, which causes patients condition to aggravate round 7 to 14 days after onset of disease. At this stage, the production of antibodies may be reduced, which results in immunocompromization. The risk of COVID-19 should be considered primarily in patients with new-onset fever and respiratory tract symptoms (e.g., cough, dyspnea)[53, 54]. It should additionally be considered in cases where severe lower respiratory tract disease has been detected without any ostensible cause[33]. Although these syndromes can arise with other viral respiratory infections, the likelihood of COVID-19 is increased if the patient:

(1) Stays in or has visited within the earlier 14 days to a place where community transmission of SARS-CoV-2 is continuing

(2) Has had close contact (Supplementary information: text box no. 4) with a confirmed or suspected case of COVID-19 in the previous 14 days, including through work in health care settings.

Text Box No. 4
Close Contact

Close contact includes being within approximately six feet (about two meters) of a patient for a prolonged period of time while not wearing personal protective equipment (PPE Kit) or having direct contact with infectious secretions while not wearing personal protective equipment.

Based on clinical manifestations, Chineses CDC report divides the disease by its severity in patients[26], as follow

1. **Mild disease:** Approximately found in 81% of patients, maybe non-pneumonic and mild pneumonia may found. Main manifestations are mild fever, dry cough, sore throat, nasal congestion, malaise, headache, muscle pain. Dyspnea is not present generally. Diarrhoea may present or may not.

2. **Severe disease:** Approximately found in 14% patients, main manifestations along with mild disease are - Cough, respiratory frequency ≥ 30/min, dyspnea (or tachypnea in children), blood oxygen saturation (SpO2) ≤ 90% on room air, the ratio of the partial pressure of arterial oxygen/ percentage of inspired oxygen (PaO2/FiO2 ratio or P/F) < 300, and/or lung infiltrates > 50% within 24 to 48 hours. The fever symptom must be checked carefully as at this stage, and it may be moderate or even absent. Cyanosis (greyish or blueish colour of nails, lips, skin or around eyes) can occur in children. At this stage, clinical diagnosis is highly recommended, and for excluding complications, radiologic imaging must be used.

3. **Critical disease:** Approximately found in 5% patients, main manifestations along with severe disease are – severe dyspnea [tachypnea in children (> 30 breaths/min)], hypoxia and sudden attack of respiratory failure (SpO2 < 93% on room air). This septic shock leads to multiple organ dysfunction (MOD) or failure (MOF) and finally may cause death[26].

Among the severe clinical indications, there are severe pneumonia, Acute Respiratory Distress Syndrome (ARDS), sepsis, and septic shock are leading and life-threatening.

The respiratory insufficiency severity and the diagnostic criteria of septic shock and sepsis can be used as a reference[55].

1. **Pneumonia:** In the occurrence of COVID-19, infection, pneumonia appears to be the most severe and frequent manifestation, characterized primarily by fever, cough, dyspnea (Shortness of breath), and bilateral infiltrates on chest imaging[35]. There are no precise clinical features that can yet consistently distinguish COVID-19 from other respiratory viral infections. Headaches, sore throat, and rhinorrhea (runny nose) also seen as less common symptoms. Additional to respiratory symptoms, some gastrointestinal symptoms such as nausea and diarrhoea have also been reported in some patients[35, 44]. Huang et al. reported that patients (n. 41) suffered from COVID-19 have symptoms of fever, dry cough, dyspnea and malaise (general feeling of discomfort due to illness). Chest computerized tomography (CT) scans of such patients showed pneumonia with abnormal findings in all cases[56]. Chest CT of COVID-19 patients shows most commonly ground-glass opacification (an act or the process of becoming opaque) with or without consolidative abnormalities, consistent with viral pneumonia[53]. Abnormalities are bilateral, have a peripheral distribution, and involve the lower lobes of lungs. Pleural thickening, pleural effusion, and lymphadenopathy (disease of the lymph nodes, in which they are strange inconsistency or in size) come under less common findings during COVID-19 pneumonia[54, 57]. Chest CT may help make the diagnosis, but no finding can completely rule-in or rule-out the possibility of COVID-19.

2. **Acute Respiratory Distress Syndrome (ARDS):** ARDS is suggestive of a severe new-onset respiratory failure. Diagnosis of ARDS requires clinical and ventilatory criteria. These are classified in three forms based on the degree of hypoxia [reference parameter is the ratio of the partial pressure of arterial oxygen/ percentage of inspired oxygen (PaO2/FiO2)][58, 59]:

   a. **Mild ARDS:** When the ratio of the partial pressure of arterial oxygen/ percentage of inspired oxygen (PaO_2/FiO_2) is more than 200 mm of Hg and less than 300 mm of Hg[58-60].

   b. **Moderate ARDS:** When the ratio of the partial pressure of arterial oxygen/ percentage of inspired oxygen (PaO_2/FiO_2) is more than 100 mm of Hg and less than 200 mm of Hg[58, 59].

   c. **Severe ARDS:** When the ratio of the partial pressure of arterial oxygen/ percentage of inspired oxygen (PaO_2/FiO_2) is less than 100 mm of Hg[58, 59].

   It is suggestive to ARDS that when PaO_2 is not available, a ratio blood oxygen saturation to the percentage of inspired oxygen (SpO2/FiO2) can be used, and it must be ≤ 315. Lungs ultrasound demonstrating bilateral opacities (lung infiltrates > 50%), chest radiograph and CT scan are some chest imaging techniques which are also utilized for diagnosis purpose. In some cases, where pulmonary oedema is prominent, echocardiography can be helpful[60, 61].

3. **Sepsis:** International Consensus defines sepsis as "a life-threatening organ dysfunction provoked due to dysregulated host response to a speculated or documented plague, with organ dysfunction"[62]. The clinical representations of COVID-19 patients with sepsis are pretty serious. The malady is characterized by an ample spectrum of manifestations and symptoms of multiorgan intentness. These manifestations and symptoms include respiratory indications such as severe hypoxemia and dyspnea, renal damage with decreased urine output, tachycardia, modified mental status, and dynamic remodeling of organs. All these can be determined by comparing the reference laboratory data to observed data of high lactate, hyperbilirubinemia, acidosis, coagulopathy, and thrombocytopenia. The reference for the evaluation of multiorgan damage and the related prognostic significance is the Sequential Organ Failure Assessment (SOFA) score, which predicts ICU mortality based on lab results and clinical data[63-65].

4. **Septic Shock:** It is a life-threatening condition caused by severe localized or system-wide infections that require immediate medical attention. In this scenario, circulatory and cellular/metabolic abnormalities such as serum lactate level greater than two mmol/L (18 mg/dL) are present, which is generally associated with increased mortality. Main manifestations are low blood pressure, pale and cool arms and legs, chills, difficulty in breathing and decreased urine output. Mental confusion and disorientation may also develop quickly. Because patients regularly suffer from persisting hypotension despite volume resuscitation, the treatment with a vasopressors agent is required to keep a mean arterial blood pressure ≥ 65 mmHg along with other emergency treatment which may include supplemental oxygen, intravenous fluids, antibiotics and other medications etc[66, 67].

EVALUATION

Most countries are employing clinical and epidemiologic data to determine who should have to be performed testing? India is also developed as a standard procedure for the evaluation and investigation of the COVID-19 disease. According to the treatment protocol to COVID-19 and epidemiological data, most COVID-19 patients have fever along with other symptoms such as acute respiratory illness (e.g., cough, difficulty in breathing). If a person who is under investigation, it is recommended that practitioners immediately put in place to control infection and takes prevention measures (isolation and quarantine measures). Initially, they recommend testing of all sources of respiratory disease[10, 68].

Furthermore, they recommend utilising epidemiologic factors to aid in decision making. There are epidemiologic factors that help in the decision on who to test. This includes everyone who has had close contact (Supplementary information: text box no. 4) with laboratory-confirmed COVID-19 patient, within 14 days of symptom onset or a history of travel from concerning geographic areas within 14 days of symptom onset[10, 69].

Collection of Sample and Processing

Samples can be collected from both the upper respiratory tract (URT) and lower respiratory tract (LRT) parts, as recommended by WHO. Usually naso- and oropharyngeal samples from URT and expectorated sputum, endotracheal aspirate, or bronchoalveolar lavage (BAL) can be collected from LRT. BAL sample collection must only be performed in mechanically ventilated patients. Advantage of BAL sample collection is that lower respiratory tract samples seem to remain positive for a more extended period after the encounter the infection[70].

The collected samples must be stored at four°C and amplify the saliva or mucus sample extracted genetic material through a reverse polymerase chain reaction (RT-PCR). Once the genetic material is sufficient, the next step is the search of those portions of genetic codes of the CoV that are conserved. For this purpose, the probes used are based on the initial gene sequence. These gene sequences are released by School of Public Health, Fudan University, Shanghai and Shanghai Public Health Clinical Center, China on Virological.org, and following confirmatory evaluation by other labs (extra checkpoint in the testing of SARS-CoV-2). If the test results are positive, it is highly recommended that the test must be repeated for confirmation. In confirmed COVID-19 patients, the laboratory evaluation should be repeated to evaluate for viral clearance prior to being released from observation or discharging from hospital to home quarantine[70, 71].

At the early stage of disease COVID-19, there is a normal or decreased total leukocyte count and a reduced lymphocyte count to have appeared as the most important laboratory examinations. As a negative prognostic factor lymphopenia may appear. On examination of liver-functions increased values of liver enzymes, LDH, muscle enzymes, and C-reactive protein can be found, but procalcitonin may be at its standard value. In severe patients, D-dimer value is raised, blood lymphocytes declined persistently, and multiorgan imbalance (high amylase, coagulation disorders, etc.) has been found as the primary laboratory diagnostic parameter[70, 72].

COMPLICATIONS AND LONG-TERM EFFECTS OF COVID-19

Roughly long-term complexities among survivors of plague with SARS-CoV-2 having clinically significant COVID-19 disease are not yet accessible. Some COVID-19 survivors may find their bodies switched into long term by COVID-19, as it is, much more than the lungs disease. The mortality rates globally remain between 3% to 7%[36, 73]. The experts say that the patients who have mild symptoms of the disease and not required ventilation during the condition can expect no lasting harm and these seen as mild cold and flu[74, 75]. Some people about 1 in 6 will have complications, including some that are life-threatening. These complications are acute respiratory failure, pneumonia, acute respiratory distress syndrome (ARDS), acute liver injury, acute cardiac injury, secondary infections, acute kidney injury, septic shock, disseminated intravascular coagulation and rhabdomyolysis[76-78]. Longer ICU patents often suffer long-term cognitive and emotional effects of being sedated termed as “post-intensive care syndrome (PICS)” or post ICU delirium which also describes it as a type of post-traumatic stress[79]. When these patients are released from ICU may develop some mental health issues like depression and anxiety. PICS patients have some combination of physical impairment (weakness and malnutrition), cognitive impairment (memory, attention, and mental sharpness or ability to solve problems all will may be decreased), and psychiatric impairment (panic disorder, obsessive-compulsive disorder). The people who are 65 years and older, living in a nursing home for a long-term care facility, having chronic lung, kidney, heart and liver disease are at most risk[80].

Covid-19 patients have a 20-30% decrease in lungs capacity and may suffer lifelong from shortness of breath. Patients go under ICU care, and required ventilation are more prone to permanent lungs damage and may develop ARDS[75]. Experience-based on SARS and MERS, it may be possible that lungs fibrosis may develop after recovery from severe disease[80]. Some COVID-19 patients in China were on ECMO life-support machine-on temporarily to support the lungs during regain of lung function; however, it may be possible that some patients never restore the lung function[81]. it is not correct to all, as it depends on how much lung tissue was destroyed by the virus[74].

It has seen that about 20% of COVID-19 patients admitted in China, have heart complications, heart injury and blood clots during the hospitalization[74, 82], another study reveals that 16% of patients developed arrhythmias while some other may develop myocarditis[75]. Also, the viral diseases may destabilize plaques in arteries, resulting in the blockade and putting patients at the risk of heart disease. Increased blood clotting is another complex problem in COVID-19 patients for doctors treating to them. In Spain, a blood clotting problem is highly prevalent in COVID-19 patients as there every patient is also treated with anticoagulants[83]. These conditions are associated with and increase the risk of in-hospital death.

According to the International Society of Nephrology, Belgium, in 25-50% of patients kidney abnormalities have been seen who develop the severe type of the disease. As COVID-19, is an infectious disease that leads to a cascade of immune change which ultimately leads to sepsis, and sepsis is characterized by compromisation in multi-organ systems. It is seen that some individuals with sepsis can get acute kidney injury[75].

Neurological manifestations are also possible in COVID -19 patients. Same as other coronaviruses, it can also invade the human nervous system of infected humans. In the brain, it can enter through the olfactory bulb travelling via olfactory neuron pathway[84]. In the brain, it can affect medulla oblongata, which controls the cardiorespiratory physiology of our body. A study conducted on COVID-19 patients from China reported that 36% of patients suffer from neurological manifestations which include dizziness, headache and impairment in smell and taste[75].

Even after the five months of COVID-19 pandemic, doctors are not yet fully aware of the effects of the new coronavirus and are trying to find out what the long-term effects of this new coronavirus can be.

MANAGEMENT AND TREATMENT OF COVID-19

There is no precise antiviral medication recommended for COVID-19, and no vaccine is possible currently. Only essential supportive treatment is provided to COVID-19 patients, and yet the role of antiviral agents is to be proved. The medication is entirely symptomatic, and oxygen therapy is the primary treatment intervention for patients with severe infection. In cases of respiratory arrest refractory to oxygen therapy, mechanical ventilation may be necessary while hemodynamic support is crucial for managing septic shock[10].

On January 28, 2020; WHO released guidelines and scientific evidence derived from the treatment of previous epidemics from HCoVs. This principle guideline addresses measures for recognizing and sorting patients with severe acute respiratory disease; infection prevention and control strategies; early monitoring and supportive therapy along with the principles for respiratory arrest, ARDS, septic shock management; prevention of complications, treatments, special considerations for pregnant patients and laboratory diagnosis are included[85].

Intubation and protective mechanical ventilation

Special precautions are necessary during intubation (**Intubation** is the procedure of inserting a tube, known as an endotracheal tube (ET), into the airway through the mouth). The ventilation procedure should be executed by an expert operator who uses personal protective equipment (PPE includes FFP3 or N95 mask, protective goggles, disposable gown long sleeve raincoat, disposable double socks, and gloves). If it is feasible, rapid sequence intubation (RSI) must be performed[86].

Non-invasive ventilation

Practically, non-invasive ventilation techniques can be used in non-severe forms of respiratory failure type of patients. But, if the condition of a patient does not improve or even worsen within a short period (1–2 hours), it is always to prefer mechanical ventilation. Non-invasive ventilation is also known as High-Flow Oxygen Therapy (HFNO). The experts' panel, points out that HFNO must be performed by systems having an excellent fitting interface, which will not create widespread dispersion of exhaled air, and their use can be considered at low risk of airborne transmission[87].

Other therapies

Among other therapies, medication with therapeutic agents is recommended. From the reports, it has been seen that applied therapeutic agents are more or less used only for symptomatic treatment. The use of systemic corticosteroids is not suggested as a therapeutic agent for the management of viral pneumonia and ARDS. Blind therapy by the inappropriate and unselective administration of antibiotics must be avoided, although some centres recommend it[88]. Although no antiviral treatments have been approved, several approaches have been proposed. Till now, in various countries, the following drugs are used against COVID-19[57] (Table 4).

Table 4: Therapeutic Agents used against COVID-19

S. No.	Drug Name
1	Lopinavir
2	Ritonavir
3	Chloroquine
4	Hydroxychloroquine
5	Remdesivir
6	Tocilizumab
7	Azithromycin
8	Ribavirin
9	Alpha-interferon

PREVENTION

Preventive measures are the best practice to limit the spread of COVID-19, until now, no effective medication/vaccine is available, and the best is prevention from exposure to the virus. Preventive strategies are mainly focused on the isolation of COVID-19 patients and careful control of infection, including appropriate procedures to be adopted during the diagnosis and clinical care to an infected patient. For instance, precautions related to droplet, contact, and airborne infection must be adopted during specimen collection, and sputum induction should be avoided. Suggested actions from Indian Government included quarantine measures and social distancing phenomenon applied on all class of peoples belongs from schools, universities, market places and industries and implementation of remote working policies, and avoidance of all non-essential travel and use of public transport[89-91].

General recommendations for prevention of COVID-19

The WHO, other health care organizations and Government of various countries, have issued the general guidelines for the preventions of COVID-19. These includes[92]

1. Avoid close contact with SARS-CoV-2 infected subjects and patients suffering from acute respiratory infections.

2. Frequently and regularly, wash your hands with soap or sanitize your hand with an alcohol-based sanitizer,

especially after getting in touch with an infected person or their environment.

3. Stay away from unprotected contact with inhouse or wild animals.

4. Patients with symptoms of acute airway infection must keep their distance, cover coughs or sneezes with disposable tissues or clothes and make to wash their hands with soap or sanitizer, and avoid contact with face and mouth.

5. Follow the rule of strict hygiene measures for the prevention and control of infections at your house and your workplace.

6. Immune-compromised individuals must avoid public gatherings.

7. Healthcare workers (Doctors, Pharmacists, Nurses and other paramedical staff), public administrative staff, police officers, media persons and all other personnel [In India all these are called Corona Warrior, the name given by Hon'ble Prime Minister of India Shri Narendra Modi[93]] who are engaged in the control, management and prevention of pandemic must utilize PPE (Supplementary information: text box no. 5). Ordinary people also should use the mask, and it may be surgical if the surgical mask is not available should cover their face and nose with clean and washed clothes.

Meanwhile, scientific research is arising to develop a coronavirus vaccine globally. In recent days, China has declared about the first animal tests[78]. Researchers from the University of Queensland in Australia have also proclaimed that, after completing the three-week in vitro study, they are moving on to animal experimentation[94]. Furthermore, in the National Institute for Allergy and Infectious Diseases, USA, has stated that a phase 1 trial has started for a novel coronavirus immunization in Washington State[95, 96].

Text Box No. 5

Personal Protection Equipment (PPE) Kit

PPE includes FFP3 or N95 mask, protective goggles, disposable gown, long sleeve raincoat, disposable double socks, and gloves.

Enhancing healthcare team outcomes

Since the initial outbreak of coronavirus (COVID-19) in Wuhan, China, the ailment is spreading globally. Persons at the extreme of ages and those who are immuno-compromised are at the most significant risk. All health care personnel should be aware of the presentation of the ailment, workup, and supportive care. Further, health care professionals should be conscious of the precautions necessary to avoid the contraction and spread of the disease[97].

EMOTIONAL ASPECTS OF COVID-19

As WHO in March 2020 declared COVID-19 a pandemic and at present time coronavirus illness is present over 210 countries and territories around the world and two international conveyances[37]. This outbreak causes an anxiety stage and emotional distress in the world community. These thoughts of distress and anxiety can occur even in people who are not at high risk, -of getting sick, in the face of a virus with which the ordinary people may be unfamiliar. A column written on Bloomberg.com under the headline “Hospitals Are Losing the Coronavirus Battle” explains the conditions of health professional working for COVID-19 patients in Britain. They tell that health workers are always dealing with high-octane situations and treating Covid-19 patients face “life-threatening” due to shortages of PPE, they also reported that four U.K. doctors have died from Covid-19, and the youngest was 55. There will be more to come if the Government doesn’t quickly resolve the shortages of personal protective equipment, or PPE, in hospitals and medical centres [98]. A lot of examples are there that medical personnel are also become COVID-19 patients and also may take the virus from hospitals to home and make infected to their dear and near ones. Dr Wendy Dean, a psychiatrist, says that health care providers are used to do anything and everything to help their patients. Still, inadequate and amateurish protective gear and triage procedures will overpower them to make “exquisitely painful” decisions and if they can’t accommodate the care they typically consider is medically crucial for their patients, they may experience a phenomenon known as “moral injury”[99].

There is a high level of stress among the local peoples have seen as there no firm estimate of how long pandemic will last and how long our lives will be disrupted or whether or not our loved ones or we will be infected[86, 100]. Reports published entitled “Vicarious traumatization in the general public, members, and non-members of medical teams aiding in COVID-19 control” and “Traumatization in medical staff helping with COVID-19 control” somewhere throw efficient light on the matter of emotional injury and traumatic situation of ordinary peoples and corona warriors[86, 100]. Li et al. reported how much people and medical staff suffer from vicarious traumatization and how this vicarious traumatization of non-front-line medical staff is more serious than that of front-line medical staff. In Italy, medical staff have to work under high workload and intermittent lack of PPE. Racism issue has also seen against the health care professionals. These health care professionals, as working front-line corona Warrier, potentially have on a higher risk of being infected and always standing as a wall between coronavirus and healthy peoples. We don’t have to forget that many doctors and nurses become infected and many of them died due to COVID-19.

Previous research has revealed a profound and broad spectrum of psychological impact that outbreaks can inflict

on people[101]. New psychiatric symptoms in people without mental illness can occur or aggravate the condition of those with pre-existing mental illness and cause distress to the caregivers of affected individuals[83]. Most health professionals working in isolation units and hospitals very often do not receive any training for providing mental health care[101]. Barbisch et al. described how the confinement "caused a sense of collective hysteria, leading the staff to desperate measures"[102].

In India and also other countries (Saudi Arabia, Britain, Germany), reported suicidal cases in some SARS-CoV-2 infected persons[103]. In Italy, two infected nurses committed suicide in a period of a few days, probably due to fear of spreading COVID-19 to patients[104]. Fear and anxiety of falling sick or dying, helplessness may drive to take the suicidal step. Finance Minister and Economist from Germany got suicide because could not able to bear and cope with the stress about the economic fallout due to COVID-19 and turned himself as a hopeless fellow who could not be able to manage citizen's expectations for financial aid. In the United States (US), the COVID-19 Pandemic's New Epicenter, a dedicated Lifeline (the National Suicide Prevention Lifeline) was activated for emotional distress related to COVID-19 to prevent suicide. Any how COVID-19 is a situation and the world have to get rid of at any cost.

CONCLUSION

COVID-19 is not only a severe outbreak for human health and wellbeing over worldwide but is set to become one of the expensive pandemics in this neoteric history. Notably, 60 years of age of people or those already with chronic diseases such as diabetes and cardiovascular issues may be affected severely by this gorgoneion pandemic. Coping with this type of emergencies is never an easy task; it will be particularly hard and unprecedented challenges for all of us from a health perspective. Thus, Institutions and countries need to work together in the spirit of global health, with the expertise and capabilities helping and interacting each other with passion and intelligence on new and often very complex issues having limited resources.

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