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The COVID-19 Pandemic and Its Prediction: A Review of Epidemiology and Preventive Measures for the Containment of Infectious Disease

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Abstract- The emergence of the Coronavirus Disease-2019 (COVID-19) outbreak, caused by the novel coronavirus Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), has led to a pandemic across the world, as declared by the World Health Organization (WHO) on March 11, 2020. The world has faced similar coronavirus outbreaks caused by the Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) in 2003 and 2013, respectively. In this review, we summarize the latest published literature on the epidemiology, dynamics of transmission, pathogenesis, clinical features, diagnosis, and management of COVID-19. Moreover, the prediction model is designed and developed to forecast the number of fatalities and affected people in a given population to improve the response to the COVID-19 pandemic. Currently, many researchers are working on preventive mechanisms and clinical trials for the development of potential therapeutics and vaccination as a global health priority for infectious disease. Furthermore, it is emphasized that the community transmission of COVID-19 can be halted by early case detection, contact tracing, and isolation of the infected individuals. The impact of social (e.g., large-scale quarantine, lock-down, and travel restrictions) and personal restrictions (e.g., physical distancing, hand hygiene, and face masks) on the current pandemic situation is analyzed in the review in detail. Lessons learned amid COVID-19 pandemic play an important role in the prevention of future outbreaks. The statistical analysis for prediction and epidemiology is mentioned as well.

Keywords- COVID-19, Coronavirus, Prevention, Infectious Disease, Public Health Measures, SARS - CoV-2

I. INTRODUCTION

The SARS-CoV-2 has emerged as one of the deadly pathogens causing respiratory infections in human beings [1]. It has the ability to cause infection in multiple host species, manifesting as a number of diseases, thus making it a complex virus [2]. The animal coronaviruses rarely infect human beings and have human to human transmission as with SARS-CoV (Severe Acute Respiratory Syndrome Coronavirus), MERS-CoV (Middle East Respiratory Syndrome Coronavirus), and now with SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus-2), which is regarded as the novel coronavirus. All of these viruses are betacoronaviruses and have an animal reservoir with their origin in bats [3-4]. Thus, the most common source of these zoonotic infections is the interaction between wild animals and human beings frequently [5]. The Coronavirus Disease is termed as COVID-19 by WHO with reference to its first case reported in Wuhan, Hubei Province, Central China in December 2019 among the patients who presented with pneumonia with a history of frequent exposure to Huanan seafood wholesale market [6-7]. It is caused by SARS-CoV-2 [8]. The SARS-CoV-2 is an enveloped virus having non segmented, positive-sense, single-stranded RNA characterized by club-like projections on its surface [2][5]. It is regarded as the seventh member of the Orthocoronavirinae subfamily causing infection in humans [6]. Prof. Yong-Zhen Zhang led his research team to publish the first genome sequencing of SARS-CoV-2 on January 10, 2020 [9]. The novel coronavirus genome shares 79.5% identical sequencing with SARS-CoV and has an approximate number of 29,700 nucleotides in its genome [10]. The large diversity in genomic characteristics and frequent genetic recombination is largely responsible

for the periodic spillover events [11].

1.1 *COVID-19 as a Pandemic:*

WHO has characterized the COVID-19 outbreak as a pandemic on March 11, 2020 [12]. It is regarded as the first pandemic due to the novel coronavirus. It is spreading worldwide due to the lack of pre-existing immunity against this new virus. In a particular pandemic, the investigation phase marks its beginning which is followed by the recognition, initiation of the disease, and an acceleration phase. At the termination of the acceleration phase, there is a peak of illnesses followed by a decrease in illnesses, known as the deceleration phase. Different phases of a pandemic can be present in different countries or in different areas of the same country at a specific time. New influenza viruses have been known to emerge resulting in four epidemics in the past century [3].

After the emergence of coronavirus in China, which was discovered in the patients with pneumonia and isolated from the epithelial cells of the human airway by unbiased sequencing of the obtained samples, it spread quickly within a month during the time of Chinese New Year when a large number of Chinese people mobilize and travel from one place to another [6][8]. Thus, causing lower respiratory tract infections inpatients with pneumonia [8]. Asymptomatic transmissions, delayed diagnosis, and insensitivity of diagnostic reagents are responsible for underestimation of the infected individuals [13]. According to the latest WHO COVID-19 Dashboard on April 21, 2020, at 09:00 (CEST), there are a total number of 84,239 confirmed cases and 16 new cases with 4,642 deaths reported in China [14]. The daily confirmed COVID-19 casualties are represented in Fig. 1 [15]. The epidemic in China spread to the rest of the world including South Korea, Thailand, and Japan, out of which 95% of the people had been to Wuhan recently [4]. WHO has declared COVID-19 a Public Health Emergency of International Concern (PHEIC) [16]. Thus, the novel coronavirus made its way to infect humans in Europe, Americas, Eastern Mediterranean, Western Pacific, South-East Asia, and Africa with Europe having the highest number of confirmed cases among the other WHO regions on April 21, 2020, at 09:00 (CEST). United States of America, Spain, Italy, Germany, The United Kingdom, France, Turkey, China, Islamic Republic of Iran, Russian Federation, Brazil, and Belgium have reported the highest number of confirmed cases while the highest numbers of deaths have been reported in USA, Italy, Spain, France, The United Kingdom, Belgium, Iran, China, Germany, Netherlands, Brazil, and Turkey. Globally, there are 2,356,414 confirmed cases, 72,397 new cases, and 160,120 deaths as reported to WHO till April 21, 2020 at 10:00 (CEST) [14]. The daily confirmed cases of COVID-19 globally are represented in Fig. 2 [15]. Whereas 8273 cases and 775 deaths were reported due to the SARS outbreak in 2003, and 1139 cases with 431 deaths were reported due to MERS in 2013 [17].

II. EPIDEMIOLOGY

The exponential growth of disease has been observed in the early outbreak before the quarantine strategies were imposed on January 20, 2020 [17]. Recently, the delayed diagnosis and reporting of the cases have become the reason for a decline in the pandemic situation [18]. The estimated value of a basic reproductive number (Ro) of COVID-19 infection in the early outbreak is 2.68, which is higher than both SARS (2-5) and MERS (<1) [17][19-22]. Ro is the average number of people to which each contagious patient of COVID-19 infection transmits the disease. The reproductive value of SARS-CoV-2 indicates that one patient is responsible for transmitting the infection to two to three individuals as Ro values have been calculated in-between 2 and 3.5 in various studies [18-19][23]. Ro value greater than 1 predicts that the pandemic will increase and efforts are required to reduce it to less than 1 [18]. The incubation period of SARS-CoV-2 ranges from 0 to 24 days with a mean of 6.4 days, greater than the incubation period of SARS-CoV (4.6 days) and MERS-CoV (5.2 days) [17][19][24-26]. The WHO assumes an incubation period of the novel coronavirus ranging from 0 to 14 days and the European Centre for Disease Prevention and Control (ECDC) assumes it to range from 2 to 12 days [25][27]. The duration of the incubation period may be shorter for asymptomatic and mildly symptomatic patients [28]. All age and sex groups are generally prone to COVID-19 infection [29]. The mean age of the infected people is 47 years [30]. More cases have been reported in males i.e. 59% of the total cases constitutes the male gender [18][31]. Early studies of transmission dynamics have shown that the children may present with milder symptoms [18]. The deaths from COVID-19 have been observed in an age group ranging from 48 to 89 years with a median age of 75 years [32]. The case-fatality rate of COVID-19 versus median age is represented in Fig. 3 [15]. Studies suggest that the Case-Fatality Rate (CFR) in Wuhan, China is estimated to be 3% [20]. CFR is the ratio between confirmed deaths and confirmed cases. In order to have a deep insight into the relationship between confirmed deaths and confirmed cases, it is analyzed for different regions of the world as represented in Fig. 4 [15].

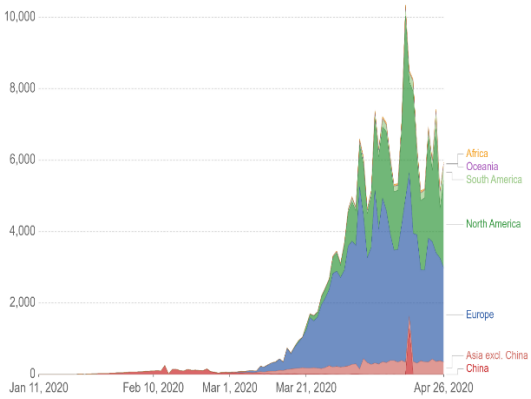


Fig. 1. Daily confirmed COVID-19 deaths

2.1. Transmission:

Studies indicate that snakes and pangolins are the intermediate hosts of the novel coronavirus while that of SARS and MERS are palm civets and dromedary camels, respectively [33-35]. The early cases of COVID-19 infection suggest animal-to-human transmission [18]. This has been demonstrated by a study which reports that almost 55% of the total 425 early cases were related to the seafood market while later it spread via a human-to-human transmission with infections in people having no contact history with Wuhan market or wild animals in the late December [18][36]. A number of infections were diagnosed among the healthcare professionals, indicating nosocomrial transmission of COVID-19 [17-18]. So, it becomes clear that SARS-CoV-2 infection occurs by viral exposure [8]. The mode of transmission of the novel coronavirus is via respiratory droplets, aerosols, aspirates, close contacts, and feco-oral transmission. Public gatherings are responsible for the presymptomatic transmission of the disease.

According to a recent report, asymptomatic individuals and convalescents may also transmit the infection. The recovered patients continue to be a potential source of COVID-19 pneumonia until 2 weeks after the termination of symptoms [37-40].

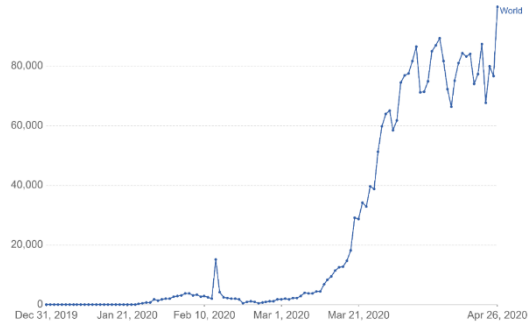


Fig. 2. Daily confirmed COVID-19 cases

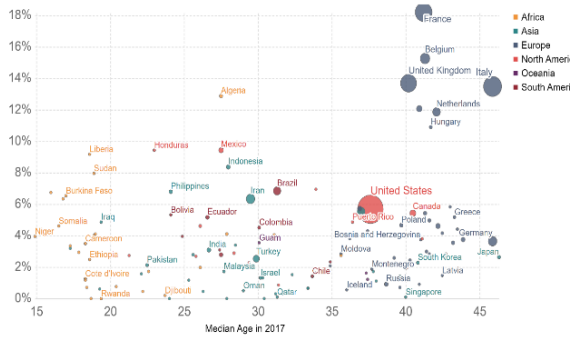


Fig. 3. Case fatality rate of COVID-19 vs. Median Age, Apr 26, 2020

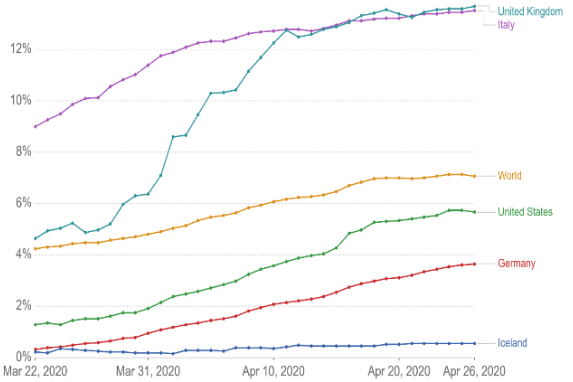


Fig. 4. Case fatality rate of the ongoing COVID-19 pandemic

Sporadically, the vertical transmission has been reported but there is no evidence of intrauterine infection to the fetus in consequence of coronavirus infection in the mother in the third trimester of pregnancy [17]. However, after 36 hours of birth, a neonate has been diagnosed to be infected with SARS-CoV-2 at Wuhan Tongji Hospital [41]. It is observed that the gestational age at MERS infection among pregnant women is lowered as compared to that of COVID-19 infected pregnant patients [40][42]. There is a 100% fetal survival rate among COVID-19 patients than that of patients with MERS-CoV (70%) [42].

III. PATHOGENESIS

Clinical evidence suggests that SARS-CoV-2 has generally less pathogenicity than SARS-CoV and MERS-CoV [20]. We find a trend that the higher the transmission, the lower is the pathogenicity of the virus as in the case of SARS-CoV-2 [20]. The Spike protein (S-protein) of the novel coronavirus has a strong affinity for human ACE2 (Angiotensin-Converting Enzyme 2) receptors, the same receptor molecule as used by SARS-CoV despite the dissimilarity in the sequence of S-protein of the two

viruses. Thus, clinical similarity could be expected between SARS-CoV-2 and SARS-CoV [8][20][43]. The receptor-binding domain of the trimeric S-protein of SARS-CoV-2 binds with the human ACE2 cell surface receptor to form a protein complex [44]. These ACE2 receptors are abundantly found in the lung and small intestine epithelia, therefore coronaviruses pass infection via the upper respiratory and gastrointestinal tracts of human beings [45].

IV. Clinical Presentation

The clinical manifestations of the novel coronavirus infection include mild flu-like symptoms to severe respiratory, gastrointestinal, and neurological symptoms [6][46]. The patients of COVID-19 might present a diverse picture of mild, moderate, severe, and critical symptoms. Mild patients present with only mild symptoms of the disease and do not have any radiographic findings. Moderate patients manifest respiratory symptoms, fever, and radiographic findings. Dyspnea with respiratory rate >30 times/min, oxygen saturation <93%, and PaO2/FiO2 <300mmHg are features of the severe patients. Critical patients may die of respiratory failure, multiple organ damage, and septic shock [17]. The majority of the cases present with mild symptoms or common pneumonia while a few cases are critical as studied by CDC China [47]. The vulnerable populations for COVID-19 include elderly people, chronic co-morbidities i.e. diabetes, hypertension, cardiovascular disease, chronic respiratory disease, liver and kidney dysfunction, and cancers, immunocompromised and individuals on long-term immunosuppressive drug therapy, and patients with a history of surgery prior to hospital admission [17-18][32][48]. The common presenting symptoms of the novel coronavirus include fever (98.6%), body aches (69.6%), dry cough, shortness of breath, and diarrhea. Sore throat, runny nose, nasal congestion, nausea, anorexia, vomiting, myalgia, chest pain, headache, confusion, ageusia, and anosmia are the symptoms that present less often among the patients [17][48-51]. Moderate or low fever might present as a symptom in severe and critical cases, or even no obvious fever. The severe and critical symptoms of COVID-19 resemble those of SARS and MERS [17]. Acute Respiratory Distress Syndrome (ARDS), acute cardiac injury, RNAaemia, and multiple organ failure constitute the complications of COVID-19 [50]. It takes a median time of 5 days for dyspnea to develop from the onset of the first symptom, hospital admission takes 7 days and ARDS develops in 8 days [49]. According to the National Health Commission of China, COVID-19 has a good prognosis in majority of the patients [17]. SARS-CoV-2 might cause renal failure along with liver and testicular damage [52-53]. Asymptomatic infections of COVID-19 have also been observed and studied [18].

4.1. Laboratory picture and imaging:

Laboratory findings of COVID-19 patients include lymphopenia, elevated levels of enzymes i.e. lactate dehydrogenase (LDH), alanine transaminase (ALT), aspartate aminotransferase (AST), and prolonged prothrombin time (PT) [49][24]. Increased Erythrocyte Sedimentation Rate (ESR) and C reactive protein are found in most patients. D-dimer is characteristically elevated in severe cases along with a progressive decrease in peripheral blood lymphocytes. Critically ill patients show high levels of inflammatory factors. D-dimer, neutrophil count, creatinine, and blood urea continue to rise in non-survivors [17][49]. The laboratory picture of COVID-19 is related to SARS and MERS [49][54]. X-Ray and Computed Tomographic Scan (CT Scan) show ground-glass opacity and bilateral patchy infiltrate as a hallmark of the disease [48]. Severe infectious diseases are being cured using several new technological methods providing deep insight to help the radiologists [55].

V. Diagnosis and Testing

The diagnostic techniques for COVID-19 include Reverse-Transcription Polymerase Chain Reaction (RT-PCR), genome sequencing, and other serological methods that include Enzyme-Linked Immunoassay (ELISA) [8][17]. Genome sequencing has been used as a diagnostic tool at the time of the early outbreak of the disease [35][56]. RT-PCR is now considered a Gold Standard technique for viral RNA detection on the basis of N-gene and Spike gene in nasopharyngeal swabs, oropharyngeal swabs, expectorated sputum, bronchoalveolar lavage, or endotracheal aspirate [56-59]. According to WHO, both the upper and lower respiratory tract specimens are required to be collected for the detection of viral nucleic acid by PCR technique. However, only lower respiratory tract samples may be elected for collection in critical patients on mechanical ventilation [59]. Quantitative PCR has the phenomenon of detecting NP and ORF1ab genomic regions of SARS-CoV-2, based on fluorescence technique [17]. However, this method of diagnosis has certain limitations [37][60]. The detection of COVID-19 is expected to improve by the ELISA method and is highly recommended [37]. It is because there are fewer sampling errors, and antibodies provide a wider detection window as compared to viruses. ELISA detects Immunoglobulin

G and Immunoglobulin M formed against SARS-CoV-2, based on a nucleocapsid protein SARSr-CoV Rp3 [56]. Flu and other diseases caused by pathogens associated with pneumonia must be ruled out as differential diagnosis is critical to confirm the cases of COVID-19 [17].

VI. Conservative Management

Symptomatic treatment and antiviral drug therapy are the mainstay therapeutics for patients infected with the novel coronavirus. Early supportive treatment, including nutrient supplementation, oxygen support, antibacterial drugs, herbal medicine, and traditional Chinese medicine, is critical for patients that present with mild symptoms in the early phase of disease. Ensuring water balance, acid-base levels, and electrolytes are important [17][59][61]. Before discharging the COVID-19 patient from the hospital, it is necessary to obtain negative results in both upper and lower respiratory tract samples [59][62]. The middle-aged and old population is generally affected by COVID-19 having poor resistance to the novel infectious disease [37]. Critical cases are treated with high-flow oxygen support, nasal catheters, invasive or non-invasive mechanical ventilation, extracorporeal membrane oxygenation, glucocorticoid therapy, and convalescent plasma is administered [17][61]. However, published literature suggests that the clinical use of glucocorticoid therapy for the regulation of cytokine production and immune reaction, and for the treatment of lung injury should be evaded [63-64]. Sepsis and progressive respiratory failure, the clinical signs of deterioration, should be monitored closely in critical patients and immediate interventions are applied. The co-morbidities of the patients are understood for the management of Intensive Care Unit (ICU) patients [59]. Ventilatory support is provided when severe hypoxemic respiratory distress is recognized. Implementation of mechanical ventilation with low tidal volume i.e., 4-8mL/kg predicted body weight (PBW) and low inspiratory pressure i.e., plateau pressure < 30 cmH2O, is recommended. Ventilation in the prone position for almost 12-16 hours per day is highly recommended for patients with severe Acute Respiratory Distress Syndrome (ARDS) [65-66].

VII. Potential Therapeutics

The pandemic of COVID-19 is a global threat to the public and is a burden on healthcare facilities. There is no definitive treatment as a cure for the disease and no vaccination is available till now [67]. Clinical trials are being conducted for the evaluation and development of effective treatment and vaccination of COVID-19 [68]. Lopinavir/Ritonavir, Interferon-α, Ribavirin, Abidor, and Chloroquine phosphate are suggested antiviral drugs. The simultaneous use of three or more of these drugs is generally not recommended [69-70]. Ribavirin and Interferon (IFN) are most commonly used in combination but no effective treatment of MERS-CoV has been documented [71]. However, IFN-β has shown a superior action as compared to IFN-α2a, IFN-α2b, IFN-γ, and IFN- universal type1 while PEG-IFN-α was responsible for demonstrating excellent cytopathic effect (CPE) inhibition in vitro studies [71-73]. In order to treat SARS, collective use of Ribavirin, Ritonavir, and Lopinavir gives better results [74]. Previous researches show that SARS-CoV is inhibited by Chloroquine [75]. The Chinese clinical trials show that Hydroxychloroquine and Chloroquine also have efficacy against SARS-CoV-2. Furthermore, greater potency has been shown by Hydroxychloroquine as compared to Chloroquine [76-77]. The clinical trials suggest that Chloroquine in higher dosage results in prolonged QTc interval and increased lethality rate and should not be, therefore, recommended to the critical COVID-19 patients, especially in conjunction with Oseltamivir and Azithromycin therapy. However, these findings are not applicable to non-severe patients [78]. Remdesivir (GS-5734) is a broad-spectrum antiviral nucleoside analog, mimicking adenosine. The mechanism of action is the inhibition of RNA-dependent RNA polymerases (RdRp) by its incorporation into the SARS-CoV-2 genome, thus halting the replication process [79-80]. It has attracted the researchers in China to put it into clinical trials, in order to determine drug therapy for the novel coronavirus infection, after its efficacy against COVID-19 was clinically observed in the recovered patients of the United States [81]. Recent studies suggest that Remdesivir effectively causes inhibition of SARS-CoV, MERS-CoV, and SARS-CoV-2 RNA viruses which is mediated by the enzymes proofreading exoribonuclease and viral polymerase [69][82-86]. As of April 25, 2020, five clinical trials are underway to test Remdesivir as potential drug therapy for COVID-19 [87]. On April 29, 2020, the Adaptive COVID-19 Treatment Trial, launched by the National Institutes of Health (NIH), showed that Remdesivir facilitates recovery in the clinically advanced patients of SARS-CoV-2, and it also reduces the mortality rate [88]. Moreover, on April 29, 2020, Gilead declared the outcomes of the Phase 3 trial of the antiviral drug Remdesivir, which is under investigation. The study indicates that similar efficacy has been observed in patients

receiving a 5-day treatment course and in those receiving a 10-day regimen of Remdesivir as the management of severe COVID-19 [89]. Based on this clinical trial, the U.S. Food and Drug Administration (FDA) issued Emergency Use Authorization (EUA) on May 1, 2020, for the emergency utilization of Remdesivir in order to make the drug readily available to the hospitalized COVID-19 patients, as a potential therapy [90].

VIII. Statistical Prediction Model for COVID-19

One of the most important parameters from the point of public health safety from COVID-19 is to predict the situation of viral spread in a specific area. This early prediction can prove useful for rapid monitoring in order to avoid a disaster [67]. According to the prediction model, the high-risk areas should be red-zoned, medium-risk areas should be orange-zoned, areas with relatively low risk should be yellow-zoned, while areas having risk probability should be blue-zoned and the relatively safe areas should be green-zoned.

A simplified predictive model for COVID-19 has been introduced by Engbert et al. [91]. This model is based on Susceptible, Exposed, Infected, Removed (SEIR) strategical methodology for the infectious disease. SEIR model is described in Fig. 5. Where 'β' is the contact parameter and is the most critical

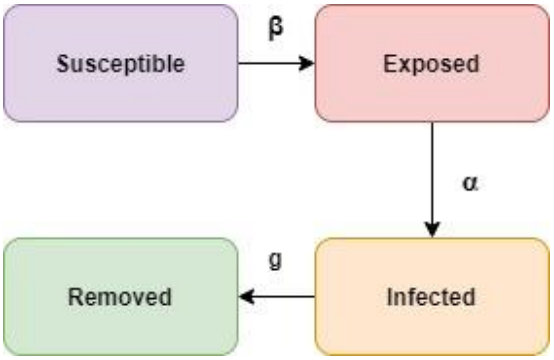


Fig. 5. SEIR model for COVID-19

element of the model [92], 'α' and 'g' are the average time for exposed and infectious periods, respectively. The susceptible, exposed, infected and recovered people can be predicted by using Eqs. 1–4 [91].

$$\frac{dS}{dt} = m - (m + \beta I)S \quad (1)$$

$$\frac{dE}{dt} = \beta SI - (m + a)E \quad (2)$$

$$\frac{dI}{dt} = aE - (m + g)I \quad (3)$$

$$\frac{dR}{dt} = gI - mR \quad (4)$$

The simplified SEIR model is further modified by Yang et al., [93] to predict the epidemic progression. In this model, the modified SEIR strategy for prediction is expressed in Eq. 5. Where, 'γ' is the probability of recovery or death, 'R(t)' is the number of the recoveries or deaths (in a province) and 'Pout[t]' is the probability of the outflowing exposed people.

$$S[t+1]=S[t]+Sin[t]-Sout[t]-\beta 1\times r[t]\times I[t]\times S[t]N[t]-\beta 2\times r[t]\times E[t]\times S[t]N[t]E[t+1]=E[t]+Ein[t]-Eout[t]+\beta 1\times r[t]\times I[t]\times S[t]N[t]+\beta 2\times r[t]\times E[t]\times S[t]N[t]-\sigma E[t]I[t+1]=\sigma E[t]+I[t]-\gamma I[t]R[t+1]=\gamma I[t]+R[t]Sin[t]=In[t]\times(1-Pout[t])Sout[t]=Out[t]\times(1-Pout[t])Ein[t]=In[t]\times Pout[t]Eout[t]=Out[t]\times Pout[t] \quad (5)$$

The model is constructed by further modifying SEIR models as presented in the literature [19][94-96]. The prediction model for the transmission of COVID-19 is represented in Fig. 6. According to this model, an area population is under COVID-19 exposure at a particular time. When exposed to SARS-CoV-2, the susceptible individuals may either become asymptomatic or symptomatic depending upon the manifestation of their symptoms. Moreover, there is a possibility that some of the individuals in the susceptible population may not contract the disease, thus contributing to the area population. The individuals who are not susceptible to the infection become part of the area population. The symptomatic individuals may present with mild symptoms which may either progress to critical symptoms or may lead to recovery. Eventually, critical cases may either die or recover from COVID-19. On the other hand, asymptomatic individuals may either recover spontaneously or may turn into mild cases following the same course of the disease as that of symptomatic patients. The recovered individuals can again be counted back in the area population.

The transmission of mild and critical cases and deaths in a given population can be predicted by Eqs. 6-8, respectively [95]. Where 'E' represents the exposed cases, 'M' represents the mild cases, 'C' represents the critical cases and 'D' represents the number of deaths. The 'a' represents the incubation period of a virus when it is exposed to a susceptible person, 'b' represents the incubation period of a virus from mild to critical phase, 'd' represents the time from the mild case to recovery, 'e' represents the time from the critical case to recovery and 'f' represents the time from the critical case to death. The 'c', 's', and' represent the critical, severe, and mild proportions, respectively.

$$\frac{dM(t)}{dt} = a\,E(t) - b\,\frac{c+s}{m}\,M(t) - d\,M(t) \quad (6)$$

$$\frac{dC(t)}{dt} = b\,\frac{c+s}{m}\,M(t) - e\,C(t) - f\,\frac{c}{c+s}\,C(t) \quad (7)$$

$$\frac{dC(t)}{dt} = f\,\frac{c}{c+s}\,C(t) \quad (8)$$

IX. METHODOLOGY

Non-pharmaceutical preventive strategies are essential to decrease secondary transmission of the disease among healthcare workers and close contacts [97]. Isolation is considered to be the most effective means for containing COVID-19 [98]. The WHO has issued preventive interventions and guidelines for public safety in order to minimize the transmission of infection in COVID-19 Strategy Update on April 14, 2020 [99]. It recommends mobilization of all sectors and community participation to prevent cases through hand hygiene, social distancing, and respiratory etiquette (maintenance of distance, covering while coughing or sneezing and using disposable tissues or cloth piece, and washing hands) [99-100]. One may also sneeze into a flexed elbow. Thus, there is a need to maintain behavioral prevention strategies at an individual level.

9.1. Public health measures:

Till the time, we do not come up with effective drug therapy and vaccination for COVID-19, prevention and public safety is a global health priority. Therefore, large-scale measures are required to be implemented aggressively to control the transmission of the infectious disease globally and to minimize the mortality and the associated socio-economic impact caused by the virus via human-to-human transmission [40][101].

9.1.1. Vaccination:

Vaccines provide an effective means for the prevention of infectious diseases [102]. Vaccines are important for the prevention of viral infections as convalescent sera improve conditions in critical patients [103]. According to a recent report, 149 mutation sites have been identified in the genome sequencing of 103 strains of SARS-CoV-2, and two subtypes of the virus have been evolved, including L and S subtype. This makes the design of a vaccine more difficult [104]. Effective measures are required to be taken in the light of various research findings, as has been done with other emerging priority diseases [105]. Various countries and their pharmaceutical companies have announced their research programs for the establishment of a vaccine against SARS-CoV-2. Some of the vaccines are being evaluated for efficacy under animal and clinical trials while most of them are still under preparation [106]. Different vaccines have been considered based on the Spike protein (S-protein), Receptor-Binding Domain (RBD), and T-cell epitopes against SARS and MERS [107-114]. S-protein is considered the most favorable antigen, in order to develop the COVID-19 vaccine, due for many reasons [115-116]. The various types of vaccines that are under development these days include, whole-cell killed vaccines, live-attenuated vaccines, subunit vaccines, messenger RNA (mRNA) vaccines, DNA vaccines, live vector vaccines, and epitope vaccines or synthetic peptide [106][117]. Recently, scientists in China developed a vaccine on the basis of yeast-expressed Spike protein which is further being evaluated in clinical trials [17]. The Chinese CDC has started research to establish an inactivated vaccine for the novel coronavirus [118]. The mRNA vaccine (mRNA-1273) has been prepared by a pharmaceutical company of the US, Moderna, on February 24, 2020, in animal experiments and is ready to be tested in clinical trials [17][106][119]. Safety is an important concern in the development and deployment of COVID-19 vaccines without adequate safety trials is not recommended [120]. As of May 4, 2020, the phase 1 clinical trial is underway to assess the safety and immunogenicity of the mRNA-1273 vaccine [121]. Currently, Stermirna Therapeutics is also working on the manufacture of mRNA vaccine samples with an advantage over traditional vaccines in terms of shorter production cycles [122]. According to the literature, two DNA vaccines are also under development by the companies [106]. These vaccines have advantages over mRNA vaccines in terms of delivery efficiency and stability, although there is a risk of host-genome mutations and vector integration [123]. GeoVax and BravoVax have announced their collaboration for the production of vaccine candidates based upon MVA-VLP (Modified Vaccinia Ankara-Virus Like Particle) platform and expertise [124]. In addition, the "Trimer-Tag" platform technology is being used by Clover Biopharmaceuticals to construct SARS-CoV-2 recombinant S-protein subunit vaccine [125-126]. On February 10, 2020, Clover Biopharmaceuticals was successful in producing S-Trimer vaccine for COVID-19 and cross-reacting antibodies were detected in sera from several recovered SARS-CoV2 patients [127]. It is observed that children are less vulnerable to the novel coronavirus pneumonia as compared to adults. This observation leads to the hypothesis of cross-resistance of vaccines. For instance, cross-resistance is created for SARS-CoV-2 by measles and rubella vaccines with which children are predominantly vaccinated [17]. Randomized control trials show that the BCG vaccine has immunomodulatory properties that provide protection

against various respiratory infections. Trained immunity is one of the beneficial non-specific effects of the BCG vaccine in which it induces epigenetic and molecular changes, thus enhancing the innate immune function in response to the subsequent infections [128-129]. Moreover, it is observed that fewer infections of COVID-19 have been witnessed in the regions where neonates are predominantly vaccinated with Bacille Calmette-Guérin (BCG) vaccine against tuberculosis [130]. However, such ecological studies may be prone to confounding [130-131]. There is no such evidence of BCG providing protection against COVID-19 pneumonia [130]. Two clinical trials are underway to assess the effectiveness of the BCG vaccine against the novel coronavirus infection [132-133]. Hence, BCG vaccination is not recommended to prevent the infection of SARS-CoV-2 by WHO in the unavailability of supportive evidence [130]. However, further research and development of vaccine prophylaxis are highly required to prevent future outbreaks of the emerging coronaviruses [17].

9.1.2. Early case detection:

WHO emphasizes early identification, testing, and treatment of severe and critical cases, along with sheltering of the high-risk population [99][59]. Therefore, it is necessary for countries to manage rapid diagnosis, contact tracing, isolation, and quarantine to stop cluster transmission and explosive outbreaks [99][134]. In case of insufficient diagnostic capacity, prioritization of testing the vulnerable populations is required; symptomatic individuals of healthcare staff, in closed settings i.e. prisons, schools, hospitals, to rapidly identify and implement isolation strategies [99]. Upper respiratory tract specimens of COVID-19 patients indicate high viral loads and the shedding pattern of the coronavirus patients resembles influenza virus patients [135]. CDC China estimated that 80.9% of the asymptomatic patients continued to release a huge amount of viruses at an early stage, posing great challenges to control the growth of COVID-19 [17]. The daily COVID-19 tests that are carried out across the different regions of the world are represented in Fig. 7 [15].

9.1.3. Personal Protective Equipment:

The nosocomial transmission of SARS-CoV-2 has rendered healthcare providers vulnerable to infectious disease [136]. Therefore, advanced infection control interventions are required to be practiced within hospitals and healthcare facilities, especially in emergency settings [100]. Triage and the provision of Personal Protective Equipment (PPE) are considered mandatory for the safety of public health workers and other vulnerable groups. These prevention measures would help to prevent nosocromial transmission of COVID-19 [99]. PPE for droplet and contact precautions include gown, gloves, medical mask, and eye protection with either face shield or goggles. After attending the patient, PPE should be taken off, discarded in the medical waste bin, and hand hygiene should also be performed [137-138]. Airborne precautions i.e. the use of N95, FFP2, or FFP3 respirators, gowns, gloves, and eye protection are necessary while performing procedures that generate aerosol including intubation, extubation, and tracheal suctioning [137][139]. Surgical masks are considered important for healthcare providers while providing treatment to the suspected and confirmed patients [140]. The shortage of PPE has also become a global challenge that calls for disinfection and reuse of the PPE material, especially of N95 respirators. Moreover, the novel coronavirus has been isolated from the PPE of healthcare providers. Studies analyze various decontamination methods including the use of 70o heat, 70% ethanol, ultra-violet radiation (260-285 nm), and vaporized hydrogen peroxide in order to inactivate SARS-CoV-2 effectively, which may be present on N95 respirators. The filtration efficiency may be affected by the type of decontamination procedure used, which is being assessed in studies. However, after single decontamination with any of the four above mentioned procedures, the filtration performance is not markedly reduced. The CDC and FDA issue certain guidelines regarding fit testing and reuse of N95 respirators which are to be followed [141-150].

9.1.4. Hand hygiene:

WHO provides comprehensive advice for public safety which includes avoiding contact with COVID-19 patients [100]. Hand hygiene can prevent the spread of microorganisms in a community [151]. It is encouraged to wash hands with soap and water or using an alcohol-based rub, in case of no immediate access to water and soap, for the containment of infection [152-153]. According to WHO Guidelines on Hand Hygiene, it is recommended to hand rub for 20-30 seconds and handwash for 40-60 seconds. The concentration of alcohol in an alcohol-based sanitizer is 70-80% v/v [151]. Two suggested formulations for local production of alcohol-based sanitizer include, 80% v/v ethanol, 1.45% v/v glycerol, 0.125% v/v hydrogen peroxide (H2O2) and the other one being 75% v/v isopropyl alcohol, 1.45% v/v glycerol, 0.125% v/v H2O2 [154]. In order to protect oneself and others from the ill effects of COVID-19, hands should be washed after sneezing or coughing, when nursing the sick, before eating, after the use of a toilet, while preparing food, and after contact with

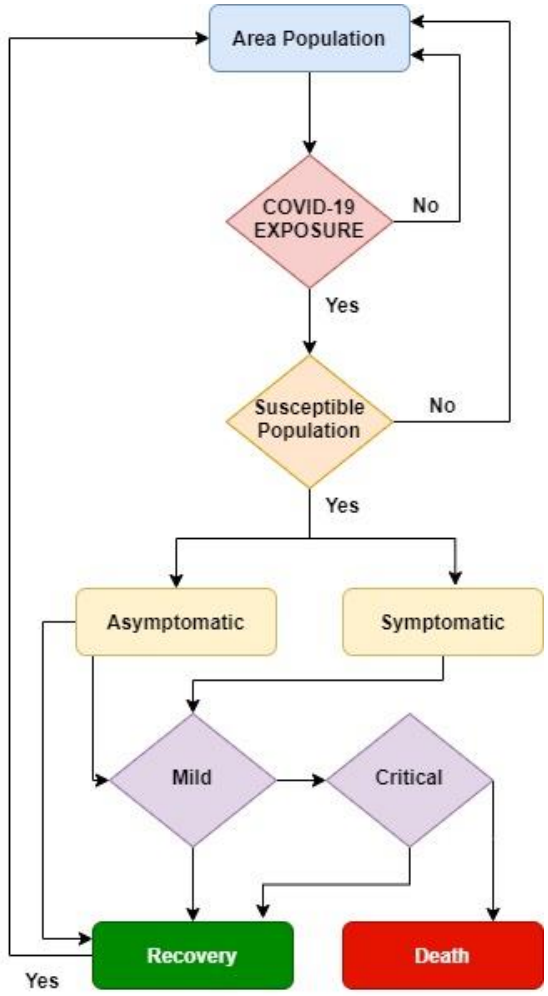


Fig. 6. Model for COVID-19 Transmission

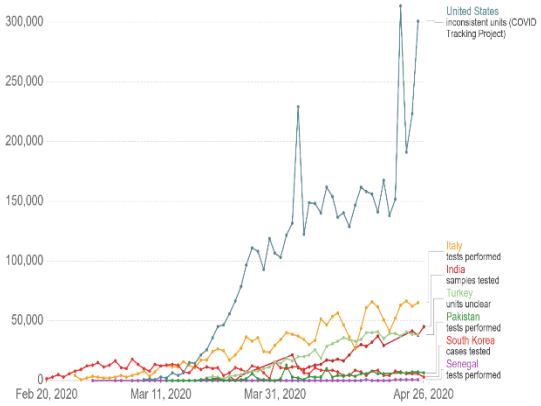


Fig. 7. Daily COVID-19 tests

animals [152]. For healthcare management, it is recommended to wash and disinfect hands after touching the immediate surroundings of a patient [151].

9.1.5. Face masks:

According to the interim guidelines on the usage of face masks issued on April 6, 2020, the WHO recommends the individuals to wear medical masks if they suffer from respiratory symptoms in-home care and health care settings. If the individuals do not suffer from respiratory symptoms, they are not supposed to use medical masks while going in public [139]. A healthy person should only wear a mask if he/she is looking after a coronavirus patient [155]. However, studies propose that community-wide wearing of the masks might lead to decreased shedding of virus in respiratory droplets and saliva from asymptomatic, pre-symptomatic, and mild patients of novel coronavirus [156-160]. Face masks prevent the droplets from dispersing during, coughing, sneezing, and talking, hence reducing environmental contamination [161]. They are only effective when used adjunctively with hand hygeine [155]. The utilization of masks in a healthy community still remains controversial and there is no mutual consensus on it to date [156][162-163]. It is important that masks should be properly used and disposed off [139]. The face masks are currently tight in supply due to an increase in their demand as the pandemic accelerates [164]. According to the WHO and CDC, medical masks should be engaged for health professionals and symptomatic individuals [156]. CDC has recommended the use of cloth face coverings, especially in high-risk regions on April 3, 2020 [165].

9.1.6. Environmental disinfection:

Environmental hygiene is an essential component of the public health interventions [137]. The surface stability of the novel coronavirus recruits the requirement of effective and rapid disinfection methods [166]. It is recommended to disinfect all the frequently touched surfaces (e.g., light switches, door handles, bed rails, bed tables, phones) especially in the hospital setting along with restrooms at least twice per day [137][167]. Surface disinfectants such as ethanol (62-71%), hydrogen peroxide (0.5%), or sodium hypochlorite (0.1%) could effectively halt coronaviruses within one minute [168]. Diethyl ether, peracetic acid, chloroform, and chlorine-based disinfectants may also be used. Exposure to the ultraviolet radiation and heat at 56 ^{o}C for about 30 minutes renders the virus inactive [169].

9.1.7. Physical distancing:

The majority of the asymptomatic individuals or those having mild symptoms can transmit the virus to the community, which makes the prevention of COVID-19 a challenging task [17][170]. Avoiding exposure to the virus is the best preventive strategy.

Therefore, it is advised to establish physical distancing of at least 3 feet (1 meter) between the two persons, one being the person who is either sneezing or coughing, as a measure of droplet precaution. Touching of the eyes, mouth, and nose should be avoided. Hands touch surfaces and may be contaminated, acting as a potential source of viral transmission. Spitting in public should be avoided [152]. The Kingdom of Saudi Arabia (KSA) has introduced decisive measures by suspending sporting and religious mass gatherings such as Umrah and by temporarily closing the mosques and educational institutions, thus imposing a curfew. These measures have been taken to ensure global health despite their religious, political, and socio-economic challenges [171-172]. The suspension of Umrah on February 27, 2020, by the KSA government, has been imposed in view of the superspreader potential among pilgrims [173-174]. The KSA authorities may have to restrict Hajj (July/August 2020) as various respiratory viruses including coronaviruses, particularly 229 E, was acquired by the pilgrims at the Hajj [175-176]. The 2020 Tokyo Olympic and Paralympic Games are scheduled to be held in the months of July and August 2020 [177-178]. Like a common cold outbreak, due to respiratory viruses i.e., coronaviruses, influenza B, has also been witnessed in the past [179]. Therefore, various preventive measures, including social distancing, are required to be implemented by the host country [177-178]. In this regard, WHO provides recommendations for the management of health issues in mass gatherings [180].

9.1.8. Quarantine:

Quarantine is stated as the separation and restriction on the mobility of the individuals exposed to the contagious infection in order to observe whether they become sick with the disease or not. On the other hand, isolation is described as the separation of sick individuals manifesting the disease symptoms for the containment and prevention of the contagious spread of the disease [181-182]. WHO suggests the individuals stay at home if one even feels mild symptoms of the infection. Certain guidelines are recommended to be adopted by the public for home quarantine [183]. Furthermore, all
the COVID-19 confirmed cases are required to be isolated immediately in hospitals and/or designated centers, or in self-isolation at home with effective support for mild to moderate cases until they recover and are no more infectious. Tracing all the close contacts of an infectious person, and their quarantine and monitoring for 14 days should be done. Community volunteers can monitor quarantined individuals and can provide support via calls or messaging [99]. However, familial cluster transmission cannot be avoided by home-quarantine due to the asymptomatic cases of COVID-19 [159][184]. On January 31, 2020, the US CDC declared that a 14-days quarantine would be considered mandatory for all the citizens arriving in the US from China [185]. This duration of quarantine is in accordance with the various published research results determining the incubation period of the novel coronavirus. It provides insight into the surveillance, active monitoring, and control of the disease [28]. China successfully adopted the policy of community quarantine to combat COVID-19 [186]. This measure of transmission control worked effectively in the containment of the disease [187]. The researchers in Singapore have also suggested the deployment of a quarantine strategy to mitigate global infectious disease [188]. Participation of the population is required to implement and maintain the strategy of quarantine. In addition, there is a need to evaluate the psychological effects of quarantine on the community members in the long run [186].

9.1.9. Lock-down:

As of January 23, 2020, 10:00, the nation-wide lock-down strategy has been found productive in the mitigation of viral transmission in Wuhan, China, by hampering human mobility. In addition to lock-down, China also adopted the policy "Stay At Home" to prevent further outbreak of respiratory infection [13][189]. These interventions greatly helped China in flattening the epidemic trajectory of COVID-19 and decreased the mean daily reproduction number from 2.35 to 1.05 on January 16, 2020 and January 30, 2020, respectively [13][190][94]. This sets new benchmarks for other countries to take similar precautionary measures as taken by China [13]. Suspension of social gatherings, closure of educational institutions and entertainment venues, non-essential workplaces, and public transport restrictions are the community-level measures to decrease the interaction between individuals, thus halting the transmission of the virus [99][189]. Temperature monitoring is a potential prevention measure to be taken at workplaces along with other precautions [191].

9.1.10. Travel restrictions:

The accelerated growth of the COVID-19 outbreak in Wuhan and across international borders, including the United States, Europe, and Asian countries is attributed to human movements globally [192-195]. Transmission of the virus via air travel has been reported in China. It indicates the need for travel restrictions to be imposed on the travelers moving across the borders to mitigate the spread of infection

and also for the prevention of travelers onboard from contracting the disease [196-197]. Health guidelines are strongly recommended to travelers before and after the travel [195]. The Centers for Disease Control and Prevention (CDC) in the US issued interim guidance for the containment of the new coronavirus outbreak. The precautionary measures include the surveillance and assessment of travelers that arrive in the US from mainland China [198-199]. WHO puts emphasis on self-monitoring of the symptoms for fourteen days if

an international traveler returns from any of the affected areas [200]. Limiting travel on national and international borders, effective airport screening, installation of thermal scanners, and quarantine measures are important to suppress importation of the virus from high-transmission zones [99][201]. It is strongly highlighted in previous studies that travel

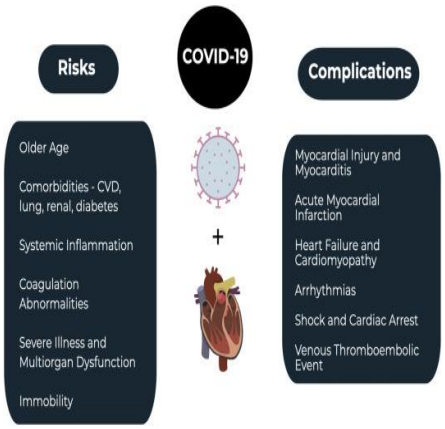


Fig. 8. Cardiological Complications due to COVID-19 [239].

history is of prime importance, rather than radiography of chest, in order to detect and isolate SARS-CoV-2 patients [202]. The health professionals should, therefore, be aware of the patients presenting with respiratory symptoms; having a recent travel history, and exposure to the affected region [203]. There could be a larger impact of ground and sea transportation on the transmission of infection in adjacent countries (e.g., Europe) [202]. Public transport has a vital role in the COVID-19 outburst. One of the important determinants of the risk of transmission is the connectivity of the destination with the epicenter. Therefore, preventive measures should be imposed aggressively in the areas having short distances from the epicenter of the disease outbreak [204]. Previously, travel restrictions had been imposed during Influenza H1N1-2009, Ebola Virus Disease (EVD), and SARS epidemics in response to the dissemination of infectious diseases [205][177][206]. Awareness should be increased among travelers about the preventive measures of COVID-19 to increase compliance with the recommendations issued by the health authorities [203].

9.1.11. Animal contact:

The emerging viruses that are transmitted from animals to humans are known to cause the deadliest diseases in mankind [105][207]. The novel virus is 96% related to the bat coronavirus [207]. Huanan wet market has been identified as the hub of initial animal-to-human transmission in China. Therefore, authorities sealed the market on January 1, 2020. This animal-to-human spread in the early cases in Wuhan suggests that close contact with animals should be minimized to ensure the prevention of COVID-19. The transmission from animals to humans can be lessened more rapidly as compared to community transmission among humans [207]. The identification of specific animals that are responsible for the spread and transmission of infection is important and the prevention and control strategies should be adopted accordingly. Screening should be performed before trading the suspected animals and there is a need to monitor the trading routes from the location of the outbreak [201]. Hand hygiene before and after animal contact is encouraged [208]. SARS-CoV-2 has been detected among pet cats [209]. Moreover, the Hong Kong Department of Agriculture, Fisheries, and Conservation have described that pet dogs could also be infected with the novel coronavirus as a dog has been found to show weakly positive results in the samples taken from the dog's oral and nasal cavities. These provoked us to believe that pet animals, particularly mammals, may present as potential carriers of the virus [210]. It is due to the fact that kidney and myocardial cells of the cats and dogs also express ACE2 receptors, which have an 85% similar amino acid sequence as that of human ACE2 receptors showing an affinity for the SARS-CoV-2 S-protein [210-211]. Surveillance and isolation are emphasized as preventive measures. Therefore, pets should not be taken to the high-risk locations and if they do, testing of the pets is required. The pets of the laboratory-confirmed COVID-19 patients should be isolated, while those of the recovered patients should be tested and quarantined to remove the chance of re-infection of the recovered owners from the virus-carrying pets [210]. Moreover, training of the pets by their owners should be avoided to reduce animal exposure and subsequently the risk of infection.

9.1.12. Precautions in pregnancy and lactation:

In the management of an outbreak of a communicable disease, the care of vulnerable

populations is the most critical component. The pregnant women along with their fetuses are particularly at a high risk of contracting an infectious disease, especially viral infections, due to a variety of physiological changes (e.g., respiratory tract edema, elevation of diaphragm, and increase in oxygen demand) and compromised immunological and mechanical functions occurring in pregnancy [40][212]. The respiratory failure occurs rapidly in the gravida, as observed in SARS and MERS which caused the death of approximately \sfrac{1}{3} rd of the affected pregnant women in the last two decades [40][213-214]. Miscarriage, spontaneous abortion, intrauterine growth retardation, and premature delivery are other adverse outcomes in pregnant SARS-CoV and MERS-CoV suspects [215-217]. No evidence supports severe SARS-CoV-2 infection effects on mothers and infants; however, risks should be kept in mind [218]. Studies show that neonatal complications may arise secondary to maternal infection, even with the negative COVID-19 results [219]. This suggests the requirement to take special precautions for the management of pregnant women and lactating mothers in the pandemic situation [220]. The quarantine guidelines should be followed if the pregnant lady has traveled to a high-risk area and she is supposed to be tested for the infection [221]. If tested positive, they should be self-monitored for COVID-19 symptoms at home for 14 days. Fetal surveillance is required for the risk of intrauterine growth restriction that includes Doppler assessments and fetal growth ultrasounds. Special considerations are taken during labor and delivery [220]. Isolation for at least 14 days and supportive treatment is recommended for neonates born with positive SARS-CoV-2 [220][222]. The physical separation between the mother and infant is recommended to avoid transmission via infectious secretions, which is also a standard practice in maternal influenza and pulmonary tuberculosis [223]. The novel coronavirus has not been detected yet in maternal milk [41]. However, there may be a risk of droplet transmission from infected mothers during breastfeeding [222]. According to the CDC, breastfeeding is not contraindicated during maternal infection until all the precautions are met i.e. hand hygiene and using a facemask. Breast milk may also be expressed by the mother following all the precautionary measures and then fed to the infant by a healthy guardian [224]. The cross-infection of healthcare workers should also be prevented during vaginal delivery and other procedures that promote close contact and droplet transmission of infection. For this purpose, the use of PPE and responsible physical distancing are mandatory [220]. Counseling of obstetric patients highlighting the risks and prevention of COVID-19 is also essential.

9.1.13. Efficient communication and education:
Health education and effective communication are essential for publicizing the information about the protective measures. Sharing of the transparent and

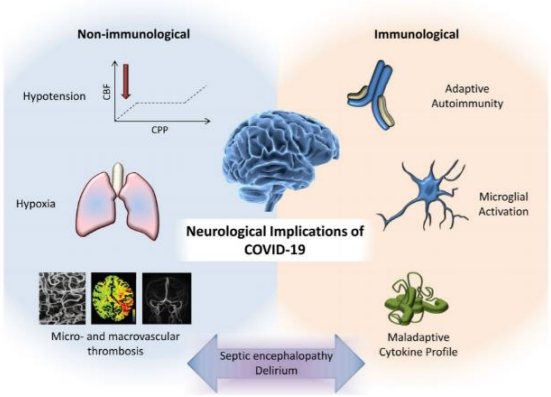


Fig. 9. Neurological Complications due to COVID-19 [240].

real-time information helps to gain trust and to increase awareness in public. It also increases the preparedness in the community and the healthcare facilities to combat the COVID-19 pandemic [208][225-226]. Coordinated efforts of communication help in minimizing the barriers that hinder the implementation of efficient and appropriate healthcare strategies. For this purpose, an updated and reliable source of guidance and information should be developed for the healthcare providers and the institutions at national and international levels [208][226]. Online presentations, web conferencing and meetings may be conducted for the awareness training of the healthcare professionals. A similar trustable and reliable source of information is important to curtail panic and to increase the consciousness of the public [208][226]. Physicians and other healthcare staff are considered an important source of health education and communication to the public [225]. The Internet is a potential tool to spread information globally. However, methods for dissemination should also consider the availability of information and guidelines to the end-user [208][226]. The facility of the internet should be made accessible to the underprivileged areas for an easy approach to health information and guidelines. Youtube and social media have been known as a popular platform of information in disease outbreaks. The appropriate internet content may also help public health organizations to enforce measures required to contain

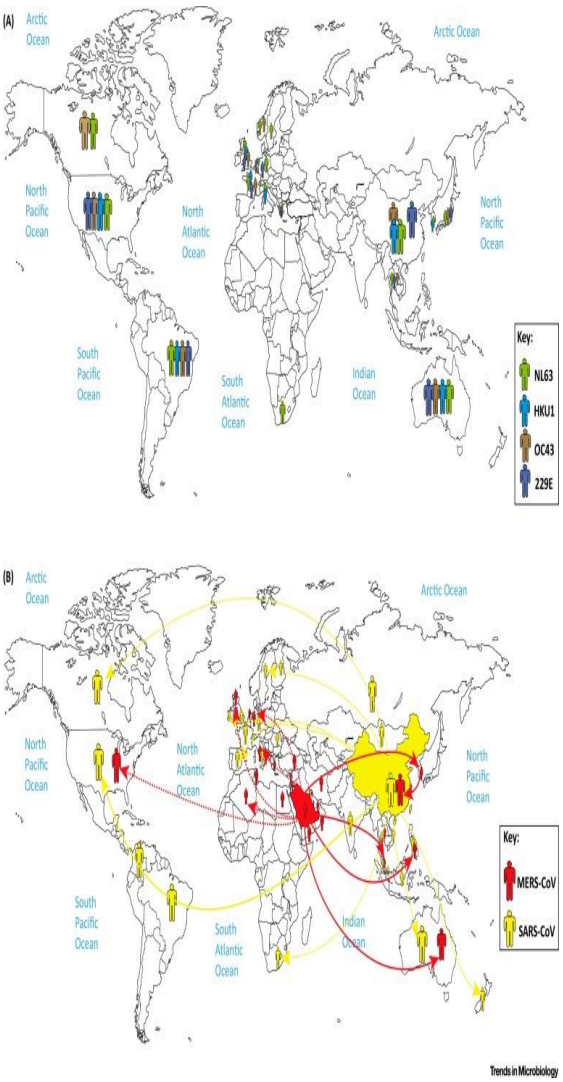


Fig. 10. Distribution of COVID-19 Epidemiology globally [241].

the disease. Academic and health institutions should broadcast more information regarding testing and screening of the disease along with the preventive measures. However, the wrong and misleading information on the internet should be screened and passed through scientific scrutiny to avoid public paranoia in the current pandemic situation [227]. The involvement of media and mass communication has an effective role in the awareness campaigns among the population for the control of infectious disease. WHO, CDC, and other health organizations make use of information technology to help protect the people from the risk of COVID-19. Evidence-based advice, reliable communication, and health promotion are the services provided by WHO via electronic platforms i.e., google, Twitter, Youtube, Facebook, WhatsApp, etc in almost 20 different languages. WHO also works to provide messaging services to tackle myths related to the disease [228]. Other ways of promoting health awareness among the public include informative videos, brochures, booklets, pamphlets, hospital posters, handouts, printed reading materials, and via telecommunication companies, radio, television, family, and friends [225][229].

9.1.14. Coping with stress:

Psychological interventions have been suggested for suspected and confirmed cases, and also for the medical staff working all day and night to combat the pandemic [230-232]. Published literature suggests that the

pandemic of coronavirus has profound psychosocial effects on the students residing away from their homelands [233]. WHO also devises ways for stress coping in this crisis that include, keeping in contact with family and friends, maintaining a healthy lifestyle (e.g., proper diet, exercise, sleep) while staying at home, engaging oneself in healthy and productive activities, and abstaining from smoking or alcohol[234]. In order to have strong immunity against various infectious diseases, a well-maintained balanced diet is essential. Prioritizing fresh products (e.g., low-fat dairy products, fresh fruits, and vegetables), eating white meat, fish, eggs, whole grains, dried fruits, beans, nuts, lentils, and seeds, preparing healthy meals at home, getting right portion sizes to avoid overeating, observing food hygiene, consuming enough fiber, limiting the intake of fat, salt, and sugar, staying hydrated, and avoiding the use of large amounts of strong tea, coffee, caffeinated and energy drinks is important for optimal health [235-236]. WHO recommends relaxation techniques (e.g., deep breaths and meditation) and physical activities to remain calm and to avoid sedentary behavior during self-quarantine due to the COVID-19 pandemic? A moderate-intensity workout or vigorous-intensity workout for 150 and 75 minutes per week, respectively, is suggested. Domestic chores (e.g., cleaning home and gardening), walking around, and playing with children are other ways to stay physically active while being at home [237]. Parents/guardians must help the children in coping with the stressful situation effectively by giving them attention and reassurance, and also by educating them on various techniques of health safety in order to prevent themselves from getting infected by the virus [238].

X. Complications of Covid-19 Infections

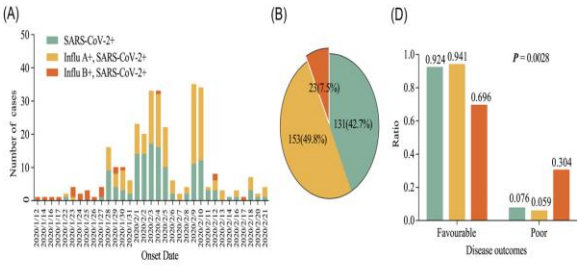
The cardiological and neurological complications caused due to COVID-19 are expressed in Figs. 9 and 10 respectively.

XI. Statistical Measures of Epidemiology

The distribution of COVID-19 around the globe and its spreadibility is mentioned in Fig. 10. Whereas, the statistical analysis for epidemiology is represented in Fig. 11.

XII. Concluding Remarks and Future Prospects

In summary, the SARS-CoV-2 has become a prominent human virus showing similarity to its preceding outbreaks of SARS and MERS. Bats are generally considered the main reservoir of the novel coronavirus. The first epicenter of the infectious outbreak was Wuhan, China from where it spread across the international borders, thus becoming the COVID-19 pandemic. To date (24-04-2020, 22:00 CEST), 183,000 people have been died due to this disease, 2.6 million population has been infected, 700,000 have been recovered and 185 countries contain laboratory-confirmed cases around the globe. The transmission among humans is mainly via the respiratory droplets, and direct or indirect contact. Asymptomatic individuals along with convalescents may also be responsible for the droplet-infection transmission. The Ro of COVID-19 infection is estimated to be 2.68 and an average incubation period of 6.4 days. The case-fatality rate is calculated to be 3% in China. Older age with co-morbidities are most commonly linked to mortality. The interaction of the SARS-CoV-2 trimeric S-protein to the human ACE2 cell surface receptor defines the pathogenesis of the virus. Mild, moderate, severe, and critical symptoms may be presented by the patients while most of the cases present with mild symptoms of the disease. The commonly occurring symptoms include fever, body aches, dry cough, shortness of breath, and diarrhea. Lymphopenia, high values of ESR and C reactive protein along with enzymes, and prolonged PT exhibit the laboratory picture of COVID-19 patients. RT-PCR and ELISA are considered important diagnostic methods. Symptomatic management is the mainstay of treatment as there is no definite antiviral drug treatment or vaccine available. Clinical trials are underway all over the world to establish potential



(C)

Indicators	Influenza-, SARS-CoV-2+	Influenza A+, SARS-CoV-2+	Influenza B+, SARS-CoV-2+	*P* value
Character	n = 131	n = 153	n = 23	
Age (years)	64 (50.5-70)	61 (46-68)	56 (43-66.5)	0.158[b]
Male	69 (52.7%)	64 (41.8%)	11 (47.8%)	0.188[c]
Female	62 (47.3%)	89 (58.2%)	12 (52.2%)	
Symptoms				
Fever	104 (79.4%)	132 (86.3%)	16 (69.6%)	0.080[d]
Cough	40 (30.5%)	38 (24.8%)	6 (26.1%)	0.556[c]
Fatigue	13 (9.9%)	5 (3.3%)	3 (13.0%)	**0.026**[d]
diarrhea	11 (8.4%)	6 (3.9%)	0 (0.0%)	0.161[d]
Difficulty breathing	9 (6.9%)	11 (7.2%)	2 (8.7%)	0.886[d]
Abnormalities on chest CT	122 (97.6%), n=125	127 (94.8%), n=134	23 (100%)	**0.401**[d]
laboratory findings (median, IQR)				
Lymphocytes ($\times 10^9$/L)	0.92 (0.68-1.19)	1.06 (0.73-1.41)	0.84 (0.68-1.27)	0.109[b]
Eosinophils ($\times 10^9$/L)	0.01 (0.00-0.03)	0.01 (0.00-0.06)	0.00 (0.00-0.01)	**0.02**[b]
Eosinophils ($\times 10^9$/L), mean (SD)	0.021±0.035	0.046±0.095	0.023±0.05	**0.049**[a]
IL-6 (pg/mL)	10.13 (3.03-25.94), n=104	9.95 (2.62-27.72), n=131	10.95 (4.69-24.15), n=20	0.981[b]
IL-8 (pg/L)	12.70 (7.25-21.73), n=102	9.95 (5.2-20.23), n=128	11.80 (7.70-18.50), n=21	0.186[b]
hs-CRP (mg/L)	36.10 (11.00-82.70), n=129	26.00 (6.20-76.45), n=152	33.50 (14.30-64.65), n=23	0.098[b]

Fig. 11. Statistical analysis of COVID-19 Epidemiology [242].

therapy along with vaccination of the COVID-19. The designed prediction model helps in the speculation of the number of infected individuals and mortalities in a given population to enhance the preparedness for the COVID-19 pandemic. Early diagnosis and contact tracing are essential to halt the explosive SARS-CoV-2 outbreak. The provision of PPE and airborne precautions while performing aerosol-generating procedures is important for healthcare providers to prevent nosocromial transmission of the virus. Hand hygiene is encouraged to inhibit dissemination of the novel coronavirus. It is recommended to wear medical masks if one is suffering from respiratory symptoms or is taking care of a coronavirus patient in-home care and healthcare settings. However, healthy individuals may use cloth face coverings to avoid the risk of asymptomatic transmission. Various methods of environmental disinfection are essential for the prevention of COVID-19. Maintaining physical distance is important among people as a measure of droplet precaution. Eyes, mouth, and nose should not be touched. Isolation of the confirmed cases, close contact tracing, and quarantine and monitoring for 14 days are recommended. Individuals are advised to home-quarantine themselves even if they feel mild symptoms of the infection. Limiting human mobility by the strategy of nation-wide lock-down has been found effective for infection prevention and control. Implementation of travel restrictions and surveillance of the travelers are the mandatory preventive measures. Travelers are bound to a 14-day quarantine after their return from the affected areas. Travel

history and exposure to the high-risk area are determining factors for the detection of COVID-19 patients. Minimizing contact with wild and farm animals mitigates the sustained animal-to-human transmission. Special precautionary measures are required to be taken in pregnancy and lactation to ensure the health of pregnant women along with their fetuses, and the nursing mothers in the pandemic situation. Strengthening public confidence by community education, engagement, and participation, aids in the containment of infectious disease. Stress coping mechanisms play an integral role in the mental wellbeing of the community to combat the crisis.

Human coronaviruses have a great potentiality of causing pandemics which poses a huge threat to the public health. Unfortunately, there has been no enough learning from the past outbreaks, thus leaving us unprepared to cope with the current obstacles of the pandemic. The Chinese government established a revolutionary control strategy in Wuhan and all the other areas and provinces where the emergency response was declared. Several other countries (e.g., Italy, Iran, and the Republic of Korea) have also demonstrated that the SARS-CoV-2 can be overcome and controlled. Hence, there is a need to learn lessons from the experiences of various countries, particularly China, in tackling the pandemic condition. Long-term planning and investing in healthcare by public health authorities lead to robust and responsive healthcare systems that are prepared to turn the pandemic tide. Prevention of coronavirus-related pandemics or epidemics highly necessitates prophylactic vaccination in the future. In a nutshell, intense surveillance, vigilance, and insight are required to prevent the risk of future outbreaks and to make the world a better place.

NOMENCLATURE

a	Incubation period of a virus when it is exposed to a susceptible person
ACE2	Angiotensin-Converting Enzyme 2
ALT	Alanine Transaminase
ARDS	Acute Respiratory Distress Syndrome
AST	Aspartate Aminotransferase
b	Incubation period of a virus from mild to the critical stage
c	Critical Proportion
C	Critical Cases
CEST	Central European Standard Time
COVID-19	Coronavirus Disease-2019
CT Scan	Computed Tomographic Scan
d	Time from mild to recovery
D	Death Cases
e	Time from critical to recovery
E	Exposed Cases
ELISA	Enzyme-Linked Immunoassay
ESR	Erythrocyte Sedimentation Rate
f	Time from critical to death
g	Average time for infectious period
ICU	Intensive Care Unit
LDH	Lactate Dehydrogenase
m	Mild Proportion
M	Mild Cases
MERS-CoV	Middle East Respiratory Syndrome Coronavirus
N	Total Population
PHEIC	Public Health Emergency of International Concern
PPE	Personal Protective Equipment
PT	Prothrombin Time
RBD	Receptor-Binding Domain
R_o	Reproductive Number
s	Severe Proportion
SARS-CoV	Severe Acute Respiratory Syndrome Coronavirus
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus-2
SEIR	Susceptible, Exposed, Infected and Removed
S-protein	Spike Protein
WHO	World Health Organization
α	Average time for exposed period
B	Contact Parameter
γ	Probability to Recover or Death

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