



Epidemiology and Pathogenesis of Coronavirus Disease (COVID-19)

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Abstract

An acute respiratory syndrome (ARDS) episode was first identified in Wuhan, China, and later officially designated as COVID-19 by the WHO. It is caused by SARS-CoV-2 that is likely associated with zoonotic transmission. Based on the live data from live reference website Worldometer which provides counters and real-time statistics for diverse topics data, COVID-19 has influenced 186 nations. China reported 25 % of cases, while 75 % of the remaining cases were reported in other nations. The clinical and genetic characteristics of SARS-CoV-2 support the similar pathogenesis pattern between SARS-CoV and MERS-CoV. The elevated level of cytokine release during the infection caused the failure of multiple organs leading to the patient death. Treatment of patients depends on the clinical course and symptoms associated with the COVID-19. Several prevention and control measures including; active surveillance, use of masks, and hand sanitizers are recommended to stop the spread of this virus. Besides, COVID-19 was sampled using a throat swab to detect the viral nucleic acid using Real Time Polymerase Chain Reaction (RT-PCR), for early detection and treatments evaluation. In this review, we comprehensively summarized the COVID-19 epidemiology, pathogenesis and diagnosis, using suitable literatures obtained from reliable sources.

Keywords: Coronavirus, COVID-19, SARS-CoV-2, MERS-CoV, Pathogenesis, Epidemiology

1. Introduction

On December 31, 2019, the WHO (World Health Organization) pronounced an obscure progressive type of pneumonia in Wuhan, China, as a Public Health Emergency of an International concern. On February 11, 2020, they termed the disease as COVID 19. On

the same day, the International Committee on Taxonomy of Virus named the coronavirus, causing the disease as SARS-CoV2. At the 26th of February, 2020, COVID 19 cases were detected in every continent except for Antarctica, with 77,041 total

confirmed cases. It surpassed the SARS outbreak cases in China detected at 2002. By March 2, 2020; around 20 nations were battling against the COVID-19 outbreak ([Tomasi, 2020](#); [Zu *et al.*, 2020](#)). Though there is enormous recently published literatures explaining COVID-19, as a global pandemic burden, this review would give extended insights on the viral source, distribution of cases, safety measures for controlling the global spread, and also provides a reference to the specialists working in this field.

2. Source of the COVID-19 virus

Coronavirus is a group of viruses. These viruses are capable of causing common flu-like symptoms to severe conditions such as; Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS). According to recent studies of [Livingston *et al.*, \(2020\)](#); [Xu *et al.*, \(2020\)](#), SARS-CoV-2 is a β Coronavirus of sub-genus *Botulinum* belongs to *coronaviridae* group, and is the third known zoonotic coronavirus. [Banerjee *et al.*, \(2019\)](#) reported that subterranean insect-eating pangolin was identified as the primary source of this virus, and based on the quality investigation; some pangolin corona viruses showed 99 % of similarity in Restriction Binding Domain with the COVID-19 virus-infecting human, which were determined with the explicit site of restriction called receptor- restricting area (RBD). A previous study of [Liu *et al.*, \(2013\)](#) noted that SARS infection imparted 99.8 % of its genome to COVID coronavirus, so it likewise considered as a wellspring of novel Corona viral diseases ([Bell *et al.*, 2004](#)).

Malayan pangolins (*Manis javanica*) illicitly brought into the Guangdong area contain coronaviruses like SARS-CoV-2 ([Fisher and Heymann, 2020](#)). In spite of the fact that the RaTG13 bat infection remains the nearest to SARS-CoV-2 over the genome, some pangolin coronaviruses showed solid closeness to SARS-CoV-2 in the Receptor Binding Domain (RBD), including every one of the six key RBD residues ([Banerjee *et al.*, 2019](#)). As a consequence of common discovery, this clearly shows

that the spike protein of SARS-CoV-2 is assertive to human like ACE2 receptor.

Previous studies conducted by [Lu *et al.*, \(2020\)](#); [Zhang *et al.*, \(2020\)](#) confirmed that current examinations expressed that COVID-19 offers over 88% homology with two bat-inferred extreme intense respiratory disorder (SARS) related coronaviruses, which are: bat-SL-CoVZC45, and bat-SLCoVZC21, and that bats might be the most probable common hosts of these viruses. Recently, [Giovanetti *et al.*, \(2020\)](#); [Jonathan *et al.*, \(2020\)](#); [Lai *et al.*, \(2020\)](#) added that although bat coronavirus does not legitimately contaminate humans yet; however, it could have been transmitted through the middle host. Generally speaking, whether the SARS-CoV-2 transmits straightforwardly from bats or through a halfway host is still yet questionable.

3. Epidemiology

The WHO documented that the COVID-19 outbreak originated from 'wet markets' in South China, selling meat of wild animals. Recently, [Lai *et al.*, \(2020\)](#); [Rothe *et al.*, \(2020\)](#); [Wang *et al.*, \(2020a\)](#) added that the outbreak was first reported on December 31, 2019, in Wuhan, China. Within few weeks, it spread throughout China, and then after a month, it extended to several other countries including; Italy, the United States, and Germany. [Wang *et al.*, \(2020a\)](#) reported that till the 30th of March, 2020, COVID 19 have become pandemic throughout the world, affecting 199 countries, infecting 722,389 people and caused 33,982 (5 %) worldwide deaths.

Disease cases are rapidly increasing in other countries across all continents except Antarctica, outpacing the rate and numbers of China. These cases were initially believed to be attributed to the migration of infected people from China to other parts of the world ([Corman *et al.*, 2020](#); [Gao *et al.*, 2020](#); [Kannan *et al.*, 2020](#); [Poon *et al.*, 2020](#); [Pullano *et al.*, 2020](#); [Wang and Jin, 2020](#); [Zhao *et al.*, 2020](#)). However, local transmission in several countries such as; Italy,

Germany, Spain, UK, France, USA, South Korea, Japan and in many other countries are becoming so high, which has driven more significant outbreaks outside of mainland of China, resulting in a massive worldwide pandemic.

Until the 30th of March, 2020; about 11% (81,470) of the confirmed cases were recorded in the mainland of China, whereas 89 % (640,919) of cases were from the rest of the world. However, the reported cases from China are continuously declining from 99.22 % at the 10th of February to 11 % at the 30th of March, 2020, with respect to the total cases. Conversely, in the other countries, the viral infection is increasing

exponentially from 0.78 % to 89 % at the same period of duration. According to [Corman *et al.*, \(2020\)](#), the global distribution of cases until the 30th of March, 2020 is shown in the Table (1). Initially, the total global cases are almost equivalent to China's total cases, but recent cases from China are negligible, and under well control ([Worldometer. 2020](#)). However, cases from the other countries excluding China are increasing exponentially, and are very close to the total global cases demonstrated in Fig. (2). Data analysis of the number of total reported COVID-19 cases and total deaths in several worldwide countries are presented in Fig. (3), in reference to [Worldometer. \(2020\)](#).

Table.1. Worldwide distribution of reported cases of infection by the COVID-19 virus

Date	Total Global	China	Other Countries	No of affected countries
22 th of January	314	309	5	4
28 th of January	4593	4537	56	14
3 rd of February	17391	17238	153	23
9 th of February	37558	37251	307	24
15 th of February	50580	50054	526	25
21 th of February	76769	75569	1200	26
27 th of February	82294	78630	3664	46
4 th of March	93091	80422	12669	76
10 th of March	113702	80924	32778	109
16 th of March	167515	81677	86438	150
22 th of March	292142	81498	210644	193
26 th of March	462684	81961	380723	196
30 th of March	693224	82447	610777	199

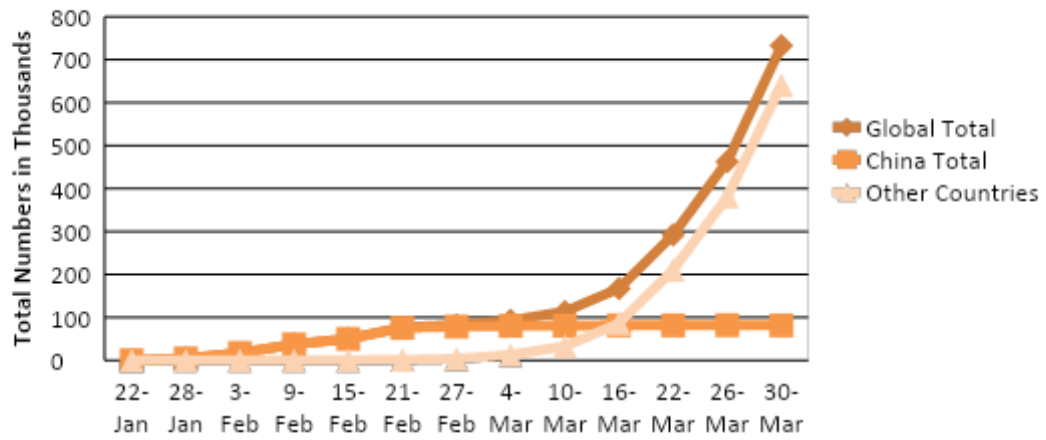


Fig.2.World wide infection trend of COVID-19

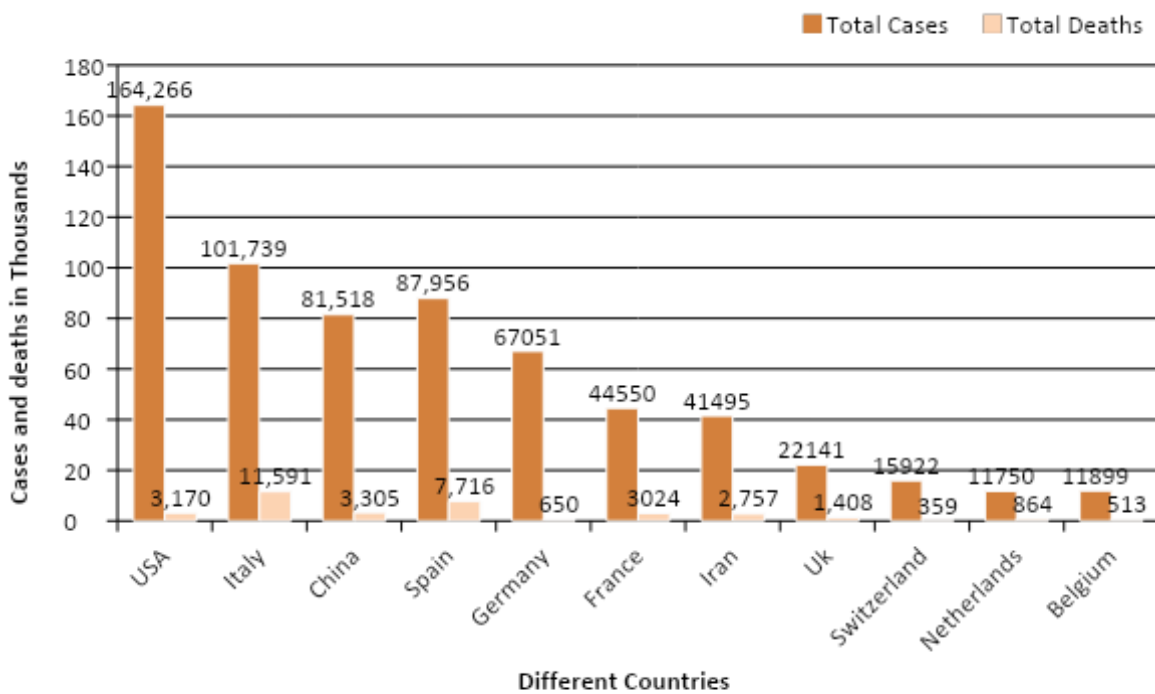


Fig.3.Total Number of Cases and Deaths Countries Wise

Till the 31th of March 31: the highest numbers of cases are reported from USA: 164,266 with deaths 3,170, followed in decreasing order by: Italy: 101,739/ 11,591; China: 81,518/ 3,305; Spain: 87,956/ 7,716; Germany: 67,051/ 650; France: 44,550/ 3,024; Iran: 41,495/ 2,757; UK: 22,141/ 1,408; Switzerland: 15,922/ 859; Netherlands: 11,750/ 864; and Belgium: 11,899/ 513. The highest mortality is however recorded from Italy (total deaths: 11591), followed by Spain (7716), and then China (3,305), in reference to [\(Wang *et al.*, 2020b\)](#). The relation between the total recorded cases of viral infections and total deaths in the top countries having cases number more than 10,000, are shown in the Fig. (3).

On the 30th of March, 2020; there are about 722,389 total confirmed cases of COVID-19 infections worldwide, since the beginning of the epidemic [\(Worldometer, 2020\)](#). The cases with outcomes are 185,775 (26 %), about 151,793 (21 %) of them are recovered and discharged, whereas about 33,982 (5 %) deaths have been recorded. Later, [Gao *et al.*, \(2020\)](#); [Wang *et al.*, \(2020b\)](#) reported that the current active cases are 536,614 (74 %), of which mild cases are 509,933 (95 %), and serious or critical cases are 26,681 (5 %). The growth factor for new cases in the 21th of March is 1.17. This means that the infections are increasing exponentially (>1). The newly infected cases (30,665 at March 20th), versus the newly recovered cases (3,411 at March 20th) have greatly increased. This shows that the pandemic is greatly expanding, particularly in Europe and the USA outside China.

Recent studies conducted by [Pullano *et al.*, \(2020\)](#); [Wang and Jin, \(2020\)](#) reported that the most affected age groups are above +80 years old: 14.8 % death rate, followed by 70-79 years: 8%, 60-69 years: 3.9 %, 50-59 years: 1.3 %, and finally the 40-49 years: 0.4 % death rate. The least affected ages are 10-39 years recording 0.2 % death rate. Males have a higher death rate of 4.7 %, followed by females with 2.8 % deaths of confirmed cases. The associated co-

morbidities are cardiovascular diseases: 13.2 % death rate, diabetes: 9.2 %, chronic respiratory diseases: 8 %, hypertension: 8.4 %, cancer: 7.6 % and 0.9 % deaths were associated with no any underlying diseases.

Although all these figures are for confirmed cases; however, the actual number of international people with COVID-19 is thought to be much higher, as people with mild symptoms are not tested. In response to the viral spread, countries around the world are ramping up measures to control the number of new cases. Governments have halted flights from virus-hit nations, locked down places, and urged people to stay at home.

According to [Barua, \(2020\)](#), many international conferences and sporting events have also been cancelled or postponed, including Six nations rugby matches, Euro 2020, Copa America, and this year's meeting of G7 leaders in the U.S. Schools, colleges, universities, hotels, and parks. In addition, many institutions are currently closed, and home isolation or quarantine is issued all around the world to fight against this pandemic. The WHO announced that it took longer than three months to reach the first 100,000 of confirmed cases globally, whereas just 12 days to reach 200,000, four days to reach 300,000 and three days to reach 400,000 and four days to reach 750,000. [Rothe *et al.*, \(2020\)](#) added that millions of people globally are living under restrictions. India and Nepal are the latest countries to impose a lockdown. About 1.3 billion people are currently prohibited from leaving their houses for weeks. In this way, not less than one-quarter of 7.8 billion people globally are living under lockdown, and social distancing because of coronavirus.

4. Pathogenesis

Homology analysis has revealed that SARS-CoV-2 has an identical confining structure to that of SARS-CoV-1, and COVID-19 may have similar pathogenesis as SARS-CoV-1 [\(Dhama *et al.*, 2020\)](#). Thus, regardless of COVID-19 severity, the known clues of

SARS-CoV and MERS-CoV can give us a lot of information about the pathogenesis of SARS-CoV-2 illness. Results of [Li *et al.*, \(2020a\)](#) demonstrated that the virus might proceed via the mucous membranes, particularly the nasal and throat mucosa, then ingress into the lungs via the respiratory tract. The alveolar epithelial cells in the lungs are found to be the fundamental cell affected by the SARS-CoV-2 virus. The S protein has been revealed as a remarkable impetus of the virus entry into host cells. The envelope spike glycoprotein ties up to its biological receptor ACE2, adjacent to alveolar epithelial cells in the lungs. After that, the SARS-CoV-2 spikes bind ACE2 with around 10 folds higher affinity than SARS-CoV. This promotes the transmission properties of SARS CoV2. Moreover, [Dhama *et al.*, \(2020\)](#); [Qiao, \(2020\)](#); [Rothe *et al.*, \(2020\)](#); [Sahin, \(2020\)](#); [Sohrabi *et al.*, \(2020\)](#); [Li *et al.*, \(2020a\)](#) added that CD209L and CD209 are believed to be elective receptors through which the virus attaches the cells; however the mechanism is poorly understood.

[Prompetchara *et al.*, \(2020\)](#); [Sohrabi *et al.*, \(2020\)](#) revealed that following entry of the virus into the cells, the viral RNA genome is liberated into the cytoplasm and is expressed into two poly proteins and structural proteins, after which the viral genome begins to replicate. The recently established envelope glycoproteins are lodged into the sheet of the Endoplasmic reticulum or Golgi gadget, and then the nucleocapsid is re-organized by the union of genomic RNA and nucleocapsid protein. Then, viral fragments sprout into the Endoplasmic reticulum-Golgi intervening section. Finally, the vesicles containing the virus fragments meld with the plasma membrane to liberate the virus by exocytosis. [Li *et al.*, \(2020a\)](#) added that the virus may enter the peripheral blood from the lungs, provoking viremia. At that time, the virus will bombard the additional targeting organs that express ACE2, such as the heart, kidney, and the gastrointestinal tract. [Mackay and Arden, \(2015\)](#); [Prompetchara *et al.*, \(2020\)](#); [Qiao, \(2020\)](#) reported that while the viral fragment enters the cell, the antigen is acquainted with the antigen-presenting cell by the

MHC/HLA system. These are seen through the unequivocal cytotoxic T-cells response. This antigen can make the sporadic T-cell response in light of prompting of the T-cell apoptosis (Fig. 4). The latest reports released by [Rothe *et al.*, \(2020\)](#); [Sohrabi *et al.*, \(2020\)](#); [Li *et al.*, \(2020b\)](#) also showed the enormous decline of the CD4⁺ and CD8⁺T cells in the peripheral blood of the COVID-19 patients.

Numerous assessments reported by [Rothe *et al.*, \(2020\)](#); [Sahin, \(2020\)](#); [Li *et al.*, \(2020b\)](#) have proposed the uncontrolled central combustible responses against the virus by the provocative cytokines (cytokine storm) such as; IFN α , INF- γ , IL - 1 β , IL-6, IL-12, IL-18, IL-3, TNF- α , TGF- β , IL-2, IL-10, MCP1, IL-1RA, etc., and by the raised degrees of chemokines including; CCL2, CCL3, CXCL8, CXCL9, CXCL10, etc. The cytokine storm triggered by the immune system generates obstructions in the respiratory system leading to Acute Respiratory Distress Syndrome (ARDS), and finally causing death ([Mackay and Arden, 2015](#); [Dhama *et al.*, 2020](#); [Prompetchara *et al.*, \(2020\)](#)). However, more immune-associated investigations are required to assist us in interpreting the pathogenesis of the disease.

5. Clinical symptoms

Recent studies conducted by [Dhama *et al.*, \(2020\)](#); [Ryu and Chun, \(2020\)](#); [Spiteri *et al.*, \(2020\)](#) proposed that, in spite the clinical appearances being exhibited are ambiguous, yet most of the assessments give a couple of symptoms that are close to COVID-19. According to the Centers for Diseases Control and Prevention (CDC), symptoms include fever, cough, fatigue, shortness of breath, having the normal brooding time of first 4 days. All symptoms usually are mild at the initial stage; however, they gradually become severe in the second seven day extend of disease, following respiratory symptoms including runny nose and sore throat. At the first stages, patients may suffer from nose runs and sickness for a couple of days before the fever, thus proposing that fever is predominant, but is not the chief effect of contamination (Fig. 5).

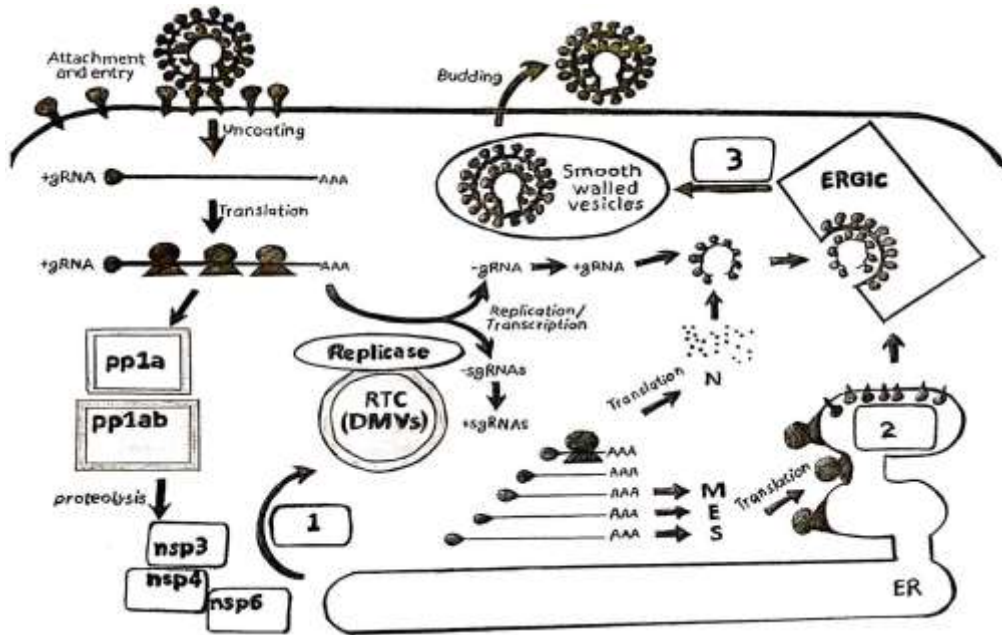


Fig. 4: Replication of the SARS-CoV inside the infected human cell

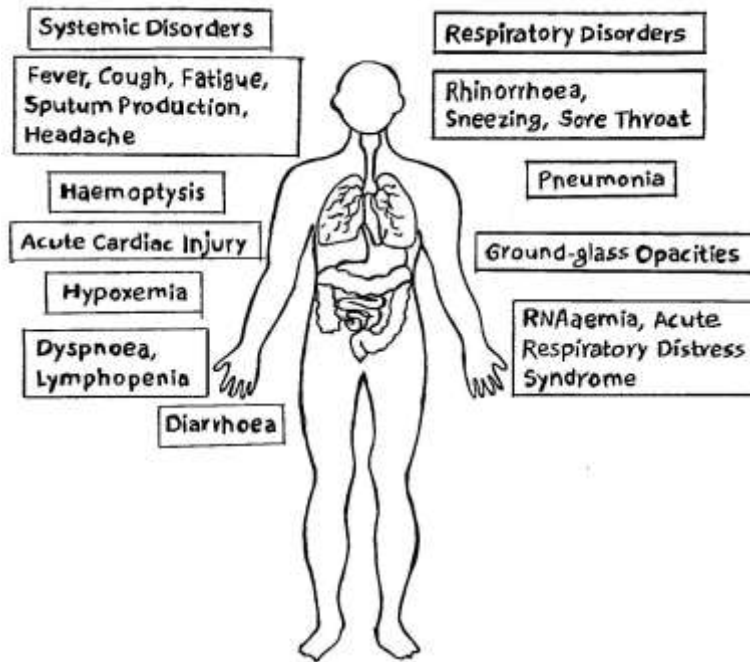


Fig. 5: The systemic and respiratory disorders in human body caused by COVID-19 infection

Moreover, [Abdulmir and Hafidh, \(2020\)](#); [Dhama *et al.*, \(2020\)](#); [Spiteri *et al.*, \(2020\)](#) added that cerebral pain or hemoptysis generally is asymptomatic in the modest number of patients. However, in several old patients influenced by comorbidities, they are bound to have respiratory disappointment, because of the serious alveolar harm. Patients suffering from organ brokenness including; stun, intense respiratory pain disorder (ARDS), intense cardiovascular injury, and intense kidney injury at the beginning of COVID-19 infection, show quick advance and even passing in serious cases as opposed to recently influenced patients. In the interim, patients may show ordinary or lower white platelet checks, lymphopenia or thrombocytopenia, with broadened initiation-thromboplastin time and expanded C-responsive protein level in the plasma or serum. Thus, a patient having fever and upper respiratory tract manifestations with lymphopenia or leukopenia ought to be of suspected infection, particularly for patients with recent introduction to Wuhan city (China), or of close contact history ([Abdulmir and Hafidh, 2020](#); [Spiteri *et al.*, 2020](#)).

6. Analysis of COVID-19 infection

The principal focus on the clinical symptoms of COVID-19 was affirmed to Wuhan's city presentation. Anyway, the expanded obscure introduced by the Chinese and American Centers of Diseases Control and Prevention (CDC) created several atomic examines, for the detection of the various infections in the clinical samples. [Majumder and Mandl, \(2020\)](#) revealed that different investigates were depicted about Real-time PCR methodologies to test for the COVID-19, by concentrating on a mixture of open reading frame (Orf), envelope (E), nucleocapsid (N), and RNA-subordinate RNA polymerase (RdRp) qualities. [Li *et al.*, \(2020b\)](#) added that On February 4, 2020; the United States Food and Drug Administration (FDA) made a significant step, by giving an approval for the US CDC's COVID-19 continuous PCR methods, along with these empowering CDC-qualified research

facilities, to play out the test. At present, there are 115 CDC-qualified research facilities in the U.S., and about 191 qualified labs around the world.

A patient suffering from fever, cough, shortness of breath within 2-14 days of exposure, has troubles in breathing with persistent pain and/or pressure in the chest, new confusion or inability to arise, and bluish lips or face is considered as a presumed case of COVID-19. On the off chance that there is no reasonable presentation history, suspected patients should meet 3 clinical conditions that include; fever, cough, and shortness of breath. In view of the fifth clinical status, chest Computed tomography (CT) scan can identify the viral pneumonia, which is viewed as a proof of the COVID-19 contamination. It is noteworthy that, the WHO didn't acknowledge the Computed tomography (CT) scan without RT-PCR affirmation until the 17th of February, 2020. In addition, the Diagnosis and Treatment Program of 2019 New Coronavirus Pneumonia (preliminary 6th form), has excluded the term of clinical examination for the diagnosis of the disease. As indicated by their clinical appearances, affirmed patients are classified into mellow, moderate, serious, and basic cases ([Qiao, \(2020\)](#); [Li *et al.*, \(2020a\)](#); [Rasmussen *et al.*, \(2020\)](#); [Rothen and Byrareddy, \(2020\)](#)).

7. Control and prevention of infection by COVID-19

There are numerous difficulties in avoiding contamination with the COVID 19 in the different fields including; the clinically mellow cases or atypical introductions, restricted inventory of individual defensive hardware, and/or respiratory disconnection rooms at the hospitals. The CDC suggests that the medical service providers should use the Personal Protective Equipment (PPE), and apply the standard, contact, and airborne safety measures, including utilization of eye insurance. [Majumder and Mandl, \(2020\)](#); [Li *et al.*, \(2020b\)](#) added that the health workers should wear protective outfits, gloves, and either an

N95 respirator in addition to confronting shields, or a fuelled air purging respirator.

According to [Lu *et al.*, \(2020\)](#), the CDC prescribes the presence of airborne contamination confinement rooms that ought to be reserved for the patients, who will experience vaporized producing procedures. The CDC prescribes also the execution of the ecological contamination controls, by guaranteeing natural cleaning and sanitization methods reliably and correctly. The usage of designing control like a physical hindrance, draperies between patients in shared regions, air dealing with a framework with proper directionality, filtration, conversion scale, and powerful contact following and seclusion, could diminish the general size of an outbreak.

The world related Safety and Health Administration had created break direction to help forestall laborer presentation to COVID-19, like regular washing of hands with cleanser and water for 20 sec, and utilization of liquor based hand rub with at least 60 % liquor. Avoid contacting eyes, nose, mouth with unwashed hands, and keep away from close contact with individuals who are wiped out. The antibody is an ideal approach to forestall and control COVID-19, yet no immunization against SARS-CoV-2 is accessible.

In terms of immunizations, vaccines are being developed, and a phase1 investigation of mRNA antibody created by the National Institute of Health (NIH) is in its preliminary stage in March, 2020 ([Lu *et al.*, 2020](#)). Because of the absence of compelling treatments, an ideal approach to manage the SARS-CoV-2 pestilence is to control the wellsprings of infections. Besides this, the successful anticipation of COVID-19 for people necessitates defensive measures including; improving individual hygiene, wearing clinical masks, adequate rest, social distancing, and keeping rooms well ventilated.

8. Discussion

The arises of novel coronavirus started from the Human fish market at Wuhan, China, where bats,

snakes, raccoon hounds and palm civets are sold, and quickly spread up to 109 nations. The zoonotic wellspring of SARS-CoV-2 is not affirmed; however, succession based examination recommended bats as the key store mediator, but the intermediate hosts are not still confirmed. According to [Lu *et al.*, \(2020\)](#), DNA recombination was included at the spike glycoprotein, which grouped SARS-CoV (CoVZXC21 or CoVZC45) with the Restriction Binding Domain (RBD) of another Beta CoV. The rapid genomic sequencing and open access data, together with advanced vaccine technology, are expected to give us more knowledge on the virus itself, including the host immune response as well as the plan for the expected therapeutic strategies in the near future. Treatment is basically based on clinical symptoms presented by the patients; however, preliminaries of immunizations and antivirals are in progress.

Currently, there are no compelling antibodies or explicit antiviral medications for COVID-19. Henceforth, we need to depend only on authorizing severe preventive and control quantifies that limit the danger of conceivable illness transmission. Results of the *in vitro* examination against COVID-19 are promising since the medications such as; Remdesivir and Chloroquine are seen as profoundly compelling in controlling the viral contamination. The S protein is viewed as a key viral antigen for creating COVID-19 immunizations, as appeared in a few preclinical examinations ([Liu *et al.*, 2020](#)). In spite of the fact that explorations to improve the avoidance, treatments, and control of COVID-19 are in progress, the reported clinical information on various restorative methodologies for COVID-19 are rare. Further researches ought to be coordinated toward the investigation of SARS-CoV-2 in reasonable creature models, for dissecting its replication, transmission, and pathogenesis.

Conclusion

This review article focuses on current research responses to the outbreak of COVID-19. During this period, numerous studies have been released involving

the study of COVID-19 disease transmission, causes, clinical appearance, avoidance and control of this new virus. However, laboratory research based scientific and pathological discoveries are urgently needed, to understand the immune-pathogenesis of the virus, and for the generation of novel curative agents such as; antivirals and vaccines, to limit the effect of this viral outbreak. Moreover, the governmental organizations have to unit their efforts, to release the logical discoveries into the open strategies at the network, regional, and at the national levels, to prevent further spread of this COVID-19 virus.

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Conflict of interest

The authors declare that there is no conflict of interests.

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Ethical approval

Non-applicable.

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