

Epidemiological characteristics, reinfection possibilities and vaccine development of SARS CoV2: A global review

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ABSTRACT

According to the World Health Organization (WHO), there are 37,704,153 cases and 10,79,029 deaths due to COVID-19 till the 13th October 2020 in the world. Day by day, rise in the number of COVID-19 deaths has created great pressure on health facilities, governmental bodies, and health workers. There is a need for knowledge regarding lifecycle, transmission, and different strains of SARSCoV2, so that countries can stop the disease as early as possible. The present study was conducted to review various epidemiological aspects along with measures used in the containment and prevention of this new pandemic. The scientific literature database was searched using the terms: coronavirus, 2019-nCoV, SARSCoV2, and COVID-19. Articles with appropriate topics fulfilling the objective of the present work were included. The epidemiological characteristics regarding life-cycle, intermediate hosts, viability on various surfaces, strains, case fatality rate, and their implication to reduce the transmission of SARSCoV2 have been identified. According to Centers for Disease Control and Prevention, Atlanta (updated till October 05, 2020) people with recurrent or persistent positive COVID-19 tests in South Korea and USA did not show to have live virus in their bodies. As per WHO web-page information till 15 October 2020, there were 42 candidate vaccines in clinical evaluation and 156 vaccines are in preclinical evaluation phase. As the virus can easily be transmitted to the people either via droplets, fomites, and may be via the fecal-oral route, knowledge regarding the above-mentioned areas is needed for time to be prepared for the next waves of the COVID-19 pandemic.

Keywords: Basic case reproduction rate, COVID-19, reinfection, SARSCoV2, vaccine

Introduction

COVID-19 pandemic is causing severe stress to the health system of affected countries in the world. According to the World Health Organization (WHO), there are 37,704,153 cases and 10,79,029 deaths due to COVID-19 till the 13th October 2020 in the world.^[1] WHO declared COVID-19 as a pandemic on 11th March 2020, when the overall number of cases raised

to 118,000 and a total of 114 countries had been affected by it.^[2] The first case of COVID-19 was identified in December 2019 and on the 12th of January, 2020 China shared the genetic structure of the SARS CoV2. On 13th January 2020, the first case outside China was reported in Thailand. WHO warned human to human transmission of the SARS CoV2 virus late in January 2020. On 18th March 2020, a solidarity trial was conducted to gather data on COVID-19's most successful therapies.^[3] The International Committee on Taxonomy of Viruses gave the name of "Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)" to this new virus on 11 February 2020, because the genome of this virus has similarities to the coronavirus

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causing the outbreak of SARS in the year 2003. “COVID-19” the name of this pandemic was given by WHO on 11 February 2020.^[4] As of 14 October 2020, there were 826,876 active cases and 110586 deaths in India.^[5] The present work was conducted to review various epidemiological aspects along with measures used in the containment and prevention of this new pandemic. Although many primary care physicians were very familiar with SARS-CoV-2 and took appropriate precautions in their day-to-day outpatient services, thither is a demand for continuous knowledge update on the new COVID-19 pandemic. So, they can prevent this pandemic and spread accurate information.

Materials and Methods

The terms: coronavirus, 2019-nCoV, SARS CoV2, and COVID-19 were used in the search of the literature in Web of Science, Science Direct, JAMA, Oxford, BMJ, The Lancet, and PubMed journals to find the articles published till to December 08, 2020 without any restrictions to language and region. Open source documents from organizations like WHO, Centers for Disease Control and Prevention (CDC)- Atlanta, European Centre for Disease Prevention and Control (ECDC), and China-CDC were also searched. Moreover, the reference lists of all studies were checked. Studies with old data and inappropriate topics were excluded from the study. The titles and summaries of the articles collected were screened separately by two authors and after reading the article, a final decision was made for eligibility.

History of Pandemic Influenza

During the last century (20th), three influenza pandemics took place. During 1918-1919, the Spanish Flu (causative agent H1N1 Virus) pandemic caused 20-50 million deaths. In 1957-1958, Asian flu (causative agent H2N2 Virus) occurred and in 1968 Hong Kong Flu (causative agent H3N2 virus) occurred. These two, Asian flu and Hong Kong flu, were milder in nature. The new century's first influenza pandemic happened in 2009-2010 (causative agent H1N1 Virus). During this pandemic, about 100,000 to 400,000 deaths occurred in the first year of the pandemic.^[6]

Similarities and differences between COVID-19 and influenza

Similarities: The mode of transmission of COVID-19 and influenza by droplets, direct contact, or indirect contact through fomites is similar. Both diseases cause respiratory illness. The spectrum of both diseases ranges from asymptomatic to mild to very severe disease and death. **Differences:** The median incubation period and serial interval for influenza virus are shorter than the SARS CoV2 virus. The estimated serial interval for influenza virus is 3 days, whereas for the SARS CoV2 virus it is 5 to 6 days. It means that the rapidity of transmission of influenza virus is more than the SARS CoV2 virus. The pre-symptomatic transmission can occur 3 to 5 days before illness in influenza, whereas the studies suggest that in COVID-19, the viral transmission occurs 1 to 2 days before the

onset of symptoms. The reproductive number, i.e., the number of secondary infections arising from one infected individual is estimated to be between 2 and 2.5 for SARS CoV2 virus. For the influenza virus, this reproductive number is less than the SARS CoV2 virus. The fraction of patients in severe infection in COVID-19 is more than influenza, and the mortality from COVID-19 infection (3–4%) appears more when compared to influenza virus infection (usually below 0.1%) by current data trends.^[7]

Origin of SARS CoV2

A few samples of bronchoalveolar lavage of pneumonia of unexplored etiology came to a hospital in Wuhan city in China in late December 2019.^[8] Epidemiological investigations showed that the animal market in Wuhan and seafood market in HuaNan were probably linked to the COVID-19 outbreak, so the market was closed on 01 January 2020.^[9] In India, COVID-19 was first found in Kerala (laboratory confirmation on 30 January 2020), in a student returned from Wuhan, China.^[10]

Distribution of SARS CoV2

According to the European Centre for Disease Prevention and Control, the cases of COVID-19 occurred are distributed in various geographical areas as shown in the Table 1.^[11]

Life Cycle of Virus

The virus causing COVID-19 is SARS CoV2 belonging to beta coronavirus having a length of 29.9 kilobases (strain found in the Wuhan seafood market) is encapsulated and round or oval in shape with a diameter of 60-140 nm.^[12,13] The main four structural proteins of SARS CoV2 are S-glycoprotein, E-glycoprotein, M-glycoprotein, and N protein and about sixteen other non-structural proteins. S-glycoprotein has a role in attachment, fusion, entry, and in transmission.^[14]

SARS CoV2 binds to cells expressing angiotensin-converting enzyme-2 (ACE2) receptors such as type 2 alveolar cells in the lungs, upper part of esophagus, and enterocytes of the ileum and colon, cardiac myocytes, urothelial cells of the urinary bladder and cholangiocytes, etc., The study also showed that the oral cavity is at high risk of SARS CoV2 infection due to the expression of ACE2.^[15] This might be a reason for patients of COVID-19 also present with symptoms of diarrhea, urinary, and

Table 1: Distribution of COVID-19 cases according to geographical areas since 31 December 2019 and as of 13 October 2020

Geographical areas	Number of cases
Africa	15,85,643
Asia	11,858,004
America	18,144,366
Europe	6,250,851
Oceania	35,862
Others	696

cardiac disorders.^[16] It is observed previously that cells expressing ACE-2 and trans-membrane serine protease 2 simultaneously are at more risk of SARS CoV entry.^[17] After the binding process, viral envelop fuses with the host–cell and genetic material are released for further translation in the nuclei followed by the formation of progenies.^[18]

Reservoirs and intermediate hosts of SARS CoV2

There is very strong evidence that natural reservoirs for SARS CoV are Chinese horseshoe bats.^[19] A study done by Wu *et al.*, showed that viral transmission to humans can occur directly from bats. *Rhinolophus sinicus* was considered as a natural host. Primates, wild variety of felidae, civet cats, goats, hyenas (spotted), golden (Syrian) hamsters might be the intermediated host of the SARS CoV2 virus. Birds and reptiles are not intermediate hosts, whereas earlier pangolins (but in later studies pangolins were found as possible intermediate host) were not supposed to be an intermediate host. When considering susceptibility, rats, mice, and guinea pigs are not susceptible to SARS CoV2 virus.^[20] The coronavirus discovered from pangolin resembled close to SARS CoV2, suggesting that pangolin might be a possible intermediate host.^[21] Also, a recent study done by Lam *et al.*, in China showed that Pangolin was considered a possible intermediate host for SARS CoV2 as the samples from Malytan pangolins found two sub-lineages of coronavirus related to SARS CoV2.^[22]

Transmission of SARS CoV2

Samples from the human upper and lower parts of the respiratory tract and bronchoalveolar lavage fluid showed the presence of SARS CoV2 RNA.^[23] When a person sneezes or coughs, different sizes of droplets come from the respiratory tract. The droplet particles which are >5–10 µm in diameter are known as respiratory droplets, and when the size of the droplet is <5 µm in diameter, it is known as droplet nuclei.^[24] A study done by Xie *et al.* (2007), of indoor behavior of droplets found that large droplets due to sneeze (exhaled air velocity of 50 m/s) are transmitted more than 6 m. During coughing (exhaled air velocity of 10 m/s), large droplets can be carried more than 2 m away and less than 1 m away during breathing (exhaled air velocity of 1 m/s).^[25] The transmission of SARS CoV2 can be via droplets and fomites. COVID-19 can be spread through airborne means if some aerosol-generating procedures (endotracheal intubation, bronchoscopy, manual ventilation, etc.) are done and airborne transmission via droplet nuclei can occur over distances greater than 1 m.^[8] SARS CoV2 genome was isolated from air samples from different areas in two hospitals and outdoor spaces in Wuhan, China.^[26] A hospital study done in Wuhan, China showed isolation of SARS CoV2 in 35% of air-samples from an intensive care unit and 12.5% of air-samples from the COVID-19 ward.^[27] A research from The University of Nebraska Medical Center showed that the SARS CoV2 viral genome was found in 63.2% air samples of 11 isolation rooms of COVID-19 positive patients and in 66.7% air samples from the hallways of the hospital.^[28] However, a study in Iran showed no positive air samples taken from 2–5 m distance from patient beds.^[29] Viable SARS CoV2

virus has been found in the fecal matter of some patients in a few case reports. Therefore, the role and significance of the fecal–oral transmission route should also be investigated.^[8]

A study conducted by Chen *et al.*, published in the Lancet showed that samples from breast milk, throat swab of newborn, cord-blood, and amniotic fluid were free from the SARS CoV2 virus and no newborn had clinical signs of infection with this virus. The results from this study showed that no chances of vertical transmission, but as the study sample size was only nine pregnant females with positive COVID-19 infection, there is a need for further studies on vertical transmission of the virus.^[30]

The spectrum of the disease

In a report WHO said that about 80% of infections of COVID-19 are asymptomatic and 15% are severe, requiring O₂ therapy and only 5% of infections are critical.^[31] Whereas, a CDC, Atlanta, U.S. study showed that about 50% among SARS CoV2 positive patients were asymptomatic.^[32] A cohort study done in China showed that among 44,415 confirmed cases about 81% had mild to moderate symptoms, about 14% had severe symptoms and 5% had a critical illness.^[33] Data from China CDC showed that among 44,672 patients confirmed COVID-19 cases, about 80.9% cases were asymptomatic or having mild pneumonia and 86.6% were aged between 30 and 79 years.^[34] Mild cases usually present with symptoms of dry cough, fever, and fatigue. Symptoms like running nose, sore throat, and nasal congestion are found in some cases. The severity of the disease usually increases after 1 week and rapid progression to acute respiratory distress syndrome, refractory metabolic acidosis, septic shock, coagulopathy, and finally to multiple organ failure.^[35]

Viability of SARS CoV2

An article showed that SARS CoV2 remained viable for 3 h in aerosol and it was stable on steel and plastic (detected up to 3 days after application). Whereas on copper, the virus was not found after 4 h.^[36] A research article published in The Lancet showed the detection of SARS CoV2 on glass and currency notes for up to 4 days. They also found that this virus viable on steel, plastic, and on surgical mask up to 7 days.^[37] Also, WHO advised the avoidance of uncooked or undercooked animal products in food.^[38]

Incubation period

According to the European CDC and WHO, the estimated incubation period of SARS Co V2 is between 1 and 14 days and on average it is 5–6 days.^[39-41] Lauer *et al.* on 181 confirmed COVID-19 positive cases with known exposure and onset of symptoms estimated the median incubation period of 5.1 days (95% CI, 4.5–5.8 days) for SARS CoV2.^[42] Whereas Backer *et al.*, in Wuhan, China estimated the incubation period range of 2.1–11.1 days (2.5th to 97.5th percentile) with a median of 6.4 days (95% CI: 5.6–7.7 days).^[43] Similar results were shown by Li *et al.*, who conducted a study on 425 confirmed cases in which they estimated mean incubation period of 5.2 days.^[44] A research

published in NEJM conducted on 1099 patients from China, estimated mean incubation period of 3.0 days (with a range of 0–24.0 days) among cases of COVID-19 disease.^[45]

Strains of SARS CoV2

Data on 11 patient-derived viral isolates from a hospital in Hangzhou, China, showed 33 mutations and 19 of which are novel when compared with 1111 genomic sequences.^[46] A population genetic analytical study of 103 SARS CoV2 genomes showed two prevalent types: L type (about 70%) and S type (about 30%); and L type strains are more virulent and contagious.^[47] A research published by Angeletti *et al.*, in a medical virology journal showed that non-structural proteins 2 and 3 (NSP2 and NSP 3) mutations play a role in the infection and differentiation ability of the COVID-19 virus.^[48] Korber *et al.*, revealed 13 mutations in spike, among which D614G is of immediate concern as this mutation spread in Europe in February 2020.^[49] An article published in Bulletin of the World Health Organization (Koyama *et al.* 2020) identified 14 other variants besides D614G. Nearly, all strains with D614G mutation also have a replicative-responsible protein mutation (ORF1ab P4715L; RdRp P323L), which may influence the virus' replication rate. The antiviral drugs, remdesivir and favipiravir, may target these proteins. The treatment-resistant strains may emerge if there is a mutation in this protein. Mutations that found in the receptor-binding domain of the spike protein may produce variants that have decreased binding affinity with ACE2, thus reducing the infectivity of the virus.^[50]

Basic Case Reproduction Rate (R0) for SARS CoV2 Virus

The basic case reproduction number means that on average the total number of healthy persons getting infected by each patient. D'Arienzo and Coniglio based on an early outbreak in Italy found that the basic reproductive number of COVID-19 may range from 2.43 to 3.10.^[51] A review article that included 12 studies from China and overseas found that the average R0 to be 3.28 and the median to be 2.79. It was higher than the WHO estimates of average R0 from 1.4 to 2.5.^[52] An article published by Sanche *et al.*, in emerging infectious diseases, CDC journal showed a median R0 value of 5.7 (95% CI 3.8–8.9) while assuming a serial interval of 6–9 days.^[53] Chen *et al.* found that the R0, 2.30 from reservoir to person and 3.58 from person to person.^[54] Lathika Rajendrakumar *et al.* found the R0 estimates ranging from 1.43 to 1.85 using the time series data available from the internet.^[55]

The Case Fatality Rate (CFR) of COVID-19

An article published in the month of March 2020 in JAMA showed a CFR among different age-groups in Italy and China. The CFR among the 70–79 age groups was 12.8% and 8.30% in Italy and China, respectively, whereas 60–69 years age group had about the same CFR (approx. 3.5%) in both countries.

The younger ones had less CFR in both countries.^[56] An article published in The Lancet showed the CFR of 4.00% per total cases and per closed cases (who either died or recovered from the disease) is 4.44% in China.^[57] Data from China CDC revealed an overall CFR of 2.3%, among confirmed cases showing a total of 1,023 deaths.^[34] Baud *et al.*, by using WHO data on the cumulative number of deaths to March 1, 2020, estimated mortality rates of 5.6%.^[58]

Using data from “worldometer” The Oxford COVID-19 Evidence Service has presented (updated until 09th June 2020, 15:21 GMT) country-level case fatalities as a percentage along with 95% confidence intervals in a forest plot. Estimates of heterogeneity and a 95% prediction interval are presented, but a pooled overall estimate is suppressed due to heterogeneity. Taking the top four countries from the graph, France had a CFR of 18.4% (95% CI; 18.75–19.14), Belgium has a CFR of 16.18% (95% CI; 15.89–16.48), Italy has a CFR of 14.44% (95% CI; 14.29–14.58), and the United Kingdom has a case fatality of 14.13% (95% CI; 14.00–14.25).^[59,60] The case fatality for COVID-19 among these developed countries is higher than the China. This can be attributed to the population structure, i.e., more geriatric population in these countries than the Chinese population. There are many factors we might rely on for variation in the epidemiology of COVID-19, like herd-immunity, cross-border travel and communication, density of population, inequalities in social groups, and the proportion of the elderly.^[61]

Interventions to Reduce Transmission

Health care workers who are at higher risk of infection than the general population should use Hazmat suits and other personal protective equipment like surgical face mask, protective goggles, shoe covers, and double gloves according to their place of posting in the hospital to reduce exposure to the virus.^[62] Most of the countries in the world have sealed their boundaries, stopped receiving international flights, even stopped domestic flights, trains, buses, and local transport services. A lot of countries have adopted full lockdown, even though it has had a dramatic impact on the economy. This is the first time in the modern era that a virus had had such a tremendous impact on the life of everyone, even healthy people. Many health agencies have started web programs for health care workers regarding COVID-19. Promotional videos regarding common symptoms, when to test, maintain social distancing, and respiratory etiquettes, etc., have been developed and spread around the social media. Many of the states here in India have done complete lockdown and hot spot containment as other countries are doing the same in different parts of the globe.

Vaccine Developments

As per WHO web-page information till 15 October 2020, there were 52 candidate vaccines in clinical evaluation and 162 vaccines are in preclinical evaluation phase. One such vaccine from

University of Oxford/AstraZeneca, whose vaccine platform is no-replicating viral vector, has been entered in phase 3 of trial.^[63] According to news published in Nature, on 11 August 2020, the Russian Federation announced the world's first COVID-19 vaccine, Sputnik V, for widespread use.^[64] Clinical trials of Russian Sputnik V vaccine have been foretold in the UAE, India, Venezuela, and Belarus. The efficacy of the Sputnik V vaccine is 91.4%, based along the second interim analysis of data obtained 28 days after administering the first dose (7 days after the second dose).^[65] Recently, a report published in BMJ (13th October 2020) said that Johnson & Johnson has paused its vaccine trial because of some adverse effects developed in the vaccine recipients.^[66] Similarly, in September Oxford and AstraZeneca paused the COVID-19 vaccine trial due to adverse events. The trial was resumed after that.^[67] Moderna, a biotechnology company based in Cambridge, Massachusetts, has stated that its RNA-based vaccine is more than 94% effective in preventing COVID-19. These results were based on a 95-case analysis in the current Phase III efficacy test.^[68] mRNA-based vaccine from Pfizer Inc and BioNTech SE was found to be more than 90% effective in preventing COVID-19 in persons without prior SARS-CoV-2 infection. Their study was conducted upon 43,538 persons, and no serious safety concerns have been found.^[69]

Recurrence Positive Tests or Person with Persistent Positive Test?

Some case reports about reinfection were published where the patients (from Hong Kong, Nevada-USA, Belgium, and Ecuador) got reinfection from SARS CoV2 virus.^[70] According to CDC, Atlanta (updated till October 05, 2020) people with recurrent or persistent positive COVID-19 tests in South Korea and USA did not show to have live virus in their bodies.^[71]

Conclusion

As the natural history of SARS CoV2 is not fully known, many studies have shown genetic mutations in the virus producing different strains, so there should be an emphasis on a molecular level as well as epidemiological interventions. Case fatality rate varies from country to country, suggesting more to explore on mutations and virulence of the viral strains. COVID-19 infection is expanding in the world, and the virus can be transmitted very long distances (up to 6 m during sneeze) with long viability on some surfaces (up to 7 days); therefore, it is required to change the social behaviors like avoiding crowded places, maintenance of social distancing, good respiratory etiquettes, not touching surfaces/currencies, and not eating raw/undercooked animal products. More time is needed to know the natural history of SARS CoV2 and a long way to go into its diagnosis and treatment.

Limitations of the Study

COVID-19 pandemic is still going on. Many research fields are untouched as the current time needs the study to be focused on the stopping of the spread of the disease.

Key Message

The number of secondary infections arising from one infected individual is estimated to be between 2 and 2.5 for SARS CoV2 virus. Large droplets due to sneeze are transmitted more than 6 m. During coughing, large droplets can be carried more than 2 m away and less than 1 m away during normal conversation or breathing. SARS CoV2 remained viable for 3 h in aerosol. It was found on steel and plastic up to 3 days and on glass and currency notes for up to 4 days. This virus was viable on steel, plastic, and on surgical mask up to 7 days. Whereas on copper, the virus was not found after 4 h.

Ethical consideration

None required.

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Conflicts of interest

There are no conflicts of interest.

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