Chapter

Epidemiology, Zoonotic and Reverse Zoonotic Potential of COVID-19

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Abstract

The demographic patterns of COVID-19 spread can provide clues to develop roadmaps for devising better prevention and control. It is high time to analyze and re-evaluate the zoonotic/reverse zoonotic spread of SARS-CoV-2 globally. To this end, lessons from epidemiology and associated determinants from previous outbreaks of SARS-CoV-1 and MERS need to be cultured and re-visited. Ways to minimize the rates of infection and promote the well-being of the masses need urgent attention owing to the subsequent waves of the global pandemic in most countries. Efforts are being directed for the provision of efficient and cost-effective diagnostics, prophylaxis and therapeutic options for COVID-19. The chapter provides insights, suggesting a potential roadmap for efficiently preventing the future outbreaks of COVID-19, based on the tools of epidemiology, transmission probabilities and public health safety concerns.

Keywords: COVID-19, Zoonotic, reverse zoonotic, Epidemiological tools, public health

1. Introduction

An outbreak with the name of CoVID-19 was reported from Wuhan, China on December 29, 2019. Initially, it was treated as pneumonia of unknown origin and reported to the local office of the World Health Organization (WHO) in China on December 31, 2019 [1]. The most recent outbreak owing to the probable zoonotic and human-human transmission of coronavirus disease virus, 2019 (COVID-19) has entrapped 220 countries and territories with 162, 773, 940 confirmed cases reported by WHO as of 17 May 2021 more than One Hundred Fifty-eight million people (WHO) affected. The host, agent and environmental factors are crucially involved in the chain of infection following the entry of the 2019 novel Coronavirus (2019-nCoV or SARS-CoV-2) in a susceptible host. The progression of the virus within the host may be as quick as 5–6 days (average), leading to severe clinical symptoms that warrant intensive care. The virus later on named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the international committee on taxonomy of viruses on February 11, 2020 [2]. Bats and Pangolins were considered the reservoir host and initially blowout through the exposure of human beings to the seafood market in Wuhan, China [3]. The worldwide distribution of the virus was attributed to commercial air travels from epidemic countries to non-epidemic countries including, Taiwan, Japan, Korea, Malaysia, Russia, America, Saudi Arabia, United Arab Emirates, Germany, France, Spain, Italy and Iran etc. [4]. To date, the number of highest positive cases has been encountered by the USA followed by India, Brazil, Europe, UK, Africa and Middle East [5]. In order to respond to the outbreak swiftly and accurately, the public health authorities and policy makers direly need to know the epidemiology and associated risk factors [6]. The risk factors may include; how much time it takes to show the symptoms and which specific individuals having specific characteristics are more prone to infection.

According to CDC, currently several registered vaccines are available in United States to provide protection against CoVID-19. These vaccines are named as Pfizer-BioNTech, Moderna and Johnson & Johnson's Janssen. Other two vaccines Novavax and AstraZeneca are in phase 3 clinical trials.

It is necessary to strictly follow the precautionary measures i.e. wearing mask, social distancing, avoid arranging events and frequently hand washing along with the vaccination because vaccines alone will not prevent the transmission or end the pandemic. Until high level of global vaccine mediated defense is attained throughout the world.

As documented by the WHO, mathematical models specifically designed in a timely fashion may play an important role in providing evidence-based knowledge to public health authorities and policy makers. Moreover, modeling can help in understanding different aspects of the outbreak including (i) the ability of transmission of disease, (ii) prediction of peaks of infections during the progression of the disease, (iii) severity of infection and (iv) the effectiveness of preventive strategies for the intervention of disease. The modelers of infectious diseases worldwide had accepted the challenge of developing simulation models for transmission and dynamics of the disease and promptly reacted to the emerging outbreak of CoVID-19. Various epidemiological models that have been developed by modelers worldwide included: In China, Susceptible-Exposed-Infected-Resistant (SEIR) Model [7–9], Bats-Host-Reservoir-People (BHRP) transmission network model [10], Markov Chain Monte Carlo (MCMC) methods [11], Susceptible individuals (S)-Asymptomatic individuals (E)- Infectious individuals with symptoms(I)- Isolated individuals with treatment (J)- Recovered individual (R) (SEIJR) dynamic compartmental model [12], Exponential growth (EG) and Maximum Likelihood (ML) estimation method [13–15], Incidence Decay and Exponential Adjustment (IDEA) model [16], Susceptible-Exposed-Infected-Recovered-Death-Cumulative (SEIRDC) model [17], Computational modeling of potential epidemic trajectories [18], Simulation of early outbreak trajectories [19], Traveling network based modeling [20], Susceptible-Infected-Recovered (SIR) model and Quarantine model [5] in Italy, Susceptible-Exposed-Infected-Recovered (SEIR) model, Exponential growth (EG), Maximum Likelihood (ML) estimation, Sequential Bayesian (SB) method and Estimation of Time Dependent (TD) reproduction numbers in India [21, 22].

All of these simulation models estimated the Basic Reproduction Number (R0) of the virus. The R0 indicates the transmissibility of the virus from an infected person to a naïve or unexposed population. A value $R0 > 1$ represents that the number of cases will increase in the future while $R0 < 1$ represents that the disease will diminish in the near future. The reason for higher R0 estimates may be attributed to lower numbers of cases and minimum onset time of infection. However, the estimation error will start to decrease as the number of cases increased and real-time pictures of the cases will be available for accurate estimates [13]. In this scenario, statistical models are primarily used to determine the basic viral replication number, the serial interval between primary and secondary cases and virus doubling time which are important epidemic parameters [23, 24]. Additionally, some other approaches may also be required to include mild or asymptomatic cases which may be missed due to limitations of diagnostic methods applied [25]. With time, treatment options of clinical patients were improved and the spread of disease is being controlled through more strict methods like the restricted movement of individuals. The effects of such measures may be measured through statistical reasoning [26, 27]. On the other hand, mathematical models are based on dynamical Equations [28] can give more details related to epidemic characteristics as compared to statistical methods [29].

2. Reverse zoonotic potential of coronaviruses

Sporadic detection of natural SARS-CoV-2 infections together with successful experimental infections of certain animals raises concerns about reverse zoonosis (also termed as zooanthroposis: transmission of the infection from humans to animals. As a result of close contact with infected humans, several cats, dogs and zoo animals tested positive for SARS-CoV-2 [30, 31]. However, the incidence of natural infections in these animals has not been ruled out due to limited information on clinical features of the infections in animals. The existing data suggest that clinical features may range from asymptomatic infections to symptomatic disorders with signs that may include sneezing, coughing, nasal discharge, respiratory distress, vomiting, diarrhea, ocular discharge, lethargy and fever etc. [32]. A study from Hong Kong in February 2020 confirmed the transmission of SARS-CoV-2 infection to asymptomatic dogs from their previously diagnosed COVID-19 positive owner. A 17-year-old Pomeranian breed dog and a 2-year-old German shepherd were tested positive for SARS-CoV-2 RNA by RT-PCR on multiple oral and nasal swabs. However, virus isolation and serological testing could not be executed [33]. A summary of potential zoonotic relations of some coronaviruses has been given in **Figure 1**.

As a result of the death of a geriatric dog; presumably due to other underlying health issues, it was concluded that the dog either was contaminated by close contact with an infected individual or had a low level of infection. Similarly, a six-year male German shepherd tested positive for SARS-CoV-2 RNA in the USA in mid-April 2020, who contracted the infection from his COVID-19 positive owner. After five days of infection, he developed active infection followed by nasal discharge, lethargy and difficulty in breathing, blood in urine and vomit, weight loss and difficulty in walking, along with heart murmurs and lymphoma [34]. A case report in March 2020 revealed a cat belonging to a COVID-19 positive owner, tested

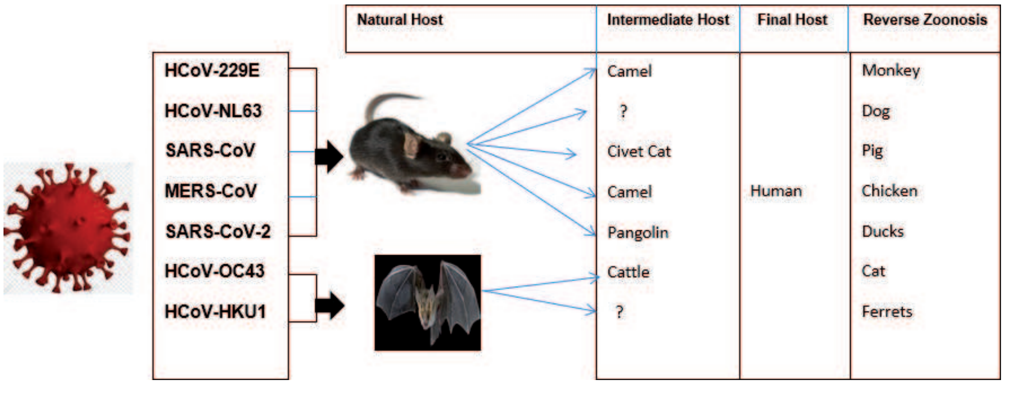

Figure 1.
Probable zoonotic potential of various coronaviruses.

positive for SARS-CoV-2 RNA by RT-PCR in Belgium, presenting gastrointestinal disease and transient respiratory disorders. While in another report on April 01, 2020, a pet cat belonging to a COVID-19 positive owner was tested positive for SARS-CoV-2 without showing disease symptoms [35]. A report on April 05, 2020, showed transmission of SARS-CoV-2 from a zoo employer who was an asymptomatic carrier of SARS-CoV-2 to one tigress, five tigers and lions at Bronx zoo in New York [35].

In the USA on August 14, 2020, 13 cases of pet cats and 14 cases of dogs were tested positive for SARS-CoV-2 by virus neutralization antibody tests or RT-PCR having close contact history with infected humans [31]. It has also been proven experimentally that susceptible pet cats can also transfer this virus to other healthy cats via short-distance aerosols or droplets due to greater similarity between ACE-2 receptors of feline and humans [36]. In a study, two dogs, two cats, three lions and four tigers were tested positive for the presence of SARS-CoV-2 due to close contact with their COVID-19 positive caretakers [37]. It also provides important information about animal management for COVID-19 control, animal models for SARS-CoV-2 and significant replication of this virus in both lower and upper respiratory tracts of ferrets and cats. Transmission of this virus can occur in ferrets through direct contact and in cats through droplets or aerosols. The presence of this virus in cats from Wuhan, China showed that cats may get infected by this virus by the environment or humans [38]. In a study, 15% of cats were tested positive for the presence of SARS-CoV-2 using an Indirect Enzyme-Linked Immunosorbent Assay while cats tested before the outbreak showed negative results [39]. A study provides important insight about the high susceptibility risk of animals having close contact with humans especially cats and ferrets while poor susceptibility risk in animals like pigs, dogs, ducks and chickens [40].

Based on these findings we may conclude that SARS-CoV-2 has the potential of reverse zoonosis as well. Although the risk of disease transmission from humans to animals and companion or zoo animals to humans or other animals is much less and it depends upon how this virus spreads in various animal species. Therefore, planned investigations, targeted surveillance and continuous monitoring of specific animal species having close contact with their COVID-19 positive or suspected owners or caretakers are mandatory at local or national levels. Although, currently there is no specific testing facility available for SARS-CoV-2 infections in animals. But the situation may change in the future to control and management of COVID-19 infections. To test samples for companion animals, a laboratory in the USA known as IDEXX Laboratories has started a test under the commercial name of SARS-CoV-2 (COVID-19) [41]. Several private and government veterinary laboratories are now trying to develop and use nucleic acid-based tests and serological assays to diagnose SARS-CoV-2 transmission in zoo and pet animals [42].

3. Reverse zoonosis in other coronaviruses

3.1 SARS-CoV

To probe into the proximal origin of SARS-CoV from china in 2002–2003, an epidemiological surveillance survey was conducted in the animal market of china and adjoining areas during the outbreak from wild, companion and livestock animals to check out their susceptibility for this virus and more importantly to devise means for the management and control of this first documented outbreak [43]. In this report, dogs and goats were tested negative while wild boars and cats were found to be positive for the presence of SARS-CoV using viral detection assays [43]. Chen et al. conducted a field-based surveillance study on different animals through antibody and antigen-based tests. In this study, two pigs were tested positive for SARS-CoV antibodies while cats, dogs and cattle were tested negative. Based on sequence data analysis this study also suggests that transmission is from human-related SARS-CoV [44].

3.2 MERS-CoV

During the MERS-CoV outbreak very few reports appeared regarding the chances of human-animal transmission of this virus [45]. Kasem et al. conducted a study to check out the incidence of MERS-CoV infections in goat, sheep and cattle samples due to close contact with MERS-CoV positive individuals. In this study, all the tested samples were negative for MERS-CoV suggesting that no cross-species transmission was occurred [46]. El-Duah et al., conducted a field-based surveillance study on MERS-CoV by taking samples from sheep, pigs, goats, donkeys and cattle of the Ghana area. This study showed that none of the samples were found to be positive for the presence of MERS-CoV [47]. Kandeli et al. conducted an epidemiological surveillance study in Tunisia, Egypt and Senegal area from the field samples received from buffaloes, sheep, cattle, goats, mules, horses and donkeys using PCR and antibody detection kit. The results of this study revealed that both antibody detection tests and PCR were found to be positive for MERS-CoV in goats, sheep, cattle and donkeys. While PCR was negative in horses [48]. These reported studies suggest that transmission of MERS and SARS-CoVs occurred in humans-wild, domestic and companion animals making the possibility of reverse zoonosis [49]. However, still it is not clear whether infected animals shed the virus and are involved in the disease transmission cycle.

4. Promoting public health

There are at least 360,497 research studies worldwide, on diagnosis, treatment and prophylaxis of coronavirus that are being supported by NIH [50]. Combined efforts of global health organizations including the World Health Organization (WHO), Centers for Disease Control and Prevention (CDC) and many International, Regional and National NGOs, Government and private bodies are funding, supporting and helping approaches for public health. Food and Drug Administration (FDA) on the other hand, is rapidly analyzing and approving medicines and diagnostics for public use. Some major areas to be considered for tackling the current situation and developing roadmaps for future pandemics have been given in this section.

4.1 Elucidating the concept of quarantine and isolation

The COVID-19 crisis is continuously becoming a grave threat to the world and the number of cases is escalating globally. The present pandemic has redefined the human strategies against the control and prevention of this contagious agent responsible for disease outspread [4]. This virus is very lethal and contagious, and the WHO devised measures to control the infectivity and spread of the virus through quarantine and isolation. Some major myths and their busters associated with COVID-19 have been re-developed using WHO research-supported guidelines in **Figure 2**.

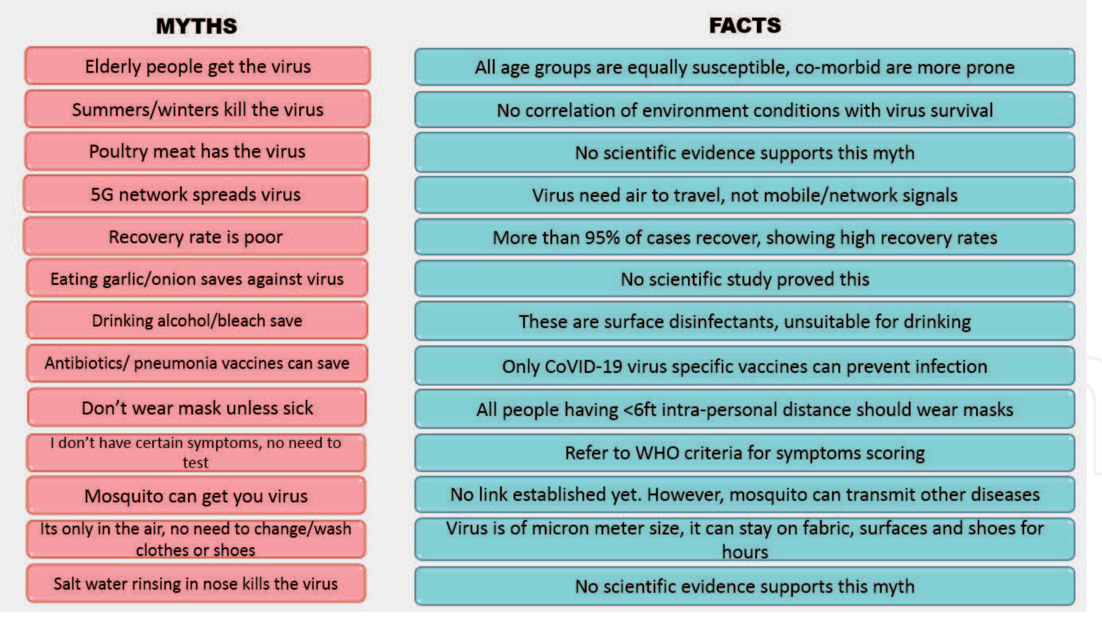

Figure 2.
Major myths and their busters associated with COVID-19.

Quarantine is separation and restricting the movement of people who have been exposed to a SARS-CoV-2 disease to see if they become sick, according to the CDC. Generally, this quarantine practice takes place at home or generalized facility or restricted movement areas specified for this practice. It can be imposed on individuals or communities constituting exposed individuals. Contact surveillance is required either passively or actively to monitor the individual if they develop the symptoms of the disease. Duration of the quarantine is based on a person's test results for disease or having experienced disease symptoms. If individual tests positive so after that, they are separated or isolated for treatment and monitoring purposes and if the individual is negative for diagnostic test and not showing any disease symptoms, then discharge from the quarantine center [8]. Monitoring must be done in case of quarantined person shows any of the disease symptoms. Government and other global authorities must implement border restriction if necessary, to overcome the spread of disease. The efficacy of this approach allows us to overcome the spread of disease with the early detection of diseased individuals.

Here the question arises after or during this "Quarantine session" what would be our approach if a person is positive for SARS-CoV-2. This question leads us to the term 'isolation'. The Center for Disease Control (CDC) has defined "Isolation" as the separation of sick people with any contagious disease from others who are not sick or at-risk population. This is important to flatten the disease curve so that fewer people become infected over a while. It can be explained as separation and restriction of movement of sick individuals who have a contagious disease, to prevent it from being transmitted to others. These measures are implemented to ensure the close monitoring of individuals with proper treatment and release after full recovery into the community or population to minimize or eliminate the risk of spread of this contagion. However, these individuals can still be monitored for weeks or two, to ensure they do not re-infect or develop severe symptoms after discharge from medical facilities.

4.2 Measures for cleaning and disinfection

From the sanitation/disinfection point of view, the Environment Protection Agency (EPA) recommends the use of List N disinfectants for use against COVID-19.

Cleaning the surfaces before applying disinfectants and observing the appropriate contact time are important considerations for efficient utilization. Among the most accessible ones are sodium hypochlorite, hydrogen peroxide, and quaternary ammonium compounds with or without alcohol or phenols. The forms of these disinfectants may be solid, vapor, wipe, dilute-able, which could be easily used to disinfect surfaces. These compounds in their commercial preparations could be safely applied to disinfect keys, doorknobs/handles, slabs, floors, switchboards, equipment, keyboards, tables, cell phones, remote controls, cars, bikes, etc.

Case definitions and their importance to the general public may be well-communicated. Also, smart solutions for handling a large number of outdoor patients may be sought. Un-necessary exposure and increase in case of loads at emergency and intensive care units could be minimized using efficient telemedicine and consultation services. For laboratory testing facilities, it is important to consider biosafety guidelines of level-3 or above, owing to the transmissibility of the virus. Also, solid waste management should be very well planned and executed to spare the risk of dissemination to the general public [51].

4.3 Management of COVID-19 patients

It is important to consider the difference of COVID-19 with other prevailing respiratory viral infections e.g. influenza that involves nasopharyngeal or lower respiratory tract infections. Polymerase chain reaction (PCR) is necessary to confirm COVID-19. Further hospitalization of patients involves various factors inclusive of which are the age of patients (≈60 years old); patient having 40% allied morbid conditions like diabetes and cardiac diseases; children exposed, pregnant women with severe illness although there are mild symptoms so far in majority cases and the onset of symptoms and admission to ICU (9–10 days critical) as two-third of patients met criteria of acute respiratory distress syndrome (https://www.ecdc.europ a.eu/en/geographical-distribution-2019-ncov-cases).

The patient's care should be divided into four categories (1) Usual critical care, (2) Modification to usual critical care, (3) Facility planning, (4) COVID-19 specific consideration. Usual critical care will include: Conservative intravenous fluid strategies; Empirical early antibiotics for bacterial pneumonia; Consideration for early invasive ventilation; Lung protective ventilation strategies; Periodic prone position during mechanical ventilation; Consideration of extracorporeal membrane oxygenation. Modification to usual critical care involves: Admission of patients with the suspected disease to private rooms when possible; Use of medical face masks for symptomatic patients during assessment and transfer; Maintain a distance of at least 2-meter distance between patients; Caution when using high-flow nasal oxygen or non-invasive ventilation due to the risk of dispersion of aerosolized virus in the health care setup with poorly fitting masks; Clinicians involved with aerosol-generating procedures should use addition airborne precautions including N95 respirators and eye protection. COVID-19 Specific consideration; Ensure staff updated training in infection prevention and control including PPE; planning at local and regional levels for a potential surge in the need for critical care resources. The facility planning involves: Antiviral or immunomodulatory therapies are yet to be approved, so patients should be left on supportive or targeted therapies.

Three lines of treatments are generally followed (a) COVID-19 with mild acute respiratory distress syndrome (ARDS), (b) COVID-19 with mild ARDS, (c) Adjunct therapies. In the first case ventilator, supply while conservative fluid therapy, and empiric antibiotics are considered. Systematic corticosteroids are uncertain to be used on this occasion. In the second phase, short courses of systemic corticosteroids are considered. In adjunct/rescue therapy (3rd phase), antiviral, chloroquine, and anti-interleukin 6 are uncertain to be used. The hypoxic conditions will be dealt with differently. It is important not to delay intubation if the situation is worsening. COVID-19 hypoxia travels to endotracheal intubation, then it is important to: follow endotracheal intubation, an expert should do intubation in the airway, N95/FFP-2 or equivalent personal protection equipment is necessary, infection control is followed, and staff in the room is minimally kept. In case if the situation is not getting better, endotracheal intubation should immediately be done.

4.4 Ensuring mental well-being

Due to social distancing and remote working, maintenance of psychological well-being is pivotal. Social, electronic, print media could play a significant positive role in effectively communicating the risks while assuring mental health. Non-professional people who have a lot of apprehensions about the current pandemic may be discussing their concerns through telecommunication [52, 53]. Another important aspect of lockdown amidst outbreaks worldwide is the less privileged or daily wager community, migrants and internally displaced persons (IDPs). The anxiety due to uncertainty of fiscal matters may affect the mental health of the masses. Also, patients with other diseases, particularly those with chronic diseases may suffer a psychological breakdown. Apart from mental health issues, India has reported suicide due to fear of contracting COVID-19 [54]. It is, therefore, high time to spread hope, offer support and positivity all around.

Studies from one highly infected country *i.e.* Iran have revealed moderate to severe anxiety symptoms in apparently healthy citizens [55]. Suspected patients and cases, belonging to different age groups, may also require support for mental well-being amidst strict isolation. The healthcare workers in the frontline of combating the pandemic may need psychological/moral support, medical insurance and proper PPE. Government, NGOs, private stakeholders, media persons, celebrities, doctors and allied healthcare staff, scientists need to develop stronger communication with the public. These people can motivate people to adopt safety measures and promote public health safety.

5. Conclusions and future outlook

The detailed understanding of epidemiological patterns and probable modeling of COVID-19 are highly important. Moreover, there's a need to disseminate the research-based findings to public health. This could be made possible by the thorough collaboration of the National and International organizations that may fetch research-supported data for prevention and ways to control or contain the pandemic at all levels.

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