**REVIEW**

# COVID-19 transmission, vulnerability, persistence and nanotherapy: a review

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## Abstract

End 2019, the zoonotic severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), named COVID-19 for coronavirus disease 2019, is the third adaptation of a contagious virus following the severe acute respiratory syndrome coronavirus in 2002, SARS-CoV, and the Middle East respiratory syndrome virus in 2012, MERS-CoV. COVID-19 is highly infectious and virulent compared to previous outbreaks. We review sources, contagious routes, preventive measures, pandemic, outbreak, epidemiology of SARS-CoV, MERS-CoV and SARS-CoV-2 from 2002 to 2020 using a Medline search. We discuss the chronology of the three coronaviruses, the vulnerability of healthcare workers, coronaviruses on surface and in wastewater, diagnostics and cures, and measures to prevent spreading.

## Abbreviations

| | |
|---|---|
| SARS | Severe acute respiratory syndromes |
| MERS-CoV, 2012, Saudi Arabia | Middle East respiratory syndrome virus |
| H2H | Human to human |
| WHO | World Health Organizations |
| HCW | Health care workers |
| CDC's | Centers for disease control and prevention |
| NHMRC | National Health and Medical Research Council |
| IARC | International Agency for Research on Cancer |
| WEPA | Water Environment Partnership in Asia |

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|---|---|
| DWAFSA | South African Department of Water Affairs and Forestry |
| NPHS | National Public Health Service for Wales |
| PCR | Real time-polymerase chain reaction |
| rt-PCR/qPCR | Quantitative reverse transcription-PCR |
| RCA | Rolling circle amplification |
| ALBO | Aluminate-based nanomaterials |
| CT | Computer tomography |
| NGS | Next generation sequencing |
| TGEV | Transmissible gastroenteritis virus |
| Quarantine, shield, and stop | QSS model |

## Introduction

The severe acute respiratory syndromes (SARS) is from a lineage of β-coronaviruses that caused the emergence of previous outbreaks-SARS-CoV in 2002 in China, and the Middle East respiratory syndrome virus MERS-CoV in 2012 i nSaudi Arabia. The β-coronaviruses such as SARS-CoV and MERS-CoV can induce infection in the lower respiratory tract followed by cough and fever and that trends to cause severe respiratory illness in humans (CDC 2020). Whereas, recent pandemic by novel severe acute respiratory syndromes (SARS-CoV-2) is a fall in α-coronavirus lineage showing similarity to these earlier CoV's such as SARS-CoV and MERS-CoV, predominately attacks alveolar epithelial cell of the lung, stimulates peripheral pneumonia-causing mass mortality up to 5% (Wu et al. 2020c). This suggests that the clinical spectrum of SARS-CoV-2 is not confined to peripheral pneumonia, but relatively indicates a multiple series of illness leading to multiple organ failure such as heart, liver, kidney, coagulation, gut or gastrointestinal tract (Robba et al. 2020) that are highly contagious than previous illness by SARS-CoV or MERS-CoV in human (Tang et al. 2020).

Hence, we review SARS-CoV-2 in correlation to previous SARS and MERS outbreaks (Dai et al. 2020; Gorrasi et al. 2020; Choi et al. 2021). We present the key scientific developments, ongoing research and rapid detection procedures from the SARS-CoV and MERS-CoV outbreaks insights to understand the gravity of the problem for possible preventive measures to control the current pandemic (Sarkar et al. 2020; Sharma et al. 2020, 2021). In addition, we present an extensive outline of the outspreading of the SARS-CoV-2, aspects responsible to the transmission, vulnerability, persistence, and addressing potential control approaches in pandemic mitigation (Prabha et al. 2020; He et al. 2021;

Mousazadeh et al. 2021). The most innovative point of this review is the correlation of the behavioral patterns of the coronavirus family in different settings and its tenacity in the environment, which should facilitate the design of epidemiological measures to avoid such pandemics in future. This study also highlights the comparative study on symptoms and various laboratory methodologies and parameters. The major aspects are the following: (1) epidemiological findings across several countries contributing toward cross-cultural and scientific influences, (2) present vulnerability data of first line exposures, healthcare workers with case fatality among them, (3) persistence of agents such as material surfaces, water, wastewater, streams, and (4) finally provide some insights & strategies learned from earlier outbreaks.

## Review methodology

The main aim of this review is to make a combinative review information for better understanding the current state of SARS-CoV-2 situation. Therefore, we have used databases like PubMed, Google Scholar, Scopus, Web of Science, and Research gate. The adapted keywords were "coronavirus" and "virus name" such as "SARS-CoV," "MERS-CoV," "SARS-CoV-2," "COVID-19" and other strings like "epidemiological," "preventive measures," "transmission," "persistency," "vulnerability," "pandemic," "human to human transmission" and "nanotheraputics," etc. Furthermore, we have excluded the inappropriate studies and selected proper articles that were additionally checked for references which will increase the scientific values of this study. Besides, we accessed the websites of the world health organizations (WHO), Centers for Disease Control and Prevention guidelines, the Council of European Union, the Australian Government National Health and Medical Research Council (NHMRC), the Canadian Federal Provincial Territorial Committee on Health and the Environment, the International Agency for Research on Cancer (IARC), the National Standard of the People's Republic of China, the Japanese Ministry of Health, Labor and Welfare, the Water Environment Partnership in Asia (WEPA), the New Zealand Ministry of Health, the South African Department of Water Affairs and Forestry (DWAFSA), the National Public Health Service for Wales (NPHS), and various health ministry's information on COVID-19 (Sun and Han 2020; Wang et al. 2020a, c). The main goal of the current review is to provide clear and comprehensive information of coronaviruses infections and current status. Additionally, this study reviewed about newly developed methods, potential technologies and further mainly focused on nanotherapeutic approaches toward COVID-19 that has been discussed.

## Natural virus hosts

The human coronavirus 229E (HCoV-229E), human coronavirus NL63 (HCoV-NL63), human coronavirus OC43 (HCoV-OC43), human coronavirus (HCoV-HKU1), SARS-CoV, MERS-CoV, and SARS-CoV-2 have a zoonotic origin from bats, mice, or domestic animals (Ye et al. 2020). SARS-CoV-2 has characteristics that are similar to SARS-CoV and MERS-CoV which shows high communicable. Epidemiological data revealed civets raccoon dogs were the first carrier of SARS-CoV- viruses (Guan et al. 2003). A subsequent study showed that for a host of SARS-CoV revealed relation to bat CoV (Li et al. 2005). Similar findings that showed MERS-CoV was closely relative to bat origin (Lau et al. 2018). Researches from Shanghai shown that the natural host is likely to be bat for SARS-CoV-2 (Ji et al. 2020). Further other studies from Perkin University suggested that snakes may be the cause (Ji et al. 2020). Later, studies try to prove that snakes were not the cause (Zhang et al. 2020a, b) and gene sequence between SARS-CoV-2 with bat coronavirus is high as 96.2% by sequencing technology (Yuen et al. 2020). These factors suggest that the possible cause of this virus could be a bat. According to findings published by the journal Nature Medicine, the novel SARS-CoV-2 is the product of natural evolution (Andersen et al. 2020). In the current situation, main sources of spread such as vulnerable population, risk groups, and factors, are considered to be affected population but is debatable regarding the incubation period and needed more research (Wang et al. 2020b).

## Clinical profiles of infected coronavirus patients

The laboratory parameters and clinical profile in patients suffering from coronavirus infections are shown in Table 1.

Findings are essential to interpret the unknown deadly viruses and its behavior more efficiently to save the mankind. From the above-mentioned references, it is easy to understand the transmissibility of COVID-19 and the innate immune process behind this phenomenon. In the next section, we discuss various routes of transmission of coronaviruses.

## Route of transmission

The first indication of human to human transmission was detected in SARS-CoV, develops primarily by nosocomial transmission. Similar indications were reported in MERS-CoV; which were linked to hospitals (Chowell et al. 2015). The hospital transmission of MERS-CoV's was the most usual route of transmission of infection among patients up to 79%, whereas up to 42% for SARS-CoV (Chowell et al. 2015). At present, spread of SARS-CoV-2 is substantially influenced by contact with the infected persons either via aerosol, airborne or object transmission (Adnan Shereen et al. 2020) (Baranwal, Mahapatra et al. 2020). This was proven by the detection of this virus in the various samples taken from the population through stool, urine and saliva. Considering the bioinformatics, digestive track is the main route of infection (Wang et al. 2020b). It was also seen

**Table 1** Common symptoms in different countries having persistent infection detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and laboratory parameters

| Symptoms | References | | | | |
|---|---|---|---|---|---|
| | Huang et al. (2020) | Wang et al. (2020a) | Chin et al. (2020) | Kong et al. (2020) | Chan et al. (2013) |
| Fever | 98% | 98.6% | N/A | 87.9% | 83% |
| Dry cough | 76% | 59.4% | N/A | 67.7% | 82% |
| Fatigue or myalgia | 44% | 69.6% | N/A | N/A | 11% |
| Sputum formation | 28% | N/A | N/A | N/A | N/A |
| Diarrhoea | 3% | N/A | N/A | Seldom | 2% |
| Haemoptysis | 5% | N/A | N/A | N/A | N/A |
| Distress syndrome | 29% | 61.1% | N/A | N/A | 17% |
| Shock | N/A | 30.6% | N/A | N/A | N/A |
| Lymphopenia | 63% | 70% | N/A | 82.1% | N/A |
| Ground-glass lung opacities | 100% | 100% | 100% | 50% | 14% |
| Symptom onset, day | Up to 8 | N/A | N/A | Median period 3 (1–24) | N/A |

N/A not applicable

that pregnant women with COVID-19 virus likely to infect infants through intrauterine vertical transmission (Chen et al. 2020a). Few studies stated that the airborne transmission through aerosols route is highly infectious and dominant for the spread of COVID-19 (Zhang et al. 2020a, b). Inhaling the virus-bearing aerosols effecting human respiratory tract directly. The inadequate awareness on SARS-CoV-2 virus hindered this pandemic globally. However, to establish these hypotheses, researchers are trying to do more experimental studies since such studies are very limited and require more verification. Until then, the development of effective mitigation policies and measurements to stop this virus has to be taken very seriously.

## Vulnerability to healthcare workers

Recent epidemiological studies suggest that elderly people i.e., 75 years and above are more vulnerable as compared to other age groups toward SARS-CoV-2 (Bonafè et al. 2020; Rabaan et al. 2020; Chandra and Roy 2020). Considering clinical aspects of COVID-19, the probable incubation period was 3 days having death symptoms in 14 days for the elderly persons were reported (CDC 2020). If we look at SARS cases, it was 4 days and 17.4 days for first death symptoms to be visible (Cho et al. 2016). Moreover, it is worthy to note that the incubation period for SARS-CoV-2 is quite shorter than another coronavirus like SARS and MERS. Additionally, 24 days of high inactivity toward transmission is also been observed. Besides, another trend was observed that 20 days for the first death symptoms arise, as a median for the aged person above 70 years and 11.5 days as shorter median. From the above, it would be suggestive that for an elderly person is more likely to get infected as compared to other hence needed to take special precautions.

According to United States-Centers for Disease Control and Prevention (US-CDC), the risks faced by healthcare workers were very high, even with protective gear, as they had a very intimate relationship with their patients. The infectious materials have potential vulnerability in direct/indirect transmission to patients comprising (1) body substances, (2) infected medical tools and instruments, (3) infected material surfaces, and (4) aerosols transmissions.

Among all the three coronaviruses, SARS-CoV-2 is the most infectious followed by MERS-CoV, SARS-CoV, respectively, as reported by World Health Organizations. To date, the healthcare workers accounted infected (deaths) by SARS-CoV-2, MERS-CoV and SARS-CoV are around 1706 (41), 450 (24), and 287,010 (2000) (WHO 2019; Xiao et al. 2020). According to the International Council of Nurses, so far more than 90,000 Healthcare workers have been infected by SARS-CoV-2 and more than 260 nurses died. Hence, the total numbers of deaths among healthcare workers are hard

to access by, but to date, more than 2000 healthcare workers died globally on treating COVID-19 patients as shown in Table 2.

Healthcare workers should take all the precautions to learn from former coronaviruses (MERS, SARS) experiences for the prevention and cure of future outbreaks. High fatality in SARS-CoV-2 indicates less understanding, and implementation in handling indicates that a thorough workup from earlier outbreaks such as SARS and MERS, causing patients, hospitals, and healthcare worker vulnerability is required.

Therefore, the vulnerability is very serious for SARS-CoV-2. Moreover, this virus is airborne which has great mobility, long surviving nature and duration of time for dispersion is quick. Due to these reasons, SARS-CoV-2 is more vulnerable specially in densely populated countries or areas.

## History of coronaviruses

In the early twenty-first century, in 2003, SARS-CoV emerged in China and a decade later in 2012 MERS-CoV was first diagnosed in Saudi Arabia. Recently, close to 2020, a new chain of SARS-CoV-2 emerged again in Wuhan, China in December 2019 with a similar character that caused the SARS outbreak in 2002. Hubei provinces, Wuhan is a hub of wholesale food markets in Huanan that supply bat soup. A medical team headed by Zheng-Li Shi consists of microbiologists that isolated the virus from a 49-year-old lady. Li Wenliang posted warnings to their colleagues and associate staff, that an unknown virus has been developed within the province of city and Hubei provinces that is similar to SARS and MERS. He stated that symptoms were fever, sore throat, and sneezing by the lady within the hospital. This novel SARS-CoV-2 is the most outreaching among all the three coronaviruses and has infected more than 200 countries so far. The coronaviruses represent a various family of positive sense ribonucleic acid (+ ssRNA) viruses capable of inflicting metastasis and enteric sickness in deferent hosts. Although, many human coronaviruses are known to cause gentle metastasis disease (Li 2015), most capable of inflicting a severe respiratory illness by infecting humans such as SARS and MERS CoV's. The SARS-CoV arose into humans in 2002, infected around 37 nations throughout its course for more than nine-month circulation in humans (Liu et al. 2020). This epidemic led to more than 8000 confirmed contagions with above 10% mortality and it was thought SARS-CoV had been eliminated until the death of recent humans with infections (Ge et al. 2013).

In 2012, another nexus of member beta-coronavirus subgroup MERS-CoV epidemic was originated in Saudi Arabia, from a patient with mucous secretion and acute respiratory

**Table 2** Gross evaluation-oriented deaths among healthcare workers around the world with possible transmission of SARS-CoV-2 and type of protection used

| Country | Number of heathcare workers | Department | Protection measures | Possible transmission |
|---|---|---|---|---|
| *SARS-CoV-2* | | | | |
| Bangladesh | 69+ | Ophthalmology, Thyroid and breast surgery, general OPD (Outpatient Department), GynecologyPhysician, Cardiology, Clinical Pathology, Infectious Disease Specialist, Emergency Medicine, Dentistry, Paramedic, Radiology, Pediatric, Otolaryngology, Hematology, Surgery, OB/GYN (Obstetrics/Gynecology), Nursing, Psychiatry | Providing personnel protective equipment (PPE) in health services includes gown, gloves, N95 mask, face shield/goggles, powered air-purifying respirator (PAPR) | Conjunctivitis, droplets and contaminated surfaces (Table), coughing, sneezing, airborne transmission |
| Brazil | 250+ | | | |
| Canada | 30+ | | | |
| China | 23+ | | | |
| Egypt | 68+ | | | |
| France | 58+ | | | |
| Georgia | 110+ | | | |
| India | 200+ | | | |
| Indonesia | 200+ | | | |
| Iran | 150+ | | | |
| Italy | 250+ | | | |
| Malaysia | 50+ | | | |
| Mexico | 200+ | | | |
| Pakistan | 100+ | | | |
| Peru | 200+ | | | |
| Philippines | 30+ | | | |
| Russia | 300+ | | | |
| South Africa | 200+ | | | |
| Serbia | 20+ | | | |
| Spain | 65+ | | | |
| UK | 150+ | | | |
| USA | 1500+ | | | |
| *MERS-CoV* | | | | |
| Saudi Arabia | 24+ | | | |
| South Korea | 5+ | | | |
| *SARS-CoV* | | | | |
| China | 53+ | | | |
| Canada | 8+ | | | |

Information assembled from Ip et al. (2004), WHO (2019), Elkholy et al. (2020), Emanuel et al. (2020), Khanna and Honavar (2020), Lee et al. (2020), Misra (2020) and Xiao et al. (2020). COVID-19 infections death estimates numbers (3 August 2020-Situation Report −196) are based on references (Ip et al. 2004; WHO 2019; Elkholy et al. 2020; Emanuel et al. 2020; Khanna and Honavar 2020; Lee et al. 2020; Misra 2020; Xiao et al. 2020; Medscape's Coronavirus Resource Center, CDC and health ministry reports of respective countries. SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

OPD: Outpatient Department; OB: Obstetrics; GYN: Gynecology

disease and nephropathy (Pavli et al. 2014). Typical symptoms were myalgia, abdominal pain, vomiting and diarrhea, and some symptoms similar to SARS-CoV such as shortness of breath, cough, sore throat, pneumonia, rigors, and fever (Assiri et al. 2013). Its fatality rate was very high and approximately one-third of infected patients died. According to World Health Organizations (WHO), more than 2494 individuals have been infected and more than 858 deaths worldwide have occurred due to MERS-CoV to date (Rahman and Sarkar 2019). The authors reported that several MERS-CoV patients in Saudi Arabia were from healthcare unit transmission and few secondary cases occurred following close contact to infected patients with severe symptoms (Pavli et al. 2014). Researchers found that the majority of MERS-CoV patients had been infected indirectly by individuals with MERS-CoV symptoms (Hui et al. 2018). Results of a later study show that there are hardly any remedial compounds for MERS-CoV, containing a synthesis of lopinavir/ritonavir (LPV/r) and Betaferon, and ribavirin (Momattin et al. 2019). Consequently, precautionary action is only to reduce the risk of spread.

Additionally, the evolution of SARS-CoV-2 is similar to MERS-CoV and SARS-CoV which is genetically associated to have a zoonotic origin. According to the Chinese Centers for Disease Control and Prevention, the patient diagnosed with virus infection may have visited the infected Wuhan seafood market. Recent investigations have been also stated that newly infected individuals may have approached the infected patient, not visiting the Wuhan market (Adnan Shereen et al. 2020). In the month of January, World Health Organizations (WHO) took the necessary step and declared COVID-19 as a global pandemic worldwide. The intervention in-order to stop the spread lies with the fact of how quick people can respond to this emergency, the early detection, the early treatment, isolation procedures with rugged implementation (Peck 2020). The major symptoms detected during this outbreak in Wuhan were flu like symptoms such as dry cough, persistent fever, and lung infiltration (Sohrabi et al. 2020). They majorly linked to the seafood initially and related live stocks like bats and snakes (Lu et al. 2020a). Recently, some of such problems resolved instantaneously but mainly in selected cases these developed symptoms converted into fatal injuries i.e., septic shock, acute respiration problems, and organ failures. Some extensive studies assisted that more than 54% are male infected patients (Chen et al. 2020b).

Based on the results to date, the human transmission potential of this virus unfurls COVID-19 to more than 200 countries in the world. According to the World Health Organization's (WHO) report, globally 93,217,287 have been infected and 2,014,957 deaths from the coronavirus have been confirmed to date. The COVID-19 conditions in America, India, and Brazil are continuously worsening,

so far total infected and deaths are 23,344,423 (389,084), 10,557,985 (152,274) and 8,393,492 (208,246) were recorded highest in the world, respectively. The fatality rate is highest in the America region i.e., 3.6% (Culp 2020). A comparative analysis of coronaviruses SARS-CoV, MERS-CoV, and SARS-CoV-2 is shown in Table 3.

Thus, in the last two decades, human population has faced three coronaviruses outbreaks. These viruses can affect children and adults severely. However, in the case of SARS-CoV-2, children showed mild symptoms than adults. Many studies have been conducted to know the zoonotic origin of three coronaviruses after continuous attacks of these viruses. In the later section, we have focused on how coronaviruses are spreading from various surfaces, objects and solid materials to human.

## Coronavirus persistence on surfaces

The studies have been done concerning the persistency of coronaviruses on several materials surfaces, such as aluminum, aerosols, copper, cardboard, disposable gown, metal, paper, plastic, steel, surgical glove, and wood. The virus existence varies from 2 h to 5 days and the temperatures ranging from 20 to 25 °C as shown in Table 4. A higher persistence showed by SARS-CoV on metals that are capable to exist for 5 days. After considering the research studies, comparative data were collected regarding the persistency of the higher side of the inoculation and is presented in Table 4. According to van Doremalen et al. (2020), it has also been observed that different surfaces have different surface stability concerning that of SARS-CoV-2 and SARS-CoV when compared on aerosol, plastic, steel, disposable gown, and cardboard. Both the CoV's (SARS-CoV-2 and SARS-CoV) remained capable of attaching onto aerosols for a span of 3 h. SARS-CoV-2 stability on common surfaces of plastic for that of stainless steel was observed more than on copper and cardboard and is stable up to 3 days. The constancy kinetics of SARS-CoV were analogous after 3 days on plastic and after 2 days on stainless steel. It has been observed that on copper and cardboard, no valid SARS-CoV-2 was detected after 4 h and 24 h, respectively. Similarly, no valid SARS-CoV was detected after 8 h on copper and cardboard, respectively (van Doremalen et al. 2020; Carraturo et al. 2020; Wang et al. 2020d, e).

An investigation showed the persistency of HCoV-229E is inactive within 1 min on stainless steel, using ethanol 70% w/v or 0.1% sodium hypochlorite (Kampf et al. 2020). Based on the previous investigation on SARS-CoV and MERS-CoV, reported no infections transmitted through food, vegetables (Vasickova et al. 2010; Yépiz-Gómez et al. 2013). However, the authors reported stable pathogens at low temperatures. Hence, avoiding uncooked food and scientific

**Table 3** Comparison of coronaviruses

| Coronaviruses | SARS-CoV | MERS-CoV | SARS-CoV-2 |
|---|---|---|---|
| Origin | Guangdong, China | Zarqa, Jordan | Wuhan, China |
| Date | November, 2002 | April, 2012 | December, 2019 |
| Natural hosts | Bat, palm civets and Raccon dogs | Bat, camel | Bat, snake |
| Transmission mode | Zoonotic virus | Zoonotic virus | Zoonotic virus |
| Receptor recognition | ACE2 | DPP4 | ACE2 |
| Infected countries | 37 | 27 countries | 235 + * |
| Infected (deaths) | 8000 (800) | 2494 (858) | 93,217,287 (2,014,957) |
| Symptoms | Fever, malaise, myalgia, diarrhea, shivering, cough and shortness of breath | Fever, Sore throat, cough, pneumonia, shortness of breath, diarrhea | Cough, fever and shortness of breath, vomiting, diarrhea |
| Vaccine developed | Under development** | Under development** | Under development** |
| Mortality rate | 10% | 35% | ~5%* |
| *R0* | 0.80 | 0.5 | 2.43–3.10 |
| References | Wang et al.(2005a, b), Cui et al. (2013) and Adnan Shereen et al. (2020) | Assiri et al. (2013), Cui et al. (2013), Alfaraj et al. (2019) and Ji (2020) | Adnan Shereen et al. (2020), Lu et al. (2020a, b) and Wu et al. (2020a, b, c) |

*Data deprived from WHO Coronavirus disease (COVID-19) as of 19 January 2021-Situation Report

**No effective vaccine has been approved yet

R0-pathogen's basic reproductive number

**Table 4** Coronaviruses persistency on various surfaces under different environmental conditions

| Surface[a] | Virus | Strain | Temperature[b] | Duration of existence | References |
|---|---|---|---|---|---|
| Aluminum | HCoV | 229E | 21 °C | 2 to 8 h | Sizun et al. (2000) |
| Aerosols | SARS-CoV-2 | MN985325.1 | 21–23 °C | 3 h | van Doremalen et al. (2020) |
| Copper | SARS-CoV | AY274119.3 | | 3 h | |
| | SARS-CoV-2 | MN985325.1 | 21–23 °C | 4 h | van Doremalen et al. (2020) |
| Cardboard | SARS-CoV | AY274119.3 | | 8 h | |
| | SARS-CoV-2 | MN985325.1 | 21–23 °C | 24 h | van Doremalen et al. (2020) |
| Disposable gown | SARS-CoV | AY274119.3 | | 8 h | |
| | HCoV | GVU6109 | 21 °C–22 °C | < 2 days | Lai et al. (2005) |
| Metal | SARS-CoV | P9 | Room temperature | 5 days | Casanova et al. (2010) |
| Paper | SARS-CoV | P9 | Room temperature | 4 to 5 days | Lai et al. (2005) |
| Plastic | SARS-CoV-2 | Isolate HCoV-EMC, MN985325.1 | 22 °C–25 °C | < 5 days | (Chan et al. 2011; Kampf et al. 2020; van Doremalen et al. 2020) |
| | MERS-CoV | | | | |
| | SARS-CoV | AY274119.3 | | 3 days | |
| Steel | SARS-CoV-2 | MN985325.1 | 21–23 °C | 48 h | van Doremalen et al. (2013, 2020) |
| | SARS-CoV | AY274119.3 | | 48 h | |
| | MERS-CoV | Isolate HCoV-EMC | 20 °C | 48 h | |
| Surgical glove (latex) | HCoV | 229E | 21 °C | < 8 h | Sizun et al. (2000) |
| Wood | SARS-CoV | P9 | RT | 4 days | Carraturo et al. (2020) |

[a]Surface can be disinfected by simple disinfectant to kill the virus and [b]Exposure may also depends upon humidity of the environment

H-CoV: Human coronavirus; SARS-CoV: Severe acute respiratory syndrome coronavirus; SARS-CoV-2: Severe acute respiratory syndrome coronavirus-2; EMC: Erasmus Medical Center

studies recommended to cook foods above 70 °C to ensure the maintenance of healthy and hygienic factors (Carraturo et al. 2020).

Above-mentioned data demonstrate the severity of SARS-CoV-2 infections and its easy dispersion from various metal objects, solid surfaces, etc. Study said, this virus can be recovered from non-porous surfaces for maximum 28 days at ~20 °C temperature and humidity. The transmission of this virus is not only spreading from aerosols or solid surfaces, but researchers have also found traces of virus in water and wastewater as well. Henceforth, we have discussed the presence of coronaviruses in water and wastewater in the following section.

## Coronavirus persistence in water and wastewater

Several researchers found CoV's such as SARS-CoV, MERS-CoV, and SARS-CoV-2 RNA in the various sample of stool, urine, hospital wastewater, domestic wastewater, and stream water in Australia, China, France, Germany, Israel, Italy, India, the Netherland, Japan, Spain, Turkey, and USA (Wang et al. 2005b; Drosten et al. 2013; Pinon and Vialette 2018; Haramoto et al. 2020; Khan et al. 2020a; Randazzo et al. 2020; Alpaslan Kocamemi et al. 2020; Wu et al. 2020b; Kumar et al. 2020; Medema et al. 2020; Carraturo et al. 2020). Thus, wastewater-based epidemiology for the monitoring of coronavirus infections is much needed to prevent it in communities. Besides, the safety aspect should be considered in sampling wastewater, containing all PPE with protective sampling kits to avoid exposure to pathogens. Nevertheless, the presence of CoV's in the feces, urine, and blood of a diseased person is therefore not unexpected, as reported researchers that SARS-CoV and MERS-CoV RNA in stool specimens gathered on 12 and 16 days comprised the virus (Drosten et al. 2013). Recently, authors observed SARS-CoV-2 RNA in the stool sample of patients in the current global pandemic (Amirian 2020). However, vitro observations demonstrated that SARS-CoV virus persistence for 2 days, 3 days, and 14 days in hospital wastewater, feces, and urine, respectively, at 20 °C (Wang et al. 2005b). In another study, the authors reported that SARS-CoV-2 RNA may be released through urine depending on the severity of patients. Besides, only 10% (2 of 20 patients) urine samples were detected SARS-CoV-2 RNA (Nomoto et al. 2020).

However, complete inactivation of SARS-CoV by adding residue chlorine over 0.5 mg/L (pure- Cl) or 2.19 mg/L for chlorine dioxide in wastewater while insignificant reduction of *E. coli* and f2 phage was reported (Wang et al. 2005b). Additionally, the chlorination disinfection approach requires to be monitored carefully for possible ecological risks of disinfection by-products (Mazhar et al. 2020). However, from the treatment aspects, very limited treatment processes in removing or inactivating coronaviruses are available. This knowledge gap could be further investigated to ensure public health by monitoring wastewater treatment plants. Henceforth, additional crucial steps in research and managements are required to comprehend the possible presence of coronavirus or any other deadly viruses in normal drinking water or wastewater (Wang et al. 2005b; Mazhar et al. 2020; Nomoto et al. 2020).

## Diagnosis and treatment of SARS-CoV-2

The current situation of SARS-CoV-2 is known for its rapid spread because the virus can tolerate harsh environmental conditions for up to 72 h. Hence, increasing global concern on how to battle coronavirus calls for a novel therapeutic strategy (Sampath Kumar, Chintagunta et al. 2020). In this respect, the use of the ever-evolving options offered by nanotechnology seems to be promising solutions against emerging pathogens including SARS-CoV-2. Nanotechnology can be exploited for quick diagnosis of coronavirus as well as the development of drug delivery treatment (Vazquez-Munoz and Lopez-Ribot 2020).

Due to the SARS-CoV-2 outbreak, fast and accurate diagnostic tools are instantly required to screen COVID-19 patients and confirm the positive cases (Abdul et al. 2020). The common and mostly used bio-molecular based diagnosis of SARS-CoV-2 are nucleic acid detection by real-time-Polymerase Chain Reaction using quantitative reverse transcription-PCR (rt-PCR/qPCR), various isothermal amplification such as loop-mediated isothermal amplification (LAMP), rolling circle amplification, nucleic acid sequence based amplification (NASBA) etc. and screened via Computer tomography scans for lungs (Yang et al. 2020) (Roy and Baranwal 2020). Furthermore, to study the behavior of SARS-CoV-2 genome and gene analysis is performed by next generation sequencing (NGS). In addition, enzyme-linked immunoassay (ELISA) based serological testing of SARS-CoV-2 is also available which is also used for surveillance tools for understanding the epidemiology of this virus (Kontou, Braliou et al. 2020). Antibody-antigen testing of viral elements is crucial to study about the clinical complications and existence cause of virus. However, these methods have many drawbacks such as these processes require high-end equipment, many costly reagents, trained/skilled laboratory personnel.

Therefore, nanotechnology and nanobiosenors can play a major role in producing scalable and inexpensive detection methods (Roy, Malode et al., Purohit, Kumar et al. 2019, Mahapatra, Baranwal et al. 2020, Shetti, Malode et al. 2020). Nano-biosensors can be used as a challenging point of care diagnostic tools even before symptoms have been shown in

patients with very low viral loads (Abdul et al. 2020). Zhu et al. (2020) stated a new study about optical bio-nanosensor that can detect the coronavirus in ~30 min directly from patient's samples without needing centralized laboratory tests. Furthermore, it can track the evolution of viruses and prevent future outbreaks (Zhu et al. 2020). Recently, thermal biosensor-based SARS-CoV-2 detection with geotagging became very influential technique for the current scenario (Reichberg, Mitra et al. 2020). Many countries have applied this technology to separate infected personnel from healthy people in terms of controlling the transmission of this virus (Rodriguez-Manzano, Malpartida-Cardenas et al. 2021).

Generally, the key factor in using nanomedicine is the nanosize of the materials, which facilitate the penetration into the living cells. Besides, nanomaterials can play a defensive role, preventing the encapsulated drug or anti-infection agent from degradation because of the shielding properties of these nano-sized materials (Wang et al. 2018).

Drug delivery has major obstacles to reach the upper respiratory tract including lower blood flow, smaller surface area, mucus layer, and filtration of foreign objects. However, the lower respiratory tract may be an ideal area for the delivery because it is connected directly to the systemic circulation via pulmonary circulation and overcome a few challenges like branched nature alveolar macrophages and pulmonary surfactant. To address these barriers, nanotechnology-based approaches can be implemented due to their characteristic features such as small size and high surface area (Khan et al. 2020b; Mahmoud 2020a, b; Nikaeen et al. 2020).

Oxygen therapy via a ventilator plays a major role in the SARS-CoV-2 treatment but it is not enough. Nanotechnology can provide a substantial role in the treatment process. Nanoparticles could be integrated into the development of nano-based therapeutic agents or vaccines against several types of coronaviruses. This is due to various phytosynthesized nanoparticles that possess antiviral and antibacterial activities to reduce the disease risk. AbdelHamid et al. (2013) highlighted that gold, silver, and Au−Ag bimetallic nanoparticles have antibacterial activities. Ag showed antibacterial activity against *E. coli and S. aureus* bacteria (AbdelHamid et al. 2013; Gomathi et al. 2017; Sudha et al. 2017).

Due to the smaller average size of Silver nanoparticles (~20 nm) than the average size of SARS-CoV-2 (120 nm), Silver nanoparticles can interact with the whole virus. Sportelli et al. (2020) reported the ability of Silver nanoparticles to inhibit the viral entry in host cells as with the HIV-1 virus, interact with cell receptors, and inhibit the viral replication (Sportelli et al. 2020). In 2020, the global consumption for health care-related nanotechnology is expected >50 tons, just for Silver nanoparticles (Salmiati et al. 2017).

Currently, the production of antibacterial papers impeded with silver nanoparticles is an international target because Silver nanoparticles can reduce SARS-CoV-2 >95% from the paper surface (Patel 2020).

We should keep in mind that COVID-19 is one of the viral diseases, not bacterial infections which are still a serious challenge in the medical field. Au nanoparticles conjugated to a swine transmissible gastroenteritis virus (TGEV) in mice/rabbits could be considered as a potential antiviral candidate for vaccine application (Staroverov et al. 2011).

Viral infections pose substantial global health challenges by affecting millions of people worldwide, with negative consequences on socio-economic development (Singh et al. 2017). Nanoparticles have been proven to be effective in the inhibition of viruses regardless of their viral structures and their drug-resistant profile. The unique properties of nanoparticles favor drug delivery and entry through the negatively charged cell membrane. This can be due to their small particle size (affects bioavailability), their large ratio of surface area to volume, and their surface functionalization. Besides, they can have biomimetic properties as in the case of dendrimers which can encapsulate several chemical moieties (Cagno et al. 2018).

Nanotechnology-based viral disinfectants have great potential to prevent the virus dissemination. Various nanomaterials can be used to promote surface oxidation by releasing toxic ions and therefore preventing viral dissemination by inhibiting binding/penetration of viral particles, either by a generation of reactive oxygen species and/or photothermal-based reactions such as heat that destroy viral membranes (Talebian et al. 2020). One approach to fight against the virus is through preventing its dissemination through disinfecting air, skin, or surrounding surfaces (Talebian et al. 2020).

Another very important and exclusively used nanomaterial is graphene in the medical fields, it possesses viral inhibition capacity. However, few studies focused on the anti-viral efficiency of graphene nanomaterials. Graphene Quantum Dots have great potentials as HIV Inhibitors when conjugated with the non-nucleoside reverse transcriptase inhibitor (CDF119) (Iannazzo et al. 2018). (Ye et al. 2015) tested the antiviral effect of graphene oxide on the *pseudorabies virus*, PRV (causes Aujesky's disease). They detected that the virus is inactivated due to its direct interaction with the sharp edges of the graphene oxide layers (Ye et al. 2015). The negative charge of graphene oxide favors electrostatic interaction with the positively charged virus and higher interactions result in the destruction and inactivation of viruses (inhibitory effect) (Innocenzi and Stagi 2020).

Even nanocomposites are now widely preferable in drug delivery and medicinal applications. For instance, GO-Ag nanocomposites increase the biocompatibility of the materials and lessening the toxicological effects of the nanosilver

as a metallic nanoparticle. Chen et al. (2016) found that graphene oxide only inhibited 16% of infection by a feline coronavirus, FCoV (represents enveloped virus) but showed no antiviral activity against infectious bursal disease virus, IBDV (non-enveloped virus) whereas Go-Ag inhibited 25% of infection by FCoV and 23% by IBDV (Chen et al. 2016).

It is noting that graphene oxide–Ag nanocomposite showed higher efficiency when compared with graphene oxide during the process of restraining viral infection. As graphene oxide sheets are negatively charged (Mahmoud 2020a, b), they can interact with the positively charged lipid membranes and Ag can bind to the sulfur groups of the viral proteins to impede the infection (Nikaeen et al. 2020).

The target mechanisms of nanoparticles are important for the drug delivery system. There are two types of targeting mechanisms. Active targeting requires the direct attachment of ligand as peptide/antibody to the nanotherapeutic of specific receptors. On the other hand, passive targeting can occur due to increased permeability or leakiness of the local vasculature which is caused by malignancy or inflammation (Singh et al. 2017). This results in the diseased area becoming more permissive to the accumulation of the nanotherapeutic agent.

The integration of nanomaterials is possible in the facemasks as it has become obligatory to wear them in public places. Unfortunately, the used facemasks are often very low quality and even N95 filters have very low protection efficiency against SARS-CoV-2 (Jokanovic et al. 2020). Recently, Jokanovic et al. (2020) concluded that their new aluminate-based nanomaterials (ALBO) nanosilver masks have significant advantages as they are safe and the sizes of Ag nanoparticles are in the range of 3–10 nm which can have high activity against viruses and bacteria. Hence, it can be concluded that researchers, are trying to get a cure for SARS-CoV-2 at the earliest. Many companies have already released various types of vaccines worldwide which were produced using these new molecular technologies and nanoparticles-based methods. In near future, there will be an exceptional implementation with advanced artificial intelligence-based technologies that will help to cure these deadly viruses in a fast and robust way.

## Mitigation and prevention

Flatten the growth curve of COVID-19 is the aim of many countries. Hence, the lockdown was applied and was at the forefront of these restrictions. Herein, we highlight some examples. China essentially authorized a country-wide shut down and built an isolation hospital within a week with around 7000 workers operating day and night. Another precaution strategy was adopted by developing a stadium in

24 h to quarantine/isolate the infected individuals (WHO 2020).

In USA, Florida initiated executive orders mandating the closure of beaches, large-scale community areas, and in-house dining as well as requiring expansion of hospital capacity. Florida authority recommends providing public health advisories about measures that can be taken to protect against COVID-19 (Sen-Crowe et al. 2021). Serological testing enhances the efficacy of early detection and medical action, including (WHO 2020) a meta-analysis. Scientific reports showed that serological examination accuracy COVID-19 can be attained by quality clinical studies (Lisboa Bastos et al. 2020). South Korea adopted maximum testing for the drivers and the authority could test around 300,000 individuals representing 17% of the total population. The prophylactic measures also control the transmission among communities. Common precaution strategies are applied and obligatory to everyone such as wearing masks outside, adopting alcohol-based hand sanitizer's, and supporting online working from home (WHO 2020).

The fever detection at the entry point by thermal scanning can be the most effective measure. It has been reported that spraying alcohol-based disinfectants in the air could tend to reduce the health risk to the masses (Syafiuddin et al. 2012; WHO 2020). Prevention and control need a multifactorial approach. Potential sources of infection both from humans or animals must be identified and separated. Furthermore, essential measures such as rinsing hands with detergents, social distancing (three feet), touching eyes, nose, and mouth should be restricted (Watkins 2020).

Recently, endorsing the QSS model (Quarantine, shield, and stop) by the governments/health ministry's helps in resilient infection in the community. Countries that strictly implement the QSS model will get better and recover with fruitful results within a short time such as China and Korea. Another important aspect in controlling pandemic is by halting travelers. Recently, Saudi Arabia, restricted religious activity (Annual Hajj) to 1000 domestic pilgrims (without international travelers) that usually packed with 3–5 million pilgrims, to prevent secondary transmission of COVID-19 into the kingdom (Memish et al. 2020).

## Conclusion

The chronological follow-up study of SARS-CoV (2003), MERS-CoV (2012), and recent SARS-CoV-2 provides important insights in combatting SARS-CoV-2 infection. The research domain thrives for such a comparison between the characteristics of SARS-CoV-2 infection with these two CoV's. The recent outbreak unveiled the inadequate infrastructure in our health care system, especially of awareness for handling emerging global pandemic. Human

to human transmission was one of the key transmission attributes of SARS-CoV, MERS-CoV, and SARS-CoV-2 infection and could be transmitted via heterophil-mediated communication, patient-to- Health Care Workers (HCW), Health Care Workers (HCW)-to-patient, and Health Care Workers (HCW)-to-Health Care Workers (HCW). The introspection for loose referral systems, such as travel restrictions, overcrowding at public areas especially in an emergency, infectious units, intensive care unit and respiratory section, lack of expertise in infection control sections, and improper control for health pandemic alarm the governing bodies to improve the healthcare system, and to spend much in controlling infectious diseases.

Some insights strategies and lessons we have learned so far, to prevent COVID-19 spread that includes:

- A sole skip in testing may trigger an outbreak
- Imposed mandatory thermal scanning of all areas including small shops, clinics/hospitals and public places
- Construction of an isolation unit. China build an isolation hospital within a week with around 7000 workers operating day and night
- Maximum testing. South Korea adopted drive-through testing and tested 17% of total population-around 300,000 individuals
- Mandatory quarantine/isolation areas for mass exposures spotted. China develops stadium in 24 h
- Free testing. Provide free and easily accessible testing
- Reduced human to human transmission by social distances and personal protection gears
- Adopt hygiene, e.g., alcohol-based hand sanitizers
- Wear masks when going outside
- Support working from home or online. Several countries support online businesses
- Lockdown. China essentially implemented a country-wide shutdown

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