# Coronaviruses Pathogens in Human in Third Millennium (SARS-CoV, MERS, COVID-19): A Review Article

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***Received: 23 Mar. 2022; Accepted: 18 Nov. 2022***

**Abstract**- This study aimed to investigate the most common Coronavirus pathogens in humans in the third millennium. In this study, all documents in English on pathogenic coronaviruses were examined from the beginning of 2002 to March 27, 2020. Articles were searched through reliable databases such as PubMed, Web of Science, Scopus, Google scholar, Science Direct, Cochrane library, and BioRxiv using the keywords "COVID-19", "Coronavirus 2019", "SARS-CoV," and" MERS-CoV." In addition, reliable health websites, such as WHO and the Centers for Disease Control and Prevention (CDC), were used to obtain new figures and information on these diseases. A total of 1563 articles and documents were extracted, and after reviewing the full texts of these articles, 100 papers and documents with necessary eligibility were finally selected in the present review study. The outbreak of pathogenic viruses, especially the latest one, i.e., COVID-19, as a severe threat can affect the entire global community, in particular medical staff who are at the forefront of fighting against the virus. It can generally be concluded that coronaviruses have high pathogenesis, with very rapid person-to-person transmission. Since human knowledge is not yet complete about the new type of this virus, i.e., COVID-19, there are no definitive treatments for the virus. Thus, the best and only way to prevent affection from this virus is currently fully implementing health protocols and preventing self-infection and the virus outbreak.



*Acta Med Iran* 2022;60(12):723-730.

**Keywords:** Coronavirus; Coronavirus disease 2019 (COVID-19); Severe acute respiratory syndrome (SARS); Middle east respiratory syndrome (MERS); Human

## Introduction

Coronaviruses are positive RNA viruses that belong to the coronaviridae family (1,2) and were first identified in the 1960s (3). They are found in humans, other mammals, and birds and can cause a wide range of severe respiratory, gastrointestinal, and neurological diseases for the host (4). Emerging viral diseases have always been highly prevalent and widespread around the world (5). Since the 21st century, the endemic of three coronavirus strains have caused human health problems. Severe acute respiratory syndrome (SARS) and Middle East Respiratory Syndrome (MERS) were respectively discovered in China in 2002-2003 and in Saudi Arabia in 2012 (6-8). Before 2002 and the incidence of SARS, coronaviruses often caused poor infection in people and were not pathogenic (1). In the early second decade of the current century (2012), a coronavirus emerged in Saudi Arabia that had not been identified formerly. These two issues (SARS and MERS) point out the risk of transmission and pathogenesis of coronavirus from other animal species and its spread in humans (9,10). By the end of 2019, a new disease called coronavirus (COVID-19) was diagnosed in China (11). On the last day of

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December, reports were published of pneumonia with symptoms very close to SARS that affected some people in China (12,13). Due to the rapid spread of the new coronavirus (SARS-CoV-2), many affected people are referred to medical wards (14). In January 2020, the WHO finally declared the spread of this disease as an emergency in the public health of different countries (15).

## Review methods

In this review study, all articles and documents in English on pathogenic coronaviruses were examined from the beginning of 2002 to March 27, 2020. Articles were searched through authentic databases such as PubMed, Web of Science, Scopus, Google scholar, Science Direct, Cochrane library, and BioRxiv using the keywords "COVID-19", "Coronavirus 2019", "SARS-CoV-2", and" MERS-CoV." In addition, authentic health websites such as WHO and the Centers for Disease Control and Prevention (CDC) were used to obtain new figures and information on these diseases. All cases, including epidemiology, history, treatment, prevention strategies, and other cases related to these viruses, were searched at reliable databases.

A total of 1563 articles and documents were extracted in an initial search, 208 of which were selected after deleting duplicate items. After reviewing the full texts of these articles and excluding those with scientific and bias problems, finally, 100 articles and documents that met the necessary criteria and conditions in the present review were selected and analyzed completely. The inclusion criteria were articles published in reliable global databases. Exclusion criteria included articles published in unreliable scientific databases and those with high error rates. All ethical and trusteeship principles were observed in all stages of the search and analysis.

## Origin of diseases

Coronaviruses have generally been observed in some animals, including bats, mice, cats, and dogs (16). Before the outbreak of SARS, two viruses that originated in bats were found in Asia and Australia. In their times, SARS and MERS were individually considered a serious threat in the world. According to previous studies, bats were probably the origin of SARS and its transmission to humans. Further studies in this regard revealed that other animals in commercial markets are not probably the source of SARS (17-20). In 2005, two research teams found, almost simultaneously but independently, that SARS probably had its origin in Chinese horseshoe bats (18,19). Researchers also consider bats to be the source of MERS (20). Results of published studies demonstrated that bats were most probably the causative agent of MERS. At the same time, camels and goats were known as intermediate hosts (21). In fact, these two pathogenic viruses are most probably derived from bats, and their genetic coronaviruses have mostly been observed in bats (1). The origin of COVID-19 has not been found so far (22). According to recent studies, the disease has spread from a local fish market in China (23). Virological analyses have shown that the COVID-19 coronavirus is similar to SARS and MERS by 79 and 50%, respectively. Research has also shown that the virus resembles the coronaviruses of horseshoe bats by 98.7%. The disease might have spread due to the presence of bats and some animals in a local fish market in China (15). Coronaviruses are generally able to mutate and infect different species (24). In this respect, Andersen *et al*., believe that this emerging disease is not a targeted (purposive) manipulated laboratory phenomenon (25).

## Epidemiology

SARS negatively impacted public health in China during 2002-2003 (26). The disease spread to 29 countries and affected 80,988 people, 774 of whom died with a 9.6% mortality (27). In a report, the WHO announced that the SARS virus was present in 32 different countries with 8422 cases and 916 deaths, with a case-fatality rate (CFR) of 11 percent (28). The SARS outbreak reappeared in 2004 but terminated without any death (29). Epidemiologic studies have shown that the disease occurs in people with a history of presence in wet markets, hence limiting and terminating these markets has played an important role in preventing the spread and endemic of the disease (20,30).

Emerged in Saudi Arabia in 2012, MERS is a severe respiratory illness capable of affecting the renal and digestive systems of people (17). However, recent research shows that the disease appeared in Jordan before Saudi Arabia (31). According to existing reports, the virus spread to 27 countries and affected 2,080 people by 2017, with a 34.71% (722) death rate (17). As announced by the WHO, the figure led to 2,494 cases and 858 deaths by the end of November 2019. An estimated mortality rate of 34.4% has been found for the disease (32). All people are prone to disease development upon exposure to the virus. There is a higher chance of developing COVID-19 due to a greater proliferation process than that of SARS (33). Reports indicate a death rate of close to 2% from COVID-19 (34). Little is known about the epidemiological characteristics of children affected by the disease (35). Research suggests that the age range of 25-89 years is more involved in patients, with a lower

presentation in children (33). In another study, a mean age of 54 years was accounted for in patients, most of whom were men. The mean incubation period was 5.2 days, and the endemic was doubled every 7.2 days. However, Chinese health officials consider an average incubation period of one week to be variable from 2 days to 2 weeks (33,36). In another study that examined 41 patients with a mean age of 49 years, men comprised nearly ¾ of the study population. Underlying conditions, including cardiovascular disease, hypertension, and diabetes, were observed in 32% of patients, 32% of whom that participated in the research were hospitalized in the intensive care unit, with a reported mortality rate of 15% (37). In Europe, an investigation was conducted on the first case of COVID-19 in January 2020. The study included five patients, comprising two women and three men, one of whom was an elderly man. Two female patients presented no clinical symptoms and were diagnosed to be affected by the virus through testing. The old man deceased after two weeks of the disease's affection and development, and the others recovered five days after his death (38).

**Transmission routes**

SARS is transmitted through direct contact with an infected person and the droplets. There is also some evidence of likely airborne transmission in a community (39). Since close contact with an infected person leads to the virus transmission, the virus spreads among families and healthcare centers (40). In MERS, close contact with a patient also transmits the disease to another person (41), and this disease is potentially transmissible from person to person (42).

COVID-19 coronavirus can be transmitted by touching contaminated surfaces and objects, contact between people, inhaling droplets impregnated with the virus, and contact with the nose, eyes, and mouth (33,43,44). Due to the presence of some gastrointestinal manifestations, researchers also suggest the gastrointestinal route as one of the transmission routes of the virus (33).

**Clinical signs**

Although the mortality rates are respectively about 40% and 10% in SARS and MERS, the clinical symptoms are close to each other (17,45). The clinical signs of SARS and MERS are present mostly in adults. The incubation period is between 2 days and 2 weeks, with an average of 5 days, for both diseases. Fever, chills, dry cough, diarrhea, nausea, vomiting, sore throat, muscle aches, and dyspnea are among the most noticeable clinical manifestations of these two diseases. Respiratory failure accounts for a major problem in diseased people. However, the presentation of symptoms is usually not severe in children (39,45-48). According to research, abnormalities were also observed in the laboratory findings of patients with SARS and MERS. Some abnormal laboratory conditions include thrombocytopenia, leukopenia, lymphopenia, elevated levels of liver enzymes (ALT and AST), increased levels of lactate dehydrogenase (LDH), infiltration and leakage in chest radiographs, and abnormal renal function (41,49,50).

Clinical signs of COVID-19 have not been determined exactly thus far (33). The main clinical manifestations in these patients include sore throat, headache, dry cough, fever, fatigue, dyspnea, chest pain, muscle aches, diarrhea, and vomiting (51,52). These symptoms have so far been reported from mild to severe. Most patients with mild symptoms recovered a week later, while those with severe symptoms developed progressive respiratory problems and even death in some cases (31). According to research, however, the viral load in the throat and nose of symptomatic patients is not different from those without clinical symptoms (53).

**Treatment**

No FDA-approved treatments have been identified for CoV infections (5). The treatment of coronaviruses is generally supportive. Analgesics, antipyretics, and, if necessary, antibiotics in cases of bacterial infections are also used in this regard. Special attention should also be paid to hydration in patients (47). Because respiratory failure is the main cause of death in patients with SARS, and this condition has been observed in almost a quarter of cases, respiratory system care, including mechanical ventilation, is critical in these patients. However, some anti-inflammatory therapies and some antiviral drugs (e.g., ribavirin) are also used in the treatment of SARS (54). Corticosteroids, such as prednisolone, are also used in cases of fever exacerbation and lung involvement at a higher level (55). In addition to SARS, no vaccines or antiviral treatments have been found and are not available for MERS as well (31,56). The treatment includes supportive care based on patients' problems and their clinical manifestations (31). Isolation can help considerably in finding the virus's origin and its infection property (57). Also, the WHO pointed to maintaining physical distance to prevent the spread of disease in people (58). Since no definitive medicine and treatment have been found for this disease, treatment is currently based on clinical manifestations and supportive care

(33,37,51). People with mild illnesses should be supported by the control of their symptoms at home. Special attention should be paid to hydration in patients, maintaining bodily electrolyte balance, providing calories, and controlling their clinical manifestations. In some cases, the use of antibiotics and antifungal drugs is on the agenda (59-62). Based on previous experience, some antiviral drugs have been used in cases of SARS and MERS (51). Some patients suffer from oxygen deficiency, which can render the need for mechanical ventilation (59-61).

**Personnel**

Extensive occupational and emotional hazards threaten nurses and treatment teams so that personnel suffers from psychological distress in dealing with SARS patients. In Saudi Arabia, a study reported that 91.8% of a medical team had a negative attitude towards providing health and medical services to people with or suspicious of MERS (63). Logistics and preparation for unknown things are major challenges (64). When there are not enough resources in hospitals, the workload of medical staff will increase considerably (14).

The health team infection is a major challenge in any type of infectious disease. The health team are the forefront of the medical field of the community and is severely threatened by the risk of disease transmission through direct communication with patients (65). Forefront healthcare personnel should have received good training (66). Out of 8098 SARS cases, healthcare personnel comprised 21% of patients (67). At the incidence of MERS, unclear instructions, which underwent multiple changes, confused nurses and health care personnel (68). According to a recent study in China, six out of 1,500 medical ward personnel affected by COVID-19 lost their lives. Therefore, the protection of medical personnel, besides regular care for patients, prevents the virus transmission to other patients (61). The use of gloves and masks plays an important role in the health of health personnel. In this respect, the WHO and the US CDC have provided the necessary recommendations. The WHO recommends health care teams wear masks during daily care with COVID-19 when the aerosol is in the production stages. On the other hand, Europe and the United States CDCs believe that masks should also be used during health activities for high-risk patients in addition to routine care for COVID patients. In this regard, some countries comply with WHO, and others perform their health activities according to the CDC (11). These contradictions have confused healthcare teams, including nurses, and have led to discussions between professionals of infectious disease prevention and service providers to these patients. These issues occurred simultaneously with the Ebola epidemic in 2014 (11,69,70). Non-compliance and preventive control by medical teams pose a high risk of infectious diseases, making them disease carriers, so their families, other people at hospitals, and the community are also exposed, in addition to the team members (65). In this regard, studies conducted on the prevention of nosocomial infections have suggested training to increase the knowledge of prevention, disinfection, isolation, protection, and care (33).

**Prevention**

Preventive methods play a key role in preventing the spread of infectious diseases (71). Nurses have historically played an important role in the prevention of infections (72). To prevent MERS, people should avoid contact with animals and eat raw meat, as cooking at high temperatures also kills microbes. Due to the fact that people with immunodeficiency are at risk for severe illness after exposure to MERS, they should implement preventive measures. Occupational health nurses need to provide necessary training to raise public awareness and keep them up-to-date about the prevention of MERS (31). Some prevention rules for MERS infection in health personnel include preventing the disease transmission via the early and timely diagnosis, isolating suspected and confirmed cases of the disease, and being in a well-ventilated environment, as well as using masks, gloves, and glasses before contact with patients and suspicious people (73).

Due to the lack of definitive treatment for patients with COVID-19, there is a strong emphasis on the need for prevention. However, prevention of COVID-19 is not an easy task because the virus can be transmitted to others before the onset of clinical manifestations during the disease incubation period. Besides, recovered individuals with alleviated symptoms may also transmit the disease and contaminate healthy people. Such people and those who are suspected of having the disease are recommended to isolate themselves from others. These patients need to learn the proper coughing technique. The use of a simple surgical mask is another recommendation to prevent the spread of infection. People taking care of patients should also use these masks. It is recommended to wash hands 3-4 times an hour. Other pieces of advice for disease prevention are to have proper ventilation and adequate lighting in residence (61).

The public is requested to refrain from attending crowded places for control and prevention purposes.

People should use their cloth or sleeve during coughing. Washing hands regularly is a method to prevent infection. People must maintain their composure and avoid spreading untrue news in society (61).

In a study, healthcare providers were recommended to wear a simple surgical mask while examining patients and to pay special attention to washing hands regularly. Patients should also wear these masks. Physicians should also be aware of the latest news and information related to the COVID-19 disease (61).

Early triage and diagnosis of disease, hand washing, and hygiene with soap and water or disinfectant gels, the use of long-sleeved clothes, disposable gloves, and the use of eye protection are among the strategies for the prevention and management of COVID-19 disease in healthcare personnel (66).

**The global spread of the virus**

Table 1 represents the top ten countries with the highest rates of the virus outbreak, according to the WHO, until April 7, 2020.

**Figure 1.** The spread of COVID-19 in the world by April 7, 2020, more pronounced areas indicate more prevalence

**Table 1. 10 countries with the highest prevalence of corona**

| Location | Number of cases | Recovered | Deaths |
|---|---|---|---|
| **Worldwide** | 1.381.014 | 292.973 | 78.269 |
| **United States** | 1.150.71 | 20.027 | 11.385 |
| **Spain** | 140.511 | 43.208 | 13.897 |
| **Italy** | 135.586 | 24.392 | 17.127 |
| **Germany** | 106.306 | 31.432 | 1.943 |
| **China** | 81.740 | 77.167 | 3.331 |
| **France** | 74.390 | 17.250 | 8.911 |
| **Iran** | 62.589 | 27.039 | 3.872 |
| **United Kingdom** | 55.242 | - | 6.159 |
| **Turkey** | 34.109 | 1.582 | 725 |
| **Switzerland** | 22.245 | 8.056 | 821 |

(Reference: PHIL: Centers for Disease Control and Prevention (CDC))

The outbreak of pathogenic viruses, especially the latest one, i.e., COVID-19, as a serious threat can affect the entire global community, in particular medical staff who are at the forefront of fighting against the virus. Due to the rapid transmission of these viruses and their widespread global outbreak, it is necessary to implement the necessary measures for the treatment and prevention of the virus outbreak. No definitive cure has yet been found due to the low human knowledge of the new COVID-19 virus and the unknown nature of some characteristics of the virus. Hence

research is ongoing on this issue. Therefore, the best way of dealing with the virus is to prevent the infection of people and the spread of the virus to cities and countries. The prevention of virus outbreaks is only achievable by implementing preventive measures such as using masks and gloves, keeping a good distance from people affected by or suspected of virus infection, regular washing of hands, and observing other health protocols by the majority of people. Furthermore, infected people should be timely diagnosed through coronavirus infection testing by governments.

## Acknowledgments

The authors of this study want to thank the vice-chancellor of Shiraz University of Medical Sciences.

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