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The Modes of Transmission and Risk Factors for SARS-COV-2

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ABSTRACT

Currently, the severe acute respiratory coronavirus type 2 (SARS-COV-2) pandemic remains widespread worldwide despite extensive prevention and control measures for close contact and droplet transmission. Previous literature has identified close contact and droplet transmission as important modes of transmission of SARS-COV-2, but other modes, risk factors, and etiologic mechanisms have not been fully described. Therefore, it is particularly necessary to explore other modes and risk factors for SARS-COV-2 transmission in the current epidemic prevention and control efforts. This review focuses on aerosol transmission as an important mode of SARS-CoV-2 transmission. We comprehensively and carefully discuss the internal and external risk factors that can increase the susceptibility associated with SARS-CoV-2 among populations. These include clinical characteristics, underlying diseases, and high-risk industries. Therefore, to carry out novel coronavirus prevention and control in a scientific and effective manner, governments and health care institutions at all levels should fully understand the multiple modes and the internal and external risk factors for SARS-CoV-2 transmission.

Introduction

The outbreak of severe acute respiratory coronavirus type 2 (SARS-COV-2) in December 2019, which is still spreading around the world, has been classified by the World Health Organization as a global pandemic with some impact on health care systems and global socioeconomic balance [1]. As a β-coronavirus with high infectivity, SARS-COV-2 causes a respiratory disease known as coronavirus disease 2019 (COVID-19) [2]. Currently, SARS-CoV-2 is thought to be transmitted mainly from person to person through close contact or respiratory droplets (> 5–10 μm in diameter) from an infected person over short distances (<1–2 m) by coughing, sneezing, talking, etc [3]. Based on the mode of transmission of the virus, a series of prevention and control measures were taken to reduce the risk of transmission of SARS-COV-2, including avoiding close contact with infected people, wearing masks in public places, travel and airport screenings, isolation, and quarantine.

However, the SARS-CoV-2 epidemic remains rampant around the world, putting enormous pressure on global health care systems. Therefore, clinical staff should pay attention to this dilemma and identify the risk factors that may cause the spread of SARS-COV-2 and enhance the susceptibility of the population as soon as possible. In addition, the risk of infection can be reduced through rational allocation of medical resources and timely adjustment of prevention and control measures. This article focuses on both the modes of transmission of SARS-CoV-2 and the risk factors for infection among populations.

Modes of Transmission

Currently, SARS-CoV-2 is predominantly transmitted by both respiratory droplets and close contact. Common modes of transmission are through coughing, sneezing, inhalation of droplets, and contact with the oral, nasal, and eye mucous membranes of people infected with SARS-CoV-2 during daily life. In addition to the above modes of dissemination, aerosol, as a common mode of respiratory infectious disease, the current research on the transmission of SARS-COV-2 remains unclear. Evidence for aerosol transmission of SARS-COV-2 is still being collected (Asadi, et al. [4]). found that SARS-COV-2 particles ≤1 μm in diameter are released during normal breathing, coughing, and conversation, while small, aerosolized particles (<5 μm in diameter) containing the virus can remain in the air for a certain time and propagate over long distances (distances > 1 m). Aerosol transmission distances far exceed droplet transmission (1–2 m) and can even reach 8 m. The transmissibility and infectivity of aerosols also depend on the presence of particulate matter in the air, which can transmit and release microorganisms, including viruses. An NIH study [5] showed that the novel coronavirus can survive in the air as an aerosol for at least 3 h, which can cause mutual infection in persons who are not in direct contact in the same confined space. Moreover, sewage pipes allow the virus to spread as aerosols between tall buildings, such as bathrooms and bedrooms. In addition, SARS-COV-2 can survive for many days on a variety of surfaces. For example, it can survive for up to seven days on the outer surface of a surgical mask. Therefore, aerosol transmission is an important mode of transmission of SARS-COV-2.

In addition, (Chirico, et al. [6]) reviewed the literature on whether air conditioning systems contribute to the transmission of severe acute respiratory syndrome (SARS)/Middle Eastern Respiratory Syndrome (MERS)/COVID-19. It was found that most of the studies on SARS and SARS-COV-2 were suspected or supported the diffusion of virus particles through air conditioning systems, and MERS has been confirmed to be infected by viruses in air conditioning systems. Moreover, aerosols often move along with air flow so that the air conditioning system promotes the long-distance transmission of respiratory droplets. Therefore, the air conditioning system may play a key role in promoting the long-distance transmission of aerosol molecules during the transmission of SARS-COV-2.

High-Risk Factors

High-Risk Industries

Health Care: Health care workers have always been on the front lines of the fight against SARS-COV-2 amid the grim global COVID-19 situation. Consequently, they are in more frequent contact with SARS-COV-2 than other industries and the key population at risk of SARS-COV-2 infection. Personal protective equipment, workplace environment, occupation, exposure, and testing are risk factors for health care workers to be infected with SARS-COV-2. (Gómez-Ochoa, et al. [7]) showed that approximately 1 in 10 health care workers in hospitals screened were diagnosed as positive for SARS-CoV-2 infection, half of whom were nurses. Then, compared with nurses and general service workers, physicians exposed to COVID-19-positive patients are at higher risk, primarily including key medical workers in respiratory departments, infection control departments, ICUs, and surgical departments. Based on the current situation, if health care workers fail to protect themselves and become infected, the strength of epidemic prevention and control will be weakened to a certain extent. Therefore, adequate prevention and control measures should be taken to protect them from SARS-COV-2.

Quarantined Hotel: Strict nucleic acid testing and isolation control should be carried out for all passengers regardless of whether they show symptoms at the time of entry to take the initiative for epidemic prevention and control. Centralized quarantine at designated hotels is one of the essential steps to prevent the importation of COVID-19. There are strict requirements on the quarantine facilities and management system. Effective centralized isolation is of great significance to prevent further transmission of SARS-COV-2. The staff of quarantined hotels are mainly responsible for indoor and outdoor disinfection, daily meal delivery, garbage disposal, and other life supplies that may have close contact with quarantined people. Therefore, workers in quarantined hotels are also at high risk for SARS-COV-2 infection (Yue, et al. [8]). Showed that the local outbreak was most likely caused by transmission of SARS-CoV-2 infection through contact with household waste from imported cases based on the results of on-site epidemiological investigation and gene sequencing analysis. Among them, the place where the epidemic occurred is adjacent to the quarantined hotel for inbound people. Additionally, the routine management of quarantined hotels also revealed that the staff did not properly manage the household waste of quarantined staff, which undoubtedly increased the risk of infection.

Clinical Features: Due to differences in sex, blood type, age, race, and behavior habits, people have different susceptibilities to SARS-COV-2.

Men: The risk of SARS-COV-2 infection, disease severity, and death in men is higher than that in women, which is consistent with previous studies that respiratory infections are more severe and will cause greater mortality in men than in women [9]. It has been reported [10] that higher levels of estradiol in women can increase the expression level and activity of a disintegrin and metalloprotease-17 (ADAM17), thereby promoting the shedding of angiotensin converting enzyme 2 (ACE2). Since the ACE2 receptor has been identified as the main functional entry receptor of SARS-COV-2 [11], decreasing the number of ACE2 receptors in the body may be a critical method to block SARS-CoV-2 entry into cells, which leads to a large difference in susceptibility between males and females to SARS-COV-2.

Type O and RH-Blood: (Zhao, et al. [12]) Demonstrated that ABO blood groups had different associations with SARS-CoV-2 infection risk. In particular, blood type A increases the risk of infection, while blood type O reduces the risk of infection. Similarly, (Ray, et al. [13]). Found that type O and Rh-blood may reduce the risk of SARS-COV-2 infection, severe COVID-19 disease, and death. The reason might be that SARS-COV-2 infections in the population could be prevented by some unspecified characteristics conferred by type O blood. Moreover, anti-A antibodies in the blood specifically inhibit the adhesion of SARS-CoV S protein-expressing cells to ACE2 receptors. SARS-CoV shares a high degree of similarity with SARS-CoV-2 in terms of nucleic acid sequences as well as ACE2 receptor binding sequences [12]. Thus, anti-A antibodies may inhibit the transmission of SARS-CoV-2.

Age: Evidence from around the world [14] showed that aging was a prominent risk factor for severe disease and death from COVID-19, with patients over 70 years of age appearing to have a 65% higher risk of contracting COVID-19 than the rest of the population. This may be related to the different immune responses of T cells to SARS-COV-2, which result from the complex effect of aging on the immune system and the potential impact of taking various drugs while suffering from various diseases. In addition, differences in the severity of symptoms in elderly patients are also associated with the expression of ACE2 and the lymphocyte count [2]. (Hu, et al. [15]). Also believed that older age was an independent risk factor for the severe Delta variation in Guangzhou, especially in those older than 58.5 years. Therefore, aging should be given adequate attention as a risk factor for SARS-CoV-2 infection. Currently, some countries have started to develop protection plans for COVID-19 outbreaks in nursing homes, which play a positive role in preventing SARS-COV-2 transmitted infections for elderly individuals.

Black, Asian, and Minority Ethnic Groups: Human evolution has always been tied to natural pathogens. For long stretches of history, different risk factors for infection among ethnic groups make the immune system gradually adapt to the environment, which eventually leads to great differences in the immune system. Thus, during the transmission of SARS-CoV-2, the organism may undergo a different immune response. A systematic evaluation of the relationship between race and SARS-COV-2 infection by (Daniel, et al. [16]). Showed that black, Asian, and minority ethnic individuals were at increased risk of SARS-COV-2 infection compared with Caucasians. Similarly, (Lusignan, et al. [17]). Found that black patients were more likely to test positive for SARS-COV-2 than other ethnic groups. Individuals of other races may be protected from SARS-COV-2 infection due to their low ACE2 expression level [18]. However, the specific mechanism needs to be further confirmed.

Smoking: Whether smoking increases the risk of SARS-COV-2 infection has become a hot research topic in recent years (Lee, et al. [19]). Studied and analyzed three independent RNA expression databases of smokers to explore the potential connection between smoking and biological behavior associated with COVID-19. This study revealed that smoking may exacerbate COVID-19-related inflammation and increase susceptibility to COVID-19. Further research suggested that inflammation and the upregulation of ACE2 may be the molecular mechanisms that increase susceptibility to COVID-19. Tobacco has elevated ACE2 activity, while e-cigarettes without flavoring and nicotine lack a correlation with ACE2 activity. Furthermore, in addition to the upregulation of ACE2 in smokers [11], the host proteases TMPRSS2 and furin are also upregulated, which increases the affinity of SARS-CoV-2 for ACE2 by modifying spike proteins. However. Showed the opposite result through epidemiological investigation, suggesting that smoking status was negatively correlated with positive SARS-COV-2 infection [20]. Nicotine may increase the number of receptors on the cell surface of the lungs and protect tissue from damage caused by SARS-COV-2 infection. Nevertheless, the claim that smoking protects against SARS-COV-2 infection is not supported by further evidence, so smoking is more likely to increase susceptibility to SARS-COV-2.

Basic Diseases: Population-based diseases often have a subtle impact on the risk of SARS-COV-2 infection. The Centers for Disease Control and Prevention stated that people of any age with certain underlying medical conditions were at increased risk of severe COVID-19 [21].

Cancer

(Lee, et al. [22]) that individuals with cancer had a 60% increased risk of testing positive for SARS-CoV-2 compared to those without cancer. In particular, the association between cancer and SARS-CoV-2 infection was stronger in men over 65 years of age than in women. Among cancer patients, current chemotherapy or immunotherapy doubled the risk of testing positive for SARS-COV-2. For example, the use of corticosteroids and other immunosuppressants can reduce the ability of the body's immune system to fight infection, thus making patients more susceptible to infection in the face of various foreign invasions [23]. Moreover, a high proportion of stage IV cancer patients were infected with SARS-CoV-2, suggesting that patients with advanced cancer may be more susceptible to SARS-COV-2 infection.

Asthma

(Sunjaya, et al. [24]) conducted a systematic evaluation of the relationship between asthma and SARS-CoV-2 infection, demonstrating that the risk of COVID-19 infection was reduced by approximately 14% in asthmatic patients compared to those without asthma. On the one hand, downregulation of ACE-2 receptors has been observed in patients with high T2 asthma. On the other hand, patients treated with corticosteroids are less susceptible to COVID-19 because of the decreased expression of ACE2 [23]. In addition, behavioral aspects may also play a vital role in reducing asthma patients' susceptibility to COVID-19 due to their better compliance during the SARS-COV-2 pandemic.

Obesity

Obesity has been identified as an independent susceptibility factor for severe cases of SARS and MERS infections [25]. The genetic similarity of SARS-CoV-2 has been 80% with SARS-CoV-2 and 50% with MERS. Moreover, obesity is very common among hospitalized COVID-19 patients, which not only increases the risk of SARS-COV2 infection but also exacerbates the severity of COVID-19 [26]. Further research showed that severe obesity (BMI≥ 35) was independently associated with the risk of acquiring COVID-19, with an odds ratio greater than 1.05. Obesity may increase susceptibility to SARS-CoV-2 for the following three reasons: First, obesity disrupts the immune system, limiting its ability to respond to new viruses such as SARS-CoV-2. Second, the expression of ACE2 is increased among obese patients, which makes them more susceptible to SARS-CoV-2. Third, the body's adipose tissue may create space for viral retention, which may slow viral clearance and exacerbate infection [27].

Rheumatic Diseases

Rheumatic diseases are also closely associated with the risk of SARS-COV-2 infection. Patients with rheumatic diseases have higher rates of SARS-COV-2 infection and mortality than the general population. Further studies by (Wang, et al. [28]). Showed that patients with rheumatic diseases had a 53% increased risk of sarS-COV-2 infection compared with the general population. The main reason may be that long-term use of glucocorticoids and immunosuppressants in patients with rheumatic diseases destroys their own immune system, resulting in reduced resistance to SARS-COV-2 [23].

Other Common Diseases

In addition to the above representative diseases associated with SARS-COV-2 infection risk, the virus may be related to the renin-angiotensin-aldosterone system (RAAS), which is closely connected with the ACE2 receptor, thus significantly increasing the risk of SARS-CoV-2 infection in the population with hypertension. Furthermore, the susceptibility to SARSCOV-2 in patients with cardiovascular disease may be increased through increased expression of ACE2 in muscle cells and vascular fibroblasts [29].

Discussion

Despite the extensive isolation control and health protection measures taken by governments and health care institutions at all levels based on the main modes of transmission of SARS-CoV-2, the epidemic trend of COVID-19 has still not been controlled in all aspects. Aerosol transmission is another important route of SARS-COV-2 transmission in addition to close contact and droplet transmission, which plays a vital role in the prevention of SARS-COV-2 transmission. Among them, the air conditioning system may promote the long-distance diffusion of aerosol molecules. At the same time, health care and quarantine hotel control are key industries and external risk factors related to the spread of SARS-COV-2. Therefore, while preventing and controlling the spread of the epidemic, it is necessary to make strict requirements on SARS-COV-2 protection. Except for focusing on external factors, it is also essential to keep an eye on internal factors. Men, aging, along with black, Asian, and minority individuals and smoking behavior can increase the risk of SARS-COV-2 infection. In addition, cancer, obesity, and rheumatic diseases increase the susceptibility of the population to SARS-COV-2, while individuals with type O and Rh-blood groups and with asthma may be at reduced risk. By exploring the mechanism of population risk factors, we found that there are two main reasons for population susceptibility to SARS-COV-2. First, the ACE2 receptor is the key structure for SARSCOV-2 to enter cells [12], which affects the expression and affinity of the ACE2 receptor. Second, the use of corticosteroids and other immunosuppressants will reduce the ability of the body's immune system to fight infection, thus making patients more susceptible to infection in the face of various foreign invasions [24].

Therefore, understanding the transmission characteristics and mechanism of SARS-COV-2 and the causes of the widespread epidemic from the perspective of genetics and molecular biology will help researchers develop an effective vaccine against the novel coronavirus as soon as possible and control the epidemic. In addition, clinicians and community health workers should also focus on the prevention of SARS-COV-2 transmission among patients with underlying diseases. When conducting COVID-19 screening, medical prevention and vaccine research and development, governments at all levels and medical and health institutions should be conscious of the risk factors and transmission routes of SARS-COV-2 infection in advance. Through targeted scientific research and prevention as well as relevant knowledge dissemination among high-risk

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groups, the self-prevention awareness of the public in preventing novel coronavirus can be strengthened. In addition, professional guidance for all epidemic prevention and control personnel will be beneficial to epidemic prevention and control, allocation of medical resources, and control of key groups.

Conclusion

When preventing the spread of SARS-COV-2, we should not only consider aerosols as an important route of transmission and external infection risk factors, such as high-risk industries related to COVID-19 but also pay attention to the influence of internal factors, such as high-risk populations and basic diseases. Comprehensive assessment of SARS-COV-2 infection risk and identification of high-risk individuals play a certain guiding significance for the prevention and control of SARS-COV-2 and lay a certain foundation for the elimination of SARS-COV-2 in the future.

Advantages and Limitations of this Study

An in-depth analysis of the internal and external factors of SARS-CoV-2 transmission was conducted in this review, with an emphasis on aerosol transmission, which has guiding significance for the future. However, the mechanism of risk factors for the spread of COVID-19 remain to be confirmed by further research.

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- Concept Proposal LX-H
- Literature search and collation YC, MZ-C, ZH-K, GR-Q, YQ-C
- Specific scheme implementation LX-H, JG, DD-H, YX-S, WX, YJ, WJ-P, LJ-Q, WW-D, YC
- Research Regulatory LX-H, JG, ZY
- Writing - Draft YC
- Writing-Proofreading and Editing LX-H, YC
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Competing Interests

The authors claim that there are no competing interests among them.

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