

# Transmission Routes of COVID-19: a Review of the Evidence

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## Abstract

Since early December 2019, the Coronavirus Disease 19 (COVID-19) infection has been prevalent in China and in the short term, the virus has spread to other countries. Due to the short duration of the virus pandemic, few studies have been reported on transmission routes. Identifying ways of transmitting the disease will be very effective in preventing its spread. We reviewed the methods of transmission of COVID-19 including droplets, contact, airborne, vertical transmission to the fetus of infected mothers and fecal-oral by using data of published articles or official websites up to Apr 19, 2020. The most important routes of transmission of COVID-19 were droplets and contacts. The presence of the virus in the stool, even after a negative nasopharyngeal swab, was another major cause of shedding of infection. No maternal to fetus vertical transmission was seen. Infant is at risk after birth only through droplets during breastfeeding. Based on limited data, droplets, contact, airborne and fecal transmissions are important ways of transmitting the disease and there is no evidence for intrauterine transmission of COVID-19 from infected pregnant women to their fetuses.

**Keywords:** Corona virus; COVID-19; Droplet; Contact, Airborne; Vertical transmission; Fecal.

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## Introduction

The novel coronavirus was first presented in Wuhan City (1). During the first weeks of January 2019, the COVID-19 virus quickly spread to other countries (2). The World Health Organization (WHO), named the novel coronavirus disease as Coronavirus Disease 19 (COVID-19), (3).

The most common manifestations of COVID-19 consist of fever, cough, and fatigue or myalgia, sputum production, and headache (4-6). Infants and children have not been featured prominently in COVID-19 case statistics.

A study conducted in China was shown that children younger than 10 years, account for only 1% of COVID-19 cases (7). Therefore, due to the low number of children involved, the number of studies conducted in this field is low.

Due to the rapid spread of the disease and the lack of specific treatment, identifying and preventing the transmission of the disease can be effective in reducing the prevalence of the disease, so the aim of this study was to investigate the ways of transmission of the COVID-19.

## Droplet & contact routs

Many studies have noted the importance of transmitting the virus through droplets and contacts. Droplet (considered to be  $>5-10\mu\text{m}$  in diameter) transmission occurs when a person is in close contact (1 meter) with a person with respiratory symptoms (cough or sneezing). Therefore, the mucous membranes of the mouth or nose or conjunctiva (eyes) are at risk of potentially infectious respiratory droplets. Droplet transmission may also occur through fomites such as clothes, utensils, and furniture in the environment around the infected person (8), so COVID-19 virus transmission can occur in two ways: 1) direct contact with infected people and 2) indirect contact with surfaces used by an infected person.

Air transfer is different from droplet transfer and refers to particles less than 5 micrometers. In fact, they are germs that are present in droplets and are the result of the evaporation of larger droplets or dust particles. They may also stay in the air for long periods of time and be transported to others over distances of more than 1 meter (9).

In the context of COVID-19, airborne transmission may be in procedures that generate aerosols are performed (i.e. intubation, bronchoscopy, open suctioning, administration of nebulized treatment, manual ventilation before intubation, turning the patient to the prone position, disconnecting the patient from the ventilator, non-invasive positive-pressure ventilation, tracheostomy, and cardiopulmonary resuscitation) (9). The investigation done by Wycliffe et.al identified seven clusters of COVID-19 in Singapore in which presymptomatic transmission likely occurred. Among the 243 cases of COVID-19 reported in Singapore as of March 16, 157 were locally acquired; 10 of the 157 (6.4%) locally acquired cases are included in these clusters and were attributed to presymptomatic transmission (10).

### Fecal & oral

Gastrointestinal (GI) symptoms including nausea or vomiting and diarrhea are less common. In a cohort of 1,099 patients with COVID-19 from 552 hospitals in China, published in the *New England Journal of Medicine*, 5.0% of patients had nausea or vomiting and 3.8% had diarrhea (11).

Several case studies have reported gastrointestinal symptoms. Some patients with SARS-CoV-2 have viral RNA virus in their feces (12).

The mechanisms by which SARS-CoV-2 interacts with the gastrointestinal tract remain unknown. SARS-CoV-2 is thought to use ACE2 as a viral receptor, and ACE2 mRNA is highly expressed in the gastrointestinal system (12). Reverse transcriptase-polymerase chain reaction (RT-PCR) is a routine method for the diagnosis of COVID-19 in oropharyngeal swabs. Recent evidence showed that SARS-CoV-2 present in fecal specimens from patients with COVID-19 so another way of transmission can be fecal-oral and hands, food, and water contamination may occur by fecal content and may cause a critical infection by invading the oral cavity and respiratory tract (13-15). Yi Xu et.al in a clinical characterization of ten pediatric patients with SARS-CoV-2 infection in China reported that none of them required respiratory support or intensive care and none of them had pneumonia, eight patients tested positive for rectal swabs, even after the nasopharynx test was negative.

The details were published as a Brief Communication in *Nature Medicine* (16).

In a study done by Zhang et al. on 14 definite COVID-19 patients, the molecular diagnostic value of COVID-19 in the stool sample was equivalent to oropharyngeal swab. At the same time, patients with a positive stool test had no gastrointestinal symptoms (13). Even in the final stages of the infection, the anal swab can be positive, while the nasopharyngeal swab is negative, and this can be shedding the infection through oral-fecal route (17).

### Vertical

The most definitive measure of intrauterine transmission of COVID-19 is the confirmation of SARS-CoV-2 proliferation in fetal lung tissue that is technically unfeasible. Practically, the approach to investigating whether there has been intrauterine viral infection is to confirm the presence of the virus in placenta, amniotic fluid, cord blood and neonatal pharyngeal swab samples. It is important to emphasize that all of these samples need to be collected immediately after delivery and using aseptic technique (18).

A study by Zhao et al. has shown that angiotensin-converting enzyme 2 (ACE2) in human placentas act as the surface receptor for SARS-CoV-2 (19, 20). Therefore, if the severe infection of the mother's lung causes hypoxemia, damage to the placental barrier can result in vertical transmission. Because little is known about COVID-19, it is unknown what side effects it can cause in pregnant women.

According to a study in Iran, three infants were born from infected pregnant mothers, two of whom died after delivery due to acute respiratory distress syndrome (ARDS), but their infants were negative COVID-19 test (21). In their study, Chen and colleagues reported no COVID-19 nucleic acid in the pathology of placentas from three infected mothers (22).

Due to the short duration of the pandemic, most studies have been performed during the third trimester of pregnancy, and most mothers have mild to moderate symptoms. Therefore, on the one hand, the time interval from clinical manifestation of COVID-19 infection to delivery was short and on the other hand, due to the low pulmonary involvement, the rate of hypoxia and subsequent damage to the placenta will be lower (18).

Recently, two studies (23, 24) evaluated the risk of vertical transmission of SARS-CoV-2 in seven pregnant women patients through specific antibodies (IgG and IgM) in neonatal serum samples. The rapid decline of SARS-CoV-2 IgG in the infant within 14 days, while there had been a decline in IgM antibodies, strongly indicates that the neonatal SARS-CoV-2 IgG was transplacentally derived from the mother, and was not actively induced by the presumed neonatal infection (23, 24). Therefore, these two studies showed that there was no vertical transmission in the uterus.

### Conclusion

Presymptomatic transmission was defined as the transmission of SARS-CoV-2 from asymptomatic infected person to another. Therefore, because the asymptomatic patient is unaware of his or her disease and it does not provide the necessary health care to prevent the spread of droplets and contacts, so it puts other people at risk.

Regarding fecal transmission, various studies have shown that despite the negative oropharyngeal swap,

even in patients without gastrointestinal symptoms, the virus is still present in the feces, so it is better to discharge criteria based on negative rectal swabs to prevent the shedding of infection via feces.

In the case of vertical transmission of the mother to the fetus, all studies have been performed on infected pregnant mothers with mild to moderate pulmonary involvement in the third trimester and no positive results were found. Therefore, long-term studies in the first or second trimester of pregnancy, or infected pregnant mothers who have severe pulmonary involvement are needed to check for vertical transmission.

However, infected mothers may be at increased risk for more severe respiratory complications. It is well known that an infected mother can transmit the COVID-19 virus through respiratory droplets during breastfeeding. Thus, the mothers with known or suspected COVID-19 should adhere to standard and contact precaution during breastfeeding.

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### Conflict of Interest

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### References

- Rasmussen SA, Smulian JC, Lednicki JA, Wen TS, Jamieson DJ. Coronavirus Disease 2019 (COVID-19) and Pregnancy: What obstetricians need to know. *American journal of obstetrics and gynecology*. 2020 Feb 24. doi: 10.1016/j.ajog.2020.02.017.
- Working Group for the Prevention and Control of Neonatal 2019-nCoV Infection in the Perinatal Period of the Editorial Committee of Chinese Journal of Contemporary Pediatrics. [Perinatal and neonatal management plan for prevention and control of 2019 novel coronavirus infection (1st Edition)]. *Zhongguo Dang Dai Er Ke Za Zhi*. 2020;22:87-90.
- World Health Organization. Coronavirus disease (COVID-19) outbreak; n.d. [accessed 2020 Mar 4]. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>.
- Ma K, Chen T, Han MF, Guo W, Ning Q. [Management and clinical thinking of Coronavirus Disease 2019]. *Zhonghua gan Zang Bing za zhi = Zhonghua Ganzangbing Zazhi = Chinese Journal of Hepatology*. 2020 Mar;28(0): E002. DOI: 10.3760/cma.j.issn.1007-3418.2020.0002.
- Zhu ZB, Zhong CK, Zhang KX, et al. [Epidemic trend of corona virus disease 2019 (COVID-19) in mainland China]. *Zhonghua yu Fang yi xue za zhi* [Chinese Journal of Preventive Medicine]. 2020 Mar;54(0): E022. DOI: 10.3760/cma.j.cn112150-20200222-00163.
- Yang HY, Duan GC. [Analysis on the epidemic factors for the corona virus disease]. *Zhonghua Yu Fang Yi Xue Za Zhi*. 2020;54: E021. doi:10.3760/cma.j.cn112150-20200227-00196.
- Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *JAMA* 2020; published online Feb 24. DOI:10.1001/jama.2020.2648.
- Ong SWX, Tan YK, Chia PY, et al. Air, Surface Environmental, and Personal Protective Equipment Contamination by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) From a Symptomatic Patient. *JAMA*. Published online March 04, 2020. doi:10.1001/jama.2020.3227
- World Health Organization. Modes of transmission of virus causing COVID-19: implications for IPC precaution recommendations: scientific brief, 27 March 2020. World Health Organization; 2020.
- Wei WE. Presymptomatic Transmission of SARS-CoV-2—Singapore, January 23–March 16, 2020. *MMWR. Morbidity and Mortality Weekly Report*. 2020;69.
- Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *New England Journal of Medicine*. 2020 Feb 28.
- Hindson J. COVID-19: faecal–oral transmission? *Nature Reviews Gastroenterology & Hepatology*. 2020 Mar 25:1.
- Zhang J, Wang S, Xue Y. Fecal specimen diagnosis 2019 novel coronavirus-infected pneumonia. *J Med Virol*. 2020.
- Holshue ML, DeBolt C, Lindquist S, et al. First Case of 2019 Novel Coronavirus in the United States. *N Engl J Med*. 2020;382:929-936.
- Yeo C, Kaushal S, Yeo D. Enteric involvement of coronaviruses: is faecal-oral transmission of SARS-CoV-2 possible? *Lancet Gastroenterol Hepatol*. 2020;5:335-337.
- Xu Y, Li X, Zhu B, et al. Characteristics of pediatric SARS-CoV-2 infection and potential evidence for persistent fecal viral shedding. *Nature medicine*. 2020 Mar 13:1-4.
- Zhang W, Du RH, Li B, et al. Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. *Emerg Microbes Infect*. 2020;9:386-389.
- Wang C, Zhou YH, Yang HX, Poon LC. Intrauterine vertical transmission of SARS-CoV-2: what we know so far. *Ultrasound in Obstetrics & Gynecology*. 2020 Apr 7.
- Yu Zhao, Zixian Zhao, Yujia Wang, Yueqing Zhou, Yu Ma, Wei Zuo. Single-cell RNA expression profiling of ACE2, the putative receptor of Wuhan 2019-nCoV. *bioRxiv* 2020. DOI: <https://doi.org/10.1101/2020.01.26.919985>.
- G. Valdesa, L A A Neves, L Anton, J Corthorn, C Chacón, A M Germain, D C Merrill, C M Ferrario, R

- Sarao, J Penninger, K B Brosnihan. Distribution of Angiotensin-(1-7) and ACE2 in Human Placentas of Normal and Pathological Pregnancies. *Placenta*. 2006, 27, 200e207. DOI: 10.1016/j.placenta.2005.02.015.
21. Tasnim Agency. Birth of a neonate from infected mother COVID-19 in Babol city; 2020; Mar 3 [Accessed 2020 Mar 4]. <https://www.tasnimnews.com/fa/news/1398/12/14/2216407/>.
  22. Chen H, Guo J, Wang C, Luo F, Yu X, Zhang W, Li J, Zhao D, Xu D, Gong Q, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *Lancet*. 2020;395:809–15. doi:10.1016/S0140-6736(20)30360-3.
  23. Zeng H, Xu C, Fan J, et al. Antibodies in infants born to mothers with COVID-19 pneumonia. *JAMA*. 2020. Online ahead of print. DOI: 10.1001/jama.2020.4861.
  24. Dong L, Tian J, He S, et al. Possible vertical transmission of SARS-CoV-2 from an infected mother to her newborn. *JAMA*. 2020. Online ahead of print. DOI: 10.1001/jama.2020.4621.