



## Review Article

## The transmission modes and sources of COVID-19: A systematic review

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## ARTICLE INFO

## Article history:

Received 19 July 2020

Received in revised form

30 August 2020

Accepted 31 August 2020

Available online 11 September 2020

## Keywords:

COVID-19

Transmission mode

Virus source

Virus load and shedding

Pandemic infection

## ABSTRACT

The current rampant coronavirus infection in humans, commonly known as COVID-19, a pandemic that may cause mortality in humans, has been declared a global emergency by the World Health Organization (WHO). The morbidity and mortality rates due to the pandemic are increasing rapidly worldwide, with the USA most affected by the disease. The source COVID-19 is not absolutely clear; however, the disease may be transmitted by either by COVID-19-positive individuals or from a contaminated environment. In this review, we focused on how the COVID-19 virus is transmitted in the community. An extensive literature search was conducted using specific keywords and criteria. Based on the published report, it is concluded that COVID-19 is primarily transmitted human-to-human via oral and respiratory aerosols and droplets with the virus-contaminated environment play a lesser role in the propagation of disease. Healthcare providers and the elderly with comorbidities are especially susceptible to the infection.

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## 1. Introduction

The first confirmed coronavirus disease 2019 (Covid-19) case was reported on November 17, 2019, in a 55-year-old resident of Hubei, Central China [1]. However, the WHO Country Office in China was only notified of the COVID-19 outbreak on December 31, 2019, which then attracted international attention to the potential pandemic. On February 1, 2020, the World Health Organization (WHO) declared that the outbreak of this respiratory illness as a Public Health Emergency of International Concern (PHEIC). Subsequently, several more cases of the infection were identified in Wuhan City, Hubei Province, China in December 2019, in patients that patronized the South China Huanan seafood wholesale and live animal marketplace in the city.

Initially, the infection was believed to be due to animal-to-human transmission without animal species association [1,2]. Later, it was realized that human-to-human transmission is, in fact, a common mode of viral spread because a growing number of patients without a history of exposure to the market had acquired the disease [3,4].

The coronavirus infection was given various names including severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the International Committee of Taxonomy of Viruses (ICTV) and novel coronavirus infection (2019-nCoV or COVID-2019) by WHO. This disease is now widely known as COVID-19 [5]. The COVID-19 had spread very rapidly throughout the world [6,7] with clustering onset especially from international air travel [8,9]. As of May 2020, more than 200 countries had been affected, reporting more than 4 million confirmed cases with more than 280,000 deaths. The USA alone reported more than 1.3 million cases and more than 80,000 deaths with the highest morbidity and mortality rate elderly with comorbidities and immunocompromised and organ transplantation patients, and individuals of any age with

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underlying chronic diseases including cancer, diabetes, kidney disease, and hypertension [10].

Coronavirus represents a large family of single-stranded, positive-sense RNA viruses found in a wide range of animals including birds, camels, cattle, cats, pigs, and bats [11], some of which are carriers of the virus. Among these animals, the rhinolophid bats are the most dangerous carriers and they do not exhibit clinical signs of infection [12]. In other animals, the virus develops severe illness such as infectious bronchitis (IB) disease in chicken, which could lead to serious economic losses to the poultry industry [13].

Coronavirus infections are not new because during the last two decades the world was shaken by several epidemics including Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) in China (2002) from civets and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) in Saudi Arabia (2012) from dromedary camels. The source of COVID-19 is not clear, although it was originally believed that the bats are the source of the infection [14].

The symptoms of COVID-19 infection are mild to severe with death reported in some cases [15]. The most common symptoms are lower respiratory tract infection, pneumonia, dry cough, fever, shortness of breath, dyspnea, and myalgia [1,16]. Headache, confusion, sore throat, hemoptysis, runny nose, chills, muscle and chest pain, rhinorrhea, and diarrhea with nausea and vomiting may occur but less commonly reported [16]. It is now known that patients can be infected with the virus without showing any symptoms. However, most COVID-19 cases have good prognoses with mild symptoms, and with supportive care, they recovered after 7–10 days of hospitalization [17]. Patients that developed pulmonary edema, acute respiratory distress syndrome (ARDS), multiple organ failure, may die from the infection [18].

There are several tests available for COVID-19 diagnosis, mostly based on molecular or serological methods. The molecular methods are Real-time Polymerase Chain Reaction (PCR) and *E* gene PCR. These tests have been effective in the detection of COVID-19 infections from respiratory secretion samples. However, confirmation of the PCR test result may be required, and this can be done by sequencing the RNA-dependent RNA polymerase (*RdRp*) gene [19,20]. The serological tests are used to determine the presence of antibodies to the coronavirus, in patients who recovered from COVID-19, or those that may have been acquired the disease but showing mild or no symptoms [21].

At present, there is no proven antiviral medication available for COVID-19. The current treatment method for infected patients is mainly supportive care [1,22]. However, it was reported that patients at Jinyintan Hospital in Wuhan, China treated with oral doses of oseltamivir, lopinavir, and ritonavir tablets and intravenous injection of ganciclovir showed faster recovery rate [18,23]. On the other hand, dexamethasone lowered 4 weeks of mortality among hospitalized patients that received either invasive mechanical ventilation or oxygen alone at randomization but not among those received no respiratory support [24]. Additionally, alpha-interferon, a combination of Hydroxychloroquine and azithromycin, arbidol, favipiravir were given some critical recovery rate in various countries [25]. In contrast, remdesivir touted as the savior drug for COVID-19 patients but failed in the first clinical trial [26].

Risk factors for transmission of COVID-19 are largely uncharacterized [27]. However, to avoid the spread of COVID-19, the CDC and WHO have instituted a preparedness and prevention agenda for the infection to be used by the public, first-responders, and healthcare providers and professionals [28,29]. Although this agenda is somewhat practiced by hospitals with confirmed COVID-19 patients, the general population is not completely compliant, thus, putting them at extremely high risk of exposure to the infections from colleagues, household members, and the community [27,30].

Clusters of local transmission must be identified [31,32] to improve control of spread through preparedness, readiness, and response actions [33]. Control of the spread of COVID-19 also requires precise information on human mobility, epidemiological, and genetic data at local, regional, and global levels. This information will ensure success in the deployment of resources in the mitigation of COVID-19 transmission [30,34].

Treatment and control of viral disease are complicated by the propensity of the virus to mutate, making development and deployment anti-viral vaccines very challenging [35,36]. In this regard, a recent study reported the initial analysis of APOBEC and ADAR deaminase-mediated mutation signature patterns in complete COVID-19 genomes from informative locations and times in China, USA and Spain identified a unique set of new putative co-ordinated Riboswitches in COVID-19 genomes and variants in common strain Haplotypes. The results reveal that COVID-19 diversifies using switching of RNA Haplotypes with minimal alteration to protein structure [37]. Thus, vaccine designs that assume that the main viral protein antigens will be the only putative protective targets could fail to produce effective and protective immunity. Therefore, the challenges for targeted drug and vaccine development for COVID-19 needs understanding COVID-19 adaptation and survival strategy and identifying the host Haplotype, and which vaccine(s) is effective for each Haplotype group [37].

However, there are other alternative means to control COVID-19 infection and preventing transmission. This can be done implementing containment, which includes isolation of known cases, quarantine of persons believed at high risk of exposure, especially during the initial phase of the outbreak, and closing regional and country borders and restricting movement and travel and screening travelers for the infection [2,38,39]. As the last resort and if necessary, the community could be placed on complete lockdown [40].

The exact source of the COVID-19 virus remains elusive [41]. To ensure that the pandemic can be curtailed, the source and mode of transmission of the infection must be precisely determined. Thus, in this review, we focused on the causative agent, the main modes of transmission, and sources of COVID-19.

## 2. Methodology

### 2.1. Document identification on COVID-19

Several pertinent online databases including PubMed, Google Scholar, Scopus, bioRxiv, medRxiv, and chemRxiv were searched to collect relevant data. Information from some articles published online by the Chinese Center for Disease Prevention and Control, and the WHO was also included in the review.

### 2.2. Inclusion criteria

All publications available in peer-reviewed journals, review, practical and technical articles addressing the main routes, modes, and sources of COVID-19 virus transmission in humans were selected, inclusive of full review articles, practical, and technical papers.

### 2.3. Exclusion criteria

Case reports, editorials, letters, letters to the editor, comments/commentaries, short/brief communications, rapid reviews, short/rapid reports, opinions, news, seminars, features, correspondences, exercises, protocols, guidance, highlights, forums, images, interviews, insights, panels, symposia, abstracts, personal views,

perspectives, preprints, podiums, policies, consensus documents, and practices were excluded from the review.

#### 2.4. Data collection

Gathering of publications from websites was done with the Medical Subject Heading (MeSH) using terms such as new Coronavirus, novel Coronavirus, COVID-19, 2019-nCoV, SARS-Coronavirus-2, SARS-CoV-2, MERS-Coronavirus-2, and MERS-CoV-2. Keywords from the title of the subject matter, such as COVID-19 mode of transmission, route of transmission of COVID-19, and source of COVID-19, COVID-19 viral load, and shedding were also used. To ensure that all relevant researches are including, the following terms were used in combination with COVID-19: transmission, spread, source, viral load, viral shed, infection, respiratory illness, pneumonia, outbreak, pandemic, quarantine, and lockdown. The titles, author list, and abstracts of these publications were evaluated to avoid data duplication.

#### 2.5. Extraction of the data

Data from selected publications were extracted and documented in the excel spreadsheet.

### 3. Results and discussion

A total number of 2036 of publications were identified. Among these publications, 235 were duplicated studies and excluded. The remaining 1801 publications were scrutinized based on exclusion criteria, and as a result, 1071 publications were removed from the study. The remaining 730 articles were again screened and finally, only 151 publications were found relevant included in the review (Fig. 1).

#### 3.1. Emergence of coronavirus

After the report of an emerging coronavirus disease epidemic in Wuhan City, China in December 2019, early in January 2020, the Chinese Center of Disease Control and Prevention of CDC China conducted an epidemiology investigation by collecting 585 collected environmental samples from the Huanan Seafood Market in Wuhan, Hubei Province, China on two occasions on January 1 and 12 2020. They discovered that 33 samples were positive for COVID-19 and suggested that wild animals sold at the market were the origin of the virus [42]. Earlier in December 2019, in the province, among lung fluid, blood, and throat swab samples collected from 41 pneumonia cases of unknown etiology, 15 were positive for virus-specific nucleic acid sequence. Upon isolation, the ultrastructure of the virus was typical of human coronavirus species [43]. The virus is related to some  $\beta$ -coronaviruses genera in bats [43–45].

#### 3.2. Genetic analysis of the virus concerning transmission

After examination of approximately 169 genomes, the COVID-19 virus can be classified into two major genotypes, namely, Type I (A and B) and II. Based on the phylogenetic investigation, Type IA almost appeared like the ancestral COVID-19 virus. Type II, which evolved from Type I, is a predominant and highly contagious form of the virus, and this virus is suggested to be one responsible for the epidemic that began in the wet-market of Wuhan City, China. People with COVID-19 that did not have direct contact with the Wuhan marketplace may have been infected with the Type I virus [46].

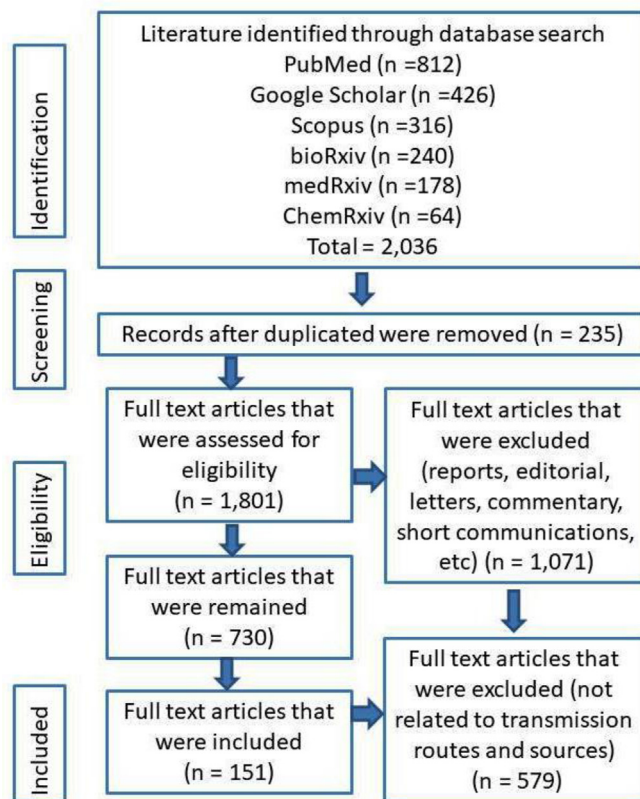


Fig. 1. PRISMA flow diagram for the current systematic review process indicating the study selection stages and analyzed results.

#### 3.3. Modes and sources of coronavirus transmission

The character and trends of current COVID-19 transmission can be used as indicators of how the COVID-19 pandemic will behave throughout the rest of 2020 and in the following years [7].

#### 3.4. Animal-to-human transmission

The transmission of COVID-19 in humans is no clear [47], although early in the pandemic, it was declared that the infection is zoonotic [48], that is, from animals to human [43,49,50].

The bat coronavirus, Beta-CoV/bat/Yunnan/RaTG13/2013 (bat/RaTG13), is similar to the human COVID-19 virus [51], suggesting bats to be the reservoir for acute infection in humans [52]. In fact, at the whole genome level, the human nCoV-2019 is 96% identical to a bat coronavirus [53]. However, in another report, Ji et al. (2020) described the homologous recombination within the spike glycoprotein of COVID-19 that favors cross-species transmission. It was also suggested snake as another probable virus reservoir for human infections because of the resampling similarity codon usage bias of COVID-19 is similar to that of *Bungarus multicinctus* snake [54]. On the other hand, recent studies had implicated the pangolins as the missing link in COVID-19 infection to humans because they provided a partial spike gene to COVID-19. The critical functional sites in the spike protein of COVID-19 in humans are nearly identical (91.02% at the whole genome level) to a virus isolated from a pangolin. Based on this finding, it was also suggested that the pangolins are a natural reservoir of the COVID-19 virus and play a major role in the transmission of the disease to humans [55–57].

Recently, many patients without a history of exposure to the marketplace in Wuhan, China, or animals elsewhere and medical



professionals had contracted the disease, which indicates that the infection is not merely animal-to-human transmission, instead, it may occur between humans [16,58–60]. This mode of transmission of the disease appears to be similar to SARS and MERS, known to infect and spread among humans through close contact and respiratory droplets from coughs and sneezes [11]. Whether COVID-19 behavior is similar to SARS or MERS needs further investigations.

### 3.5. Human-to-human transmission

Current data showed that there is the human-to-human transmission of COVID-19 [61], suggesting that to be the main mode of transmission of the disease in the current pandemic [62]. Thus, there is a need for rigorous surveillance and testing to prevent further expansion of the pandemic [63–65]. Generally, patients showing symptoms of COVID-19 will spread the disease to those in close contact [66,67]. However, many COVID-19 patients are asymptomatic and can serve as carriers and unknowingly transmit the virus [68–70]. This may be the reason for the number of COVID-19 cases increased drastically and rapidly in some societies that lax in the practice of isolation and social distancing [59,71,72], and within families with asymptomatic infected individuals [73] (Fig. 2).

The COVID-19 is a fast expanding pandemic, which caught many countries off-guard. In many countries, the control of the infection is hindered by inadequate emergency settings, suboptimal logistics, and scarcity of personal protective equipment (PPE) [74]. This had endangered front liners and healthcare providers that were directly involved in the handling of COVID-19 cases. This situation suggests the need for other treatment means, like telemedicine, which is ideal for medical practitioners to evaluate, diagnose and treat patients from a distance, thus, while avoiding contact with and exposure to infected patients [66,67]. Telemedicine is especially ideal because [75,76] physicians can simultaneously attend to patients at several distant locations. In pandemics, where the medical practitioners are stretched to provide services, telemedicine will serve to provide the means to obtain the much need medical attention to a large number of patients [77].

Currently, it is difficult to determine whether a COVID-19 case is imported, secondary, and the result of tertiary transmission [78,79]. However, there are confirmed cases of secondary and tertiary transmission of COVID-19 [80,81], and these cases are believed to

be the leading causes for rapid cycles of disease transmission from one generation to the next [35]. There are now many pieces of evidence of chains of at least four generations (highest level of first-generation) infections, which unequivocally suggest the existence of sustained human-to-human transmission [63,82–84].

This type of human-to-human COVID-19 transmission includes:

#### 3.5.1. Horizontal Transmission

Based on the latest guidelines from Chinese health authorities, there are 3 main transmission routes for the COVID-19 virus in humans [85–87], namely direct contact, aerosol, and droplets.

**3.5.1.1. Direct Contact Transmission.** Direct contact transmission may occur through direct contact with virus-contaminated objects or surfaces and infecting people through the mouth, nose, or eyes [88,89]. Healthcare providers attending COVID-19 patients are especially at risk of being infected via this mode of disease transmission [84], one reason there are numerous nosocomial infections [54,86]. In direct contact transmission, the fomites are suspected to be the main source of infectious particles [90,91]. The transmission of COVID-19 can be minimized by frequent washing of hands with an alcohol-based hand rub or soap and water and avoiding touching eyes, nose, and mouth with contaminated hands [92].

**3.5.1.2. Aerosol Transmission.** Although the COVID-19 virus is not principally an airborne virus [93], the aerosols from expired coughs, and sneezes that contaminate the immediate environment [88,89] are among media for virus spread [94–96]. Aerosol transmission is not just from people with symptoms of the disease, even asymptomatic COVID-19-positive people can be the source of infection [69,97]. In close environments, the virus-containing aerosol may persist in the air for long periods and at high concentrations, further increasing the rate of transmission [82]. The virus remains viable for at least 3 h in aerosols and 48–72 h on stainless steel and plastic surfaces [98].

Nosocomial transmission of the COVID-19 [99] is a serious threat to healthcare providers. Nosocomial infections through aerosols can occur when they perform procedures on the respiratory pathway, perform dental care [94] and hemodialysis [100], and manage of intensive care unit (ICU) [101]. Management of respiratory diseases and disorders often requires the use of high-flow nasal oxygen or endoscopy, procedures that may generate COVID-19 virus-laden aerosols into the environment, and infecting inadequately protected people. To minimize the risk of infection among healthcare providers, the CDC had formulated recommendations on the use of PPE including gowns, gloves, N95 respirators, face-shield, or goggles. In extreme cases, a powered, air-purifying respirator (PAPR) should be used to aid respiration healthcare providers. These precautions should be concurrent with the practice of social distancing [102–104].

**3.5.1.3. Droplet Transmission.** Respiratory air normally contains an abundance of droplets of sizes less than 5  $\mu\text{m}$  in diameter. Coughing and sneezing cause increased expulsion of droplets from the oral cavity and respiratory tract. In COVID-19 patients these droplets contain a virus that if inhaled or ingested or landing on the mucous membranes will cause disease in people [98,105]. This mode of transmission is the most dangerous form of COVID-19 spread among healthcare providers [106]. The use of PPE with efficient barriers to the droplets and maintenance of personal and environmental hygiene will limit the rate of infections [107].

COVID-19 viral transmission may also occur via feces, tears, and conjunctival secretions [101,108–110].

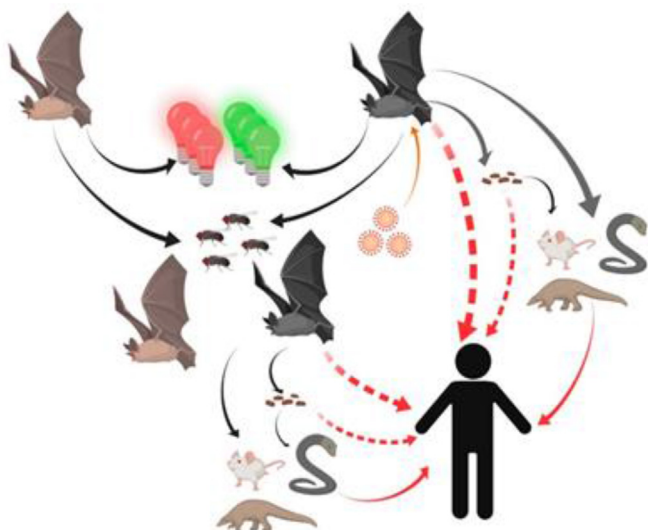


Fig. 2. Main routes of transmission for COVID-19 to humans [71].

### 3.6. Fecal-oral transmission

The role of feces in the transmission of COVID-19 is unclear [111]. There have been suggestions that the gastrointestinal system is a critical route for the spread of this virus [112]. The COVID-19 virus infects cells via the surface angiotensin-converting enzyme 2 (ACE2). Incidentally, it was shown that there are high expressions of ACE2 in gastric glandular, colon and ileum absorptive enterocytes, duodenal and rectal cells suggesting the virus spread via the fecal-oral route [97,107,113]. It seems, that using immunofluorescent staining, the ACE2-positive cells are rarely detected in esophageal mucosa. This is probably of the predominance of esophageal squamous epithelial cells that express less ACE2 than glandular epithelial cells [114].

Specimens collected from the surface of the toilet bowl, in the sink, and the door handles of toilets used COVID-19-positive patients without diarrhea, were all positive for the virus [108]. However, these toilets were negative for the virus after it has been thoroughly sanitized. Therefore, public toilets with poor sanitation may pose infection risks to users through contact transmission. Sharing of toilets between healthy and COVID-19-positive individuals, although still contentious [52], may facilitate the transmission of the infection through the fecal-oral route [115].

It seems that the feces of recovered COVID-19 patients negative for the virus in their respiratory secretions may contain viral RNA that remains viable in feces for long periods. It may be that gastrointestinal infection with this virus and fecal-oral transmission of COVID-19 can still occur even after the respiratory tract of COVID-19 patients had become clear of the virus [116]. Clearance of the COVID-19 virus in the respiratory tract occur within two weeks, whereas the feces can remain positive for viral RNA for longer than 4 weeks, after abatement of fever [117]. Thus, although the respiratory secretion of recovered patients may appear negative for the virus, according to the principles of transmission-based Precautions, the feces should be checked for the presence of the virus, to ensure that they have completely virus-free and completely recovered from the infection [114].

### 3.7. Transmission through organ transplantation and surgical operations

The COVID-19 virus resides principally in the respiratory tract and its secretions. These pose risks to healthcare providers if these patients require surgery. This is particularly true in organ transplantation procedures. Recipients of organs, especially, because being place in the immunocompromised state, which is necessary for the procedure, are at high risk of being infected with COVID-19 [17,118]. Thus, unless necessary, it would be advisable to delay organ transplantation procedures until the COVID-19 pandemic has gone through its full course and no longer a health threat. However, emergency surgical interventions should be followed in the COVID-19 population in case of severe appendicitis; abortions that need caesarian section, strangulated inguinal hernias, intestinal/respiratory obstructions, severe toothache, aggressive tumor, painful kidney stone and even severe trauma caused by a gunshot or car accident [119].

Although until the beginning of April 2020 there was no published data on cases of transmission of COVID-19 from patients to surgeons, healthcare providers, and other hospitalized patients during the surgical operation, hospitalization, and treatment [120]. But later on, it was confirmed by the Chinese Center for Disease Control and Prevention that 3.8% of reported cases were healthcare personnel from which 15% were classified as severe cases with only 0.2% mortality rate. In COVID-19 patients, there is an evidence of the virus in the sputum (93%), blood (1%), stool (29%), and maybe

some organs contain the virus, which may expose surgeons, or operating room staff [121]. Taken together, this suggests that pulmonary and upper respiratory surgeries are likely to be higher risk, but that colorectal and gastrointestinal surgeries may also have a greater risk of transmission [122].

#### 3.7.1. Vertical Transmission

The COVID-19 pandemic puts pregnant women and fetuses at risk of being infected by the virus. This is primarily due to the high expression of ACE2 receptors in the human maternal-fetal interphase. This ACE2 receptor structure of the COVID-19 virus is analogous to that of SARS. Thus, like SARS, COVID-19 can potentially be transmitted vertically [116,123,124]. The first case of possible vertical transmission of COVID-19 was reported in March 2020. The neonate of a COVID-19-positive mother, 2 h after birth, showed elevated blood IgM and cytokine levels [125]. Other cases similarly showed neonates to be positive for the COVID-19 virus, shortly after birth [126], while the amniotic fluid, cord blood, breast milk after the first lactation of their mothers were negative of the virus [127,128]. The mothers acquired the infection in the last trimester of their pregnancy, thus, it is still not clear of the perinatal outcome had the infection occurred early in the pregnancy [129]. Not all neonates of COVID-19-positive mothers acquired the disease [130] because one study showed that none of the neonates born of 31 mothers infected with COVID-19 had the disease [130,130]. Although cases of vertical COVID-19 transmission are few and maybe incidental, the potential of vertical transmission of COVID-19 should not be ruled out.

Learning from the previous SARS outbreak, the Canadian Society of Obstetricians and Gynecologists guidelines suggested immediate clamping of the umbilical cord to avoid potential transmission of the COVID-19 following delivery [131,131]. As an additional precaution, newborns of mothers with suspected or diagnosed COVID-19 infection should be isolated and monitored for clinical manifestations of the infection for 14 days after birth [132]. Since the breast milk of COVID-19-mothers is virus-free, breastfeeding is safe for the newborn [133,134]. However, mothers should be wearing masks during breastfeeding to minimize the risk of transmitting the infection to the newborns through droplets and aerosols [135].

#### 3.8. Viral load and shedding

The pathophysiological characteristics of COVID-19 have not been determined and there is much uncertainty regarding the mechanism of shedding and spread of the virus [136,137]. Recent estimates suggested that COVID-19 has a median incubation period of 3 days (range: 0–24 days) [138] with potential asymptomatic transmission [139,140]. Epidemiological evidence showed the virus can be transmitted during the incubation period [141], especially during the late stages [142]. Interestingly, the viral could not be detected early in diseased patients from the tertiary transmission, thus, it could be speculated that the infectivity of COVID-19 will gradually decrease with the level of transmission [143]. The highest viral load in COVID-19 patients are in the sputum, saliva, and upper airway secretions [144], although the virus may also be found in blood, pharynx, and anus [145].

The most critical characteristics of a COVID-19 virus are their high capacity for shedding, transmission, and spread [146,147]. The median period of COVID-19 viral release from the time patients nasopharyngeal swab tested positive, is 12 days, although some patients shed virus after one week. In these patients, the virus may be present in stool, whole blood, and urine [23,151,152]. In COVID-19-positive patients at Wuhan Pulmonary Hospital, China, there were more positive anal than oral swabs, which suggests a possible fecal-oral route for the transmission of the disease [148].

The COVID-19 virus exhibits gastrointestinal tropism and may account for the frequent occurrence of diarrhea in infected patients. The shedding of the virus in feces facilitates the spread of the disease via fomite transmission and aerosolized toilet plume [149].

The nasopharyngeal viral load of patients with COVID-19 peaks within the first few days of onset of symptoms and viral shedding in nasopharyngeal secretions will persist for at least another 24 days [150]. Most COVID-19 patients show a high prevalence of the virus in saliva. However, saliva viral load decreases with time [151]. Thus, the saliva is a convenient noninvasive sample for the diagnosis of COVID-19, especially, at the stages of the disease.

Patients with symptoms of COVID-19 should be immediately triaged and separated from the community preferably in well-ventilated facilities while keeping safe distances of at least 2 m from other individuals [152]. Contact tracing for exposure to COVID-19-infected people is essential to identify potential hotbeds and to institute disease control and containment measures [153–155]. Healthcare providers are at high risk of acquiring the disease, thus, must be subjected to regular testing, practice self-monitor, report signs of illness, and voluntarily isolate themselves if they exhibit symptoms of COVID-19 [94,156]. Since the COVID-19 virus is known to survive on surfaces for hours or days [157], the healthcare providers must practice strict hygiene, regularly and conscientiously cleaning workspaces and personal items such as stethoscopes, mobile phones, keyboards, dictation devices, land-lines, and nametags. The hospital must provide disinfectants for the use of personnel and patients [158].

### 3.9. Testing strategy to prevent viral transmission

The testing strategies that should be followed to prevent COVID-19 vertical/horizontal modes of transmission during surgery include detection of the viral RNA using Polymerase Chain Reaction

(PCR) and detection of the host's response (antibodies) to the virus using serological techniques [159].

The former technique is more accurate and considered as a gold standard for this virus using swabs from the nasopharynx and/or oropharynx. Since COVID-19 can infect anyone and result in transmission before the onset of symptoms or even without individuals ever developing symptoms, testing/screening of asymptomatic patients has been considered [160].

Whereas, the latter includes detection of IgM, IgA, IgG, or total antibodies in the blood although this virus is not typically present in blood in which COVID-19 infection causes white blood cells (WBC) to make antibody proteins that help the immune system identify the viruses and stop them or mark infected cells for destruction. This process is host-dependent and takes 7–11 days after exposure to the virus, although some patients may develop antibodies sooner. Therefore, this technique is not useful in the setting of an acute infection [159].

### 3.10. Protection strategies

Standard surgical personal protective equipment (PPE) includes a face shield, high-performance filtering mask, waterproof gown, double gloves, and shoe covers that must be implemented properly (Table 1) [161]. However, there is some disagreement about the type of respiratory protection N95 respirator, powered air-purifying respirator (PAPR), and standard surgical mask that should be used for surgical procedures on patients with COVID-19. Mask is considered as the main item of PPE as it is easy to obtain, cheap, and available in almost all hospitals including low-income countries. A surgical mask is capable of blocking the gross inhalation of respiratory droplets, while a well-fitted N95 respirator is proficient in filtering aerosols [162,163]. On the other hand, high-performance filtering masks including FFP1, FFP2, and FFP3 masks have a high

**Table 1**

Recommended personal protective equipment (PPE) to be used against COVID-19 infection, according to the setting, personnel and type of activity. Reprinted from World Health Organization, 2020.

Setting	Target personnel or patients	Activity	Type of PPE or procedure
<b>Healthcare facilities</b>			
<b>Inpatient facilities</b>			
Patient room	Healthcare workers	Providing direct care to COVID-19 patients.	Medical mask Gown Gloves Eye protection (goggles or face shield). Respirator N95 or FFP2 standard, or equivalent.
		Aerosol-generating procedures performed on COVID-19 patients.	Gown Gloves Eye protection Apron Medical mask Gown Heavy duty gloves
	Cleaners	Entering the room of COVID-19 patients.	Eye protection (if risk of splash from organic material or chemicals). Boots or closed work shoes
Other areas of patient transit (e.g., wards, corridors).	Visitors	Entering the room of a COVID-19 patient	Medical mask Gown Gloves
	All staff, including healthcare workers.	Any activity that does not involve contact with COVID-19 patients.	No PPE required
	Healthcare workers	Preliminary screening not involving direct contact	Maintain spatial distance of at least 1 m. No PPE required
Triage	Patients with respiratory symptoms.	Any	Maintain spatial distance of at least 1 m. Provide medical mask if tolerated by patient.
	Patients without respiratory symptoms.	Any	No PPE required
Laboratory	Lab technician	Manipulation of respiratory samples.	Medical mask Gown Gloves Eye protection (if risk of splash)

Table 1 (continued)

Setting	Target personnel or patients	Activity	Type of PPE or procedure
Administrative areas	All staff, including healthcare workers.	Administrative tasks that do not involve contact with COVID-19 patients.	No PPE required
<b>Outpatient facilities</b>			
Consultation room	Healthcare workers	Physical examination of patient with respiratory symptoms.	Medical mask Gown Gloves Eye protection PPE according to standard precautions and risk assessment. Provide medical mask if tolerated.
	Healthcare workers	Physical examination of patients without respiratory symptoms.	Any
	Patients with respiratory symptoms.	Any	No PPE required
	Patients without respiratory symptoms.	Any	No PPE required
	Cleaners	After and between consultations with patients with respiratory symptoms.	Medical mask Gown Heavy duty gloves Eye protection (if risk of splash from organic material or chemicals). Boots or closed work shoes Provide medical mask if tolerated. Immediately move the patient to an isolation room or separate area away from others; if this is not feasible, ensure spatial distance of at least 1 m from other patients.
Waiting room	Patients with respiratory symptoms.	Any	No PPE required
	Patients without respiratory symptoms.	Any	No PPE required
Administrative areas	All staff, including healthcare workers.	Administrative tasks	No PPE required
Triage	Healthcare workers	Preliminary screening not involving direct contact	Maintain spatial distance of at least 1 m. No PPE required
	Patients with respiratory symptoms.	Any	Maintain spatial distance of at least 1 m. Provide medical mask if tolerated.
	Patients without respiratory symptoms.	Any	No PPE required
<b>Community</b>			
Home	Patients with respiratory symptoms.	Any	Maintain spatial distance of at least 1 m. Provide medical mask if tolerated, except when sleeping.
	Caregiver	Entering the patient's room, but not providing direct care or assistance.	Medical mask
	Caregiver	Providing direct care or when handling stool, urine or waste from COVID-19 patient being cared for at home.	Gloves Medical mask Apron (if risk of splash)
	Healthcare workers	Providing direct care or assistance to a COVID-19 patient at home	Medical mask Gown Gloves Eye protection No PPE required
Public areas (e.g., schools, shopping malls, train stations).	Individuals without respiratory symptoms	Any	No PPE required
<b>Points of entry</b>			
Administrative areas	All staff	Any	No PPE required
Screening area	Staff	First screening (temperature measurement) not involving direct contact	Maintain spatial distance of at least 1 m. No PPE required
	Staff	Second screening (i.e., interviewing passengers with fever for clinical symptoms suggestive of COVID-19 disease and travel history).	Medical mask Gloves
	Cleaners	Cleaning the area where passengers with fever are being screened.	Medical mask Gown Heavy duty gloves Eye protection (if risk of splash from organic material or chemicals). Boots or closed work shoes Maintain spatial distance of at least 1 m.
Temporary isolation area	Staff	Entering the isolation area, but not providing direct assistance.	Medical mask Gloves
	Staff, healthcare workers	Assisting passenger being transported to a healthcare facility.	Medical mask Gown Gloves Eye protection
	Cleaners	Cleaning isolation area	Medical mask Gown Heavy duty gloves Eye protection (if risk of splash from organic material or chemicals). Boots or closed work shoes
Ambulance or transfer vehicle	Healthcare workers	Transporting suspected COVID-19 patients to the referral healthcare facility.	Medical mask Gowns Gloves Eye protection

(continued on next page)

Table 1 (continued)

Setting	Target personnel or patients	Activity	Type of PPE or procedure
	Driver	Involved only in driving the patient with suspected COVID-19 disease and the driver's compartment is separated from the COVID-19 patient. Assisting with loading or unloading patient with suspected COVID-19 disease. No direct contact with patient with suspected COVID-19, but no separation between driver's and patient's compartments.	Maintain spatial distance of at least 1 m. No PPE required  Medical mask Gowns Gloves Eye protection Medical mask
	Patient with suspected COVID-19 disease. Cleaners	Transport to the referral healthcare facility.  Cleaning after and between transport of patients with suspected COVID-19 disease to the referral healthcare facility.	Medical mask if tolerated  Medical mask Gown Heavy duty gloves Eye protection (if risk of splash from organic material or chemicals). Boots or closed work shoes
<b>Special considerations for rapid response teams assisting with public health investigations</b>			
<b>Community</b>			
Anywhere	Rapid response team investigators.	Interview suspected or confirmed COVID-19 patients or their contacts.  In-person interview of suspected or confirmed COVID-19 patients without direct contact.  In-person interview with asymptomatic contacts of COVID-19 patients.	No PPE if done remotely (e.g., by telephone or video conference). Remote interview is the preferred method. Medical mask Maintain spatial distance of at least 1 m. The interview should be conducted outside the house or outdoors, and confirmed or suspected COVID-19 patients should wear a medical mask if tolerated. Maintain spatial distance of at least 1 m. No PPE required The interview should be performed outside the house or outdoors. If it is necessary to enter the household environment, use a thermal imaging camera to confirm that the individual does not have a fever, maintain spatial distance of at least 1 m and do not touch anything in the household environment.

filtration efficiency of 80%, 94%, and 99% respectively, while N95 mask blocks at least 95% of solid and liquid aerosol test particles. Thus, the FFP3 is likely to be twice as effective as the FFP2 mask, and broadly both are equivalent or superior to an N95 mask.

In this regard, a study in 4 hospitals at Wuhan, China on 420 fully protected (implemented appropriate PPE) healthcare professionals (116 doctors and 304 nurses) with an average age of 35.8 years and an average work of 16.2 h each week in intensive care units that had direct contact with COVID-19 patients and performed at least one aerosol-generating procedure for 6–8 weeks has been conducted. The results revealed that during the deployment period, none of the participants reported COVID-19 related symptoms and when the participants returned home, they all tested negative for COVID-19 specific nucleic acids and IgM or IgG antibodies [164].

### 3.11. Recently developed vaccines

Very recently chimpanzee adenovirus-vectored vaccine (ChAdOx1 nCoV-19) expressing the SARS-CoV-2 spike protein has been developed in the University of Oxford, UK in collaboration with AstraZeneca Company in a ½ phase, single, blind randomized controlled trial on healthy adults aged 18–55 years with no history of COVID-19 infection or COVID-19-like symptoms. But, this vaccine produced side effects in vaccinated individuals such as pain, slight fever, chills, muscle ache, headache, and malaise which were reduced by the use of prophylactic paracetamol. However, it presented an acceptable safety profile, and homologous boosting improved antibody responses [165].

Moreover, a recombinant adenovirus type-5-vectored COVID-19 (Ad5-vectored COVID-19) vaccine in healthy adults aged 18 years or older with no history of HIV and COVID-19 infections were developed in Beijing Institute of Biotechnology, Wuhan, China in a randomized, double-blind, placebo-controlled, phase 2 trial. This vaccine seemed to be safe and induced significant immune responses in the majority of recipients after a single immunization [166].

Furthermore, a COVID-19 RNA Vaccine Candidate (BNT162b1) has been developed by both Pfizer and BioNTech Companies, Germany in the placebo-controlled, observer-blinded dose-escalation study among healthy adults, 18–55 years of age, randomized to receive 2 doses, separated by 3 weeks, of various amounts of a lipid nanoparticle-formulated, nucleoside-modified, mRNA vaccine that encodes trimerized SARS-CoV-2 spike glycoprotein RBD. Local reactions and systemic events were seemed to be dose-dependent, generally mild to moderate, and transient [167].

Finally, the mRNA-1273 vaccine is developed by Moderna Company, the USA in phase 1, dose-escalation, open-label trial including 45 healthy adults, ages 18–55 years who received 3 different doses of 2 vaccinations at 4 weeks interval. Besides, this vaccine produces immune response but more than half of the participants showed adverse effects such as fatigue, chills, headache, myalgia, and pain at the injection site especially after 2nd vaccination with high doses of mRNA-1273 [168].

## 4. Conclusion

COVID-19 infection may have begun from animal-to-human infection, however, the virus has evolved into a form that causes



rapid human-to-human transmission through aerosols, droplets, and direct contact. Nosocomial transmission of COVID-19 patients to healthcare works can be controlled by instituting adequate safety measures. However, control of COVID-19 transmission in the community may not be as straightforward because this depends on strict societal compliance to the standard operating procedure for control of the COVID-19 pandemic, which includes social distancing, wearing masks, personal hygiene, and avoiding crowds. These precautions are even more critical for the elderly and those with comorbidities such as cardiovascular and kidney diseases, diabetes, and other chronic diseases. Measures were taken by the government to lock down the country are probably the most effective means of controlling the pandemic. However, the country mustn't be too hasty in the lifting of lockdown because of the pressure to restart the economy. Lifting lockdown prematurely, when the disease is not adequately contained, poses the risk of a flare-up in second and third wave pandemic.

#### 4.1. Strength and limitation of the studies

The review applied a systematic and rigorous search strategy to retrieve relevant articles based on the objectives of this review. The information in this review is current at the point of publication. New information on the COVID-19 pandemic is being published every day, however, much is still not known about the COVID-19 pandemic. For example, there are gaps in knowledge on the mode, source, and mechanism of transmission of COVID-19 and the rate of mutation of the virus in the community. This information must be acquired to ensure containment of the pandemic through the use of vaccines or institutions of new normal physical and psychological behaviors, which with luck will eradicate the virus from the community.

#### Ethical approval

No patient samples were used.

#### Funding

No fund is obtained for this review article.

#### Author contribution

**Heshu S. Rahman:** Conceptualization, Writing-Original draft preparation, Reviewing and Editing.

**Masrur S. Aziz:** Data Analysis, Resources and Visualization.

**Ridha H. Hussein:** Writing-Original draft preparation.

**Hemn H. Othman:** Writing-Original draft preparation.

**Shirwan H. Omer:** Writing-Original draft preparation.

**Eman S. Khalid:** Resources and Visualization.

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**Kawa Amin:** Writing-Original draft preparation.

**Rasedee Abdullah:** Writing-Original draft preparation, Reviewing and Editing.

#### Conflict of interest statement

Authors declared that there is no conflict of interest to this manuscript.

#### Guarantor

Prof. Dr. Heshu Sulaiman Rahman.

#### Research registration number

There is no human participants and this is a review article.

#### Consent

No studies on patients has been done and this is a review article.

#### Acknowledgments

Our sincere thanks go to all the experts who contributed to the writing of this review.

#### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijso.2020.08.017>.

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