



Review Article

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Coronavirus Disease (COVID-19) Possible Transmission Routes and Alleviation Strategies

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ABSTRACT

Coronavirus disease is a contagious respiratory ailment that has spread significantly around the world. Most cases of COVID-19 are spread from person to person by coming into contact with respiratory droplets that are released when an infected person coughs or sneezes. In this manuscript, we have highlighted the possible transmission of COVID-19 through food, water, air and paper. In the case of food, we have extensively covered the transmission of COVID-19 through meat, frozen foods, food packaging and food market along with the incidences worldwide. In the next section, we have highlighted the different components of air which are responsible for the transmission and also covered its relation with PM 2.5 incidence. The SARS-CoV-2 was isolated from sewage water/wastewater of various countries namely the United States, India, Australia, Netherlands and France signifying that wastewater can be a mode of virus transmission. The paper circulation by the infected COVID-19 patients can also be a virus conveyance route. It can be concluded that SARS-CoV-2 can therefore be transmitted indirectly through food via the workers involved in food packing or food marts. By following general safety precautions (wearing masks, using hand sanitisers, cleaning and disinfecting contact surfaces, and avoiding close contact), heating and using chemicals like ethanol (67-71%), sodium hypochlorite (0.1%) and hydrogen peroxide (0.5%) on environmental surfaces, along with vaccination, it is possible to reduce the spread of the SARS-CoV-2 virus.

Key words: COVID-19, Transmission, Food, Wastewater, Mitigation

INTRODUCTION

The World Health Organization (WHO) briefly designated the pneumonia-like SARS-CoV-2 disease that was reported from the Chinese city of Wuhan as coronavirus disease (COVID-19) in December 2019 [1]. The entire world has been affected by COVID-19's three waves, while some countries have experienced the fourth wave also, which has resulted in human deaths and economic losses. Up until December 19, 2022, there have been 649,038,437 confirmed cases of COVID-19 in more than 200 nations, resulting in 6,645,812 fatalities (<https://covid19.who.int/>). Coronaviruses are positive-stranded, non-segmented enveloped viruses that are members of the Coronaviridae family. These viruses are pleomorphic particles that have a diameter of 80–220 nm. SARS-CoV-2 is the latest coronavirus to spread overseas. The pandemic has focused our attention on the potential transmission channels of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the pandemic's causative agent [2].

COVID-19 is a respiratory infection that spreads mostly through proximate contact (touch, blood and body fluids, saliva) as well as close interaction with respiratory secretions produced when an infected individual sneezes and coughs. However, food, water, insects and fomites might also be a mode of transmission. SARS-CoV-2, unlike other viruses, can persist after leaving the host for a while, albeit it hasn't been determined for how long it may be identified on surfaces. The duration of the virus's survival outside of the host is largely influenced by the physical and chemical characteristics of the surface as well as the surrounding factors, such as the weather, light, temperature, humidity, and so on [3, 4]. SARS-CoV-2 survived for seven days on a plastic surface and four days on a stainless-steel surface at room temperature, according to studies by Chin *et al.*, and Doremalen *et al.*, although it sustained much less well on paper documents, money, and mail wrapping paper [3, 5].

Transmission of coronavirus through food

SARS-CoV-2 is capable of surviving the gastrointestinal fluids and enzymes and establishes an effective infection in the intestine. Thus, this finding supported the notion that food and waterborne transmission of SARS-CoV-2 are plausible [6]. Food contamination can happen at any point along the food supply chain, including before, during and after production, distribution and immediately before consumption. Few epidemiologic investigations have shown that numerous cases were linked with a 'wet wholesale market' in Wuhan, China known as the Huanan South Seafood Market. This study suggested that COVID-19 could be the very first respiratory outbreak to be food-borne [7]. Following the finding of SARS-CoV-2 on frozen foods, including their packaging materials and storage conditions, food transmission evidence was found in China in early July 2020, with two re-emergent cases connected to contaminated food sources. Some incidences of coronavirus are reported in **Table 1**.

Table 1. Incidences of COVID-19 transmission through food

Country	No. of individuals/ positive cases	Duration	Food type	Reference
China	38	July 2020 – August 2020	Seafood	[8]
Auckland, New Zealand,	4	August 2020	Frozen Food	[9]
Beijing, China	1	June 2020	Frozen salmon	[10]
China	9	July-August 2020	Imported frozen raw foods	[2]
Tiajin, China	3	November 2020	Imported foods	[9]
America	117 crew members	June 2020	Seafood	[11]
Singapore	-	January 2020	Sharing of Food	[12]
Llangefni, UK	204	June 2020	Chicken Factory	[13]
China	6	February-March 2020	Family Dinner	[14]

Patients with latent phase and asymptomatic illnesses may contaminate cold chain food during preparation, packing, handling and shipping in severe COVID-19 areas, catalysing the subsistence of SARS-CoV-2 on frozen foods and their surfaces as shown in **Figure 1**.



Figure 1. Transmission of coronavirus through foods and food packaging

Studies by Chin *et al.*, have highlighted that low temperatures could expand the grit on SARS-CoV-2; thus, frozen and refrigerated foods have been viewed as the potential vectors of the virus [3]. Heparin and heparan, which are important for SARS-CoV-2 viral adhesion onto target tissues, are abundant in meats including seafood, beef and chicken, hinting that viral dissemination by the consumption of meat and animal products is conceivable [15, 16]. In the Xinfadi agricultural produce wholesale market of Beijing, SARS-CoV-2 was detected on a chopping board used to prepare imported salmon on June 12, 2020. This was the most alarming instance [17]. A possibility of SARS-CoV-2 transmission across international borders through cold chain food sources [2] has been speculated due to the ongoing identification of SARS-CoV-2 on imported frozen foods and their packaging materials [10].

Transmission through meat

Covid-19 outbreaks linked to fresh meat and seafood industries in several nations were described by Hu *et al.*, raising worries about SARS-CoV-2 transmission through food. Out of the first 53 persons who tested positive for SARS-CoV-2, 48 had worked, three had gone shopping and two were found connected to the seafood market of Beijing [9]. Vast groups of COVID-19-positive cases, associated with the fish processing industry, were identified in Portugal [18] and linked to slaughterhouses in Germany as well as in Australia. According to some evidence, SARS-CoV-2 can infect pigs and rabbits, suggesting that viral propagation through meat products may be feasible. Evidence also indicated that one way the virus might spread to the public is through consuming food made from infected palm civets [19]. Pangolins, which are used for their meat as well as traditional Chinese medicine, was also mentioned as a possible source of the virus in several articles [20].

Transmission through frozen foods

Apprehension has been sparked worldwide by the discovery of SARS-CoV-2 in frozen aquatic food, animal species or their derivatives, including their packaging materials [2]. Consistent low temperatures during the preservation and shipping of cold-storage foods create favourable conditions that drastically prolong the virus's survival. Adulteration has been discovered in frozen shrimp, salmon, pork, and shellfish, creating a systemic danger of transmission in the current epidemic [18]. Titres of SARS-CoV-2 remained persistent and upheld their infectivity on refrigerated and frozen foods. Han *et al.*, first recognized a novel coronavirus in actual food *s.i.e.* from frozen chicken wings imported from Brazil [2]. So, frozen foods are the conveyors for a wide range of transport of SARS-CoV-2 during the ongoing pandemic.

Transmission through food packaging

An instance of SARS-CoV-2 RNA was reported on the packaging of Ecuadorian shrimp and the interior of a shipping container [2, 21]. SARS-COV-2 has been identified on the surface and in containers of cold chain food items from South America in Dalian, Quindao, and other cities in China since July 2020 [22]. From July to October 2020, Dalian customs identified SARS-COV-2 on the external packaging surface of frozen South American white shrimp from Ecuador and on the imported frozen cod outer package's surface, which indicated that imported frozen food industry could bring in SARS-CoV-2. It was suggested that cases in Qingdao were caused by SARS-CoV-2 contamination of cod outer package during production or cold-chain transportation [22, 23]. Even after long-distance transit, SARS-COV-2 remains viable on the exterior of contaminated frozen food. In the second half of 2020, the spread of the virus through imported cold chain food packaging befell [23-25].

Since cold chain foods are kept at temperatures below -18°C, SARS-COV-2 can persist on the surface of the outer packaging for an extended time and may spread globally. Although structured research is inadequate, and these cases are scarce, it still evoked people to shield themselves against the virus outspread of cold chain food [26]. Food contact surfaces, which often consist of stainless steel, plastic, wood, rubber, ceramics, or glass, include all the areas that come into contact with the food items during preparation (such as cutting boards, tables, cutlery, etc.), production, processing, and packing [15]. These areas might harbour harmful bacteria and viruses that could infect the food as well as the persons handling it.

Through food markets

Grocery stores and supermarkets pose a heightened risk of transmission due to the convergence of various risk factors, such as a confined environment, difficulties in maintaining physical distance, and numerous frequently touched surfaces and products by a variety of users [2]. Within the first half of 2020, the United Food and Commercial Workers stated that 12,405 supermarket workers had been infected among its members.

Transmission through air

Environmental factors can have an impact on viral transmission and persistence in addition to public movement and interpersonal interactions. Factors that contribute to disease spread, such as air pollution, can have an impact on the decisions needed to control epidemics. Airborne pathogens have the potential to spread over vast expanses [27]. The majority of Patients with COVID-19 experienced severe acute respiratory infections, including fever, coughing and breathing difficulties which ultimately resulted in death. Although it is feasible for a virus to disseminate on surfaces, the survival of an aerosolized virus should be investigated. SARS-CoV-2 was still detectable in aerosols after the experiment's three hours were up, but its infectious titre fell from 103.5 to 102.7 TCID50 per litre of air. SARS-CoV-2 had a similar drop in aerosolized plasma concentrations as SARS-CoV-1. In aerosols, both SARS-CoV-2 and SARS-CoV-1 showed similar half-lives [5].

Climatic factors such as air temperature, humidity, wind speed and rainfall are important in SARS-CoV-2 transmission. When investigating how the weather affected the COVID-19 pandemic, several studies found a negative correlation between the speed of the wind, humidity in the air and temperature as weather variables and COVID-19 instances [28-30]. In Chinese cities, there was shown to be a substantial relationship (Poisson regression model) between the air quality index and COVID-19 transmission [31]. Within a range of variable humidity conditions, cases can spread continually and develop quickly [32]. It can be concluded that environmental changes alone will not result in significant reductions in case frequencies unless comprehensive public health actions are implemented. Under experimental conditions, HCoV-19 and SARS-CoV showed identical persistence [5]. HCoV-19 is expected to spread via aerosol and fomites because the virus may survive for several hours in aerosols and many days on surfaces.

Because chronic airway disease brought on by prolonged exposure to air pollution can worsen lung inflammation and increase vulnerability to air pollution, high levels of nitrogen dioxide (NO₂) may raise the COVID-19 fatality rate [33]. The impact of particulate matter and indoor and environmental factors on SARS-CoV-2 transmission was also reported. COVID-19 lethality increased with both short and long-term exposure to PM 2.5; nevertheless, assessment of PM 2.5 incidence is essential for experimental and epidemiological investigations [34]. SARS-CoV-2 was transmitted indoors and outdoors via HVAC (heating, ventilation, and air conditioning) systems [35]. COVID-19 pandemic control can be more effective if this transmission channel is controlled.

Transmission through wastewater

Transmission of SARS-CoV-2 perhaps occurs via droplets and also by aerosols [36] it is proved that the atmospheric environment affects the viral spread. Saliva, sputum and faeces are examples of body excreta that shed live SARS-CoV-2 and viral RNA and are subsequently disposed of in wastewater, as depicted in **Figure 2**.

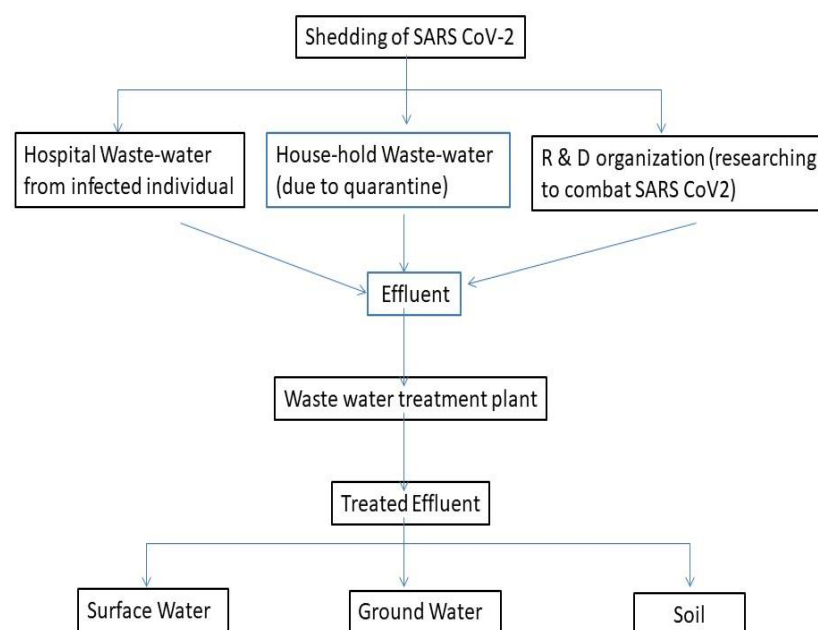


Figure 2. Schematic representation of transmission of coronavirus through wastewater

Due to their low concentrations, inability to spread through human faeces, and ease of inactivation in aquatic conditions, encapsulated viruses in municipal sewage generally pose little risk of infection. Some encapsulated viruses produced from infected human faeces, on the other hand, can live in aquatic settings for days to months [37]. SARS-CoV, for example, can live for more than 17 days at 4°C, 3 and 17 days in faeces and urine at 20°C, and 3 days at 20°C in hospital sewage, municipal wastewaters and chlorine-free potable water [1]. As a result, speculation about SARS-CoV-2 presence in wastewater arose. SARS-CoV-2 RNA has been discovered in influent water from sewage treatment plants around the world, and its concentration rises in proportion to the number of infected people in a given area [38, 39]. A study of COVID-19 biomarkers based on sewage epidemiology could help forecast SARS-CoV-2 infection rates at the community level [40, 41]. Notably, SARS-CoV-2 may be found in wastewater before the first confirmed case is published, demonstrating the sensitivity of wastewater-based epidemiology to detect SARS-CoV-2 [42].

The World Health Organization's most recent public recommendation emphasised the importance of safe human sanitary waste management, including avoiding faecal contamination of hands, preventing aerosolized faecal matter, and managing faecal sludge during pandemics. SARS-CoV-2 is shed as faeces in the environment in low-income countries due to a lack of basic sanitation, contributing to the spread of COVID-19. Only a few investigations have revealed SARS-CoV-2 virus/RNA in sewage/wastewater in developing nations, such as SARS-CoV-2 virus RNA recently reported in Indian municipal wastewater treatment facilities [43, 44]. In India, the genetic material of the coronavirus in sewage grew in a linear relationship with the number of COVID-19 confirmed cases [45]. With inadequate wastewater treatment and disposal practices, sewage-related exposure to SARS-CoV-2 poses a risk to the public's well-being due to its prevalence in developing countries [46].

Excreta of both symptomatic and asymptomatic individuals infected with the virus have shown the presence of SARS-CoV-2 [47]. The virus SARS-CoV-2 was discovered in the urine of patients who had been infected with the virus implying that the infections were induced by the patients' open defecation behaviours [48, 49]. Even in asymptomatic patients, the virus may be present in faeces and can be detected for several days [50]. Coronavirus has been reported in untreated wastewater in developed nations [38, 42] hinting that the virus could be found in wastewater.

Sewage is considered to be one of the most important sources of transmission, areas with a lack of sanitation and wastewater treatment facilities are at greater risk of infection [1, 46]. The coronavirus is considered a potential waterborne pathogen and studies have confirmed that sewage treatment facilities contain SARS-CoV-2 RNA and COVID-19 can be identified in human faeces even after the patient has tested negative for the virus [51]. An economical solution for COVID-19 surveillance in wastewater/sewage is monitoring.

Transmission through paper

Since inviting laboratory studies for patients is mainly done manually and on paper, healthcare personnel such as doctors, chemists, and nurses, as well as medical and laboratory professionals, have a considerable probability of contracting COVID-19. SARS-CoV strain P9 has been reported to persist on a variety of non-living surfaces, including paper, for up to 4-5 days at room temperature [52]. SARS-CoV strain GVU6109 survived for 24 hours on paper at normal temperature, according to Lai *et al.*, [53]. According to studies, SARS-CoV may survive on inanimate objects and paper for 9 days and 1–5 days, respectively; SARS-CoV-2 is predicted to act analogously. Hasan *et al.*, evaluated the risk of Covid-19 transmission through laboratory paper and found that 432 (83%) out of 520 forms for laboratory investigations were obtained in the lab within 24 hours while the remaining 88 (17%) forms took much time. Receptionists, technicians, and pathologists had daily paperwork interaction times of 2.7 minutes, 5.5 minutes, and 54.6 minutes, respectively. The bulk of the paper forms (80%) were dealt with by laboratory recruits in less than 24 hours, posing an elevated risk of viral spread because about 21% of the paper forms emerged in high-risk divisions such as the emergency room, intensive care unit, and quarantine section, while 79 percent originated in moderate-risk departments such as wards, outpatient departments and operating rooms [54].

Therefore, to guarantee the safety of employees and personnel, particularly during such a pandemic, pathology laboratories must build an electronic request-handling system [55]. Hospitals should adhere to the World Health Organization's standard for laboratory safety and good clinical practices to protect personnel from infected documents].

Risk factors

When compared to Ebola, MERS, and H1N1, COVID-19 infection has a first reported reproduction number that ranges from 1.4 to 6.5, with an average of 3.6, indicating that the infection is exceedingly contagious [56]. The virus can survive for prolonged periods of transport and export on frozen surfaces, so processing and packaging of infected foods pose a severe contamination risk to the handlers and the consumers [9]. Because the viral dose required for infection is minimal, the virus survives longer on internationally traded food products. This could lead to the global diffusion of COVID-19 and its reawakening along the cold food supply chain. Thus, frozen foods, meat and poultry processing facilities serve as the locations that may be the potential “hotspots” of COVID-19 [2]. Although food-to-human transmission is less likely than other routes (air, water, and paper), it must not be ignored as a threat concern considering the enormous quantities of chilled foods transported corner to corner across nations and regions, as well as their human contact with a broad consumer base. Even though several countries are rapidly vaccinating against COVID-19, safety precautions must be followed because the virus is evolving.

Alleviation of COVID-19

COVID-19 disease can be mitigated by the below-mentioned strategies which are depicted in **Figure 3**.

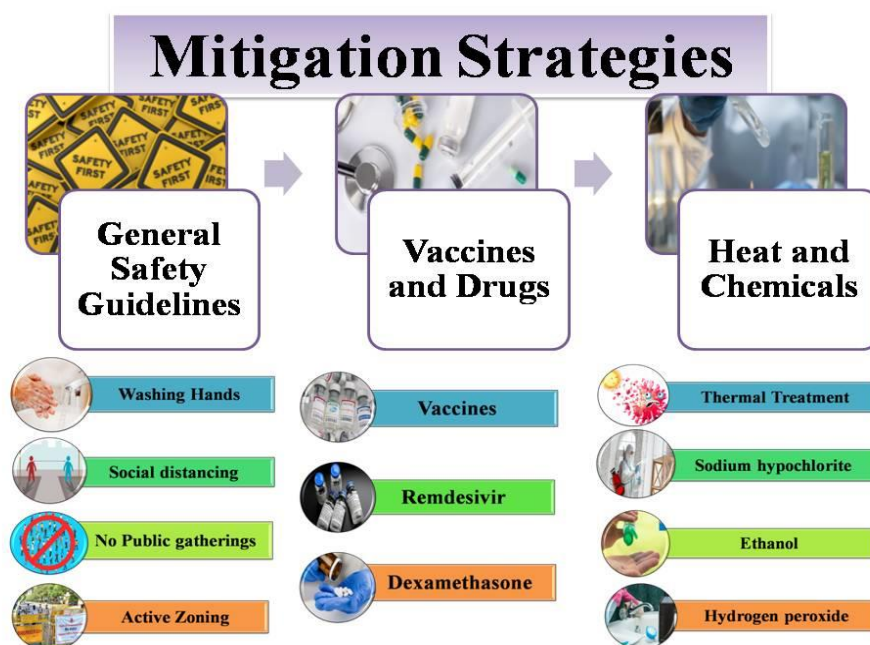


Figure 3. Mitigation strategies to combat COVID-19

By following general safety guidelines

Washing hands for at least 20 seconds, sneezing into the elbow, avoiding touching surfaces, contactless payments, household waste disposal guidelines, preventing waste collectors and waste processing staff from coming into contact with infectious waste, and worker protection are all hygienic practises that can help to mitigate COVID-19 [57]. Mobility restrictions aim to lower the number of individuals who can contract the virus from both symptomatic and non-symptomatic uncontained cases by limiting people's movement to control or impede the spread of the virus [58]. Active zoning, the suspension or reduction of public transportation, temporary or permanent restrictions on air traffic, and limitations on the use of private vehicles and outdoor activities are all examples of mobility restrictions which can be useful against COVID-19. Physical distancing measures are used to prevent social isolation, especially for vulnerable populations like the elderly, as long as there is a sufficient distance (now defined as between 1.5 and 2 m) which includes virtual social ties.

By heat and chemicals

Kampf *et al.*, revealed 5 different types of Coronaviruses suspended in liquid media including SARS-CoV-1 and MERS-CoV, can be reduced by at least four logs via heat treatments such as 60°C for 30 min, 65°C for 15 min or 80°C for 1 min after carrying out analysis of ten different investigations [59]. After heat treatment of 70°C for 5 min, Chin *et al.*, found that SARS-CoV-2 was reduced by about seven logs [3]. Furthermore, the issue of sufficient

heat treatment of food was examined by ANSES and it was concluded that exposure of food to 63°C for 4 minutes would be enough to kill the virus [60]. Since freezing is a technique for preservation, it is conceivable that SARS-CoV-2 might endure freezing in particular media. Studies have demonstrated that after 1 minute of exposure at room temperature, 0.1% sodium hypochlorite, 0.5% hydrogen peroxide, and 62-71% ethanol can considerably diminish coronavirus presence on environmental surfaces [61]; similar effects have been seen with SARS-CoV-2 [3].

Health Canada releases a list of approved hand sanitisers and disinfectants for use against the SARS-CoV-2 virus. The European Chemical Agency (ECA) and the US Environmental Protection Agency (USEPA) have posted lists of coronavirus disinfectants on their websites, titled "COVID-19 List of Disinfectant Active Substances and Products" and "List N: Coronavirus Disinfectants (COVID-19)," respectively. The destruction of CoVs, especially SARS-CoV-2, is made possible by antimicrobial treatments including halogen-based, quaternary ammonium compounds, and oxidants. For the eradication of CoVs, particularly SARS-CoV-2, halogen-based, quaternary ammonium compounds and oxidants are very efficacious [62].

Vaccines and drugs

A SARS-CoV-2 protein mRNA-based vaccine called mRNA-1273 has been created by Moderna and the NIAID vaccine research centre [63]. With the help of self-amplifying mRNA, uridine mRNA, and nucleoside-modified mRNA, BioNTech and Pfizer are developing vaccine candidates [64]. Additionally, IntelliStem (IPT-001 peptide vaccine), Bharat Biotech/FLugen (CoroFlu), Seqiris (MF59), IRBP (RespiResponse IR101C), Dynavax (CpG 1018), Takeda (TAK-888), and Tonix (TAK-888) have vaccines in preclinical testing [65]. Overall, the most promising method of battling the SARS-CoV-2 pandemic is the widespread use of vaccines to create herd immunity.

Nucleotide analogue Remdesivir is a broad-spectrum anti-viral medication that has shown promise in vivo and in vitro efficacy in animal models, predominantly against the viral diseases MERS and SARS [66]. These encouraging findings provide sufficient proof to continue investigating Remdesivir as a viable treatment for SARS-CoV-2. Dexamethasone, an inexpensive drug, is a long-acting corticosteroid that lowers neutrophil migration and inflammatory mediator synthesis. It offers highly ill COVID-19 patients who need oxygen ventilation an effective kind of care.

As of 12 January 2022, the vaccines that have obtained WHO Emergency Use Listing are Pfizer/BioNTech Comirnaty vaccine, SII/COVISHIELD and AstraZeneca/AZD1222 vaccines, Janssen/Ad26.COVID.2.S vaccine made by Johnson & Johnson, Moderna COVID-19 vaccine (mRNA 1273), Sinopharm COVID-19 vaccine, Sinovac-CoronaVac vaccine, Bharat Biotech BBV152 COVAXIN vaccine, Covovax (NVX-CoV2373) vaccine, and Nuvaxovid (NVX-CoV2373) vaccine. Vaccination was a very effective strategy to combat COVID-19.

CONCLUSION

In our extensive review, various pieces of evidence demonstrated the significant risk of SARS-CoV-2 transmission and infection along the entire fresh and frozen animal produces supply chain, from initial breeding, in-between processing to final sales. Although we can say SARS-CoV-2 can be transmitted indirectly through food via the workers involved in food packaging or food marts. It is crucial to thoroughly clean and disinfect all food contact surfaces since touching infected surfaces followed by touching your mouth, nose, or eyes is one of the ways that SARS-CoV-2 can be transmitted. Virus transmission and survival can be influenced by environmental stakeholders in addition to public movements and person-to-person connections, but little information on this novel pathogen is accessible. Despite the unidentified transmission of SARS-CoV-2 through potable water, sewerage lines and ambient air disclosed by available guidelines, the researched data show strong potential for environmental diffusion through these pathways and therefore research on various environmental transmissions should be emphasized. The SARS-CoV-2 can be mitigated by following general safety regulations i.e. use of masks, and sanitisers, cleaning and disinfection of contact surfaces, social distancing etc. Heat treatment and use of chemicals like ethanol (67-71%), sodium hypochlorite (0.1%) and hydrogen peroxide (0.5%) on environmental surfaces can also be used for mitigation of COVID-19 disease along with the vaccination and recommended drugs. We are hopeful that the fourth wave of COVID-19 can be combated through vaccination and the above-mentioned safety precautions.

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