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Article Review

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Indirect exposure to novel coronavirus (SARS-CoV-2): an overview of current knowledge

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HIGHLIGHTS

- People may get infected from contact with surfaces, wastewater and air
- The virus can be transported in the air up to 6 m from the source depending on wind speed

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ABSTRACT

This review chronicles the indirect transmission method which seems to be overlooked by most people and makes attempts to document the various transmission ways with a hope that such information may strengthen the knowledge base of researchers towards methods of eradicating the pandemic. Current knowledge of transmission and exposure of SARS-CoV-2 has been explained. Various researchers have put forward different ways of exposure and transmission. Literature does not reveal whether the indirect transmission route is the dominant one. However, total lockdown could be a veritable means to reduce both direct and indirect transmission routes. In many countries where the indirect transmission has been reduced, the scourge of the virus is less. The work creates awareness on the need to watch out for those routes of transmissions that may not be popular and suggested vital knowledge gaps that need to fill.

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1. INTRODUCTION

The global pandemic of coronavirus disease 2019 (COVID-19) that is ongoing is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and is currently a public health emergency of international concern (WHO, 2020). As of April 21st, 2020, data showed that there are two million, four hundred and ninety thousand, five hundred and sixteen (2,490,516) cases of SARS-CoV-2 infection in 215 countries with the death of one hundred and seventy thousand, five hundred and ninety (170,590) (death rate 6.8 %).[1] This trend is on the continuous increase daily as more cases are being recorded, despite the global efforts to stop the outbreak. This, therefore, is responsible for the global lockdown or movement restriction and thus the global economy is being affected.[2] Other efforts to stop the spread involve encouraging proper hygiene which includes, hand washing, social distancing and other personal hygiene directives such as avoid face touching especially the eyes, nose and mouth.[3]

Generally, three possible transmission routes of COVID-19 by the patient to people have been identified including symptomatic, pre-symptomatic and asymptomatic transmission. By way of definition, a symptomatic COVID-19 case is a case that has developed signs and symptoms compatible with COVID-19 virus infection. The pre-symptomatic transmission occurs during the incubation period (5-14 days) for COVID-19, i.e. between the infected time to time when symptoms begin to manifest while the asymptomatic transmission is an infected person without showing any symptoms but transmits the virus to another person. However, to date, there are no reports of asymptomatic transmission, but few documents of laboratory-confirmed cases exist (WHO, 2020). The reported symptoms of COVID-19 patients include cough, fever, difficulty in breathing and diarrhoea. SARS-CoV-2 ribonucleic acid (RNA) has been detected in faeces of not only symptomatic but also asymptomatic patients and on surfaces, in aerosols and wastewater.[4,5,6,7,8,9,10] In other to document clearly the various ways of transmission and exposure for this new virus, we as a result of this present an overview on the current knowledge on the sources of the exposure of human to COVID-19. This will provide an overall quick, concise yet precise reference material with both scholars and public office holders for public enlightenment and could assist policymakers in formulating policies that would help reduce the spread of this virus.

2. REVIEW METHOD

Materials such as preprint servers, statistical bulletins, blogs, journals articles and conference/workshop/seminar papers that were published online were used for sourcing information. In other to maintain our idea of current information, we focused on publications within March and April 2020. All searches were restricted to articles from articles written in English and focused mainly on SARS-CoV-2, and few other articles searched with the following keyword "coronaviruses", "microplastics" "nano plastics" and "airborne particulates". Information not backed by empirical data was avoided, and interviews were completely left out. Overall, 5 preprint (not peer-reviewed) papers included were Zhang et al.,(2020)[5]; Wu et al., (2020)[11]; Santarpia et al., (2020)[12]; Enyoh et al., (2020)[3] and Dipak et al., (2020)[13].

3. RESULTS AND DISCUSSION

Indirect exposure routes to SARS-CoV-2

Preventing the transmission in the family settings, public and healthcare systems is of importance to prevent any further spread of the virus. Two possible routes of exposure include the direct or indirect transmission of the virus from an infected person to an uninfected person or a new host.

Direct exposure: Direct exposure is one of the major routes of transmission of coronavirus from person-to-person. This has been described both in hospitals where medical personnel contact the diseases from patient or healthy person contacting the disease from an infected medical personnel. In this case, it could be said to be a nosocomial infection. Another typical direct exposure route involves family settings.[14] Here, a member of the family transmits the virus to one or other members of the same family.

Indirect exposure: Indirect viral transmission involves an uninfected person coming in contact either by hand or with a contaminated surface. Transmission of coronaviruses from contaminated dry has been demonstrated and reviewed.[15] Another indirect route could be from inhaling contaminated air or ingesting, swallowing, and/or breathing in untreated wastewater spray or mist. The schematic below emphasizes the indirect exposure routes to SARS-CoV-2 based on current information are presented in Figure 1.

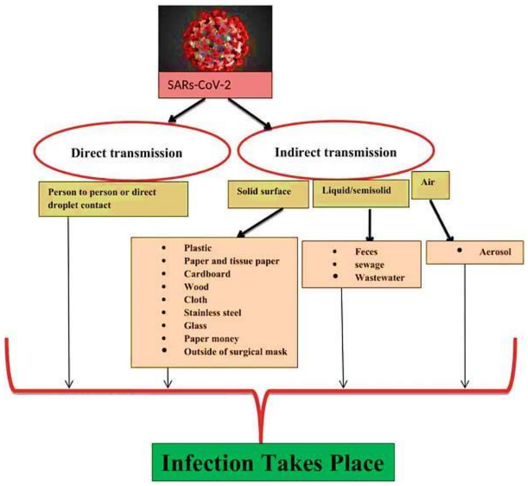

Figure 1. Overview of plausible exposure pathway to SARS-CoV-2 based on current information

Solid surfaces/fomites

This route is based on contact transmission when viral particles emitted from the respiratory tract of an infected individual are deposited on a solid surface such as plastic, paper and tissue paper, cardboard, wood, cloth, stainless steel, glass, paper money and outside of surgical masks. Then the virus can infect another person when the person comes in contact with the contaminated surface by hand and then touches their nose, mouth or eyes, then sneaks into the body via the mucous membranes. The survival and stability of SARS-CoV-2 on surfaces has been shown in some reports, in both laboratory and natural settings. These studies are summarized in Table 1. Viral particles found on surfaces such as toilets, and frequently touched surfaces at the University of Nebraska Medical Center.[12] Similarly, on March 26th, the CDC (Center for Disease Control) published a report on the coronavirus-stricken Diamond Princess Cruise ship in which they found traces of RNA from SARS-CoV-2 on surfaces throughout the cruise ship, in the cabins of both symptomatic and asymptomatic infected passengers, up to 17 days later.[16]

In hospital settings, there will be high risks of infection by contact with surfaces especially in low and middle-income countries (LMICs) with inadequate health care systems[13], where patient's documentation is mostly done using paper-based records. Most of the hospitals in LMICs are using paper to keep patient records, owing to poor funding and lack of proper databases. Each record file is exchanged many times between health care workers, patient caretakers as well as various administrative people in the hospital. These paper files and records also it travels to different wards or rooms for various purposes along with patients during medical check-up and treatment. The virus could be transmitted during this process. At present, very little is known regarding the surface distribution of SARS-CoV-2 in hospitals of LMICs which rely on paper documentation of patients. However, this pathway of infection may also occur in public places. In other studies, it was indicated that surfaces in general hospital wards and intensive care units are infectious, of which the highest rates were for computer mice, followed by trash cans, sickbed handrails and doorknobs.[17,18] The further study revealed that sleeve cuffs and gloves of medical staff presented significant positive results for the virus.[19] Due to these findings, encouraged proper hygiene such as proper handwashing or sanitizing be practised by medical staff immediately after patient contact.[17]

Table 1. Persistence of novel coronavirus on surfaces at different conditions

Surface	Strain/ isolate	Inoculum (Viral Titer in $TCID_{50}$ per mL)	Temperature (ºC)	RH (%)	Persistence	Reference
Plastics	SARS-CoV-2 nCoV-WA1-2020 (MN985325.1)	$10^{5.25}$	21 to 23	40	≤ 3 days	Neeltje et al., 2020
	N/A	$10^{7.8}$	22	65	4 days	Chin et. al., 2020
Paper and tissue paper	SARS-CoV-2 nCoV-WA1-2020 (MN985325.1)	$10^{5.25}$	21 to 23	40	3 hours	Neeltje et. al., 2020
	N/A	$10^{7.8}$	22	65	< 1 hour	Chin et al., 2020
Cardboard	SARS-CoV-2 nCoV-WA1-2020 (MN985325.1)	$10^{5.25}$	21 to 23	40	24 hours	Neeltje et al., 2020
Copper	SARS-CoV-2 nCoV-WA1-2020 (MN985325.1)	$10^{5.25}$	21 to 23	40	≤ 3 days	Neeltje et al., 2020
Stainless steel	N/A	$10^{7.8}$	22	65	4 days	Chin et al., 2020
	SARS-CoV-2 nCoV-WA1-2020 (MN985325.1)	$10^{5.25}$	21 to 23	40	4 hours	Neeltje et al., 2020
Wood	N/A	N/A	N/A	N/A	4 days	WebMD Medical Reference (2020)[a]
	N/A	$10^{7.8}$	22	65	< 2 days	Chin et al., 2020
Ceramics	N/A	N/A	N/A	N/A	≤ 5 days	WebMD Medical Reference (2020)[a]
Aluminium					2 ≤ 8 hours	
Glass	N/A	N/A	N/A	N/A	≤ 5 days	WebMD Medical Reference (2020)[a]
	N/A	$10^{7.8}$	22	65	2 days	Chin et al., 2020

Metal	N/A	N/A	N/A	N/A	≤ 5 days	WebMD Medical Reference (2020)[a]
Cloth	N/A	$10^{7.8}$	22	65	< 2 days	Chin et al., 2020
Banknote	N/A	$10^{7.8}$	22	65	2 days	Chin et al., 2020
Masks	N/A	$10^{7.8}$	22	65	4 days (inner layer) and 7 days (outside layer)	Chin et al., 2020

RH: Relative Humidity; N/A: Not available. A peer-reviewed medical web, but did not make the used references visible.

Liquid and/or semisolid

Feces/stool

According to the World Health Organization[20], a significant proportion (16 – 73%) of patients with SARS tend to have diarrhoea in addition to respiratory symptoms. As one of the symptoms of COVID-19 is diarrhoea, the patient tends to excrete faeces/stool often. Recent reports show that SARS-CoV-2 has been detected in stool samples of COVID-19 patients[21,22,14,8,23,24] and for more than nine days after the patients recovered.[4]

The shedding of SARS-CoV-2 was studied in a cluster of 9 cases and was 10000000 RNA copies/g faeces one week after symptom onset and decreased to 1000 RNA copies/g three weeks after symptom onset.[10] In another study, reported up to 1000000 viral particles per mL in a single faecal sample.[5] Although these studies did not evaluate the replication in culture, they, revealed the likelihood of infection through contact with contaminated stool or faeces, even though, there are currently no reports of infection through this process. Further, because the virus is detectable in the faeces just like the previous coronaviruses.[25] Therefore aerosolization of the virus in contaminated faeces during toilet flushing was believed to be the mode of transmission of this outbreak similar to the previous coronaviruses.[26]

Wastewater

By adopting a wastewater - based epidemiology (WBE) approach, the prevalence of viruses in a particular wastewater treatment plant (WWTP) catchment population was understood by researchers because wastewater contains viruses excreted from symptomatic and asymptomatic individuals in a catchment.[27,6] The WBE approach is essential in predicting and providing early warning for a potential outbreak of disease. Therefore, informing the efficacy of public health interventions, as previously demonstrated for enteric viruses, such as norovirus, hepatitis A virus, and poliovirus.[28,29] The viruses mentioned above are, however, not enveloped like SARS-CoV-2 virus and may not behave exactly alike in wastewater. Recent studies have shown that SARS-CoV-2 is present in untreated wastewater suggesting a potential, significant source or route of infection to the people of most community.[22] The presence of SARS-CoV-2 in untreated wastewater is linked to the stool of an infected person passed into the sewer system. In stool samples with high RNA copies, viable SARS-CoV-2 was detected.[21] Although it is unlikely that wastewater will become a critical transmission pathway for SARS-CoV-2, increasing the circulation of the virus in the population will increase the virus load into the sewer systems of our cities.[30]

The N_Sarbeco and NIID_2019-nCOV_N assays were used by Ahmed in their study to detect SARS-CoV-2, and subsequently sequencing the RT-qPCR (quantitative reverse transcription-polymerase chain reaction) products recorded to avoid false results due to wastewater being a complex matrix.[6] Results showed that 22.2 % (2 out of 9) of wastewater samples analyzed were positive for SARS-CoV-2 using the N_Sarbeco assay while NIID_2019-nCOV_N assay failed to detect. Prevalence in the wastewater based on excreted human faeces was estimated according to Eq. (1). Results suggest a median SARS-CoV-2 infection of 0.096 %

in the catchment basin during the study period. By implication, the clinical prevalence would be equivalent to 450 cases in the catchment, but the upper bound of the 95 % confidence interval around the median would suggest up to 764 total cases to 314 undiagnosed cases or roughly seven undiagnosed infections for every ten diagnosed infections.

$$Infected\ person = \frac{\left({}^{RNA\ copies}/_{Wws\ (L)}\right) * \left({}^{Wwt\ (L)}/_{day}\right)}{\left({}^{g\ feces}/_{person-day}\right) * \left({}^{RNA\ copies}/_{faeces}\right)} \quad (1)$$

Note: Wws = wastewater sample in liters; Wwt = total wastewater collected per day in liters.

By use of PEG 8000 (polyethylene glycol) concentration method, Wu et al., (2020) were able to recover SARS-CoV-2 successfully from wastewater. Following a 24h flow-dependent composite sample, the authors assayed using CDC N1, N2, and N3 primers with a virus concentration of ~ 10 to 240 Copies 40 mL^{-1}, ~ 40 to 140 Copies 40 mL^{-1} and ~ 10 to 160 Copies 40 mL^{-1}. The prevalence rate was estimated to range from 0.000001 to 0.000035 %. Similarly, Medema (2020) followed a 24h flow-dependent composite sampling technique in collecting tested sewage samples of 7 cities in the Netherland.[30] With the use of RT-PCR against three fragments of the nucleocapsid protein gene (N_{1-3}) and one fragment of the envelope protein gene (E), the samples were analyzed. No SARS-CoV-2 detected in samples with N_2 throughout the study period while others had a detection rate of 58.3, 33.3 and 20.8% respectively. The prevalence rate was estimated to range from 0.000001 to 0.000035% (Table 2).

Overall, the information provided by these studies shows that not only there is a risk to sewage workers, but also the circulating SARS-CoV-2 in the communities can be monitored through sewage surveillance. They were thereby complementing the limited current clinical surveillance done in many world countries (e.g. mostly low and middle-income countries), where tests are mainly done when there are severe symptoms. Furthermore, it could be used as an early warning tool for increased circulation in the rainy period on unaffected populations. However, there is no evidence to date that SARS-CoV-2 has been transmitted via sewerage systems, with or without wastewater treatment. We, therefore, recommend that future wastewater sampling efforts and analysis adhere to already established safety procedures to curb the potential spread.

Air

The transmission of SARS-CoV-2 in the air is aided by aerosols as people emit aerosol particles when talking, and that louder speech volumes correlate to more aerosol particles being emitted. The transportation of aerosols is largely depended on environmental factors such as airflow and direction, humidity, ambient temperature, wind speed and gravity as well as landscape and densities of buildings.[31,32,33,34] Recent studies have demonstrated this scenario of SARS-CoV-2 surviving in aerosols.[35,17] Neeltje (2020) used the SARS-CoV-2 nCoV-WA1-2020 (MN985325.1) strain in their study and compared the stability in aerosols (< 5 µm).[35] Using a three-jet nebulizer, the aerosol was filled with viruses with 50% tissue-culture infectious dose; $TCID_{50}$ mL^{-1} of $10^{5.25}$. The decay rate was determined to measure stability at different environmental conditions such as temperature (21 to 23 ^{o}C) and relative humidity of 40 %. Results showed that SARS-CoV-2 was stable and remained throughout the period of study (three hours). In a hospital setting, Zhen-Dong (2020) collected air samples in intensive care units (12 air supplies and 16 air discharges hour $^{-1}$) and general wards (8 air supplies and 12 air discharges hour^{-1}).[17] Results from the study showed that 35 % and 12.5 % of the air samples were contaminated respectively, indicating that the virus can travel in the air. Overall, the aerosol mainly concentrated downstream up to 13 feet from the source while smaller quantities were found up to 8 feet upstream with the maximum transmission of ~ 4 meters from the source. However, there are limitations to the study.[17] First, the results of the nucleic acid test do not indicate the amount of viable virus. Second, for the unknown minimal infectious dose, the aerosol transmission distance cannot be strictly determined. Although we have warning signs, there is still a lack of evidence of transmission via aerosols as the minimal viral load is unknown. These studies (Neeltje, 2020 and Zhen-Dong**,** 2020) did not fully mimic real-life outdoor scenario considering many other environmental factors.[35,17]

Following this need for a deeper understanding of the fluid and particles transport emanating from our respiratory tracts from coughing, sneezing, speaking, or breathing, Dbouk and Dimitris (2020) using an advanced three-dimensional model was able to study the phenomenon.[36] The applied model which is based on fully coupled Eulerian-Lagrangian techniques taking the flowing factors into account including droplet phase-change, relative humidity, evaporation, turbulent dispersion forces, and breakup in addition to the interactions of droplet–droplet and droplet–air. Results from their study showed that saliva-disease-carrier droplets from a mild human cough at the temperature of 20°C, relative humidity of 50% and at wind speeds which vary from 4 to 15 km/h could travel up to 6 meters (farther than the current recommended 2 meters distance between people). However, at a wind speed of 0 km/h, the droplets could not travel 2 meters (current recommended distance between people).

Reviewed studies have confirmed that SARS-CoV-2 aerosol exposure poses significant risks. Therefore, there is a need for more studies on indoor and outdoor environments where many environmental factors are in play such as the presence of airborne microplastics and other particulates in the ambient environment that may aid in the transmission of the virus over longer distances (> 4 m). While indoor activities are ongoing, whether in the hospital or household setting, large volume/quantity of small size plastics (microplastics or nano plastics) are often generated and deposited (could be as high as > 11, 000 particles day^{-1} m_2^{-1}) on ground surfaces.[33]

Virus emitted from a patient can drop on the surface of these particles and can be accommodated up to 3 days if the room isn't cleaned properly. During the period of accommodation, the particles can be re-suspended in the air with dust particles when there is a disruption of indoor air, thereby putting inhabitant at risks of infection when these plastic particles (with the virus) are inhaled. Following a simulated study, MPs particles as much as 272 particles can be inhaled by inhaling indoor air.[37] In the outdoor environment, the process is similar except that the virus may potentially be transported with particles over long distances depending on the wind events, relative humidity, ambient temperature and anthropogenic activities as well as particle shape, size and length.[3]

4. CONCLUSION

SARS-CoV-2 can be transmitted indirectly through contact with solid surfaces or fomites, liquid or semisolids, including wastewater and faeces as well as through air (aerosol). Although reports have not shown any case transmitted through these pathways, the likelihood is high as suggested by available data. The survival and stability of SARS-CoV-2 on surfaces is largely depended on environmental factor such as relative humidity, temperature and pH as well as the surface morphology. Smooth surfaces will increase the chances of survival by becoming more stable. Wastewater Based Epidemiology (WBE) may be an effective tool in monitoring outbreaks of this virus, and there is a need to treat wastewater before disposing of in the environment. The primer-probe used in wastewater studies included N_Sarbeco, E_Sarbeco, NIID_2019-nCOV_N, and CDC (N_{1-3}) of which CDC N_2 and NIID_2019-nCOV_N have poor detection rate. The virus can be transported in the air up to 4 m from the source (at current, in the confined environment) and human saliva-disease-carrier droplets may travel up to 6 m, depending on the wind speed. Therefore there is a need to review or re-evaluate the current guideline of generally keeping 2 m distance between people (both in confined and open places) as recommended by WHO.

Further studies should focus on the contribution of airborne plastic particles such as MPs and NPs on the survival and transport of the virus in the air over long distances. Studies should also be conducted on the survival of the virus food produce as previous coronaviruses have been shown to survive on lettuce at low temperature. Studies should also be conducted on the survival of the virus in drinking water as previous coronaviruses have been shown to survive. As people died from COVID-19, they are buried in the soil. So, the potential impact on groundwater should be studied. These studies would inform on the extent of risks of exposure and damage this unwanted virus would cause to the public and ecosystems health.

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Table 2. Available data on the detection of SARS-CoV-2 in wastewater samples

Location	Sampling date	Sampling technique	Assay used	Detection rate (%)	Virus concentration ([a]Copies/100 mL [b]Copies/40 mL)	Prevalence rate (%)	References
Southeast Queensland, Australia	24/02/20 to 01/04/20	Composite grab sample and autosampler (conventional refrigerated and/or submersible in-situ high-frequency autosampler)	N_Sarbeco NIID_2019-nCOV_N	22.2 0	Approx. 1.90 to 12.0[a] ND	0.096 N/A	Ahmed et. al., 2020
Massachusetts, USA	18/03/20 to 25/03/20	24h flow-dependent composite sample	CDC N_1	N/A	Approx. 10 to 240[b]	0.026	Wu et. al., 2020
			CDC N_2	N/A	Approx. 40 to 140[b]	0.026	
			CDC N_3	N/A	Approx. 10 to 160[b]	0.026	
7 locations in Netherlands	5/02/20 to 5/03/20	24h flow-dependent composite sample	CDC N_1 CDC N_2 CDC N_3 E_Sarbeco	58.3 0 33.3 20.8	N/A N/A N/A N/A	0.000001 N/A 0.000035 0.000035	Medema et al., 2020

*Primer probe were CDC N_1, N_2, N_3 = nucleocapsid protein gene (N_{1-3}) (USA); Sarbeco N = envelope protein gene (N) and E = envelope protein gene (E); NIID_2019-nCOV_N (Japan)
*N/A = Not available; ND = No data