Detection and disinfection of COVID-19 virus in wastewater

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Abstract
The coronavirus disease 2019, COVID-19, caused by the severe acute respiratory syndrome coronavirus 2, SARS-CoV-2, appears as a major pandemic having adverse impact on public health and economic activities. Since viral replication in human enterocytes results in its faecal shedding, wastewater surveillance is an ideal, non-invasive, cost-effective and an early warning epidemiological approach to detect the genetic material of SARS-CoV-2. Here, we review techniques for the detection of SARS-CoV-2 in municipal wastewater, and disinfectants used to control viral spread. For detection, concentration of ribonucleic acid involves ultrafiltration, ultracentrifugation and polyethylene glycol precipitation. Identification is done by reverse transcriptase amplification, nucleic acid sequence-based amplification, helicase dependent amplification, loop-mediated isothermal amplification, recombinase polymerase amplification, high throughput screening and biosensor assays. Disinfectants include ultraviolet radiations, ozone, chlorine dioxide, hypochlorites and hydrogen peroxide. Wastewater surveillance data indicates viral presence within longer detection window, and provides transmission dynamics earlier than classical methods. This is particularly relevant for pre-symptomatic and asymptomatic COVID-19 cases.

Keywords COVID-19 · Pandemic · SARS-CoV-2 · Wastewater surveillance · Wastewater treatment plants · Disinfection

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Abbreviations
ATP Adenosine triphosphate
CPE Cytopathic effect
DNA Deoxyribonucleic acid
dPCR Digital polymerase chain reaction
HTS High throughput sequencing
LAMP Loop-mediated isothermal amplification
NASBA Nucleic acid sequence-based amplification
PCR Polymerase chain reaction
POC Point-of-care
qPCR Quantitative polymerase chain reaction
qRT-PCR Real-time quantitative polymerase chain reaction
RNA Ribonucleic acid
RPA Recombinase polymerase amplification
RT-qPCR Reverse transcriptase quantitative polymerase chain reaction
SARS-CoV-2 Severe acute respiratory syndrome coronavirus
Introduction

In December 2019, China declared an emergence of an acute form of pneumonia outbreak in Wuhan, Hubei Province, to World Health Organization and its association with novel coronavirus SARS-COV-2 was conclusively established soon thereafter through shotgun metagenomic sequencing of bronchoalveolar lavage samples (Zhu et al. 2020). Since its first reported case in late 2020, the COVID-19 global pandemic has now been confirmed in 222 countries and territories with 101,406,059 confirmed cases and 2,191,898 confirmed deaths as per official data available on World Health Organization website on January 30, 2021 (WHO 2021).

Whilst countries around the world are now progressively starting to reopen and restart after imposing extensive lockdown, the COVID-19 pandemic is still catastrophic and yet to be resolved (Ng et al. 2020; WHO 2021; Chen et al. 2021). World Health Organization along with various international and national health agencies are continuously working synergistically to explore the ways to detect, diagnose, prevent, contain and treat the highly infectious COVID-19 cases at community level. Worldwide, medical researchers and epidemiologists are still finding and exploring new ways to scrutinize, prevent and treat the disease (Dai et al. 2020; He et al. 2021). One of the new ways of analysing the coronavirus is through monitoring the municipal wastewater (Gostin et al. 2020; Lahrich et al. 2020). The viable SARS-CoV-2 and its ribonucleic acid released through human faeces, saliva and sputum eventually find ways in wastewater (Bar Or et al. 2020; Sun and Han 2020). In March 2020, in the Netherlands, scientists found the presence of SARS-COV-2 ribonucleic acid in the sewage samples collected from premises of Schiphol airport, Amsterdam (Medema et al. 2020a). The results came within a week after the first case of COVID-19 was confirmed in the country. These findings opened newer opportunity of utilizing water-based epidemiology (or wastewater surveillance) to determine the spread, persistence and detection of SARS-COV-2 in communities where clinical diagnostic testing is not widely accessible. Water-based epidemiology is an efficient approach to analyse water samples to identify and isolate the microorganisms for public health monitoring (Larsen and Wigginton 2020; Sims and Kasprzyk-Hordern 2020). The water-based approach is not new, as this has been previously used to detect the presence of viruses and bacteria (Kataki et al. 2020).

SARS-COV-2 ribonucleic acid sooner or later ends up in the municipal sewage system, and consequently, wastewater surveillance offers several advantages in comparison with clinical testing of COVID-19 patients as this approach is cost-effective, noninvasive and efficient in providing larger population-wide data (Fig. 1). A study from China revealed the detection of a strain of coronavirus from human faeces samples before the onset of symptoms,
thus indicating the advantage of an early detection (Chan et al. 2020). Further, Yale University researchers showed that monitoring coronavirus strain in sewage water could envisage COVID-19 outbreaks 6–7 days before person testing and 2–3 days before hospital admissions (Peccia et al. 2020). It concludes that water-based approaches are a promising indicator to identify hot spots in the local areas or in a community. Consequently, water-based epidemiology can serve as a cheap, early caution to recognize new pandemic, parameters in current outbreaks and frequency of infections (Rothan and Byrareddy 2020). Numerous research and commercial laboratories have now gained precious knowledge in monitoring water samples for analysis of the virus (Prem et al. 2020).

Environmental scientists are continuously developing effective tools and equipment which can measure and monitor the activities related to the status of health of the entire population over the last 20 years. Nowadays, water-based approaches are beginning to apply for the monitoring of SARS-COV-2 to enumerate the community (Nemudryi et al. 2020). Here, we review technologies available for detection and differentiation of SARS-COV-2 in wastewater samples. Various factors configuring the transmission, survival and infection potential along with their fundamental mechanism is also discussed. The analyses and findings are hence forth represented in this review under various sections and subsections. Current research works on the detection of SARS-COV-2 in wastewater using sensing techniques along with future perspectives are suggested.

**Persistence and detection of COVID-19 virus in wastewater**

Contemporary data on SARS-COV-2 and numerous viruses evince that wastewater-based epidemiology is a pragmatic way to assess and palliate viral outbreaks (Randazzo et al. 2020b). Elementary and viable approaches are accessible for the concentration of wastewater samples in order to detect the virus. Conversely, the process controls are recommended as depicted in Fig. 2. The extensively used

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Fig. 2 Techniques available for the reliable and rapid detection of severe acute respiratory syndrome coronavirus or SARS-CoV-2 virus in municipal wastewater. Reverse transcriptase quantitative polymerase chain reaction remains the widely used method of COVID-19 virus detection. In addition, immunological assays, viral cultivation in animal cell cultures, transmission electron microscopy and biosensor-based portable devices are also available. Next-generation high-throughput sequencing is also considered a method of choice for larger sample analyses.
real-time quantitative polymerase chain reaction test allows rapid nucleic acid detection provided the probe and primer selection is accurate and optimized. Regardless of the fact that infectivity state of the specific virus is not appropriate for epidemiological monitoring, the SARS-CoV-2 survival within sewage throughout the treatment process requires a complete analysis to evaluate the health risks. Specific and nonspecific sequencing of sewage viruses probably facilitates tracking the outbreak of target variants and detects mutations that may affect viral identification in a clinical framework. To evaluate viral endurance, culturing-based approaches and integrity assays are practised. Amplicon, as well as complete genome sequencing, is exorbitant and laborious, yet having the potential to detect emerging viral strains/species, thus being beneficial for early detection of epidemiological viruses.

Technologies available for COVID-19 virus detection and identification

Wastewater concentration method

For sensitive identification of viral strains in municipal wastewater, samples are concentrated prior to quantification. Manifold approaches are prevalently exploited (Bofill-Mas and Rusiñol 2020). Monitoring SARS-CoV-2 entails centrifugation and filtration of wastewater samples in order to obliterate debris and subsequently electronegative membrane filtration (Ahmed et al. 2020), ultrafiltration or polyethylene glycol precipitation (Balboa et al. 2020), aluminium flocculation/ultra-centrifugation (Randazzo et al. 2020b) allowing and facilitating 20 ×–800 × concentration (Wurtzer et al. 2020). Sludge sample is treated by ribonucleic acid extraction explicitly (Peccia et al. 2020) or initiated by virus elution followed by polyethylene glycol precipitation from the matrix (Zhang et al. 2020). Most of the concentration approaches are cost-effective and less arduous howbeit with high sample possessing high turbidity; these techniques emerge as intricate and laborious. The major snag of such approaches is co-concentration of superfluous organic compound, viz. humic substance, impeding the downstream process of virus detection. Withal, concentration efficacy varies among various samples albeit it has been determined in two investigations only intended to identify SARS-CoV-2 within wastewater (Randazzo et al. 2020a) demonstrating 3–50% of viral retrieval (Table 1). In order to evaluate concentration efficiency, the amount of viral indicator scilicet, gut-associated phages must be collated between processed and unprocessed sample (Medema et al. 2020b).

Viral nucleic acid-based methods

Several technologies have been reported and implemented for the detection and differentiation of viral nucleic acids in wastewater and sewage. These methods include the following.

Quantitative polymerase chain reaction-based techniques

Polymerase chain reaction technique aims to target the specific genes of the virus and offers an effective, convenient and reliable solution for wide-scale environmental studies. The conventional approach for monitoring viruses is real-time/quantitative polymerase chain reaction predominantly combined with reverse transcription phase to enumerate ribonucleic acid targets. Polymerase chain reaction performed on a microfluidic platform reduces the time and expenditure of the assay. Microfluidic–based quantitative polymerase chain reaction detects manifold viruses from water samples. Although it utilizes low amount sample and exiguous amplification reaction mixes with increased detection efficiency, as exemplification 150 copies/μl (Woelfel et al. 2020), yet it not considered to be standard for most environmental samples.

The prominent technique for quantification of the virus is digital reverse transcriptase polymerase chain reaction where reaction mixes are disseminated within thousand to million separate wells placed on-chip/H2O–oil droplets and further quantification is computed based on + or – signals. Digital reverse transcriptase polymerase chain reaction is a rapid and extremely sensitive technique facilitating the strain-level identification of nearly one to ten genome copies in approximately 1 to 4 h. This method is more advantageous over quantitative polymerase chain reaction due to executing absolute quantification, without the requirement of any standards. Comparative analysis manifests that digital polymerase chain reaction is highly sensitive and is seldom affected by any sort of inhibitors rather than quantitative polymerase chain reaction techniques (Jahne et al. 2020). Howbeit, digital quantitative polymerase chain reaction features a narrower range of quantification compared to its quantitative counterpart (Qiu et al. 2020); therefore, sample bearing high viral concentration, viz. wastewater samples, must be diluted prior conducting digital reverse transcriptase polymerase chain reaction. Probe-based quantitative polymerase chain reaction using TaqMan, a target-specific probe, is multiplexed, allowing the parallel identification of two to four targets within single well (Ahmed et al. 2020). This might prove propitious for concurrent quantification of the animal as well as a human for tracking the source. Commercially available multiplex quantitative polymerase chain reaction testing is used to detect viral pathogens excretes (Hirvonen 2019). A duplex assay in which digital reverse transcriptase
polymerase chain reaction is multiplexed, allowing detection of the virus in clinical trials (Yurick et al. 2019). The disadvantages associated with digital reverse transcriptase polymerase chain reaction method include exorbitant cost, long turnaround time and unavailability for remote settings which in turn limit the extensive use of the aforementioned techniques in environmental investigations and routine monitoring.

Isothermal amplification

Isothermal amplification techniques including helicase-dependent amplification, loop-mediated isothermal amplification, recombinase polymerase amplification and nucleic acid sequence-based amplification possess the ability to determine the low concentration of desired deoxyribonucleic acid and/or ribonucleic acid within 15–60 min at 37 °C to 65 °C. These approaches can detect pathogens within environmental samples (Zhang et al. 2020). In loop-mediated isothermal amplification, three sets of primers are used, thus allowing the formation of loop sequence and addition in primer binding sites, through each of the amplification. Thus, loop-mediated isothermal amplification is considered vastly specific and generates significantly more amplicons compared to polymerase chain reaction with less time period and excluding thermal cycler. This technique can further be multiplexed via implementing reverse transcriptase step for detecting ribonucleic acid targets (Zhang et al. 2018). Moreover, loop-mediated isothermal amplification has minimum sensitivity towards inhibitors rather than polymerase chain reaction (Huang et al. 2018). Considering its inherent convenience, reliability and preciseness,
the loop-mediated isothermal amplification approach can be performed in the assessment of virus in wastewater and sewage collected in municipal wastewater treatment plants. Nucleic acid sequence-based amplification and recombinase polymerase amplification operate with a combination of enzymes in order to promptly amplify multiple nucleic acid targets. Unlike other amplification techniques, nucleic acid sequence-based amplification directly amplifies from the target sequence, thereby not demanding reverse transcription step. Conversely, the complexity of recombinase polymerase amplification and nucleic acid sequence-based amplification render them susceptible to slowing down compared to other techniques (Rames and Macdonald 2019). It has been proposed that due to the ability of nucleic acid sequence-based amplification, it can be implemented for environmental viral load detection (Hønsvall and Robertson 2017). However, the challenges in producing reliable results and the high cost of nucleic acid sequence-based amplification limit its wider applications as a regular method for detection of virus in environment samples (Walker et al. 2017).

High-throughput sequencing

High-throughput sequencing can be utilized to identify nucleic acids of several viral pathogens from freshwater, wastewater and sewage samples. Therefore, high-throughput sequencing has the potential to detect emergent viruses and related pathogens in environment water bodies (Adriaenssens et al. 2018). To recover the whole genome of noncultured viruses from metagenomics data generates genotype-level detection and assists the quantitative polymerase chain reaction assays for better scale surveying (Huang et al. 2019). High-throughput sequencing for target amplicon sequencing produces finer resolution geographical distribution (Young et al. 2020) as well as diversity (Hata et al. 2018). However, quantitative polymerase chain reaction and high-throughput sequencing at times yield conflicting indication on the occurrence of target viruses whilst data processing provides chimeric sequences and artefacts. Long-read sequencing facilitates to overcome such limitations, despite that it yields nearly 15% error rate (Rang et al. 2018). However, some disadvantages of high-throughput sequencing approach, i.e. high cost, complex setup, need for expertise and voluminous computational analysis, limit its application in routine analysis of wastewater.

Assessment of viral infectivity

The nucleic acid detection systems do not provide any reliable information about the virulence of the pathogens. Culturing human-associated viruses entails particular equipment, for example, CO₂ incubator and inverted microscope. It also requires finely maintained cell lines, yet not often exploited in regular viral monitoring (Pang et al. 2019). In contrast, the existing approaches, for instance, the cytopathic effect for examining cell lysis induced by the morbific virus, take weeks. However, the aforementioned approach has the potential to determine the viral infectivity, which is crucial for wastewater treatment. Researchers are endeavouring to simplify and promote viral culturing methods (Farkas et al. 2020a). Integrated cell culture along with reverse transcription quantitative polymerase chain reaction reduces the time needed for culturing. It provides results of virus detection within 1–4 days, where the concentration of nucleic acid elevates because of viral propagation which can further be accurately examined via reverse transcriptase quantitative polymerase chain reaction. Lately, such available techniques are being implemented for identifying enteric viruses in environmental water bodies (Sedji et al. 2018). Further, time periods of the aforementioned assays can be curtailed up to hours via virus identification done during the initial stage of cell attachment (Zou et al. 2020). Reverse transcriptase quantitative polymerase chain reaction has an advantage where only a single cell line is used for procreation of various viral strains, allowing the estimation of diverse targets within water sample different (Pang et al. 2019). In viral culturing, the main focus is expressed on the proliferation of human norovirus. From the time 2016, three techniques have been established, exploiting zebrafish embryos (Van Dycke et al. 2019), human B cells (Jones et al. 1939), intestinal epithelial cells (Sato et al. 2019) and human stem cell-extracted enteroids (Etayebi et al. 2016). The aftermath of these approaches exhibits augments in genome copies in 2 to 4 days. But, implementing these methods for environmental sample analysis has not been conducted.

Assessment of viral structural integrity

By virtue of several drawbacks encountered in ribonucleic acid and deoxyribo nucleic acid and culturing-based virus detecting assays, the uncomplicated and cost-effective assays have been established for estimating the integrity of virus in terms of morbific particle intact with it.

Obliteration of free viral nucleic acids

Elimination of free ribonucleic acid and deoxyribonucleic acid is done via enzymatic treatment DNase/RNase, by which nonencapsidated viral ribonucleic acid and deoxyribonucleic acid deteriorate, prior polymerase chain reaction assay for quantification. Enzymatic assays manifest moderate elimination of free ribonucleic acid and deoxyribonucleic acid (Leblanc et al. 2019). Oftenly, DNase/RNase enzymatic assay is coupled with proteinase K processing that deteriorates the capsid proteins, allowing nucleases to approach ribonucleic acid and deoxyribonucleic acid.
from noninfective viral particles. Howbeit, proteinase K action causes impairment to morbid viral particles; also, ergo must be processed with caution (Langlet et al. 2018). Another discrete method to annihilate free ribonucleic acid and deoxyribonucleic acid is viability treatment, where intercalating dyes are used. These dyes are capable of penetrating viral capsids and on the exposure of lights samples covalently bind to ribonucleic acid and deoxyribonucleic acid molecules, thereby precluding polymerase amplification (Leifels et al. 2019). The most extensively used dyes are ethidium monoazide and propidium monoazide. In other viability treatment, the binding substances used are cis-dichlorodiammineplatinum and platinum chloride and do not require light exposure to bind with ribonucleic acid and deoxyribonucleic acid. The aforementioned substances happened to be tested chlorinated/inactivated viral samples (Canh et al. 2019). The outcomes of these treatments evince that most ribonucleic acid and deoxyribonucleic acid molecules are eliminated, barring variations among various samples and viral strains (Monteiro and Santos 2018). Propidium monoazide treatment can be advanced via adding surfactants (Randazzo et al. 2018) or can be coupled with ethidium monoazide (Canh et al. 2019). These assays are propitious as not being strain-specific, therefore allowing multiple target analysis in a single sample.

Capsid functional integrity assay

In this test method, the affinity binding occurs between viral capsid and proteins. Due to high variation exhibited by capsid protein, one assay is applicable for few species/strains only but must belong to the same family. The latest investigations emphasize capsid integrity concerning noroviruses, specifically genotype II, estimated via histo-blood group antigens such as porcine gastric mucin. For these proteins, immobilization is done on magnetic beads/plate wells (Tian et al. 2018). Binding of virus particles with proteins after sample addition followed by washing steps assists in the elimination of viral ribonucleic acid as well as inhibitors that may hinder polymerase chain reaction-based identification. This method is simpler rapid and convenient; it can be practised in nearly all laboratories. Yet it seems ineffective for norovirus genotype I compared to genotype II (Farkas et al. 2020).

Biosensors

Biosensors convert biological responses into quantifiable signals subsequent to the association with a specific target (Shen et al. 2019). Biosensors based on aptamer referred as aptasensors contain single-stranded ribonucleic acid or deoxyribonucleic acid oligonucleotides, having the potential to attach target deoxyribonucleic acid/proteins, possessing high affinity and specificity moreover producing quantifiable signals upon binding. Aptasensors based on colorimetric, electrochemical, fluorescence and surface plasmon resonance detection platforms are established for norovirus identification (Weerathunge et al. 2019) and may prove favourable for viral identification in aquatic samples. Aptamers usually can outlast environmental inhibitors, allowing more recoveries and higher detection within minutes (Schilling et al. 2018). Few aptamers have the ability for multiple detections in various norovirus strains (Shen et al. 2019). As the need for rapid diagnosis of COVID-19 cases is escalating, point-of-care or POC biosensors gained tremendous environmental (Kalyani et al. 2020) and diagnostic importance (Choi 2020). Both chip-based and paper-based biosensors are useful for the detection of SARS-CoV-2 owing to their low cost, high sensitivity, portability, ease of handling, amenability miniaturization and multiplexing, and quick result outcomes (Choi 2020; Parihar et al. 2020). In the present demanding situation for COVID-19, research focus is oriented towards development of optical, electrochemical, microfluidics and paper-based biosensors for reliable and sensitive diagnosis of SARS-CoV-2 infection, especially in emerging COVID-19 hot spots (Parihar et al. 2020).

Electronic biosensors

Field-effect transistors, amperometric and 3 electrodepotentiometric systems are fundamental electronic biosensors extensively applicable in the identification of biological molecules and causative agents. The chief advantage of aforesaid biosensors is compactness, cost-effective and abundant manufacturing. Field-effect transistors are effortlessly designed in complementary metal oxide semiconductor setups (Syu et al. 2018), albeit manifold portable electrochemical biosensors are available for sale in markets (Stoian et al. 2020). Earlier numerous electrochemical biosensors were established for viral pandemics. Researchers designed single microfluidic electrochemical biosensor for identification of H7N9, H1V1 and H5N1, amalgamated with zinc oxide nanorods (Han et al. 2016; Jyoti and Tomar 2017), and amplification approaches were utilized for sensitive diagnosis of H1N1 via electrochemical biosensors (Li et al. 2012), electrochemical identification of Middle-East respiratory syndrome virus employing carbon electrodes (Layqah and Eissa 2019), screening of severe acute respiratory syndrome virus (Ishikawa et al. 2009) and various other proceedings exploiting disposable screen-printed electrodes as well as paper-based substrates to detect diverse viruses (Malecka et al. 2016). Few investigations foster to develop procedures for early identification of COVID-19 outbreak. Researchers notified a field-effect transistor biosensor for identifying SARS-CoV-2 in clinical samples (Seo et al. 2020). These sensors are made of graphene sheets coated on transistors.
containing an antibody specific to SARS-CoV-2 spike protein. These biosensors have the potential to detect SARS-CoV-2 spike protein at 11 fg/ml concentration in buffer solvents formulated in the laboratory as well as 100 fg/ml of biological samples. This is an epitome of how biosensors are used for detection of viral strains at minimal concentration and devoid of sample pretreatment/labelling.

Microfluidic biosensor

Microfluidics method is meticulous and manipulates microscale fluids (Reboud et al. 2019). The elementary operating units, viz. detection, extraction, preparation and reaction, concerning many processes are amalgamated on the microchip. These microfluid channels, detectors, pumps, sensors and valves are fabricated on polymer, silicon or metal via micromachining approach. Previously, microfluidics has been implemented using numerous analytical technologies such as mass spectrometry, electrochemical analysis, chemiluminescence and fluorescence analysis (Zhang et al. 2019). Microfluidic setup is categorized into electrokinetic, capillary, centrifugal, pressure-driven and acoustic systems based on liquid propulsion standards (Nasseri et al. 2018). Over the years, microfluidic biosensors were employed to detect infectious diseases within the medical sector. For instance, acoustic wave biosensors bearing horizontal surface were acknowledged for multiple identifications of anti-gp 41 and anti-p 24 antibodies associated with human immunodeficiency virus (Gray et al. 2018). Microfluidic biosensors have the potential to discern human immunodeficiency virus biomarkers in 5 min using a little amount of sample (6 μl of plasma), thereby being a cost-effective and rapid diagnostic tool. Another microfluidic bio-sensor based on silicon nanowire was established to identify reverse transcriptase quantitative polymerase chain reaction derivatives associated with Dengue serotype 2 (Zhang et al. 2010). During COVID-19 pandemic, prompt diagnostic tools/approaches are of tremendous significance for timely detection of SARS-CoV-2, leading to adequate treatment. Microfluidic biosensors have many advantages over rudimentary methods, viz. a culture-based and molecular approach. The aforesaid method is economical, rapid, precise, portable, highly reproducible, consumption of less sample/reagent and high-throughput processing (Nasseri et al. 2018).

Wastewater biosensors

Wastewater-based epidemiology is an analytical method employed to divulge discernments about public health via examining contents of desired regions sewage. Wastewater-based epidemiology is a significant tool to trace the dissemination of viruses in the public sector, thereby endowing with opportunities to assess its prevalence, diversity and distribution (Ahmed et al. 2020). The technique entails chemical analyses of samples collected from sewage plants. This technique enables us to get insights, to obtain effective information about human health, pathogens, diseases, illicit and licit drugs (Mao et al. 2020). Human viruses including salivirus, enteroviruses, rotaviruses, astroviruses and noroviruses have been identified in water and wastewater via wastewater-based epidemiology, suggesting their presence to be an efficacious approach for early detection of the viral outbreak through consistent monitoring of the diversity as well as the concentration of pathogens in wastewater (O’Bannon 2020). Scientists are trying to explore wastewater-based epidemiology to precisely monitor the outbreak of COVID-19 from sewage. SARS-CoV-2 has been detected in faecal samples of positive cases across various countries such as China (Chen et al. 2020), Germany (Woelfel et al. 2020), Korea (Kim et al. 2019), USA (Holshue et al. 2020) and Singapore (Young et al. 2020), thereby increasing viral load within wastewater of infected area. Consequently, wastewater-based epidemiology can be employed as an early detecting tool for the prevalence of COVID-19 onset, whilst providing an accurate estimation of the spread of pandemic (Corman et al. 2020). Researchers are carrying out a study to implement wastewater-based epidemiology technique to deal with an ongoing pandemic (Verma and Rani 2020). Biomedical and chemistry are being integrated in order to fabricate wastewater-based epidemiology as rapid and effective means to monitor the spread of SARS-CoV-2 (Mao et al. 2020; Sharma et al. 2020).

Optical biosensors

Numerous optical biosensors predominantly based on the concept of plasmonics (Qiu et al. 2020) basically where the transduction standards exploit optical constituents including, lasers (Ma et al. 2019), waveguides (Rodriguez et al. 2019), photonic crystals (Rodriguez et al. 2019) and fibre optics (Socorro-Leránoz et al. 2019) are categorized as optical sensors. Optical biosensors, for example, surface plasmon sensors, comprising localized surface plasmon resonance are accessible for commercial sale since the 1990s. It is used to identify viral strains, mostly the one that is associated with H1N1 (Kamikawa et al. 2012), influenza (Takemura et al. 2017), severe acute respiratory syndrome (Seo et al. 2020) and Middle East respiratory syndrome (Layqah and Eissa 2019). Various plasmonic approaches possessing sophisticated surface chemistry render high sensitivity, rapid response for detection of pathogen and selectivity. The challenge in operating this technique remains enormous size and expenditure of instrumentation required for fabricating plasmonic systems. Yet these sensors have accuracy in detecting viruses during a pandemic. Researchers established a biosensor for precise detection and analyses of SARS-CoV-2.
cases employing a plasmonic photothermal effect, and localized surface plasmon resonance is assembled as transduction standards (Qiu et al. 2020). Primarily, the deoxyribonucleic acid receptors are utilized to identify desired sequences obtained from SARS-CoV-2 via nucleic acid hybridization. Using nanoparticles and illumination in localized surface plasmon resonance sensing a prominent thermoplasmonic frequency is generated. Researchers claim to improve the in situ hybridization temperature by implementing thermoplasmonic heat that can facilitate the meticulous perception of similar gene sequences. Optical biosensors can perform remarkably in high-resolution imaging of viral strains during pandemic conditions.

**Disinfection methods against SARS-CoV-2 in wastewater**

Disinfection of wastewater having COVID-19 viruses is as important as disinfection of healthcare facilities, medical instrumentation public transport and other public use amenities for containing the spread of COVID-19 (Crini and Lichtfouse 2019; Li et al. 2020; Wang et al. 2020; Choi et al. 2021). The various methods applicable for wastewater treatment specific to COVID-19 virus are mentioned in Fig. 3 and described below:

**Ultraviolet radiations**

Ultraviolet radiations having wavelengths ranging from 200 to 400 nm have been extensively employed to disinfect drinking water as early as in 1910 (Leifels et al. 2019). Ultraviolet radiations can be segregated into four wave bands on the basis of distinct wavelengths, comprising ultraviolet A (315 to 400 nm), ultraviolet B (280 to 315 nm), ultraviolet C (200 to 280 nm) and vacuum ultraviolet (100 to 200 nm). Therein, vacuum ultraviolet cannot be implemented for disinfection, as it gets absorbed by wastewaters. Wavelength ranging between 200 and 300 nm deteriorates the genetic materials of microorganisms, including bacteria and viruses, thereby preventing protein synthesis. Ultraviolet B and Ultraviolet C can be utilized for disinfection of wastewaters due to excellent bactericidal effect. It is usually considered that the wavelength of 253.7 nm is optimum for ultraviolet disinfection. In contrast to chlorine disinfection, the ultraviolet disinfection is meant to be significantly more economical. Howbeit, intermittently ultraviolet C is regarded unsatisfactory due to inadequate depth of penetration and includes some health risks as well. The possibility
for eradicating micropollutants from wastewater is ultra-
 violet light or hydrogen peroxide as an advanced oxidation
 process (Shu et al. 2016). Lately, the Gold Bar Wastewater
 Treatment Plant implemented this approach in Edmonton,
 Canada, to remediate secondary sewage (Cuerda-Correa
 et al. 2019). Thereafter, this method has gained enough
 attention, due to the presence of hydroxyl radical, which is
 extremely reactive to impair intractable compounds present
 in wastewater (Chollom et al. 2020). Advanced oxidation
 processes including ultrasonic process, Fenton processes
 photo-catalysis, ozone combined with ultraviolet/catalysts/
 hydrogen peroxide or both ultraviolet and hydrogen peroxide
 have been efficiently used to treat wastewater.

 **Chlorine-based disinfectants**

 Disinfection approaches liberating free available chlorine
 such as hypochlorous acid and hypochlorite ion persist as
 the most effective way to address viral contamination (Lee
 et al. 2018). Most eminent sources of free available chlo-
 rine are sodium hypochlorite, calcium hypochlorite chlo-
 ride dioxide, elemental chlorine, chloroisocyanurates and
 chloramines. Hypochlorite being a powerful oxidizing agent
 is potent for oxidizing organic pollutants; however, undis-
 sociated hypochlorous acid is predominantly the microbi-
 cidal agent. Inactivation of chlorine is caused by various
 factors including oxidation of sulfhydryl enzyme and amino
 acids, reduced nutrient uptake, ring chlorination of amino
 acids, reduced oxygen uptake, loss of intracellular contents,
 inhibited protein synthesis, reduced oxidation of respira-
 tory products, downregulation of deoxyribonucleic acid
 synthesis, decreased adenosine triphosphate production and
 deoxyribonucleic acid fragmentation (Leifels et al. 2019).
 Research has affirmed the efficacy of chlorine upon viruses;
 howbeit, viruses exhibit more tolerance towards chlorine
 disinfectants relatively than bacteria, and it might be due
 to the virus attribute, which is lack of metabolic enzyme
 system. Conventionally, 30–50 mg/l and 15–25 mg/l of
 chlorine are supplemented to wastewater subsequent to pri-
 mary and secondary treatment of wastewater (Zhang et al.
 2020). Earlier findings emphasized that free chlorine residue
 ranging between 0.2 and 0.5 mg/l for municipal wastewater
 is adequate to disinfect severe acute respiratory syndrome
 virus promptly (Lu et al. 2013), pH is a decisive factor in
 inactivation of viruses, at low pH, the inactivation rate is
 more compared to high pH. The pH is a modulating fac-
 tor that determines the dissociation of hypochlorous acid
 to lesser microbicidal form hypochlorite ion (Zhang et al.
 2020). The primary concern in efficacious chlorination is
 pH, the demand for chlorine and the presence of ammonia.

 **Hypochlorites**

 Aqueous solutions of 5.25% to 6.15% sodium hypochlorite
 are most commonly used chlorine disinfectant. Hypochlo-
 rite is considered to be a more effective virus disinfectant
 compared to chlorine dioxide against SARS-CoV (Zhang
 et al. 2020). It was observed that the chlorine solution deliv-
 ered through hypochlorite in the concentration of > 10 mg/l
 could entirely inactivate the SARS-CoV after a contact
 time of 30 min. Studies reported the absolute inactivation
 of SARS-CoV when incubated at 0.05% hypochlorite solu-
 tion in less than 1 min of time. However, it is regarded as a
 broad-spectrum microbicidal disinfectant, whilst at high pH
 hypochlorite ion acts as a slower virus disinfectant. It can be
 used on a small scale as a virus disinfectant due to its mod-
 erately low residual toxicity, robust activity, easy handling,
 cost-effective and stable performance.

 **Chlorine dioxide**

 Chlorine dioxide disinfectant is more convenient than chlo-
 rine. It is exemplary for virus inactivation and is considered
 an alternative for chlorine (Lee et al. 2018). Chlorine dioxide
 is adsorbed in proteins (capsomeres) of viruses, where it
 reacts with ribonucleic acid. Previously, the effectiveness
 of chlorine dioxide was explored against coxsackievirus
 B5, bacteriophage f2, human rotavirus, poliovirus l, simian
 rotavirus and echovirus 1. Chlorine dioxide was potent at a
 wider range of pH, dosing at 1.0 mg/L. Chlorine dioxide has
 more efficacy than chlorine and ozone towards few viruses.
 Howbeit, for SARS-CoV, it shows less effectiveness than
 chlorine (Zhang et al. 2020). Chlorine dioxide can inactivate
 SARS-CoV adequately after 30 min of exposure time and
 at the dose of 40 mg/L. Also, inactivation of murine coro-
 navirus was successful soon after the exposure to chlorine
dioxide gas at the dosage of 0.16 ppm/min (Kim et al. 2016).

 **Hydrogen peroxide**

 In numerous organic treatment techniques, hydrogen perox-
 ide is supplemented as a wellspring of dissolved oxygen in
 pretreatment of high-quality wastewater where biotreatment
 may not be pragmatic and in predigestion of wastewaters
 containing inconsistent levels of toxic substances. The syn-
 thetic liquid disinfectant may be preferably utilized because
 of easy handling, expeditious start-up; however, utilization
 of hydrogen peroxide for full-scale wastewater treatment
 is paltry (McDonnell 2014). It is safe, more advantageous
 oxidizing alternative commonly accessible at the concentra-
 tion of 3% which is powerful at combating against micro-
 scopic organisms including yeast, bacteria, spores, fungi
 and viruses. Hydrogen peroxide excessively damages the
 viral genetic material, lipids and other cell components, as
the virus is devoid of repair mechanism and thus cannot escape this damage generated by OH− radicals of hydrogen peroxide. Exposure of hydrogen peroxide vapour in the concentration of 20 µl to a coronavirus surrogate for nearly 2 to 3 h on stainless steel consequently reduces the virus load (Goyal et al. 2014). Hydrogen peroxide is regarded risk-free as it produces water and oxygen during dissolution, thereby being a nonpollutant.

Ozone

Ozone is a reliable, clean oxidizing agent with powerful microbicidal impact against viruses, bacteria and protozoan (Tizaoui 2020). Ozone is successful in obliterating viruses by destroying the viral protein. Microorganisms get inactivated via ozone as it reacts with the cytoplasmic membrane, thereby breaking lipid components at various bond sites (Mecha and Chollom 2020; Zucker et al. 2021). Additionally, during ozone contact with a virus, it yields capsid proteins, protein hydroperoxides and protein hydroxides, generating oxidative stress, for which the virus is incapable of combat. Lately, none of the reports is available on ozone disinfection for wastewater against SARS-CoV-2, despite that it is envisaged to be effective against viruses, as ozonation manifests positive results in disinfecting SARS-CoV-1 (Martínez-Sánchez et al. 2020). The current analysis recommends exploitation of ozone as powerful oxidant against SARS-CoV-2, where it distorts the proteins and lipids of the viral membrane (spike and envelope), specifically tryptophan, oleic acid, methionine cysteine, linoleic acid and arachidonic acid and N-glycopeptides of the spike protein. Viruses display better tolerance mechanism to ozone compared to bacteria. Ozone is a substantial disinfectant which can enhance biological water quality in less time and concentration at higher efficacy.

Effect of environmental factors on transmission, survival and infectivity

Temperature and humidity

Seasonal change, a ubiquitous attribute, is associated with several acute infections, and predominantly with viral respiratory ailments (Martínez 2018). For example, influenza recurrence transpires every winter within the temperate realm. An epidemiological paradigm in the USA manifested that absolute humidity influenced the influenza prevalence (Shaman et al. 2010). Furthermore, an outbreak of severe acute respiratory syndrome (SARS) in China during November 2002, entirely abated by July 2003 (Ma et al. 2020). Case study investigations in Beijing, Hong Kong, Taiyuan and Guangzhou evinced that the severe acute respiratory syndrome virus outbreak was notably associated with temperature variations (Xie and Zhu 2020). Epidemiological data and emerging laboratories indicate that diverse environmental conditions may influence the ongoing COVID-19 pandemic (Brassey et al. 2020). A promulgated laboratory analysis stated that SARS-CoV-2 is significantly stable at 4° C, however, susceptible to high temperature. The survival time of virus declined to 5 min when subjected to higher incubation temperature (70° C). Epidemiological investigations suggest an association between SARS-CoV-2 and environmental parameters, yet the outcome of studies is controversial (Yao et al. 2020). About 1° C increase in mean temperature (~3° C) raised the daily cases of COVID-19 by 4.861% (Xie and Zhu 2020). A study reported the positive relationship between everyday deaths from COVID-19 and daytime temperature, and a negative relation with relative humidity (Ma et al. 2020). Howbeit, another study stated no association between COVID-19 cases and transmission with temperature in china (Yao et al. 2020). Another finding exhibited that humidity and temperature are inversely correlated with COVID-19 (everyday, fresh cases and deaths). Increase in temperature by 1° C lowered the daily new cases by 3.08% whilst as deaths also declined by 1.19%, whereas 1% increase in humidity reduced daily new cases by 0.85% and deaths declined by 0.51%, the aforementioned analysis was done by 196 countries (Wu et al. 2020). Global transmission of SARS-CoV-2 is very rapid; therefore, the impact of meteorological parameters towards the spread of SARS-CoV-2 must be examined in order to predict the progression in combating COVID-19, whilst several other factors may influence the advancement of COVID-19 pandemic.

Bioaerosols

Direct/indirect mode of contact entails the vulnerable individual to touch each other physically, viz. hands contaminated with the virus. Direct mode signifies person-to-person contact spreads the virus between the carrier and susceptible individual scilicet, handshake, whereas, indirect mode indicates transmission through fomite, for instance, virus-contaminated handrail, tissue paper, etcetera. Contrastingly, airborne transmission transpires via distinct modes and demands no physical contact between the individual (infected and susceptible). In comparison, sneezing/coughing virus-laden droplet with the size of 5 µm in diameter scatters and targets susceptible hosts. A vulnerable individual inhales evaporated respiratory microscopic bioaerosols, and these tiny droplets (<5 µm) remain airborne up to hours (Asadi et al. 2020). Airborne-associated disease investigations prior to COVID-19 pandemic emphasized violent expiratory incidents, viz. sneeze/cough (Lindsley et al. 2013). Numerous infected persons transmitting
SARS-CoV-2 have mild symptoms or are nonsymptomatic. Various researches reported the transmission of the virus from asymptomatic individuals who tested positive for COVID-19 (Rothe et al. 2020). Asymptomatic carriers usually do not sneeze/cough to some considerable extent, denoting mode of transmission via bioaerosols (Zou et al. 2020). Research executed during the SARS epidemic in 2003 demonstrates that hospitalized individuals infected with SARS release viable virus (aerosols) into the environment (Booth et al. 2005). Reportedly that epidemic was induced by SARS-CoV-1, which is closely associated to the ongoing pandemic (SARS-CoV-2). Both these viruses are not identical. However, research carried out by van Doremalen et al. (2020) revealed that aerosolized SARS-CoV-2 retained in the air for hours and inferred that transmission via fomite and bioaerosols is plausible, as SARS-CoV-2 remains viable in aerosols and various surfaces for hours to several days.

**Major challenges**

Sample handling and processing are the critical issues in detection of SARS-CoV-2 which occurs at a low concentration in wastewater and sewage. Several primary data indicate that ribonucleic acid-based polymerase chain reaction test and single-step reverse transcriptase droplet digital polymerase chain reaction can elucidate virus quantification. Such approaches possess significant specificity as well as sensitivity, yet they are laborious, require skilled personnel and take a long time for data processing and analysis. Engrossingly, paper analytical apparatus has appeared as a suitable platform for the cost-effective detection of ribonucleic acid sequences of viral strains. The whole process can be executed via simple folding of paper-based apparatus in different ways devoid of any power supply or supplementary tools; therefore, several time-consuming drawbacks of polymerase chain reaction assays are subdued. This approach was effectively implemented in the determination of malaria parasites from blood samples (Reboud et al. 2019). Also, still there exist many challenges, including the requirement of establishing systemic and reliable quantification protocol for viruses, the availability of inadequate data for executing a quantitative assessment for SARS-CoV-2 exposure pathways ascertaining the half-life of viable SARS-CoV-2 within sewage and setting up a sampling protocol and schedule which would serve as representative of the population. Moreover, the amount of virus shed with faeces by an individual is obscure. Additionally, due to limited global resources, the surveillance of SARS-CoV-2 should be cautiously investigated prior to application as per location facilities and involvement of other measurements.

Scientific research has made remarkable progress towards use of biosensors in SARS-CoV-2 detection, and the consequential challenge persists in surpassing the complications associated with translating pragmatic data promptly into commercially feasible prototypes via industries, thereby addressing intricate regulatory matter obligatory for the clinical setting, particularly during pandemic situations. Howbeit, another notable challenge lingers in technology shift of most biosensors and sophisticated instrumentation. Hands-on expertise from subjects which are radically opposite, including biology and electronics, is often required for operating sensing instruments. The technical drawback is being the adoption of biosensor processing protocols, accuracy and reliability of sensors. Rudimentary science and engineering require the discovery of novel materials which must be physically, chemically and intrinsically stable and pioneer techniques and methods to render more reliability in measurements. There are significant ethical concerns also revolving around these technologies; for instance, ownership, privacy and data confidentiality are highly challenging to tackle in a brief period, resulting in less adoption of technology by society. Howbeit, it is contemplated that early SARS-CoV-2 detection in sewage would signify a noninvasive warning to aware communities towards SARS-CoV-2 contagion (Orive et al. 2020).

**Conclusion**

COVID-19 global pandemic has emerged as most challenging global health crisis ever faced humanity. Its nearly uncontrollable transmission in human population across international borders despite aggressive curbing measures has surprised the health agencies and administrative authorities and projected a never expected risk of overloading and subsequent collapse of public health systems. Encouragingly, the affected countries are quick enough to implement control measures at community, public health, transport and economic levels to flatten the curve of the COVID-19 pandemic. SARS-COV-2 is an increasing health risks among human population worldwide, and it is imperative to control the spread of the disease in the present time. Since only limited vaccines and antiviral agents are available, only meticulous preventive measures and implementation can bring some significant triumph in this matter of concern. Presently, we are only equipped with isolation and quarantine measures being employed throughout most of the world and hence an urgent need is realized to reduce direct and indirect contact (through contaminated object or surface) or close contact with an infected person to flatten the curve of the pandemic. The very imperative thing is about the testing process, the number of tests done regularly, the rate of positivity and whether this number of positive cases stays steady or erratic. Currently, clearcut and straightforward methods are available for the detection of the virus in the
wastewater samples. However, the use of parameters (for instance, spiking the sample with an animal virus with a structure similar to the target pathogen before concentration) is highly recommended. The most widely used reverse transcriptase polymerase chain reaction techniques provide quick viral ribonucleic acid quantification, but, the primers and probes should be selected cautiously.

To conclude, considering the paramount challenges and threats to human health and survival due to SARS-CoV-2 pandemic, there is an urgent need for research collaborations, data sharing and synergistic vaccine development efforts at war scale. At the same time, emphasis towards development of availability of rapid, cost-effective, sensitive, portable and early diagnostic tools is equally essential. Detection of SARS-CoV-2 from wastewater and sewage in municipal wastewater treatment plants can accelerate the COVID-19 diagnosis at mass scale even before clinical diagnostic testing can reach every single person. Therefore, continuous monitoring of COVID-19 threat in sewage and wastewater along with environmental monitoring of public places and development of better suited disinfection methods will hold promise to control the spread and threat of COVID-19 global pandemic. It can be safely concluded that the technology advancements in the areas of viral detection and disinfection will facilitate better preparedness of scientific community and healthcare organization to tackle possible future biological threats and viral pandemics.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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