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Review

Surveillance of omicron variants through wastewater epidemiology: Latest developments in environmental monitoring of pandemic

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HIGHLIGHTS

• Environmental concerns of highly mutated SARS-CoV-2 B.1.1.529 are described.
• Wastewater surveillance can serve as an early warning system.
• Robust sample strategies with successive fast detection approaches are discussed.
• Various benefits of SARS-CoV-2 B.1.1.529 surveillance are presented.
• Opportunity and major challenges for epidemiology are provided.

ABSTRACT

WBE has been a monitoring system that can give purposeful and inclusive real-time assessments of civic society as well as environmental health. This concept review introduces WBE as a surveillance scheme and initial warning outbreaks of contagious diseases caused by harmful SARS-CoV-2 with pandemic potential. Examining biomarkers of contagious diseases as evidence in polluted water taken from wastewater treatment plants suggests that these systems can be examined to get epidemiological data for checking the transmission of infectious B.1.1.529 to different areas. Thereafter, various benefits of surveillance are provided to analyse health information and pinpoint different problems that may be occurring in the workstaton. Surveillance is followed by intervention steps that improved the work environment and prevent further progression of the disease. This information will help to improve early detection strategies, designing a prevention strategy to reduce their spread, infection control and therapies, thus, strengthening our global preparedness to fight future epidemics. In the end, a comprehensive discussion on the remaining challenges and opportunities for epidemiology has been given for future research perspectives.

Keywords:
Human health risks
Infectious disease
Virus
COVID-19
SARS-CoV-2 B.1.1.529
Variant of concern
Transmission
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1. Omicron variants: next phase of pandemic

The whole world is exhausted by the pandemic and is still worried about the extensive negative social, economic, and psychological effects of COVID-19 (Soni et al., 2022; Sun et al., 2022). Following Alpha (α), Beta (β), Gamma (γ), and Delta (δ) another novel variant of severe acute respiratory syndrome-Corona Virus-2 (SARS-CoV-2) was identified in South Africa and globally announced as Omicron i.e., Pango lineage; B.1.1.529. SARS-CoV-2 has disturbed the whole world’s budget, limited free movement, affected people in trillions, and placed too much burden on the medical workers exhausted, physically as well as emotionally vulnerable (Ma et al., 2022; Rosato et al., 2022). Phylogenetic tree analysis strongly demonstrated that among all known variants of concern, the highly mutated B.1.1.529 was not present on an intermediate evolutionary branch as shown in Fig. 1, indicating that it may have not evolved in a human host (Sun et al., 2022). When compared to other known variants, the B.1.1.529 variant has a distinctive mutation profile containing mutations that are rare in clinical samples. It is the 5th mutation of SARS-CoV-2 reported on 24.11.2021 that multiples approximately 75 times quicker than the δ variant in the lungs bronchi (Behl et al., 2022). The highly mutated B.1.1.529 variant belongs to a variant of concern that has fifty nonsynonymous mutations, eight synonymous mutations, and two non-coating mutations (Nasiri and Dimitrova, 2022). Transmutations in the B.1.1.529 receptor-binding domain region of S protein are mainly associated with the enhanced transmission, and immune evasion thus has potential consequences for the current pandemic. Severely reduced neutralization of B.1.1.529 variant by the antibodies caused three times more reinfection than the previously discovered α, β, γ, and δ variant. B.1.1.529 variant enters the cells of the host via the interactions of its spike like “S protein” with the entry receptor angiotsensin-converting enzyme-2 of host (Hirose et al., 2022). The shift in the target site infection from the lower respiratory to the upper respiratory and its high environmental stability might be potential factors for its unwarranted spread. According to Chinese scientists in vitro research analysis, mutations at N440K, T478K, and N501Y sites are responsible for its higher infectivity i.e., 2 times than “8” and 10 times higher than another initial SARS-CoV-2 variant. The research findings suggested that the highly mutated B.1.1.529 variant evades our immunity more rapidly in comparison to other discovered variants. The entrance, survival as well as the transmissance of B.1.1.529 variant in sewage and the threat of pollution of water reservoirs are much significant in developing countries like India.

A multi-layered strategy is thus required to be implemented mainly when immune escape and possible vaccine failure are posing a significant concern. Based on clinical data trends and the emergence of this variant as a variant of concern, researchers are using the WBE approach to determine the presence of B.1.1.529 variant in wastewater samples. Till date, very few reports on detection of B.1.1.529 genomic in sewage have been studied and it is observed that insufficient treatment of wastewater in developing countries can lead to the subsequent spreading of viruses to the water bodies. In this present article, we review the unwarranted spread, survival, and chance of contagion by the B.1.1.529 variant in contaminated water and the potential of wastewater surveillance. This review paper aims to share the early successful detection and monitoring of the B.1.1.529 in wastewater and will present the latest methodology and approaches for detecting the B.1.1.529 variant in wastewater samples as part of WBE. Various roles of WBE in pandemics have emphasized that are having great potential for initial cautionary of highly contagious SARS-CoV-2 spread. For better understanding, we compared the B.1.1.529 variant to understand its similarities and differences with other discovered SARS-CoV-2 variants of concern. Several transmutations in SARS-CoV-2 B.1.1.529 lead to enhanced transmissibility as well as immune evasion. In densely populated developing countries like India, there is a great challenge to stop harmful viruses such as SARS-CoV-2 from entering and ensuring complete removal from the water cycle. To tackle the growing SARS-CoV-2 B.1.1.529 pandemic, herein we discussed various strategies that mainly involved the government organizations and the strict measures for the operative implementation of prevention, control as well as preparedness interventions.

2. Environmental concerns of Omicron

Highly mutated B.1.1.529 variant has various negative impacts on the environment; (a) generation of biomedical waste (Chevance et al., 2020; Saadat et al., 2020) (b) reduction in the waste recycling and the generation of municipal waste; management of waste is an efficient method to reduce the environmental pollution and to conserve nature (Sharma et al., 2021). According to the latest survey, the death rate during the pandemic mainly depends on the level of environment contamination and is more prominent in people with 65+ age suffering from kidney troubles, high blood sugar and pressure level (Hirose et al., 2022; Soni et al., 2021). COVID-19 displayed long as well as short term environmental impacts which are significant for sustainable development of the environment (Coltman and Miller, 2020; Saadat et al., 2020). Various environmental factors including atmospheric temperature, humidity, stability on fomites, ventilation as well as filtering systems in healthcare centers, restaurants, hotels or residential houses where there is close contact of people, could have a significant influence on the B.1.1.529 infection (Axiotakis et al., 2021). The survival rate as well as half-life might vary reliant on the external environment and the composition of the body fluid containing the SARS-CoV-2 B.1.1.529. Establishing feasible and reliable ways to diagnose SARS-CoV-2 infections is critical to successfully fighting the epidemic and improving our readiness in the event of a re-emergence of the virus (Chassalevris et al., 2022; Wolfe et al., 2022). Precisely, RNA of SARS-CoV-2 was identified in the stools up to 14 days after the virus was released into the respiratory tract,
irrespective of the disease severity (Wolfe et al., 2022). Although, mutated SARS-CoV-2 is an airborne, as well as respiratory, the literature related to the causative SARS-CoV-1 of 2003 the SARS outbreak suggested the chances of fecal-oral spread based on the identification of SARS feces using RT-qPCR (Arts et al., 2022). Wastewaters can also collect SARS-CoV-2 present in the mouth as well as in the upper respiratory tract during personal hygiene (Loan et al., 2014). This implies that contaminated water may contain SARS-CoV-2 particles/RNA which may be used as a diagnostic tool for epidemiological surveillance monitoring (Davoury and Dutta, 2021). Considering that SARS-CoV-2 was found both in the stool of asymptomatic carriers and in recently recovered patients as previously described, several authors use WBE as a tool to monitor the pandemic (Medema et al., 2020). Sufficient control of different environmental parameters as well as suitable human behaviour by these conditions play an important role in reducing the unwarranted spread of COVID-19 (B.1.1.529) (Hirose et al., 2022).

3. Role of wastewater epidemiology in pandemics

Monitoring contaminated water for new SARS-CoV-2 genetic variants has been proposed for initial identification and targeting alleviation measures where variants of concern (VOC) are increasing (Jian et al., 2020). Concerning the pandemic, wastewater-based epidemiology (WBE) is used to identify SARS-CoV-2 B.1.1.529 in contaminated water to test potential pathogens and provide an initial warning of COVID-19 epidemics (Loan et al., 2014; Raizada et al., 2021). WBE is an effective method having great potential for initial cautionary of highly contagious SARS-CoV-2 spread as well as outbreaks (Lawal et al., 2022). For instance, COVID-19 studies identified SARS-CoV-2 RNA (40.5%) in the stools of infected persons and 7.4% reported diarrhoea indicating that majority of SARS-CoV-2 shedders shed virus in the formed stool (Larrarte and Pons, 2011; Medema et al., 2020). Results analysed by another research group showed that SARS-CoV-2 was probably under-going local community transmission at the time (Chassalevris et al., 2022; Chevance et al., 2020). Increased RT-qPCR signal in wastewater collected in late February and early April 2020 strongly during incipient cases suggested that WBE is an effectual stratagem for the epidemiological surveillance of highly mutated COVID-19 (Randazzo et al., 2020). Karrkhikeyan et al. scrutinized that out of a total of 59 positive cases among college students, 84.5% cases were diagnosed with contaminated water samples either in the early days or on the day of the diagnostic test. However, rest of the 8% cases were diagnosed as negative, indicating that the contaminated water system was very sensitive in identifying SARS-CoV-2 B.1.1.529 infected cases. Likewise, Ahmed et al. on 25.11.2021 putatively detected the SARS-CoV-2 B.1.1.529 in the contaminated aircraft water sample through positive results on the CDC N1, CDC N2, as well as del (69–70) RT-qPCR assays as per direction from the World Health Organization.

Fig. 1. Transmutation profiles of the α, β, γ, δ, and B.1.1.529 variant of concerns considered by the world health organization. Reprinted from ref. Sun et al. (2022).
Organization (Ahmed et al., 2022). Therefore, there is a need to monitor and treat B.1.1.529 variant contamination in the wastewater before its reuse by society.

Conclusively, wastewater investigation is comparatively less invasive, simpler and cheaper than other traditional surveillance systems for quickly intervening and controlling infectious disease epidemics. Moreover, the WBE can provide well-timed examinations which permit community services to react more rapidly and accept potential health interventions before the unwarranted spread of contagious diseases. It could be used to track the source and location of potential SARS-CoV-2 carriers, and provide an initial warning to the community. Thus, because of the cost and structural challenges, WBE offers benefits when compared to biomonitoring tools that emphasize small target groups, hence retaining the anonymity of people.

4. Benefits of surveillance omicron variants

Most literature reports on wastewater surveillance discuss the applications with the great incidence of COVID-19 mainly to trace trends and detect hotspots (Thakur and Kanta Ratho, 2021). During the pandemic, WHO had advised implications for surveillance and their epidemiological interrelation to better understand the measuring steps to combat circulating SARS-CoV-2 variants. The percentage share of B.1.1.529 variant globally with confirmed cases till March 29, 2022 as depicted in (Fig. 2a, b)

Fig. 2. (a). Global percentage share of Omicron variant, reprinted with ref. Sharma et al. (2022) (order number-501726026), Copyright Wiley 2022, (b) several SARS-CoV-2 B.1.1.529 variant cases in the Asia-pacific region till March 29, 2022, based on different countries. The data in the bar graph is used from the source available at https://www.statista.com/statistics/1287427/apac-number-omicron-variant-by-country/#professional.
Moreover, this new variant of unknown origin directs the surveillance of B.1.1.529 variants to be held in developing countries (economically) and in the environment to better assess its spread and remain prepared for future contagions virus diseases. To get a better knowledge of severe threats caused by the B.1.1.529 drive scientists to fold and evaluate significant data in a short period. According to an epidemiological study, community health measures, social intercessions, immune responses, diagnostic approaches etc. necessitates the analysis of the worldwide population (Organization, 2021). The medical background of the COVID-19 WHO scheme permits the sharing and assembling of medical data of patients in the hospital that significantly assist in the formulation of treatment guidelines. The surveillance failure of the COVID-19 variant strain surveillance (NS3) program for spike gene was further improved and achieved by the center for disease control and prevention (CDC) in association with community health test labs in the US (CDC, 2021). In the race of sequencing genomic diversity, an appropriate substitution of the VOC-21NOV-01 (BA.1) variant i.e., VOC-22JAN-01 (BA.2) variant was detected with no amino acids present at the 69 and 70 positions of the S-protein along with specimen data (Fig. 3) (Nyberg et al., 2022).

The main objective of surveillance is to propose data for well-versed policy making. There exist some challenges associated with conventional variant of concerns surveillance as per genotyping of medical samples, including, labor/resources demand, people sampler methodology, and available sequencing measurements. Wastewater-based COVID-19 variants surveillance establishes an effective scheme without any requirement of prevailing sampling and proposes cost-effective and appropriate evidence on the prevalence of the disease (Hasija et al., 2022; Hasija et al., 2021). Wastewater surveillance of Omicron variants was applied to analytically notice viral RNA traces in wastewater, mainly as an early warning scheme of local viral integration and transmission. This scheme was intended to supplement additional surveillance, specifically person testing, advising earmarked acts for public health such as local detections from public health surveillance and improved capacity for individual examinations (Cutrupi et al., 2022). Benefits of wastewater surveillance permit community-wide testing/screening without any behaviourally varied needs from the public health; collective public sample to organize the absence or presence of omicron variants in a distinct community; minimum favoritisms realized with clinical testing. The complexity of the wastewater analyses as a surveillance implement comprises definite challenges including testing of bacterial and viral publics in complex matrices such as the presence of inhibitors (RNAase), wastewater, lack of adequate laboratory coverage, and small viral concentration, that might result into restricted treatment, diagnosis, and detection of human disease (Panchal et al., 2021b).

After the disruption, the SARS-CoV-2 B.1.1.529 variant in Australia’s earlier positive community health response to the epidemic, the significance of the surveillance scheme was enhanced in November 2021 (McMahan et al., 2021). The spread of these variants is evidenced to be more contagious and tough to control than previous alpha (B.1.1.7) and ancestral variants and mandates an adaptive surveillance strategy to assist decision making. Despite early distrust in Australia, this surveillance scheme has approved as a vital module of the population health response with a low pervasiveness of COVID-19 cases. In a study, the advancement of a novel RT-PCR-assisted methodology was done, since easily available in analytical laboratories and found proficient in quantifying and detecting the SARS-CoV-2 variants in wastewater concentrations of existing predominant variants (Chassalevris et al., 2022). This study indicated that targeting B.1.1.529 variant methodical surveillance in wastewater samples precisely apprehended the sequence of Delta to B.1.1.529 transition (50.2 % in 10 days and 91.09 % in 19 days) among the inspected community. The wastewater epidemiology technique unveiled several advantages over conventional sequencing related variant surveillance performs due to its faster efficiency, low labor-intensive, low-cost and more practical.

5. Opportunity and challenges for epidemiology

The wastewater tracking data of SARS-CoV-2 B.1.1.529 could not find the existence of a particular variant due to their inability in investigating all variant-defining changes on a single-genome. Moreover, the main shortcomings in tracking SARS-CoV-2 B.1.1.529 includes unpredictable detections with the varying present epidemiology, poor quality sequencing test, irregular detections, and discovery of mutation related to one specific variant. However, circumstances that enhance assurance in the outcomes included a diagnosis of multi-variant related mutations, exceptional mutations (independent of other variants) or connected mutations (present on the same sequence systems), the increase in concentration of RNA concentration with time, diagnosis of sequential samples or by multiple approaches, and sequencing abundant data for multi-variant-related mutations curving together (Kirby et al., 2022; Patial et al., 2022b).

Ma et al. studied the genomic characteristic of SARS-CoV-2 B.1.1.529 with sequencing data obtained from 108 infected patients which were formulated by the Network for Genomic Surveillance (South Africa) and gambled that SARS-CoV-2 B.1.1.529 is different from the other variants generated through recombination or mutations (Ma et al., 2022). Further, the main challenges for wastewater surveillance experienced particularly in developing countries have been illustrated as follows (Panchal et al., 2021a):

- Inadequate wastewater treatment facilities: The lack of suitable drain system led to the irrelevant collection of waste-water and few established treatment plants were the reason for a rare sampling of influent of treatment plants with 8–28 % of wastewater treatment (Panchal et al., 2021a).
- Mismanagement of Wastewater: More infective exposure due to inappropriate separation of offloaded waste coming from domestic effluents and other sewage sources.
- Unavailability of analytical services: Lack of proper treatment facilities with expensive equipment, skilled laboratory staff and laboratories, due to which no regular monitoring of physicochemical variations could be possible.
- Open-defecation: The open evacuation is predominant in densely populated areas (like India) with the worst kind of cleanliness. The practices notably enhanced consequences to community health with virus-infected population. Thereby, increasing the complexity of the sample matrix impeding the diagnosis of SARS CoV-2 B.1.1.529. A survey report carried out in a rural area of India to examine the impact on the biological and physicochemical quality of water because of open-defecation activities in

![Fig. 3. Regular confirmed VOC-22JAN-01 (BA.2) sequences constituting S-genomic diversity with no amino acids positioned at 69 or 70 along with specimen dates. Reprinted with ref. Nyberg et al. (2022).](image-url)
villages with open-defecation and without open-defecation displayed 48 % and 17 % of fecal pollution in drinking water (Tambekar and Rajigire, 2012).

Despite these above-mentioned challenges, wastewater-based surveillance is an emerging method for early detection of contagious risk of infection. This technique might be effectively used in developing countries where human diagnosis that would cost billions of bucks using conventional methods is complex to prevent at wider scale.

6. Concluding remarks

Considering the potential health risk, worldwide researchers are enthusiastically exploring an efficient solution to battle the current COVID-19 (SARS-CoV-2 B.1.1.529) pandemic. It is assumed that an operative monitoring scheme is significant to prompt intervention as well as control of an infectious disease epidemic. Sewage and Wastewater Treatment Plant are available in the center of this potential transmission line and can play a significant role in detecting as well as controlling the unwarranted spread of SARS-CoV-2. For detection, WBE provides comprehensive and complete real-time health data at the community level. SARS-CoV-2 B.1.1.529 was undergoing public transmission before previously anticipated, suggesting that wastewater analysis may be critical and an inexpensive COVID-19 epidemiological surveillance strategy. In addition to the current global epidemiological surveillance strategy. In addition to the current global undergoing public transmission before previously anticipated, suggesting that wastewater treatment facilities across Ontario in the era of emerging SARS-CoV-2 variants of concern. Microbiol. Resour. Data. e00362-22

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