



Review

Epidemiological surveillance of enteric viral diseases using wastewater in Africa – A rapid review



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ABSTRACT

Viral enteric pathogens remain an important cause of diarrhoeal outbreaks among children in sub-Saharan Africa (SSA). Consequently, diarrhoeal illness remains a significant cause of morbidity and mortality in the under-fives in SSA. These outbreaks associated with viral pathogens tend to be seasonal and early warning systems for impending outbreaks could be very crucial for triggering preventive public health response and building public health resilience to deal with increased demand for medical services. Wastewater surveillance for pathogens is an important epidemiological component that could inform early warning systems. The objective of this rapid review was to evaluate the use of wastewater for epidemiology surveillance of enteric viral pathogens. Nine studies met the inclusion criteria. Eight viral pathogens were reviewed and analysed from 6 countries that performed wastewater analysis. Six studies explored the epidemiologic significance of viral pathogens in wastewater. The findings of this review revealed that monitoring of wastewater can provide an additional tool to determine the epidemiology of viral pathogens circulating in the community thereby providing early warning of potential outbreaks using wastewater-based epidemiology methods. Five of the included studies revealed the occurrence of viral pathogens in raw sewage and treated wastewater as an indication of inefficient elimination of viruses leading to potential release into water sources which presents a public health risk, increasing the risk of inducing gastroenteritis in the population. Six studies revealed the need for public health authorities to realise the potential benefit of environmental surveillance (ES) as an additional tool to determine the epidemiology of viral pathogens circulating in each community. Despite the significant public health challenge associated with enteric viral pathogens in sub-Saharan Africa, there remains remarkable underinvestment in potentially epidemiologically beneficial research, including wastewater-based epidemiology for these infections.

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Introduction

Viral pathogens remain an important cause of infectious diseases outbreaks in sub-Saharan Africa (SSA) [1]. In particular, enteric pathogens with a tendency to epidemic diarrhoeal outbreaks in young children are common, causing significant outbreaks in this population [2,3]. Consequently, the diarrhoeal illness remains a significant cause of morbidity and mortality in the under-fives in SSA [4], and together with acute viral respiratory illnesses contribute significantly to disease burden and consumption of a sizeable amount of public health resources [2]. The World Health Organisation (WHO) estimates that there are approximately 1.7 billion cases of diarrhoea in children, with 525,000 deaths in under-fives [5], the majority of which are preventable through the provision of safe drinking water and adequate hygiene and sanitation. Whilst bacterial pathogens such as *Escherichia coli* and *Shigella* species are significant aetiological agents, Rotavirus is the leading cause of acute watery diarrhoea in children in low-to-middle income countries, even despite the availability of rotavirus vaccination [5,6].

The outbreaks associated with viral pathogens tend to be seasonal [7,8], and early warning systems for impending outbreaks could be very important for triggering preventive public health interventions and contribute to public health sector capacity to deal with increased demand for healthcare [9]. Surveillance for pathogens in wastewater/sewage is an important epidemiological component that could inform early warning systems, and inform community infection trends for enteric or genitourinary pathogens [9]. It has been observed that the concentration of some pathogens in wastewater in communities with well-developed reticulation systems closely mirrors community infection trends [10–12], and hence could serve as a useful adjunct to traditional surveillance systems such as active case finding and sentinel surveillance. This could be more important in resource-limited settings or communities where access to healthcare services is limited for socio-economic reasons. Hence, in Africa where substantial proportions of the population are economically disadvantaged, wastewater surveillance could be utilized to inform the public health system.

In a previous review of the utilization of wastewater surveillance for the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in Africa, we noted this to be poor, retrieving a meagre 8 studies, of which only four were primary studies, and mainly in South Africa [13]. To take stock of the utilization of wastewater surveillance for enteric viral pathogens in SSA and adequately inform public health of the level of utilization and need for further studies, we undertook a systematic review. Our main objectives were to determine the viral pathogens for which wastewater surveillance has been utilized in SSA, the sources of the wastewater, the types of the analyses that were done and the uses to which the results were put.

Methodology

a. Information sources and literature search

We searched PubMed, Google Scholar, SCOPUS, and the World Health Organization library databases for relevant studies. The key search terms included “Wastewater”, “Waste water”, “Sewage”, “Sewer”, “Environmental”, “Surveillance”, “Disease”,

“Feces”, “wastewater-based epidemiology”, “Environmental surveillance”, “Environmental Epidemiology”, “Wastewater Surveillance”, “Environmental Monitoring”, “Wastewater Monitoring”, “Viral Pathogens” and “Virus”. All database searches were conducted from 10¹ to 13 January 2022. Due to the rapid nature of this review, a modified Population, Intervention, Control and Outcomes (PICO) framework informed the development of the search strategy to ensure that the boundaries of the research question were clearly defined:

Search # 1 – Population (Studies conducted in African Countries),
Search # 2 – Intervention ~ the environmental matrix of interest (Wastewater-based surveillance, role in management / monitoring of viral pathogens)

Search # 3 – Outcomes (the utilization of, acceptability of, and significance of wastewater-based surveillance in the management/ monitoring of viral pathogens).

The reference lists of all full-text articles screened were searched for relevant studies.

b. Study selection and inclusion criteria

We searched for reports and primary research studies. The review included studies conducted within Africa that described the utilization of wastewater surveillance for viral pathogens.

c. Screening process

We developed a screening criterion *a priori* for each of the three stages, title and abstract and full text. Two researchers screened the articles independently. Differences in screen results at the full-text stage were resolved by discussion. Covidence, an online tool for conducting various types of reviews (www.covidence.org) was used to review the titles and abstracts for inclusion/exclusion based on the criteria described in the modified PICO framework. Next, articles were single screened during full text using the same inclusion/exclusion criteria.

d. Data abstraction and synthesis

A data abstraction form was developed, discussed, and revised *a priori*. Data extraction was completed using the following endpoints: [1] country; [2] study aim; [3] study design (if applicable); [4] description of wastewater surveillance methods [5] sources of water surveilled [6] pathogens investigated [7] key findings any other significant findings—; two reviewers abstracted data from the included studies. For collating, summarizing, and reporting the findings, first, the reviewers familiarized themselves with the content of the articles. Second, findings reported in the papers were grouped into categories based on the reported findings, and a narrative was provided.

Results

Our initial keyword database search found 1398 potentially eligible articles. Following title screening, 126 articles were eligible for inclusion in abstract screening. These articles were imported into Covidence and 13 duplicates were removed, leaving 113 articles included in the abstract screening. Eighty-one studies were excluded following abstract screening, leaving 32 articles for full-text screening. Twenty-three articles (Supplementary File 1) were excluded after full article screening, leaving nine articles for data extraction (Supplementary File 2). Of the excluded articles 18 were

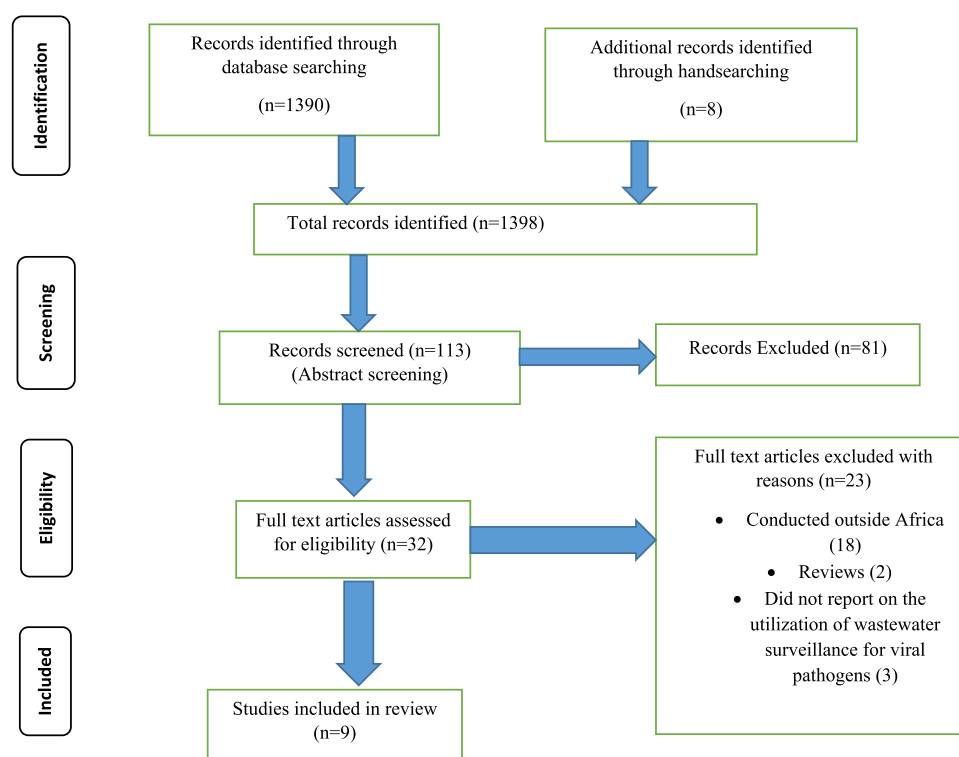


Fig. 1. PRISMA flow diagram.

conducted outside Africa, two were review articles and three did not report on the utilization of wastewater surveillance for viral pathogens. More details are presented in Fig. 1.

Fig. 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart.

a) Characteristics of included studies

Of the nine articles included in the study, three were from Tunisia [14–16], two from Nigeria [17,18], and one each from Senegal [19], Uganda [20], South Africa [21], Egypt [22]. Three were cross-sectional studies, and six experimental studies. More details are presented in Supplementary File 2.

b) Study findings

i. Testing methodologies and pathogens investigated

The studies reviewed analyzed the occurrence of rotavirus [16,18,20], norovirus [15,18,21], poliovirus [17], enterovirus [19,20], adenovirus [20], hepatitis A [14,20], aichi virus and human bocavirus [22], in wastewater. In three studies that were conducted in Tunisia [16], Uganda [20] and Nigeria [18], sewage samples were used to determine the viral load, genomics, and comparing strains of rotaviruses in clinical, animal, and environmental samples. Two other studies conducted in Tunisia [15] and South Africa [21] assessed wastewater for norovirus variants. In another study in Nigeria [17], raw flowing sewage samples were shipped at 4°C to a polio laboratory for concentration to survey for poliovirus. Studies aimed at evaluating the complex enterovirus circulation patterns and quantification in human populations have been conducted in Senegal [19] and Uganda [20]. A cross-sectional study conducted in Tunisia assessed the occurrence of hepatitis. In six of the studies [14–16,20–22], the viral pathogens were extracted from wastewater treatment plants (WWTP). The other three studies conducted in Nigeria [17,18] and Senegal [19] collected and analyzed sewage samples collected using the grab method and processed following the World Health Organization (WHO) guidelines [23].

Seven of the studies [14–16,18–21] utilized reverse transcriptase-polymerase chain reaction (RT-PCR) extraction methodology. In an experimental study conducted to determine the distribution of G and P types of group A rotaviruses (RV-A) using RT-PCR in sewage samples in Tunisia utilized a one-step kit TaqMan RNA-to-CT (Applied Biosystems, Foster City, CA) [16]. A multi-country study that included Senegal [6] utilized a qScript XLT qPCR Toughmix system (Quantabio) in a Rotor-Gene Q instrument (Qiagen) extraction methodology. In Nigeria, Motayo et al. [18] used a total RNA purification kit and SCRIPT cDNA synthesis kit (Jena Bioscience® GmbH, Germany) for extraction. For the study conducted in South Africa [21], norovirus extraction was done using norovirusGI@ceeramTools and norovirusGII@ceeramTools™ kits (Ceeram S.A.S, La Chapelle sur Erdre Cedex, France). A cross-sectional study conducted in Nigeria [17] characterized poliovirus using a 2-phased separation method. Shaheen et al. [22] conducted conventional PCR using QIAamp Viral RNA and DNA kits (Qiagen, Inc., Valencia, CA, USA).

ii. Viral pathogens in Wastewater: Epidemiological Significance and Environmental Risks

Six studies explored the epidemiologic significance of viral pathogens in sewage and wastewater [15,16,18–21]. Although not supported by study findings, five studies [15,16,19–21] suggested that monitoring of sewage and wastewater can provide an additional tool to determine the epidemiology of viral pathogens circulating in the community thereby providing early warning of potential outbreaks using wastewater-based epidemiology methods. In a prospective analysis of sewage from five states in Nigeria [18], all the rotavirus genotypes detected were linked to genotypes that have caused outbreaks in Nigeria. The same study went on to further highlight the importance of wastewater molecular epidemiology of rotavirus in the identification of emerging rotavirus strains to augment rotavirus disease prevention and control.

Five studies argued the occurrence of viral pathogens in raw sewage and treated wastewater as an indication of inefficient

elimination of viruses from sewage leading to potential release into water sources which presents a public health risk [15,16,20–22]. In studies conducted in Tunisia, Hassine-Zaafane et al. [15,16] found numerous rotavirus and norovirus (NoV) strains that were not efficiently eliminated by the sewage treatment process with chances of it spreading to surface waters increasing the risk of inducing gastroenteritis in the population. A study in South Africa [21] revealed that the presence of NoVs in effluent water samples is suggestive of inefficient removal of potentially harmful pathogens. In Uganda, effluent from the wastewater treatment plant appeared to impact surface water, as samples taken from surface water downstream of the treatment plant had higher viral concentrations of adenovirus, enterovirus, rotavirus, and hepatitis A than samples taken upstream.

iii. Gaps revealed from included studies

Six studies [16,20–22] revealed the need by public health authorities to realise the potential benefit of environmental surveillance (ES) as an additional tool to determine the epidemiology of viral pathogens circulating in each community. A study in Nigeria [17] revealed that environmental surveillance is still constrained to poliovirus high-risk states with its national expansion subject to viral epidemiology, laboratory capacity and financial support. Continuous monitoring of wastewater can contribute to learning about pathogens circulating in a population. A study in South Africa [21] showed that at least 16 norovirus genotypes were circulating in the Free State and Gauteng provinces. In another study, Beji-Hamza et al. detected five unique variants of hepatitis A that had not been previously reported in clinical cases [14]. The detection of viral pathogens in post-treatment effluent and downstream water sources [15,16,20–22] calls for the urgent need to add viral parameters to water quality surveillance as most people in low-income countries live in informal settlements with no proper sanitation and clean running water where contaminated surface waters are a public health risk.

Discussion

This systematic review revealed a significant paucity of wastewater surveillance studies in sub-Saharan Africa, retrieving only nine studies, of which only three were primary cross-sectional studies, and four were reviews. This is the first notable significant gap, which places limitations on the synthesis of the studies. Additionally, out of the whole of sub-Saharan Africa, the retrieved studies were from six countries, namely Egypt, Uganda, Tunisia, South Africa, Senegal and Nigeria. Despite the significant public health challenge associated with enteric viral pathogens in sub-Saharan Africa, there remains remarkable underinvestment in potentially epidemiologically beneficial research, including wastewater-based epidemiology for these infections. A similar rarity of primary studies was noted in a previous rapid review of the utilization of SARS-CoV-2 wastewater surveillance in Africa [13].

The studies reviewed investigated wastewater for the presence of rotavirus, norovirus, poliovirus, enterovirus, adenovirus, hepatitis A virus, echovirus and human bocavirus. Amongst these, rotavirus has the greatest public health significance due to its aetiological role in acute watery diarrhoea in under-fives [6], and the resultant morbidity mortality. Detection of community infection trends of rotavirus through wastewater surveillance would therefore be informative for public health; unfortunately, only two [16,18] of the retrieved studies examined its presence. Hepatitis A virus, norovirus, enterovirus and adenovirus also remain with relative public health significance. On the other hand, poliovirus is generally near-eradicated or eradicated in most countries, and cases of acute flaccid paralysis have been low. However, of late there have been reports of some cases in Malawi, which would necessitate all forms of

surveillance for early detection of the virus and mitigation against the serious morbidity associated with the disease.

According to our current review, a variety of methods were used for viral genome extraction, PCR and sequencing. Whilst in six of the studies [14–16,20–22], the viral pathogens were extracted from wastewater treatment plants (WWTP), three studies conducted in Nigeria [17,18] and Senegal [19] collected and analyzed sewage samples collected using the grab method. Both collections points can be used in well-developed urban communities that have modern reticulation systems emptying into a common point. However, in most of sub-Saharan Africa, including Zimbabwe, most rural areas lack such infrastructure hence community ablution facilities at points such as schools, shopping points and churches could be investigated for utility for wastewater surveillance. The commercial extraction (NucliSens, Jena Bioscience, Qiagen) and nested/semi-nested PCR (Quantibio, norovirusGIceeramTools) methods used can be applied in other SSA countries riding upon already existing poliovirus surveillance programs. However, further localised cost per test studies are needed to evaluate the cost-effectiveness in the context of long-term public health surveillance.

The clinical significance of the detection of viral pathogens is a bone of contention. There remains an argument that the detection of these pathogens in water indicates inefficient elimination. In communities with poor infrastructure and frequent leakage of raw sewage in the streets, the presence of the pathogens could serve as a source of contamination of water and food sources, triggering diarrhoeal diseases outbreaks. This may also affect toddlers who frequently play in the streets. Therefore, apart from indicating the community infections trends with the viral pathogens, the presence of these viruses in sewage could pose public health hazards. More examinations into the viability and pathogenic potential of viral pathogens in wastewater or sewage are therefore indicated. However, the major significance of detecting viral pathogens in wastewater could be the triggering of early warning systems and informing public health preparedness and response. Resource-limited settings in sub-Saharan Africa need to continue extensively exploring the utility of wastewater surveillance for viral pathogens as a way of detecting outbreaks or impending outbreaks early and instigating adequate preventive measures to mitigate against overwhelming diarrhoeal disease outbreaks. This is important as many of these communities remain with limited capacity and resilience to deal adequately with large scale disease outbreaks, with resultant excess avoidable morbidity and mortality, which further strains scarce resources.

Conclusion

This review reveals serious gaps in the utilization of wastewater surveillance in Africa, and a paucity of studies to conclusively determine its utility. There is, therefore, need for more primary studies, and an investment in testing capacity to enable appropriate diagnostics. Due to its limitations in interpretation, wastewater surveillance may not be used in isolation, but must be utilized and interpreted in the context of other aspects of surveillance, including testing and treating of active cases, active case finding and sentinel surveillance. Together, these can provide more robust information regarding the epidemiology of enteric viral pathogens in communities. Despite that fact that wastewater is proven to contribute to identification of viral enteric pathogens linked to outbreak, little is known about most African countries effort to include wastewater surveillance among the epidemiological surveillance activities.

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CRediT authorship contribution statement

Conceptualization, TD and GM (Grant Murewanhema); Methodology, TD, GP and PGI, EM; Writing – original draft, TD and GM (Grant Murewanhema); Writing – review & editing, KM, IC, GM (Godfrey Musuka). All authors have read and agreed to the final version of the manuscript.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jiph.2022.05.010.

References

- [1] Chetty M. Global burden of diseases in Sub-Saharan Africa. *Medi Chron* 2018;2018(10):50.
- [2] Mujuru HA, Burnett E, Nathoo KJ, Ticklay I, Gonah NA, Mukaratirwa A, et al. Cost estimates of diarrhea hospitalizations among children < 5 years old in Zimbabwe. *Vaccine* 2020;38(43):6735–40.
- [3] Mujuru HA, Yen C, Nathoo KJ, Gonah NA, Ticklay I, Mukaratirwa A, et al. Reduction in diarrhea- and rotavirus-related healthcare visits among children < 5 years of age after national rotavirus vaccine introduction in Zimbabwe. *Pediatr Infect Dis J* 2017;36(10):995–9.
- [4] Ugboko HU, Nwinyi OC, Oranusi SU, Oyewale JO. Childhood diarrhoeal diseases in developing countries. *Heliyon* 2020;6(4):e03690.
- [5] WHO. Diarrhoeal disease Factsheet. 2017 Available from <https://www.who.int/news-room/fact-sheets/detail/diarrhoeal-disease> Accessed August 14, 2021.
- [6] Musuka G, Dzinamarira T, Murewanhema G, Cuadros D, Chingombe I, Herrera H, et al. Associations of diarrhea episodes and seeking medical treatment among children under five years: insights from the Zimbabwe Demographic Health Survey (2015–2016). *Food Sci Nutr* 2021;9(11):6335–42.
- [7] Fares A. Factors influencing the seasonal patterns of infectious diseases. *Int J Prev Med* 2013;4(2):128–32.
- [8] Moriyama M, Hugentobler WJ, Iwasaki A. Seasonality of respiratory viral infections. *Annu Rev Virol* 2020;7:83–101.
- [9] Mao K, Zhang K, Du W, Ali W, Feng X, Zhang H. The potential of wastewater-based epidemiology as surveillance and early warning of infectious disease outbreaks. *Curr Opin Environ Sci Health* 2020;17:1–7.
- [10] McCall C, Wu H, Miyani B, Xagorarakis I. Identification of multiple potential viral diseases in a large urban center using wastewater surveillance. *Water Res* 2020;184:116160.
- [11] Wade MJ, Jacomo AL, Armenise E, Brown MR, Bunce JT, Cameron GJ, et al. Understanding and managing uncertainty and variability for wastewater monitoring beyond the pandemic: lessons learned from the United Kingdom national COVID-19 surveillance programmes. *J Hazard Mater* 2022;424:127456.
- [12] CDC. Public Health Interpretation and Use of Wastewater Surveillance Data. Available from <https://www.cdc.gov/healthywater/surveillance/wastewater-surveillance/public-health-interpretation.html> Accessed 21 March 2022.
- [13] Dzinamarira T, Murewanhema G, Iradukunda PG, Madziva R, Herrera H, Cuadros DF, et al. Utilization of SARS-CoV-2 wastewater surveillance in Africa—a rapid review. *Int J Environ Res Public Health* 2022;19(2):969.
- [14] Béji-Hamza A, Khélifi-Gharbi H, Hassine-Zaafraane M, Della Libera S, Iaconelli M, Muscillo M, et al. Qualitative and quantitative assessment of hepatitis A virus in wastewaters in Tunisia. *Food Environ Virol* 2014;6(4):246–52.
- [15] Hassine-Zaafraane M, Sdiri-Loulizi K, Kaplon J, Salem IB, Pothier P, Aouni M, et al. Molecular detection of human Noroviruses in influent and effluent samples from two biological sewage treatment plants in the region of Monastir, Tunisia. *Food Environ Virol* 2014;6(2):125–31.
- [16] Hassine-Zaafraane M, Kaplon J, Ben Salem I, Sdiri-Loulizi K, Sakly N, Pothier P, et al. Detection and genotyping of group A rotaviruses isolated from sewage samples in Monastir, Tunisia between April 2007 and April 2010. *J Appl Microbiol* 2015;119(5):1443–53.
- [17] Johnson Muluh T, Hamisu AW, Craig K, Mkanda P, Andrew E, Adeniji J, et al. Contribution of environmental surveillance toward interruption of poliovirus transmission in Nigeria, 2012–2015. *J Infect Dis* 2016;213(Suppl_3):S131–5.
- [18] Motayo BO, Adeniji JA, Faneye AO. Species A Rotavirus (RVA) isolated from Sewage in Nigeria, 2014: close genetic relatedness of partial G, P, and NSP4 gene sequences encoding G1 with cogent genes of other Asian and African rotaviruses. *J Pathog* 2018;2018.
- [19] Majumdar M, Sharif S, Klapsa D, Wilton T, Alam MM, Fernandez-Garcia MD, et al. Environmental surveillance reveals complex enterovirus circulation patterns in human populations. *Open Forum Infectious Diseases*. US: Oxford University Press; 2018.
- [20] O'Brien E, Nakyazze J, Wu H, Kiwanuka N, Cunningham W, Kaneene JB, et al. Viral diversity and abundance in polluted waters in Kampala, Uganda. *Water Res* 2017;127:41–9.
- [21] Mabasa VV, Meno KD, Taylor MB, Mans J. Environmental surveillance for Noroviruses in selected South African wastewaters 2015–2016: emergence of the Novel GII.17. *Food Environ Virol* 2018;10(1):16–28.
- [22] Shaheen MN, El-Daim A, Sahar E, Ahmed NI, Elmahdy EM. Environmental monitoring of Aichi virus and human bocavirus in samples from wastewater treatment plant, drain, and River Nile in Egypt. *J Water Health* 2020;18(1):30–7.
- [23] WHO. Guidelines for environmental surveillance of poliovirus circulation. Available from https://polioeradication.org/wp-content/uploads/2016/07/WHO_V-B_03.03_eng.pdf Accessed 18 March 2022.