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Spectrum of environmental surveillance of SARS-CoV-2 fragments: Questions, quests, and conquest
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Abstract
This work examines the entire spectrum of ‘Environmental Surveillance (EnvSurv)’ of SARS-CoV-2 fragments i.e. the questions, quests, and conquests of the technology since early year 2020. The prime focus of the present work to document the journey with achieved objectives and remaining ambitions associated with the technology. Despite the EnvSurv may be regarded as the techniques, which rather achieved more than expected, will it win the struggle for its existence or lose its way once the pandemic and fear associated with it completely fades. Pertaining to this discussions, major researched topics were investigated, followed by enlisting of ten bullets of the past experiences along with corresponding challenges, and finally key targets for the techniques are enlisted. The article targets to be a simple guide of the journey of EnvSur in terms of its effectiveness for treatment, infectivity, monitoring & estimation (TIME) till date.

Introduction
After several thousand articles on wastewater surveillance for accurately monitoring the COVID-19 pandemic from the expertise interfaces of microbiologist, environmental engineers, data scientists, civil engineers, remote sensing experts, and modelers to integrate their findings on the above topics to etch out the probability of relative environmental risks and human health challenges infected persons based on wastewater surveillance, it is time to have a look on general awareness, learning, policy and mitigation strategies that could be yielded by the technique. While some researchers kept on dealing with effective disinfection methods, analysis and interpretation of the data of RNA count of SARS-CoV-2 virus, predicting near to accurate number of symptotic/asymptotic/incubated patients, possible infection risk due to treated/un-treated wastewater or natural water environment, and issues as well as improvements in current wastewater based epidemiological (WBE) surveillance methodologies; the rest kept on applying the techniques with more and more logical and precise way in new city/community types/country/region/states. Even the absence of wastewater treatment plant could not stop researchers to implement WBE studies in the remote location against all the odds. Figure 1 depicts a simple word cloud of the most used word in the publications pertaining to the domain [1–30, 31–51].

On the other hand, after nearly three years of active experience on WBE applicability, the majority of the limitations have also become evident. Various range of questions are posed on the continuing relevance of the techniques and academic research challenges. In some part of the globe, core researchers are wrapping-up the projects, while in another part, public health organisations and stakeholders are starting it up to convert the generated knowledge into the policy. Under the light of above discussion, this opinion work is taking a look at the questions with which methodologies kicked off amidst the peak of pandemic, followed by what have been major milestones that brought recognition to the techniques, and finally what remains to conquer. The article is expected to help policy makers to take a quick synaptic view that matters the most for policy implementation in the One Health monitoring of the planet Earth.
The argument in support of this belief was the fact that raw wastewater contains the RNA excreted by both symptomatic and asymptomatic individuals; and also its previously proven effectiveness for the monitoring of other enteric viruses, such as poliovirus, hepatitis A, and norovirus. The consensus was global and hence it was globally trusted to perform and have the answer to the question and thus be capable of providing meaningful public health interventions. It leads to the formation of global collaborative to maximise contributions in the fight against COVID-19.

While WBE remain a technique to provide approximation of pandemic trend rather the exact number of infected people in a given community, capability to detect new variants made EnvSur i.e. genomic surveillance an indispensable technique for public health. We all know that had genomic surveillance would have been in place, probably death owing to variant B.1.1.7/ B.1.617, that have been linked to increased transmissibility and an ability to evade immune protection, could have been minimised considerably. Later various mutants like omicron could be identified on time and thus adverse impacts cold be negated on time.

**Quests**

It is arguably agreed that WBE could outperformed clinical tests, served better on community and watershed scale, understood easily by the general public, health worker and policy makers, exhibited no conflict on its capability to predict a rise of active cases early, proved handy in hotspot zonation, curfew allocation, effectiveness of vaccine drive, as well as actually supplemented the individual testing during the various phases of pandemic. The main quests pertaining to environmental surveillance have been as follows [1–35]:

- Proof of the concept of wastewater surveillance for COVID-19 tracking.
- Profile tracking of active cases through the wastewater loading of SARS-CoV-2 RNA.
- Epidemiological application including the most accepted benefits of early warning.
- Effective in identifying co-occurring indicator pathogens for COVID-19 and likely exposure rates.
- Passenger tracking mainly of international air, and thus provided another line of check.
- Comparison of treatment technologies and their efficacy of SARS-CoV-2 RNA removal.
- Predicted occurrence, ecotoxicological risk and environmentally acquired resistance of antiviral drugs associated with COVID-19 in environmental waters
- Detection of SARS-CoV-2 genetic material in the wastewaters (both effluents, influents, and in between the steps involved in treatment system), in the University campuses, vicinity of COVID-19 isolation centre, in the ambient urban waters, Bay areas, along the sewer network, as well as full scanning of the city.
- WBE based city zonation for pandemic preparedness powered by early warning
- Perspectives of short and long-term temporal variations in SARS-CoV-2-RNA prevalence along the COVID-19 surges and dips.
- Merging of co-infection, antimicrobial and anti-viral resistance along with COVID-19.
- Unravelling the early warning capability of wastewater surveillance for COVID-19 and the variations in lag-time
- Adding an extra layer for the protection of environmental and health security.
- Tracking attenuation and exposure risk following the wastewater mediated discharge of SARS-CoV-2 in natural water bodies.
- Tracking the decay of SARS-CoV-2 RNA along the various wastewater treatment systems.
- Comparisons of sample concentration, detection and data-normalisation techniques.
- Could be applied on surface waters (river, drain, lake).
- Detection of mutations as explicitly proven for the case of Delta/omicron variants of SARS-CoV-2 i.e. effective application of bioinformatics
- Effective in studying the proclivity and consequence of SARS-CoV-2 migration to aquatic environment.
- Potential emergence of antiviral-resistant pandemic viruses via environmental drug exposure of Animal Pools
- Diagnosis, seasonality, environmental fate, prognosis, treatment, transport, transmission, inactivation, anti-viral drug resistance, and epidemiology.
- Perspectives of modelling and monitoring of SARS-CoV-2 in aquatic environment for COVID-19 pandemic
- Assisting the community with online portal on weekly update of genome concentration with accessibility provided to the public and policy makers.
- Effective application of quantitative microbial risk assessment (QMRA) framework.
- Unprecedented precision in identifying a single active case on dormitory scale i.e. highly effective for campuses.
- Capable of predicting pathogen diversity (bacterial/viral) from wastewater in order to establish early sign of WBE as prediction tool.
- Picked and implemented by several concerned authorities and policymakers around the globe for upgradation of existing COVID-19 surveillance in their ward/community/city/campuses/country.

Once we will have a longer valuable time series surveillance data, we will have the following advantages/capabilities:

- Efficacy of vaccination on COVID-19 cases and secondary transmission.
- Further understanding on the robustness in early warning capability of the techniques.
- Capabilities to have better benefits of making WBE data accessible for public.
- Possibility to perform various modelling and simulation to advance the surveillance protocols, as well as the subtle signals like monitoring of co-infections like monkeypox.
- Understanding the potential risk through water-oral route under QMRA framework, and the impact of heavy antibiotic use during COVID-19 treatment on environment
- Ways to provide interactive publicly accessible genome concentrations data on web with various lag to general public, public health workers, policy makers and water managers.
- For various risk evaluation studies and producing higher resolution with signs indicative of temporal variation in COVID-19 patient loadings.

Conquests

Some of the challenges for WBE can be argued as follows [1—30, 31–51]:

- Effect of solid—liquid partitioning and role of biofilm on the final results of WBE.
- Is it possible to have a wrong signal of peak owing to the condition of sink (sludge/biofilm) becoming the source (releases the RNA fragments)?
- What influence different treatment steps will may have on WBE results if sampled water is not raw water?
- Discrepancies among the monitored genes:
  - Which genes Ct value should be considered for gene copy calculation?
  - Does treatment really remove RNA, if yes up to what extent?
- What are the effects of treatment type or STP size on RNA removal or WBE results? Case A: 10 MLD Traditional STP
- What to compare with active/recovered/cumulative COVID-19 cases?
  - S-gene, ORF-gene, N-gene, which is the best for comparisons with active cases or the average.
- Need of coefficient that may convert Ct to gene copies to number of infected person.
  - Will it ever be possible?
  - How would method precision can help in better prediction or take aways of the results.
- Implementation/Application of the obtained information.
- City zonation can help the management?
- Lock-down component especially.
- Seasonality effect on the WBE results especially in monsoon dominated tropical countries is still to observe.
- How to apply in a city with no wastewater treatment facilities or rural areas or in a low sanitation country
- Not detected is just a notion of below detection.
- Can river/drains be monitored for WBE and used as the indicator for regional and national health.
- Economics and real-world problems with WBE.
- What should be the frequency (weekly/monthly) of sampling? How much samples are enough for a city?
- How would catchment size, sewage connections, efficient waste collections will affect the WBE results?
- Regional/case-specific normalisation factor.
- Would WBE be economically worth if used for COVID-19 only? How to include WBE in the policy of a country, province or municipality.
- How to use the early capability of WBE for COVID-19 management. Can online portal of such surveillance be helpful in this regard?
- What further can be derived using long-term weekly resolution of SARS-CoV-2 RNA data?
- What impact (on antibiotic resistance) has been already there due to the unprecedented use of antivirals/antibiotics for the treatment of COVID-19?
- How successful is the vaccine in each community?
- What is the pathogen diversity (viral and bacterial) in the wastewater?

Conclusion

While WBE has established itself as a technique of tomorrow, it must deal with the economics of surveillance by including several other health indicators under its purview. A consensus among the researchers must be there so that WBE can be incorporated at policy scale. It is quite clear that we need a strong surveillance as we cannot afford lose so many lives. Also we never know that what extent of co-infections like monkeypox, black fungus, or after effects like AMR are going to be in the near future. No country should overlook it to have it in place formally. Ignorance can kill, if WBE that subscribes and assists the ethos of ‘One Health’ is not implemented on the core of environmental monitoring. On the other hand, technology will be benefitted from the development of practical guide and pandemic management tools can by integrating the virtues of information technology with early warning capability of wastewater surveillance. Further, a confidence will be spawned through instilling informed understanding among the commons about the efficacy of techniques. It will be then easy to convince government agencies and thus be adopted in the policy of using WBE as a regular environmental monitoring tool.

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Given his role as Guest Editor, Manish Kumar had no involvement in the peer-review of this article and has no access to information regarding its peer-review. Full responsibility for the editorial process for this article was delegated to Payal Mazumder.

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.

Data availability

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This paper discusses the use of hospital wastewater for tracing patient numbers correlated with hospitalized patient numbers.

This paper discusses the first detection of SARS-CoV-2 genetic material in the vicinity of COVID-19 isolation Centre in Bangladesh: variation along the sewer network.

This article reports the first detection of SARS-CoV-2 viral RNA in wastewater and their trends with the reported was same as clinical cases.

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