USING WASTEWATER-BASED EPIDEMIOLOGY AS A POTENTIAL INSTRUMENT FOR THE PREDICTION AND CONTROL OF COVID-19 DISEASE OUTBREAKS

Natalie Lowe, Vladimír Bencko

Institute of Hygiene and Epidemiology, First Faculty of Medicine, Charles University and General University Hospital in Prague, Prague, Czech Republic

SUMMARY

The COVID-19 pandemic has revealed a significant number of cracks in the current vigilance techniques that stand to minimise outbreaks of SARS-CoV-2. There is a serious inadequacy of the testing capacity of healthcare systems worldwide, which can be attributed to the lack of appropriate testing and monitoring methods for a disease such as COVID-19. The current tools in use for COVID-19 surveillance are either expensive, not applicable to large populations or yield results after the outbreak has already occurred. The immense contagiousness in combination with a wealth of asymptomatic carriers means that RT-PCR testing is not feasible on a mass scale. It is evident that new methods are required for the monitoring of COVID-19 and a range of new epidemiological tools must be implemented if public health systems worldwide want to make relevant predictions on the patterns of disease spread and increase the efficacy of their decisions. In addition to this, the pandemic has highlighted the necessity for redirecting biomedical research towards early diagnosis and rational therapy of respiratory viruses in particular, as well as prevention of their spread by conventional means. An efficient early detection system would save lives and allow countries to return to pre-pandemic standards of living. At the forefront of this lies wastewater-based epidemiology, which carries immense potential as a means of pre-symptomatic diagnosis and population-based surveillance.

Key words: wastewater-based epidemiology, COVID-19, outbreaks, prevention, PCR, SARS-CoV-2, surveillance, epidemiology

Address for correspondence: N. Lowe, Institute of Hygiene and Epidemiology, First Faculty of Medicine, Charles University and General University Hospital in Prague, Studničkova 7, 128 00 Prague, Czech Republic. E-mail: Natalielowe111@gmail.com

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INTRODUCTION

The global pandemic caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is one of the greatest public health threats of this century. To date 494,587,638 people have been infected and 6,170,283 lives have been claimed by the coronavirus disease 19 (COVID-19), which has now produced cases in every single country on Earth (1).

SARS-CoV-2 is an enveloped, single-stranded RNA virus (2), which infects lung alveolar epithelial cells via receptor-mediated endocytosis and utilises the angiotensin-converting enzyme II (ACE2) receptor to gain entry. If the virus leads to a symptomatic infection, individuals typically tend to present with symptoms that range from a fever, loss of smell, headache, and general malaise to pneumonia and shock (3, 4).

On 30 January 2020, the WHO declared a global health emergency of international concern and by 11 March 2020, a global pandemic was publicised (2, 3). SARS-CoV-2 is classified as "Risk Group 3" meaning it entails a substantial risk to the population, due to its effect on health and the global economy (5). The standard of testing is based on polymerase chain reaction (PCR); its high sensitivity and selectivity yields highly accurate results when testing individuals; however, it was not designed for the mass surveillance of populations. PCR testing encompasses time-consuming sampling, long turnaround times for results and it is an expensive testing modality (6).

The combination of limited diagnostic testing capacity with the possibility of individuals presenting with asymptomatic/oligosymptomatic infection of COVID-19, unfortunately results in significant uncertainty of the estimated numbers of those infected with SARS-CoV-2 at any one time (4). Recent studies have shown that persons infected with SARS-CoV-2 shed viral remnants in their faeces prior to symptom onset. This acts as the foundation that wastewater-based epidemiology (WBE) can be used to revolutionise the surveillance of COVID-19 infections within a population (7). Wastewater-based epidemiology provides the ability to incorporate the asymptomatic population of individuals into the true prevalence statistics, which therefore allows for a more appropriate epidemiological response (2).

The Problem: Early Identification of Infected Individuals

The early identification of infected individuals is crucial for the successful prediction and control of COVID-19 outbreaks. Early detection can be done through epidemiological surveillance of the virus, which so far has proved a challenge to public health systems worldwide (8, 9). The surveillance of COVID-19 involves tracking the spread of the disease throughout communities and populations in order to predict and identify patterns, which in turn allows for the application of measures of prevention and control (5).

Despite the knowledge surrounding the need for the implementation of COVID-19 surveillance methods, public health departments worldwide are experiencing difficulty concerning the early identification of COVID-19 amongst the population, in addition to the prediction and early assessment of patterns of disease spread (9).

Recent studies display evidence that the mean incubation period of COVID-19 is approximately five days, despite the range being from zero to twenty-four days (10). The time taken from entry of the virus until infectivity of the individual is two to three days, which means that there are up to 22 days those individuals may be unknowingly contagious. There lies a significant number of individuals that have an extended pre-symptomatic or completely asymptomatic infection, meaning the spread of the virus between individuals is probable throughout the whole course of infection (11).

The current epidemiological tools for the identification of infectious individuals are based upon individuals coming forward for reverse transcriptase polymerase chain reaction (RT-PCR) testing if they suspect they may have symptoms or have been in contact with an infected individual. RT-PCR detects genetic fragments of SARS-CoV-2 within the samples of secretions taken from nasal and pharyngeal mucous membranes (11).

This method of epidemiological testing poses several problems; first, there is a hugely undetermined number of asymptomatic individuals, who are unlikely to come forward for testing due to the lack of symptoms. Secondly, RT-PCR is a highly specific but also very costly method for the detection of SARS-CoV-2. It is designed for the detection of SARS-CoV-2 in individuals and is not economically or epidemiologically efficient as a tool for screening or surveillance. It is time-consuming and expensive, which means that it is not applicable in many countries worldwide (8).

Moreover, there is currently no method implemented for the monitoring of infected patients. The current standards of control involve a 14-day isolation period, after which, the individual is presumed to have cleared the infection and is deemed non-infectious again; this poses a number of problems. First, the 14-day isolation period begins from the point of diagnosis, which could be at any point throughout the time of infection; so many individuals remain in quarantine for much longer than necessary. This usually means they are unable to work in addition to a plethora of personal problems that come with self-isolation. Unnecessary quarantine also puts a huge number of people out of work, which causes problems for businesses and institutions as well as service providers within the public sector (12).

The Solution: Wastewater-based Epidemiology

Wastewater provides an excellent source of chemical and biological markers, which in turn serve as tools to decipher human activity. These markers can be analysed to reveal qualitative and quantitative data based on a certain population within a given area (13). Previous uses of WBE includes the monitoring of the use of pharmaceuticals, tobacco, alcohol and illicit drug use within the community; however, the implementation for observation of population health is a rapidly expanding field, which has shown enormous potential (13). One of the most renowned uses of WBE was the implementation during the worldwide eradication of polio, whereby it was invoked to assess the presence of polio within the community as well as to monitor the efficacy of the vaccination programme. The approach of WBE is based on the assumption that any substance that is excreted in the waste of humans can be quantified and used to back-calculate the original concentration within a specific population, provided the substance is stable in wastewater (14, 15).

One of the greatest advantages of WBE is its capability to expose outbreaks at an early stage. Presymptomatic or asymptomatic transmission of SARS-CoV-2 is one of the driving forces behind the rapid spread of the virus, which often goes undetected due to lack of symptoms or the exhibition of non-specific symptoms. However, as long as these individuals develop viral shedding via faeces, WBE can detect infected individuals (16). For example, if an area which previously had a low viral load of SARS-CoV-2 suddenly spikes, it is likely that an outbreak is imminent and decisions can be made to limit the spread of the virus within this given community (16).

The use of WBE for detection of SARS-CoV-2 is based on the principle of viral shedding in stool samples, that is thought to be due to the viral infection of gastrointestinal cells. The viral shedding of SARS-CoV-2, although there is no current consensus, is not considered to be a faecal-oral disease; hence, the viral remnants are inactive and are not able to elicit an infection (2,17).

The ability of WBE to include the asymptomatic and oligosymptomatic population means that the evaluated infectivity of the population is almost always underestimated. Studies have shown that in France and Spain, there have been documented concentrations of at least two orders of magnitude higher than the concentrations estimated by other means (2).

Using WBE as a surveillance tool for COVID-19 will allow the spatial display of infection within communities and highlight localisations as ‘hotspots’. Individuals living within these ‘hotspots’ should be tested using RT-PCR, which will give accurate individual results and ensure the early quarantining of individuals, thereby diminishing or even preventing an outbreak of COVID-19. Studies have shown that the spread of this virus is heterogenous, meaning it is strongly influenced by local outbreaks (2). Using WBE in this way will target the epidemiological characteristics of disease spread, unveiling its potential to control and prevent large outbreaks of COVID-19. An example of the application WBE for the early warning of COVID-19 outbreaks was shown by the University of Arizona. Scientists were able to discover high levels of SARS-CoV-2 in the wastewater coming from a student dormitory in August 2020. Using this data, the University was able to take early action and test all the 311 residents of the dormitory using PCR. Clinical testing revealed there were two asymptomatic carriers of the virus, which would have likely caused a significant outbreak of the disease when considering the intimate living spaces and concentration of individuals within a student dormitory (16).

WBE also poses solutions to other problems. A huge number of countries worldwide are struggling due to limited resources and urgency of a clinical testing programme on a country-wide scale. WBE allows for analysis of the levels of contagions within a given population, removing the burden of numbers on the PCR testing process (16).

WBE Limitations

It is important to mention that the quantitative ability of WBE to determine the relationship between levels of viral RNA in sewage and infectivity of the population is dependent on many variables. The main limitation for the estimation of SARS-CoV-2 within the community using WBE is the lack of a reliable stool-shedding rate. In asymptomatic individuals, the rate of viral shedding is typically much lower than in symptomatic patients. In addition to this, there are several variables that affect the shedding rate including the duration of infection, levels of viremia, the age of the patient in addition to the stage and severity of the disease. Therefore, it should be used in combination with clinical testing data when making public health decisions (2, 14).

Another deliberation of using WBE for population surveillance of COVID-19 are the ethical considerations. Using WBE for tracking illicit drug use within populations raises ethical discussions, because if the data is published, this can lead to the unfair labelling of these specific areas, which in turn can have detrimental effects within said communities. As WBE does not currently focus on individual data, the number of ethical considerations is low; however, when using WBE for viral load in sub-populations, this raises some ethical considerations. For instance, these areas of concern may undergo changes implemented by the public health authority, which can lead to stigmatising behaviours (14).

When considering the potential limitations of WBE for surveillance of SARS-CoV-2 amongst the population, it is important to discuss a number of variables. The viability and confidence interval of WBE relies on the lowest possible prevalence level of viral RNA that can be detected in sewage. This value in turn is determined by several variables including the sewage network itself, size of the sampling area, shedding profile of individuals as well as the methods of quantification of the viral RNA and back-calculation models (16). Another potential limitation when considering the viability of WBE is the responsiveness to data. Even if the sensitivity of detection is accurate, if the data is not delivered to and used by authorities in a timely manner then it is ineffective.

Furthermore, there may be areas where the faecal shedding of SARS-CoV-2 may be consistently detected; these areas require close monitoring for sudden increases in viral RNA remnants in wastewater. The shedding profile of individuals is another important variable. It directly influences the viral load and in turn determines the levels of viral RNA detected within wastewater (17). Zhu et al. describes the three elements that constitute the shedding profile: the shedding rate, the start of the shedding and the duration of the shedding. The shedding profile can vary greatly both intra- and inter-personally. The uncertainty in this area means it may affect the sensitivity of detection in addition to affecting some of the factors which govern the back-calculations of data (16).

In clinical data testing bias can be present, which depends on a multitude of factors, ranging from the screening of individuals, limitations in testing supply as well as the methods of testing. The nasopharyngeal swab is notoriously uncomfortable for patients, meaning that many tests are not carried out sufficiently, resulting in unreliable data. On the contrary, WBE methods of data collection do not encounter the same bias, as it is a completely non-invasive way of data collection; despite this, WBE may be affected by the uncertainty associated with spatial and temporal variations of molecular signals within the sewers. The impact of fluctuations in rainfall on the dilution of viral remnant concentrations also poses a potential problem on the overall quantification of individuals infected with the virus (2).

The early detection of the presence of SARS-CoV-2 within communities can also give healthcare authorities time to prepare for potential outbreaks, ensuring they have the correct supplies, including ventilators, ICU beds and available staff. The population will also benefit from the appropriate preventative controls implemented by local public health departments (7).

DISCUSSION

The information that WBE can provide regarding the detection of SARS-CoV-2 within the community has the potential to shape the decisions made by public health authorities, which may implement specific warnings, social rules or administrative guidance and reduce the scale of viral spread (16, 18). COVID-19 has already had an enormous impact on the functioning of many aspects of the economy and society. Numerous important decisions need to be made daily, that have a huge impact on people's lives. These arrangements need to be based on reliable scientific data and from reliable sources. It is therefore of vital importance that public health officials have an arsenal of data sources available to them when making decisions (2).

The combination of prior experience with SARS-1 in addition to the dedication of scientists, vaccine developers and the pharmaceutical industry; there are several highly effective vaccines currently in circulation around the globe, which have significantly reduced the death rate of COVID-19. However, despite the presence of the vaccine, the number of infected persons with SARS-CoV-2 continues to increase and there are still a significant number of outbreaks occurring worldwide (1). This highlights the need for alternative epidemiological tools for the prediction, detection and control of COVID-19 outbreaks in order to successfully manage community transmission of the disease (19).

The reality is, that large-scale diagnostic testing with RT-PCR is not feasible in most countries due to the massive costs and existing problems surrounding the production and supply of these tests (8, 18). WBE can perform an integral role in the understanding of overall infectivity numbers within a population, in addition to minimising the occurrence in the number of case surges, which is what overwhelms the hospitals and healthcare centres (8).

CONCLUSION

Despite the successful development and distribution of vaccines, the number of cases of COVID-19 continues to increase (1). The ongoing pandemic has highlighted the necessity for redirection of biomedical research to focus on the early diagnosis of potential pathogenic threats, especially respiratory viruses (15).

The current tools in use for SARS-CoV-2 disease surveillance are either expensive, not applicable to large populations or yield results after the outbreak has already occurred. It is evident that new methods are required for the monitoring of COVID-19 and a range of new epidemiological tools must be implemented if public health systems worldwide want to make relevant predictions on the patterns of disease spread and increase the efficacy of their decisions.

The potential for the use of WBE in the prediction and management of outbreaks is enormous. At a low cost and easy implementation into society, along with its minimal ethical considerations, WBE provides a tool, which at this moment in time would greatly solve many of the problems surrounding early risk identification.

It is evident that a legitimised viral surveillance system is critical in order to prevent future pandemics from novel pathogens.

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Conflict of Interests

None declared

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