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A Prevalence Risk Analysis of Waterborne Transmission of SARS-CoV-2

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Abstract

We statistically analyzed 31 published studies comprising 113 water samples collected from 17 countries for SARS-CoV-2 positivity. The pooled estimated prevalence of viral RNA in the tested samples was 64.1% [95% CI:51.6%, 74.9%] with considerable heterogeneity (I2: 90.1%, P<0.001). Notably, wastewater, sewage, hospital septic-tank, biological sludge, and effluent demonstrated statistical significance (P<0.05) for RNA positivity. The country-wise pooled estimated prevalence for Germany, India, Turkey, Spain, the Netherlands, Italy, the USA, and Japan were 88% (76%, 94%), 85% (33%, 98%), 83% (43%, 97%), 78% (54%, 92%), 60% (41%, 77%), 53% (36%, 70%), 53% (27%, 77%), and 25% (13%,43%), respectively. Further subgroup analyses showed that the prevalence of SARS-CoV-2 among the tested water samples was significantly higher in middle-income countries compared to high-income groups. Our data, therefore, suggests wastewater-based epidemiological surveillance as an important tool for community-wide monitoring of SARS-CoV-2.

Keywords: SARS-CoV-2; COVID-19; Fecal Shedding; Waterborne Spread; Wastewater Surveillance.

1. Introduction

Waterborne enteric or diarrheal viruses are generally shed in the gastrointestinal tract and feces of symptomatic as well as asymptomatic individuals. Such viruses are therefore transmitted through the fecal-oral route even at low infectious titers [1]. Most of the human enteric viruses, such as adenovirus, astrovirus, enterovirus, cytomegalovirus, rotavirus, norovirus, and coronavirus, are either asymptomatic or cause self-limiting gastroenteritis, diarrhea, or respiratory infections [2]. Several respiratory coronaviruses (CoVs), including six humans CoV viz., HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-HKU1, the severe acute respiratory syndrome CoV (SARS-CoV-1) and the Middle-East respiratory syndrome CoV (MERS-CoV), are also known for their gastrointestinal manifestation and fecal shedding [3–5].

The recently emerged SARS-CoV-2, which has caused the devastating CoV-2 disease-19 (COVID-19) pandemic, is the seventh and third most pathogenic CoV after SARS-CoV-1 and MERS-CoV [6, 7]. Similar to SARS-CoV-1 and MERS-CoV, transmission of SARS-CoV-2 from 'asymptomatic' individuals during the 'pre-symptomatic' state has also been observed [8, 9]. Notably, a proportion of SARS-CoV-2-infected patients have also shown gastrointestinal and hepatobiliary manifestations, including fecal shedding of high-titer infectious particles [10–18]. In the last two years of

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the COVID-19 pandemic, there have been a growing number of reports on the worldwide detection of SARS-CoV-2 in wastewater, raw sewage, hospital septic tanks, biological sludge and effluent, lakes, and rivers [19]. In view of the highlighted fecal contamination of water, a potential risk of waterborne transmission of SARS-CoV-2 in countries with poor sanitation and inadequate wastewater management has been envisaged. Here, we have statistically analyzed the global prevalence of SARS-CoV-2 in different water sources based on published reports, and accessed the risk of waterborne spread of COVID-19.

2. Materials and Methods

2.1. Literature Search Strategy

A structured online search for peer-reviewed articles published in English (2020–2021) was conducted on PubMed, Europe PMC, MEDLINE, EMBASE, and Google Scholar portals, including the Cochrane Library, using phrases: enteric or diarrheal coronaviruses or SARS-CoV-2, gastrointestinal or fecal shedding of SARS-CoV-2, Waterborne or fecal-oral transmission of COVID-19, detection of SARS-CoV-2 in wastewater or water samples, etc. The present study followed the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-analysis, or PRISMA [20], and Meta-analysis of Observational Studies in Epidemiology, or MOOSE [21]. The quality of the study was appraised using the Newcastle-Ottawa quality scale [22].

2.2. Inclusion Criteria

The eligibility of each published study followed the inclusion criteria: (i) original research or observational studies; and (ii) study samples of wastewater-based epidemiological surveillance for SARS-CoV-2. The exclusion criteria consisted of articles published in other languages or as conference abstracts, especially reporting on biological or excretory fluid specimens from COVID-19 patients to avoid inter-study variance. Study eligibility was independently assessed by the authors, and any disagreements were resolved by mutual discussion and consent.

2.3. Process of Systematic Review and Data Retrieval

All retrieved full articles were first screened for their titles and abstracts to determine their eligibility before systematic review and meta-analysis. Further, standardized data on the first author's name, year of publication, country of origin, study design, sample size, method of water concentration, and diagnostic technique of SARS-CoV-2 detection were collected for the analysis.

2.4. Measurements and Statistical Analysis

The prevalence of SARS-CoV-2 in water samples in each region subjected to statistical analysis was expressed in percentage (%). All data were presented as mean±standard deviation (SD) or event rate with a 95% confidence interval, and $P<0.05$ was considered statistically significant. All statistical analyses were performed using comprehensive meta-analysis software. Data were also assessed for Higgins I2 statistics, which quantify heterogeneity levels as minimal (1–40%), moderate (30–60%), substantial (50–90%), and considerable (90–100%).

3. Results and Discussion

3.1. Quantitative Detection of Viral Load in Water Samples

Since the first report on the detection of SARS-CoV-2 in the fecal sample of clinically confirmed COVID-19 patients [23], its plausible waterborne transmission through contaminated water has become an important water-based epidemiological issue [19]. Subsequently, ample data on wastewater or sewage surveillance for SARS-CoV-2 has emerged from across the world [24]. Of these, several studies have reported the detection of SARS-CoV-2 RNA in water samples collected from different sources (Table 1). Our analysis of the published data from different countries and water sources on the occurrences of SARS-CoV-2 confirmed by detectable viral RNA was in accordance with the set eligibility criteria. Of these, most studies employed the molecular diagnostic test (RT-PCR) to detect the viral RNA rather than quantifying RNA (RT-qPCR) expressed as genome copy (gc) number. Notably, higher titers of SARS-CoV-2 were reported in wastewater samples as compared to clinical specimens [17].

Owing to the samples' origins in different water sources and geographic regions of variable endemicity or socioeconomic status, variable occurrences of SARS-CoV-2 were reported. The use of different sample volumes, methods of virus filtration or concentration, and RNA quantifications in different units therefore greatly challenged our comparative analysis between studies. Nonetheless, the overall detection rate of SARS-CoV-2 in raw sewage or wastewater samples ranged between 13.0% and 100%, with optimal viral RNA over 106 gc/L. Notably, the first published report on SARS-CoV-2 detection in Dutch untreated sewage samples used the ultrafiltration method and RT-qPCR for RNA quantification in the range of 2.6×103 to 2.2×106 gc/L (Table 1). In contrast, while polyethylene glycol precipitation and ultracentrifugation of American raw sewage samples had SARS-CoV-2 RNA loads ranging 103−105 gc/L [17], viral RNA concentrations in French wastewater samples ranged between 5×104 and 3×106 gc/L (Table 1). Further examples include the use of aluminum flocculation-based concentration methods and the quantification of SARS-CoV-2 RNA as 2.5 ×105 gc/L in Spanish wastewater [25], which corroborated the German data based on ultracentrifugation and ultrafiltration of viral RNA [26]. Interestingly, a comparatively lower level of SARS-CoV-2

RNA (2.5×103 copies/L) was reported in secondary-treated wastewater samples in Japan, suggesting the importance of water treatment in reducing the viral contamination (Table 1).

Table 1. Country-wise quantitative detection of SARS-CoV-2 RNA in various water sources

Country	Source	RNA (gc/L)	Study name
Australia	Raw wastewater	19–120	Ahmed et al. (2020) [27]
France	Raw wastewater	3×10^6	Wurtzer et al. (2020) [28]
	Raw wastewater	5×10^4	Wurtzer et al. (2020) [28]
Spain	Raw wastewater	7.5×10^3–15×10^3	Balboa et al. (2020) [29]
	Primary sludge	0.1×10^5–4×10^4	Balboa et al. (2020) [29]
	Biological sludge	7.5×10^3–10×10^3	Balboa et al. (2020) [29]
	Raw wastewater	2.5×10^5	Randazzo et al. (2020) [25]
	Secondary effluent	2.5×10^5	Randazzo et al. (2020) [25]
	Raw Wastewater	5.2–5.9 log10	Randazzo et al. (2020) [25]
Italy	Raw wastewater	N/A	La Rosa et al. (2020) [30]
	Raw wastewater	N/A	Rimoldi et al. (2020) [31]
	River water	N/A	Rimoldi et al. (2020) [31]
Germany	Raw wastewater	3.0×10^3 – 20×10^3	Wu et al. (2020) [26]
	Secondary effluent	2.7–37×10^3	Wu et al. (2020) [26]
	Effluent	2.0×10^3 – 3.0×10^6	Agrawal et al. (2020) [32]
China	Hospital septic tank	0.5 – 18.7×10^3	Zhang et al. (2020) [13]
Netherlands	Airport wastewater	N/A	Lodder et al. (2020) [33]
	City wastewater	N/A	Lodder et al. (2020) [33]
	Sewage water	2.6×10^3-30×10^3	Medema et al. (2020) [34]
USA	Raw wastewater	$>3\times10^4$	Nemudryi et al. (2020) [35]
	Raw wastewater	0.1×10^5 – 2×10^5	Wu et al. (2020) [17]
	Raw wastewater	42.7×10^3	Wu et al. (2020) [17]
	Primary sludge	1.7×10^6– 4.6×10^8	Peccia et al. (2020) [36]
	Raw wastewater	3.2 log10	Sherchan et al. (2020) [37]
	Raw wastewater	10^2–10^5	Rosiles-Gonzalez et al. (2021) [38]
	Raw wastewater	66–390	Weidhaas et al. (2020) [39]
UK	Sewage water	3.5 – 4.2 log10	Martin et al. (2020) [40]
Japan	Raw wastewater	2.1×10^4 – 4.4×10^4	Hata & Honda (2020) [41]
	Treated wastewater	2.4×10^3	Haramoto et al. (2020) [42]
India	Sewage water	0.78×10^2 – 8.05×10^2	Kumar et al. (2020) [43]
	Raw wastewater	3.08×10^4 – 2.19×10^5	Hemalatha et al. (2021) [44]
	Raw wastewater	N/A	Arora et al. (2020) [45]
	Raw wastewater	N/A	Sharma et al. (2021) [46]
Iran	Sewage water	0.1×10^4	Tanhaei et al. (2021) [47]
Pakistan	Raw wastewater	N/A	Sharif et al. (2020) [48]
UAE	Wastewater	2.8×10^2 – 2.9×10^4	Hasan et al. (2021) [49]
Israel	Sewage water	N/A	Orive et al. (2020) [50]
Turkey	Raw sewage	2.9×10^3–1.8×10^4	Kocamemi et al. (2020) [51]
	Raw sewage	1.1×10^4 – 4×10^4	Kocamemi et al. (2020) [51]
Ecuador	River water	2.9×10^5– 3.2×10^6	Guerrero-Latorre et al. (2020) [52]

NA: not applicable (RNA not quantified).

3.2. Prevalence Risk Analysis of SARS-CoV-2 in Water Sources

Further, the random effect pooled analysis of the published reports indicated the prevalence and risk of SARS-CoV-2 in various water sources as 64.1% [95% CI: 51.6%, 74.9%] with considerable heterogeneity (I2: 90.1%, P <0.001) (Figure 1). Of the different water sources analyzed, the prevalence of SARS-CoV-2 RNA was higher among biological sludge, effluent, raw sewage, and wastewater, ranging from 80-90% (Figure 2). Further, analysis of SARS-CoV-2 contaminated water sources indicated a high risk of COVOD-19 spread from raw wastewater with a prevalence of 62% [95% CI: 51, 72], followed by sewage water with a prevalence of 61.2% [95% CI: 31%, 84.9%] (Table 2).

Study name	Event rate	Lower limit	Upper limit	Total
Agarwal, 2020	0.863	0.739	0.933	44 / 51
Ahmed, 2020	0.444	0.177	0.749	4 / 9
Arora et al. 2020	0.353	0.168	0.596	6 / 17
Balboa, 2020	0.880	0.687	0.961	22 / 25
Gonzalez, 2020	0.606	0.536	0.672	120 / 198
Green, 2020	0.818	0.604	0.930	18 / 22
Guerrero-Latorre, 2020	0.875	0.266	0.993	3 / 3
Haramoto, 2020	0.200	0.027	0.691	1 / 5
Hasan, 2020	0.846	0.697	0.929	33 / 39
Hata, 2020	0.259	0.129	0.453	7 / 27
Hemalatha. 2020	0.984	0.789	0.999	30 / 30
Kocamemi et al. 2020	0.875	0.614	0.969	14 / 16
Kumar. 2020	0.833	0.194	0.990	2 / 2
La rosa, 2020a	0.500	0.244	0.756	6 / 12
Lodder, 2020	0.833	0.194	0.990	2 / 2
Martin, 2020	0.900	0.326	0.994	4 / 4
Medema, 2020	0.583	0.383	0.759	14 / 24
Nemudryi, 2020	0.938	0.461	0.996	7 / 7
Or, 2020	0.176	0.058	0.427	3 / 17
Peccia, 2020	0.100	0.073	0.136	36 / 360
Randazzo, 2020a	0.667	0.553	0.764	50 / 75
Remoldi, 2020	0.556	0.330	0.760	10 / 18
Sharif. 2020	0.269	0.183	0.378	21 / 78
Sharma, 2021	0.929	0.423	0.996	6 / 6
Sherchan, 2020	0.133	0.034	0.405	2 / 15
Tanhae, 2021	0.800	0.459	0.950	8 / 10
Weidhaas, 2020	0.612	0.543	0.676	126 / 206
Westhaus, 2021	0.964	0.616	0.998	13 / 13
Wu, 2020	0.714	0.439	0.889	10 / 14
Wurtzer, 2020	0.935	0.776	0.984	29 / 31
Zhang, 2020	0.333	0.084	0.732	2 / 6
	0.641	0.516	0.749	

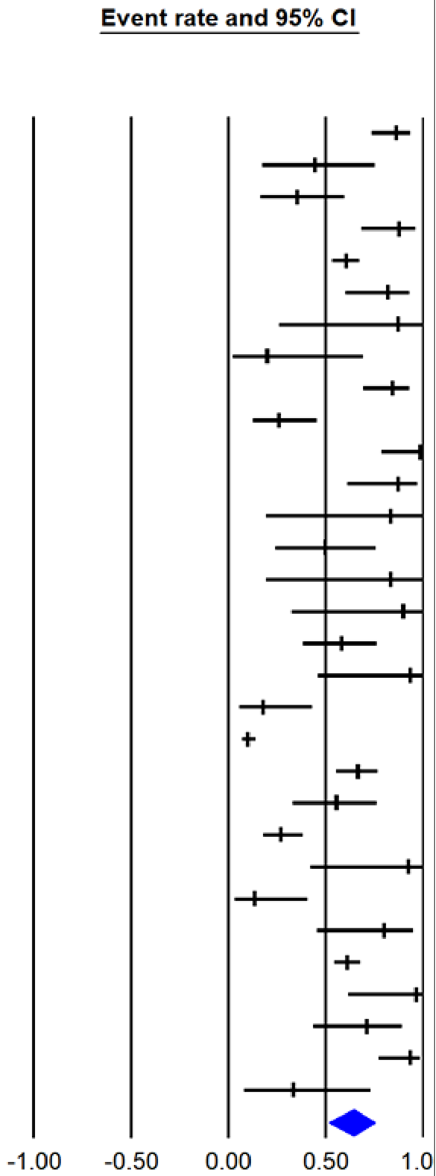

Figure 1. Forest plot demonstrating the risk of waterborne spread of SARS-CoV-2

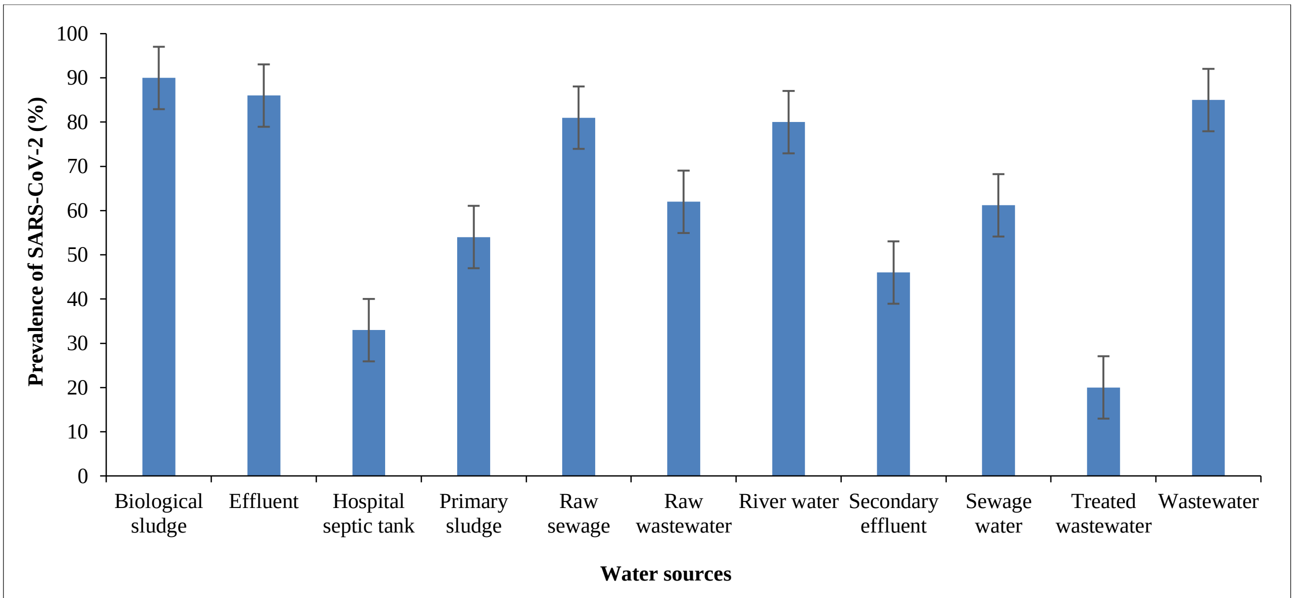

Figure 2. Prevalence of occurrences of SARS-CoV2 in various water sources

Table 2. Prevalence risk of waterborne spread of COVID-19 across various water sources

Sample source	Study (n=38)	Prevalence (%)	95% L CI (%)	95% U CI (%)	P	I^2	Model
Biological sludge	1	90	53	99	<0.001	NA	FE
Effluent	1	86	74	93	<0.001	NA	FE
Hospital septic tank	1	33	8	73	<0.001	NA	FE
Primary sludge	2	54	0.8	99	0.94	91.2	RE
Raw sewage	2	81	50	94	0.05	31	RE
Raw wastewater	20	62	51	72	0.02	71	RE
River water	2	80	40	96	0.124	0	FE
Secondary effluent	2	46	1.3	98.2	0.94	85	RE
Sewage water	5	61.2	31	84.9	0.47	67.9	RE
Treated wastewater	1	20	3	69	0.21	NA	FE
Wastewater	1	85	70	93	<0.001	NA	FE

FE: Fixed effect; RE: Random Effect, NA: Not available.

3.3. Country-Wise Prevalence Risk of Waterborne Spread of SARS-CoV-2

In the country-wise analysis, seven studies from the USA demonstrated a prevalence of 53% [27%, 77%], followed by four studies from India with a prevalence of 85% [95% CI: 33%, 98%] with substantial heterogeneity (Table 3). Of these, while the highest prevalence of waterborne SARS-CoV2 RNA was observed in France, the UK, Germany, and Ecuador, the least prevalence was observed in Israel, followed by Japan (Figure 3).

Table 3. Prevalence risk of waterborne spread of SARS-CoV-2 across different countries

Country	Study (n=33)	Prevalence (%)	95% L CI	95% U CI	P	I^2	Model
USA	7	53%	27%	77%	0.85	96	RE
India	4	85%	33%	98%	0.17	78	RE
Spain	3	78%	54%	92%	0.025	72.33	RE
Germany	2	88%	76%	94%	<0.001	NA	FE
Turkey	2	83%	43%	97%	0.097	31.8	RE
Netherlands	2	60%	41%	77%	0.29	0	FE
Italy	2	53%	36%	70%	0.72	0	FE
Japan	2	25%	13%	43%	0.01	0	FE
France	1	94%	78%	98%	<0.001	NA	FE
UK	1	90%	33%	99%	0.14	NA	FE
Ecuador	1	88%	27%	90%	0.2	NA	FE
UAE	1	85%	70%	93%	<0.001	NA	FE
Iran	1	80%	46%	95%	0.08	NA	FE
Australia	1	44%	18%	75%	0.74	NA	FE
China	1	33%	8%	73%	0.42	NA	FE
Pakistan	1	27%	18%	38%	<0.001	NA	FE
Israel	1	18%	6%	43%	0.02	NA	FE

FE: Fixed effect; RE: Random Effect, NA: Not available.

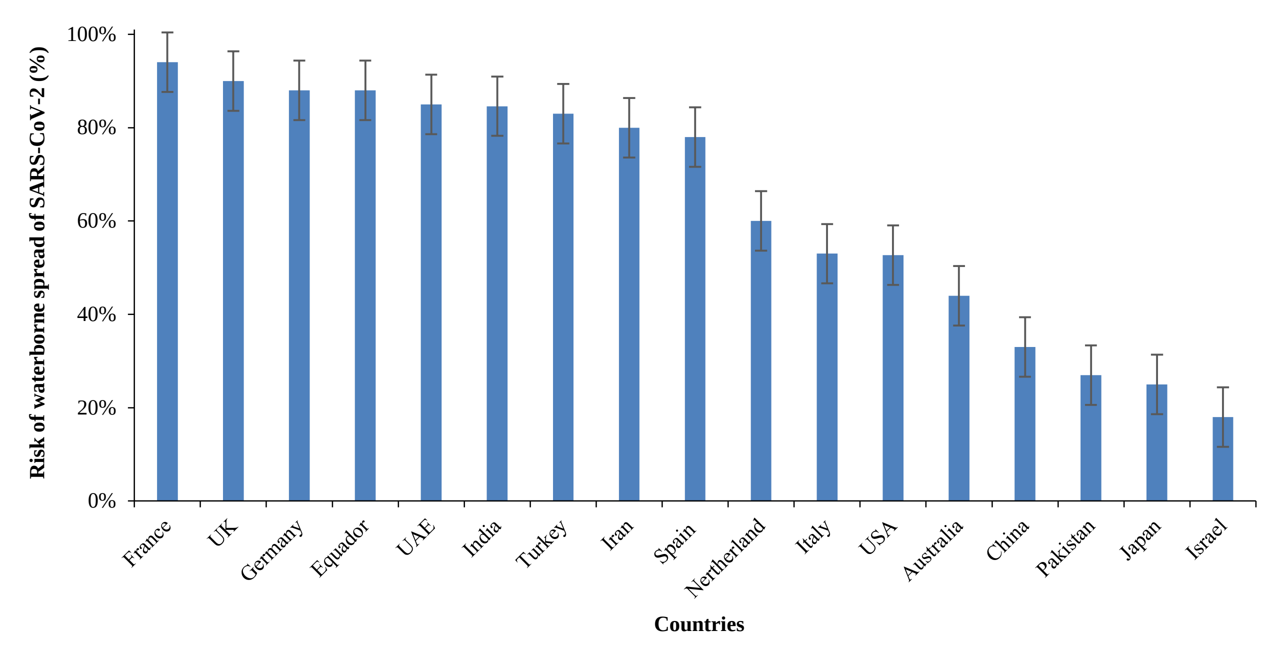

Figure 3. Prevalence risk of waterborne spread of COVID-19 cases across different countries

4. Conclusion

The fecal shedding of high-titer SARS-CoV-2 in COVID-19 patients has been recently corroborated with several reports on the detection of SARS-CoV-2 in wastewater, raw sewage, hospital septic tanks, biological sludge and effluent, lakes, and rivers worldwide. In view of this, our meta-analysis of pooled samples showed data about a 64% prevalence risk of waterborne transmission of SARS-CoV-2 with considerable heterogeneity. Of the various water sources, wastewater, raw sewage, hospital septic tanks, biological sludge, and effluent demonstrated statistically significant contamination with SARS-CoV-2. The pooled estimation of country-wise prevalence of SARS-CoV-2 was substantially high in Germany, India, Turkey, and Spain, moderate in the Netherlands, Italy, and the USA, and minimal in Japan. In addition, the prevalence of SARS-CoV-2 among water samples was significantly higher in middle-income countries compared to high-income countries. This is very likely due to the lack of focused water surveillance on enteric coronaviruses in general and the knowledge gaps in their circulation, persistence, and post-treatment inactivation. Because costly and time-consuming diagnostics are not feasible in such a pandemic situation, wastewater-based epidemiological surveillance should be considered an important tool for community-wide monitoring of COVID-19. However, tracking the source of SARS-CoV-2 contamination and spread, as well as its genetic variants, in near real-time would be most challenging.

5. Declarations

5.1. Author Contributions

Conceptualization, M.K.P.; resources, M.A.P. and A.R.A.; data curation, A.R.A. and M.A.P.; writing—original draft preparation, A.R.A. and M.K.P.; writing—review and editing, M.K.P. All authors have read and agreed to the published version of the manuscript.

5.2. Data Availability Statement

The data presented in this study are available in the article.

5.3. Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

5.4. Institutional Review Board Statement

Not applicable.

5.5. Informed Consent Statement

Not applicable.

5.6. Declaration of Competing Interest

The authors declare that there is no conflict of interests regarding the publication of this manuscript. In addition, the ethical issues, including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, and redundancies have been completely observed by the authors.

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