



Research article

Assessment of rotavirus and norovirus emitted from water spray park: QMRA, diseases burden and sensitivity analysis

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ABSTRACT

A quantitative model on exposure to pathogenic viruses in air of recreational area and their corresponding health effects is necessary to provide mitigation actions in content of emergency response plans (ERP). Here, the health risk associated with exposure to two pathogenic viruses of concern: Rotavirus (RoV) and Norovirus (NoV) in air of water spray park were estimated using a quantitative microbial risk assessment (QMRA) model. To this end, real-time Reverse Transcriptase polymerase chain reaction (real-time RT-PCR) was employed to measure the concentration levels of RoV and NoV over a twelve-month period. The probability of infection, illness and diseases burden of gastrointestinal illness (GI) caused by RoV and NoV for both workers and visitors were estimated using QMRA and Monto-Carlo simulation technique. The annual mean concentration for RoV and NoV in sampling air of water spray park were 20 and 1754, respectively. The 95% confidence interval (CI) calculated annual DALY indicator for RoV (Workers: 2.62×10^{-4} – 2.62×10^{-1} , Visitors: 1.50×10^{-5} – 2.42×10^{-1}) and NoV (Workers: 5.54×10^{-3} – 2.53×10^{-1} , Visitors: 5.18×10^{-4} – 2.54×10^{-1}) were significantly higher than the recommended values by WHO and US EPA (10^{-6} – 10^{-4} DALY pppy). According to sensitivity analysis, exposure dose and disease burden per case (DBPC) were found as the most influencing factors on disease burden as a consequence of exposure to RoV and NoV, respectively. The comprehensive information on DALY and QMRA can aid authorities involved in risk assessment and recreational actions to adopt proper approach and mitigation actions to minimize the health risk.

1. Introduction

The diarrhoeal death is known as hot issues all over the world, in particular, in middle and low-income countries, so that WHO (2014) reported 1.5 million deaths attributed to diarrhoeal diseases [1]. Over 58% of diarrhoeal deaths are associated with exposure to untreated or improperly treated water resources; it covers 1.5% of total global burden of diseases (BOD) [2, 3]. Despite the extensive presence of pathogens in water worldwide, the magnitude of microbial data and microbial risks following human exposure to waterborne viruses in developing countries remains unelucidated [4, 5]. Enteric viruses including Rotavirus (RoVs) and Noroviruses (NoVs) are extensively known as prominent viral agents of diarrhoeal and gastrointestinal diseases [6, 7]. The evidence indicated that NoV cause annually approximately 20 million gastroenteritis in U.S [8, 9]. The NoVs and RoVs excreted from feces of infected individuals

may be found in reclaimed water and natural recreational water resources [10, 11]. These pathogenic viruses due to non-enveloped structure are highly resistant to environmental stressors and survive for some days in the environment; RoV and NoV can be considered as markers of fecal contamination in water resources [12, 13]. RoV and NoV cause a wide spectrum of symptoms associated with diarrhoeal diseases including mild diarrhea, severe diarrhea and death from diarrhea [14]. The exposure to RoV and NoV through fecal-oral route are the most common cause of childhood gastroenteritis [8, 15]. However, the pathogenic viruses can be spread out from water resources following mechanical activities and wind erosion in bioaerosol form [16, 17]. The airborne particles containing both living and non-living components such as bacteria and viruses can be easily transferred and inhaled by the human which activate surroundings [18, 19]. Furthermore, the risk for human health following exposure to pathogenic viruses emitted from

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water resources is dependent on type of reclaimed water, the area of water environment, the load of viruses, the mechanical equipment, and immunity levels of human bodies [17, 20]. A numerous research have concentrated on bioaerosols emitted from wastewater treatment plant (WWTP), land application and wastewater irrigation of wastewater for agricultural crops [16, 17, 21, 22, 23]. For instance, Pasalari and et al. (2019) surveyed the temporal variation of RoV and NoV emitted from the aeration tank in WWTP. The authors reported that the annual mean concentration levels of these two pathogenic viruses of concern were measured to be 27 and 3099 (Viruses/m³.h), respectively [23]. Cheng Yan and et al. (2020) investigated the properties of bioaerosols emitted from WWTP and their corresponding microbial risk for human exposure [19]. However, the monitoring of bioaerosols emitted from water spray in recreational water resources, specially, in parks remain unclear. People choose the parks to spend a time with a fresh breaths to work out, likewise, the existence of RoV and NoV in spray water park feed with reclaimed water and effluent from the WWTP in an improper way can threaten the human health, especially the children [24]. Monitoring and screening the enteric viruses including RoV and NoV emitted from the water spray park can aid to minimize the human health risk [6]. In addition, the health effects associated with exposure to bioaerosols are highly dependent on (1) the concentration of enteric viruses, (2) meteorological parameters, (3) the inactivation rate of viruses in atmosphere, and (4) inhalation rate of exposed people [16, 25]. Microbial source tracking (MST) compiled with quantitative microbial risk assessment (QMRA) make desired for understanding the proportion of gastrointestinal infections and diseases occurring in the community level which never refer to medical places and considered in medical records [17, 26, 27]. The QMRA allows the development of computational tools to accurately ascertain the proportion of different pathogenic viruses present in water resources [6, 28]. To this end, QMRA estimate the potential risk of infection and diseases consequential to exposure any amount of enteric viruses according to a four-step procedure: hazard identification, exposure assessment, dose-response assessment and risk characterization [27]. In addition, the authorities are able to compare the health effects attributed to tolerable risk level for water resources enacted by world health organization (WHO) (10⁻⁴ pppy) [29, 30]. QMRA based on Monto Carlo simulation is a recommended technique by WHO to estimate quantitatively the annual probability of infection and diseases following exposure to pathogenic viruses [31, 32]. Furthermore, disability adjusted life years (DALY) metric is known as a complementary tools to estimate the burden of diseases attributed to environmental pollution [33]. Here, a QMRA was developed for the first time to estimate BOD and probability of infection and illness caused by exposure to RoV and NoV emitted from

the water spray park in Tehran, Iran using Monto Carlo simulation model.

2. Methods and materials

2.1. Site description

Present study was performed at Laleh park, known as a largest park in the center of Tehran, the capital of Iran. Laleh Park with area over than 35 ha is located in the center of Tehran with easy accessibility. This park with advantages of different infrastructures for exercises and work-out is of interest for people living surroundings and youth from other restricts of Tehran. In addition, the presence of water spray park in the center of this park is the focus of attention and gathering of people, especially the children. A schematic representation of water spray park is shown in Figure 1. As per speech view and the information recorded on <https://zibasazi.tehran.ir>, the people enter the Laleh park and usually spend over 1.5 h in this park.

2.2. Bioaerosol sampling procedure

To detect the bioaerosols and viruses in the air of water spray park, the air sampling were performed monthly in different 12 months of a year between July 2020 and June 2021. The air samples were taken 1.5 above adjacent the water spray park area. The sampling was conducted at 9:00 AM to 13:00 PM, to enhance the survival of bioaerosols due to weak solar radiation and high humidity. In this study, an ace-glass impinger with total volume of 100 mL containing phosphate buffer saline (PBS) (40 mL) equipped with a SKC pocket pump (SKC Inc., PA, USA) was employed to measure the RoV and NoV in air adjacent the water spray park. The flow rate of 4 L min⁻¹ was regulated and calibrated for pocket pump with aim of simulation the human breathing and personal exposure. After sampling period, the impingers covered with a sheath was immediately transported at 4 °C in insulated cool box for further analysis to the laboratory. Then, the samples were kept at refrigerator and -70 °C for further experiments. Table S1 summarizes the main meteorological characteristics for different days of sampling during the study period acquired from <http://www.wunderground.com>.

2.3. Detection of RoV and NoV

The viral loads of two viruses of interest in air of water spray park were measured using a quantitative real-time Reverse Transcriptase PCR (real-time RT-PCR) assay. NucleoSpin R RNA Virus Extraction Kit



Figure 1. A Schematic representation of water spray park in Laleh Park, Tehran. * Sampling Location.

(Macherey-Nagel, Germany) and cDNA using cDNA Synthesis Kit (Biofact TM RT Series cDNA Synthesis Kit, South Korea) were used to extract the RNA of viral viruses and conversion of isolated RNA to cDNA as per the manufacture instruction. The forward and reverse primer sequencing targeting VP6 the specific human viruses 5'-CAC CAG CGG TAG CGG CATT A-3' and 5'-ATT GTT TCG CTT GCG TCGGC-3', respectively with amplicon size of 124 bp. Of note, the detailed information on RNA extraction, CDNA conversion, and forward and reverse primer sequences are described in our previous study [23].

2.4. Statistical analysis

The statistical analyses were performed in Minitab 17.0 to determine the correlation coefficient between meteorological parameters (temperature, humidity, and wind speed) and concentration levels of RoV and NoV within the study period (Spear-man's correlation). In addition, the difference between the concentration levels of two viruses of concern in different seasons of a year was analyzed using Kruskale-Wallis statistical test.

2.5. QMRA and estimation of infection and illness probabilities

In this work, a QMRA model was performed to estimate probability of infection and illness associated with inhalation of air with RoV and NoV for people refer to park and workers employed. To this end, the QMRA model suggested by [34] was incorporated to appraise quantitatively the exposure levels to these two pathogenic viruses of concern for workers and people refer to Laleh park for work-out. Generally, the QMRA consist of four steps: hazard identification, exposure assessment, dose-response assessment, and risk characterization. The detailed information associated with present study are described as follows.

2.5.1. Hazard identification

As earlier mentioned, workers employed and people refereeing to Laleh Park are subjected to inhalation the air containing RoV and NoV and respective risks. Thus, in this study, we focus on these two viruses of concern and their corresponding probabilities of infection and illness.

2.5.2. Exposure assessment

To assess the potential levels of exposure of people and workers to RoV and NoV in the air of water spray park, the daily inhalation was calculated according to Eq. (1) [23]:

$$D_e = C * ET_{inhalation} * IR \tag{1}$$

where D_e refers the exposure dose ($GC.day^{-1}$), C denotes virus concentration (GC/m^3), $ET_{inhalation}$ represents the exposure duration (h), and IR is inhalation rate ($0.83 m^3/h$). The time of exposure for people refereeing to Laleh park and employee were considered 1.5 and 8 h, respectively. In addition, the background concentration levels of two pathogenic viruses (RoV and NoV) were considered zero, denoting assumption of these pathogenic viruses in ambient air away from any pollution sources. Furthermore, a simplified approaches without ages of people and susceptibility equal to 1 was considered to represent the worst-case estimation which is advisable in QMRA [35].

2.5.3. Dose-response assessment

Given known pathogen doses, the dose-response model assesses the likelihood of risk of outcomes (e.g. infection or illness). The mathematical function estimates the probability of infection (P_{inf}) and illness (P_{ill}) as the endpoints based on amount of pathogen inhaled by individuals within 1 day or 1 year. An exponential model was employed to analysis the data as a results of inhalation the RoV and NoV according to <http://bit.ly/29uHt8R>:

In case of probability of infection (P_{inf}), Eq. (2) was employed. The P_{inf} represents the outcome when individuals are exposed to a single pathogen dose “d”

$$P_{inf(d)} = 1 - \exp(-rd) \tag{2}$$

In exponential models, r denotes the parameter associated to viral infectivity constants.

It is important to note that, the dose harmonization [36] was employed to overcome the disadvantages imposed by real-time RT-PCR about the effectiveness of viruses. The specific parameters values for dose harmonization of each pathogenic viruses of interest are described in Table 1.

The risk of infection for different time of exposure including daily and annual exposure to NoV and RoV through inhalation the air in water spray park were estimated through Eq. (3) (<http://bit.ly/29uHt8R>).

$$P_{inf(D:A)}(d) = 1 - [1 - P_{inf(d)}]^n \tag{3}$$

where P_{inf} (A, D) represent daily and annual probability or risk of infection due to “n” exposure (n = 1 for daily exposure and n = 365 for annual exposure).

2.5.4. Risk characterization

The risk characterization was done according to dose-response model and information from earlier procedures in order to determine the probability of illness (Pill) as a consequence of infection [33] (See Eq. 4).

$$P_{ill} = P_{inf(A:D)}(d) * P_{ill_{inf}} \tag{4}$$

where, $P_{ill_{inf}}$ refers to the probability of illness to infection ratio. In case of RoV and NoV, $P_{ill_{inf}}$ are 0.5769 [37] and 0.5 [38], respectively.

Furthermore, disease burden by considering the gastrointestinal illness caused by exposure to RoV and NoV were estimated through Eq. (5) [39].

$$DB = Pill (A) * S * DBPC \tag{5}$$

where DB refers to burden of disease (pppy), Pill (A) denotes the probability of illness, S is susceptible fraction of population ($S = 1$) and DBPC represents the disease burden per case (DALY/year). Disease burden calculation consider both premature mortality and loss of healthy years due to morbidity. Table S2 summarizes the values corresponding to disease outcomes, duration, severity and DBPC for both RoV and NoV [40].

2.5.5. Model implementation

The model based on Monte Carlo simulation technique (MC2D) and R software was employed to represent the propagation of variability in DB as a response. It is important to mention that, the MC2D model with 10000 iterations for different distribution of each input parameter was run. The type of influencing parameters in the model and their corresponding distribution are described in Table 2. In addition, the best fitted distribution for viral concentration samples withdrawn from air of water spray park was selected using fit distribution extension from @Risk software (Palisade Corporation, Newfield, New York). The sensitivity analysis according to rank-order correlation and tornado charts illustration was used in order to calculate the relative importance of different input variable on DB as a response.

Table 1. Species-specific parameter values and dose harmonization for RoV and NoV.

Pathogen	Exponential r	Concentration of infectious virus.	Concentration of genome.	Source
RoV	0.0173	1 focus forming unit	1900	(Jonsson et al., 2009)
NoV	0.722	1 Virus	18.5	(Mcbride et al., 2013)

Table 2. QMRA model input parameters and their distributions.

Parameter	Unit	Distribution type (values)	References
RoV concentration (C)	GC/m ³ .h	Beta (shape1 = 0.300, shape2 = 0.589)	This study
NoV concentration (C)	GC/m ³ .h	Beta (shape1 = 0.3080, shape2 = 0.6306)	This study
ETinhalation	h	Uniform (1.5,8)	This study
Inhalation rate (IR)	m ³ /h	(Lognormal, meanlog = 0.83, sdlog = 0.15)	(Stellacci et al., 2010)
Dose (D _e)	GC/day	RoV: Exponential (rate = exposure) NoV: Exponential (rate = exposure)	(Ward et al., 1986) (Messner et al., 2014)
Days of exposure per year (n)	Days	Uniform (1,365)	(Courault et al., 2017)
Disease burden per case (DBPC)	DALY per case	RoV: Uniform (Min:0.00172, Max:0.525) NoV: Uniform (Min:0.00092, Max:0.522)	This study
Illness: Infection (I _{ill} /I _{inf})	Proportion	RoV (0.5769) NoV(0.5)	(Timm et al., 2016a) (Teunis et al., 2008)
Susceptible fraction of the population (S)		Constant (1)	This study

3. Results

3.1. Enteric viruses quantification

The loads of two viruses of concern: RoV and NoV in air of water spray park during the sampling period is presented in Figure 2. As shown in Figure 2, the monthly concentration of NoV within the sampling period was significantly higher than the other virus of interest, RoV. Surprisingly, contrast to previous comparable research focused on NoV and RoV in diverse contexts, the presence of these two pathogenic agents were identified whole the time of study period in air of water spray park [41]. According to statistical ANOVA analysis, a significant difference was found between the average concentration of two viruses of interest in different seasons of a year (p-value < 0.001). The annual mean concentration levels of NoV and RoV were 1754 and 20, respectively. In addition, the highest (NoV: 3767, RoV: 38) and lowest (NoV: 737, RoV: 11) concentrations of two viruses of interest were observed in autumn and spring season, respectively. The great numbers of hospitalization may be attributed to highest concentration of these two pathogenic agents in inhaled air by the people [23]. Furthermore, in the present research, we surveyed the relationship between meteorological parameters as a most important influencing parameters [42] on the variation of NoV and RoV concentration levels in air of water spray park by statistical spearman's analysis. Table S3 shows the spearman's correlation coefficients between

NoV and RoV concentration and meteorological parameters including temperature, wind speed and humidity.

The low temperature aid the viruses to survive for longer time in the ambient air [43]. Therefore, the higher concentration of viruses in cold seasons a year consequently bring about the higher risk of infection and diseases for people exposed.

3.2. Estimation the probabilities of infection and illness using the QMRA

According to experimental data on concentration of NoV and RoV, the Beta distribution as the highest probability of fitness was obtained to estimate the QMRA and DALY following exposure to these two viruses of interest in air of spray park. The probabilities of infection (P_{inf}), annual infection (P_{inf,A}), annual disease (P_{ill}), and disease burden (DB) were estimated for both workers and people coming into to workout in Laleh park and for 8 and 1.5 h per day. Table 3 summarizes the probabilities of daily and annual infection following the inhalation of RoV and NoV for both workers and people visitors. According to Table 3, 95% confidence interval (CI) for calculated the daily infection related to RoV and NoV for employees varied from 5.62 × 10⁻⁵ to 1 and from 3.68 × 10⁻³ to 1, respectively. While the 95% CI of daily P_{inf} for people visitors for 1.5 h exposure to air containing RoV and NoV were calculated to be between 4.73 × 10⁻⁶-1 and 4.57 × 10⁻⁴-1, respectively. In addition, 95% CI for annual infection probability for workers as a consequence exposure to

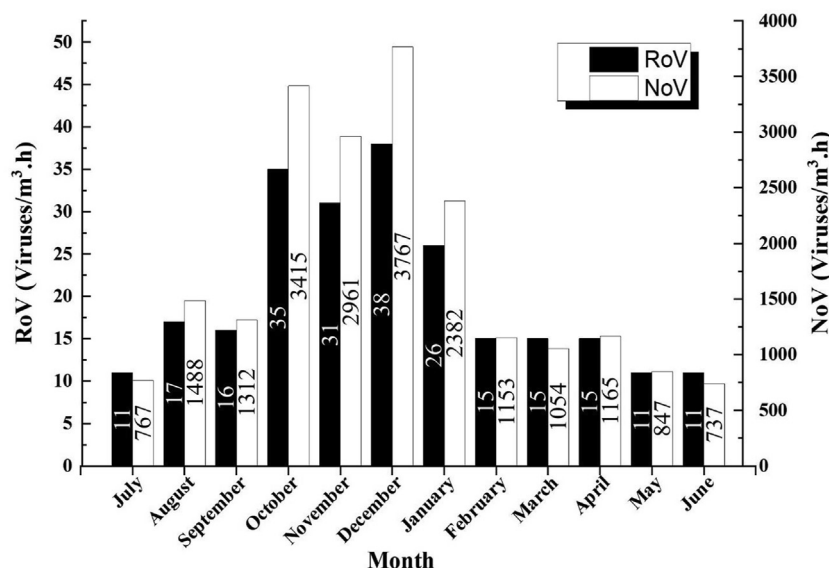


Figure 2. The concentration levels of NoV and RoV during the study period.

Table 3. Daily (Pinf) and annual Probabilities infection for workers and visitors in water spray park.

		Probability	2.5%	25%	50%	75%	97.5%
RoV	Workers	Daily (Pinf)	5.56×10^{-5}	0.000775	0.00316	0.0277	1
		Annual (Pinf A)	4.17×10^{-3}	0.0950	0.385	0.987	1
	Visitors	Daily (Pinf)	4.73×10^{-6}	0.00167	0.00637	0.0549	1
		Annual (Pinf A)	1.96×10^{-4}	0.192	0.629	1	1
NoV	Worker	Daily (Pinf)	3.68×10^{-3}	0.0761	0.275	0.937	1
		Annual (Pinf A)	3.47×10^{-1}	1	1	1	1
	Visitors	Daily (Pinf)	4.57×10^{-4}	0.156	0.479	0.995	1
		Annual (Pinf A)	1.09×10^{-2}	1	1	1	1

RoV and NoV for 8h per day were estimated to between 4.17×10^{-3} –1 and 3.47×10^{-1} to 1, respectively. While, the 95% CI of Pinf.A of exposure to RoV and NoV for people visiting Laleh park for 1.5 h per a day were estimated to be 1.96×10^{-4} –1 and 1.09×10^{-2} –1, respectively (See Table 3).

Furthermore, in the present study, the probabilities of illness (Pill) for daily and annual exposure to RoV and NoV for both personnel or workers and people visiting Laleh park were estimated in order to explain more the risk. The information on Pill for workers and people who visit Laleh park for work-out are summarized in Table 4. As shown in Table 4, the 95% CI of Pill for workers due to exposure to RoV and NoV were calculated to be 2.09×10^{-3} –0.5 and 1.73×10^{-1} –0.5, respectively. These values for people visitors for 3 h exposure per day to RoV and NoV ranged between 9.81×10^{-5} –0.5 and 9.98×10^{-3} , respectively. In addition, Table 4 shows the 95% CI of annual disease burden (DB) following exposure to RoV and NoV for both workers and people visiting the Laleh park. Of note, the DB was computed using the uniform distribution assigned to disease burden per case (DBPC) with uniform distribution [44]. The DBPC values containing a spectrum of symptoms between mild diarrhea (Minimum) and death from diarrhea (Maximum). According to Table 4, the 95% CI of annual DB estimated for workers and people due to inhalation of RoV were 2.62×10^{-4} – 2.62×10^{-1} and 1.50×10^{-5} – 2.42×10^{-1} , respectively. While the 95% CI of DB attributed to inhalation of NoV by workers and people during a year were estimated to be 5.54×10^{-3} – 2.53×10^{-1} and 5.18×10^{-4} – 2.54×10^{-1} . Furthermore, a comparison of the estimated DB for both worker and people visiting the Laleh park with recommended values by WHO (10^{-6} pppy) and US EPA (10^{-4} pppy) [45] are presented in Figure 3.

Figures 4 and 5 illustrate cumulative distribution plots (CDP) for annual DB estimated as a consequence of RoV and NoV exposure. The 95% and 50% uncertainty range of each quantile are stratified with light and gray bands by the R software.

A sensitivity analysis with 10000 iterations was conducted in order to determine the influence of variability of input variable on DB as the response variable. Figure 6 shows the tornado chart of input U and VU parameters (exposure time, concentration, inhalation rate, dose, n, and DBPC) in model on DB (pppy). According to Figure 6(a), sensitivity analysis identified the Dose as the most relevant factor on DB related to exposure to RoV in water spray park. However, in case of NoV, the

uncertainty in DBPC was selected as the most influencing factor on DB (Figure 6(b)).

4. Discussion

4.1. The load of viruses (RoV and NoV)

For better understanding about the risk of exposure to pathogenic agents in different environments of exposures, the quantitative data measured using a proper approach is needed. In the present study, the numbers RoV and NoV were measured using promising real-time RT-PCR techniques. According to Figure 2, the annual mean concentrations of concentrations of RoV and NoV in water spray park were 1754 and 20, respectively. To best of our knowledge, this is the first study focused on the concentration of pathogenic agents in water spray park, to date. However, the concentration of these two viruses of concern in air of water spray park were lower than those measured in air of wastewater treatment plant in France [46] and Iran [23]. The comparative concept of risk analysis indicated that the people who work out in water spray park are subjected to lower exposure of air containing RoV and NoV and consequently lower risk of infection and illness. Furthermore, as expected, the highest concentration level of RoV and NoV were found in the autumn. The lower temperature can aid the survivability of pathogenic agents in air for prolonged time. In addition, the correlation spearman correlation analysis indicated that temperature and wind have more importance to compared to humidity in numbers of RoV and NoV in air of water spray park. These lower temperature and lower wind speed simultaneously tend to favor the survival and formation of pathogenic viruses and consequently higher human exposure [19, 42].

4.2. QMRA

The QMRA technique is mathematical approach to determine the probability of infection (Pinf) and illness (Pill) caused by exposure to pathogenic viruses in different environments [47]. The quantitative results obtained by QMRA can be utilized as an early health warning tool for authorities to establish a correct strategy for mitigating efforts in context of emergency response plans (ERP) [48, 49]. In the current research, Pinf and Pill of exposure to two main viral agents of

Table 4. Probabilities of illness (P_{ill}) and disease burden (DB) for workers and visitors in water spray park.

		Probability	2.5%	25%	50%	75%	97.5%
RoV	Workers	Pill	2.09×10^{-3}	0.0475	0.193	0.494	0.5
		DB	2.62×10^{-4}	0.00788	0.0340	0.1028	0.262
	Visitors	Pill	9.81×10^{-5}	0.0962	0.314	0.500	0.5
		DB	1.50×10^{-4}	0.0146	0.0523	0.125	0.242
NoV	Worker	Pill	1.73×10^{-1}	0.5	0.5	0.5	0.5
		DB	5.54×10^{-3}	0.0585	0.0978	0.189	0.253
	Visitors	Pill	9.98×10^{-3}	0.5	0.5	0.5	0.5
		DB	5.18×10^{-4}	0.0620	0.126	0.193	0.254

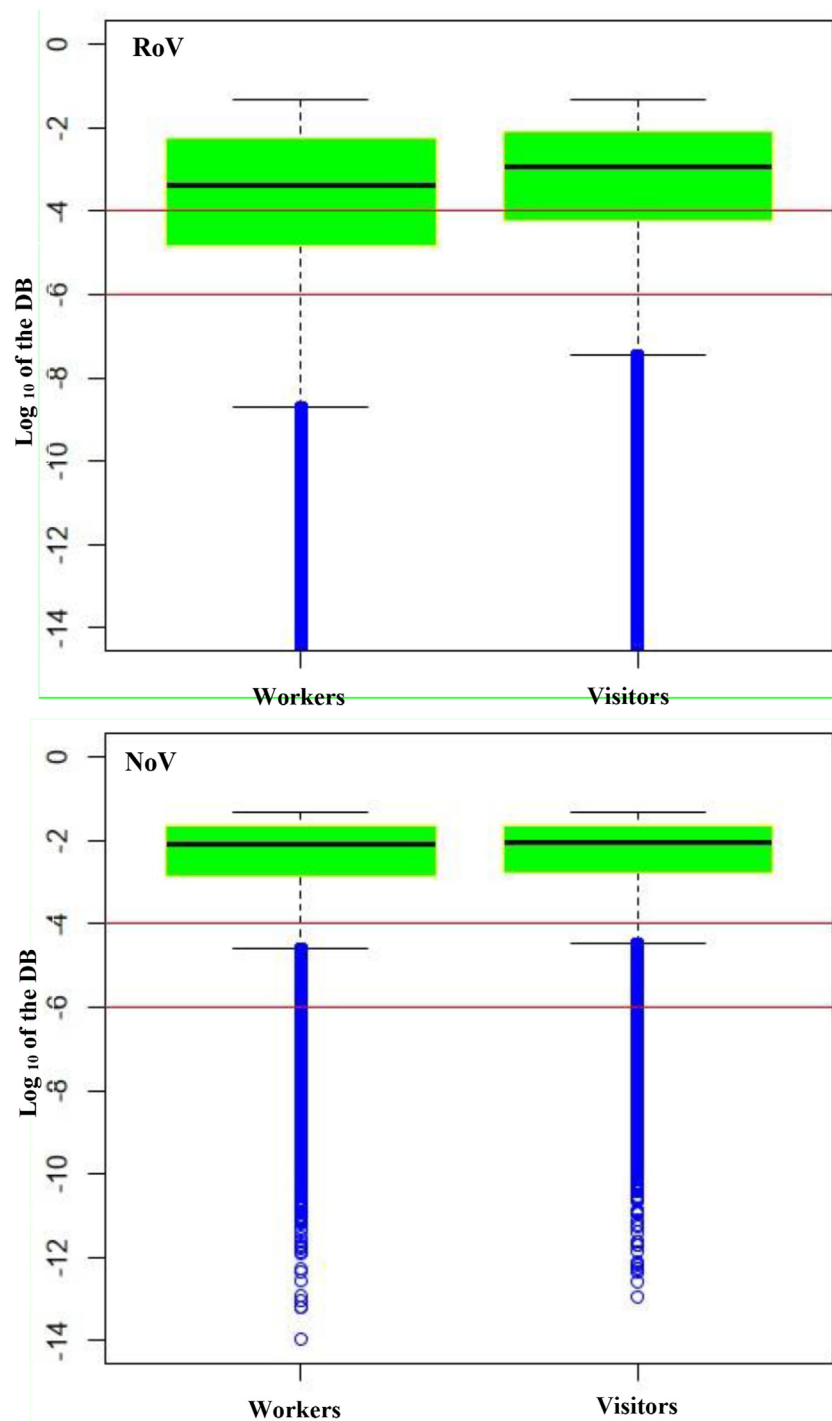


Figure 3. The disease burden (DB) (pppy) estimated for workers and people visiting water spray in the Laleh Park and WHO (10^{-6}) US EPA (10^{-4}) guidelines.

gastrointestinal illness, namely RoV and NoV in air of water spray park was calculated using QMRA. To date, there is no such work available on these two viral agents of concern in water spray park. Therefore, such a procedure would advise the health authorities to inform the existing risk of exposure and consequently mitigate and minimize the detrimental effects [50, 51]. The daily and annual Pinf of exposure to RoV and NoV in air of water spray park for both workers and people visiting the Laleh park are described in Table 3. Generally, the Pinf associated with exposure to both RoV and NoV for workers were calculated to be higher than that for people who visit the water spray park. This highlights the role of exposure time in risk assessment and QMRA; the exposure time for workers and visitors are 8 and 1.5 h per a day. In addition, the higher Pinf

and Pinf.A for NoV compared to those for RoV are attributed to higher dose harmonization for NoV [23]. Until now, some few studies have mainly focused on QMRA of bioaerosols in air, mostly on estimated probability of infection and illness due to exposure to pathogenic viruses in air of wastewater treatment plant (WWTP) [16, 17, 19, 23, 31]. For instance, Cheng Yan et al. (2021) estimated the probability of infection (Pinf) due to exposure to microbial bioaerosols in air of WWTP in China. The results suggested that Pinf for workers were 1–2 orders of magnitude higher than the recommended values by WHO and US.EPA with 10^{-6} pppy and 10^{-4} pppy, respectively [19]. Emmanuel de-Graft Johnson Owusu-Ansah et al. (2017) investigated the annual probability of infection for NoV from wastewater irrigated-vegetables in Gahna and the

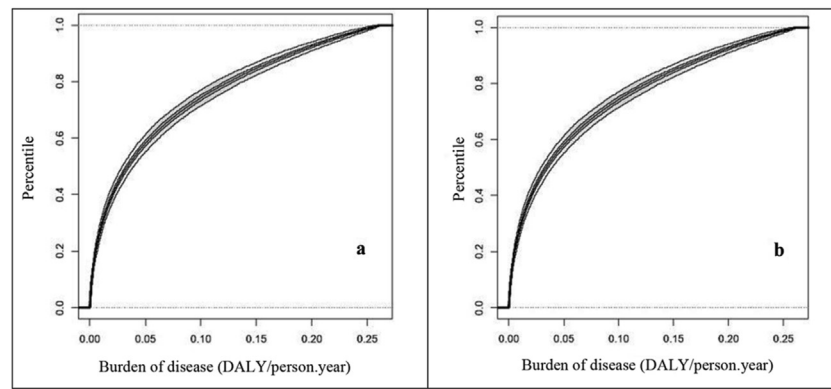


Figure 4. Cumulative distribution plots of RoV with different percentiles (Y-axis) for workers (a) and visitors (b). * Five curves in each plot displays the 2.5th, 25th, median, 75th, and 95th percentile of cumulative distribution function from left to right, respectively.

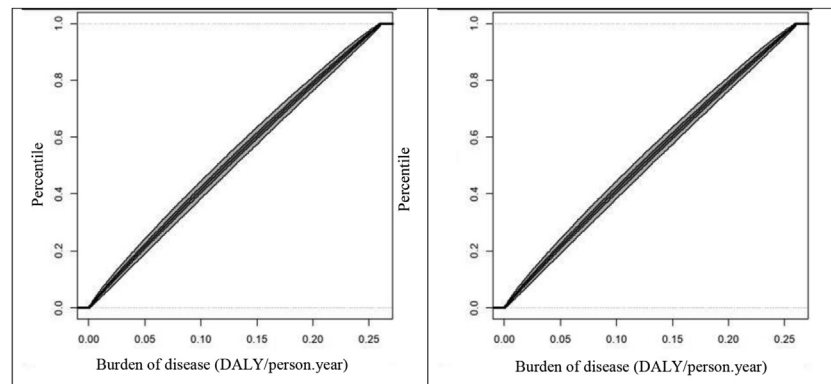


Figure 5. Cumulative distribution plots of NoV with different percentiles (Y-axis) for workers (a) and visitors (b). * Five curves in each plot displays the 2.5th, 25th, median, 75th, and 95th percentile of cumulative distribution function from left to right, respectively.

result indicated that Pinf for all NoV genomes were 9.2×10^{-1} to 9.4×10^{-1} [21]. In addition, Courault et al. (2017) reported that Pinf.A associated viruses emitted from WWTP and pond stabilization in distance of 500 m away were 1.5×10^{-2} pppy [46]. Therefore, since the type of viruses are different in numerous studies, the best scenario for assessment the current situation and QMRA in specific environment is comparison the value with values recommended by WHO (10^{-6} pppy) and US.EPA (10^{-4} pppy). Therefore, the Pinf.A of RoV and NoV in air of water spray park are higher than the mentioned recommended values; mitigation actions are required to reduce the health risk as a consequence of exposure to pathogenic viruses.

4.3. DALY calculation

DALY is a widely acknowledged as a metric to perceive the burden of disease and risk management [32, 52]. WHO evaluate DALY indicator to estimate the health risk due to uncertainty of dose-response models, in particular, with spare data [19, 53]. DALY indicator aids authorities involved in risk management to better discuss the regulatory processes and overcome the uncertainties in risk analysis [54]. The data on the Pill and DB due to exposure to RoV and NoV for workers and visitors are summarized in Table 4. According to Table 4, the medium estimated DB for RoV and NoV for both workers are lower than those calculated in our previous study focused on estimated RoV (5.76×10^{-2}) and NoV (1.23×10^{-1}) in air of Ekbatan WWTP in Tehran, Iran [23]. Yan-huan Chen (2020) surveyed the QMRA corresponding to bacterial bioaerosols under different aeration mode in WWTP and reported that DB for workers exceeded significantly the WHO recommended value ($\leq 10^{-6}$ pppy) [31]. However, the median annual disease burden estimated through the

numeration the norovirus in vegetables irrigated with wastewater was 1.8×10^{-5} – 6.7×10^{-5} , which is lower than the DB estimated here [21]. Therefore, it can be concluded that the exposure pathway is also the important factor in DALY and risk management. Furthermore, as shown in Figure 3, the median estimated DB for RoV and NoV in case of both exposed population, namely workers and visitors in Laleh park are higher than recommended values by WHO and US.EPA with 10^{-6} pppy and 10^{-4} pppy, respectively [45]. To best of our knowledge, estimation the DB for NoV and RoV in water spray park is the first studies in this field. Therefore, such a high airborne concentration and consequently higher DB can be considered as alarming figures for authorities to employ mitigation action to minimize the health risk [55].

4.4. Sensitivity analysis

As in present study, the sensitivity analysis was performed to analyze the level of influence of each UV and U input variables on RoV and NoV annual disease burden [21]. Tornado plot was applied to depict how much each input variable influence the variation of RoV and NoV annual disease burden [56]. The Tornado plot was designed in R version 3.5.1 based on Monto Carlo approach. According to Figure 6(a and b) the most influencing input parameters on variability of DB due to exposure to RoV and NoV were Dose and DBPC, respectively. In case of DB for RoV, the most important influencing were Dose, Concentration and DBPC. While the three influencing parameters on RoV disease burden were DBPC, Dose, Concentration. It is important to note that Dose is influenced by three parameters including concentration, inhalation rate and exposure time, as denoted in Eq. (1). Yan-huan Chen et al. (2021) showed that aerosol ingestion rate, exposure time, and breathing rate are three most

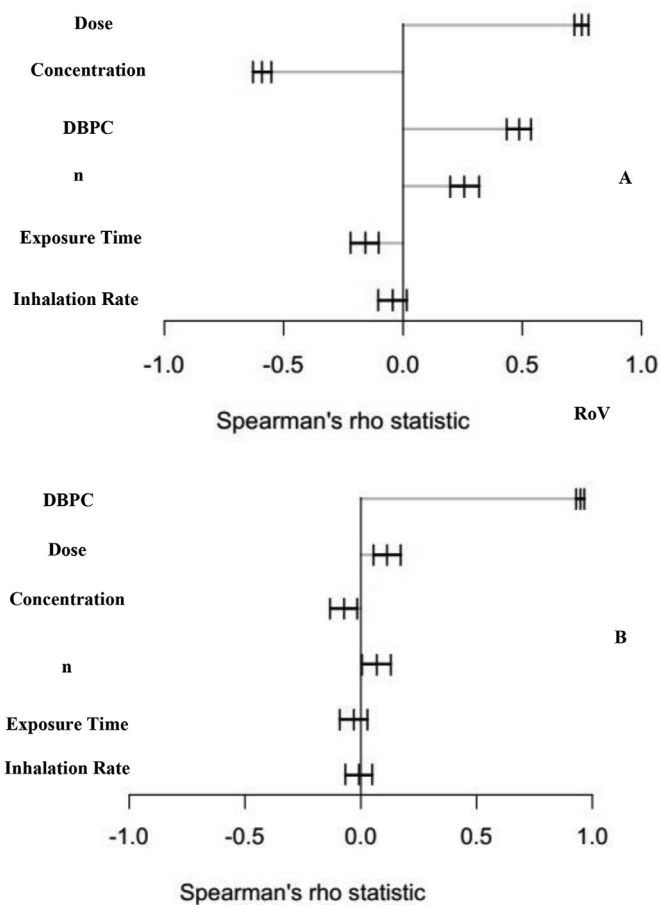


Figure 6. Tornado charts based on spearman's rank correlation shows the correlation between the median estimations of the input factors and the burden of illness (RoV: (A), NoV: (B)).

influencing parameters on variation of response value and health risks [31]. Generally, the sensitivity analysis with important statistical tools identifies the most influential parameters in model and output variable. Therefore, the most influencing parameters should be given much attention when building exposure model; the authorities involved in risk assessment should focused mostly on these parameters [57, 58].

5. Conclusion

In the present research, the viral loads of RoV and NoV, two pathogenic viruses of concern in water spray park were determined by real-time RT-PCR technology. The findings indicated that the highest viral load of RoV and NoV were found in autumn season which are consistent with the great numbers of hospitalization. Among the different meteorological parameters influencing on the concentration levels of viruses, the temperature has the higher appropriation. The risk analysis using Monto Carlo approach indicated that Pinf and DB of exposure to RoV and NoV for both workers and visitors in Laleh park were significantly higher than the recommended values by WHO and US.EPA with 10^{-6} pppy and 10^{-4} pppy, respectively. Therefore, the authorities involved in risk management and wastewater treatment are expected to employ the practical mitigation action to lower the risk of inhalation exposure of these two viruses of great concerns. The most obvious limitation of this study is stratification of risk values for different group of ages with different disease susceptibility, which is due to lack of information on people refer to water spray park.

Declarations

Author contribution statement

Hasan Pasalari: Conceived and designed the experiments; Performed the experiments; Wrote the paper.

Hesam Akbari: Conceived and designed the experiments; Analyzed and interpreted the data.

Angila Ataee-Pirkooh: Performed the experiments; Analyzed and interpreted the data.

Amir Adibzadeh: Contributed reagents, materials, analysis tools or data; Wrote the paper.

Hamed Akbari: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper.

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Data availability statement

Data will be made available on request.

Declaration of interest's statement

The authors declare no conflict of interest.

Additional information

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