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Article

The mediatory role of water quality on the association between extreme precipitation events and infectious diarrhea in the Yangtze River Basin, China

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ABSTRACT

Extreme precipitation is exacerbating the burden of infectious diarrhea in the context of climate change, it is necessary to identify the critical and easy-to-intervene intermediate factors for public health strategies. Water quality may be the most important mediator, while relevant empirical evidence is limited. This study aimed to examine the role of water quality in the process of infectious diarrhea caused by extreme precipitation. Weekly infectious diarrhea cases, meteorological factors and water quality data in Yangtze River Basin in China between October 29, 2007 to February 19, 2017 were obtained. Two-stage statistical models were used to estimate city-specific extreme precipitation, water quality and infectious diarrhea relationships that were pooled to derive regional estimates. A causal mediation analysis was used to assess the mediation effect of water quality. In Yangtze River Basin, extreme precipitation events had a significant impact on infectious diarrhea (Incidence Rate Ratios [IRR]: 1.027, 95% Confidence Interval [CI]: 1.013~1.041). After extreme precipitation events, the dissolved oxygen (DO) in surface water decreased (-0.123 mg/L, 95%CI: -0.159 mg/L~-0.086 mg/L), while the un-ionized ammonia (NH(3)-N) increased (0.004 mg/L, 95%CI: 0.001 mg/L~0.006 mg/L). The combined overall effect of DO and NH(3)-N on infectious diarrhea showed that both low and high concentrations were associated with an increased risk of infectious diarrhea. The causal mediation analysis showed that the mediation proportion of the two water quality indexes (DO and NH(3)-N) is 70.54% ($P < 0.001$). To reduce the health effects of extreme precipitation, in contrast to current population-oriented health strategies, those that take into account more direct and easy-to-intervene water quality indicators should be encouraged by future policies.

1. Introduction

Infectious diarrhea is a typical climate-sensitive disease caused by a variety of microorganisms such as bacteria, viruses, fungi, or parasites [1]. Meteorological factors can directly affect the reproduction, virulence and transmission of diarrhea pathogens [2], and at the same time affect the vulnerability of the population, destroy the protective social infrastructure [3], and eventually lead to infectious diarrhea infection [4]. Epidemiological evidence indicates that high temperature may increase the risk of infectious diarrhea [5,6]. Besides, water (including precipitation, surface water and ground water) has been shown in a plurality of studies to dramatically affect the transmission dynamics of Infectious diarrhea from the microbial level to the host level [7,8].

Climate change leads to changes in the total amount of water resources and their redistribution in temporal and spatial distribution, ultimately increasing the frequency and intensity of extreme weather events such as extreme precipitation, flood and drought [9]. According to the Blue Book on Climate Change in China (2022), extreme precipitation events in China showed an increasing trend during 1961–2021 [10]. And the results of climate prediction models show that this phe-

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nomenon will continue to develop [11]. China is a sensitive area of climate change, the change of extreme precipitation is significant and prominent [12], and its impact on the natural environment, economic development and population health is more intense [13]. In addition to directly causing casualties [14], extreme precipitation events could also result in increased risk of infectious diseases such as infectious diarrhea [15–17]. And because of China's large population, the enormous burden of infectious diarrhea, caused by extreme precipitation events has become a growing problem ravaging public health [18]. This underscores the need for effective public health strategies in the context of improving understanding of environmental coupling.

Although it has been recognized that extreme precipitation can lead to a prominently increased risk of infectious diarrhea, the disease burden still remained significant. This phenomenon is fundamental due to the inadequate understanding of current research on infectious diarrhea and extreme precipitation events, which remains in a simple association study [19]. In fact, many links are also embedded in the process of extreme precipitation events leading to infectious diarrhea [20]. Identifying intermediate factors would provide a more feasible and efficient implementation idea for public health interventions.

To date, some researchers have conducted theoretical studies on the mechanism of extreme precipitation leading to infectious diarrhea, and found that water quality is probably the key intermediate link [20,21]. As one of the typical water-borne diseases, diarrhea pathogen spreads through water to infect people and thus induce disease. Extreme precipitation events, as the most common hydro-meteorological disasters, will bring pathogens and pollutants in the soil environment and air into the water through "runoff effect" and "sedimentation effect" respectively, which will affect the water quality indicators closely related to the survival and reproduction of pathogenic microorganisms in the water [22,23]. In addition, the decline of water quality will affect the water purification efficiency of domestic water treatment system. Meanwhile, extreme precipitation events will damage domestic water treatment equipment [24], or cause combined sewer overflow events [25]. Eventually, people may contact and ingest contaminated water, leading to the occurrence of infectious diarrhea [25,26].

In exploring the specific pathways by which extreme precipitation events lead to infectious diarrhea, high priority should be placed on water quality as a key intermediate. However, insufficient evidence has been provided in existing empirical studies, which are rather fragmented. Yangtze River Basin in China (Fig. 1) is one of the areas with the most frequent extreme precipitation events in China [27]. It is also the area with the highest burden of infectious diarrhea in China. Based on the monitoring of water quality and infectious diseases in the whole Yangtze River Basin, a regional study will be conducted in 97 cities in Yangtze River Basin. Firstly, the basic association between extreme precipitation, water quality, and infectious diarrhea will be evaluated respectively. Then, causal mediation analysis will be continued to assess the role of water quality in the relationship between extreme precipitation and infectious diarrhea.

2. Methods

2.1. Study area

Yangtze River Basin in China has two distinct climatic zones. One is the Alpine Plateau climate in the upper reaches and the other is the subtropical monsoon climate in the middle and lower reaches. The upper reaches of Yangtze River Basin are cold and dry, with little precipitation. The middle and lower reaches have four distinct seasons and abundant rainfall. The different climatic zones imply the exposure in this study, that is, the patterns of extreme precipitation events are quite different. Therefore, in this study, Yangtze River Basin is divided into these two regions based on their natural and geographical characteristics.

A total of 97 prefecture-level cities were included in the study (including 2 municipalities directly under the central government and 95 prefecture-level cities). There are 33 cities in the upper reaches and 64 cities in the middle and the lower reaches.

2.2. Data collection

2.2.1. Diarrhea data

According to the classification in *Chinese Diagnostic Criteria for Infectious Diarrhea* and the *Law of the People's Republic of China on the Prevention and Treatment of Infectious Diseases*, infectious diarrhea in addition to cholera, dysentery, typhoid and paratyphoid are classified as other infectious diarrhea (OID). From October 29, 2007 to February 19, 2017, the anonymous data of patients with diarrhea, including age, onset date, disease type and administrative code information of cities, were extracted from China National Infectious Disease Monitoring System (NDSS) and were verified. We aggregated the individual infectious diarrhea data and counted the weekly number of diarrhea cases by city for further statistical analyses.

2.2.2. Water quality data

Weekly surface water quality data from 37 stations over the study period were acquired from the China National Environmental Monitoring Centre (http://www.cnemc.cn/), with 7 stations in the upper reaches and 30 stations in the middle and lower reaches. The site published data on four water quality indicators: pH, dissolved oxygen (DO), unionized ammonia (NH(3)-N) and permanganate index. Based on previous studies, it is likely that DO [28] and NH(3)-N [29] are involved in the survival and reproduction of pathogenic microorganisms in water and can reflect the level of biological contamination in surface water [30]. Therefore, the effects of DO and NH(3)-N are mainly considered in this study. In addition, the pH value was included as a control variable in the analysis of the relevant data since it may affect the concentration of DO and NH(3)-N in surface water. The weekly water quality data were interpolated to each city in the study area respectively by the inverse distance weighted (IDW) interpolation technique in ArcGIS 10.2 (Environmental System Institute, Redland, California, USA). IDW is a deterministic method that takes into account spatial autocorrelation among water quality observations and estimates the value of a given location by weighted average of observations from monitoring stations within a specific search window [31].

2.2.3. Meteorological data

The baseline meteorological data came from the ERA5 reanalysis data set of the European Centre for Medium-Range Weather Forecasts (ECMWF, https://www.ecmwf.int/). These data included the daily temperature, precipitation, relative humidity and other grid meteorological data in China during this study. The grid resolution is $0.25^\circ * 0.25^\circ$. Based on this, the average value of all grid data covered by each city was calculated to assess the daily mean temperature, precipitation, relative humidity and other meteorological data of this city. Afterward, all meteorological data were aggregated to a weekly resolution.

2.2.4. Sociodemographic data

Besides, the annual population of residents and urbanization rate of each city were retrieved from China Statistical Yearbook (http://www.stats.gov.cn/tjsj/ndsj/) to allow for standardization and comparability. The effect of water quality on human health may be significantly affected by the coverage of sanitary toilets, the level of infrastructure construction and the economic development level in rural areas [32]. In this study, the urbanization rate was used as a substitution variable to control these variables that are unavailable.

2.3. Statistical analysis

2.3.1. Association analysis

The two-stage modeling approach was mainly adopted: firstly, the model was built separately in the 97 cities in Yangtze River Basin.

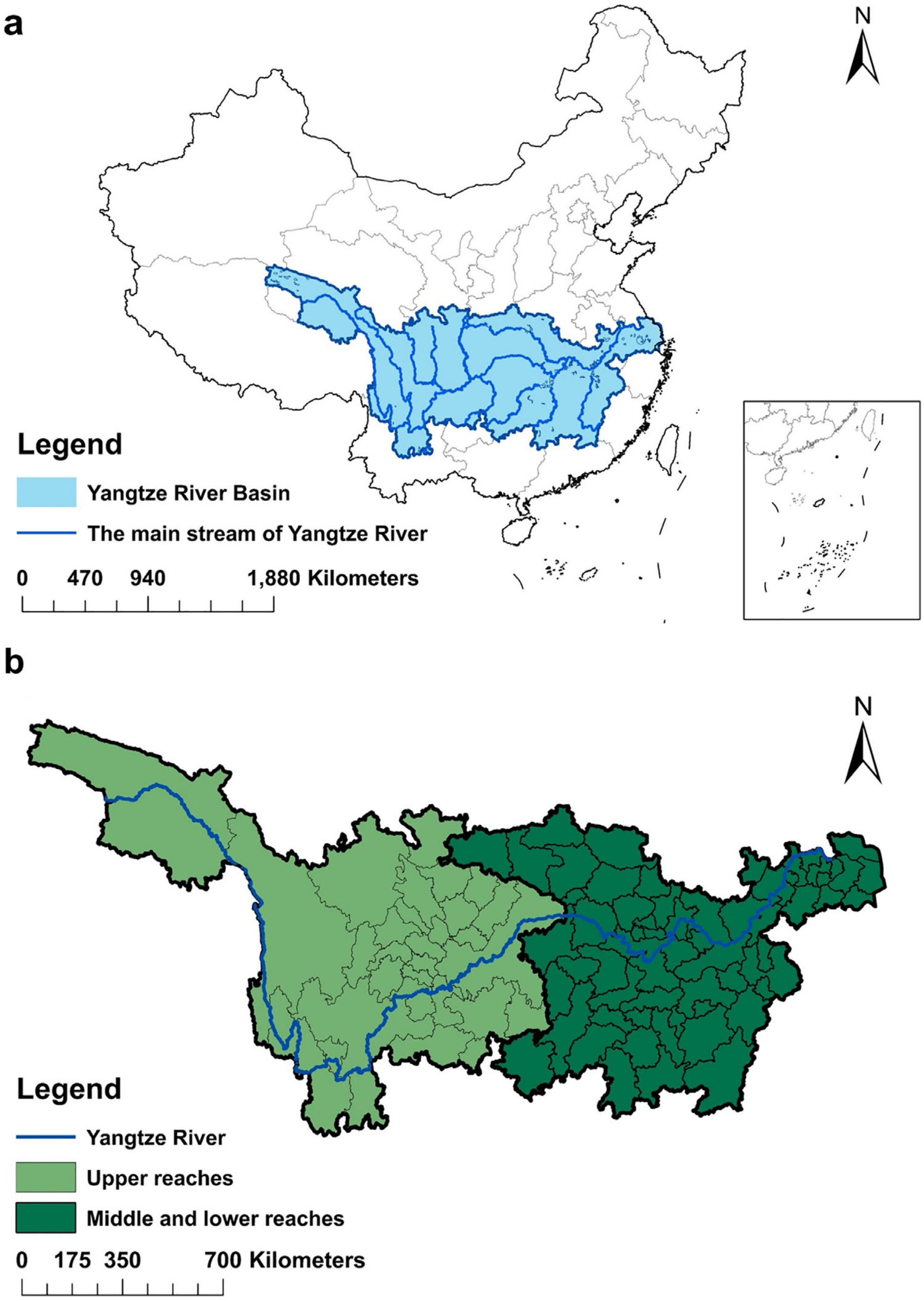

Fig. 1. Location of Yangtze River Basin in China (a) and subregions of Yangtze River Basin (b). Note: These maps were made based on the standard map (approval number: GS (2019)1822) downloaded from the standard map service of the Ministry of Natural Resources of the People's Republic of China, and the base map was not modified.

Afterward, the pooled effects in the whole Yangtze River Basin, the upper reaches of the Yangtze River and the middle and lower reaches of the Yangtze River were estimated by the meta analysis.

A generalized linear model with quasi-Poisson distribution was used to establish the association between extreme precipitation events and infectious diarrhea. (Model 1)

Model 1:

$$\begin{aligned} logE\left[\textstyle\sum_t^{t+L} Count_{it}\right] &= \alpha + \beta_1 Extreme_{it} + s_1\left(Tem|df\right) + s_2\left(Hum|df\right) \\ &+ s_3\left(WeekNumber_{it}|df = 11\right) + \beta_2 UR_{it} \\ &+ \log\left(Population_i\right) + \varepsilon \end{aligned}$$

In this study, extreme precipitation events were defined as the daily precipitation level greater than 95th quantiles of historical city precipitation during the study. $Extreme_{it}$ is a binary variable. If an extreme precipitation event occurred at least once in city i within the week t, this variable is defined as 1. Where $E[\sum_t^{t+L} Count_{it}]$ was the expected accumulated weekly all-cause infectious diarrheal counts in city i from week t to week $t + L$. L was the maximum lag week, the subsequent period L was set to 4 weeks. The degrees of freedom were chosen based on the minimum quasi-AIC (Akaike Information Criterion). The long-term trends of temperature, humidity and time and the urbanization rate were further controlled by using natural cubic splines for Week Number in the study, with 11 degrees of freedom for the 11 years of the study. Moreover, the population was added as an offsetting item for better comparison between cities.

A generalized linear model with Gaussian distribution was used to establish the association between extreme precipitation events and two water quality indicators (DO and NH(3)-N). (Model 2)

Model 2:

$$E\left[WQ_{it}\right] = \alpha + \beta_1 Extreme_{it} + s_1(Tem|df) + s_2(Hum|df) \\ +s_3(WeekNumber_{it}|df = 11) + \beta_2 UR_{it} + \epsilon$$

where $E[WQ_{it}]$ was the expected concentration of water quality indicators (DO, NH(3)-N) in city *i*. And all the other variables were defined for model 1.

The effect of DO and NH(3)-N on the incidence of infectious diarrhea was established respectively with the generalized linear model combined with a distributed lag nonlinear model (DLNM). (Model 3)

Model 3:

$$log E\left[Count_{it}\right] = \alpha + cb(DO_{it}) + cb(HN3.N_{it}) + s_1\left(pH_{it}|df\right) \\ +s_2(WeekNumber_{it}|df = 11) + \beta_1 UR_{it} \\ +\log\left(Population_i\right) + \epsilon$$

where $cb()$ was a bidimensional cross-basis natural cubic spline function. Weekly mean DO concentration was applied with the cross-basis natural cubic spline function with 2 weeks of lag for both response (degrees of freedom, *df* = 6) and lag dimension (*df* = 3). While, weekly mean NH(3)-N concentration was applied with the cross-basis natural cubic spline function with 4 weeks of lag for both response (*df* = 4) and lag dimension (*df* = 3). $E[Count_{it}]$ were the expected accumulated weekly all-cause infectious diarrheal counts in city *i* during week *t*. And pH_{it} represented the pH in the surface water of city *i* during the week *t* was also controlled by a natural cubic spline. All the other variables were defined for model 1 and 2.

2.3.2. *Causal mediation analysis*

Causal mediation analysis was performed to evaluate the proportion of the relationship between extreme precipitation event and all-cause infectious diarrheal diseases mediated by DO or/and NH(3)-N at the region level. Causal mediation analyses are a seminal methodological development for mediation focuses on evaluating the causal mediation effects based on a counterfactual or potential outcomes approach to mediation analysis [33]. Its purpose is to reveal the relation between independent variables and dependent variables. The mediating effect is multiple causalities composed of independent variables, mediators, and dependent variables. The regression-based method was used to evaluate the total natural indirect effect (TNIE) and the total natural direct effect (TNDE) [34]. TNIE represents the effect of extreme precipitation events on infectious diarrhea by acting on mediators. TNDE means the direct effect of extreme precipitation events on infectious diarrhea. Afterward, the proportion of association of mediators (TNIE/[TNDE+TNIE]) can be estimated to quantify the size of mediators [34].

We chose 0.05 (two-sided) as our statistical significance level. All data management and analyses were conducted in ArcGis (version 10.2) and R (version 4.2.1; R Development Core Team) (http://www.r-project.org), using packages "dlnm", "tsModel", "mvmeta", and "CMAverse".

3. Results

As reported by the China National Infectious Disease Monitoring System, a total of 2,806,995 cases of infectious diarrhea occurred in Yangtze River Basin during the study period, including 1,841,311 occurred in the middle and lower reaches of the Yangtze River, accounting for 84.37% of all cases. Specifically, OID (77.75%) and dysentery (20.77%) were the main types of infectious diarrhea. Most cases occurred in the summer, followed by those in the autumn (Table 1). Furthermore, although the diarrhea cases in the two regions mainly were OID, the proportion of dysentery cases in the upper reaches of the Yangtze River was much higher than the middle and lower reaches. The urbanization rate, mean temperature, weekly cumulative precipitation and mean relative humidity in the middle and lower reaches of the Yangtze River were higher than those in the upper reaches of the Yangtze River. In terms of water quality data, the average pH value and DO concentration in the middle and lower reaches were lower than those in the upper reaches, while the average concentration of NH(3)-N was higher than that in the upper reaches (Table 2).

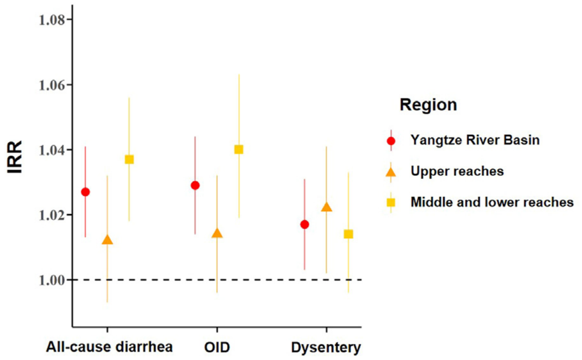

Fig. 2. The incidence rate ratios for the association between an extreme precipitation event and infectious diarrhea by region. Abbreviations: IRR, incidence rate ratios; OID, other infectious diarrhea.

The risk of infectious diarrhea increased after extreme precipitation events. However, different types of infectious diarrhea were mainly affected by extreme precipitation events in different regions and different seasons. As shown in Fig. 2, a significant increase in the incidence of all-cause infectious diarrhea caused by extreme precipitation could be observed in Yangtze River Basin (Incidence Rate Ratio [IRR]: 1.027, 95% Confidence Interval [CI]: 1.013~1.041). Stratified analysis showed that the incidence of both OID and dysentery increased significantly after extreme precipitation events (IRR: 1.029, 95%CI: 1.014~1.044; IRR: 1.017, 95%CI: 1.003~1.031, respectively). OID was significantly associated with extreme precipitation events only in winter (IRR: 1.078, 95%CI: 1.048~1.108). In terms of dysentery, the effect was only significant in summer (IRR: 1.016, 95%CI: 1.000~1.032) (see Table S1 for the results of seasonal stratified analysis).

The results of the analysis by regions showed that the incidence of all-cause infectious diarrhea in the middle and lower reaches of the Yangtze River increased significantly after extreme precipitation (RR: 1.037, 95%CI: 1.018~1.056), while the effect was insignificant in the upper reaches (RR: 1.012, 95%CI: 0.993~1.032). In addition, there were differences in the specific types of infectious diarrhea sensitive to extreme precipitation events between the two regions. In the middle and lower reaches of the Yangtze River, extreme precipitation events mainly resulted in an increase in the risk of OID. However, in the upper reaches of the Yangtze River, extreme precipitation events mainly led to a significant increase in the risk of dysentery. The further seasonal stratified analysis showed that the effect of extreme precipitation events in the upper reaches was significant only in winter. In the middle and lower reaches, however, extreme precipitation in summer was associated only with an increased risk of dysentery, and extreme precipitation in winter was associated only with an increased risk of OID.

In Yangtze River Basin, after extreme precipitation events, the DO in the surface water decreased significantly (decreased by 0.123 mg/L, 95% CI: −0.159 mg/L~−0.086 mg/L), while the NH(3)-N significantly increased (increased by 0.004 mg/L, 95% CI: 0.001 mg/L~0.006 mg/L) (Fig. 3). However, this change was insignificant in the upper reaches of

Table 1
Summary statistics of infectious diarrhea in Yangtze River Basin during October 29, 2007 to February 19, 2017.

Characteristics	Yangtze River Basin (*N* = 2806,995)	Upper reaches (*N* = 965,684)	Middle and lower reaches (*N* = 1841,311)
	N (%)	*N* (%)	*N* (%)
All-cause diarrhea	**2806,995**	**965,684**	**1841,311**
Cholera	426 (0.02)	210 (0.02)	216 (0.01)
Typhoid	41,225 (1.47)	20,302 (2.10)	20,923 (1.14)
Dysentery	582,909 (20.77)	256,971 (26.61)	325,938 (17.70)
OID	2182,435 (77.75)	688,201 (71.27)	1494,234 (81.15)
Season[a]			
Spring	547,006 (19.49)	203,775 (21.10)	343,231 (18.64)
Summer	844,972 (30.10)	277,610 (28.75)	567,362 (30.81)
Fall	780,412 (27.80)	259,348 (26.86)	521,064 (28.30)
Winter	634,605 (22.61)	224,951 (23.29)	409,651 (22.25)

Abbreviations: OID, other infectious diarrhea.

[a] Seasons are divided according to the following rules: Spring from March to May, Summer from June to August, Fall from September to November, and Winter from December to February.

Table 2
Distributions of climate condition, water quality and urbanization rate at different reaches of Yangtze River Basin (2007–2017 average).

Characteristic	Yangtze River Basin Mean (SD)	Upper reaches Mean (SD)	Middle and lower reaches Mean (SD)
Climate			
Mean Temperature (°C)	15.03 (8.73)	13.01 (8.40)	16.07 (8.72)
WAP (mm)	24.95 (30.67)	19.62 (24.94)	27.70 (32.90)
Mean RHU (%)	74.74 (10.42)	74.12 (12.38)	75.07 (9.23)
Water quality			
pH	7.69 (0.26)	7.83 (0.22)	7.61 (0.25)
DO (mg/L)	8.15 (1.35)	8.15 (1.06)	8.14 (1.48)
NH(3)-N (mg/L)	0.30 (0.20)	0.24 (0.15)	0.33 (0.22)
Urbanization Rate (%)	47.80 (14.14)	39.96 (12.63)	51.84 (13.14)

Abbreviations: WAP, weekly cumulative precipitation; DO, dissolved oxygen; NH(3)-N, un-ionized ammonia; SD, standard deviation.

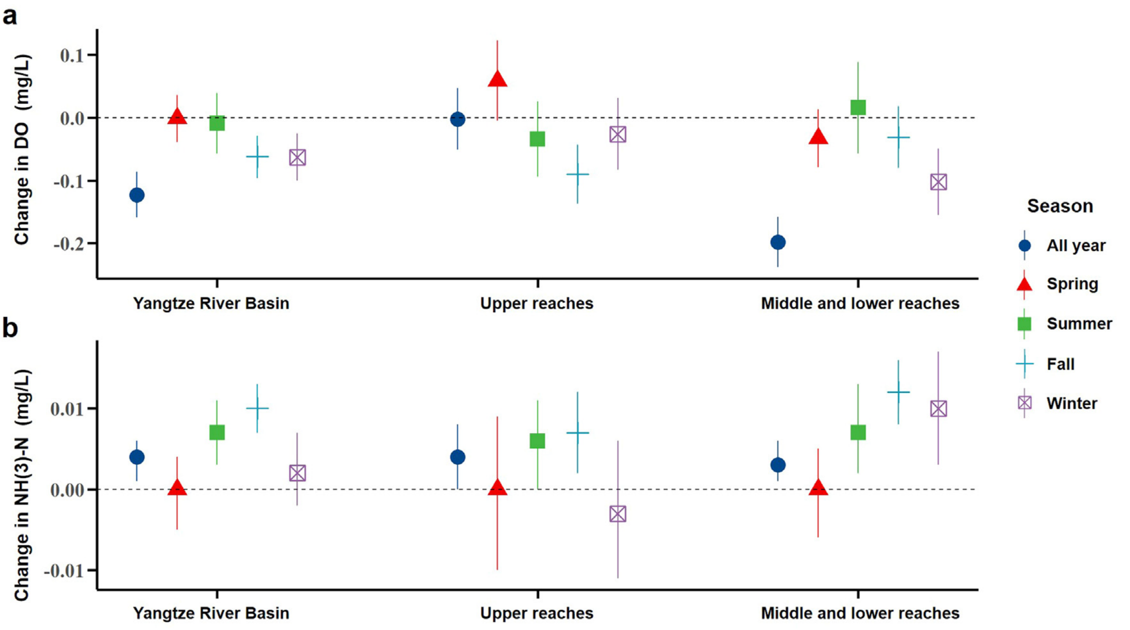

Fig. 3. Changes in water quality after an extreme precipitation event by different region and season. Abbreviations: DO, dissolved oxygen; NH(3)-N, un-ionized ammonia.

the Yangtze River. Besides, different water quality indexes were affected by extreme precipitation events by different seasonal patterns. The stratified analysis showed that the DO mainly decreased significantly in winter (decreased by 0.063 mg/L, 95%CI: −0.100 mg/L~−0025 mg/L), while NH(3)-N mainly increased significantly in summer (increased by 0.007 mg/L, 95%CI: 0.003 mg/L~0.011 mg/L).

Seasonal patterns in the middle and lower reaches of the Yangtze River were similar to those in the whole Yangtze River Basin. Nonetheless, in the upper reaches of the Yangtze River, neither DO nor NH(3)-N showed significant change after extreme precipitation events. But a stratified analysis showed that significant effects of extreme precipitation on surface water quality can still be observed in specific

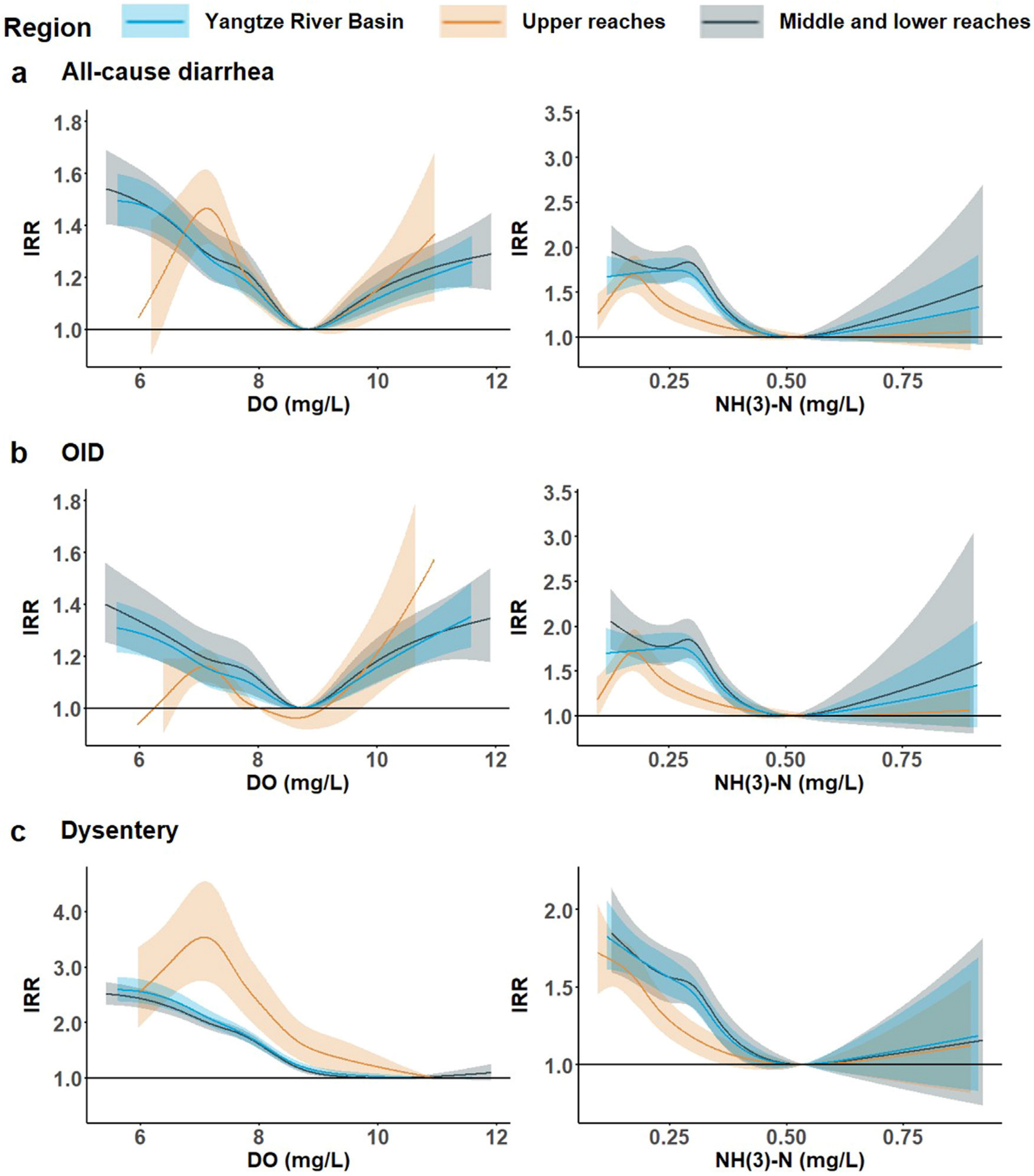

Fig. 4. Pooled estimates of water quality effect on infectious diarrhea in Yangtze River Basin, China. Abbreviations: IRR, incidence rate ratios; DO, dissolved oxygen; NH(3)-N, un-ionized ammonia; OID, other infectious diarrhea.

seasons. In the upper reaches, a significant decrease in the DO concentration was observed in autumn, while a significant increase in the concentration of NH(3)-N was observed in both summer and autumn.

The low or high concentrations of DO and NH(3)-N in the surface water were associated with the increase in the incidence of all-cause infectious diarrhea, but the patterns in which different types of diarrheas were affected by water quality were different. Fig. 4 shows the pooled associations between the two water quality indexes and different types of infectious diarrhea. The pooled overall effect of DO on all-cause infectious diarrhea was a U-shaped curve. An increase in the risk of all-cause infectious diarrhea could be observed under both low and high concentrations of DO. Similarly, the overall effect of NH(3)-N on all-cause infectious diarrhea was also an approximate U-shaped curve. Moreover, after the stratification by the regions and diarrhea types, the association between dysentery and DO was observed to be significant only under low DO concentration; the effect of high DO concentration on dysentery almost disappeared.

To summarize the above correlation analyses results, we could find two different patterns between the upper reaches of the Yangtze River and the middle and lower reaches of the Yangtze River. In the middle and lower reaches of the Yangtze River, extreme precipitation events might result in a significant increase in the incidence of dysentery mainly by increasing the concentration of NH(3)-N in the surface water in summer, and lead to a significant increase in the incidence of OID mainly by decreasing the concentration of DO. Nevertheless, in the upper reaches of the Yangtze River, extreme precipitation events might result in a significant increase in the incidence of OID and dysentery mainly by decreasing the DO concentration in surface water.

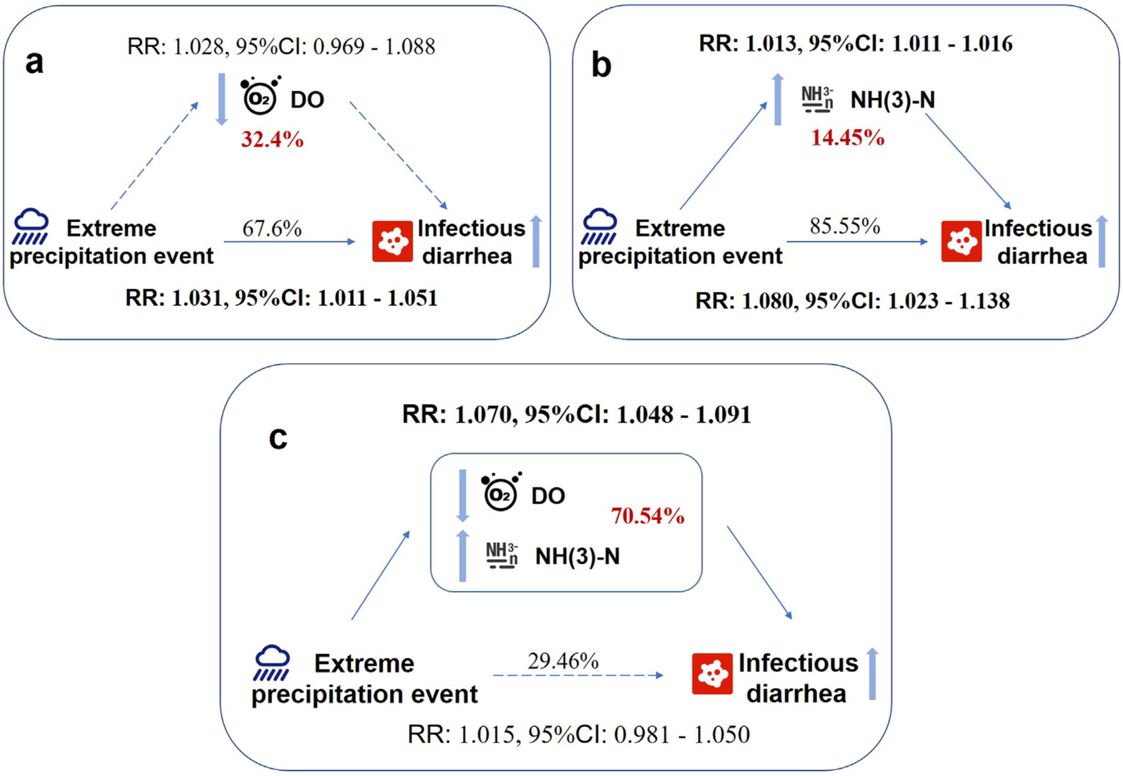

Fig. 5. Directed acyclic graphs of the mediating effect between extreme precipitation event and infectious diarrhea. Abbreviations: RR, rate ratios; CI: confidence interval; DO, dissolved oxygen; NH(3)-N, un-ionized ammonia. Crude association between extreme precipitation and infectious diarrhea mediated by DO (a), NH(3)-N (b) and both (c). Dashed horizontal arrows indicate the total natural direct effect, i.e., the association between extreme precipitation and infectious diarrhea that is not attributable to DO. Solid oblique arrows indicate the natural indirect effect, i.e., the association between extreme precipitation and infectious diarrhea that is attributable to DO.

Both DO and NH(3)-N play an intermediary role between extreme precipitation and infectious diarrhea. Moreover, when DO and NH(3)-N were simultaneously considered, the proportion of the mediating effect increased significantly. Table S2 and Fig. 5 showed the proportion of the direct and indirect association and mediation between extreme precipitation events and all-cause infectious diarrhea. Both DO and NH(3)-N showed significant mediator effect in the pathways in which diarrhea was affected by extreme precipitation. The mediation proportion was 32.40% ($P < 0.001$) and 14.45% ($P < 0.001$), respectively. According to the results of the single mediator model considering DO, the main effect of extreme precipitation events on infectious diarrhea was reflected in the direct effect of extreme precipitation events (TNDE: 1.031, 95%CI: 1.011, 1.051), while the indirect effect of causing infectious diarrhea by acting on DO was insignificant (TNIE: 1.028, 95%CI: 0.969, 1.088). According to the results obtained with the NH(3)-N -considering single mediator model, both direct and indirect effects are significant. The direct effect of extreme precipitation events on infectious diarrhea was 1.080 (95%CI: 1.023, 1.138), while the indirect effect was 1.013 (95%CI: 1.011, 1.016).

The multi-mediators causal mediation analysis showed that the proportion of the mediating effect increased significantly under the joint action of DO and NH(3)-N and was 70.54% ($P < 0.001$). At this time, the effect of extreme precipitation events on infectious diarrhea was dominated by the indirect effect mediated via DO and NH(3)-N (TNIE: 1.070, 95%CI: 1.048, 1.091), while the direct impact of extreme precipitation events was insignificant (TNDE: 1.015, 0.981, 1.050).

Sensitivity analysis were performed to examine the robustness of all main findings at regional level. We repeated our analyses defining extreme precipitation event at the 90th and 99th percentile. The results of sensitivity analyses remained similar to the main model. And the results showed similar patterns of pooled association with infectious diarrhea (Fig. S1) and water quality indexes (Fig. S2).

In addition, in order to explore whether it is appropriate to combine the middle and lower reaches of the Yangtze River into one region, this study separate them into two regions in the sensitivity analysis to determine if there are differences in the main results between the two regions. The sensitivity analysis shows that the main results of this study are consistent in the middle reaches and the lower reaches. After extreme precipitation events, the risk of infectious diarrhea increased significantly in both the middle and lower reaches (IRR: 1.017, 95%CI: 1.002~1.032; IRR:1.116, 95%CI: 1.085~1.149, respectively). In the middle reaches and the lower reaches, the concentration of NH(3)-N in surface water both increased (0.004, 0.000~0.016; 0.046, 95%CI: 0.021~0.071, respectively), and the concentration of DO both decreased (−0.026, 95%CI: −0.033~−0.020; −0.033, 95%CI:−0.044~−0.023, respectively) after extreme precipitation event. It was also observed in both regions that low or high concentrations of DO and NH(3)-N in surface water were associated with increased incidence of all-cause infectious diarrhea (Fig. S3).

4. Discussion

This is the first epidemiological study to evaluate the role of water quality in the association between infectious diarrhea and extreme precipitation events at the city and regional levels. It was found that extreme precipitation events had a close bearing on infectious diarrhea in Yangtze River Basin. After the extreme precipitation event, the concentration of DO in surface water decreased and the concentration of NH(3)-N increased. The effect curves of DO and NH(3)-N on infectious diarrhea showed that the low concentration of DO and high concentration of NH(3)-N in surface water were all associated with the increased incidence of infectious diarrhea. Finally, further causal mediation analysis showed that water quality is the key intermediary factor, and that 70.54% of the effect of extreme precipitation events on all-cause infectious diarrhea was caused by influencing DO and NH(3)-N concentrations in surface water.

The results of our extreme precipitation-diarrhea analyses are consistent with those of previous studies [35,36]. In contrast to previous studies, we further divided our study areas and subdivided infectious diarrhea into OID, dysentery. In this study, extreme precipitation events were shown to markedly increase the risk of dysentery in the upper reaches of the Yangtze River, and other infectious diarrhea in the middle and lower reaches of the Yangtze River. This probably results from the backward level of economic development, the relatively low penetration rate of tap water and rural sanitary toilets, and the developed animal husbandry in the upper reaches of the Yangtze River, making it easier to spread dysentery through fecal-oral transmission [4]. For the middle and lower reaches of the Yangtze River, where population density is higher, people may be more severely affected by OID, considering that a large proportion of OID in China is viral diarrhea caused by rotavirus and norovirus [18].

No matter in the upper reaches or the middle and lower reaches of the Yangtze River, the changes of water quality after extreme precipitation events showed the pattern of DO concentration decreasing and NH(3)-N concentration increasing. A multinational study also reported a negative association between dissolved oxygen and precipitation [37]. The reason for this concentration changes phenomenon may be that extreme precipitation events strengthen the circulation of nutrients and organic substances between the affected areas and water sources, which may lead to increased nutrient concentrations that promote algal blooms and consume large amounts of DO in surface waters [38].

In addition, extreme precipitation events will result in the “runoff effect” by flushing microorganisms, nitrogenous fertilizer pathogens, and human/animal waste from the soil into surface waters [39]. After extreme precipitation, a large amount of NH(3)-N in human and animal feces pollute the surface water in a short time [40], and directly lead to the increase of NH(3)-N concentration in water [41,42]. In areas with developed animal husbandry, backward economic levels, and low penetration of sanitary latrines, there are more human and animal feces enriched with diarrheal pathogens in the soil environment. The “runoff effect” of extreme precipitation events in these regions may be more significant. Extreme precipitation events may also bring nitrogen-containing dust and gas pollutants from the atmospheric environment into surface water through “sedimentation effect”, resulting in an increase in NH(3)-N concentration [43]. In regions with high level of urbanization and heavy air pollution, the “runoff effect” may not be significant. In that case, the “sedimentation effect” of extreme precipitation events may play the main role in increasing the concentration of NH(3)-N in surface water.

Low or high concentrations of DO and NH(3)-N in surface water have a close bearing on increased risk of infectious diarrhea. For one thing, these water quality indicators can affect the reproduction of diarrhea pathogens in surface water; for another, they can also reflect the changes of water quality and microorganisms in surface water. Specifically, there are many kinds of pathogens that can cause diarrhea, among which aerobic and facultative anaerobic bacteria depend on oxygen to survive and reproduce in the water environment. Therefore, increased dissolved oxygen concentrations in surface water provide a more suitable living environment for these diarrhea pathogens, which eventually leads to an increased risk of infectious diarrhea. In case of water eutrophication, or when the “runoff effect” of extreme precipitation events leads to a large number of exotic microorganisms (including diarrhea pathogens) entering the surface water, water contaminated by pathogens will increase the risk of infectious diarrhea [44,45]. In addition, eutrophic water sources will flood the water supply and sanitation infrastructure, which will also increase the risk of infectious diarrhea [46]. In this case, the number of microorganisms in water increases rapidly, consuming a large amount of dissolved oxygen, which is reflected in the decrease of dissolved oxygen concentration in water. It is concluded that low concentration of DO is correlated with the increased risk of infectious diarrhea.

For the association between NH(3)-N and infectious diarrhea, when human or animal feces enter the surface water, the concentration of NH(3)-N in the water will increase significantly [40]. Infectious diarrhea pathogens, mainly infected through fecal-oral transmission, will contaminate surface water, leading to an increased risk of infectious diarrhea [47]. In this case, high levels of NH(3)-N in surface water were observed to be associated with an increased risk of infectious diarrhea. In addition, NH(3)-N, as a nitrogen source existing as free ammonia and ammonium ions in water, is an important nutrient for microorganisms. When diarrheal pathogens and a large number of other microorganisms enter surface water from atmospheric or soil environments, the NH(3)-N in surface water are rapidly consumed. In this case, low concentrations of NH(3)-N surface water were observed to be associated with an increased risk of infectious diarrhea.

To our knowledge, only one empirical study in northern Botswana systematically explored the relationship between precipitation, water quality and diarrhea. In the study conducted by Alexander et al. [39], the impact of rainfall on water quality (including the bimonthly *E. coli* count and total suspended solids), diarrhea cases of children under 5 years old, and the impact of water quality on children’s diarrhea were investigated. The study showed that in rainy season, rainfall had a significant impact on diarrhea of children under 5 years old. Rainfall, minimum temperature and river height predicted the concentration of Escherichia coli, while the increase of *E. coli* in rivers was positively correlated with diarrhea cases. Nevertheless, only the association between these three factors was explored in this study, while whether water quality was a mediator of the rainfall diarrhea association was not further verified.

Based on the association study, causal mediation analysis was further employed in this study. It was shown that when only the single factor mediation of DO and NH(3)-N was considered, the mediation ratio of DO and NH(3)-N was relatively low. However, when both DO and NH(3)-N were included, the mediation ratio increased significantly. Under such circumstances, the direct impact of extreme precipitation on infectious diarrhea became negligible. This indicates that extreme precipitation may affect infectious diarrhea mainly by affecting DO and NH(3)-N simultaneously. On the other hand, this also suggests the possibility of complex interactions between DO and NH(3)-N, which together mediate the incidence of infectious diarrhea.

In this study, we have explored the environmental components of climate-disease relationship that could drive disease dynamics. Water quality is the key intermediate between extreme precipitation and diarrhea, which relevant public health intervention can act on to ameliorate future negative impacts of climate change and disease burden [19,20]. The results of this study also showed that the water quality mainly affected by extreme precipitation events varies in different regions and different seasons. More accurate measures should be taken according to local conditions when carrying out relevant interventions. In addition, China’s current standards on the quality of surface water or source water only consider the ecological and environmental significance [48], while ignoring the influence on human health. In the future, standards need to be further updated to guide water quality monitoring and management interventions more scientifically.

Several limitations are still visible in this study. First, the total impact of extreme precipitation events may be underestimated. Diarrhea data in this study were extracted from the National Notifiable Disease Surveillance System, which is reported by clinicians. However, many patients may not choose to go to the hospital considering the usual lack of severity of infectious diarrhea. Community-based disease active surveillance networks could be recommended in the future to better respond to extreme precipitation events and public health risks. Secondly, only physical (pH) and chemical (DO, NH(3)-N) indicators of water quality were considered in this study due to the availability of data. However, other indicators closely related to microbial growth and reproduction, such as water temperature, total suspended solids and microbial indicators that can directly reflect pathogens in water (including: total bacteria, total *E. coli* and total fecal *E. coli*), were not taken into account. Although these water quality indicators may not have much impact on our existing results, some other intermediate links might be hidden. Finally, factors such as the penetration rate of tap water, the penetration rate of sanitary toilets and the purification efficiency of tap water significantly affect the impact of water quality on human health. In this study, only the urbanization rate was used as a proxy variable, which may not reflect the actual impact of the above factors and lead to some bias in the results.

5. Conclusion

Our study suggests water quality is an important mediating factor for the association between extreme precipitation events and infectious diarrhea. Increased risk of infectious diarrhea has been found after extreme precipitation events in Yangtze River Basin. And extreme precipitation could also cause decreased DO and increased NH(3)-N concentration in the surface water. Low concentrations of DO and high concentrations of NH(3)-N were related to increased risk of infectious diarrhea. Our findings have remarkable implications for targeted emergent responses by providing a specific and important index that is the water quality for relevant departments to take an intervention.

Declaration of competing interest

The authors declare that they have no conflicts of interest in this work.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.fmre.2023.05.019.

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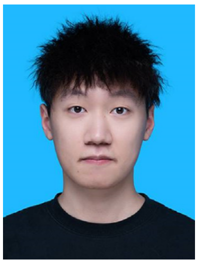

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