Impacts of Meteorological Factors on the Incidence of Infectious Diarrhea in Urban Shanghai, China

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Abstract

Objective: This study aimed to analyze the epidemiology of infectious diarrhea in Yangpu district of Shanghai, from 2006 to 2015, and investigate the associations between meteorological factors and the incidence of infectious diarrhea.

Methods: The epidemiological characteristics were analyzed by descriptive analysis, and the generalized additive model was employed to examine the association between meteorological variables and the incidence of infectious diarrhea.

Results: A total of 3606 infectious diarrhea cases were reported. The average annual crude incidence rate was 33.20/105 and age-standardized incidence rate by world standard population was 63.36/105. Proportion of rotavirus infection accounted for 90.11% of infectious diarrhea cases in 0-4-year-old patients, whereas 56.92% of 5-year-old or older patients were infected with Vibrio. Monthly average maximum temperature below 6.38°C and above 24.59°C, minimum temperature below 5.12°C and above 24.03°C, and precipitation below 1.48 mm and above 7.40 mm had positive effects on the incidence of infectious diarrhea.

Conclusion: High temperature and excess precipitation increase the incidence of infectious diarrhea caused by *Vibrio parahemolyticus* in 5-year-old or older people. Low temperature and little precipitation increase the incidence of infectious diarrhea caused by rotavirus in 0-4-year-old children. These findings might be references for the prophylaxis and control of infectious diarrhea in urban areas of developing world.

Keywords: Epidemiology; Generalized Additive Model; Incidence; Infectious Diarrhea; Meteorological Factors

Introduction

Approximately 1.7 billion cases of diarrheal disease occur worldwide. Diarrheal disease is the second leading cause of death in 0-4-year-old children, killing around 760,000 children every year [1]. Diarrheal disease accounts for 10.03% of deaths among children aged 1-59 months in the Americas and 31.3% of death among children in South East Asia [2]. Infectious diarrhea is referred to diarrheal disease which is most often caused by infections with viral, bacterial, and parasitic pathogens. According to the web-based real-time disease surveillance system-China Information System for Disease Control and Prevention, infectious diarrhea is grouped into three classes, including class A (cholera), class B (bacillary dysentery, typhoid and paratyphoid) and class C (other infectious diarrhea). In China, a total of 836,591 class C infectious diarrhea cases were reported and the incidence rate was 62.39/105 in 2011 [3]. Among overall diarrheal disease cases, 0-4-year-old children accounted for 52.13%, and the incidence rate was 447.06/105 [3]. Despite remark improvement of public health disease system after the 2003 SARS outbreak, infectious diarrhea poses a great threat to public health, particularly in 0-4-year-old children.

Infectious diarrhea is vulnerable to the influence of meteorological factors, and the occurrence and prevalence of infectious diarrhea are closely related to meteorological factors including temperature, precipitation, relative humidity, and air pressure [4-7]. For example, temperature can directly affect the replication and survival of pathogen and predict the number of

bacillary dysentery patients. Two time-series analyses reported that 1°C rise of maximum temperature resulted in 11.40% (95%CI:10.19%-12.69%) and 16% (95%CI:13%-19%) increase in the number of bacillary dysentery, respectively [8,9]. Precipitation may influence the quality of drinking water via contaminating the supply of drinking water, and there is a positive association between heavy precipitation and risk of infectious diarrhea [8,10]. Moreover, climate changes usually affect the behavior habits of human beings, and increase human exposures to environmental pathogens [8,11,12].

The geographical position of Shanghai is unique, facing the Huangpu River and bordering the East China Sea. Tide level of the Huangpu River is susceptible to many meteorological and hydrological factors such as temperature, ocean tide, upstream flood, local precipitation and runoff. As a city with a subtropical humid monsoon climate, Shanghai is characterized by a mild climate, abundant precipitation, adequate light, and four distinct seasons. It has a sufficient supply of fresh water and reaches the highest temperatures in July and August. Spring in Shanghai is from March to May (recently described as until June). Summer in Shanghai is long, from June to September. There is a particular "Plum Rain Season" (Meiyu Season) from mid-June to early July, and it lasts for nearly one month commencing in early summer. During this period, the precipitation often equals to 25% of the annual total. Autumn of the region comes in October and November, and winter begins from December to the next February. The coldest period starts from the end of January to early February.

In this study, we described the epidemiological and etiological characteristics of infectious diarrhea cases among permanent residents in Yangpu district of Shanghai, China, from 2006 to 2015, and examined the associations between the meteorological factors and the incidence of infectious diarrhea.

Materials and methods

Study area

Yangpu district is one of the 16 districts of Shanghai, China. It is located at 31°27' north latitude and 121°52' east longitude, in northeastern part of downtown Shanghai, bordering the Huangpu River on the east and south. Yangpu district has a total area of 60.61km^2 and about a population of 1.1 million [13,14].

Meteorological and demographic data

Meteorological data of Yangpu district from 2006 to 2015 were downloaded from China Meteorological Data Network. The meteorological variables included daily wind velocity, daily sunshine time, daily air pressure, daily maximum temperature, daily minimum temperature, daily vapor pressure, daily relative humidity, and daily precipitation. Demographic data during the study period were obtained from the Public Security Bureau of Yangpu Administration.

Disease surveillance data

Disease surveillance data used in this study were obtained from the National Notifiable Disease Surveillance System (NDSS), which was approved by Municipal Center for Disease Control and Prevention of Shanghai. Infectious diarrhea cases included cholera, bacillary dysentery, typhoid, paratyphoid, and other infectious diarrhea in NDSS. All infectious diarrhea cases were diagnosed by clinical symptoms and identified by the serological tests and stool specimen tests. Information of reported cases included age, gender, and residential address, type of disease, date of onset, and pathogens. According to the National Communicable Disease Control Act of the People's Republic of China, physicians in hospitals have the responsibility to report every case of infectious diarrhea to the local center for disease control and prevention within 24 hours.

Statistical analysis

The epidemiological characteristics of infectious diarrhea cases in Yangpu district from 2006 to 2015 were analyzed by descriptive analysis. Categorical variables were tested by either χ^2 test or Poisson approximation. Kruskal-Wallis test was employed to compare the monthly distributions of infectious diarrhea cases among age groups and Nemenyi method was introduced in multiple comparisons. The generalized additive model (GAM) was employed to examine whether these meteorological variables were correlated to the incidence of infectious diarrhea. The GAM method is usually used to perform linear and nonlinear regression analysis in time-series studies with a Poisson regression [15]. GAM has been widely used in studies of association between meteorological variables and incidence of infectious diarrhea, because of its strength in nonparametric adjustment of confounding effects of seasonality and long-term trends [16-18]. In this study, the error distribution and correlation function in GAM were the Poisson distribution and Log correlation, respectively. Smoothing spline method was used in the form of non-linear function, and generalized cross validation was chosen to estimate non-linear function. The GAM regression model was described as follows:

$$Y = \sum_{i=1}^{q} \beta_i X_i + \sum_{j=1}^{m} f_i(Z_j) + \varepsilon + \beta_0$$

Where Y represented the monthly number of infectious diarrhea cases. β_i and f_i represented linear and non-linear functions based on their regression effects in the model, respectively. ε was random-error term and β_0 represented the intercept of regression equation. The degree of freedom was specified based on the result of cross validation, and the possible lag effects (up to seven days) of meteorological factors were assessed in GAM. The effects of meteorological factors on the incidence of infectious diarrhea were described by effective value. The effective value above 0 meant

that meteorological factor had a positive effect on the incidence, whereas the effective value under 0 meant a negative effect. The statistical analyses were conducted using SAS 9.4 (SAS Institute, Inc., Cary, NC), and two-tailed $P<0.05$ was considered statistically significant.

Results

Epidemiological characteristics of infectious diarrhea

Of 3606 infectious diarrhea cases in Yangpu district from 2006 to 2015, 1843 (51.1%) were male and 1763 (48.9%) were female, with a male-to-female sex ratio 1.05. The annual crude incidence rate ranged from $20.10/10^5$ to $57.94/10^5$, with an average annual crude incidence rate was $33.20/10^5$ and an age-standardized incidence rate by world standard population (ASIRW) of $63.36/10^5$ during 2006-2015 period. The average annual crude incidence rate was $366.13/10^5$ in 0-4-year-old patients, and this rate was significantly higher than that of $24.13/10^5$ in 5-year-old or older patients ($u=99.42$, $P<0.001$). The incidence rates of infectious diarrhea were highest in 2009, and crude incidence rates were $57.04/10^5$ in male, $58.86/10^5$ in female, $57.94/10^5$ in total,

Year	Male				Female				Total			
	Case	Population	Crude incidencea	ASR(W)a	Case	Population	Crude incidencea	ASR(W)a	Case	Population	Crude incidencea	ASR(W)a
2006	118	554774	21.27	34.33	99	524781	18.87	24.05	217	1079555	20.10	29.42
2007	100	552302	18.11	18.86	122	525003	23.24	22.22	222	1077305	20.61	20.45
2008	283	551412	51.32	142.29	268	527962	50.76	114.97	551	1079374	51.05	129.08
2009	315	552204	57.04	195.29	313	531761	58.86	156.99	628	1083965	57.94	176.73
2010	249	553123	45.02	111.49	237	535804	44.23	95.67	486	1088927	44.63	103.83
2011	150	552502	27.15	50.10	151	539420	27.99	41.02	301	1091922	27.57	45.70
2012	129	551345	23.40	49.66	112	541378	20.69	41.40	241	1092723	22.05	45.62
2013	176	549281	32.04	58.50	162	542042	29.89	51.88	338	1091323	30.97	55.27
2014	166	547036	30.35	40.24	173	541979	31.92	38.61	339	1089015	31.13	39.41
2015	157	544656	28.83	33.96	126	542008	23.25	24.72	283	1086664	26.04	29.44
Total	1843	5508635	33.46	70.80	1763	5352138	32.94	59.56	3606		33.20	63.36
a per/100000 person-year; ASR(W): Age-world-standardized incidence rate												

Table 1: The incidence of infectious diarrhea cases in Yangpu district of Shanghai, China, from 2006 to 2015.

Occurrence of infectious diarrhea cases in 0-4 year-old patients usually peaked at period from November to next January, while the peak time of 5-year-old or older patients was from July to September (Figure 1).
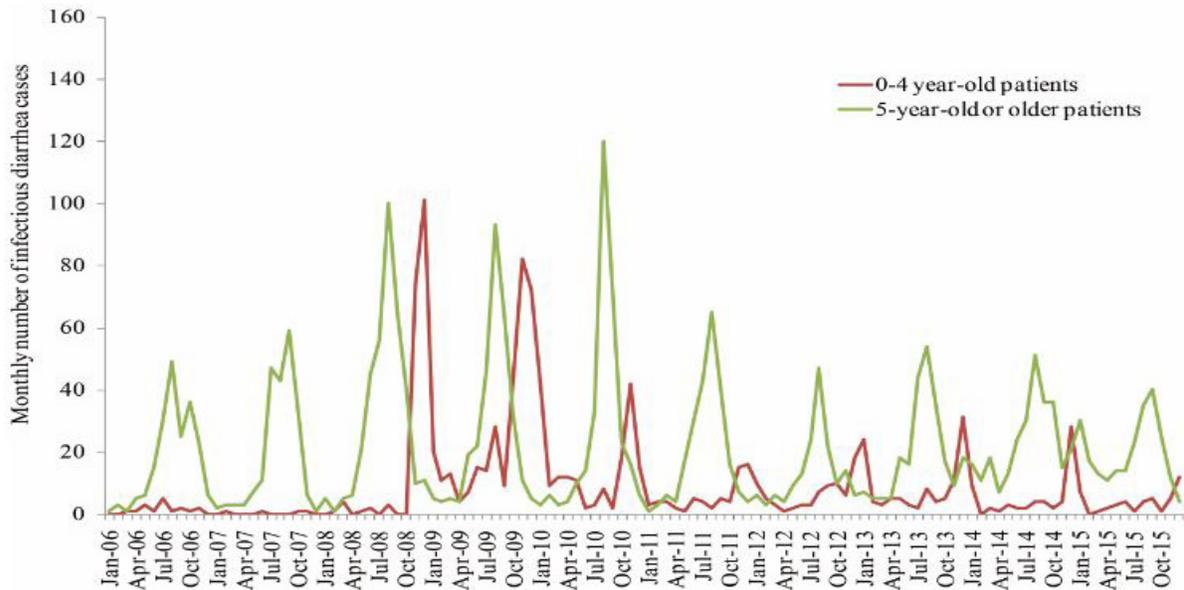
Figure 1: Monthly distributions of reported infectious diarrhea cases in Yangpu district of Shanghai, China, from 2006 to 2015

The age stratification analysis showed that infectious diarrhea cases had statistically different monthly distributions for each age group between 2006 and 2015 (χ^2=199.95, P<0.001) (Figure 2). Moreover, a significant difference in the monthly proportion of each age group was found between 0-4-year group and 15-59 year group (χ^2=31.37, P<0.001) and between 0-4 year group and >60 years group (χ^2=17.24, P<0.005), respectively.
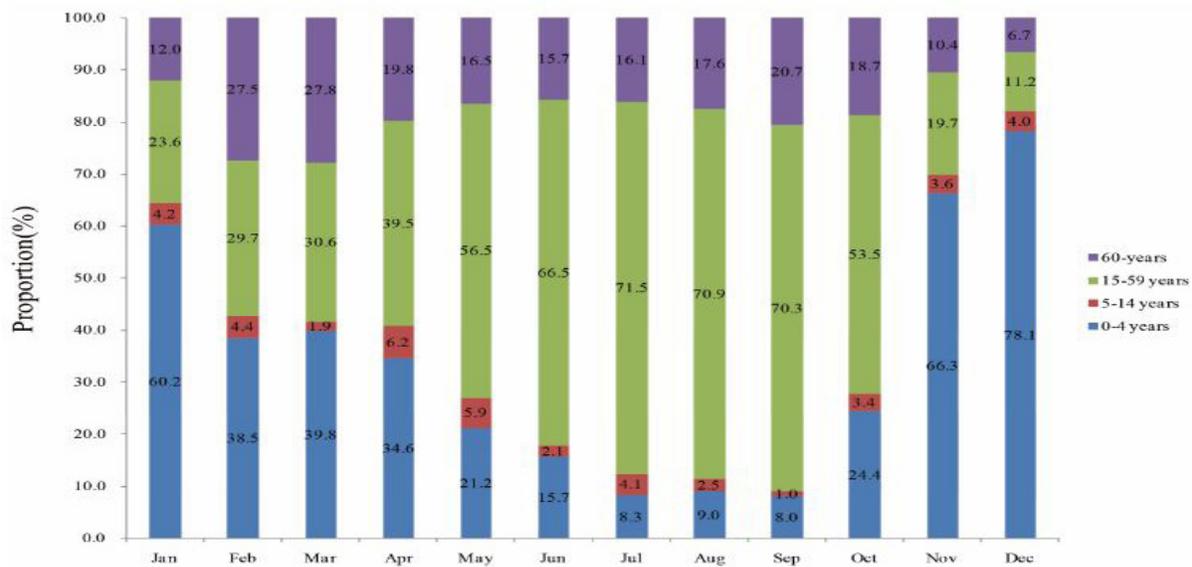

Figure 2: Monthly distributions of infectious diarrhea cases in different age groups

Pathogen spectrums of infectious diarrhea cases from 0-4-year-old patients and5-year-old or older patients

A total of 2809 cases with pathogen information were reported from 3606 infectious diarrhea cases. Due to different types of pathogens causing infectious diarrhea in patients at different age groups, we analyzed the pathogen spectrums from 910 cases of 0-4-year-old patients and 1899 cases of 5-year-old or older patients, respectively. In 0-4-year-old patients, rotavirus accounted for 90.11% (820/910)

and was the dominant pathogen followed by *Salmonella* (8.02%, 73/910), *Shigella* (1.76%, 16/910) and *Campylobacter jejuni* (0.11%, 1/910). The top five pathogens were *Vibrio* (56.92%, 1081/1899), *Salmonella* (15.38%, 292/1899), *Shigella* (15.17%, 288/1899), norovirus (5.11%, 97/1899), and rotavirus (4.11%, 78/1899) in 5-year-old or older patients (Figure 3). Among the 1081cases of *Vibrio* infected patients, *Vibrio parahemolyticus* was the predominant bacterial pathogen with a high proportion of 98.43% (1064/1081).
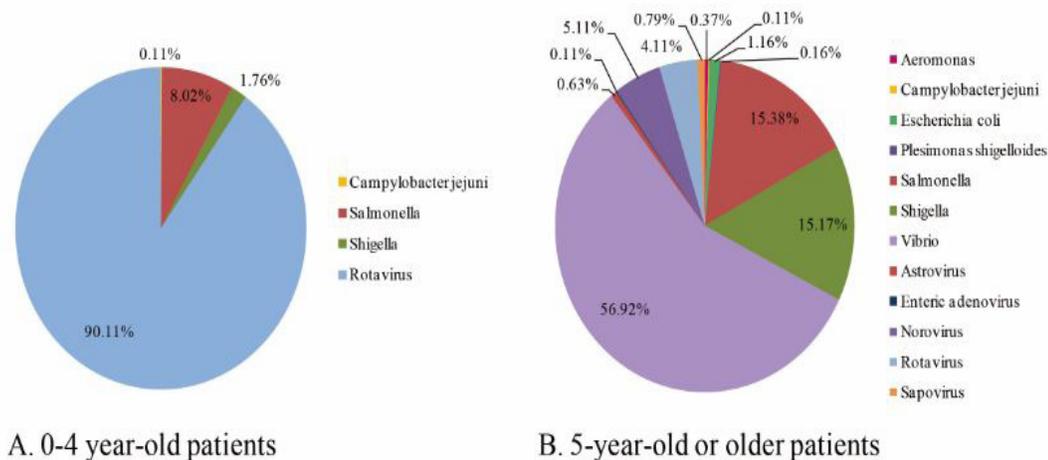

Figure 3: Pathogen spectrums of infectious diarrhea cases in different age groups.

The association between the incidence of infectious diarrhea and meteorological factors

The GAM result of 0-4-year-old patients was similar to the result of 5-year-old or older patients, so GAM result was shown in the form of total patients. Monthly average wind velocity, sunshine time, air pressure, vapor pressure, and relative humidity were automatically excluded during the subsequent selection process. Monthly average maximum temperature, minimum temperature and precipitation were introduced into the non-linear part of model. Degrees of freedom (df) for the non-linear functions were set as 3. The lag effects were insignificant and excluded in the final GAM. The final GAM was shown as follows:

log *[E(Y)]* =f(maximum temperature, df=3)+f(minimum temperature, df=3)+f(precipitation, df=3)+ε+β0

As shown in (Figure 4), with the increase of monthly average maximum temperature, minimum temperature and precipitation, the effective value gradually decreased and then increased, which was similar to binary curve. Monthly average maximum temperature below 6.38°C and above 24.59°C had positive effects on the incidence of infectious diarrhea. Monthly average minimum temperature below 5.12°C and above 24.03°C had positive effect on the incidence of infectious diarrhea. Monthly average precipitation below 1.48 mm and above 7.40 mm had positive effects on the incidence of infectious diarrhea.
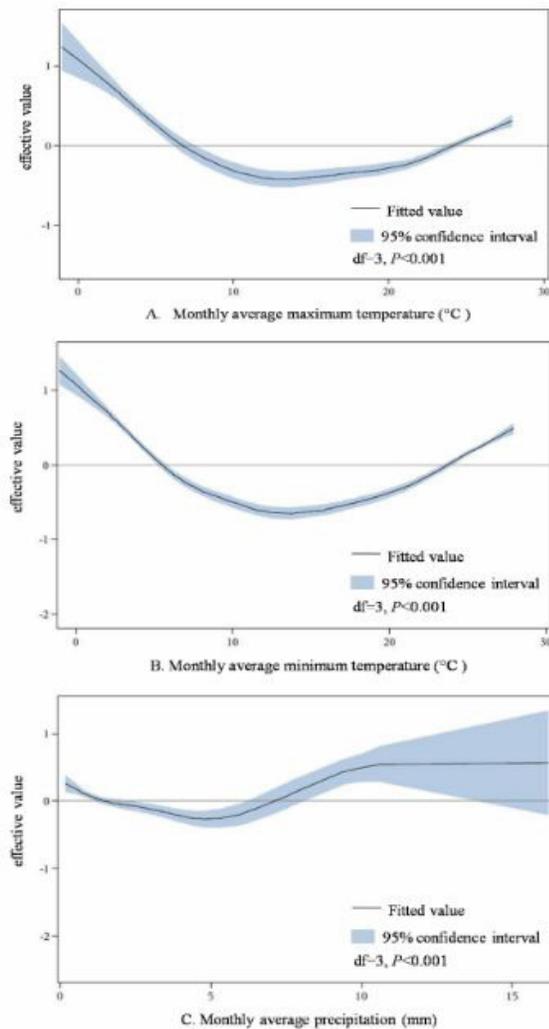
Figure 4: Effect diagram of the associations between the incidence of infectious diarrhea cases and meteorological factors

Discussion

Our study described the epidemiology of infectious diarrhea cases and analyzed the association between the meteorological factors and incidence of infectious diarrhea cases in Yangpu district from 2006 to 2015. This study revealed that the average annual crude incidence rate was $33.20/10^5$ and the ASIRW was $63.36/10^5$ during 2006-2015 period, which were relatively low compared with other provinces in China [3]. The average annual crude incidence rate was $366.13/10^5$ in 0-4-year-old patients, whereas this rate was $24.13/10^5$ in 5-year-old or older patients. Based on this significant difference, we divided overall patients into 0-4-year-old and 5-year-old or older patients for further analyses, such as peak time, pathogen spectrums and the associations between meteorological factors and the incidence of infectious diarrhea.

Our results were consistent with other studies in China showing that infectious diarrhea cases in 0-4-year-old patients usually peaked at period from November to next January, while the peak time of 5-year-old or older patients was from July to September [19,20]. The monthly distributions of infectious diarrhea cases were statistically different among different age groups. For example, the cases of 15-59 years group mainly occurred in June, July and August, but 0-4years group cases occurred in November, December and January. We further investigated the reason why pathogen spectrums might differ among different age groups. Proportion of rotavirus accounted for 90.11% of infectious diarrhea cases and was the dominant pathogen in 0-4-year-old patients, whereas it was only 4.11% in 5-year-old or older patients. Rotavirus is one of the major reasons of diarrhea diseases in 0-4-year-old patients, and about 30%-60% of hospital admissions for diarrhea diseases in young children were infected with rotavirus [21-23]. In order to control the prevalence of rotavirus, several kinds of hygienic measures, such as supplement of clean water and good sanitation, are recommended. We suggest that rotavirus vaccine is the most economical and effective means to prevent rotavirus related infectious diarrhea in 0-4-year-old children. Rotavirus vaccine has been proved to be responsible for a 67% reduction in laboratory-confirmed rotavirus infections for 0-4-year-old children in England [24]. In addition, 56.92% of 5-year-old or older patients were infected with *Vibrio*, but there were no patients infected with *Vibrio* in the 0-4-year-old patients. *Vibrio parahemolyticus* was the predominant bacterial pathogen among *Vibrio* infected patients. *Vibrio parahemolyticus* has a halophilic characteristic and is often isolated from seawater and seafood. Shanghai is a coastal city and the consumption of contaminated seafood is the main cause of acute diarrhea in adults [25]. To strengthen the supervision of hygiene conditions in the sale, transportation and consumption of seafood may help reduce the occurrence of infectious diarrhea in adults.

The incidence of infectious diarrhea and meteorological factors varied widely in different regions in mainland China [3], the analysis in a certain area can provide more accurate and detailed information. With a population of about 1.1 million, Yangpu district can be a good candidate for the impact of meteorological factors on the incidence of infectious diarrhea. Because of its strengths in the time series analysis, the GAM has been widely used in the studies of the association between climate changes and incidence of infectious diseases [16-18].

We observed that maximum temperature below 6.38°C and above 24.59°C had positive effects on the incidence of infectious diarrhea. The minimum temperature below 5.12°C and above 24.03°C had positive effects on the incidence of infectious diarrhea. Our results suggested that the effects of maximum temperature and minimum temperature were similar. High and low temperatures were associated with an increasing number of infectious diarrhea

cases. The following are the possible reasons for this phenomenon. Firstly, the possible etiological and meteorological explanations might be that temperature influences the replication and activity of pathogens. For example, the stability of rotavirus is higher under low temperature and it allows rotavirus to survive longer in contaminated environment, providing more opportunities of virus transmission and infection. The highest level of rotavirus was occurred in the colder and drier months, and the rotavirus infectivity was weaker at $37^{\circ}C$ than $4^{\circ}C$ or $20^{\circ}C$ [26]. Moreover, food poisoning which was caused by bacteria such as *Vibrio parahaemolyticus* and *Salmonella*, was common in summer, because food was easy to be rotten in high temperature [27]. A $1^{\circ}C$ increase in temperature was associated with a 10.6% increased risk of bacillary dysentery [28]. Secondly, in winter, people usually stay indoors to keep warm and avoid low temperature, providing more chances for person-to-person contacts and rotavirus spread via fecal-oral route and contaminated surfaces in closed environment [29].

We found that precipitation above 7.40 mm had a positive effect on the incidence of infectious diarrhea. More precipitation was associated with an increased risk of infectious diarrhea caused by *Vibrio parahaemolyticus*. Increased precipitation exerts an effect on the survival and transmission of waterborne disease pathogens and leads to a lack of clean water and food supply [30]. Because of contamination of the water distribution systems, more precipitation can trigger higher risk of diarrhea outbreaks [7]. Excess precipitation is positively associated with risk of infectious diarrhea in Beijing [28], Fiji [31], Taiwan [18] and Bangladesh [32]. There are three possible mechanisms in which increased precipitation might influence the quality of water supply and hence the risk of infectious diarrhea outbreaks. Firstly, increased risk of sewer overflows caused by more precipitation might result in water supply contamination [33]. Secondly, excess precipitation will increase the runoff of manure and animal excreta on soil and surface, leading to higher waterborne pathogen concentrations in surface water [34,35]. Thirdly, excess precipitation increases turbulences and sediment resuspension, leading to wide distributions of accumulated pathogens [36,37]. Moreover, precipitation below 1.48 mm also had a positive effect on the incidence of infectious diarrhea. Less precipitation in winter and spring was associated with more infectious diarrhea cases caused by rotavirus. And the infectivity of rotavirus was increased by 0.3% when the precipitation had a decrease of 10 mm [38].

Several limitations should be acknowledged. Firstly, although there have been large improvements in the reporting of NDSS, under-reporting is an inevitable issue in the surveillance of infectious diarrhea [9]. Because of its prosperous economic, yangpu district has a large number of mobile populations, such as tourists or individuals who are on a business trip for a short period of time. Some individuals with mild symptoms might do not go to the hospital or take medicine by themselves. To a certain

extent, the NDSS includes the surveillance information of these mobile populations, but it is difficult to avoid the missing data. Under-reporting would weaken the assessment of the association between meteorological factors and infectious diarrhea incidence. Secondly, lack of complete microbiological etiology might limit the evaluation of effect of meteorological variables on each class of infectious diarrhea. Thirdly, the multicollinearity caused by significant correlations among some meteorological variables, such as a positive correlation between temperature and precipitation, might result in the instability of model parameters.

In conclusion, our study suggested that residents in Yangpu district of Shanghai had a relatively low risk of infectious diarrhea. The average annual crude incidence rate, the peak time and the pathogen spectrums of infectious diarrhea cases were distinct between different age groups. In 0-4-year-old patients, rotavirus was the dominant pathogen. And *Vibrio parahemolyticus* was the predominant bacterial pathogen in 5-year-old or older patients. High temperature and excess precipitation had positive effects on the incidence of infectious diarrhea caused by *Vibrio parahemolyticus* in 5-year-old or older people. Low temperature and little precipitation had positive effects on the incidence of infectious diarrhea caused by rotavirus in 0-4-year-old children. Our findings have suggested that meteorological factors can impact the incidence of infectious diarrhea, and might be references for the prophylaxis and control of infectious diarrhea in urban areas of developing world.

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