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Associations of *Salmonella* hospitalizations with ambient temperature, humidity and rainfall in Hong Kong

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ABSTRACT

Background: Little is known about the relationship between *Salmonella* infection and meteorological parameters other than air temperature. This study aimed to explore associations of *Salmonella* hospitalizations with temperature, relative humidity (RH) and rainfall.

Methods: With negative binomial distribution assumed, time-series regression model adjusting for season and time trend were constructed employing distributed lag non-linear models and generalized additive models. Meteorological variables including mean temperature, RH, and daily total rainfall as well as indicator variables including day of the week and public holiday were incorporated in the models.

Results: Higher temperature was strongly associated with more hospitalizations over the entire range of temperatures observed. There was a net 6.13 (95%Confidence Interval (CI) 3.52–10.67) relative risk of hospitalization at a temperature of 30.5 °C, relative to 13 °C, lag 0–16 days. Positive associations were found for RH above 60% and rainfall between 0 and 0.14 mm. Extreme high humidity (96%) and trace rainfall (0.02 mm) were associated with 2.06 (95%CI 1.35–3.14), lag 0–17 day, and 1.30 (95%CI 1.01–1.67), lag 0–26 days, relative risks of hospitalizations, relative to 60% and no rain, respectively.

Conclusions: High temperatures, high RH and light rainfall are positively associated with *Salmonella* hospitalizations. The very strong association with temperatures implies that hotter days will lead to increases in *Salmonella* morbidity in the absence of other changes, and the public health implications of this could be exacerbated by global climate change.

1. Introduction

The earth is warming up, and the world has been alerted to the mounting threat of climate change (The Lancet, 2014). The impact of climate change on the distribution and spread of infectious diseases is of significant public health concern.

Non-typhoidal *Salmonella* infection, also known as salmonellosis, is caused by *Salmonella* species other than *Salmonella* Typhi and *Salmonella* Paratyphi, and is one of the most widespread foodborne diseases (fecal-oral transmission can also occur) with tens of millions of cases occurring every year all over the world (World Health Organization, 2013). It has been estimated that 93.8 million gastroenteritis cases and 155,000 associated deaths occur yearly worldwide (Majowicz et al., 2010). In a nine-year investigation between 2003 and 2011 in Hong Kong, of the 4230 bacteria-caused food poisoning outbreaks reported to the Centre for Health Protection, 763 were associated with non-typhoidal *Salmonella*, and a total of 3250 persons were affected, ranking it the second most common bacterial agent of food poisoning outbreaks in Hong Kong during that period (Centre for Health Protection, 2011). However, the worsening situation from 2011 to 2017 has already made it the most common bacterial causative agent among confirmed cases of food poisoning (Centre for Health Protection, 2017).

Most prior studies of associations between *Salmonella* and meteorological variables have focused on temperature (Lake et al., 2009; Fleury et al., 2006; Zhang et al., 2010; Britton et al., 2010; Uejio, 2017; Jiang et al., 2015; Akil et al., 2014). Higher temperatures have consistently been found to be associated with higher incidence of *Salmonella* infection, although association magnitudes and lengths of lagged effects have varied (Lake et al., 2009; Fleury et al., 2006; Zhang et al.,

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2010; Britton et al., 2010; Uejio, 2017; Jiang et al., 2015; Akil et al., 2014). The association of *Salmonella* infection with relative humidity (RH) and rainfall has been less well studied. A few studies from Australia have examined rainfall, with conflicting results reported (Zhang et al., 2010; Stephen and Barnett, 2016; Zhang et al., 2008), with positive associations being reported for Brisbane and Townsville (Zhang et al., 2010) and Queensland (Stephen and Barnett, 2016) while a negative association was found in Adelaide (Zhang et al., 2008). Another study in Maryland, USA found that exposure to extreme precipitation 90th percentile was associated with a 5.6% increase in the risk of salmonellosis (Jiang et al., 2015). A recent study from Singapore reported a 1% increase in the mean RH was associated with a 1.3% decrease in reported cases six weeks later. However, no cumulative association was assessed and the use of weekly data might not capture the true lag dependency (Aik et al., 2018). Accordingly, the present study aimed to investigate associations between hospitalizations for non-typhoidal salmonellosis and RH, rainfall, and temperature in Hong Kong, a subtropical Chinese city.

2. Methods

Hong Kong has a total area of 1106.34 km^2 and a total population of 7.34 million as of 2016 (Hong Kong Special Administrative Region Government, 2018). Daily counts of admissions of *Salmonella* infection from January 1st, 2002 through December 31st, 2011 from all public hospitals in Hong Kong were obtained from the Hong Kong Hospital Authority and extracted and reclassified according to primary discharge diagnosis from The International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM, code for non-typhoidal salmonellosis: 003.0), Sixth Edition. Daily values of meteorological variables including daily means of temperature, RH, and daily total rainfall for the same period were retrieved from the Hong Kong Observatory.

Time-series regressions were used to model hospitalizations for *Salmonella* infection as a function of mean temperature, mean RH and daily total rainfall. Distributed lag nonlinear models (DLNMs) (Gasparrini, 2011), with the capability of assessing potentially nonlinear exposure-response dependencies and their delayed effects at the same time, were constructed together with generalized additive models (GAMs) (Wood, 2006), with a negative binomial distribution assumed to account for over-dispersion. Day of the week and public holiday (government-designated days off with the exclusion of Sundays) in Hong Kong were incorporated as indicator variables in all models, while day of the year and day of the study period were included as smooth terms of thin plate regression splines with certain degrees of freedom (*df*), respectively, to adjust for seasonality and long-term trend. The model family can be formulated as follows:

$$\log[E(Y_t)] = \beta_0 + \sum cb(\text{meteorological variables}, df_1, \text{lag}, df_2) + s(\text{DOY}, df_3) + s(t, df_4) + factor(\text{DOW}) + factor(\text{holiday})$$

where $E(Y_t)$ is the expected daily count of *Salmonella* infection admissions on day t; t is the day of the study period from 2002 through 2011; β_0 is the intercept; *cb()* represents the crossbasis function in the distributed lag models describing the potential exposure-response and lag-response associations with their corresponding degrees of freedom; *s()* denotes a thin plate penalized spline function; DOY represents day of the year adjusting for seasonality; DOW and holiday represent indicator variable for day of the week and binary variable for public holiday, respectively. The maximum lag was defined as 21 days for mean temperature and RH, and 30 days for total rainfall. The longer lag for rainfall was employed as the authors felt that there could be an extended time window between rainfall and drinking water or food contamination that could impact on pathogen transmission (Wang et al., 2016). Moreover, this impact could be further delayed due to the determent of heavy rainfall for people from seeking medical care. Three to six degrees of freedom were tried for the crossbasis and spline functions to assess the model robustness and the goodness-of-fit among the models were compared and validated using the regression coefficient (R^2) and Akaike's information criterion (AIC). All results, summing up all the contributions from the first day (same day) of the environmental exposure up to the maximum lag, were reported as the relative risk (RR) of a chosen percentile value of certain meteorological variable with corresponding 95%confidence interval (CI), compared to a pre-defined reference value. If a linear or approximately linear association was found, the 3rd percentile of the value of the variable would be used as the reference value. If a hockey-stick-shaped association was identified, the value with the lowest risk would be adopted. As for rainfall, all RRs were calculated relative to no rain for ease of interpretation. All statistical analyses were performed in R software version 3.3.0.

3. Results

A total of 4828 hospitalizations (including 6 deaths) due to *Salmonella* infection were reported from January 1st 2002 through December 31st 2011, among which 3396 cases were recorded during six hottest months in Hong Kong (from May through October). Of all hospitalizations, 2665 (55.2%) patients were male, and 2858 cases (59.2%) occurred among children aged 1 year old or younger, 1395 (28.9%) were aged 2–14 years, 225 (4.7%) were between 15 and 44, 129 (2.7%) were between 45 and 64, 70 (1.4%) were 64–74, and 151 (3.1%) were 75 or older (a total 575 (11.9%) were 15 years old or older). Descriptive statistics for daily cases of *Salmonella* infection and conditions for mean temperature, RH and daily total rainfall are summarized in Table 1. Fig. 1 shows the time series of daily counts of admissions of *Salmonella* infection and of the three meteorological parameters during the entire study period. There was a clear summer peak of *Salmonella* infection and most of the rain fell during the same season.

Six and four degrees of freedom were chosen for day of the year and day of the study respectively since they best captured seasonality and time trend throughout the study period. Fig. 2 depicts the duration of effects of extreme values (99th percentile) of weather variables (and trace rainfall for total rainfall), with a maximum lag of 21 days for mean temperature and RH and 30 days for total rainfall. The positive association between high temperature (30.5 °C, 99th percentile) and *Salmonella* hospitalizations persisted for 16 days, with a reference temperature of 13 °C. Very high RH (96%) was modestly associated with fewer hospitalizations for the first three days (lag 0–2) but positively

Table 1
Descriptive summary for hospitalizations of *Salmonella* infection, mean temperature, mean relative humidity and daily total rainfall in Hong Kong from 2002 through 2011.

	Mean (SD)	Min.	P[a] (1st)	P (25th)	Median	P (75th)	P (99th)	Max.
Salmonella hospitalizations	1.3 (1.3)	0	0	0	1	2	5	9
Length of stay (days)	4.3 (4.1)	1	1	2	3	5	16	94
Mean temperature (°C)	23.5 (5.1)	8.2	11.3	19.4	24.6	27.8	30.5	31.8
Relative humidity (%)	78 (10.3)	31	47	73	79	85	96	98
Daily total rainfall (mm)	6.2 (20.7)	0	0	0	0.01	1.4	100.4	307.1

[a] P represents percentile.