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Research article

High ambient temperature increases the number of emergency visits for upper urolithiasis in Hefei City, China

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A R T I C L E I N F O

Keywords:
Ambient temperature
Upper urolithiasis
Time-series analysis

A B S T R A C T

Background: Few studies have examined the effect of ambient temperature on upper urolithiasis in developing countries, with even fewer considering individual factors.
Methods: The present study analyzed data on emergency department visits for upper urolithiasis from three hospital sites of a large hospital in Hefei, China, during 2016–2020. Data on environmental factors during the same period were also analyzed. A time series analysis employing a generalized Poisson regression model (GPRM) combined with a distributed lag non-linear model (DLNM) was conducted to evaluate the effect of ambient temperature on the number of emergency department visits for upper urolithiasis.
Results: We found that ambient temperatures above 9 °C were positively associated with the frequency of upper urolithiasis visits, with the relationship being most significant on the current day and with a one-day lag. In the single-day lag effect, the most significant relative risk (RR) for mild heat (75th percentile) and high heat (95th percentile) was 1.229 (95% CI: 1.100–1.373) and 1.337 (95% CI: 1.134–1.577), respectively. The cumulative lag effect was significantly higher than the single-day lag effect, with maximum relative risks (RRs) of 1.779 (95% CI: 1.356–2.335) and 2.498 (95% CI: 1.688–3.697), respectively. The maximum lag time was 7 days. RRs were also higher among women and individuals aged 30–44 years.
Conclusions: Increased ambient temperature is a risk factor for upper urolithiasis, and there is a hysteresis effect. Women and individuals aged 30–44 years are the most susceptible.

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Table 1
Statistical characteristics of meteorological variables and emergency visits for urolithiasis in Hefei, 2016–2020.

Group	Sum	Mean ± SD	Percentiles						
			Minimum	P5	P25	P50	P75	P95	Maximum
T_{mean} (°C)	–	16.76 ± 9.33	−5.9	1.9	8.6	17.3	24.6	30.5	35.6
DTR (°C)	–	8.96 ± 4.35	0.6	2.2	5.5	8.9	12.0	16.4	21.5
RH (%)	–	77.23 ± 12.16	33.0	56.0	69.0	78.0	86.0	96.0	99.0
WS (m/s)	–	2.03 ± 0.85	0.3	0.9	1.4	1.9	2.5	3.6	6.2
SH (h)	–	4.94 ± 4.24	0	0	0	5.2	8.8	11.4	12.9
Rainfall (mm)	–	3.35 ± 11.00	0	0	0	0	1.0	19.4	197.0
$PM_{2.5}$ ((μg/m^3)	–	48.50 ± 31.19	5.0	15.0	27.0	40.0	61.0	112.0	235.0
NO_2 ((μg/m^3)	–	43.81 ± 19.12	10.0	20.0	29.0	39.0	55.0	80.0	139.0
SO_2 ((μg/m^3)	–	9.57 ± 5.44	2.0	3.0	5.0	9.0	12.0	20.0	58.0
All visits	9090	4.98 ± 3.39	0	1	2	4	7	11	21
Sex									
Male	6830	3.74 ± 2.76	0	0	2	3	5	9	17
Female	2260	1.24 ± 1.28	0	0	0	1	2	4	7
Age									
0–14 years	34	0.02 ± 0.14	0	0	0	0	0	0	2
15–29 years	2557	1.46 ± 1.35	0	0	0	1	2	4	9
30–44 years	3279	1.88 ± 1.67	0	0	1	1	3	5	13
45–59 years	2264	1.30 ± 1.31	0	0	0	1	2	4	10
≥60 years	956	0.55 ± 0.79	0	0	0	0	1	2	5

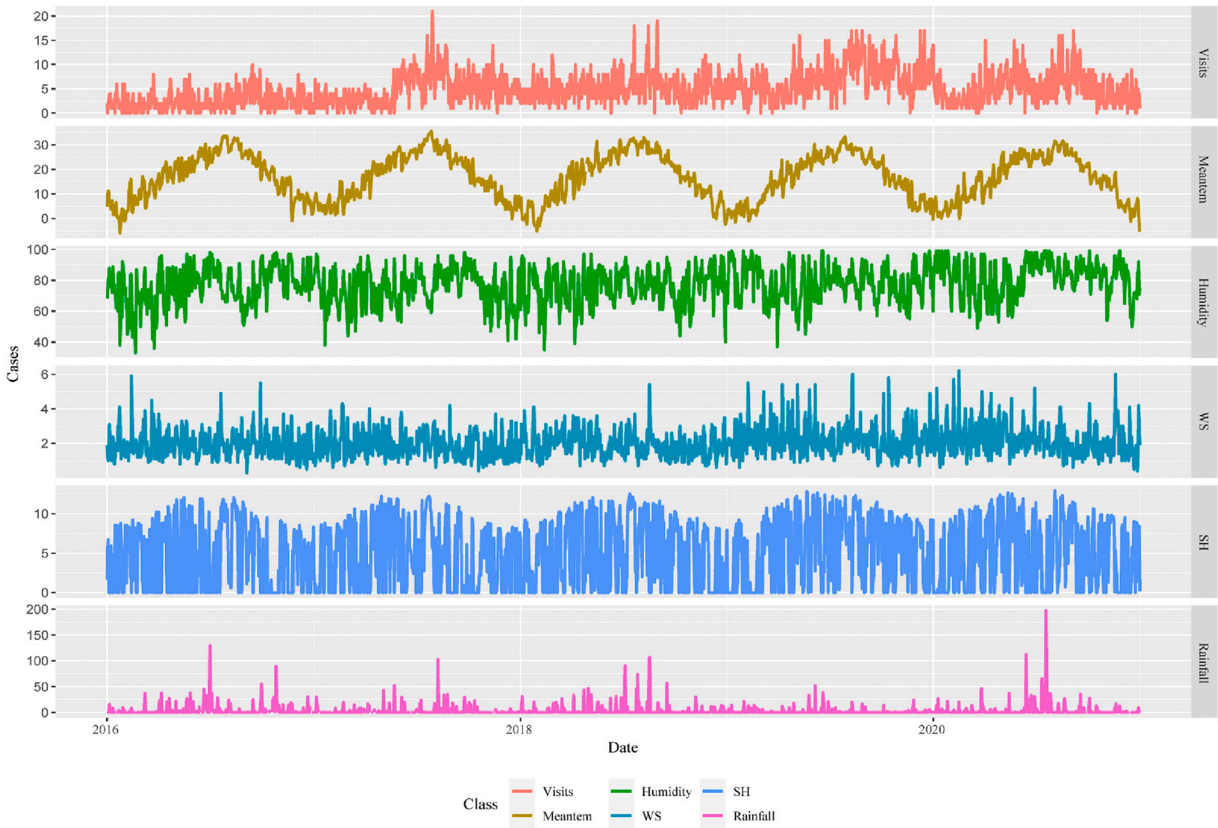

Fig. 1. Daily distribution of emergency department visits for upper urolithiasis and meteorological variables during 2016–2020.

1. Introduction

Upper urolithiasis is among the most common urinary tract diseases, affecting approximately 10% of adults worldwide [1]. In recent years, the prevalence of upper urolithiasis has been assessed in different locations throughout the world, and the results have shown that it is now 1–19% in Asia, 4% in South America, and 5–10% in Europe [2,3]. Similarly, the prevalence of upper urolithiasis in

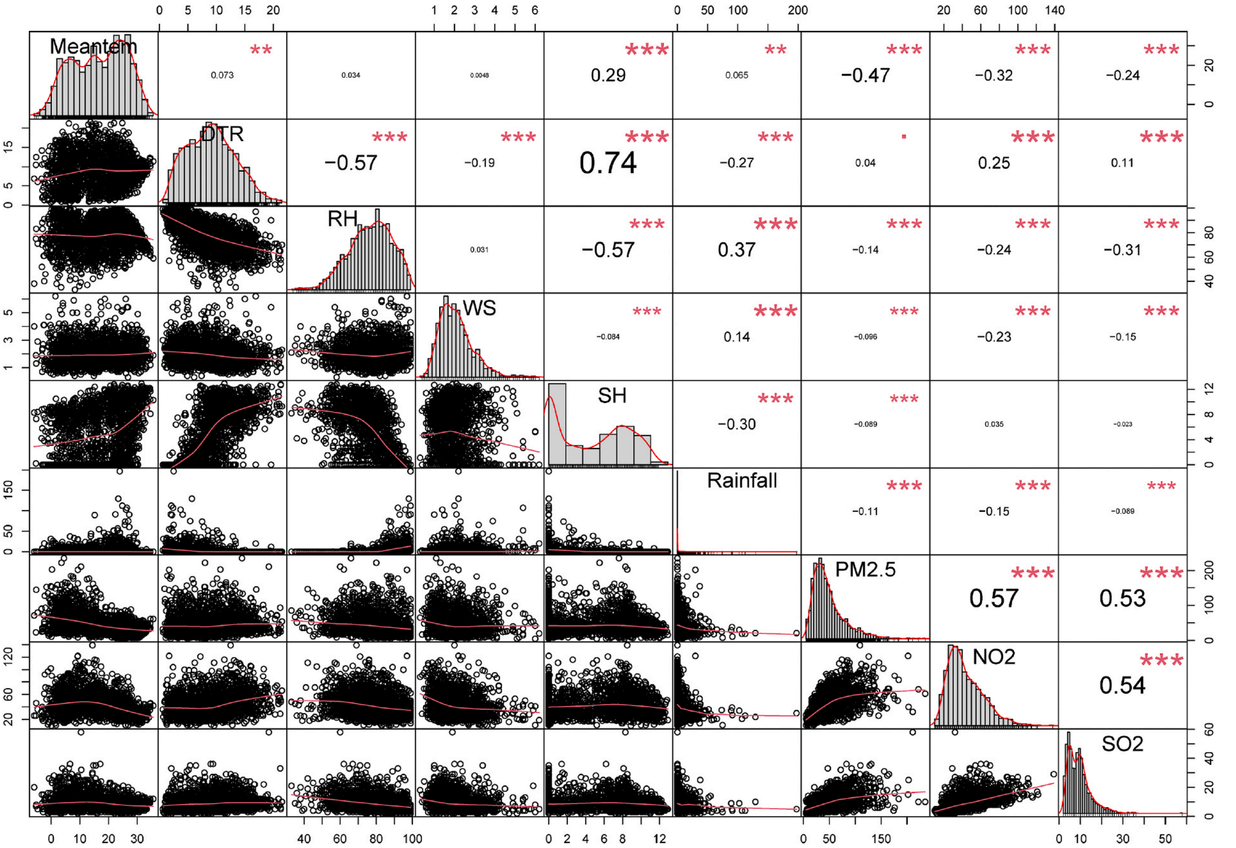

Fig. 2. Spearman's correlation coefficients between weather conditions and major pollutants *P < 0.05, Spearman's correlation coefficients at the top and scatter plot at the bottom.

China is growing annually and is presently 5.8–7.5% [4,5]. Among the main factors related to the prevalence of upper urolithiasis are sex, race, age, geography, occupation, metabolic syndrome, lifestyle, and climate [6,7].

Climate change is of increasing concern to nephrologists because the kidney is one of the main organs vulnerable to heat stress [8]. Previous studies in multiple countries have shown that the incidence of upper urolithiasis is associated with higher temperature months, and that high ambient temperatures increase the risk of urolithiasis and the development of acute symptomatic stones [9-11]. Both gender and age have an impact on these relationships, but the effect of these individual factors appears to vary in different regions. A study of emergency data from Cuneo, Italy, showed that thermal factors played a role in the development of renal colic caused by kidney stones only in women [12]. Furthermore, a Japanese study showed that male patients over 50 years of age were more likely to suffer from colic due to upper urolithiasis during the hot season [13]. A study on the emergency departments of four hospitals in Seoul, Korea, showed that men under 40 years of age were at the highest risk of developing urinary stones when exposed to high temperatures [14]. However, most previous studies on this topic have only focused on developed countries and regions with few studies examining this problem in developing countries. Therefore, we conducted a time-series analysis to quantify the effect of ambient temperature on the number of emergency department visits for upper urolithiasis, corrected for sex and age.

2. Materials and methods

2.1. Study region

Hefei is one of China's largest cities in the east. It has a population of approximately 9.46 million people and a total area of 11,445 square kilometers. The climate is classified as humid subtropical monsoon and features four distinct seasons, including sweltering summers and mild winters.

2.2. Data collection

We collected data on daily visits for upper urolithiasis from the emergency departments of the three hospital sites of a large tertiary hospital from January 1, 2016, to December 31, 2020. Essential information included visit date, name, sex, age, and residence address.

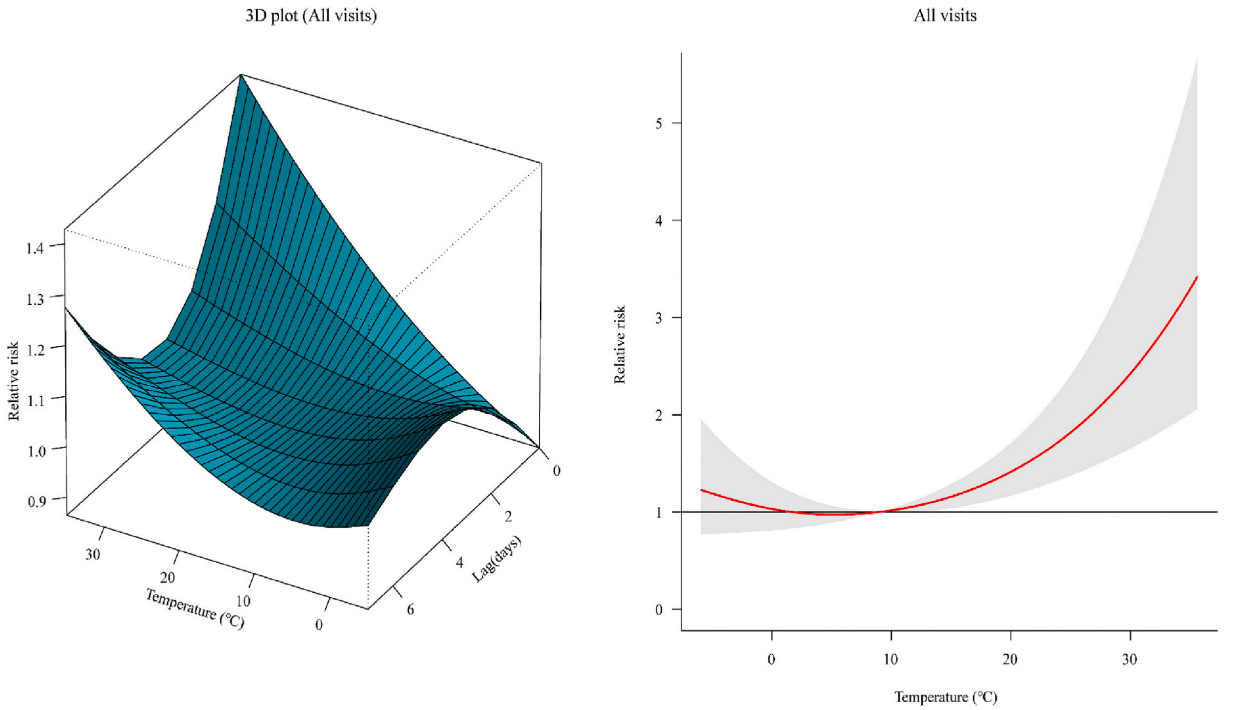

Fig. 3. The overall exposure response relationship between mean temperature and upper urolithiasis emergency department visits.

Table 2
The lag effects of high temperatures (75th and 95th percentile) on emergency visits for urolithiasis, refer to 9.

Single-day (day(s))	Relative risk (95% confidence interval)		Multi-day (day(s))	Relative risk (95% confidence interval)	
	P75(24.6 °C)	P95 (30.5 °C)		P75(24.6 °C)	P95 (30.5 °C)
0	1.229 (1.100, 1.373)*	1.337 (1.134, 1.577)*	0–0	1.229 (1.100, 1.373)*	1.337 (1.134, 1.577)*
1	1.114 (1.057, 1.174)*	1.171 (1.083, 1.265)*	0–1	1.368 (1.170, 1.601)*	1.565 (1.241, 1.975)*
2	1.037 (0.987, 1.090)	1.063 (0.987, 1.146)	0–2	1.419 (1.201, 1.677)*	1.665 (1.301, 2.131)*
3	1.004 (0.946, 1.066)	1.020 (0.932, 1.116)	0–3	1.425 (1.195, 1.699)*	1.698 (1.311, 2.199)*
4	1.004 (0.951, 1.061)	1.023 (0.943, 1.109)	0–4	1.431 (1.180, 1.735)*	1.736 (1.309, 2.304)*
5	1.029 (0.984, 1.077)	1.061 (0.992, 1.133)	0–5	1.473 (1.194, 1.818)*	1.841 (1.355, 2.503)*
6	1.072 (1.009, 1.140)*	1.125 (1.027, 1.232)*	0–6	1.580 (1.256, 1.987)*	2.071 (1.487, 2.885)*
7	1.126 (1.017, 1.247)*	1.206 (1.036, 1.405)*	0–7	1.779 (1.356, 2.335)*	2.498 (1.688, 3.697)*

*$P < 0.05$.

The diagnosis of upper urolithiasis relied on clinical presentation, physical examination, and imaging. After a comprehensive assessment, the physician indicated in the outpatient electronic medical record system whether the case had a confirmed or suspected diagnosis; the diagnosis was coded according to the International Classification of Diseases, Tenth Revision (ICD-10, N20). We screened the visit data through the outpatient electronic medical record system. Patients were included if they (1) had a confirmed diagnosis of upper urinary tract stones; (2) came to the emergency department with related symptoms; or (3) had complete basic information. Patients were excluded if they (1) had unknown time of onset; (2) either lacked an exact residential address or their residential address was not in Hefei; (3) had a suspected diagnosis; or (4) had unknown age and sex.

The meteorological data from January 1, 2016, to December 31, 2020, were obtained from the Hefei Meteorological Bureau. The meteorological monitoring methods were conducted according to the Chinese ground-based meteorological observation norms. We obtained information on daily mean temperature (T_{mean}), relative humidity (RH), wind speed (WS), sunshine duration (SH), and rainfall from the Meteorological Bureau database. The diurnal temperature difference (DTR) was calculated by subtracting the daily minimum temperature from the daily maximum temperature. Air pollutant data for the same period were obtained from the Hefei Environmental Monitoring Center. This institution has ten fixed monitoring stations widely distributed in Hefei to monitor hourly air pollutant concentrations. We obtained the concentrations of particulate matter with an aerodynamic diameter of 2.5 μm (PM2.5), nitrogen dioxide (NO2), and sulfur dioxide (SO2) by averaging the daily concentrations of air pollutants from these stations.

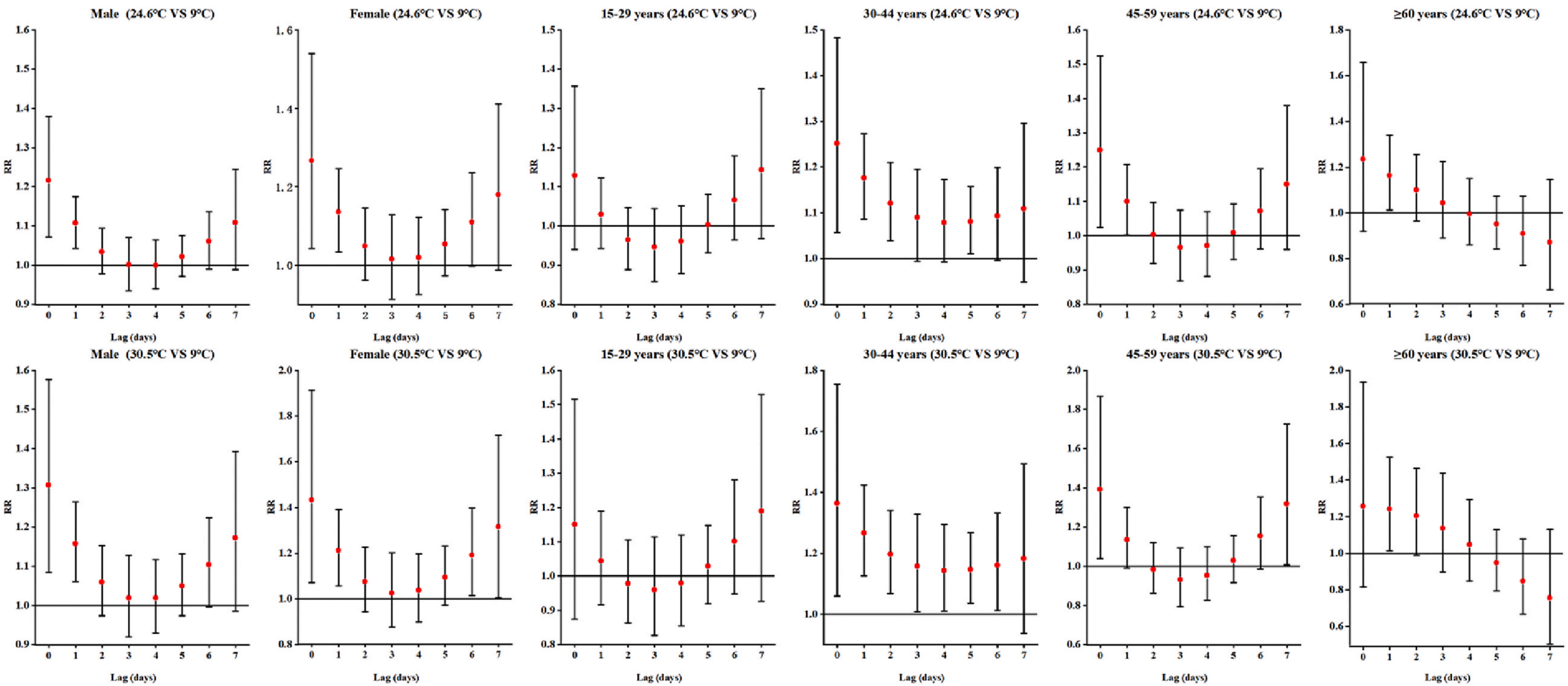

Fig. 4. The single day lag effects of the 75th and 95th percentile mean temperatures in the different subgroups.

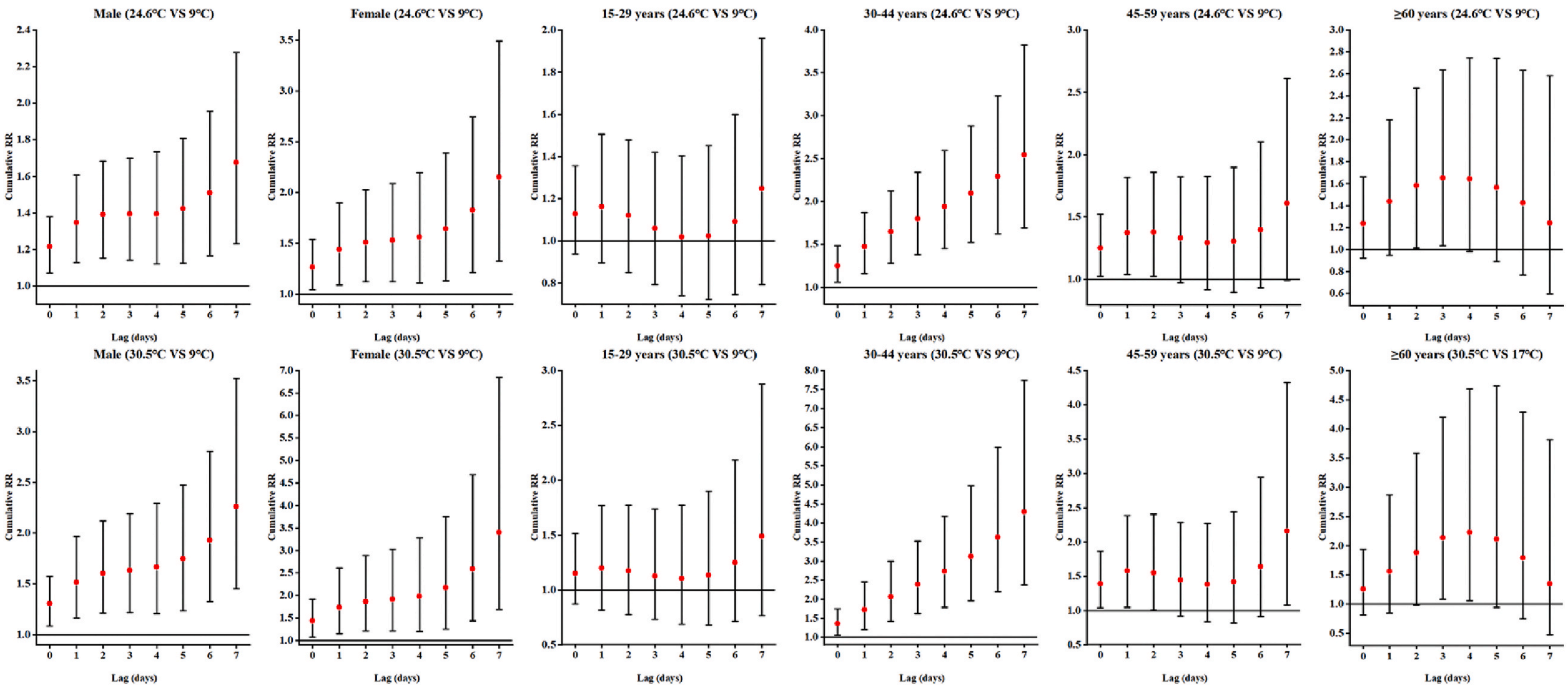

Fig. 5. The cumulative day lag effects of the 75th and 95th percentile mean temperatures in the different subgroups.

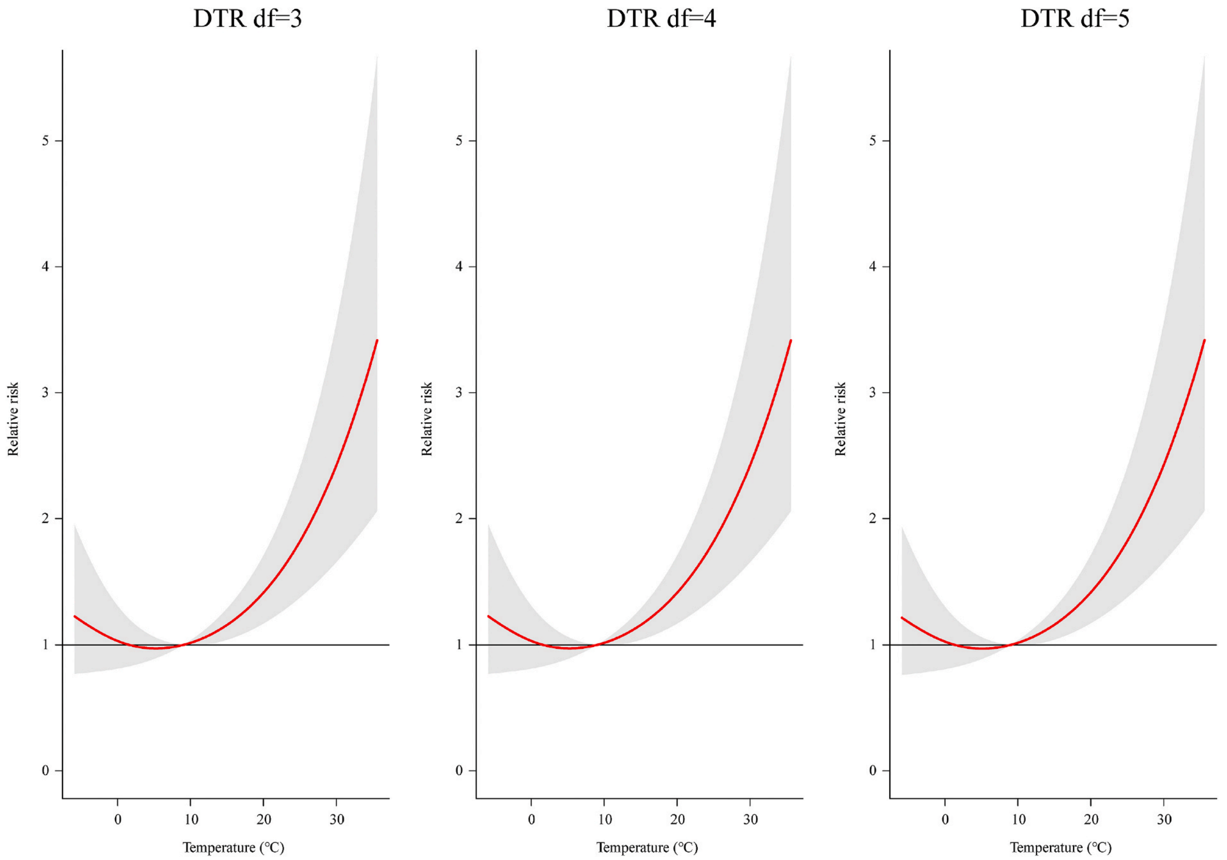

Fig. 6. Sensitivity analysis when altering the degrees of freedom (df = 3–5) for DTR in the model.

Ethical approval

This study was approved by the Ethics Committee of our institution (PJ2022-03-38). The Institutional Review Board disregarded the requirement for informed consent because the information primarily concerned the number of outpatient hospital visits and did not include personal identifiers. The research was conducted in line with the Helsinki Declaration.

2.3. Statistical analysis

Studies have shown that meteorological factors show lagging and non-linear effects on urinary tract stones [15,16]. Therefore, this study used a generalized Poisson regression model (GPRM) combined with a distributed lag non-linear model (DLNM) to quantify the effect of ambient temperature on the number of emergency visits for upper urolithiasis. The model controlled for confounding factors such as long-term trends, day of the week, and holidays, and avoided the effect of excessive dispersion on the results [17,18]. To eliminate multi-collinearity of multiple factors, a Spearman analysis of the daily emergency department visits for upper urolithiasis and the meteorological and air pollution data (see Supplementary Material Fig. S1) was undertaken, and DTR, WS, rainfall, and PM2.5 were identified as the confounders. The ideal degree of freedom was determined using the quasi-Akaike information criterion (QAIC) [19]. The specific equation for the combination of the two models is as follows:

$$Y_t \sim \text{quasi-Poisson}\ (\mu_t)$$

$$\text{Log}(\mu_t) = \alpha + \beta T_{mean\ t,l},3 + ns(DTR_{t,l},3) + ns(WS_{t,l},3) + ns(Rain_{t,l},3) + ns(PM2.5_{\ t,l},3) + ns(Time_t,7) + \gamma Dow_t + \delta Holiday_t$$

where the subscripts t and l represent the observation time and lag days, respectively; Y_t denotes the number of emergency department visits for upper urolithiasis seen on observation day t; Log() denotes the link function; α denotes the intercept; $T_{mean\ t,l}$ denotes the DLNM cross-basis matrix of the mean temperature; β denotes the matrix coefficient of the mean temperature and uses 3 degrees of freedom; ns denotes the natural cubic spline function; DTR_t denotes the diurnal temperature range on day t with 3 degrees of freedom; WS_t denotes the wind speed on day t with 3 degrees of freedom; $Rain_t$ denotes the rainfall on day t with 3 degrees of freedom; $PM2.5_t$ denotes the PM2.5 on day t with 3 degrees of freedom; $Time_t$,7 denotes the time trend with 7 degrees of freedom; and γ and δ are matrix coefficients for Dow and Holiday, respectively, that control the effects of the day of the week and holidays, respectively.

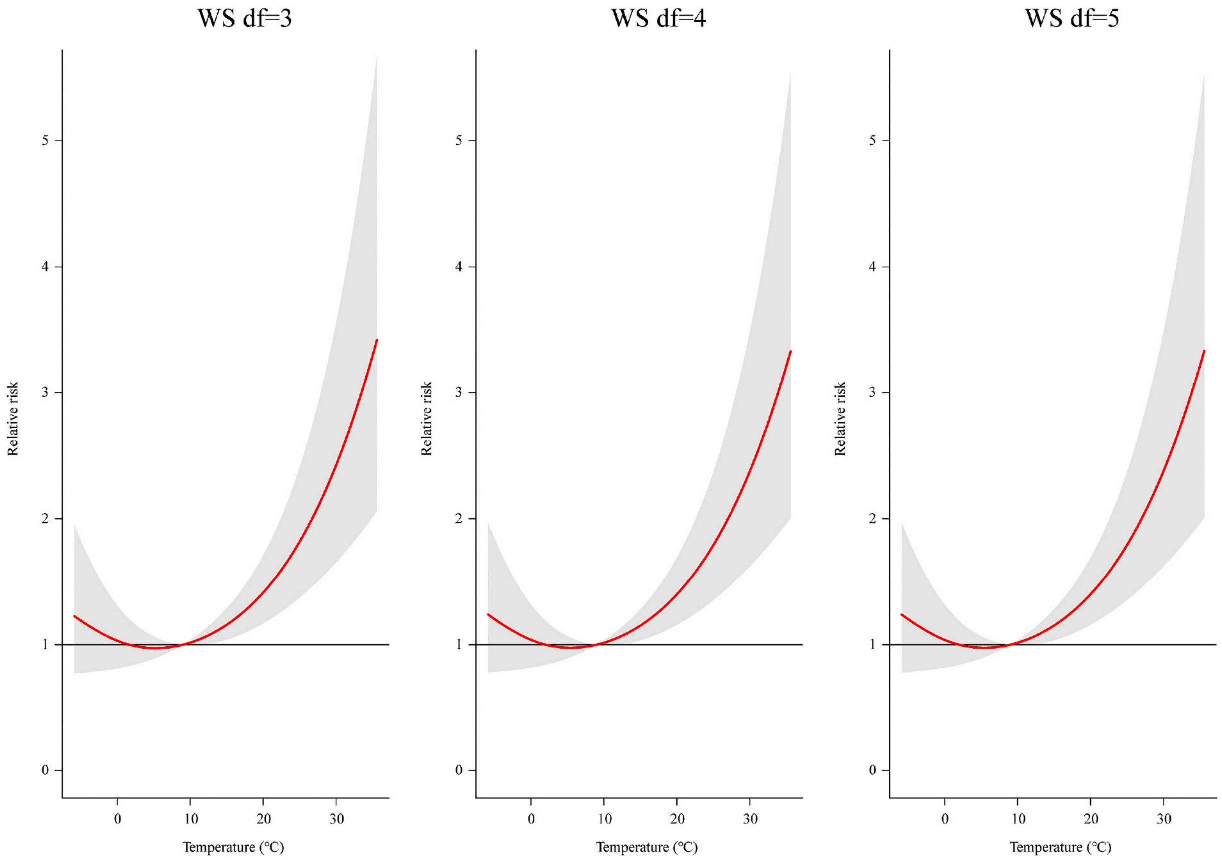

Fig. 7. Sensitivity analysis when altering the degrees of freedom (df = 3–5) for WS in the model.

We used the fitted model to derive a curve of the overall exposure-response relationship between mean temperature and emergency department visits for upper urolithiasis (best linear unbiased prediction) [20]. The minimum impact point temperature of 9 °C can be observed in Fig. 3. The relative risks (RR) were estimated for two high temperatures (mild heat: 75th percentile; high heat: 95th percentile) using the temperature at the minimum effect point (9 °C) as a reference [21]. Potential heat correction effects due to individual patient factors were analyzed by stratifying by sex (men and women) and the age group (0–14, 15–29, 30–44, 45–59, and 60 years and above).

In addition, we conducted sensitivity analyses. We varied the degrees of freedom for diurnal temperature range (df = 3–5), wind speed (df = 3–5), rainfall (df = 3–5), PM2.5 (df = 3–5), and time (df = 6–8). In addition, we adjusted for the maximum number of lag days (7 and 14 days). Details are given in the Supplementary Material Figs. S2–S7.

All statistical analyses were conducted using R (version 4.1.1). $P < 0.05$ was set as the significance level for the two-sided test.

3. Results

3.1. Descriptive statistics

The data on the daily emergency department visits for upper urolithiasis and the meteorological and air pollution data are depicted in Table 1. During the study period, there were 9090 visits to the emergency room for upper urolithiasis. Of these, 6830 (75.14%) were men. The highest number of cases was seen in the 30–44 years age group at 3279 cases (36.07%). Thirty-four cases (0.37%), 2557 cases (28.13%), 2264 cases (24.91%), and 956 cases (10.52%) were observed in the 0–14, 15–29, 45–59 and ≥ 60 years age groups, respectively. The mean daily temperature, DTR, RH, WS, SH, rainfall, PM2.5, NO_2, and SO_2 were 16.76 °C, 8.96 °C, 77.23%, 2.03 m/s, 4.94 h, 3.35 mm, 48.50 μg/m^3, 43.81 μg/m^3, and 9.57 μg/m^3, respectively. Fig. 1 depicts the distribution of the daily emergency department visits for upper urolithiasis from 2016 to 2020, as well as the mean temperature, RH, WS, SH, and rainfall. During seasons of higher temperatures, there were more visits than at other times of the year. The climate variables demonstrate a distinct seasonal variation.

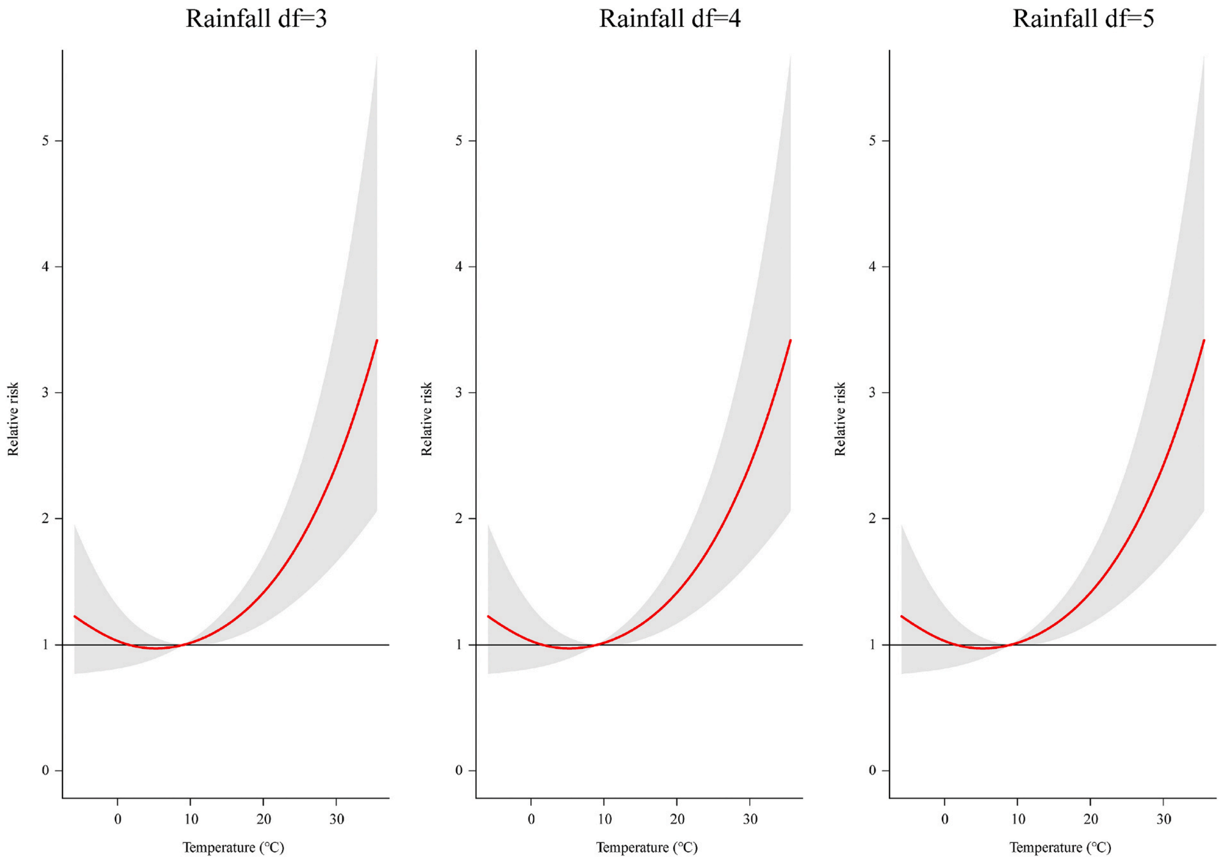

Fig. 8. Sensitivity analysis when altering the degrees of freedom (df = 3–5) for rainfall in the model.

3.2. Correlation analysis of major environmental factors

Fig. 2 demonstrates the Spearman correlation between the main environmental factors that are strongly associated with upper urinary tract stones. Mean ambient temperature is negatively correlated with PM2.5, NO2 and SO2 and positively correlated with DTR and rainfall.

3.3. The overall effect of mean temperature on emergency visits for upper urolithiasis

Fig. 3 demonstrates the overall exposure-response association between mean temperature and emergency department visits for upper urolithiasis. As the mean temperature rose above 9 °C, the number of emergency visits for upper urolithiasis dramatically increased. Lower temperatures appeared to have a protective effect on upper urolithiasis. However, this protective effect was not significant. Fig. 3 also demonstrates the delayed effect, displaying a maximum lag time of 7 days.

3.4. Lag effects for specific average temperatures

The single-day and cumulative lag effects of the 75th and 95th percentiles of mean temperature on the emergency visits for upper urolithiasis are shown in Table 2, refer to 9 °C. The effect of high temperature on upper urolithiasis visits was acute. The effect of high heat (30.5 °C) was more significant overall than mild heat (24.6 °C). The highest RRs were observed on the current day for the single-day lag effects of mild heat and high heat [1.229 (95% CI: 1.100–1.373) and 1.337 (95% CI: 1.134–1.577), respectively]. The single-day lag effect decreased and then increased over time, lasting approximately 4 days. The cumulative lag effect was more significant than the single-day lag effect, with the maximum relative risks for mild heat and high heat reaching 1.779 (95% CI: 1.356–2.335) and 2.498 (95% CI: 1.688–3.697), respectively.

Figs. 4 and 5 depict the single day and cumulative lag effects of the 75th and 95th percentiles of mean temperatures in all the groups, when 9 °C is used as a reference. The cumulative lag effect was much more significant than the single-day lag effect, and the overall effect of high heat was greater than that of mild heat. The single-day lag effect showed a U-shaped trend. The maximum single-day lag effect for both mild heat and high heat occurred on the current day for women and the 30–44 age group. The single-day lag effect of mild heat on women lasted only two days, while the effect of high heat lasted for a total of 4 days. The single-day lag effect of

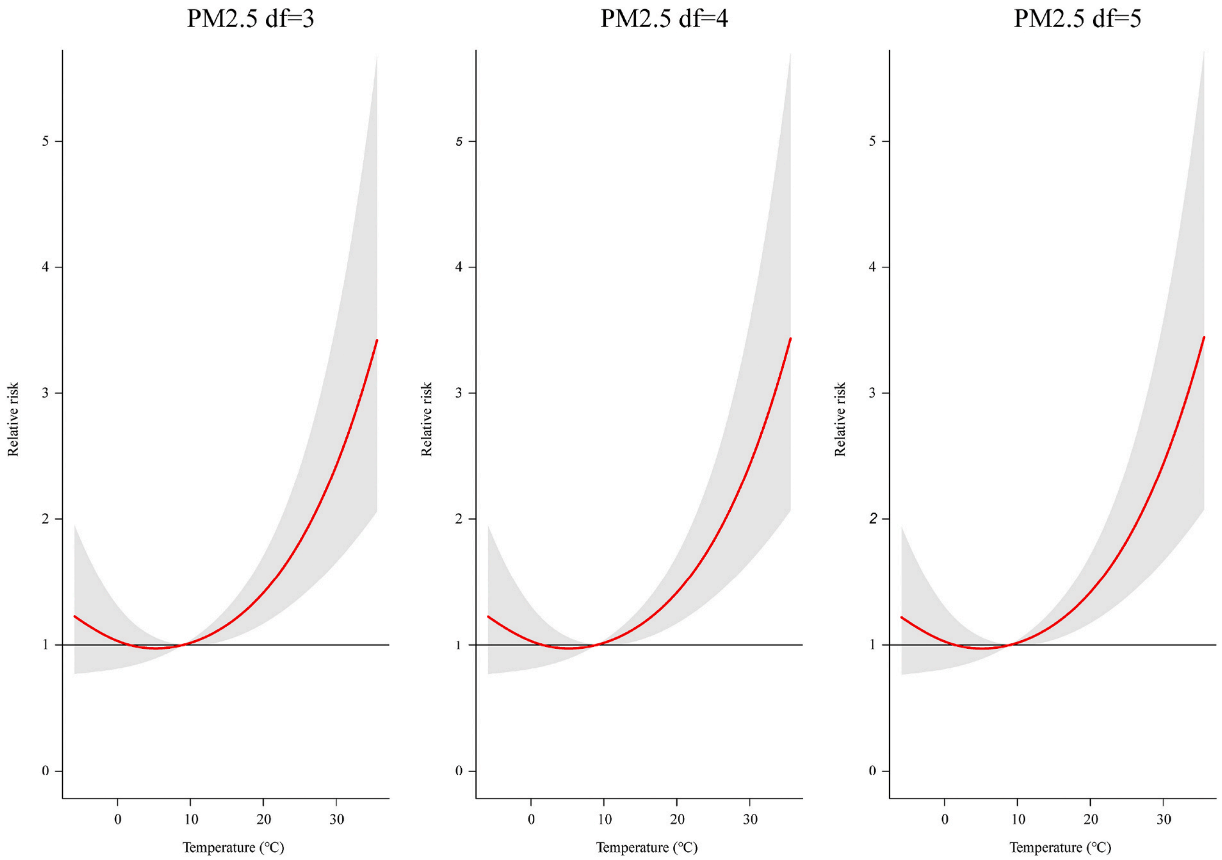

Fig. 9. Sensitivity analysis when altering the degrees of freedom (df = 3–5) for PM2.5 in the model.

high heat on the 30–44 age group continued through day 6. The cumulative lag effect for the 30–44 age group showed an approximately linear increase.

3.5. Sensitivity analysis

The sensitivity analysis indicated that the exposure-response curves were similar across the varying degrees of freedom for diurnal temperature range (df = 3–5), wind speed (df = 3–5), rainfall (df = 3–5), PM2.5 (df = 3–5), and time (df = 6–8) in the model (Figs. 6–10). Furthermore, the exposure-response curves followed a similar trend when we adjusted the maximum lag days to 14 days (Fig. 11). This indicated that our model was stable.

4. Discussion

This study utilized a GPRM combined with a DLNM to investigate the association between ambient temperature and upper urolithiasis. We discovered a significant positive correlation between ambient temperatures above 9 °C and the incidence of emergency department visits for upper urolithiasis. This effect was more significant on the current day and the lag day, gradually diminishing thereafter. No protective effect of low temperature against upper urolithiasis was observed. Our study clearly shows that high temperature is a risk factor for developing upper urolithiasis. In addition, we discovered that women and individuals between the ages of 30 and 45 years were more susceptible to the effects of high temperatures. To our knowledge, this is the first study to examine the effect of temperature on emergency visits for upper urolithiasis across demographic subgroups in a developing country.

In previous studies, numerous meteorological factors, including ambient temperature, rainfall, sunlight hours, and humidity have been considered to be influencing factors in the formation of urolithiasis and renal colic attacks [22–24]. In a single-center retrospective investigation, it was discovered that PM2.5 contributes to the disease development [25]. However, there have been no conclusive findings indicating the role of environmental variables in urolithiasis [26]. Urolithiasis may be caused by a hot and dry climate [27]. The idea that high temperature is a favorable factor for urinary stone formation is supported by ample evidence. One piece of evidence is the seasonal variation, with higher incidence in the warmer summer months than in the cooler winter months [24,28,29]. The prevalence of kidney stones in the southeastern United States is nearly 50% higher than that in the cooler northeast, creating a “rock belt” [30,31]. Some studies on specific workers who live in high temperature environments for long periods of time

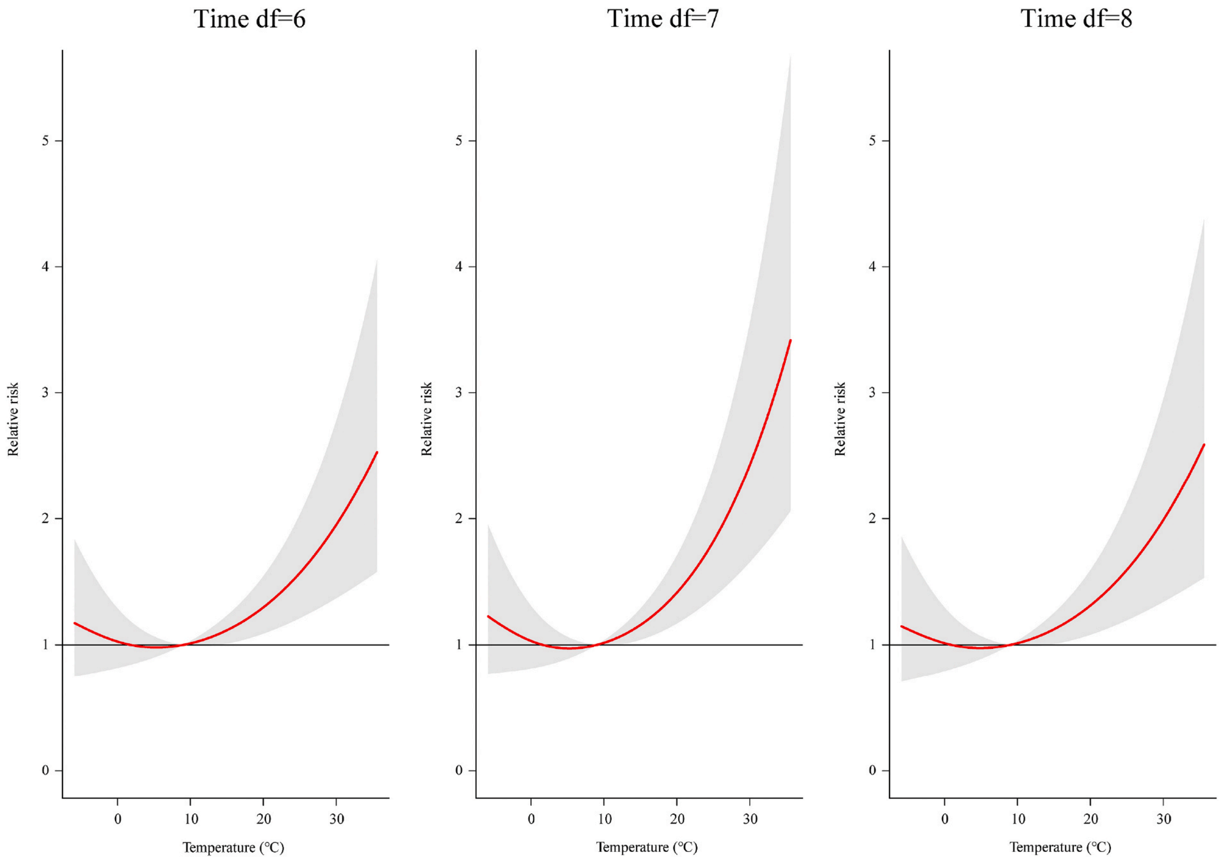

Fig. 10. Sensitivity analysis when altering the degrees of freedom (df = 6–8) for controlling for the long-term trend and seasonality in the model.

have shown that high temperatures significantly increase the risk of kidney stones [32,33].

The exact mechanism of the effect of high temperature on upper urinary tract stones is unknown, but the association is biologically plausible. Firstly, dehydration caused by the high temperature environment is an important factor. As the body sweats more in a hot environment, serum osmolality increases, stimulating the release of the pressor hormone (antidiuretic hormone) from the posterior pituitary gland. This leads to an increase in the urinary concentration, leading to supersaturation of calcium oxalate and calcium phosphate in the urine, which is then deposited in the kidneys [34-36]. An important evidence supporting this inference is that increased fluid intake is associated with fewer urinary tract stones [37,38]. Secondly, a hotter climate is associated with increased intake of sugary sodas. In addition to increasing urinary concentration, fructose stimulates adenosine triphosphate (ATP) citrate lyase, which reduces urinary citric acid concentration, thereby creating a favorable environment for kidney stone formation [39-41].

A confounding factor control was introduced to the model to prevent the potential effects of other environmental variables when examining the effect of ambient temperature on urolithiasis. Consistent with the findings from most developed countries, we found that high ambient temperature increased the number of acute visits for upper urolithiasis. For example, studies in countries such as the United States, Italy, Japan, Korea, Canada, and New Zealand have found that high temperature increases the incidence of urolithiasis or renal colic [11–14,23,42]. However, few of these previous studies quantified this effect in different populations. Our study also found a transient hysteresis effect of high temperature on urinary tract stones. This may be because we used patients with symptomatic stones as study subjects, and the lag effect may respond to the accelerated phase of stone formation, where stones that were asymptomatic expand to become symptomatic.

There are age and sex disparities in susceptibility to the effects of ambient temperature on urolithiasis. However, the disparities noted were not consistent across different study regions. In previous studies, men in Japan, Canada and Korea were found to be more susceptible to heat-induced renal colic or urinary stones [13,14,42]. A study in Cuneo, Italy, observed the opposite effect [12]. Similarly, in our study, women were more sensitive to thermal factors. In a study of 423,396 Canadian patients with renal colic, the 40–69 age group was found to be more sensitive to thermal factors [42]. Moreover, a study in Seoul, Korea, showed that younger people (under 40 years of age) were more likely to develop kidney stones due to heat [14]. The present study demonstrates similar findings, showing a higher risk associated with high temperatures in individuals aged 30–44 years. Several physiological factors (e.g., larger body surface area to body weight ratio, higher subcutaneous fat content, and hormonal fluctuations) can increase a woman's susceptibility to high temperatures [43,44]. There may be a correlation between differences in age-related sensitivity and differences in the duration of exposure to ambient temperature at different ages. However, these variations could also be attributable to climate,

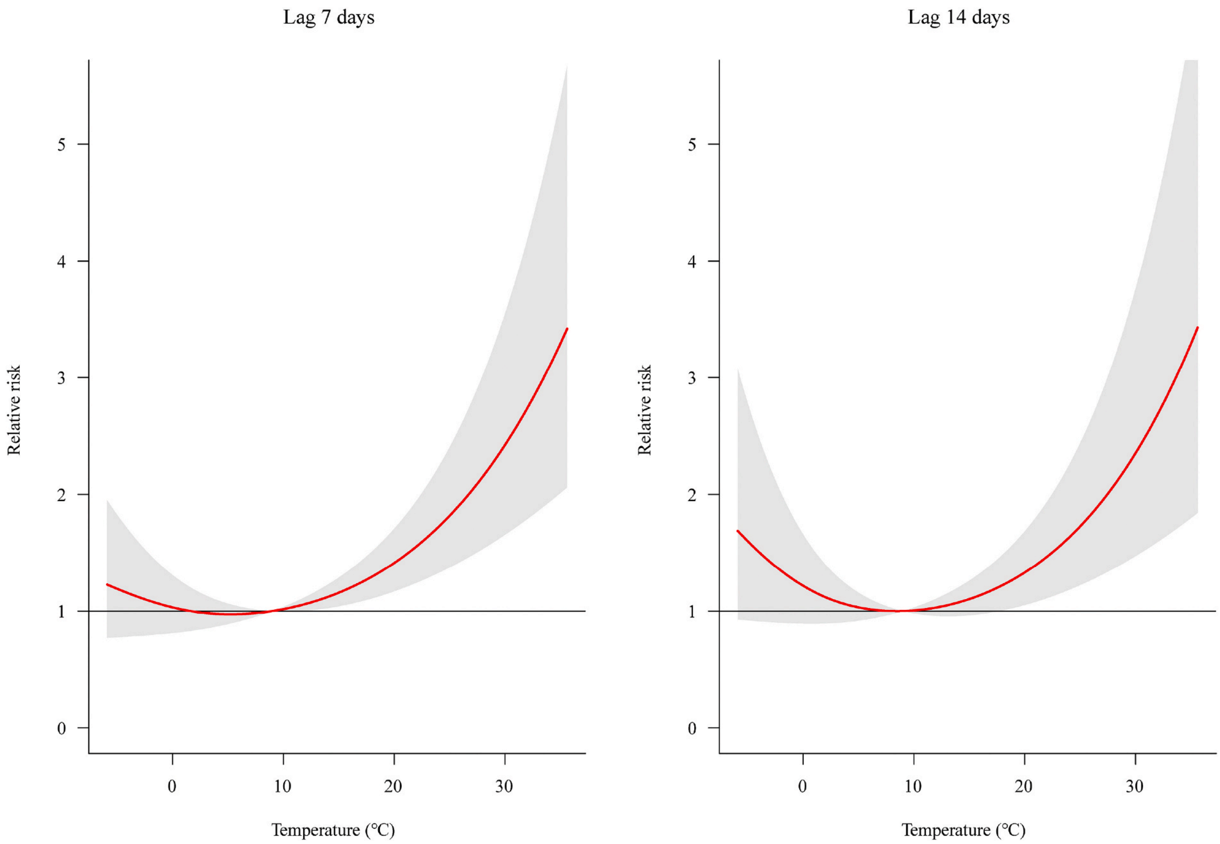

Fig. 11. Sensitivity analysis when altering the maximum lag days (7 and 14) in the model.

ethnicity, and economic levels in the study location and must be confirmed in different regions.

In a study from Padua, Italy, Boscolo-Berto et al. found a correlation between ambient temperatures exceeding 27 °C and an increase in renal colic [45]. A time-series analysis in Guangzhou, China, revealed a significant rise in the incidence of renal colic at temperatures above 21 °C [46]. In most cases, temperatures exceeding 10 °C led to an increased risk of kidney stone formation, according to a five-city US study [11]. Another time-series study in Seoul, Korea, found an increased risk of urolithiasis at temperatures above 13 °C [14]. The present study determined that ambient temperatures above 9 °C led to a significant increase in the number of cases of renal colic caused by urolithiasis. This result suggests that the critical temperature values for the effects of urolithiasis vary across different regions. This result may be indicative of the fact that populations in different regions are uniquely adapted to heat. However the effects of factors such as the methodology of these studies, other climatic conditions, diet, occupation, and other factors cannot be excluded.

The present study has several advantages. Firstly, we used emergency department data for our study, which are more current than general outpatient and inpatient data and provide a more sensitive response to the relationship between temperature and urolithiasis. Secondly, we included atmospheric pollutants as one of the confounding factors, and therefore, the results are likely more accurate than those of previous studies. Thirdly, we quantified the relative risk of high temperature for urolithiasis in different groups, which may facilitate timely decision-making by the public health system.

Our study has certain limitations. First, the use of ambient temperature indicators does not reflect the actual environmental conditions individuals are exposed to, which may have led to some bias in the results. Secondly, this study used only 5 years of data from one city, and more such studies in other areas are necessary to draw conclusions. Thirdly, there was a lack of information on stone types in the present study; therefore, the effect of environmental temperature on different stone types needs to be further investigated. Moreover, all individuals in the population we chose to study are from the same region, and the local population has similar dietary habits and lifestyles. As this is an ecological study, individual differences in socioeconomic status, family background, literacy, and medication use cannot be adjusted for, and ecological fallacies will inevitably occur.

5. Conclusion

In conclusion, our study shows that high temperatures increase the risk of developing upper urolithiasis, especially in women and individuals aged 30–44 years. This study offers developing nations evidence to guide public health preventive measures.

Author contribution statement

Haoxiang Sun, Xiaosong Wang and Xiaoyu Zhang: Conceiving and designing the experiments; Performed the experiments; Analyzed and interpreted the data; Wrote the paper. Linlin Wang: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data. Min Tao, Ying Wang, Jidan Yang, Yuting Lei, Changqing Jin, Shuang Zhao and Yue Hu: Contributed reagents, materials, analysis tools or data. Huaqing Hu: Conceiving and designing the experiments; Performed the experiments; Wrote the paper.

Data availability statement

Data will be made available on request.

Additional information

No additional information is available for this paper.

Declaration of competing interest

The authors declare no conflict of interest.

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