



Epidemiological characteristics of gonorrhoea and its influential meteorological factors: a 14-year retrospective assessment in China

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Abstract

This study aimed to investigate the seasonal variation of gonorrhoea in China, and to analyze the relationship between the incidence of gonorrhoea and meteorological factors. Data from gonorrhoea cases were obtained from the Disease Prevention and Control Bureau and the Data-Center for China Public Health Science, Chinese Center for Disease Control and Prevention, and the incidence of gonorrhoea in China from 1 January 2006 to 31 December 2019 was analyzed. Meteorological data from the same period were obtained from the South China Meteorological Data Sharing Center, including the average monthly temperature, relative humidity, atmospheric pressure, sunshine hours, number of rainy days, and precipitation. The ratio-to-moving average method and seasonal subseries plots were used to analyze the seasonality of gonorrhoea cases. The distributed lag non-linear model and attribution risks were used to investigate the effects of meteorological indexes on gonorrhoea cases. The number of gonorrhoea cases showed seasonal variation, with a peak in the third quarter and a decline in the first quarter. The Spearman assay showed that the reported number of patients with gonorrhoea was positively correlated with the monthly temperature, relative humidity, precipitation, and number of rainy days. The risk of gonorrhoea onset was highest at 6–11 °C, and the highest risk occurred when the average monthly temperature was 7 °C (resulting in an increase of 14.5% compared with 13 °C); a similar result was found regarding the cumulative risk of gonorrhoea onset in relation to temperature. The attribution score of temperature to the onset of gonorrhoea was 5.02% (95% confidence interval: –3.84%, 13.88%). The study findings suggest that increased emphasis should be placed on screening for gonorrhoea during summer and autumn, and that education on safe sexual behavior should be promoted during these times.

Keywords Gonorrhoea · Meteorology · Seasonality · Distributed lag non-linear model · Attribution risks

Introduction

Seasonal variation is a well-known phenomenon in life and health sciences, even for sexually transmitted diseases (STDs) such as gonorrhoea (Kakran et al. 2015). The

seasonality of gonorrhoea was first reported in the USA in 1971 (Cornelius 1971) and then from 1999 to 2003 (Shah et al. 2007), with peak rates of gonorrhoea in summer and early autumn (Cornelius 1971; Schroeder et al. 2001; Wright & Judson 1978). Two studies performed in the UK from 1972 to 1976 and 1984 to 1989 have shown

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a two-peak seasonal distribution in gonorrhoea incidence, with peaks in both the first and third quarters of the year (Ross & Scott 1992; Wellings et al. 1999). A study of gonorrhoea and urethritis rates in Burkina Faso, West Africa, also reported seasonal differences, with the highest rates occurring from January to May (Damiba et al. 1990).

Since the first case of gonorrhoea was reported in Changsha City in 1977, gonorrhoea has become prevalent in China. The reported incidence of gonorrhoea increased from 10.09 cases per 100,000 population in 1991 to 18.57 cases per 100,000 population in 2001 (Gong et al. 2002), followed by a decline from 22.92 cases per 100,000 population in 2000 to 7.61 cases per 100,000 population in 2013 (Gong et al. 2015). The gonorrhoea incidence then increased to reach 9.59 cases per 100,000 population in 2018, which is a 36.03% increase compared with the incidence in 2014 (Yue et al. 2019). Thus, gonorrhoea is now an important public health issue in China. To develop effective strategies for gonorrhoea prevention and control, there is a need to evaluate the seasonality and potential main determinants of seasonal fluctuations in disease patterns. However, no study has evaluated the seasonal trends of gonorrhoea in China. Therefore, we performed the present study with the following aims: (1) to determine if there were any seasonal trends in gonorrhoea incidence in China from 2006 to 2019; (2) to investigate the potential relationship between meteorological factors and gonorrhoea infection.

Material and methods

Data sources

The gonorrhoea case data were obtained from the Disease Prevention and Control Bureau (http://www.nhc.gov.cn/jkj/new_index.shtml) and the Data-Center for China Public Health Science, Chinese Center for Disease Control and Prevention (<https://www.phsciencedata.cn/Share/>), and the incidence of gonorrhoea in China from 1 January 2006 to 31 December 2019 was analyzed.

Gonorrhoea is diagnosed based on the following three aspects: epidemiological history, clinical manifestations, and laboratory findings. A positive epidemiological history includes: a history of unsafe sex, multiple sexual partners or sexual partners with infections, or a history of close contact with a person with gonorrhoea; children with a history of sexual abuse; newborns whose mothers have a history of gonorrhoea. Clinical manifestations include urethritis for males, and cervicitis, urethritis, vestibular adenitis, and perianal inflammation for females. Positive laboratory findings include: (1) gram-positive diplococcus on microscopic examination; (2) positive *Neisseria*

gonorrhoeae culture; (3) positive nucleic acid test for *N. gonorrhoeae*. Gonorrhoea is suspected in patients with a positive epidemiological history and clinical manifestations, and is definitively diagnosed when a suspected case has one of the positive laboratory findings (Wang et al. 2020).

Meteorological data from the same period were obtained from the South China Meteorological Data Sharing Center, including the monthly average temperature, relative humidity, atmospheric pressure, sunshine hours, rainy days, and precipitation.

Study design

This was an ecological study in epidemiology that analyzed aggregate gonorrhoea, meteorological, and socioeconomic data from 1 January 2006 to 31 December 2019 in Chinese mainland. Gonorrhoea time-series data were analyzed and the seasonality of gonorrhoea was analyzed by the ratio-to-moving average method (Kakran et al. 2015) and seasonal subseries plots.

A secondary analysis was performed to correlate the number of patients with gonorrhoea and meteorological factors using the Spearman assay, and the attributable risks of meteorological indexes on gonorrhoea cases was analyzed using the distributed lag non-linear model (DLNLM).

Ratio-to-moving average method

Seasonal indices were calculated quarterly using standard methods (Croxtton 1944). The first to fourth quarters were defined as January to March, April to June, July to September, and October to December, respectively.

The basis of the moving average ratio method is the multiplication model $Y = T \times S \times C \times E$, where T is the long-term change trend, S is the seasonal change trend, C is the periodic change trend, and E is the irregular random change. The following calculation steps were used:

- (1) The four-quarter moving average was used to eliminate seasonal changes and irregular changes, and the $T \times C$ value was calculated.
- (2) $Y / (T \times C)$ was calculated to obtain the estimated value ($S \times E$) of seasonal and irregular changes (the moving average ratio).

The seasonal index of the moving average of each season was calculated and corrected by averaging the moving average ratio of the same season in previous years, remove the influence of the irregular change E from $S \times E$, and obtaining

the estimated value of the seasonal change S , which is the seasonal index.

Seasonal subseries plots

Seasonal subseries plots are a specialized graphical technique that detects seasonality in a time series. This technique was used to detect the seasonality of gonorrhoea cases. Excel was used to make a cycle plot; the Excel functions “sum of”, “average”, “offset”, and “trend offset” were used to calculate and plot the averages and trends for different quarters (Kyd 2008).

Analysis of the effect of meteorological factors on gonorrhoea cases using the distributed lag non-linear model

The general Poisson distribution was used as the connection function of the DLNM to fit the time series of gonorrhoea onset and meteorological factors. Other potential risk factors (including time, season, relative humidity, air pressure, sunshine hours, rainy days, and precipitation) were also incorporated into the model.

$$\text{Log}(Y_t) = \alpha + \beta \times T_{t,l} + \text{ns}(\text{Time}, \text{df}_{\text{Time}}) + \text{ns}(\text{RH}, \text{df}_{\text{RH}}) + \text{ns}(\text{Rainday}, \text{df}_{\text{Rainday}}) + \text{ns}(\text{Rainfall}, \text{df}_{\text{Rainfall}})$$

Y_t is the number of new onset gonorrhoea cases in the t -th month; α is the intercept; $T_{t,l}$ is obtained by the cross basis function in the DLNM matrix of monthly average temperature (l is the number of months of temperature lag); β is the coefficient vector of the matrix $T_{t,l}$; ns represent natural cubic spline function, which used to generate the B-spline basis matrix for a natural cubic spline; time is the sequence of months in the study period (1, 2, ..., 156); RH is the average monthly relative humidity; Rainday is the average monthly number of rainy days; Rainfall is the average monthly rainfall.

In accordance with the principle of minimizing partial autocorrelation function, the degree of freedom (df) of time was set to 1 df/year (i.e., $\text{df} = 1 \times 13 = 13$) to control the long-term and seasonal trends. The temperature $\text{df} = 3$, relative humidity $\text{df} = 7$, pressure $\text{df} = 6$, sunshine hours $\text{df} = 3$, monthly rainy days $\text{df} = 4$, and precipitation $\text{df} = 6$. In the cross-basis function, the distribution functions of temperature (t) and lagging months (l) were set to ns , $\text{df} = 6$, the number of knots nodes was 5 (temperature distribution was uniformly set); the maximum number of lagging months was set to 6, $\text{df} = 4$, and the number of knots nodes was set uniformly using the log knots function. The effect value was estimated with the median level of the monthly mean temperature as a reference.

Statistical methods

The statistical analysis was performed using R software (version 3.6.1). The DLNM was implemented using the “DLNM” package. The statistical tests were two-sided, with the mean value set at 0.05.

Patient and public involvement

Patients or the public WERE NOT involved in the design, or conduct, or reporting, or dissemination plans of our research.

Results

Overview of gonorrhoea infection from January 2006 to December 2019

The overall number of gonorrhoea cases showed a U-shaped trend, with a significant decrease from 2006 (156,679) to 2012 (69,365) and rebound reaching 140,655 in 2017 (Fig. 1). The baseline characteristics of the aggregate gonorrhoea cases are showed in Fig. 1 (age distribution) and Fig. 1 (regional distribution). Most patients with gonorrhoea were

in the sexually active age group of 16–49 years and lived in East and South China, which are economically developed areas.

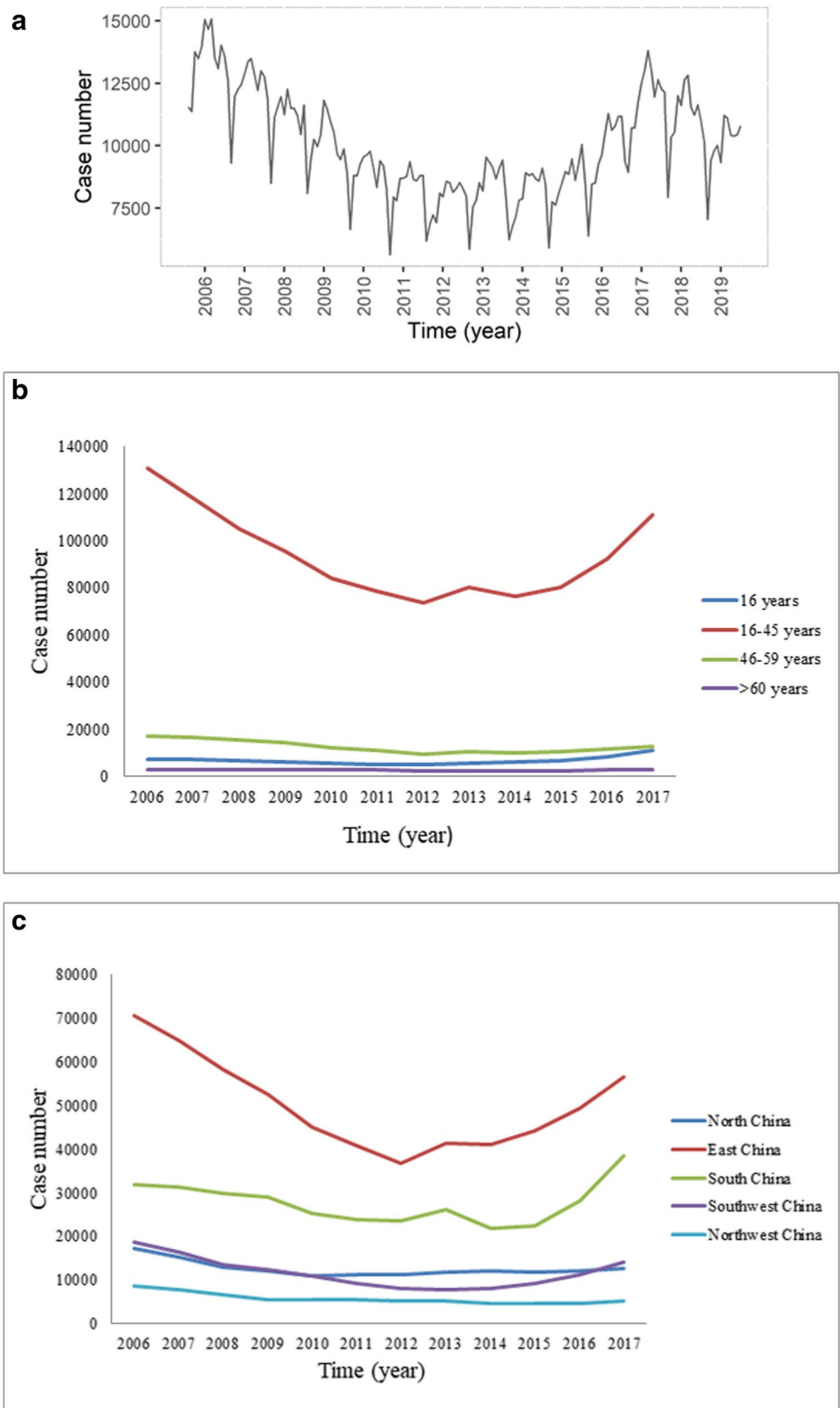
The national monthly average temperature, relative humidity, air pressure, sunshine hours, rainy days, and rainfall showed significant seasonal cyclic changes (Supplementary Fig. 1).

Seasonal variation of gonorrhoea cases from January 2006 to December 2019

Similar to the seasonality seen with the ratio-to-moving average method, the seasonal subseries plots showed that the number of gonorrhoea cases peaked in the third quarter and declined in the first quarter. The average number of gonorrhoea cases was highest (32,541.07) in the third quarter and lowest (26,437.64) in the first quarter (Fig. 2).

Table 1 shows the overall seasonal indices after seasonal adjustment of the data from 2006 to 2019. A decrease in gonorrhoea cases occurred in the first quarter of each year. The seasonally adjusted average ratio of gonorrhoea cases was highest in the third quarter (108.78%) followed by the fourth quarter (105.07%), while a trough was observed in the second quarter (99.11%) and first quarter (87.03%).

Fig. 1 Gonorrhoea incidence and seasonality from 2006 to 2019. **A** Gonorrhoea incidence from January 2006 to December 2019. **B** Age distribution of the reported gonorrhoea cases. **C** Regional distribution of the reported gonorrhoea cases



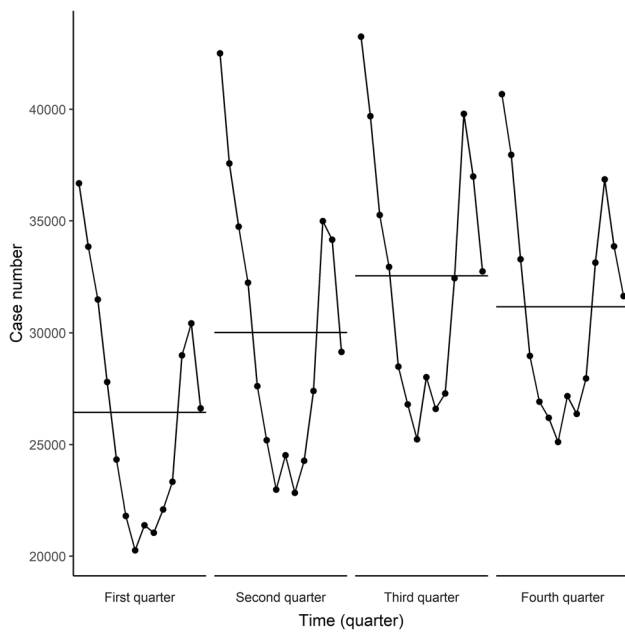


Fig. 2 Seasonal subseries plots demonstrating the trends during the four quarters. The first plot shows the data for the first quarter of every year, the second plot shows the data for the second quarter, and so on. The horizontal lines represent the means for each quarter

Correlation between gonorrhea infection and meteorological factors

The results of the Spearman assay showed that the reported number of patients with gonorrhea was positively correlated with temperature, relative humidity, precipitation, and number of rainy days, all of which were simultaneously included in the model (Fig. 3).

Lag effects evaluated by the distributed lag non-linear model

Lag effects of monthly mean temperature on the risk of gonorrhea onset

In the model with a lag time of 0 month, the risk of gonorrhea onset was high at 6–11 °C, with a significant difference compared with the annual average temperature of 13 °C. The risk of gonorrhea onset was highest at 7 °C (relative risk [RR]: 1.145; 95% confidence interval [CI]: 1.028–1.274); that is, compared with the risk of gonorrhea onset at an average monthly temperature of 13 °C, the risk of gonorrhea onset was increased by 14.5% at an average monthly temperature of 7 °C. The risk of gonorrhea onset was the

Table 1 Quarterly moving average ratio and correction of gonorrhea in China from 2006 to 2019 (%)

Year	The first quarter (Jan–Mar)	The second quarter (April–Jun)	The third quarter (July–Sep)	The fourth quarter (Oct–Dec)
2006	–*	–*	107.0	103.1
2007	88.2	99.9	107.4	104.5
2008	88.9	101.4	106.1	102.5
2009	87.3	103.9	109.6	99.7
2010	87.2	101.9	107.4	103.9
2011	85.9	100.4	108.0	107.7
2012	84.9	97.7	107.2	105.2
2013	87.6	98.0	111.0	108.8
2014	85.6	93.9	109.3	107.0
2015	88.7	96.3	106.8	107.1
2016	86.0	96.4	108.9	105.4
2017	87.0	100.9	112.6	104.1
2018	87.0	99.8	110.8	104.9
2019	85.5	96.2	–*	–*
Sum of each quarter moving averages after removing extreme value	1129.8	1286.7	1412.1	1363.9
Mean of each quarter moving averages after removing extreme value	86.90769	98.97692	108.6231	104.9154
Seasonally adjusted average	87.03322	99.11988	108.78	105.0669

*: Some quarterly moving average ratio cannot be calculated because of lacking corresponding data. As only the data of 2006.1–2019.12 were collected in this study, the quarterly moving average ratio of the first and second quarters in 2006 can't be calculated because of data lack of 2005–11 and 2005–12, and the quarterly moving average ratio of the third and fourth quarters in 2019 can't be calculated because of data lack of 2020–01, 2020–02. The 1st quarter: Jan–Mar; The 2nd quarter: April–Jun; The 3rd quarter: July–Sep; The 4th quarter: Oct–Dec. Correction Factor: $400/399.4231 = 1.001444$

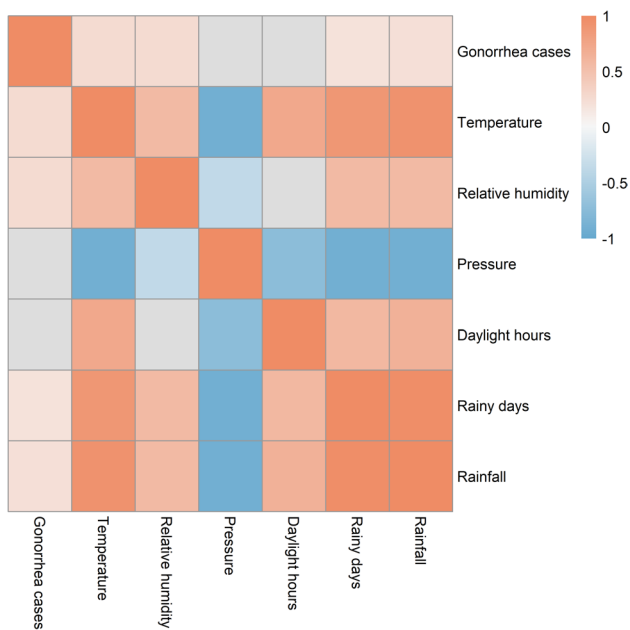


Fig. 3 Correlation between gonorrhea infection and meteorological factors. Orange/red represents positive correlation, blue represents negative correlation, and gray represents no correlation (no statistically significant difference, $P > 0.05$)

second highest at an average monthly temperature of 6 °C (RR: 1.135; 95% CI: 1.005–1.282) (Fig. 4A).

In the model with a lag time of 1 month, the risk of gonorrhea onset was high at 7–11 °C, and significantly differed at various temperatures. The risk of gonorrhea onset was highest at an average monthly temperature of 7 °C (RR: 1.108; 95% CI: 1.006–1.219), followed by an average monthly temperature of 8 °C (RR: 1.097; 95% CI: 1.015–1.186) (Fig. 4B).

The risk of gonorrhea onset did not significantly differ in accordance with the average monthly temperature in other lag time models (Fig. 4C–G).

Lag effects of monthly mean temperature on the cumulative risk of gonorrhea onset

The cumulative risk of gonorrhea onset was high at 6–11 °C, and the RR at 7 °C with a lag time of 2 months was 1.362 (95% CI: 1.025–1.809). The difference was statistically significant compared with the annual average temperature of 13 °C, and the effect lasted for up to 2 months (Supplementary Fig. 2A–C).

At 8–10 °C, the impact of temperature lasted for 3 months. In the model with a lag time of 3 months (Supplementary Fig. 2A–D), the RRs of the cumulative risks of gonorrhea onset at 8 °C, 9 °C, and 10 °C were 1.377 (95% CI: 1.008–1.881), 1.285 (95% CI: 1.023–1.615), and 1.180 (95% CI: 1.017–1.369), respectively.

The estimation of the cumulative relative risk of gonorrhea onset after a monthly average temperature of 8 °C for 3 months showed that the RR was 1.377, and 95% CI was 1.008–1.881; that is, relative to an average monthly temperature of 13 °C, the cumulative risk of gonorrhea onset after 3 months with an average temperature of 8 °C was increased by 37.7%.

Extreme temperature analysis

The national monthly average temperature was 11.80 ± 9.23 °C (range –5.61 °C to 24.61 °C) and the median annual temperature was 13 °C. The 2.5 percentile of the annual temperature (–3 °C) was defined as the extremely low temperature to estimate the effect of low temperature, while the 97.5 percentile of the annual temperature (24 °C) was defined as the extremely high temperature to estimate the effect of high temperature. The results showed that neither an extremely low temperature nor an extremely high temperature had an effect on the incidence of gonorrhea (Supplementary Table 1).

Attributable risks of gonorrhea due to short-term temperature exposure

Using the “backward perspective” method, the monthly average temperature of 13 °C was set as the baseline exposure level, and the cumulative lag was set between 0 and 6 months. The attribute number was 86,518 gonorrhea cases due to exposure to temperatures of 5–12 °C (95% CI: –71,224 to 244,560), and the attribution score was 5.02% (95% CI: –3.84%, 13.88%).

Discussion

Gonorrhea is caused by *N. gonorrhoeae* and is one of the most common STDs worldwide. Gonococcal infections are asymptomatic in 10% of males and most females (Detels et al. 2011), which exacerbates transmission. As antibiotic treatment of gonorrhea is effective, the focus is on prevention and control, which requires good understanding of the mechanism of disease transmission.

Seasonal variation in gonorrhea incidence has been reported in many countries; however, the seasonality varies. Cornelius (1971) first reported that the incidence of gonorrhea in the USA is highest in the third quarter and lowest in the first quarter, which is the same as the present findings in China. In contrast, the number of gonorrhea cases in India is highest in the second quarter and lowest in the fourth quarter (Kakran et al. 2015). Gonorrhea is most prevalent in the summer months in Israel from 1978 to 2008 (Mimouni et al. 2010). Aside from the meteorological factors related to the

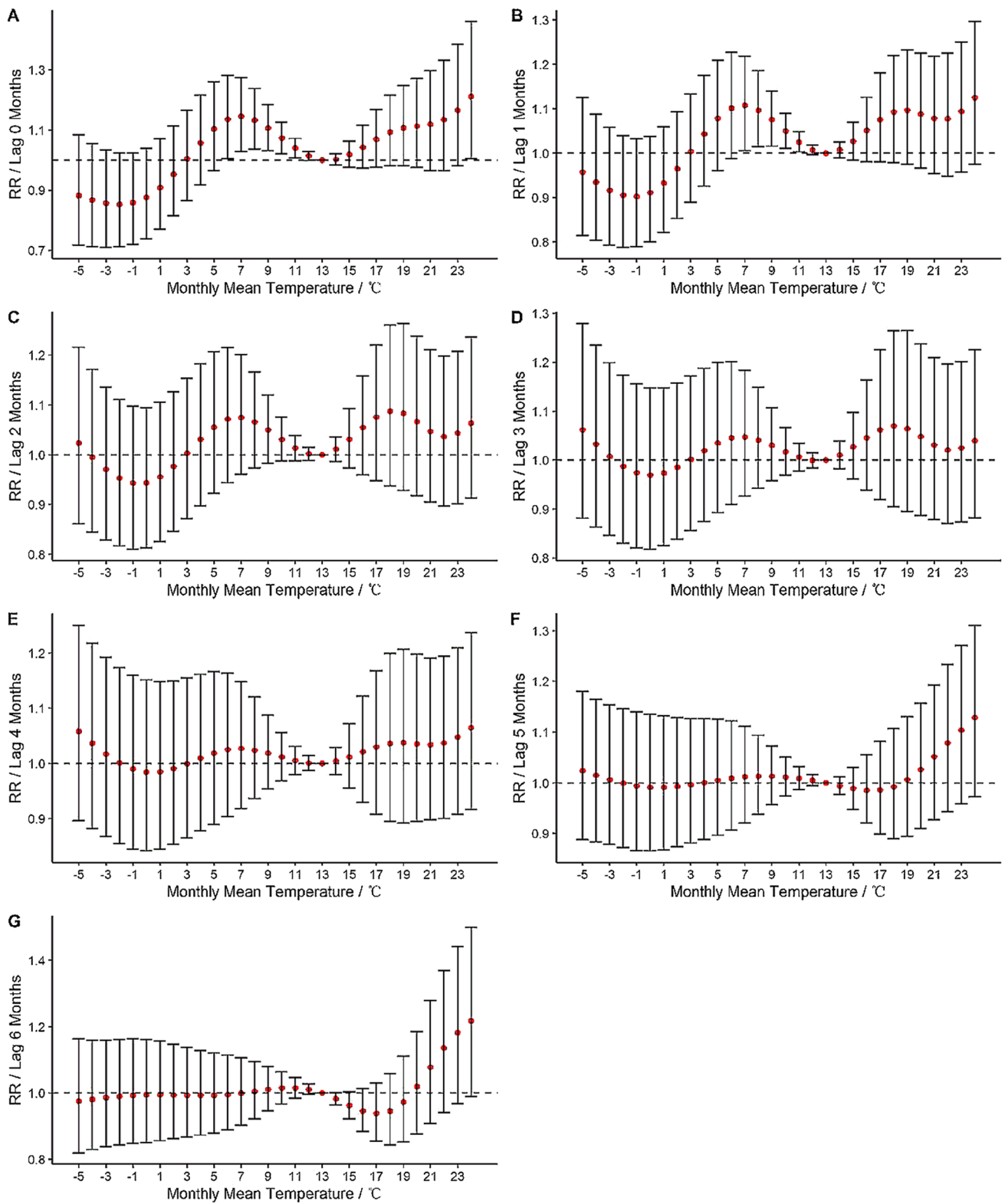


Fig. 4 Lag effects of monthly mean temperature on the risk of gonorrhea onset. **A** Lag effects of 0 month; **B** lag effects of 1 month; **C** lag effects of 2 months; **D** lag effects of 3 months; **E** lag effects of 4 months; **F** lag effects of 5 months

geographical environment, the differences between countries in the seasonality of gonorrhoea may be associated with the sexual behavior and humanities and social habits of local populations. For example, the highest reported gonorrhoea incidence is from January to May in Burkina Faso of West Africa, which correlates with the harvest season and reflects increased sexual contact among young, mobile men (Damiba et al. 1990). India has the highest culture-positive gonorrhoea incidence in the second quarter followed by the third quarter, which represent summer vacation periods for schools and colleges, and celebrations and social gatherings after harvesting in April; both factors are associated with increased sexual activity and partner changes (Kakran et al. 2015). Shah et al. (2007) reported significant 3-month cycles for all STDs (including gonorrhoea), with prominent peaks evident in March, May, August, and November from 1999 to 2003 in the USA. The authors proposed that the March and May peaks may be associated with the sexual activities of young adults during spring break, the August peak is representative of summer sexual activity of youths during school recess, and the November peak may be an expression of an endogenous annual rhythm in human biology, characterized by elevated levels of testosterone in young males (Shah et al. 2007). In the UK, an increase in sexual activity and unsafe sex occurs at or around the Christmas period, and a longer but less pronounced subsidiary period of increased sexual activity and unsafe sex coincides with the summer vacation period (Wellings et al. 1999). However, no study has investigated the relationship between the seasonality of gonorrhoea numbers and the season itself (i.e., the meteorological factors). Therefore, the current study investigated the effects of meteorological factors (monthly average temperature, relative humidity, atmospheric pressure, sunshine hours, rainy days, and precipitation) on the incidence of gonorrhoea.

The present study was the first to assess the seasonal variation of gonorrhoea in China. We found that the number of patients with gonorrhoea was positively correlated with temperature, relative humidity, and precipitation, which provides a better understanding of the seasonal trends of *N. gonorrhoeae* infection, resulting in better implementation of the optimal control strategies for this STD.

The DLNM not only considers the hysteresis effect of exposure factors, but also considers the nonlinear relationship between exposure and response, which is suitable for the study of health effects of time-series data like temperature (Gasparrini et al. 2015; Gasparrini & Leone 2014; Kim et al. 2019). We established this DLNM and found that compared with the average monthly temperature of 13 °C, the risk of gonorrhoea onset was most increased at 7 °C (risk increased by 14.5%), followed by 6 °C, and the cumulative risk of 3 months at 8 °C was increased by 37.7%. Therefore, the risk of gonorrhoea infection was highest at the temperature range of 6–11 °C, and more attention should be paid to

the temperature exposure in the past 3 months of individuals with unsafe sexual behavior.

The attribution score of temperature to gonorrhoea infection was 5.02% for exposure at 5–12 °C. The influence of meteorology on this infectious disease is consistent with that of a previous study that reported an attribution score of less than 18% (Ma et al. 2020). The present study confirmed the effects of temperature on reported gonorrhoea cases, which is worthy of more attention because a relatively small percentage (5.02%) of cases attributable to temperature causes a huge actual absolute number of potentially infected persons (more than 85,000).

The present study has the following limitations. First, the incidence data were based on monthly aggregation; incidence data with a higher resolution (such as the daily incidence) obtains much more accurate results. Second, based on the analysis of national data, exposure levels vary widely among regions. Further studies with accurate data from each area and time are necessary. As the meteorological factors contribute to less than 20% of the variation in infection transmission (Ma et al. 2020), a complex model including multiple biomedical environmental and social factors should be considered.

In conclusion, the present study shows that the reported number of gonorrhoea cases was positively correlated with temperature and humidity, and reached a peak in July–September, followed by October–December. However, the seasonality of reported gonorrhoea cases is not particularly obvious, suggesting that sexual behavior or other social economic factors may interfere or weaken the effect of meteorological factors on the disease. The present findings suggest that increased emphasis should be placed on screening for gonorrhoea infection during summer and autumn, and that education on safe sexual behavior should be promoted during these times.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s11356-021-17823-6>.

Author contribution BJ and CJ provided overall guidance and managed the project. LY and ZLJ set up the statistical model of the data and finished the manuscript on the basis of comments from other authors. All other authors provided data, developed models, reviewed results, provided guidance on methods, or reviewed the manuscript.

Data availability The data of gonorrhoea cases were obtained from the Disease Control and Prevention Bureau (http://www.nhc.gov.cn/jkj/new_index.shtml) and the Data-Center for China Public Health Science, Chinese Center for Disease Control and Prevention (<https://www.phsciencedata.cn/Share/>). The meteorological data of the same period were obtained from the South China Meteorological Data Sharing Center. The data that support the findings of this study are available from Dr. Jin Bu (dr.jinbu@gmail.com) upon reasonable request.

Declarations

Ethics approval and consent to participate Not applicable.

Consent for publication Not applicable.

Conflict of interest The authors declare no competing interests.

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