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ORIGINAL PAPER

Impact of meteorological changes on the incidence of scarlet fever in Hefei City, China

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Abstract Studies on scarlet fever with meteorological factors included were few. We aimed to illustrate meteorological factors' effects on monthly incidence of scarlet fever. Cases of scarlet fever were collected from the report of legal infectious disease in Hefei City from 1985 to 2006; the meteorological data were obtained from the weather bureau of Hefei City. Monthly incidence and corresponding meteorological data in these 22 years were used to develop the model. The model of auto regressive integrated moving average with covariates was used in statistical analyses. There was a highest peak from March to June and a small peak from November to January. The incidence of scarlet fever ranges from 0 to 0.71502 (per 10^5 population). SARIMAX $(1,0,0)(1,0,0)_{12}$ model was fitted with monthly incidence and meteorological data optimally. It was shown that relative humidity ($\beta = -0.002$, $p = 0.020$), mean temperature ($\beta = 0.006$, $p = 0.004$), and 1 month lag minimum temperature ($\beta = -0.007$, $p < 0.001$) had effect on the incidence of scarlet fever in Hefei. Besides, the incidence in a previous month (AR(β) = 0.469, $p < 0.001$) and in 12 months before (SAR(β) = 0.255, $p < 0.001$) was positively associated with the incidence. This study shows that scarlet fever incidence was negatively associated with monthly minimum temperature and relative humidity while was positively associated with mean temperature in Hefei City, China. Besides, the ARIMA model could be useful not only for prediction but also for the analysis of multiple correlations.

Keywords Scarlet fever · Meteorological factor · Auto regressive integrated moving average model · Time series analysis

Introduction

In addition to relation to age, sex, health service level, and immunity of body, incidence of infectious diseases is associated with environmental factors in which meteorological factors are important component, such as temperature, atmospheric pressure, rainfall, or relative humidity, etc. Meteorological variation not only affects the immunity of body but also affects the reproduction, development, and transmission of infectious diseases (Medlock and Leach 2015; Rossati et al. 2014). Especially given that global temperature has been generally warming, more attention has been paid to the relationship of infectious diseases with meteorological factors. Some studies were found to report the relationship between them (Lin et al. 2012; Soebiyanto et al. 2014).

Among these infectious diseases, scarlet fever is an acute respiratory infectious disease arising from group-A beta-hemolytic streptococci (GAS) (You et al. 2013). Lacking of specific protective measure, scarlet fever outbreaks still occurred in some areas during the twenty-first century, such as the scarlet fever outbreak with 50 cases in two nurseries in southwest England in 2006 (Hoek et al. 2006), 45 cases in a secondary school in China in 2006 (Yang et al. 2007), and a large outbreak in mainland China and Hong Kong in 2011 (Chen et al. 2012; Davies et al. 2015). If effect of meteorological factors on the incidence of scarlet fever was demonstrated, prevention and controlling of it would be promoted greatly.

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Duncan et al. (1996) found that the dynamics of the scarlet fever epidemics could be represented by a linear mathematical model and its epidemics were significantly correlated with dry conditions in spring/summer and with an oscillation in wheat prices in England and Wales. Briko et al. (2003) found that scarlet fever morbidity had a pronounced seasonal (autumn-winter) pattern in Moscow and Russian Federation. Although these studies about the relationship between the incidence of scarlet fever and meteorological factors were reported, only the seasonal factor had been included without other meteorological factors. Additionally, reports from China are lacking.

In this study, we performed a time series analysis on the relationship between the monthly incidence of scarlet fever and monthly meteorological factors in past 22 years in Hefei City, China. We aimed to find out meteorological factors and lag incidence's effects on monthly incidence of scarlet fever.

Materials and methods

Climate and geography of Hefei City

Hefei City, located in the middle of China with the north latitude of 32° and east longitude of 117°, is about 11, 408.48 km^2 in land size, between the Changjiang River and Huaihe River, belongs to moist monsoon climate of semi-tropics and has the traits of clear distinction among the four seasons, temperate climate, moderate rainfall, and polytropic spring temperate. The population of Hefei City grows from 3, 487,317 to 4,646,440 over these 22 years.

Data of scarlet fever

Time series of monthly incidence of scarlet fever was gathered from the center for disease control and prevention of Hefei City. Cases of scarlet fever, diagnosed according to the criterion from Health Ministry of China, were collected from the report of legal infectious disease of Hefei City from 1985 to 2006. The scope of surveillance was the resident population of Hefei City. The average population was obtained from Public Security Bureau of Hefei City.

Meteorological data

Meteorological data, including mean temperature, minimum temperature, relative humidity, atmospheric pressure, and rainfall which were presented monthly from 1985 to 2006, were obtained from weather bureau of Hefei City. Daily mean temperature is the mean temperature value of 2, 8, 14, and 20 o'clock in a day, and the monthly mean temperature is the average of all days in a month. Monthly minimum temperature is absolute minimum temperature in observed period. These data cover the study period without any missing values.

Statistical analysis

Spearman's rank correlations were used to do univariate analysis to find correlation between meteorological factors and incidence of scarlet fever.

Auto regressive integrated moving average (ARIMA) model was composed of auto regression (AR) with lag number denoted by p, integrate (I) with lag number denoted by d and moving average (MA) with lag number denoted by q (Hillmer and Tiao 1982). The model ARIMA (p, d, q) could be written as follows:

$$\phi(B)(1-B)^d X_t = \theta(B)\varepsilon_t,$$
$$\phi(B) = 1-\phi_1 B-\ldots-\phi_p B^p,$$
$$\theta(B) = 1-\theta_1 B-\ldots-\theta_q B^q,$$

in which X_t represents the value of time series at time t, ε_t represent a white noise series, B is a backward shift operator ($B^p X_t = X_{t-p}$), $\phi(B)$ is the autoregressive operator, and $\theta(B)$ is the moving average operator.

When the seasonal trend existed in time series, the ARIMA(p, d, q) extend to the multiplicative seasonal auto regression integrated moving average model SARIMA(p, d, q)(P, D, Q)$_s$. The seasonal parameter P represents seasonal autoregression, D represents seasonal differencing, Q represents seasonal moving average, and s represents seasonal cycle, which means the SARIMA model could be expressed in following form:

$$\Phi(B^s)\phi(B)(1-B)^d(1-B^s)^D X_t = \Theta(B^s)\theta(B)\varepsilon_t,$$
$$\Phi(B^s) = 1-\phi_{(s,1)}B-\ldots-\phi_{(s,P)}B^P s,$$
$$\Theta(B^s) = 1-\theta_{s,1}B-\ldots-\theta_{s,Q}B^{Qs}$$

SARIMAX model was an extension of SARIMA which included covariates as input series such as mean temperature, atmospheric pressure, and other meteorological factors:

$$X_t = \sum_{i=1}^{k} \frac{\theta_i(B)}{\phi_i(B)} B^{l_i} x_{it} + \frac{\Theta(B^s)\theta(B)}{\Phi(B^s)\phi(B)(1-B)^d(1-B^s)^D}\varepsilon_t$$

In the above model, x_i represents input series of the ith covariate, l_i represents the lag number of backward shift, $\phi_i(B)$ represents the autoregressive operator of this series, and $\theta_i(B)$ represents the moving average operator of this series.

The Ljung-Box Q test was applied to test whether residual series were white noise. An optimal ARIMA model would be mainly diagnosed by normalized Bayesian information criterion (BIC) value and determination coefficient (R^2). Bayesian information criterion is a comprehensive method to measure the overall fit of a model. It is a score based upon the mean square error (MSE). It also includes a penalty which removes the advantage of models with more parameters, so that different models for the same series can be compared by this statistics objectively (Akinbobola and Omotosho 2013).

Spearman's rank correlations and time series model were performed in SPSS 20.0. Augmented Dickey-Fuller (ADF) test whose probability level was $\alpha = 0.01$ was done by Stata 13.0. Probability level less than 0.05 in two-tailed test were used as a criterion of significance in ARIMA model.

Results

Description and univariate analysis

There were 1639 scarlet fever cases in the last 22 years in Hefei City. Monthly average incidences of scarlet fever in each year were 0.1233, 0.1076, 0.0532, 0.1014, 0.2019, 0.2626, 0.2849, 0.1708, 0.2292, 0.1639, 0.3016, 0.2137, 0.1823, 0.1197, 0.1791, 0.1405, 0.1366, 0.1016, 0.0650, 0.2511, 0.3727, and 0.2001 per 10^5 population, respectively.

The sequence of monthly incidence among 22 years included 264 values. The trend of incidence of scarlet fever from January to December in 22 years was shown in Fig. 1, where the bold curve represents the mean level of 12 months. On the whole, it was found that there was a highest peak from March to June and a small peak from October to January. Incidences in warm and cool seasons were higher than those in cold and hot seasons.

The highest monthly incidence is 0.71502 (per 10^5) in April 2005, the lowest monthly incidence is 0 in 13 month overall which were February 1986, September 1986, January 1987, August 1987, January 1988, September 1994, September 1995, November 1996, December 1996, December 2000, September 2002, October 2002, and December 2003, respectively. More parameters about incidence and meteorological factors were shown in Table 1.

Correlation of the incidence of scarlet fever with meteorological factors was shown in Table 2. The mean temperature, relative humidity, and minimum temperature were negatively correlated with the incidence of scarlet fever in Hefei City.

ARIMA model

Some transformations like square root, natural logarithm on dependent variable, and meteorological series were done, but the effect was not obvious and R^2 was even smaller than former after fitting the model. The detailed comparison results could be seen in Table 3. In this case, we used the original data to develop the ARIMA model.

An ARIMA model with 264 monthly incidence data in last 22 years and without any covariates was developed firstly. Time series graph (Fig. 2) was drawn to show the overall trend of incidence in last 22 years, and ADF test was done to show that the time series was stationary ($p < 0.001$). So, there was not necessary to do differencing and seasonal differencing ($d = D = 0$). Then, graphs of ACF and PACF (Fig. 3) were plotted to help determine the possible values of p, q, P, and Q. It was found that the ACF value of lag12 and lag24 whose lag number was multiple of 12 had obvious auto regression which has statistical significance. So, there could be seasonal cycle of 12 month (S = 12), and SARIMA model could be applied. After this, model identification and parameter estimation were done to analyze whether it is statistical significant. By these processes, several suitable models were conducted and Box-Jenkins Q test was performed to testify whether their residuals were equivalent to white noises (significant level $p > 0.05$). The comparison result was shown in Table 4. The final step was selecting optimal ARIMA model which had the lowest BIC value. It can be seen that ARIMA(1,0,0) is optimal non-seasonal model whose normalized BIC value is −4.408 and

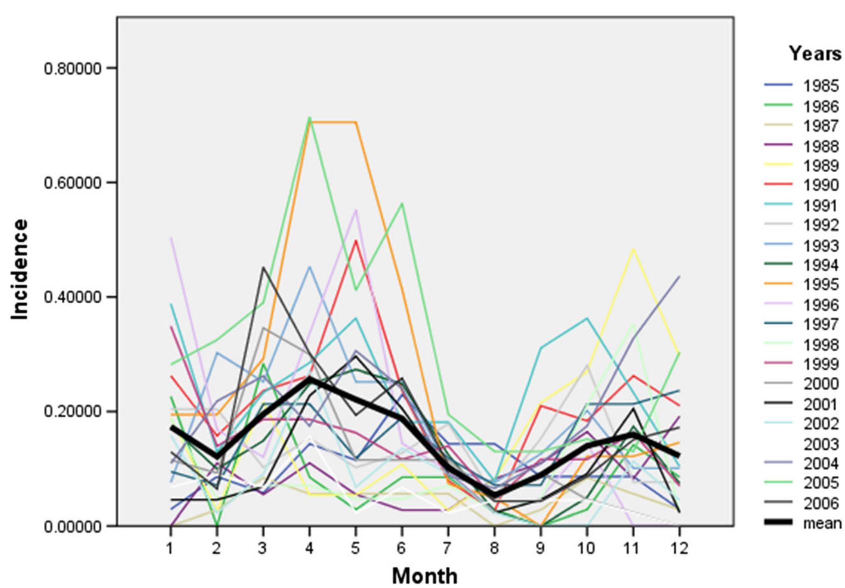


Fig. 1 Incidence of scarlet fever monthly in last 22 years

Table 1 Description of monthly meteorological factors and incidence of scarlet fever

	Median	Q_L~Q_U	Min	Max
Incidence (/10^5)	0.11519	0.559604~0.2109682	0	0.71502
Rainfall (mm)	66.250	32.225~115.575	0	448.1
Air pressure (hPa)	1012.600	1004.025~1012.600	998.7	1026.7
Mean temperature (°C)	17.100	7.350~24.375	0.7	30.6
Relative humidity (%)	76.00	70.00~79.00	55	87
Minimum temperature (°C)	6.450	−2.00~15.65	−13.5	23.6

SARIMA$(1,0,0)(1,0,0)_{12}$ is optimal seasonal model which has the lowest normalized BIC value (−4.470).

ARIMAX model

Meteorological factors were added as covariates into the model above. Only the covariates which had significant estimated parameter and could lower the normalized BIC value were selected. The process of different covariates entering models was shown in Table 5. It can be seen that SARIMAX$(1,0,0)(1,0,0)_{12}$ with covariates of relative humidity, minimum temperature, and mean temperature is optimal model whose R^2 (40.5 %) and normalized BIC value (−4.489) were more adequate. Relative humidity ($\beta = -0.002$, $p = 0.020$) and 1 month lag minimum temperature ($\beta = -0.007$, $p < 0.001$) were significant negative factors of scarlet fever incidence in Hefei City, while mean temperature ($\beta = 0.006$, $p = 0.004$) was a positive influence factor. In addition, p value of Ljung-Box Q test for this model was equivalent to 0.392 and RMSE was equivalent to 0.100. Finally, the best model can be written as follows:

$$\hat{Y}_t = 0.469Y_{t-1} + 0.255Y_{t-12} - (0.469 \times 0.255)Y_{t-13} - 0.002X_{\mathrm{RH},t}$$
$$-0.007X_{\mathrm{Tmin},t-1} + 0.006X_{\mathrm{Tmean},t} + 0.280$$

In the equation, covariates of mean temperature, minimum temperature, and relative humidity were abbreviated as X_{Tmean}, X_{Tmin}, and X_{RH}, respectively. The symbol t in subscript represents the terms of each covariate.

Discussion

At present, the rule of onset of scarlet fever remains unclear. The incidence from 1985 to 2006 in Hefei City was relatively low. However, there was a highest peak from March to June and a small peak from November to January, which was contradictory to the result of Briko et al.'s research (Briko et al. 2003). It might be related to the different climates of different areas.

In our research, relative humidity, mean temperature, and minimum temperature monthly were found to be related to the incidence of scarlet fever in Hefei City through univariate analyses. In addition, relative humidity, mean temperature, and minimum temperature were found to be influential factors of the incidence after fitting ARIMA model. Relative humidity was negatively associated with the incidence of scarlet fever ($\beta = -0.004$, $p < 0.001$). The larger the relative humidity was, the lower the incidence. It is not determined by how the relative humidity affects the incidence of scarlet fever. Lowen et al. (2007) had explored the mechanism through an animal experiment which showed how it affected the transmission of influenza virus. Aydogdu et al. (2010) found that monthly total outdoor bacterial counts were negatively associated with mean relative humidity and mean rainfall. Based on their studies, we further explored the mechanism from the two points as follows: the ability of producing toxin and enzyme from beta-hemolytic streptococcus under different relative humidity was discrepant; the second mechanism might act at the level of the vehicle, the respiratory droplet. At low relative humidity, evaporation of water from exhaled bioaerosols would occur rapidly, leading to the formation of droplet nuclei; conversely, at high relative humidity, small respiratory droplets would take on water, increase in size, and settle more quickly out of the air (Lowen et al. 2007). The second mechanism is more reasonable, which is in accord with the result of our research.

Mean temperature in every month had a positive effect on monthly incidence ($\beta = 0.006$, $p = 0.004$). There were several studies in accord with our result, for example, Rubio (Rubio 2004) found that *Streptococcus pneumoniae* increases

Table 2 Correlation between scarlet fever incidence and meteorological factors

		Rainfall	Atmospheric pressure	Mean temperature	Relative humidity	Minimum temperature
Incidence/(10^5)	r_s	−0.118	0.071	−0.137	−0.297	−0.159
	p	0.056	0.249	0.026*	<0.001*	0.010*

*p value < 0.05

Table 3 Comparison between different transformations on incidence of scarlet fever in ARIMA model

Model	Transformation	R^2 (%)	Normalized BIC	Ljung-Box Q test		
				Statistic	DF	Significance
SARIMA$(1,0,0)(1,0,0)_{12}$	None	34.6	*−4.470*	18.511	16	0.295
SARIMA$(1,0,0)(1,0,0)_{12}$	Square root	32.8	−3.947	14.558	16	0.557
SARIMA$(1,0,0)(1,0,0)_{12}$	Arcsine square root	33.5	−3.743	15.020	16	0.523
SARIMA$(1,0,0)(1,0,0)_{12}$	Natural logarithm	35.3	−3.824	16.460	16	0.421

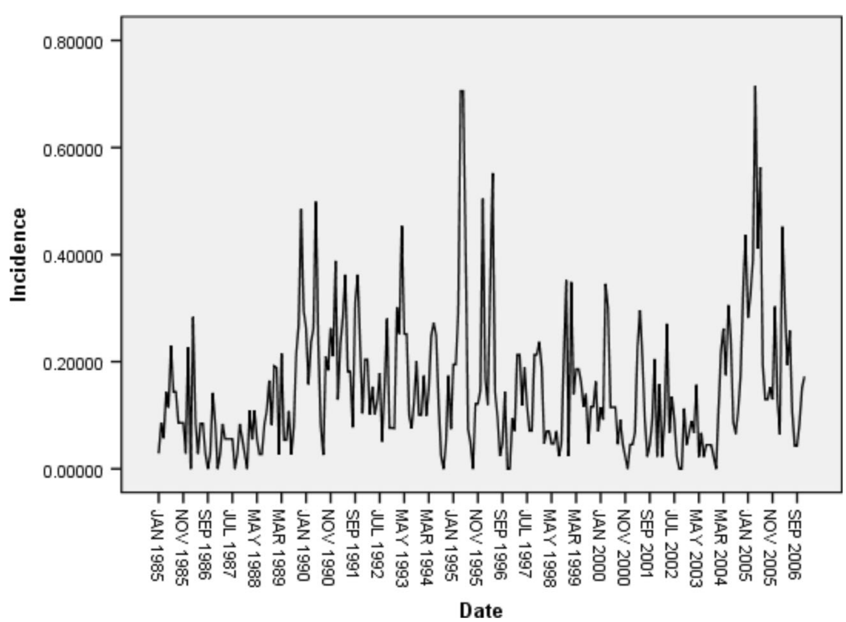
(>3.4 %) in March, November, and December, and in addition, with the mean temperature rising, *Streptococcus pneumoniae* also increases. Influenza also had similar effect from mean temperature which was reported by Hu et al. (2015). They explored the weather variability and influenza A (H7N9) transmission and found H7N9 incidence rate was significantly associated with fortnightly mean temperature (relative risk, 1.54; 95 % credible interval, 1.22–1.94). According to these studies, when the temperature was suitable for pathogen transmission, the higher mean temperature it was, the quicker pathogens reproduce which would cause more infection. However, minimum temperature played an inverse role in incidence of scarlet fever (β = −0.007, $p < 0.001$). This is mainly because of human indoor activities. In cold environment, people stayed more time in their room with windows and doors closed to keep warm which lead to terrible ventilation and increase the infection chance (Choo and Jalaludin 2015).

Although rainfall was not included in our model, it was still viewed as an influence factor. Rainfall and relative humidity had high correlation (r_s = 0.573, $p < 0.001$) and may had similar effect on incidence as it was reported in other studies (Huang et al. 2013). It might not influence incidence directly but through change of relative humidity and human activities (Dangi et al. 2014). These studies also found that atmospheric pressure showed significant inverse relationship with influenza A and also indirectly affect other meteorological factors derive seasonality of influenza virus transmission (Dangi et al. 2014). However, these two meteorological factors failed to show significant relationship and lower normalized BIC value in our study, so they were not fitted in our model.

The incidence of a previous month was also a significant predictor in our research. It was positively associated with the incidence of scarlet fever (AR(β) = 0.469, $p < 0.001$) which accords with other infectious diseases study (Wangdi et al. 2010). The incidence of the same month a year before had a positive effect on scarlet fever incidence (SAR(β) = 0.255, $p < 0.001$), as well. So, the incidence of a previous month and incidence in the previous 12 months can be important influencing factors for incidence of scarlet fever.

In summary, the meteorological factors' effect on scarlet fever in Hefei City was presented in our report clearly, but

Fig. 2 Time series plot of the incidence of scarlet fever over the last 22 years



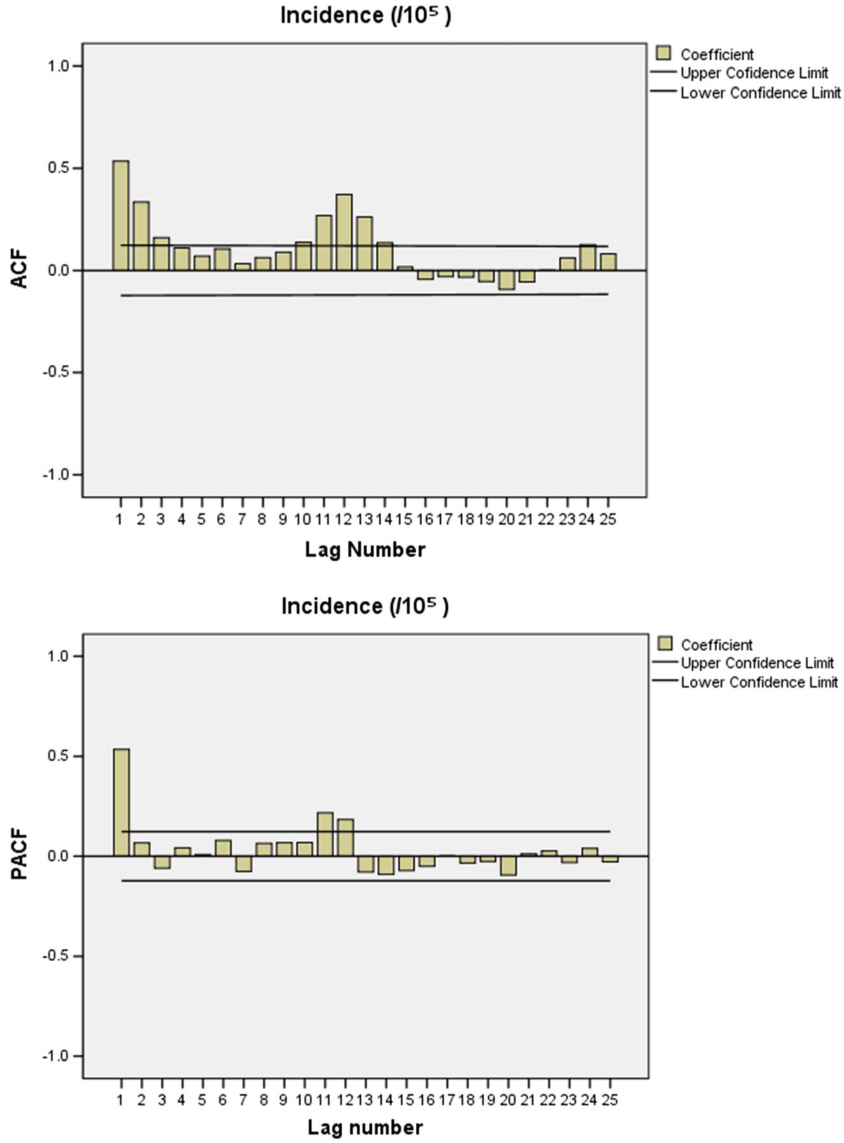


Fig. 3 Autocorrelation function (ACF) and Partial autocorrelation function (PACF) plot of original incidence

the conclusion should be further tested and explored with more data after 2006 in Hefei City. However, the incidence data after 2006 from CDC is incomplete, so further research cannot be taken at once.

Conclusions

This study shows that the incidence of scarlet fever was negatively associated with the monthly minimum temperature and

Table 4 Comparison between different non-seasonal and seasonal ARIMA models of scarlet fever incidence without covariate

Model	R^2 (%)	RMSE	Normalized BIC	Ljung-Box Q test		
				Statistic	DF	Significance
ARIMA(1,0,0)	28.7	0.108	*−4.408*	35.781	17	0.005
ARIMA(2,0,0)	29.0	0.108	−4.388	36.880	16	0.002
ARIMA(1,0,1)	28.9	0.108	−4.387	36.776	16	0.002
ARIMA(1,1,1)	22.5	0.109	−4.373	35.536	16	0.003
SARIMA(1,0,0)(1,0,0)$_{12}$	34.6	0.104	*−4.470*	18.511	16	0.295
SARIMA(1,0,0)(1,0,1)$_{12}$	35.3	0.103	−4.456	21.085	15	0.134
SARIMA(2,0,0)(1,0,0)$_{12}$	36.6	0.102	−4.452	12.938	14	0.531

Table 5 ARIMA models of monthly non-transformed scarlet fever incidence with different meteorological factors in Hefei

Model	Constant	AR			SAR			Meteorological factors				R^2 (%)	Normalized BIC
		Lag	β	p	Lag	β	p	Variables	Lag	β	p		
ARIMA(1,0,0)	0.015	1	0.535	<0.001	0	–	–	–				28.7	−4.408
ARIMAX(1,0,0)	0.336	1	0.484	<0.001	0	–	–	RH	0	−0.003	0.003	36.5	−4.449
								T_{mean}	0	0.005	0.004		
								T_{min}	1	−0.007	<0.001		
SARIMA$(1,0,0)(1,0,0)_{12}$	0.149	1	0.494	<0.001	1	0.291	<0.001	–				34.6	−4.470
SARIMAX$(1,0,0)(1,0,0)_{12}$	0.369	1	0.478	<0.001	1	0.261	<0.001	RH	0	−0.003	0.004	36.5	−4.475
SARIMAX$(1,0,0)(1,0,0)_{12}$	0.370	1	0.476	<0.001	1	0.257	<0.001	RH	0	−0.003	0.005	36.6	−4.451
								T_{min}	0	−0.001	0.585		
SARIMAX$(1,0,0)(1,0,0)_{12}$	0.373	1	0.472	<0.001	1	0.260	<0.001	RH	0	−0.003	0.009	38.5	−4.481
								T_{min}	1	−0.003	0.006		
SARIMAX$(1,0,0)(1,0,0)_{12}$	4.866	1	0.474	<0.001	1	0.252	<0.001	RH	0	−0.003	0.005	40.0	−4.480
								T_{min}	1	−0.006	<0.001		
								AP	0	−0.004	0.012		
SARIMAX$(1,0,0)(1,0,0)_{12}$	0.280	1	0.469	<0.001	1	0.255	<0.001	RH	0	−0.002	0.020	*40.5*	*−4.489*
								T_{min}	1	−0.007	<0.001		
								T_{mean}	0	0.006	0.004		

AR autoregressive, *SAR* seasonal autoregressive, *RH* relative humidity, T_{min} minimum temperature, T_{mean} mean temperature, *AP* atmospheric pressure

relative humidity while was positively associated with mean temperature in Hefei City, China. The seasonality and regularity of scarlet fever we found could be helpful for further incidence forecasting and disease prevention. We also recommend that ARIMA model could be a useful method not only for prediction but also for the analysis of multiple correlations of incidence and meteorological data. This method could be applied in some series data and was used to control the influence of data itself and revealed the correlation with other factors more clearly.

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Compliance with ethical standards

Conflict of interest The authors declare that this paper does not induce any conflicts of interests.

Ethical standards Our research was in compliance with the Helsinki Declaration (Williams 2008) approved by the ethics committee of Anhui Medical University.

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