

# Alarming increase of scrub typhus incidence in Yunnan province, southwest China, 2006–2017

**Peiying Peng** (✉ [peiyinpeng@hotmail.com](mailto:peiyinpeng@hotmail.com))

Qujing Medical College <https://orcid.org/0000-0001-9544-1527>

**Lei Xu**

Qujing Medical College

**Gu-Xian Wang**

Qujing Medical College

**Hui-Ying Zhang**

Qujing Medical College

**Lei Gong**

Qujing Medical College

**Wen-Yuan He**

Qujing Medical College

**Ben-Shou Yang**

Qujing Medical College

**Ting-Liang Yan**

Qujing Medical College

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## Research article

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## Abstract

**Background:** The bacteria *Orientia tsutsugamushi* is the causative agent of scrub typhus, mite-borne disease, which causes an acute febrile infectious illness in humans. An epidemiologic study was conducted to understand the characteristics of scrub typhus in Yunnan province and assist public health prevention and control measures.

**Methods:** Based on the data on all cases reported in Yunnan from 2006 to 2017, we characterized the epidemiological features. Q-type cluster method of hierarchical cluster analysis was adopted to analyze the incidence of scrub typhus. Together with the results of clustering, geographical distribution of scrub typhus was described.

**Results:** In total, 27,838 scrub typhus cases were reported in Yunnan during 2006-2017. Of these, 49.53% (13,787) were male and 50.47% (14,051) were female ( $P>0.05$ ). Most patients were children aged 0-5 years (13.16%) ( $P<0.01$ ) and farmers (68.41%) ( $P<0.05$ ). An almost twenty-fold increase in the number of patients was observed in 2017 (6,337 cases) compared to 2006 (307 cases). Baoshan city and Lincang city had the most cases accounting for 41.94%, while Diqing prefecture had the lowest incidence (only 3 cases). The majority of confirmed cases occurred yearly in August with a high temperature and rains. Sixteen cities (prefectures) infected of Yunnan were classified into three groups numbered in sequence.

**Conclusion:** The study results showed that the incidence of scrub typhus in Yunnan province is high and the annual incidence increased noticeably over time. Our results also indicate that surveillance and public education need to be focused on Baoshan City, Lincang City and Dehong Prefecture.

## Background

Scrub typhus (Tsutsugamushi disease) is an ancient infectious disease primarily endemic in several Asia-Pacific nations [1, 2]. It is an infection caused by the pathogen *Orientia tsutsugamushi*, which can be transmitted occasionally to humans after being bitten by infected Chigger mites (trombiculid mites)[3, 4]. *O. tsutsugamushi* spreads throughout the body via the blood and lymphatic vessels, so that patients infected with this microorganism manifest a variety of clinical symptoms and signs such as myalgia and diffuse lymphadenopathy [5]. The larval stage is the only parasitic stage when the pathogen is transmitted to people and other vertebrates [6, 7]. Rodents are important to maintenance of the disease in that they are known as incidental hosts for chigger mites [8]. It is estimated that more than half of the world's population live in tsutsugamushi disease endemic areas and that about 1 million cases occur annually [9]. Up to now, however, there is still no point-of-care diagnostics available and no reliable and effective human vaccine against tsutsugamushi disease, which will pose a significant threat to public health [2].

Scrub typhus is also widely distributed in China, including 16 cities or prefectures of Yunnan province [10, 11]. In recent years, local outbreaks of scrub typhus have occurred in many areas of Yunnan, and recently identified endemic foci of scrub typhus are reported to be expanding [12–14]. The increased incidence of tsutsugamushi disease in Yunnan offers an opportunity to enhance our understanding of the epidemiological trends of this reemerging and infectious disease. The results from our study will provide an authentic and reliable evidence for local health-care authorities to design strategies to alleviate the health effects of scrub typhus.

## Methods

## **Study area**

Yunnan, an inland province at a low latitude and high elevation, lying between 21°8'–29°15'N and 97°31'–106°11'E in southwestern China, has a vast territory with diversified and unique nature resources. Located in the southwest of China, Yunnan harbors around 45.97 million residents in its 16 cities or prefectures with a total land area of nearly 394000 km<sup>2</sup> ([http://stats.yn.gov.cn/tjsj/tjnj/201912/t20191202\\_908222.html](http://stats.yn.gov.cn/tjsj/tjnj/201912/t20191202_908222.html)). It mainly features a subtropical plateau monsoon climate type. Mean temperature for the hottest month (typically in July in Yunnan) is 19°C– 22 °C, while mean temperature for the coldest month (typically in January)

is 6 °C–8 °C. The annual average precipitations in most areas is more than 1000 mm (<http://www.yn.gov.cn/yngk/>).

## **Data collection and management**

In China, scrub typhus is a notifiable disease that must be reported to the China Center for Disease Control and Prevention. The case definition for tsutsugamushi disease consists of an individual who has traveled to an endemic area or reported contact with chigger mites or rodents within three weeks before the onset of illness, along with clinical manifestations (such as high fever, lymphadenopathy, skin rash, and eschars or ulcers), and at least one of the following laboratory criteria: an agglutination titer $\geq$ 1:160 in the Weil-Felix test using the OX<sub>K</sub> strain of *Proteus mirabilis*. A 4-fold or more rise of antibody titer against *O. tsutsugamushi* using the

indirect immunofluorescence antibody assay, detection of *O. tsutsugamushi* by PCR (polymerase chain reaction) in clinical specimens, or isolation of *O. tsutsugamushi* from clinical specimens [15]. Patients with other established causes of fever were excluded. A standard form was adopted by local physicians to collect individual information on each scrub typhus case, including epidemiological exposure histories, age, sex, address, date of onset, diagnosis, and laboratory test results. Routine case reporting is done by hospitals via the National Notifiable Disease Report System within 24 hours [15]. To describe epidemic characteristics and explore the incidence clustering of confirmed cases of scrub typhus in Yunnan China at the city (prefecture) level, we used surveillance data reported confirmed scrub typhus cases from 2006 to 2017, routinely collected by the Yunnan Provincial Notifiable Disease Report System. Population data at the city (prefecture) level were obtained from the National Bureau of Statistics of China, which is based on the Sixth National Census in 2010.

## **Statistical analysis**

The differences in the incidence rates of scrub typhus cases by sex,

age group, and occupation were analyzed using the chi-square test. *P* values <0.05 were considered statistically significant. Q type cluster method of hierarchical cluster analysis method together with Z-score standardization and squared Euclidean distance were adopted in the calculation clustering analysis under the statistical software package SPSS (v.25). The clustering result was presented in a dendrogram. The spatial distribution characteristics were showed in the form of a map of the incidence by ArcGIS 10.6.

## **Results**

A total of 27,838 clinically diagnosed and laboratory confirmed cases were reported in Yunnan province during 2006–2017, among whom 11 patients died. The overall case fatality was 0.04%. The annual incidence ranged

from 0.65/100,000 to 13.36/100,000, with a rapid uptrend observed year by year and with an average annual incidence rate of 4.87/100,000. Natural focus expansion was found. The number of confirmed scrub typhus cases peaked in 2017, when there

were 20.64 times more reported cases than in 2006. Scrub typhus cases, the incidence rate (1/100,000) and the mortality rate (1/100,000) have been increasing rapidly from 2006 to 2017 in Yunnan province, southwest China (Table 1, Fig. 1 & Fig. 2).

Table 1  
Epidemiologic features of scrub typhus cases in Yunnan province China, 2006–2017

| Year                       | No. of cases (%) | Incidence rate*<br>(1/100,000) | No. of deaths (%) | Mortality<br>rate<br>(1/100,000) | CFR# (%) |
|----------------------------|------------------|--------------------------------|-------------------|----------------------------------|----------|
| 2006                       | 307 (1.10)       | 0.65                           | 0 (0)             | 0                                | 0        |
| 2007                       | 365 (1.31)       | 0.77                           | 0 (0)             | 0                                | 0        |
| 2008                       | 526 (1.89)       | 1.11                           | 0 (0)             | 0                                | 0        |
| 2009                       | 1,045 (3.75)     | 2.20                           | 0 (0)             | 0                                | 0        |
| 2010                       | 1,155 (4.15)     | 2.44                           | 0 (0)             | 0                                | 0        |
| 2011                       | 1,346 (4.84)     | 2.84                           | 0 (0)             | 0                                | 0        |
| 2012                       | 1,884 (6.77)     | 3.97                           | 1 (9.09)          | 0.002                            | 0.05     |
| 2013                       | 2,707 (9.72)     | 5.71                           | 1 (9.09)          | 0.002                            | 0.04     |
| 2014                       | 3,836 (13.78)    | 8.09                           | 1 (9.09)          | 0.002                            | 0.03     |
| 2015                       | 3,176 (11.41)    | 6.70                           | 1 (9.09)          | 0.002                            | 0.03     |
| 2016                       | 5,154 (18.51)    | 10.87                          | 5 (45.45)         | 0.011                            | 0.10     |
| 2017                       | 6,337 (22.76)    | 13.36                          | 2 (18.18)         | 0.004                            | 0.03     |
| Total                      | 27,838 (100.00)  | 4.87                           | 11 (100.00)       | 0.002                            | 0.04     |
| * Annual average incidence |                  |                                |                   |                                  |          |
| # case fatality rate       |                  |                                |                   |                                  |          |

The scrub typhus cases occurred in all 16 cities or prefectures of Yunnan, the cases were reported from 118 of 129 counties. Baoshan city and Lincang city had the most cases accounting for 41.94%, while only 3 cases were confirmed in Diqing prefecture. The majority of confirmed cases of scrub typhus during 2006–2017 in Yunnan occurred yearly in August (Fig. 3). Farmers were the primarily affected occupation, accounting for 68.41%, followed by students (2650 cases) and young children (4867 cases). The total cases of scrub typhus was 26 562, accounting for 95.42% in these three groups. While sex-specific scrub typhus incidence from 2006 to 2017 did not change significantly over time, the ratio of male (49.53%) to female (50.47%) was 0.98:1 ( $P>0.05$ ) and most patients were children aged 0–5 years (13.16%) ( $P<0.01$ ).

The results of Hierarchical cluster analysis on the incidence of scrub typhus are described in Fig. 4. Sixteen cities or prefectures of Yunnan province are classified into three groups numbered in sequence. Baoshan City (1), Lincang City (2) and Dehong Prefecture (3) with highest incidence formed the first group in the clustering dendrogram. Chuxiong Prefecture (4), Honghe Prefecture (5), Puer City (6), Xishuangbanna Prefecture (7), Yuxi City (8), Dali Prefecture (9) and Nujiang Prefecture (14) formed the second separated clustering group. The third group with lowest incidence is Kunming City (10), Zhaotong City (11), Wenshan Prefecture (12), Lijiang City (13), Qujing City (15) and Diqing Prefecture (16) (Table 2, Fig. 5).

Table 2  
Incidence of scrub typhus in Yunnan Province, China (2006–2017, 1/100,000)

| Area | 2006 | 2007 | 2008 | 2009  | 2010 | 2011  | 2012  | 2013  | 2014  | 2015  | 2016  | 2017  |
|------|------|------|------|-------|------|-------|-------|-------|-------|-------|-------|-------|
| 1    | 0.56 | 2.11 | 4.07 | 7.18  | 8.42 | 13.17 | 24.66 | 38.03 | 42.42 | 28.21 | 38.87 | 53.03 |
| 2    | 0.21 | 2.35 | 3.37 | 6.71  | 7.24 | 10.49 | 16.50 | 19.84 | 22.30 | 24.28 | 39.18 | 59.09 |
| 3    | 0.17 | 0.08 | 0.17 | 4.05  | 9.66 | 18.41 | 16.02 | 21.14 | 38.98 | 45.75 | 67.13 | 74.57 |
| 4    | 1.30 | 0.63 | 1.79 | 4.99  | 5.40 | 3.09  | 4.47  | 5.77  | 19.63 | 9.87  | 20.86 | 25.67 |
| 5    | 0.80 | 2.24 | 2.16 | 3.38  | 4.38 | 3.35  | 3.58  | 5.15  | 7.07  | 4.20  | 7.40  | 9.78  |
| 6    | 0.00 | 0.00 | 0.04 | 0.08  | 0.08 | 0.55  | 3.34  | 4.17  | 5.11  | 8.65  | 15.97 | 18.80 |
| 7    | 0.53 | 1.76 | 8.02 | 17.72 | 9.35 | 11.29 | 5.11  | 6.35  | 10.05 | 10.76 | 14.46 | 11.11 |
| 8    | 0.26 | 0.13 | 0.17 | 0.61  | 1.52 | 1.30  | 1.87  | 5.34  | 8.94  | 6.34  | 11.28 | 8.38  |
| 9    | 3.27 | 1.74 | 0.87 | 1.07  | 0.72 | 0.84  | 0.93  | 1.65  | 2.29  | 0.75  | 2.98  | 2.20  |
| 10   | 1.06 | 0.45 | 0.58 | 0.79  | 0.90 | 0.44  | 0.54  | 0.81  | 0.75  | 0.87  | 1.40  | 1.21  |
| 11   | 0.02 | 0.00 | 0.02 | 0.33  | 0.77 | 0.12  | 0.17  | 0.06  | 0.61  | 1.50  | 2.34  | 3.30  |
| 12   | 0.00 | 0.03 | 0.00 | 0.11  | 0.14 | 0.06  | 0.28  | 0.80  | 2.42  | 1.34  | 2.81  | 2.93  |
| 13   | 0.08 | 0.08 | 0.40 | 0.48  | 0.72 | 1.12  | 2.73  | 3.45  | 5.94  | 3.05  | 4.34  | 3.94  |
| 14   | 0.19 | 0.19 | 0.00 | 0.00  | 0.37 | 0.37  | 0.75  | 0.75  | 1.12  | 3.37  | 7.68  | 9.93  |
| 15   | 0.03 | 0.03 | 0.02 | 0.00  | 0.02 | 0.05  | 0.03  | 0.15  | 0.07  | 0.09  | 0.20  | 0.38  |
| 16   | 0.00 | 0.25 | 0.00 | 0.00  | 0.00 | 0.25  | 0.00  | 0.00  | 0.00  | 0.00  | 0.25  | 0.00  |

1. Baoshan City; 2. Lincang City; 3. Dehong Prefecture; 4. Chuxiong Prefecture; 5. Honghe Prefecture; 6. Puer City; 7. Xishuangbanna Prefecture; 8. Yuxi City; 9. Dali Prefecture; 10. Kunming City; 11. Zhaotong City; 12. Wenshan Prefecture; 13. Lijiang City; 14. Nujiang Prefecture; 15. Qujing City; 16. Diqing Prefecture

## Discussion

In China, scrub typhus was removed from the National Notifiable Disease Reported System since 1989. It was legally redefined as a notifiable disease and must be reported to the China Center for Disease Control and Prevention in 2006. And the number of the cases of scrub typhus reported is on the rise since 2006 [15]. In our study, the results indicate that from 2006 to 2017 there has been an alarming increase in the number of reported cases of scrub typhus in Yunnan province, indicating that scrub typhus remains an important public health

problem throughout the province. Given the trends identified in this study, our findings suggest that scrub typhus incidence will likely continue to increase in the future.

As we know, chigger mites are the only vector of tsutsugamushi disease [16, 17]. The complicated topographic landform and high biodiversity of Yunnan may contribute the extremely high species diversity of chigger mites in this province [18], which indirectly leads to a large number of scrub typhus cases. There are several possible factors to explain the rapid increase of cases in Yunnan: (1) The special environment of Yunnan province provides the uncommon natural landscape resources and graceful eco-tourism condition to the tourism. With the development of Yunnan tourism, tourism has expanded to forests and grasslands, which makes more people have chances of getting infected by chiggers. (2) The number of farmers working in the field, field operators (logging, road construction workers, geological surveyors, etc.), field training units and field tourists have increased. Therefore, they are more likely to be attacked by chigger mites and are prone to infection. (3) People living in Yunnan, a province of education in undeveloped, have poor knowledge of scrub typhus.

The results of our study identified seasonal differences in the onset and duration of tsutsugamushi disease that suggest the existence of both summer and autumn transmission of scrub typhus (summer-autumn type) in Yunnan, which is not in accordance with scrub typhus type in other provinces of China [19–21]. In our study farmers and children aged less than 5 years old were the groups most at risk due to lower awareness of scrub typhus, poor protection during agriculture or field recreational activities and reduced use of protective measures when playing in grassland or woods for children [22].

The results of our study indicated that from 2006 to 2017 scrub typhus occurred mainly in Baoshan City, Lincang City, Dehong Prefecture, Chuxiong Prefecture and Honghe Prefecture. Actually, the classification by hierarchical cluster analysis has produced results that correspond to the rate of incidence of scrub typhus in Yunnan province. Our results also indicated that surveillance system, public education and public health efforts to control and prevent scrub typhus need to be focused on the areas with highest incidence. Baoshan City, Lincang City and Dehong Prefecture were the areas with the highest incidence of scrub typhus in Yunnan province. Located in southwest of the province, the three cities have high temperature, intense sunshine, abundant rainfall and relatively low atmospheric pressure, which made an ideal environment for living of chigger mites [23, 24].

## Conclusions

In our study, the incidence of tsutsugamushi disease in Yunnan province is on the rise, and the epidemic area is expanding. We should strengthen the ability of early diagnosis and detection, carry out

health education, monitor the epidemic situation and risk factors of tsutsugamushi disease, and prevent the harm of tsutsugamushi disease. A set of preventive strategies including public health education and personal protection facilities should be promoted in high-risk populations (the elderly, farmers and children aged less than 5 years old) and cities (Baoshan City, Lincang City and Dehong Prefecture) in Yunnan province.

## Abbreviations

PCR polymerase chain reaction; SPSS (v.25):Statistical Product and Service Solutions (version 25); ArcGIS:Arc Geographic Information System.

# **Declarations**

## **Ethics approval and consent to participate**

The research protocol was approved by the human ethics committee of Yunnan Center for Disease Control and Prevention. All study-related data were anonymized before analyses.

## **Consent for publication**

Not applicable.

## **Availability of data and materials**

The data of scrub typhus cases were routinely collected by the Yunnan Provincial Notifiable Disease Report System.

## **Competing interests**

The authors declare that they have no competing interests.

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This work was supported by the grants from Qujing medical college (2019L001). The funding body had no role in study design, data collection, analysis, and interpretation or writing the manuscript.

## **Authors' contributions**

P-YP collected the data and wrote the manuscript.

LX, G-XW, H-YZ and LG used ArcMap 10.6 to map the geographical distribution of scrub typhus cases in Yunnan.

B-SY and T-LY revised the manuscript.

P-YP and W-YH analyzed the data and interpreted the results.

All authors have approved the submitted version.

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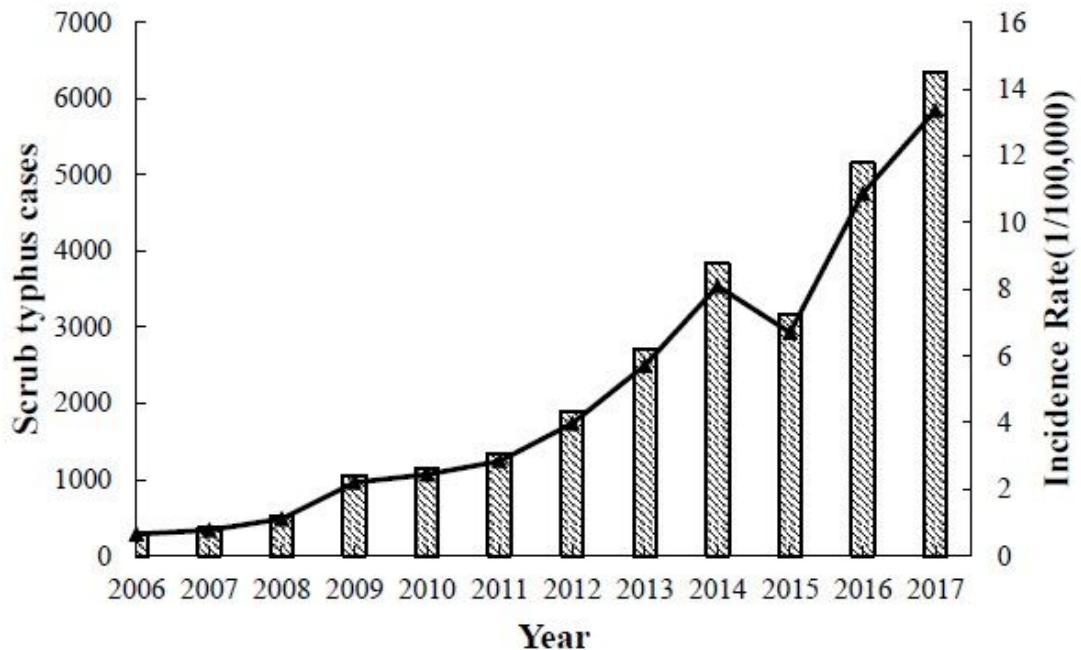
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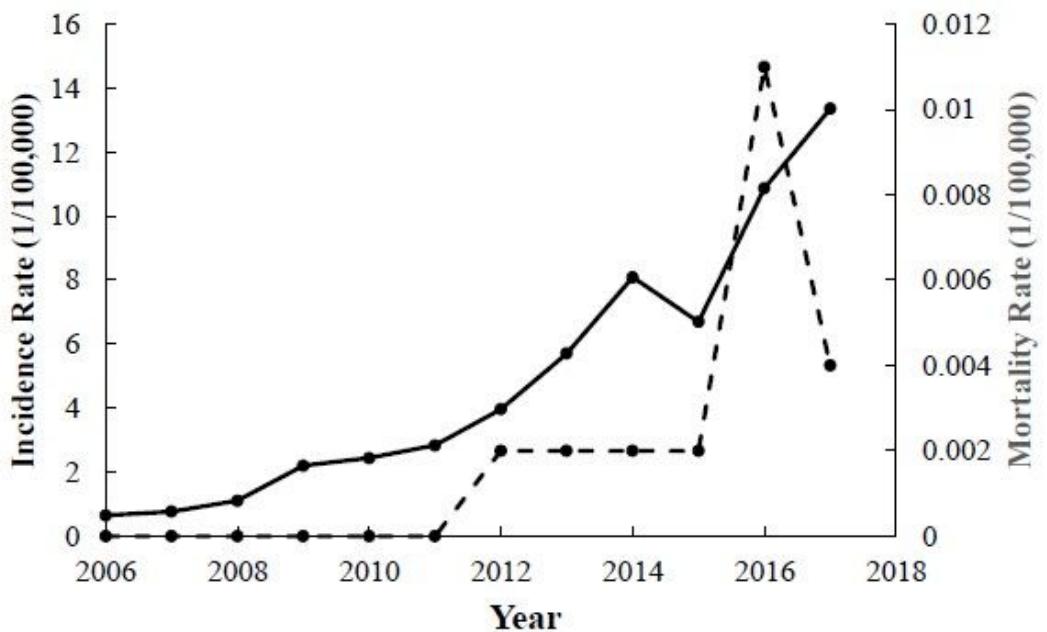
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## Figures



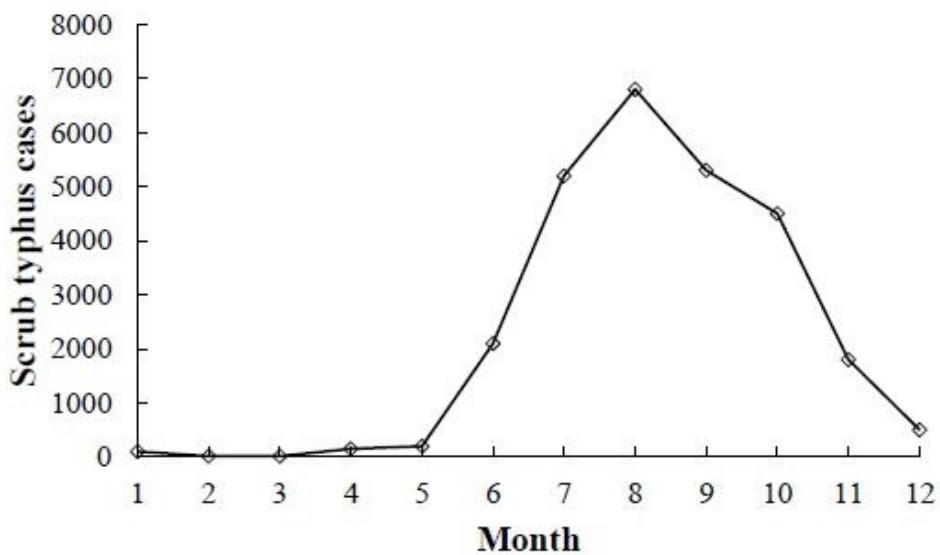
**Figure 1**

Overall trend of scrub typhus cases and incidence in Yunnan province during 2006 to 2017 (The bar charts with shadow effect represent the scrub typhus cases and the black line represents the annual incidence of the scrub typhus)



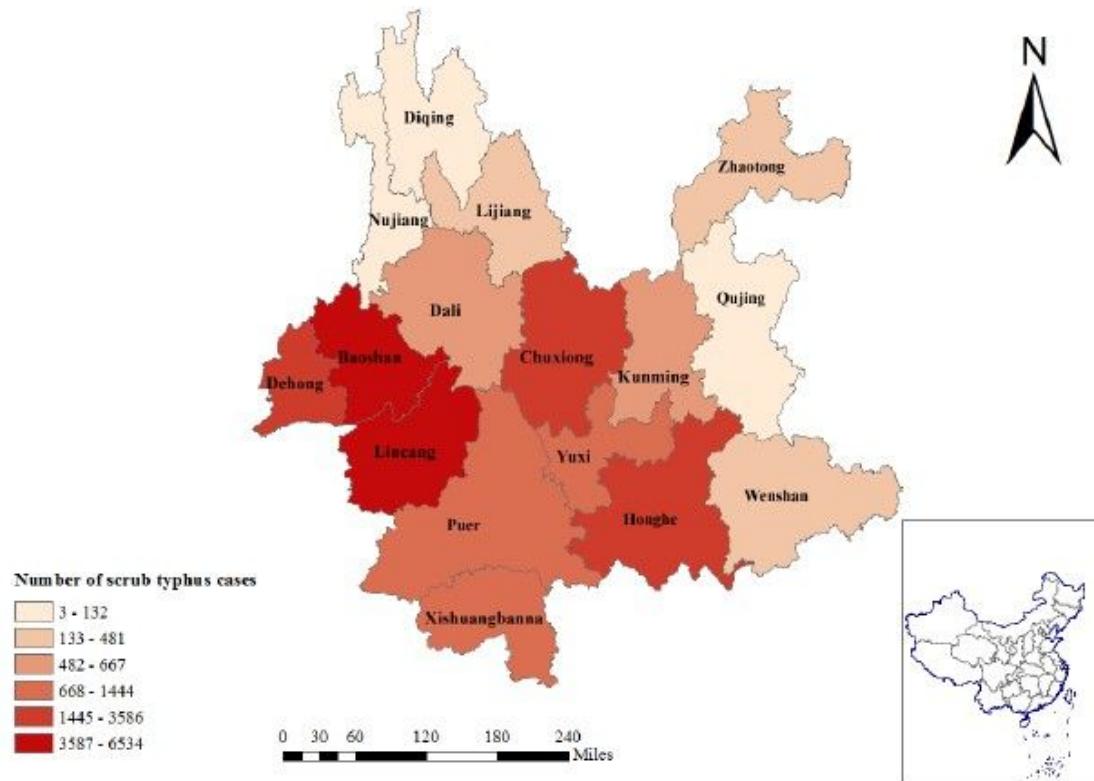
**Figure 2**

Epidemic features fluctuation of scrub typhus cases along year in Yunnan Province, China [straight line represents the incidence rate (1/100,000); broken line stands for the mortality rate (1/100,000)]



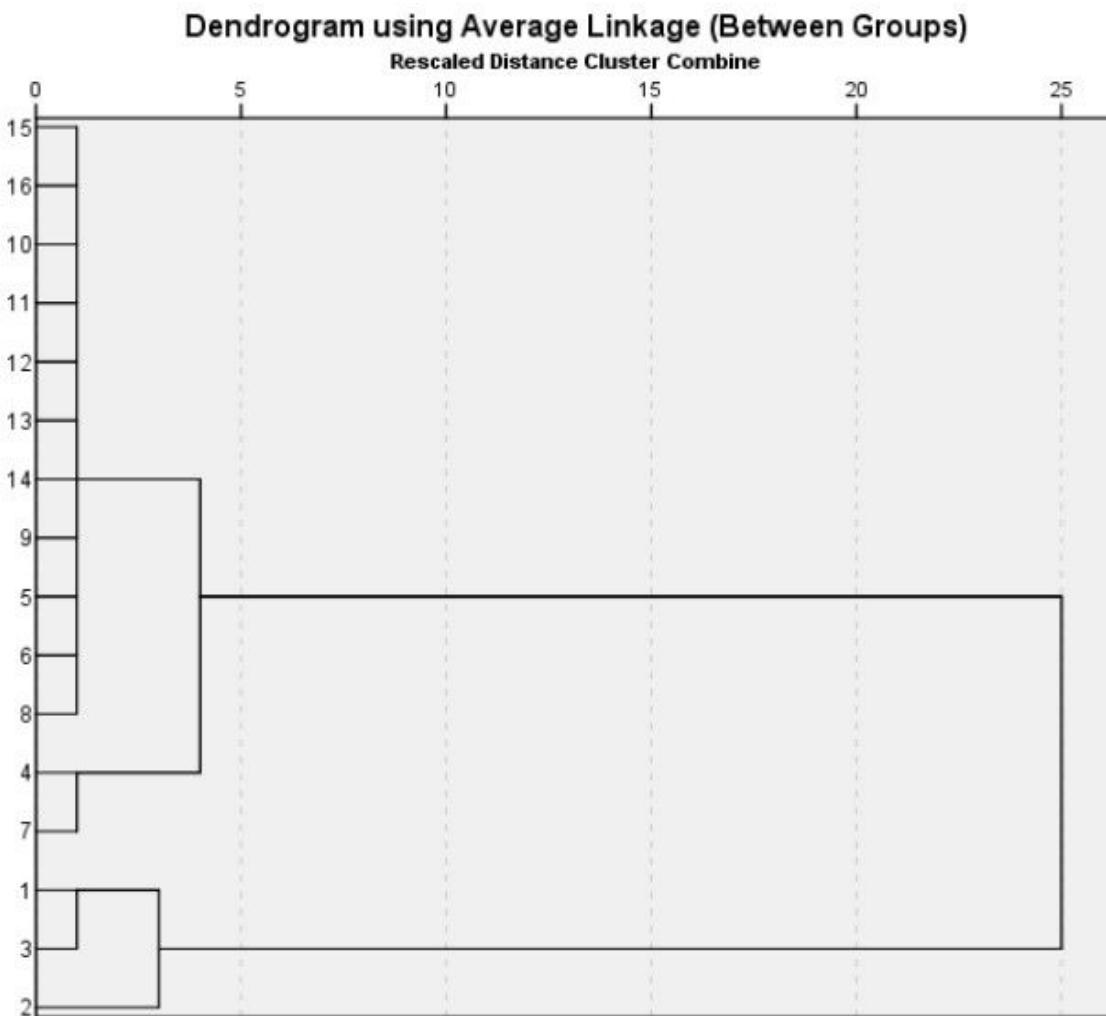
**Figure 3**

Seasonal distribution fluctuation of scrub typhus cases reported of Yunnan Province from 2006 to 2017



**Figure 4**

Geographical distribution of scrub typhus cases in Yunnan southwest China, 2006-2017



**Figure 5**

Hierarchical clustering dendrogram on the incidence of scrub typhus in Yunnan province, China (2006-2017)

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