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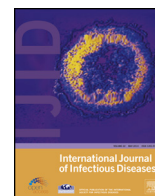
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Short Communication

The first human infection with severe fever with thrombocytopenia syndrome virus in Shaanxi Province, China



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SUMMARY

Background: Severe fever with thrombocytopenia syndrome (SFTS) is an emerging infectious disease discovered in China in 2009. In July 2013, the first human infection with SFTS virus (SFTSV) was detected in Shaanxi Province, Western China.

Methods: A seroprevalence study among humans was carried out in an SFTS endemic village; specifically, serum samples were collected from 363 farmers in an SFTS endemic village in Shaanxi Province. The presence of SFTSV antibodies in serum was determined using an ELISA.

Results: SFTSV antibodies were found in a total of 20 people (5.51%), with no significant difference between males and females (6.93% and 4.42%, respectively; Chi-square = 1.29, $p = 0.25$). Moreover, the SFTSV antibody positive rate was not significantly different across different age groups (Chi-square = 2.23, $p = 0.69$).

Conclusions: SFTSV readily infects humans with outdoor exposure. The results of the serological study indicate that the virus circulates widely in Shaanxi Province. SFTSV represents a public health threat in China.

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1. Introduction

Severe fever with thrombocytopenia syndrome virus (SFTSV) is a newly identified novel *Phlebovirus* of the *Bunyaviridae* family,¹ which has been implicated as the causative agent of severe fever with thrombocytopenia syndrome (SFTS) in China.² The clinical symptoms of SFTS are non-specific and include high fever, gastrointestinal symptoms, thrombocytopenia, leukocytopenia, multi-organ dysfunction, and hemorrhagic tendency.¹ Most reported SFTS cases have involved hospitalized patients with relatively serious clinical symptoms, with an average case-fatality rate of 12%.³ Fatal cases of infection with SFTSV have recently been reported in South Korea and Japan as well.^{4,5} *Haemaphysalis*

longicornis ticks have been implicated as the vectors of SFTSV, and a high seroprevalence of SFTSV has been reported in domestic animals.¹

The first human case of SFTS in a rural area of Long County in Shaanxi Province led to a seroprevalence study in the same village where the first case was detected, with the goal of estimating the seroprevalence of SFTSV in this population.

2. Methods

2.1. Sample and data collection

We conducted a seroprevalence study in the village in Long County where the first case of SFTS was detected. A total of 363 serum samples were collected from 363 healthy volunteers. A standardized questionnaire was used to collect information on demographic characteristics including age, gender, and residential address. The sampled population was divided into five age groups: 0–6, 7–19, 20–39, 40–59, and ≥60 years.

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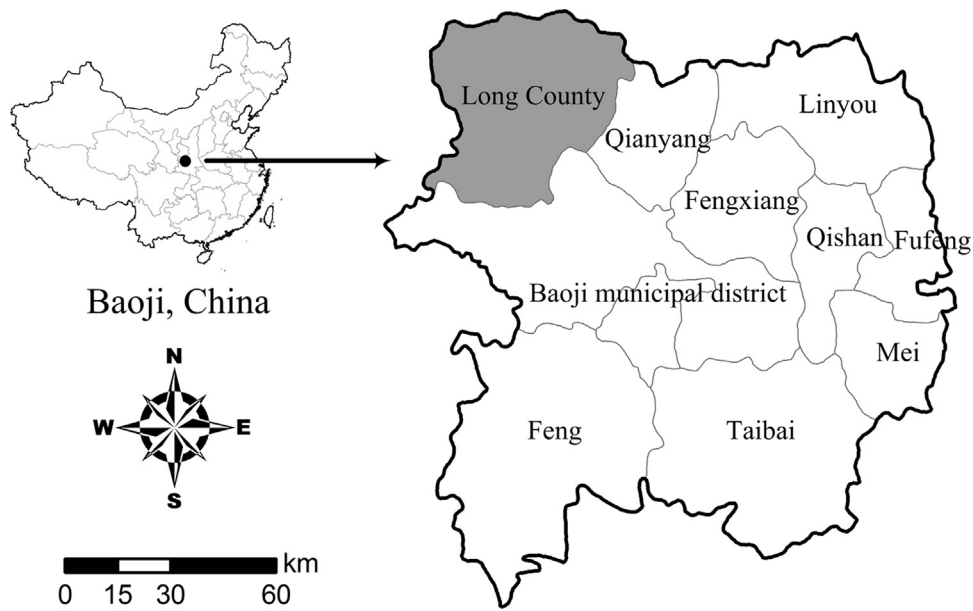


Figure 1. Location of Baoji in China and the location of selected districts where serum samples of healthy persons were collected and tested in 2013.

Long County is located in Central China (Figure 1) and had a population of a quarter million at the end of 2010. It has an annual average temperature of 8–16 °C, and the average rainfall is 600 mm.

2.2. Serological testing

Samples were tested for the presence of SFTSV RNA by quantitative real-time reverse transcription PCR (RT-PCR). Antibodies (including IgG and IgM) in serum samples were detected using a double-antigen sandwich ELISA, as described previously.⁶ Positive samples were further diluted to determine the antibody titers.

2.3. Case definition

The patient was diagnosed based on the diagnosis and treatment programs for severe fever with thrombocytopenia syndrome issued by the Chinese Ministry of Health. The clinical features include abrupt onset of fever (≥ 38 °C) and respiratory tract or gastrointestinal symptoms, followed by a progressive decline in platelets and white blood cells. A confirmed case of SFTS was defined as a person who met these criteria and who also had at least one of the following laboratory criteria for diagnosis: (1) detection of SFTSV RNA by a molecular method, (2) seroconversion

or a 4-fold rise in antibody titers between two serum samples collected at least 2 weeks apart, and (3) SFTSV isolated from clinical specimens.

2.4. Statistical analyses

All statistical analyses were performed using SPSS 17.0 (SPSS Inc., Chicago, IL, USA); the statistical significance level was set at 0.05. The Chi-square test or Fisher's exact test was used to assess differences in SFTSV seroprevalence by gender and age group.

3. Results

The first human case of SFTS in Shaanxi Province was a 66-year-old man who had a sudden onset of fever on July 11, 2013, with a temperature of 38 °C, accompanied by chills, pharyngeal pain, nausea, vomiting, and abdominal pain. The patient's family is located in a rural area of Long County. The patient did not have a history of outdoor activities before illness onset, and the patient's cattle had reportedly not been out of the village for the last 3 years.

Of the 363 volunteer participants, 173 (47.6%) were male and 190 (54.9%) were female. The ages of the participants ranged from 3 years to 80 years, and the median age was 42 years. A total of 363 serum samples were obtained from the healthy volunteers and sent to the laboratory of Shaanxi Provincial Center for Disease

Table 1
Seropositivity for SFTSV among healthy humans in Shaanxi, China

	Number of serum samples tested	Number SFTSV-IgG seropositive	Percentage seropositive	Chi-square	<i>p</i> -Value
Gender				1.29	0.25
Male	173	12	6.93		
Female	190	8	4.42		
Age, years				2.24	0.69
≤ 6	59	1	1.69		
7–19	54	3	5.56		
20–39	68	4	5.88		
40–59	128	9	7.03		
≥ 60	54	3	5.56		
Total	363	20	5.51		

SFTSV, severe fever with thrombocytopenia syndrome virus.

Control and Prevention (CDC). Overall, 6% (20/363) of serum samples were seropositive for SFTSV (6.93% among males and 4.21% among females). There was no statistically significant difference in seroprevalence between males and females (Chi-square = 1.29, $p = 0.25$) (Table 1).

The sampled population was divided into five age groups (0–6, 7–19, 20–39, 40–59, and ≥ 60 years) and the corresponding seroprevalence levels were 1.69% (1/59), 5.56% (3/54), 5.88% (4/68), 7.03% (9/128), and 5.56% (3/54), respectively. Statistical analyses showed that the seroprevalence of antibodies against the virus did not increase with age (Table 1). None of the seropositive participants reported any of the disease symptoms that are associated with SFTSV infections.

4. Discussion

We found an SFTSV seroprevalence level of 5.51% in an SFTSV endemic village, which is similar to that reported in Hubei Province (6.37%) and Zhejiang Province (5.51%), but much higher than that reported in Shandong Province (0.84%) and Jiangsu Province (0.94%).^{7–9} This discrepancy may be attributed to the season of sample collection, age and sex of the subjects, previous exposure or low level of infection, or differences in detection methods employed in different studies. Furthermore, the seropositive volunteers in our study had not had contact with the first reported patient before onset, which suggests that other infections in the village may have resulted from natural exposure to a reservoir.

There was no statistical difference observed by sex, indicating that men and women in rural areas of Shaanxi are equally exposed to SFTSV; this is in line with the results of a prior study conducted in Jiangsu Province, China in 2011.¹⁰ However, surveillance data from 2012 and 2013 in Jiangsu Province have indicated that SFTSV antibodies are more prevalent in males than in females.¹¹ Further studies are needed to clarify this difference.

Our study demonstrated that seroprevalence varied with age. Specifically, there were significant differences among studied age groups for SFTSV infection. The incidence rate of SFTS was higher in patients between 20 and 60 years of age compared to patients aged < 20 years. This suggests that the older age groups have participated in long-term outdoor activities more than the other age groups. However, the seroprevalence of SFTSV in healthy people was not significantly different among age groups in Shandong Province, although SFTS patients were mainly elderly.¹²

In conclusion, our study indicates significant levels of SFTSV antibodies among healthy humans, which suggests subclinical SFTSV infections or a relatively mild form of SFTS illness. More

emphasis is needed on this novel disease, including enhanced surveillance activities related to the virus in ticks and domestic animals.

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Ethical statement: The study was approved by the ethics review committee of Shaanxi Provincial Center for Disease Control and Prevention. The sera were collected with the consent of the volunteers.

Conflict of interest: None for all authors.

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