JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Original Article

Epidemiological trends and clinical characteristics of human leptospirosis in Wenzhou, Zhejiang Province, China, 2020–2022

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Abstract

Objective: To observe the clinical characteristics and epidemic trends of human leptospirosis in Wenzhou, Zhejiang Province, China, from 2020 to 2022 and to provide a scientific basis for prevention and control in this area.

Methods: Descriptive epidemiological methods were used in Wenzhou, China, from 2020 to 2022. *Leptospira* antibodies were detected by a microscopic agglutination test (MAT), and laboratory tests were conducted to analyse the prevalence of *Leptospira* in the population.

Results: From 2020 to 2022, a total of 41 cases of human leptospirosis were reported in Wenzhou, China, with no deaths and an average annual incidence of 0.1428/100,000. The highest incidence was in 2021 (30 cases, incidence rate: 0.31/100,000), and the lowest incidence was in 2022 (three cases, incidence rate: 0.04/100,000). The high-incidence season was from August to October, in which a total of 36 cases were reported, accounting for 87.80% of total cases, most of which were males. The main occupation was farming, which accounted for 70.7% of the total number of cases. 90.2% of cases had fever symptoms, and the body temperature was between 36.5 ℃ and 40.1 ℃. A total of 32 positive samples were detected by MAT in six main groups, mainly the *Autumnalis* serogroup.

Conclusions: The incidence of leptospirosis in Wenzhou, China, was at a moderate level from 2020 to 2022. Localities should actively strengthen the monitoring of leptospirosis host animals and populations, understand the infection rate and floral changes and prevent leptospirosis outbreaks.

Key words: Leptospirosis; clinical features; descriptive epidemiology; incidence; microscopic agglutination test.

J Infect Dev Ctries 2024; 18(11):1709-1714. doi:10.3855/jidc.18434

(Received 25 April 2023 – Accepted 07 August 2023)

Introduction

Leptospirosis is an acute infectious disease caused by pathogenic leptospirosis of various serotypes. In China, it is spread mainly by rodents and pigs. After an environment is contaminated by urine, infection enters the human body through the skin, especially damaged skin [1]. Leptospirosis has a greater impact on poorer populations, and the burden of the disease cannot be ignored [2].

Since China listed leptospirosis as a notifiable infectious disease in 1955, there have been dozens of large-scale leptospirosis epidemics. From 1955 to 2016, a total of about 2.4 million cases were reported in China, with about 20,000 deaths [3]. The disease burden of leptospirosis is heavy [4]. In recent years, the incidence of leptospirosis in China has declined significantly, and the incidence rate has remained at a low level. The number of annually reported cases is now less than 1,000 [5]. However, local outbreaks still occur occasionally, and prevention and control situations remain serious [6]. The epidemic areas of leptospirosis in China are mainly distributed in the Yangtze River, Pearl River, and Lancang River basins in the south. Among them, Sichuan, Hunan, and Jiangxi in the Yangtze River Basin, Guangxi and Guangdong in the Pearl River Basin, and Yunnan in the Lancang River Basin are the six provinces with the most serious leptospirosis in China, especially Sichuan, Yunnan, and Hunan [5]. Leptospirosis, with natural epidemic characteristics, remains one of the most important public health problems to threaten the health and safety of human beings worldwide.

Leptospirosis is widespread in Zhejiang Province and is concentrated mainly in the mountainous areas of central and southern Zhejiang. Shi *et al.* [7] reported the results of leptospirosis monitoring from 2005 to 2014, with a total of 131 cases, three deaths, and a reported incidence rate of 0.0252/100,000. In the past decade, the long-term trend of leptospirosis in Zhejiang Province has been stable. However, since the mid-

1980s, the prevalent strain, *Leptospira*, has changed in Zhejiang Province, and the newly emerging flora has become the main type in some areas. In 2007, an outbreak of leptospirosis occurred in Pan'an County, with the infected bacteria mainly from the *Autumnalis* group [8]. The epidemic flora of an outbreak in 2017 included the *Autumnalis* group, the seven-day-fever group, and the jaundice bleeding group, suggesting that regional epidemic strains may change, and related monitoring work should not be relaxed [9].

China's provincial, municipal and county centres for disease control and prevention have carried out monitoring work on human epidemics, host animal carrier rates in epidemic, and changes in flora. To reveal the epidemic trend and strain changes in leptospirosis in Wenzhou, China, from 2020 to 2022 and provide a basis for the prevention and control of leptospirosis, the analytical results of leptospirosis monitoring data are reported as follows.

Materials and methods

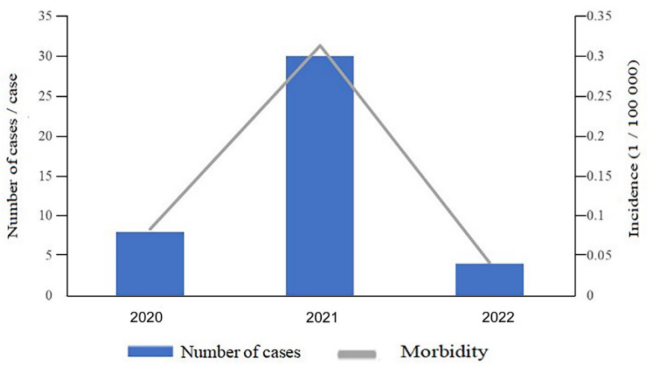
Materials

The human epidemic data were obtained from all fever cases registered in the outpatient hospital information system in Wenzhou, China, from January 2020 to December 2022, including all cases of infusion reaction after antibiotic use.

Methods

According to the requirements of the leptospirosis surveillance programme in Zhejiang Province, China, a standard leptospirosis case questionnaire was used for the case investigations; it collected basic information (age, gender, occupation, smoking history, etc.), disease status, clinical symptoms, laboratory test results, contact history, and treatment.

Figure 1. Annual incidence trend of human leptospirosis in Wenzhou, Zhejiang Province, China, 2020-2020.



Two blood samples (2~3mL) were collected at the early stage and the recovery stage, respectively. The *Leptospira* antibody was detected by a microscopic agglutination test (MAT). Using 8% rabbit serum phosphate buffer, namely, Kothorf's medium enrichment, 15 groups of Leptospira-type bacteria and 15 standard strains commonly used in China as antigens were analysed. A MAT was used to detect human antibodies, and a single serum antibody titre ≥ 1:400 or a double serum antibody titre that increased by more than four times was considered positive [10].

Diagnostic standard

The cases of leptospirosis included clinical diagnoses and laboratory-confirmed cases. The diagnosis of leptospirosis was performed according to WS 290-2008 'Diagnostic Criteria for Leptospirosis' [11] and was based on the following:

1. Epidemiology: 1~30 days before the onset of the disease, the patient had contact with infected water, infected animal urine, or infected animals.
2. Clinical manifestations: early clinical manifestations of three symptoms, including fever, muscle pain, fatigue, conjunctival congestion, gastrocnemius tenderness, and enlarged lymph nodes.
3. Laboratory testing:
   i. *Leptospira* was isolated from blood, cerebrospinal fluid, or urine.
   ii. *Leptospira* nucleic acid was detected in blood, cerebrospinal fluid, or urine.
   iii. *Leptospira* antibodies in the patient's recovery serum were fourfold or higher than in earlier serum or had a single serum antibody potency ≥ 1:400.

Statistical methods

The data were statistically analysed using SPSS 26.0 software, and Excel 2016 was used to create the database and organise and plot the data. A normality test for quantitative data was performed using the Kolmogorov–Smirnov test, quantitative data conforming to a normal distribution were described as the mean ± standard deviation ($\bar{x} \pm s$), and skewed data were described by interquartile range. A value of $p < 0.05$ was considered statistically significant.

Results

General characteristics

From 2020 to 2022, a total of 41 cases of human leptospirosis were reported in Wenzhou, China, with an

average annual incidence of 0.1428/100,000 and no deaths. Five cases (12.1%) had a history of harvesting rice in paddy fields, and 13 cases (31.7%) had a history of smoking. The average admission time was 3.34 ± 2.05 days after onset, and the average diagnosis time was 7.93 ± 4.31 days.

Epidemiological characteristics

Time distribution

From 2020 to 2022, the overall incidence of human leptospirosis in Wenzhou, China, initially increased and then decreased. The highest incidence was in 2021 (30 cases, incidence: 0.31/100,000), and the lowest incidence was in 2022 (three cases, incidence: 0.04/100,000) (Figure 1).

From 2020 to 2022, no cases were reported from January to May, and the incidence began to increase from June, reaching a peak in August and September (Figure 2). August to October was an obvious high-incidence season, with a total of 36 cases reported, accounting for 87.80% of the total number of cases.

Regional distribution

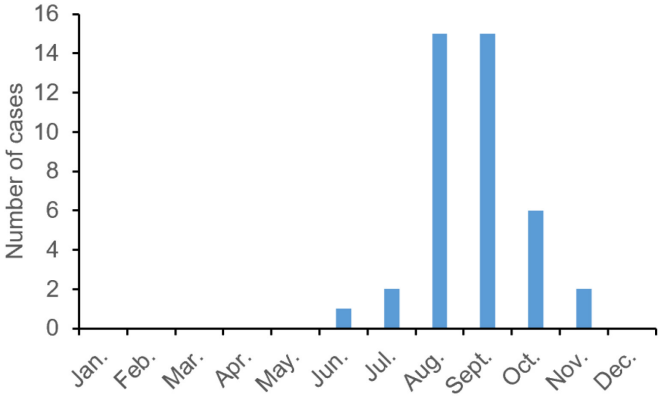
All case reports from 2020 to 2022 were from Yongjia and Lucheng in Wenzhou, China. Among them were 38 cumulative cases in Yongjia, with an average annual incidence of 1.46/100,000. There were three cumulative cases in Lucheng, with an average annual incidence of 0.09/100,000 (Table 1).

Population distribution

From 2020 to 2022, the cases of human leptospirosis in Wenzhou, China, were mainly male, with a total of 36 cases, accounting for 87.8% of total cases, and five cases were female, accounting for 12.2% of total cases. The ratio of male to female cases was 7.2:1. Farmers accounted for 70.7% of the total number of cases (100.0%, 66.6%, and 33.33% in the 3 years, respectively).

In terms of age distribution, no cases were reported in the under-20 age group, with cases concentrated in the 50–79 age group. A total of 33 cases were reported in 2020–2022, accounting for 80.5% of total cases. Among them, as shown in Figure 3, the 60–79 age group was the highest risk group among males, and 50–69 age group among female.

Figure 2. Monthly incidence trends of human leptospirosis in Wenzhou, Zhejiang Province, China, 2020-2020.



Clinical symptoms

From 2020 to 2022, human leptospirosis cases in Wenzhou, China, were accompanied by different clinical symptoms. Among them, 90.2% of cases had a fever with a body temperature of between 36.5°C and 40.1°C. Twenty-five cases presented with fatigue, 17 cases presented with gastrointestinal symptoms, 14 cases presented with coughs, 11 cases presented with expectoration, 10 cases presented with muscle soreness, and 8 cases presented with headache, vomiting, and nausea (Table 2).

Figure 3. Incidence of human leptospirosis by age and gender in Wenzhou, Zhejiang, China, 2020-2020.

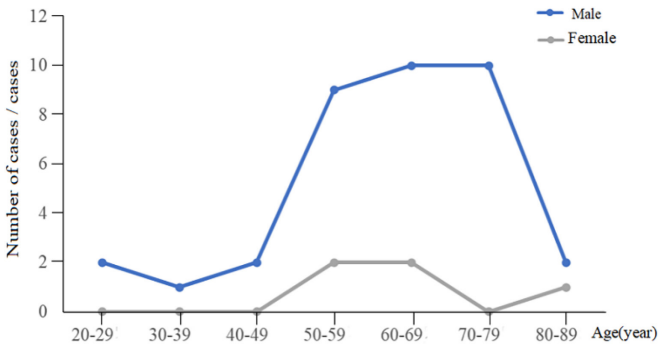


Table 1. Incidence of human leptospirosis in Wenzhou, Zhejiang Province, China, 2020-2022.

Year	Yong Jia		Lu Cheng	
	Number of cases	Incidence (1/100000)	Number of cases	Incidence (1/100000)
2020	8	0.92	0	0.00
2021	27	3.11	3	0.26
2022	3	0.35	0	0.00
Total	38	1.46	3	0.09

There are 869548 permanent residents in Yongjia, and 1167164 permanent residents in Lucheng.

Table 2. Distribution of clinical symptoms of human leptospirosis in Wenzhou, Zhejiang Province, China, 2020-2022.

Clinical symptoms	*n* = 41	Percentage
Fever	37	90.2
hypodynamia	25	61.0
Gastrointestinal symptoms	17	41.5
Cough	14	34.1
Expectoration	11	26.8
Muscle soreness	10	24.4
Nausea	8	19.5
Vomiting	8	19.5
Headache	8	19.5
Diarrhea, abdominal distension	7	17.1
Panting	4	9.8
Dry cough	3	7.3
Jaundice	3	7.3
Yellow sputum	3	7.3
Nasal obstruction	2	4.9
Hemoptysis	2	4.9

Laboratory index

The laboratory test results of patients with human leptospirosis in Wenzhou, China, from 2020 to 2022 are as follows. The results showed that the patients' neutrophils were elevated; lymphocytes, eosinophils, and haematocrit were decreased, and there were no obvious changes in leukocytes, platelets and haemoglobin (Table 3).

Population epidemic flora

From 2020 to 2022, a total of 32 positive cases of human leptospirosis were detected by serum MAT in Wenzhou, China, belonging to six groups. The number of positive cases detected in 2021 was the highest, mainly in the *Autumnalis* group. The *Leptospira* flora infected by the positive cases detected in 2020 were from the *Leptospirosis icterohaemorrhagica* group and the *L. grippotyphosa* group; the positive cases detected in 2022 were infected with the *Autumnalis* group (Table 4).

Treatment

From 2020 to 2022, all cases were treated with antibiotics as standard treatment for human patients with leptospirosis in Wenzhou, China. Twelve (29.3%) cases were treated with piperacillin–tazobactam, and 16 (39.00%) cases were treated with dexamethasone or methylprednisolone injections in different doses during hospitalisation. Twelve (29.3%) cases were treated with vasopressor drugs, mainly norepinephrine. Four cases (9.70%) used continuous renal replacement therapy.

Table 3. Laboratory test results of human leptospirosis cases in Wenzhou, Zhejiang Province, China, 2020-2022.

Indexes	x ± s	normal range
Leucocytes ($\times 10^9$/L)	9.31 ± 4.32	(4.0, 10.0)
Neutrophils ($\times 10^9$/L)	8.09 ± 4.01	(2.0, 7.0)
Lymphocytes ($\times 10^9$/L)	0.66 ± 0.44	(0.8, 3.5)
Eosinophils ($\times 10^9$/L)	0.03 ± 0.03	(0.02, 0.5)
Thrombocyte ($\times 10^9$/L)	101.56 ± 55.06	(100, 300)
Hematocrit (%)	20.27 ± 16.70	(37, 54)
Hemoglobin (g/L)	118.37 ± 18.53	(110, 160)

The above indicators are absolute values.

Prognosis

From 2020 to 2022, among the patients with human leptospirosis in Wenzhou, China, 41 cases improved and were discharged. The time from onset to improvement was 14.12 ± 3.02 days, and there were no deaths.

Discussion

The results of this study showed that the incidence of leptospirosis in Wenzhou, China, initially increased and then decreased from 2020 to 2022, with an average annual incidence of 0.1428/100,000. It was higher than the 10-year incidence rate (0.0252/100,000) reported by Shi Xuguang *et al.* [7] in Zhejiang Province from 2005 to 2014. August to October was the high-incidence season, with 36 cases reported, accounting for 87.80% of total cases. This was consistent with the epidemiological characteristics of *Leptospira* in Guizhou Province reported by Yang *et al.* from 2001 to 2008 [12]. August to October is the peak season for harvesting rice, which was also a rainy season, thus increasing the opportunities to contract leptospirosis. In addition, the cases were mainly males and farmers, which was consistent with the characteristics of leptospirosis in paddy fields [13].

Among the leptospirosis cases in Wenzhou, China, in the past 3 years, middle-aged and elderly people aged 50–79 accounted for 80.5% of the total number of cases. This is a major change from the previous data in 2005, where the incidence of leptospirosis in China was the highest in young adults aged 15–34 (about 70%) [14]. This reminds us that in China, middle-aged and elderly people have replaced young adults as the country's

Table 4. Results of serum microscopic agglutination test of human leptospirosis cases in Wenzhou, Zhejiang Province, China, 2020-2022.

Year	Positive number	Type of flora					
		Icterohaemorrhagiae group	Grippotyphosa group	Javanica group	Autumnalis group	Pomona group	Australis group
2020	3	1	1	0	0	0	0
2021	28	5	2	3	11	3	4
2022	1	0	0	0	1	0	0

main population susceptible to leptospirosis. Most of the left-behind and field workers in rural areas are middle-aged and elderly people, which directly leads to a large number of cases in this group. Moreover, due to limited access to information for the middle-aged and elderly population, access to information on measures related to the prevention and control of infectious diseases is hard to obtain, resulting in insufficient understanding of leptospirosis and inadequate awareness. Therefore, health departments should expand the scope of publicity and education on leptospirosis, improve self-protection awareness in middle-aged and elderly people and in middle-aged and elderly manual workers and encourage people to take effective protective measures to protect their own health.

In this study, the main strain was the *Autumnalis* group, which is different from the epidemic flora reported by Liu *et al.* [5] during the national epidemic situation from 2006 to 2010. However, it is the same as the main infectious flora in the outbreak of leptospirosis in Pan'an County, Jinhua City reported by Li *et al.* in 2007 [15]. In the present study, 12.1% of cases had a history of harvesting rice in paddy fields. The practice of livestock rearing in rural areas of Zhejiang Province is widespread, and farmers' self-protection awareness is weak; protective measures are lacking in farming, and people have increased opportunities to contact contaminated water, which can easily cause infection. From the monitoring of host animals in recent years, the *Autumnalis* group is the first dominant flora in Zhejiang Province. It can be seen from the cases that the infectious flora showed a trend of diversification in recent years, suggesting possible diversity in the host of these positive cases. The source of infection needs further study, and the monitoring of hosts and suspected cases needs to be strengthened. In addition, we should remain alert to outbreaks caused by changes in flora and the lack of population immunity. Therefore, we should continue to strengthen publicity and education on leptospirosis health and disease prevention, change the practices of livestock breeding and farming, and strengthen prevention measures, such as the drainage of non-flowing water.

The results of laboratory examinations in this study showed that the absolute value of neutrophils in peripheral blood increased significantly, which was consistent with the results of Zhang *et al.* [16]. Our results showed that the proportion of neutrophils increased to 90.40%. The absolute values of lymphocytes, eosinophils and haematocrit were significantly reduced.

At present, there is no report on lymphopenia in leptospirosis in China. Jauréguiberry *et al.* [17] first found that 29 (85%) of 34 cases of early leptospirosis in north-western France had lymphopenia in 2005, but Lopes *et al.* [18] analysed the clinical data of 253 cases of leptospirosis and found that lymphopenia accounted for only 17%. In addition, Scott *et al.* [19] found that lymphocytes decreased significantly in the early stage of leptospirosis infection, but with the recovery of the immune response, lymphocytes gradually increased. Lymphocytopenia, which is a common clinical feature of leptospirosis, may be caused by the release of metabolites, Lipopolysaccharide, and other toxins in the circulation of *Leptospira* in the early stage of infection. The mechanism needs further study. At present, the phenomenon of lymphocytopenia in leptospirosis in China is in the initial stage of exploration, and there are many problems to be further investigated, such as whether lymphocytopenia is common in all patients with leptospirosis and whether its occurrence is related to regional differences, affected populations or leptospirosis serotypes.

Finally, antibiotics were used in all cases in this study (100%). A total of 39% (16/41) of patients were treated with dexamethasone or methylprednisolone injections to varying degrees during hospitalisation, and the discharge rate reached 100%, suggesting that antibiotics and hormones were effective drugs for treating *Leptospira*. Vaccination is the most effective measure to prevent and control leptospirosis. However, the biggest problem in the prevention and control of the disease is that there are many leptospirosis serogroups and types (28 serogroups and more than 250 serotypes); furthermore, the prevalent leptospirosis serogroups and types in different countries and even in different regions of the same country are very different, and the antibodies against the serogroups and types are weak or even ineffective.

There are some limitations in this study; one is that the epidemic data came from passive surveillance and lacked survey data, and there may have been cases that were missed. The selected survey and monitoring area was not broad enough, and the representativeness was somewhat weak. We will further refine it accordingly in subsequent studies.

Conclusions

In summary, the incidence of leptospirosis in Wenzhou City, China, from 2020 to 2022 was at a medium level. August to October was the high-incidence season, and males, farmers and 50–79-year-olds were identified as high-risk groups. Additionally,

there were changes in the flora of leptospirosis. Therefore, disease prevention and control departments and medical personnel should be alert to the possibility of infection, and it is necessary to conduct long-term continuous monitoring.

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of Wenzhou Central Hospital. Approval number is L2022-04-038. Written informed consent was obtained from all participants.

Authors' contributions

Zhou YY, Wang XM, Li HJ and Wu ZX conceived of the study, and Pan N, Ning HY and Liu SD participated in its design and data analysis and statistics and Ye XC, Qiu CC,Wu KJ and Shi JC helped to draft the manuscript. All authors read and approved the final manuscript.

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Conflict of interests: No conflict of interests is declared.