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Epidemiological features of human rabies in China from 2015 to 2021

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ABSTRACT

Objective: This study aims to enhance the understanding of the epidemiological characteristics, laboratory diagnostic levels, and changes in pathogenic populations of rabies in China by studying the status of the human rabies epidemic in China from 2015 to 2021, and provides useful information for guiding rabies disease prevention and control strategies.

Methods: We analyzed the incidence, distribution and laboratory testing of human rabies in mainland China using statutory surveillance data from 2015 to 2021; through a literature review, the study summarizes the recent updates of the RABV population in each province based on the previous monitoring.

Results: , A total of 3,032 rabies cases were reported from 2015 to 2021 in China, there were year over year decreases in total number of cases. Most of the cases (75.19%) were distributed in Hunan, Henan, Guangxi, Guizhou, Hubei, Yunnan, Jiangsu, Anhui, Guangdong and Sichuan, with 13 counties (districts) reporting over 50 cases in 7 years. The number of reported counties (districts) decreased from 512 in 2015 to 116 in 2021. Farmers accounted most of the cases (73%); 50-75 age group accounted for the highest proportion (54.62%). No changes of epidemic populations were detected in China; The laboratory diagnosis rate of cases increased from 4.74% in 2015 to 22.93% in 2021.

Conclusions: The rabies epidemic situation in China decreased steadily from 2015 to 2021, with a marked contraction in the geographical scope. In the future, it is necessary to continue to carry out large-scale dog immunization and strengthen the surveillance and laboratory diagnosis of rabies.

Key words: rabies; epidemiological characteristics; populations; laboratory diagnosis

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BACKGROUND

Rabies, commonly known as "hydrophobia", is an acute fatal zoonotic infectious disease that mainly damages the central nervous system. Its clinical manifestations are fear of water, wind and other specific symptoms[1]. Rabies virus (RABV) which belongs to the Rhabdoviridae family and the Lyssavirus(LYSSA) genus is the most important pathogen affecting the worldwide rabies epidemic[2]. Since the establishment of the People's Republic of China, the country has experienced three epidemics circumstances(1950s, 1980s and early 21st century), among which the largest number of cases were reported in 1956, 1981 and 2007, with 1,942, 7,037 and 3,300 cases respectively[3]. According to the national morbidity and mortality tables of legal infectious diseases issued by the Ministry of Health, the number of rabies deaths has been the highest for many years after entering the 21st century[4]. In the third pandemic, the Chinese government took a series of targeted measures to control the rabies epidemic[5]. In 2005, the Chinese Center for Disease Control and Prevention (CCDC) began sentinel surveillance for 15 cities and counties in 6 provinces with a high incidence of rabies[6]. From 2007, the number of reported cases continued to decline, falling below 2,000 cases in 2011 and below 1,000 in 2015, and then the rate of decline slowed down. The year 2015 marks the beginning of the next decade of rabies surveillance, and in the phase of epidemic elimination, analyzing the rabies data from 2015 to 2021 will further clarify the epidemic characteristics, laboratory diagnostic levels and changes in pathogenic populations of the epidemic in China, so as to provide a scientific basis for precise prevention and control.

METHODS

Sources of information

The data is from China's National Notifiable Disease Reporting System (NNDRS).

Case definition

Rabies cases were diagnosed according to the unified diagnostic criteria (WS281-2008) issued by Chinese Ministry of Health. Human rabies cases include "clinically diagnosed cases" and "confirmed cases".

Research Methodology

Statistical analysis was performed using SPSS (v25.0, SPSS Inc, Chicago, IL, USA) and Excel (version 2019, Microsoft Corporation, Redmond, Washington, USA). The geographic distribution map was drawn using ArcGIS (version 10.2, Environmental Systems Research Institute, Inc., Redlands, California, USA). The adopted data includes the reported incidence, mortality, occupation, laboratory diagnosis rate, etiology changes and other various indexes of all provincial-level administrative divisions (PLADs) in the mainland of China.

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RESULTS

Overall epidemic trend

From 2015 to 2021, China reported 3,032 human rabies cases with a yearly average of 433 and the incidence rate of 0.0313/100,000. In particular, the cumulative number of reported cases in the seven years was lower than that in 2007(3,300), and the annual reported cases were all less than 1,000. The highest number of cases was observed in 2015(801 cases, 26.42%). Since then, the number of cases have gradually decreased, reaching a record low since 1951 in 2021(157 cases, 5.18%). The reported incidence rate also decreased from 0.059/100,000 population in 2015 to 0.011/100,000 in 2021.

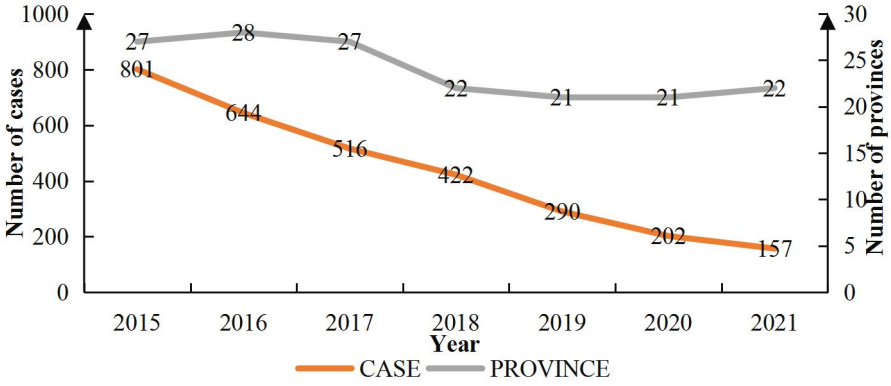

Figure 1. The number of reported human cases and case distribution provinces, 2015-2021

Epidemiology situation and analysis

Spatial distribution

Regional distribution of cumulative cases from 2015 to 2021:

From 2015 to 2021, 3,032 cases were reported in 1,116 counties(82.85%) within 253 cities(86.35%) across 31 provinces (excluding Hong Kong, Macao and Taiwan), and most of the countries were interconnected. The top ten PLADs with total cases for seven years successively Hunan, Henan, Guangxi, Guizhou, Hubei, Yunnan, Jiangsu, Anhui, Guangdong and Sichuan sequentially, accounting for 75.19%(2,280 cases) in total cases reported in the nation. There are

A total of 13 counties reported more than 50 cases in seven years, among which Yuncheng District of Hunan Province (86), Xiantao City of Henan Province (84) and Dongming County of Hebei Province (83) were the top three counties.

Comparison of the distribution of districts and counties in 2015 and 2021:

From 2015 to 2021, the number of counties with reported cases decreased year over year. In 2015, human rabies cases were reported in 512 counties, accounting for 38% of the total counties; the counties(districts) with ≥10 cases and single case accounted for 1.37%(7/512) and 67.38% (345/512), respectively. In 2021, the number of counties(districts) reporting cases dropped to 116(4%), which was 80% lower than that in 2015; no county reported over ten cases, only one county in Hunan reported ≥5 cases, and 75.86% (88/116) of the counties(districts) only had single case, indicating that the scope of the epidemic is shrinking.

The epidemic trend of key provinces:

The number of provinces reporting cases decreased from 27 in 2015 to 22 in 2021, and the number of provinces reporting less than 10 cases increased from 9 to 17 over the same period. Notably, except for Hunan, the rabies epidemic situation in other provinces decreased significantly(50%

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higher than that in 2015), especially in the southwest and southeast border provinces represented by Yunnan and Guangxi. Guangxi, Yunnan and Hebei were the provinces with high incidence of rabies in 2015, accounting for 26.34% of the total reported cases. In 2021, these provinces have the most obvious decline, with a rate of decline exceeding 90%, and the number of decreased cases accounted for 31.21% of all. Therefore, the epidemic changes in these three provinces largely affected the overall epidemic situation. Compared with 2015, the number of provinces reporting fewer than 10 cases per year increased from 9 to 26, with no case reported in Beijing, Tianjin, Liaoning, Jilin, Heilongjiang, Shanghai, Tibet, Qinghai and Xinjiang. However, during the study period, some areas with no case reports have experienced fluctuations and re-emergence in the epidemic, such as Tianjin (no case reported in 2018-2019 and 1 case reported in 2020), Heilongjiang Province (no case reported in 2015-2018 and 1 case reported in 2019), Fujian Province (no case reported in 2018-2019 and 1 case reported in 2020 and 2021), Shandong Province (no case reported in 2020, 1 case reported in 2021), Hainan Province (1 case reported in 2019 and 2021), Chongqing Municipality (2 cases reported in 2021), Gansu Province (1 case reported in 2020 and 2021). Details are shown in Figure 2.

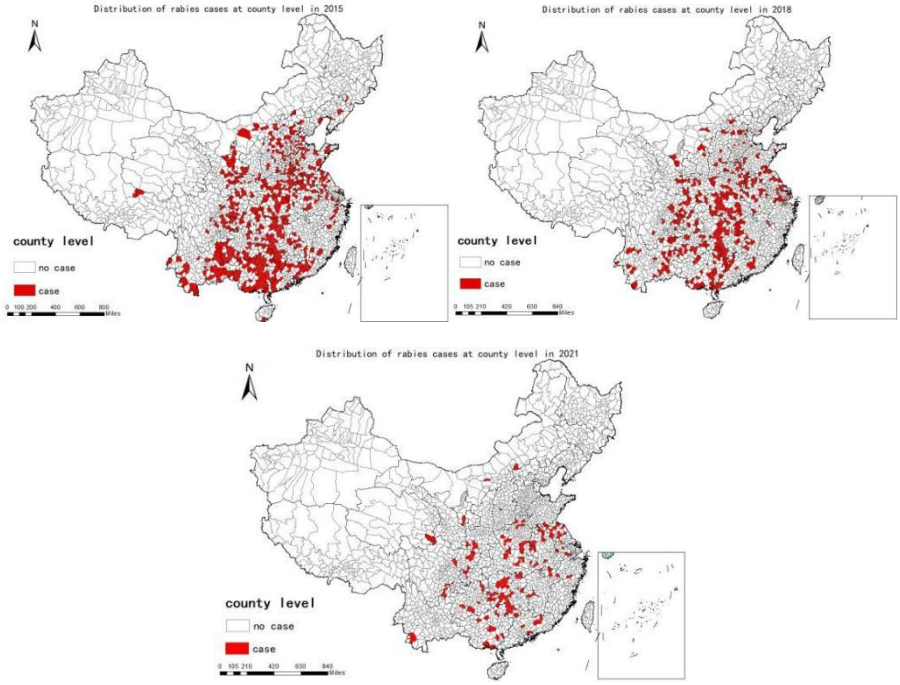

Figure 2. Regional distribution of rabies cases in China from 2015 to 2021

Time distribution

From 2015 to 2021, the onset of human rabies appeared throughout the year. Compared to other months, the months of August, September, and October had the highest incidence (Figure 3).

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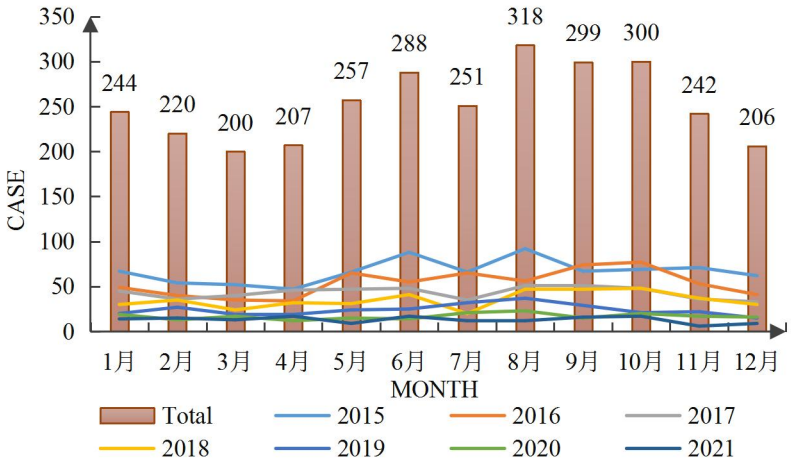

Figure 3. Total number of reported human rabies cases in each month in China, 2015-2021

Demographic features

During 2015-2021, the overall male-to-female ratio of 2.48:1(2162:870), is significantly more common in males than females; the incidence rate of the 50-75 years old group was higher, accounting for 54.62% of the total number of cases(Figure 4). The number of human rabies cases in 2015-2021 primarily affected farmers (73%), among which students, homemakers and unemployed, and scattered children comprised 7.26%, 5.44%, and 4.91%, respectively. Compared to 2015, the proportion of cases aged 50-75 years old and over 75 years old increased from 50.44% and 6.87% to 66.24% and 8.92%, while in other age groups showed a downward trend. The proportion of farmers increased from 74.53% to 84.25%, and the other occupational types decreased to varying degrees. For example, the proportion of cases among students decreased from 6.37% to 5.73%, which wasn't obvious, whereas children in the diaspora showed a significant decline, with their percentage of cases dropped from 5.87% to 1.91%.

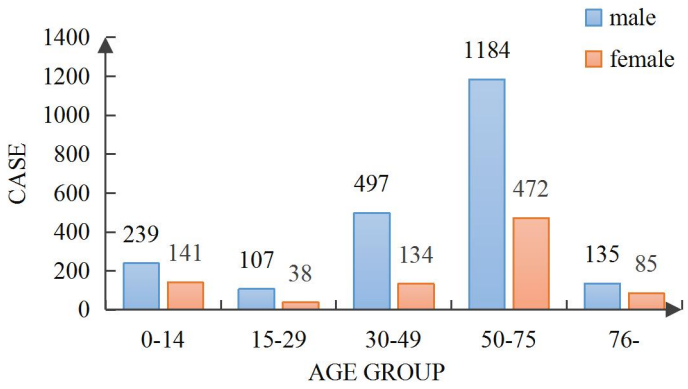

Figure 4. Age and sex distribution of human rabies incidence reported in China, 2015-2021

The division of rabies epidemic areas in China from 2015 to 2021

The number of human rabies cases in each province was used as an indicator for cluster analysis. According to the results and the incidence of rabies in each region, the rabies epidemic areas in China from 2015 to 2021 were divided into 4 categories: high epidemic regions (reported cases＞200), medium epidemic regions (reported cases＞50 and≤200), low epidemic regions (reported cases＞10 and≤50), and very low epidemic regions (reported cases≤10). Details are shown in Table 1.

Table 1 The division of rabies epidemic areas in China from 2015 to 2021

Category	Province	Counting
High epidemic regions	Guangxi, Hunan, Henan, Guizhou	4
medium epidemic regions	Hubei, Yunnan, Jiangsu, Anhui, Guangdong, Sichuan, Chongqing, Hebei, Shaanxi, Shandong, Shanxi, Zhejiang, Jiangxi	13
Low epidemic regions	Gansu, Beijing, Inner Mongolia, Hainan, Ningxia	5
Very low epidemic regions	Xinjiang, Qinghai, Tibet, Liaoning, Jilin, Heilongjiang, Shanghai, Fujian, Tianjin	9

Laboratory diagnosis rate

Viral testing is essential for disease surveillance and control. In the absence of exposure history or typical symptoms, clinical diagnosis of rabies can be difficult, and laboratory methods should be used to confirm a diagnosis whenever possible[7]. Most reported rabies cases in China were clinically diagnosed, while the proportion of lab-confirmed cases were very low, with an average annual laboratory diagnosis rate of 1.2% from 2004 to 2014[8]. However, this proportion increased in recent years, with 38(4.74%, 38/801) laboratory-confirmed cases in China in 2015, and 36(22.93%, 36/157). Details are shown in Table 2.

Table 2 Laboratory diagnosis rates of rabies in China from 2015 to 2021

Year	Reported cases	Confirmed cases	Laboratory diagnosis rate (%)
2015	801	38	4.74
2016	646	53	8.20
2017	518	47	9.07
2018	423	51	12.06
2019	291	49	16.84
2020	202	36	17.82
2021	157	36	22.93

Pathogenetic analysis

Understanding the genetic evolution characteristics of pathogens is the key to the prevention and control of infectious diseases[9]. Therefore, it is important to summarize and update the evolutionary characteristics and population type changes of rabies pathogens in a timely manner. Based on the previous monitoring, we summarized the update of RABV populations in the provinces in recent years[10]. In recent years, the monitored populations of rabies pathogens have

been reported in Shandong and Hunan provinces. In 2020[11], Shandong reported the detection and population division of specimens collected from 2010 to 2015, with 13 RABV strains (2 from case saliva and 11 from canine brain) belonged to China Ⅰ group. In 2022[12], the testing results of canine brain specimens collected from 2012-2017 in Hunan showed that 84% of the strains (21 strains) belonged to the China I and the remaining 4 strains belonged to China II. There were seven RABV populations (China Ⅰ-China Ⅶ) in China, which were different among provinces and regions[10]. Hunan is one of the provinces with the largest number of prevalent population types(four populations of China Ⅰ, China II, China Ⅲ and China V[12]), while Shandong has two populations (China Ⅰ and China Ⅱ) [11]. At present, there are no new endemic populations in China, and the types of endemic populations in the provinces have not increased.

DISCUSSION

From 2015 to 2021, a total of 3,032 rabies cases have been reported in China, which is lower than the peak of the third rabies epidemic in China (2007: 3,300 cases). The number of human rabies cases in China constantly and stably decreased from 801 cases in 2015 to 157 cases in 2021. The scope of the epidemic has been significantly reduced and the trend of spreading is obvious.

As shown in Figure 1, the spatial distribution of cases in China gradually narrowed from 27or28 PLADs in the early period (2015-2017) to 21or22 PLADs in the recent four years (2018-2021). The regional decline was more obvious at the level of districts and counties. Compared with the epidemic scope of 984 counties(districts) in the third epidemic peak (2007),

Comparing to the extent of the epidemic involved in 984 districts and counties at the third peak of the epidemic (2007)[13], the number of endemic areas decreased by 47.96% (512 districts/counties) in 2015 and by 88.21% (116 districts/counties) in 2021. Going back to the surveillance[8] from 2007 to 2011, the geographical distribution (district/county level) did not shrink when the epidemic decreased[13]. In contrast, during 2015-2021, the number of counties decreases steadily with the number of reported cases (Figure 2); the epidemic area of rabies has steadily shrunk, and the prevention and control results have been further consolidated.

In 2021, the number of reported rabies cases in China dropped to a record low (157 cases) since 1951, with significant decreases in the number of cases in some major provinces, indicating remarkable achievements in prevention and control. Among them, Guangxi Province actively adopted the comprehensive prevention and control measure of "active prevention and control as the main and passive prevention and control as the auxiliary"[14], such as animal rabies vaccination program for domestic dogs, extensive rabies prevention and control knowledge publicity work, rabies vaccine into the New Agricultural Cooperative Scheme[15] and so on. In 2016[16],the dog immunization rate in Guangxi reached 70%, and achieved good prevention and control effect. Guangxi is a model of epidemic prevention and control in high-incidence provinces. Its outbreak severity dropped from the top in 2015 to seventh in 2021, with the annual number of reported cases dropping from 117 to 7. Shandong, which has long been in a mid-endemic region, took dog immunization as the core of prevention and control work, actively promoted and steadily promotes[17-18], and successfully achieved a breakthrough from more than 30 cases annual to zero cases (2020), providing valuable experience for the local elimination of rabies.

The World Health Organization (WHO) points out that animal immunization is the most cost-effective way to prevent human rabies, and the immunization coverage of dogs can effectively prevent the spread of rabies by reaching more than 70%[19]. The experience of many countries also shows that the eradication of rabies depends on the control of the number of dogs and the formation of an immune barrier[20]. In recent years, China has continuously strengthened the management of dogs, improved the immunization rate of dogs, promulgated and updated the Animal Epidemic Prevention Law of the People's Republic of China and other relevant laws and regulations to ensure the implementation of dog registration and immunization. With the implementation of compulsory dog immunization, the immunization rates in Beijing, Shanghai, Guangxi[15][21-22] and other provinces and regions have exceeded 70%, but there are still some regions, especially in the key rabies infected areas, where dog immunization coverage is low[8][23], and the immune status of dogs varied greatly among different regions. Dog management and immunization work needs to be coordinated throughout the country to make up for shortcomings and promote effectively.

Routine surveillance combined with laboratory diagnosis is a prerequisite for the control and elimination of outbreaks[24]. Laboratory diagnosis can reduce the problems of missed diagnosis and misdiagnosis in clinical diagnosis, and further etiological analysis can provide scientific basis for epidemic traceability and precise prevention and control[25]. The laboratory diagnosis rate of rabies cases in China is low but has increased in recent years, from 1.2% (2004-2014)[8] to 22.93% (2021), contrary to the decrease of the number of cases year by year, the following factors are considered to be involved. Firstly, local CDC departments have more time and energy to collect specimens, since no many cases reported. In addition, annual trainings on rabies detection were organized in the countrywide, and some provinces have established testing laboratories to confirm the diagnosis of rabies. As the prevention and control of rabies epidemics in China has entered the elimination phase, there is a call for a corresponding national surveillance program to be introduced as soon as possible，with a clear requirement that samples are collected for laboratory testing in every case, and to effectively increase the rate of confirmed cases. At the same time, continue to emphasize the importance of specimen collection and testing, strengthen the standardized training and assessment of laboratory testing, train qualified staff, and establish a laboratory surveillance network with wider coverage to pave the way for rabies attack and elimination efforts.

In summary, the epidemic situation of national human rabies from 2015 to 2021 decreased year by year, with a marked contraction in the geographical scope of the epidemic and remarkable results in prevention and control. All PLADs should continue to carry out mass immunization of dogs, strengthen the surveillance of rabies pathogens and laboratory diagnostic capacity, and make steady progress towards the goal of eliminating human rabies by 2030.

Ethics statement

Not applicable.

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CONFLICTS OF INTERESR

The authors declare no competing interests.

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