



ORIGINAL ARTICLE

# Epidemiologic Features of Human Rabies in China from 2015-2021

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## ABSTRACT

**Objective:** This study aimed to enhance the current understanding of the epidemiologic 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 2015-2021 and provide 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 2015-2021. Based on a literature review, the study summarizes the recent updates of the rabies virus population in each province based on previous monitoring.

**Results:** A total of 3032 rabies cases were reported in China from 2015-2021, with a year-after-year decrease in the 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 > 50 cases in 7 years. The number of reported counties (districts) decreased from 512 in 2015 to 116 in 2021. Farmers accounted for most of the cases (73%), and the highest proportion of cases (54.62%) occurred in individuals 50-75 years of age. No changes in endemic 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 in China decreased steadily from 2015-2021, with a marked contraction in the geographic scope. In the future it will be necessary to continue to carry out large-scale dog immunization and strengthen the surveillance and laboratory diagnosis of rabies.

**Keywords:** rabies, epidemiologic characteristics, populations, laboratory diagnosis

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## BACKGROUND

Rabies, commonly known as “hydrophobia,” is an acute fatal zoonotic infectious disease that mainly injures the central nervous system. The clinical manifestations of rabies include a 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 (1950s, 1980s, and early 21st century), among which the largest number of cases was reported in 1956, 1981, and 2007, with 1942, 7037, and 3300 cases respectively [3]. As indicated in 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]. The number of reported cases has continued to decline since 2007, falling below 2000 cases in 2011 and below 1000 in 2015, after which the rate of decline slowed. 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 2015–2021 will further clarify the epidemic characteristics, laboratory diagnostic levels, and changes in pathogenic populations of the epidemic in China, which provide a scientific basis for precise prevention and control.

## METHODS

### Sources of information

The data were obtained 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 the Chinese Ministry of Health. Human rabies cases included “clinically diagnosed cases” and “confirmed cases.”

### Statistical analysis

Statistical analysis was performed using SPSS (version 25.0; SPSS, Inc, Chicago, IL, USA) and Excel (version 2019; Microsoft Corporation, Redmond, WA, USA). The geographic distribution map was drawn using ArcGIS (version 10.2; Environmental Systems Research Institute, Inc., Redlands, CA, USA). The adopted data include 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.

## Ethical statement

This study was approved the Ethical Review Committee of National Institute for Viral Disease Control and Prevention (Chinese Center for Disease Control and Prevention).

## RESULTS

### Overall epidemic trend

China reported 3032 human rabies cases, with a yearly average of 433 and an incidence of 0.0313/100,000 between 2015 and 2021. The cumulative number of reported cases in the 7 years was lower than 2007 ( $n=3300$ ) and the annual reported cases were all  $< 1000$ . The highest number of cases was reported in 2015 ( $n=801$  [26.42%]). Since then the number of cases have gradually decreased, reaching a record low since 1951 in 2021 ( $n=157$  [5.18%]). The reported incidence also decreased from 0.059/100,000 population in 2015 to 0.011/100,000 population in 2021. Details are shown in Fig 1.

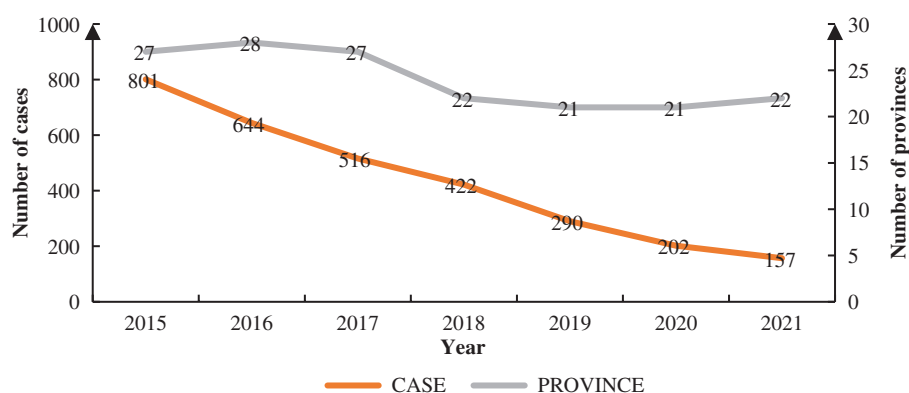
### Epidemiologic features and analysis

#### Spatial distribution

**Regional distribution of cumulative cases from 2015–2021:** From 2015–2021, 3032 rabies cases were reported in 1116 counties (82.85%) and 253 cities (86.35%) across 31 provinces (excluding Hong Kong, Macao, and Taiwan); most of the counties were interconnected. The top 10 PLADs with total cases for 7 years were Hunan, Henan, Guangxi, Guizhou, Hubei, Yunnan, Jiangsu, Anhui, Guangdong, and Sichuan (in decreasing order), accounting for 75.19% (2280 cases) of total cases reported in the nation. A total of 13 counties reported  $> 50$  cases in 7 years, among which the Yuncheng District of Hunan Province (86), Xiantao City of Henan Province (84), and Dongming County of Hebei Province (83) were the top 3 counties.

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

The number of counties with reported cases decreased year-after-year from 2015–2021. Human rabies cases were reported in 512 counties in 2015, accounting for 38% of all counties. The counties



**FIGURE 1** | The number of reported human cases and case distribution provinces, 2015–2021.

(districts) with  $\geq 10$  cases and a single case accounted for 1.37% (7/512) and 67.38% (345/512) of all counties, respectively. The number of counties (districts) reporting cases decreased to 116 (4%) in 2021, which was 80% lower than 2015. No county reported  $> 10$  cases, only 1 county in Hunan reported  $\geq 5$  cases, and 75.86% (88/116) of the counties (districts) only had 1 case, indicating that the scope of the epidemic was shrinking.

**Epidemic trends in key provinces:** The number of provinces reporting cases decreased from 27 in 2015 to 22 in 2021, and the number of provinces reporting  $< 10$  cases increased from 9 to 17 over the same period. Indeed, with the exception of Hunan, the rabies epidemic in other provinces decreased significantly (50% higher than 2015), especially in the southwest and southeast border provinces represented by Yunnan and Guangxi. Guangxi, Yunnan, and Hebei were the provinces with the highest incidence of rabies in 2015, accounting for 26.34% of the total number of reported cases. These provinces had the most apparent decline in the number of cases in 2021, with a rate of decline in number of cases exceeding 90%; the decrease in number of cases accounted for 31.21% of all cases. Therefore, the epidemic changes in these three provinces largely affected the overall epidemic status. Compared with 2015, the number of provinces reporting  $< 10$  cases per year increased from 9 to 26, with no cases reported in Beijing, Tianjin,

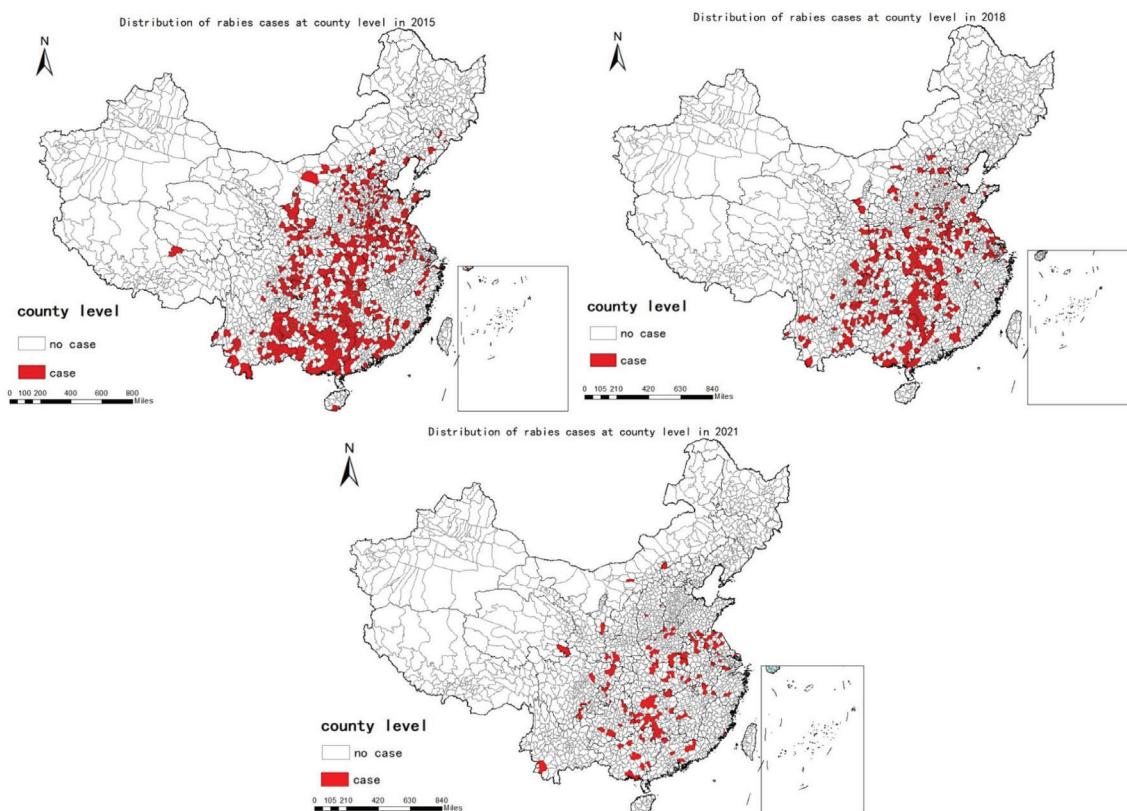
Liaoning, Jilin, Heilongjiang, Shanghai, Tibet, Qinghai, and Xinjiang. During the study period, however, some areas with no case reports experienced fluctuations in the number of cases and re-emergence of cases during the epidemic, such as Tianjin (no cases reported in 2018–2019 and 1 case reported in 2020), Heilongjiang Province (no cases reported in 2015–2018 and 1 case reported in 2019), Fujian Province (no cases reported in 2018–2019 and 1 case reported in 2020 and 2021), Shandong Province (no cases reported in 2020 and 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); the details are shown in Fig 2.

### Time distribution

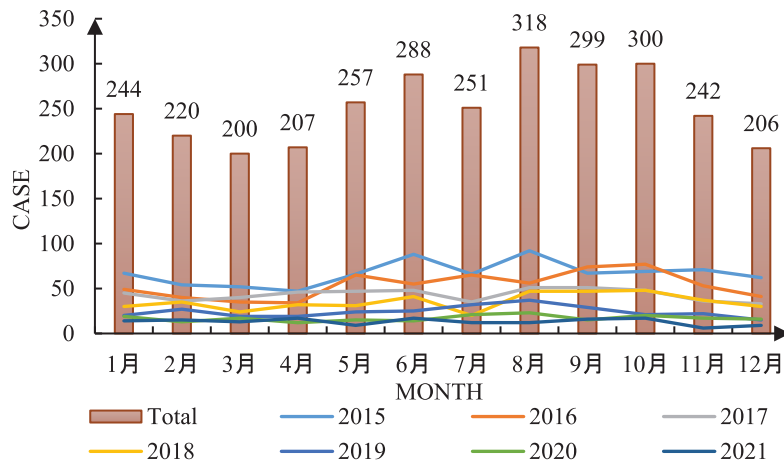
The onset of human rabies occurred throughout the year from 2015–2021. Compared to other months, the months of August, September, and October had the highest incidence (Fig 3).

### Demographic features

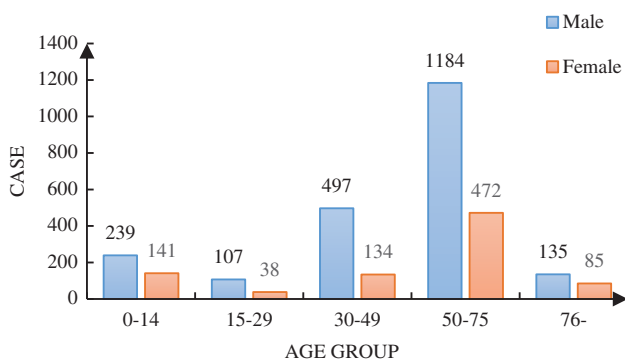
From 2015–2021, the overall male-to-female ratio of cases was 2.48:1 (2162:870), was significantly more common in males than females. The incidence of cases among individuals 50–75 years of age was higher, accounting for 54.62% of the total number of cases (Fig 4). The number of human rabies cases in 2015–2021 primarily affected farmers (73%);



**FIGURE 2** | Regional distribution of rabies cases in China from 2015-2021.



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



**FIGURE 4** | Age and gender distribution of human rabies incidence reported in China, 2015-2021.

**TABLE 1** | The division of rabies epidemic areas in China from 2015-2021.

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

students, domestic and unemployed, scattered children comprised comprised 7.26%, 5.44%, and 4.91% of cases, respectively. Compared to 2015, the proportion of cases 50-75 years of age and > 75 years of age increased from 50.44% and 6.87% to 66.24% and 8.92%, respectively, while in other age groups there was a downward trend. The proportion of farmers infected with rabies 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 was not obvious, whereas children in the diaspora showed a significant decline, with the percentage of cases dropping from 5.87% to 1.91%.

### Division of rabies epidemic areas in China from 2015-2021

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 2015-2021 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); the details are shown in Table 1.

### Laboratory diagnosis rate

Viral testing is essential for disease surveillance and control. In the absence of exposure history or typical symptoms, the clinical diagnosis of rabies can be difficult and laboratory methods should be used to confirm a diagnosis whenever possible [1]. Most reported rabies cases in China were clinically diagnosed, while the proportion of lab-confirmed cases was very low, with an average annual laboratory diagnosis rate of 1.2% from 2004-2014 [7]; 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]) in 2021; the details are shown in Table 2.

### Pathogenetic analysis

Understanding the genetic evolution characteristics of pathogens is the key to the prevention and control of infectious diseases [8]. 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 [9]. In recent years, the monitored populations of rabies pathogens have been reported in Shandong and Hunan provinces. In 2020 [10], Shandong reported the detection and

**TABLE 2** | Laboratory diagnosis rates of rabies in China from 2015-2021.

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

population division of specimens collected from 2010–2015, with 13 RABV strains (2 cases from saliva and 11 cases from canine brains) belonged to the China I group. In 2022 [11], the testing results of canine brain specimens collected from 2012–2017 in Hunan showed that 84% of the strains (21 strains) belonged to China I and the remaining 4 strains belonged to China II. There were seven RABV populations (China I–VII) in China, which were different among provinces and regions [9]. Hunan is one of the provinces with the largest number of prevalent population types (four populations [China I, II, III, and V [11]]), while Shandong has two populations (China I and II) [10]. At present, there are no new endemic populations in China, and the types of endemic populations in the provinces have not increased.

## DISCUSSION

Between 2015 and 2021 a total of 3032 rabies cases were reported in China, which was lower than the peak number in the third (2007) rabies epidemic (3300 cases). The number of human rabies cases in China has continuously and stably decreased from 801 in 2015 to 157 in 2021. The scope of the epidemic has been significantly reduced and the trend of spreading is evident.

As shown in Fig 1, the spatial distribution of cases in China gradually narrowed from 27 or 28 PLADs in the early period (2015–2017) to 21 or 22 PLADs in the most recent 4 years (2018–2021). The regional decline was more apparent at the district and county levels.

Compared to the scope of the epidemic involving 984 districts and counties during the third peak epidemic (2007) [12], the number of endemic areas decreased by 47.96% (512 districts/counties) in 2015 and by 88.21% (116 districts/counties) in 2021. Based on the 2007–2011 surveillance [7], the geographic distribution (district/county level) did not shrink when the epidemic decreased [12]. In contrast, the number of counties decreased steadily with respect to the number of reported cases in 2015–2021 (Fig 2); the epidemic area of rabies 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 measures. Among the provinces, 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,” [13] such as an animal rabies vaccination program for domestic dogs, extensive rabies prevention and control knowledge publicity work, and rabies vaccines into the New Agricultural Cooperative Scheme [14]. In 2016 [15] the dog immunization rate in Guangxi reached 70% and achieved a good prevention and control effect. Guangxi is a model of epidemic prevention and control in high-incidence provinces. The outbreak severity in Guangxi dropped from first in 2015 to seventh in 2021, with the annual number of reported cases decreasing from 117 to 7. Shandong, which has long been in a mid-endemic region, adopted dog immunization as the core of preventive and control efforts. Specifically, dog immunization was actively promoted [16,17] and successfully achieved a breakthrough from > 30 cases annually to zero cases in 2020, providing valuable experience for the local elimination of rabies.

The World Health Organization (WHO) concluded that animal immunization is the most cost-effective method by which to prevent human rabies. The immunization coverage of dogs effectively prevents the spread of rabies when > 70% of dogs are immunized [18]. The experience of many countries also showed that eradication of rabies depends on control of the number of dogs and the formation of an immune barrier [19]. In recent years China has continuously strengthened the management of dogs, improved the immunization rate of dogs, and 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 [14,20,21], 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 [7,22], and the immune status of dogs varies greatly among different regions. Dog management and immunization work needs to be coordinated throughout the country to make up for shortcomings and effective promotion.

Routine surveillance combined with laboratory diagnosis is a prerequisite for the control and elimination of outbreaks [23]. Laboratory diagnosis can reduce the problems of missed diagnosis and misdiagnosis in clinical diagnosis, and further etiologic analysis can provide a scientific basis for epidemic traceability and precise prevention and control [24]. The laboratory diagnosis rate of rabies cases in China is low but has increased in recent years from 1.2% (2004–2014) [7] to 22.93% (2021), in contrast to the



decrease in number of cases year-after-year, the following factors are thought to be involved. First, local CDC departments have more time and energy to collect specimens because few cases have been reported. In addition, annual training on rabies detection was organized country-wide, and some provinces have established testing laboratories to confirm the diagnosis of rabies. Because 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, emphasis on the importance of specimen collection and testing continued, the standardized training and assessment of laboratory testing are strengthened, qualified staff are trained, and a laboratory surveillance network is established with wider coverage to pave the way for rabies attack and elimination efforts.

In summary, the epidemic status of national human rabies from 2015–2021 decreased year-after-year, with a marked contraction in the geographic scope of the epidemic with 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.

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#### CONFLICTS OF INTEREST

The authors declare no competing interests.

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