Policy Forum

Factors Influencing the Number of Rabies Cases in Children in China*

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To understand the epidemic situation and factors influencing rabies cases in children in China, we obtained an overview of the current epidemic based on individual data of rabies cases in children and a descriptive analysis was carried on the prevalence and related factors. The results showed that the rabies cases in children accounted for 21.3% of the total number of rabies cases in China, 97.0% of these cases occurred in rural areas, they were mainly caused by dogs (81.5%), and were primarily level III exposure (47.7%). More than half of the cases were not treated with wound care, vaccination rate was extremely low (15.7%), and only 5.9% of cases were injected with antibodies. Furthermore, 25.4% of cases adopted incorrect treatments such as extruding bleed and wound closure, cases vaccinated with 5 injections accounted for only 22.5%. In conclusion, the prevalence of rabies cases in children in China remains a serious concern, the number and immune status of dogs in rural areas, and knowledge of rabies by risk populations should be considered in future rabies prevention and control programs.

Rabies is an acute zoonotic infectious disease caused by Rabies virus (RABV). Rabies prevalence is most serious in Asia and Africa, resulting in about 55,000 deaths every year[1]. Children is the high risk group of rabies, in India about 35% of human rabies cases came from children[2]; for patients who receiving post-exposure prophylaxis and treatment in Asia and Africa, children under the age of 16 accounted for 30%-50%[1]. Children act as deliver of human civilization, whose healthy growth also reflects human civilization, protecting children from the danger of rabies is the responsibility of human beings. In China, the national rabies surveillance system was implemented in 2005, and the national statutory notifiable communicable diseases reporting system started from 2004, based on these surveillance and case reporting systems it is possible to have deep investigation on disease epidemiology and the related factors. From the data of human rabies surveillance in China, there are hundreds of children died of rabies every year. In order to understand the reasons of high prevalence of rabies in children in China and explore the effective measures to protect children's health and life, avoiding the harm of rabies, we collected the data of children rabies cases under the age of 15 and analyzed the epidemic situation and influencing factors of rabies in children in China, to provide the preventive suggestions, hoping to arouse the whole society attention to rabies in children.

The focus of this study was children under the age of 15. The epidemic situation and individual data of rabies cases in children were collected through the national statutory notifiable communicable diseases reporting system of the Chinese Center for Disease Control and Prevention. A total of 5 088 rabies cases were reported in children during 2003-2012 and detailed individual case data were collected from 287 of these cases.

Analysis Methods To analyze rabies cases in children, the epidemiology, distribution, exposure history and post-exposure prophylaxis and treatment, as well as the clinical characteristics were considered. Excel 2007 and SPSS 16.0 were used for the management and statistical analysis of data, MapInfo 7.0 was used for creating the map presented in this work. Based on the results of these analyses, the efficacy of existing prevention and control measures for preventing children rabies

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were considered together with possible additional measures that could assist in the reduction of cases in the future.

Abbreviation In this paper, vaccine refers to rabies vaccines for human use, antibody refers to passive immune preparation of rabies antibodies, human rabies immunoglobulin (HRIG) is abbreviated as RIG, antiserum refers to rabies serum used as antiserum, post-exposure prophylaxis (PEP) refers to post-exposure prophylaxis and treatment. Correct PEP includes wound washing, vaccination with 5 doses of vaccines and RIG treatment (for category III exposure)[3].

Epidemic Situation of Rabies in Children in China From 2003-2012, a total of 5 088 rabies cases were reported in children under the age of 15 corresponding to an annual average of 508.8 cases and accounting for 21.3% of the total rabies cases in China. The most rabies cases in children cases occurred in 2006 year (763 cases), but the annual number of cases has subsequently each year (Figure 1A).

Distribution of Rabies Cases According To Age and Gender From 2003-2012, the rabies cases were broadly distributed by age (Figure 1B), but fewest cases were observed for children aged 0-4 years old (23.9%), and most cases in children aged 5-9 years old (40.5%). There were 10 cases in infants less than 1 year old.

Investigation of the distribution of cases according to gender reveals that there have consistently been more cases in boy (Figure 1C), with -2.3 times as many cases male cases compared to female cases. This suggests that boys preferred to contact and play with dogs or cats compared with girls, resulting the increase of infection risk.

The distribution of cases in geography and provinces was also analyzed (Figure 2). With the exception of Xinjiang, Tibet, and Jilin provinces, the remaining 28 provinces all had reports of cases in children cases, with the majority of cases distributed in southern provinces south of the Yangtze River. Previous reports have highlighted that Guizhou, Guangxi, Guangdong, and Hunan were the provinces with the most serious rabies epidemic, and the number of reported children cases was also highest in these four provinces, with the highest proportion of children cases in Guizhou (31.7%) and the lowest proportion in Hunan (20.4%).

Investigation of the detailed location of the 4 953 cases in children under the age of 15 from 2004 to 2012 according to case report cards, revealed that 97.0% of cases were distributed in rural areas and 82.0% of them were located in villages.

PEP of Rabies Cases in Children We next collected each report card for 287 rabies cases in children in 2010-2011 through the national rabies surveillance system and analyzed the exposure information and recorded PEP (Table 1). The cases were mainly exposed to dogs (81.5%), followed by cats (5.6%), which was consistent with reports at the

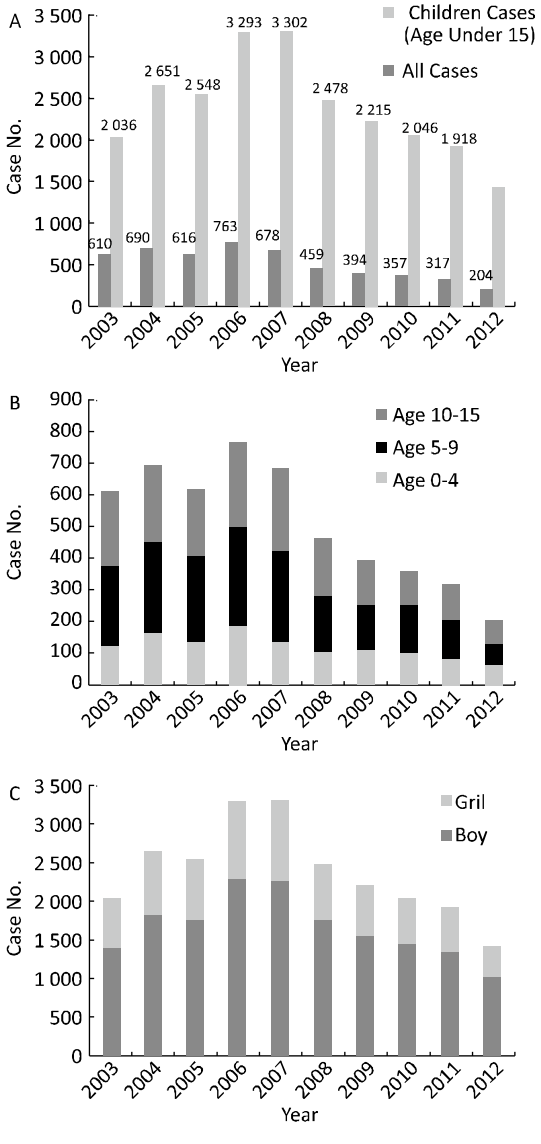

Figure 1. Prevalence and distribution of rabies case in children (less than 15 years) in China from 2003 to 2012. (A) Number of rabies cases in children and the whole population. (B) Age distribution of rabies case in children. (C) Gender distribution of rabies case in children.

Table 1. Exposure History of 287 Children Rabies Cases

Exposure History	No of Cases.	Ratio (%)	Percentage (%)
Exposed Animals			
Dog	234	81.5	90.7
Cat	16	5.6	6.2
Other	8	2.8	3.1
Type of Contact with Animals			
Bite	189	65.9	77.5
Scratch	38	13.25	15.6
Other	17	5.9	7.0
Exposure Category			
Category I	22	7.7	9.9
Category II	63	22.0	28.4
Category III	137	47.7	61.7
Exposuresite			
Head, face	68	23.7	25.6
Neck	7	2.4	2.6
Trunk	10	3.5	3.8
Arm	28	9.8	10.5
Hand	89	31.0	33.5
Upper limb	19	6.6	7.1
Lower limb	45	15.7	16.9

on human rabies cases nationwide. The modes of exposure were predominantly by bites (65.85%), followed by scratches (13.2%), which was also consistent with the observations for human rabies at the national level. The exposure degrees in children were mainly category III (47.7%) and in the cases with serious exposure, the risk of infection increased if PEP was not carried out or followed through for the entire recommended course of treatment. The regions of exposure of these cases in children mainly occurred on their hands (31.0%), and in the head, face of neck (28.2%).

The exposure history and PEP for 287 rabies cases in children were also considered (Table 2). In more than half of these cases (59.6%), the patient did not receive wound care at any level by a family member or in a medical institution and the vaccination rate was extremely low (15.7%). Although 47.7% of cases were with category III exposure, only 5.92% of the patients were injected with RIG or antiserum. Very low PEP rate was the main reason for the deaths of 287 children rabies cases. Only 12.9% of cases received wound care in medical institutions, which suggested that further treatment (vaccination, antibody injection, etc.) was unlikely. Of the 82.0% of cases that occurred in villages,

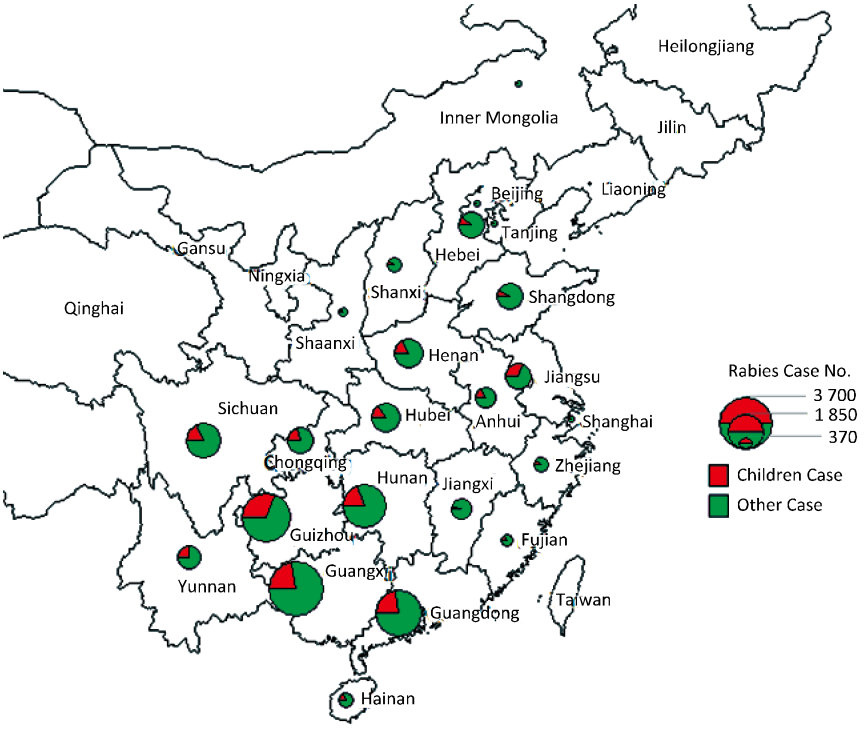

Figure 2. Geographical distribution of rabies case in children (less than15 years) in most part of China between 2003 and 2012.

Table 2. PEP of 287 Children Rabies Cases

Post-exposure Prophylaxis	Case no.	Ratio (%)	Percentage (%)
Wound Treatment			
No treatment	171	59.6	69.8
Self treatment	37	12.9	15.1
Treatment in medical institutions	51	12.9	15.1
Vaccination			
Yes	45	15.7	17.6
No	211	73.5	82.4
Antibody Injection			
Yes	17	5.9	7.0
No	226	78.8	93.0
Wound Treatment Institutions			
Village clinic	9	3.1	12.0
Town clinic	18	6.3	24.0
County hospital	24	8.4	32.0
Other	24	8.4	32.0
Vaccination Institutions			
Village clinic	10	3.5	22.7
Town clinic	18	6.3	40.9
County hospital	13	4.5	29.6
Other	3	1.1	6.8
Wound Treatment Method			
Extrusion bleeding	14	4.9	11.1
Washing	48	16.7	38.1
Disinfecting	37	12.9	29.4
Stitching wounds	18	6.3	14.3
Other	9	3.1	7.1
Vaccination Dosage			
1 dose	1	0.4	2.5
2 dose	1	0.4	2.5
3 dose	14	4.9	35.0
4 dose	15	5.3	37.5
5 dose	9	3.1	22.5
Sort of Antibody			
HRIG	17	5.9	89.5
Antiserum	2	0.7	10.5

Note. 'Case no.' include the recording data, not to be cover the missing data. Ratio's denominators are 287. Percentage's denominators are corresponding category recording cases total among 287 cases.

only a few of them (3.14%) received wound care in village clinics. A larger percentage (8.4%) received wound care in county hospitals but only half of them (4.5%) received vaccination. 25.4% of cases adopted incorrect treatments such as extruding bleed and wound suture, reflecting insufficient knowledge and skills on rabies prophylaxis by local medical staff. Although some cases were vaccinated, the cases vaccinated with the full treatment of 5 injections accounted for only 22.5% (9/40), indicating that failure to follow the correct vaccination procedure was an important reason for immunity failure. The main antibody used was RIG (89.5%), which is significantly more expensive than antiserum, which might be one of the reasons for patients failing to seek vaccination. Only 2 cases received wound washing, vaccination with 5 doses of vaccines and RIG treatment. However, wound closure was performed, which is not recommended and maybe lead to PEP failure. In all of the 287 cases at least one critical part of PEP was omitted, and there were no reports of vaccine failure where correct PEP procedure was documented.

The 287 rabies cases in children were then analyzed in terms of the timeliness of PEP. Full data was available for 67 cases (Table 3). Among these cases most children (60 cases) were treated with wound care at the day of exposure, but few of them were injected antibody or vaccinated at the same time. In the most extreme cases, subjects were treated at the 32nd day after exposure.

Clinical Characteristics of Rabies Cases in Children

Finally, the 287 rabies cases in children were investigated in terms of their clinical features. The incubation periods were from 0 to 3 452 d (9.5 years) with

Table 3. Timeliness of PEP of 67 Children Rabies Cases

Treatment Time (day)	Wound Treatment	Antibody Injection	Vaccination
0	60	11	31
1	2	-	1
2	-	1	-
4	1	-	-
6	-	2	-
22	-	-	1
28	-	-	1
30	-	-	1
32	1	1	1

a median of 43 d. The clinical course was from 0 to 34 d, with a median of 2 d. The median incubation period for all rabies cases nationwide (for all age groups) was about 60 days, and the median clinical course was about 4 d[4-6]. Thus, the incubation periods and course in children rabies cases were much shorter. The main clinical symptoms of children cases were agitation, hydrophobia, and aerophobia (80%-84%), followed by photophobia, convulsions (55%-57%), consistent with the typical clinical symptoms of other age rabies cases, but a higher rate of mental disorders (24.4%) were present in the children cases, which might be related to the shorter course in children cases, the more rapid progress leading to significantly more damage to the nervous system.

In this study, we analyzed the epidemic situation of rabies in Chinese children. The results showed that the prevalence of rabies in children remains a course for serious concern. Cases were mainly distributed in rural areas, especially in southern provinces. The prevalence of cases in these regions may be associated with the traditional custom of raising dogs to act as guard dogs in rural areas, and the increase in the migrant worker population has likely exacerbated the problem. In Guizhou, Guangxi, and other rural areas, the tradition of eating dog meat also contributed to the rising dog population, and 80.8% of dogs in these areas are allowed to roam unrestricted[7], which further increased the chances of children contacting with dogs. Finally, in rural areas, the extremely low immunization rate of dogs further increases the risk of children becoming infected with rabies virus. Dog is the primary infection source of human rabies, so the most effective measure for reducing rabies in human population is to increase the immunization coverage in dog population.

This study showed that 28.2% of children cases were bitten at head, face and neck, indicating a poor self protection ability in children, and their smaller size means their head, face and neck are more readily exposed to biting animals. Most child cases did not receive wound care treatment after exposure, which might be a consequence of insufficient knowledge about the prevention and treatment of rabies in children, the survey conducted in Guizhou and Guangdong, found that more than a half elementary students bit by animals did not receive wound care treatment in a timely manner[8].

From this investigation we also found that the incubation periods of children cases were much shorter and likely to be associated with more mental disorders, suggesting poor resistivity to infection, resulting in a rapid progress of disease after infected with rabies and severe exposure. Therefore, timely prophylaxis and treatment was necessary once exposed. However most of these children cases failed to get timely treatment, especially vaccination and antibody injection, which was an important reason for rabies prevalence in children. One more important reason for PEP failure is medical staff mistake cure among two cases whose wounds are stitched though they finished wounds, vaccine and RIG treatment.

Children cases with category III exposure in this investigation accounted for 47.7% of cases, but only 15.7% of these cases were vaccinated and 5.9% were injected with antibodies. When children had category III exposure, the bites were serious, but in spite of this, the children weren't brought to medical institutions for vaccination or antibody injection, indicating insufficient knowledge regarding rabies in these responsible adults. The low immunization rate of dogs in rural areas was also related with an insufficient awareness about the prevention of rabies in people. Cases in children occurred mainly in rural areas, and notably in infant cases under the age of one, suggesting insufficient care of children by parents and other adults, especially for preschool children who receive limited monitoring from adults due to absence of kindergartens in rural areas. The vaccination sequence of most children was less than the recommended 5 injections, also suggesting insufficient awareness of the importance of vaccination by parents or supervising adults.

This study showed that 82.0% of children cases were distributed in villages, but only 3.1% of cases received wound care in village clinics, indicating that the medical condition of village clinics was poor or didn't possess facilities or skills for the treatment of severe wound, affecting timely wound care for rabies cases. 25.4% of cases adopted incorrect treatments such as extruding bleed and wound closure, indicating insufficient knowledge and skills regarding treatment of rabies in medical staff. In this study, most children with severe exposure didn't receive antibody injection, and the vaccination rate was relatively low, which is a consequence of the financial burden on rural families. At present the antibody used for rabies prophylaxis in China is primarily immunoglobulin, which remains prohibitively expensive for many rural households with annual net income of a few thousand Yuan.

Thus, many households forgo antibody injections, increasing the risk of rabies in children. In 2011, the percentage of children comprising the national population in India is 29.8%, almost twice of that of China (16.5%)[9], which may help to explain why children cases are even more in India (35%) compared to China (21.3%).

Based on these factors identified above, we propose the following measures should be actively implemented for the prevention and control of rabies in children in China: (1) to control the number of dogs in rural areas, the feeding model of dogs should be changed and their ability to roam restricted should be reduced, their immunization and vaccination should be increased, and vaccination coverage should be improved. (2) The education of children regarding rabies should be improved, mainly through knowledge about how to be protected oneself in the presence of a potentially infected animal, how to inform parents and other adults after injury, and what treatment should be sought after exposure. (3) After potential rabies exposure, wound care should be sought as soon as possible, together with vaccination and antibody injection. (4) To strengthen the education of rural adults regarding the prevention and control of rabies, prevention concept of rabies should be promoted, care for children should be enhanced, immunization should be given to domestic dogs, and exposed children should be taken to medical institution for timely treatment. (5) To improve the medical conditions in rural areas, especially in village clinics, facilities and skills for wound care should be available, reserves of vaccine and antibody in medical institutions should be able to meet local needs, training of medical personnel should be strengthened, the standard treatment rate should be improved, and the expense of post-exposure treatment should be reduced, or incorporated into medical insurance such as the new rural cooperation medical system, for further reimbursement.

AUTHORS' CONTRIBUTIONS

SONG Miao drafted the manuscript. TANG Qing, Rayner Simon, and TAO Xiao Yan revised the manuscript in detail. SHEN Xin Xin and LIANG Guo Dong made significant contributions to this work by providing assistance and helped in the data collection, data manipulation and analysis.

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