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The epidemiology and clinical features of post-exposure prophylaxis for rabies: A retrospective study of 9772 cases

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ABSTRACT

Background: In December 2015, the World Health Organization, the World Animal Health Organization, and the Food and Agriculture Organization of the United Nations convened the International Congress on the elimination of rabies in Geneva. How to use epidemiological factors of post-exposure prophylaxis to prevent rabies has become the focus of attention.
Objective: To analyze the epidemiological characteristics of 9772 patients with rabies in a four-year period in one hospital, to clarify the outbreak law of rabies and to explore the corresponding prevention and control strategies.
Methods: The epidemiological data of rabies patients were collected from the infectious disease reporting information management system of the hospital from July 2018 to June 2022. The distributional characteristics of 13 influencing factors were analyzed using the chi-square test and linear regression.
Results: There was a significant correlation between the number of wounds and age, and the numbers of female and male patients were close. People over the age of 44 were more likely to get bites or scratches on their lower extremity ($P<0.0001$). There was a greater possibility for elderly people to be bitten by dogs ($P<0.0001$). Dogs preferred to bite or scratch lower limbs ($P<0.0001$), while cats upper limbs ($P<0.0001$). Upper limbs were more possibly attacked by animals at home ($P<0.0001$). There were significant correlations among exposure grade, wound treatment and number of wounds. Conclusions: Lower extremity protection is needed for the elderly and when encountering dogs, and more attention needs to be paid to the upper extremities when encountering cats and household pets, as well as pets that are cute but need to be protected from bites or scratches.

1. Introduction

Rabies is an acute zoonotic disease caused by rabies virus infection, and its clinical manifestations are endemic fear, water phobia, pharyngeal muscle spasm, and progressive paralysis. Rabies is currently the most lethal and highly prevalent infectious disease worldwide, with a fatality rate of almost 100%, causing approximately 59,000 deaths and the loss of more than 3.7 million disability adjusted life years (DALYs) annually [1]. At present, rabies is endemic in more than 100 countries and regions throughout the world, becoming the leading cause of death in zoonotic diseases [2–3]. A vast majority of rabies cases originate from the rural areas of Africa and Asia [4], where the number of annual deaths from rabies ranks the first in the world (estimated 30,000 people) [5]. Rabies is preventable by vaccination [6–7]. Now rabies elimination is achieved in Western European countries, Australia, Canada, the United States, Korea, Japan, and some Latin American countries [8,9]. Rabies cases have been significantly reduced through mass vaccination and management of dogs in recent years [10–11]. However, the recently increasing number of pets such as dogs and cats makes rabies still one of the important factors threatening human health [12]. In December 2015, the World Health Organization, the World Animal Health Organization, and the United Nations Food and Agriculture Organization convened the International Congress on the elimination of rabies in Geneva. The Congress proposed the goal of achieving global elimination of human rabies caused by canines by 2030 [13]. The prevalence of rabies in exposed and traumatized animals from the rabies immunization clinic of our hospital from 2018 to 2022 was analyzed, so as to improve the understanding of rabies in the general population and

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provide evidence for effective prevention and control of rabies.

2. Material and methods

2.1. Definition and labeling of exposures

Exposure to rabies refers to the situation that an animal suspected of rabies or a healthy animal possibly carrying a rabies virus bites, scratches, or licks the broken skin mucosa of a person, or the mucosa of an open wound contacts with the saliva or tissue of an animal that may carry rabies virus.

Exposure grading: Rabies exposure levels are generally categorized into three classes according to the nature and severity of exposure [6]. The exposure was rated as Class I if any of the following three conditions occurred. (1) The patient was exposed to or fed rabid animals or humans (without contacting their secretions and excretions). (2) The intact skin was licked by a rabid animal. (3) The intact skin was in contact with the secretions or excretions of a rabid animal or a human rabies case. The exposure was defined as Grade II when (1) the exposed skin was lightly bitten or (2) the patient did not bleed and had no minor scratches or abrasions. The exposure was defined as Grade III if (1) the patient had single or multiple bites or scratches on the skin, (2) the broken skin was licked by an animal, (3) open wounds or mucous membranes were contaminated by the saliva of a germy animal or a human being, or (4) the patient was exposed to a bat. The incubation period of the rabies virus is usually 2 to 3 months and rarely exceeds 1 year [6].

Patients included in this analysis were divided into rural and urban groups according to whether they lived in the countryside or town. When there were plots, roads and streets contained in the detailed residential address, the patients were classified into the urban group. When the address was marked as a village with few roads, the patients were assigned to the rural group.

Age groups were divided as per the WHO definition of age. Specifically, patients were classified as young adults (44 years old or under), middle-aged adults (45–59 years old), the young old (60–74 years old), the elderly (75–89 years old), or the super-aged (90 years old or above). The super-aged patients were excluded from this analysis due to the relatively small sample size.

2.2. Data collection and analysis

This retrospective study was carried out at Wenling Hospital of Traditional Chinese Medicine from 2018 to 2022. Medical records of patients with animal bites or scratches were checked. The information of 9772 cases, including age, gender, occupation, residential address, animal species, and injured site, was collected from the infectious disease reporting information management system of the hospital from July 2018 to June 2022. Patients were divided into different groups according to their age, gender, occupation, residential address, animal species, or injured site. The relationship between age and the chance of being bitten was analyzed by the regression equation method. Data were compared between or among different groups to clarify the associations of other factors. Data analysis was made using GraphPad (version 8.0). A p value of less than 0.05 was considered a significant difference. The Bonferroni test was used for multiple-comparison correction.

3. Results

3.1. General situation

The fact sheets for each of the influencing factors are shown in Table 1. The age distribution of the 9772 cases is presented in Fig. 1. Young and middle-aged patients make up the bulk of the population. At the same time, there is a significant correlation between the number of wounds and age according to the regression analysis: $y = -0.044 \times 2 + 2.7895\times + 104.6$, $R^2 = 0.7179$ (Fig. 2). There were 46.14%($n = 4509$)

Table 1
Case information.

Demographic	Specific conditions	Value (n/mean, median and range)
Gender	Male	4509(46.14%)
	Female	5263(53.85%)
Age		37.00 ± 20.52,34,0–98
Occupation	Housekeeping and unemployed	180(1.84%)
	Free occupation	175(1.79%)
	Professional technician	32(0.33%)
	Civil servant	69(0.71%)
	Individual operator	116(1.19%)
	Worker	399(4.08%)
	Farmer	1331(13.62%)
	Student	1655(16.93%)
	Staff	401(4.10%)
	Child-care worker	201(2.06%)
	Retired	201(2.06%)
	Teacher	106(1.08%)
	Others	4906(50.21%)
Native place	Local county-level cities	8832(90.37%)
	Other cities outside the province	172(1.77%)
	Other provinces	751(7.68%)
	Unknown	18(0.18%)
Residential address	Rural	4911(50.26%)
	Urban (containing streets and residential quarters)	4861(49.74%)
Date of getting injured	Q1 (January–March)	1984(20.30%)
	Q2 (April–June)	2477(25.35%)
	Q3 (July–September)	3102(31.74%)
	Q4 (October–December)	2209(22.61%)
Place of getting injured	At home	7683(78.62%)
	Near home	998(10.21%)
	Outside the neighbourhood, on the roadside (not of a field) (including streets and communities)	293(3.00%)
	In other places	798(8.17%)
Animal species	Dog	6603(67.57%)
	Cat	2563(26.23%)
	Mouse	464(4.75%)
	Other animals	142(1.45%)
Exposure grade*	I	51(0.52%)
	II	7678(78.57%)
	III	2043(20.90%)
Site of the wound	Upper extremity	6269(64.15%)
	Body	223(2.28%)
	Head and face	216(2.21%)
	Lower extremity	3064(31.36%)
Number of wounds	Multiple	736(7.53%)
	Single	9036(92.47%)
Wound management	Self-treatment	7728(79.09%)
	In the outpatient of medical institutions	2044(20.91%)
Whether to get vaccinated	No	6(0.06%)
	Yes	9766(99.94%)

* The exposure was rated as Class I if any of the following three conditions occurred. (1) The patient was exposed to or fed rabid animals or humans (without contacting their secretions and excretions). (2) The intact skin was licked by a rabid animal. (3) The intact skin was in contact with the secretions or excretions of a rabid animal or a human rabies case. The exposure was defined as Grade II when (1) the exposed skin was lightly bitten or (2) the patient did not bleed and had no minor scratches or abrasions. The exposure was defined as Grade III if (1) the patient had single or multiple bites or scratches on the skin, (2) the broken skin was licked by an animal, (3) open wounds or mucous membranes were contaminated by the saliva of a germy animal or a human being, or (4) the patient was exposed to a bat.

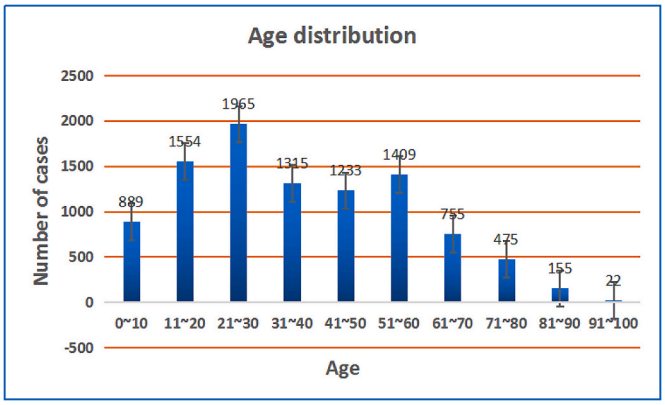

Fig. 1. Age distribution of patients. Young and middle-aged patients accounted for the majority.

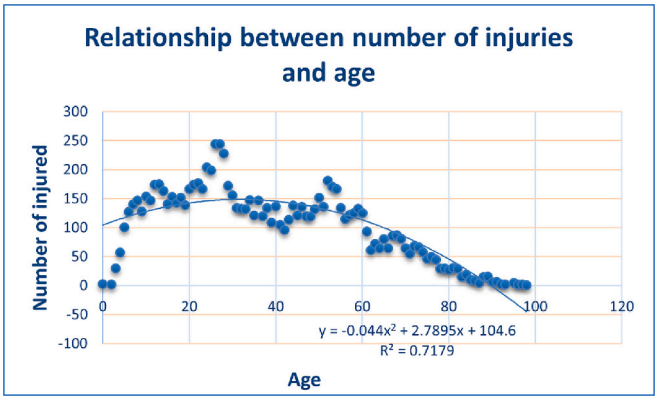

Fig. 2. Relationship between number of wounds and age (R^2 = 0.7179). The graph and the regression curve showed that there was a strong correlation between age and the possibility of being bitten or scratched by an animal.

males and 53.85% (n = 5263) females in the patients included (Fig. 3A). The incidence of rabies was 16.93% (n = 1655) in students and 13.62% (n = 1331) in farmers. Among all the occupations, these two occupations are the most easily to develop rabies (Fig. 3B). The majority of the patients included were local residents, accounting for 90.37% (n = 8832) (Fig. 3C). The numbers of rural and urban cases were close [50.26%(n = 4911) and 49.74%(n = 4861), respectively] (Fig. 3D). Most rabies infection events occurred in the third quarter [31.74%(n = 3102)], followed by those in the second quarter [25.35%(n = 2477)] (Fig. 4A). 78.62% (n = 7683) of bites took place at home (Fig. 4B). 67.57% (n = 6603), 26.23% (n = 2563), and 4.75% (n = 464) of the patients were bitten by dogs, cats, and mice, respectively (Fig. 4C). 78.57%(n = 7678) and 20.90%(n = 2043) of the wounds were classified as grades II and III, respectively (Fig. 4D). 64.15% (n = 6269) of the patients were bitten on their upper limbs and 31.36% (n = 3064) of them on the lower limbs (Fig. 5A). 92.47% (n = 9036) of the patients had single wound, and 7.53% (n = 736) of them had multiple wounds (Fig. 5B). 79.09% (n = 7728) of the patients handled the wounds by themselves, and 20.91% (n = 2044) of them sought help from the outpatient of health care facilities (Fig. 5C). 99.7% (n = 9766) of 9772 individuals received the rabies vaccine (Fig. 5D).

3.2. Association of age with animal species and wound site

Getting bitten or scratched on the lower extremity was correlated with age. The probability of getting bites or scratches on the lower extremity differed significantly among the four age groups (P<0.0001) (Table 2). It can be seen from the table that there was a correlation between age and getting bitten on the lower extremity. No comparisons of patients older than 90 were made on account of the small number of patients (Fig. 6). The data of the patients in the 4 age groups indicated in Table 2 were compared. The P value was corrected by the Bonferroni method. Specifically, by dividing the p value of a significant difference by 6, the corrected p value was obtained, which was 0.0083 (0.05 divided by 6) or 0.0017 (0.01 divided by 6). According to analysis results, the probability of getting bitten or scratched on the lower extremity in patients aged 0–44 was significantly different from that in patients aged 45–59, 60–74, and 75–89. It indicates that people over the

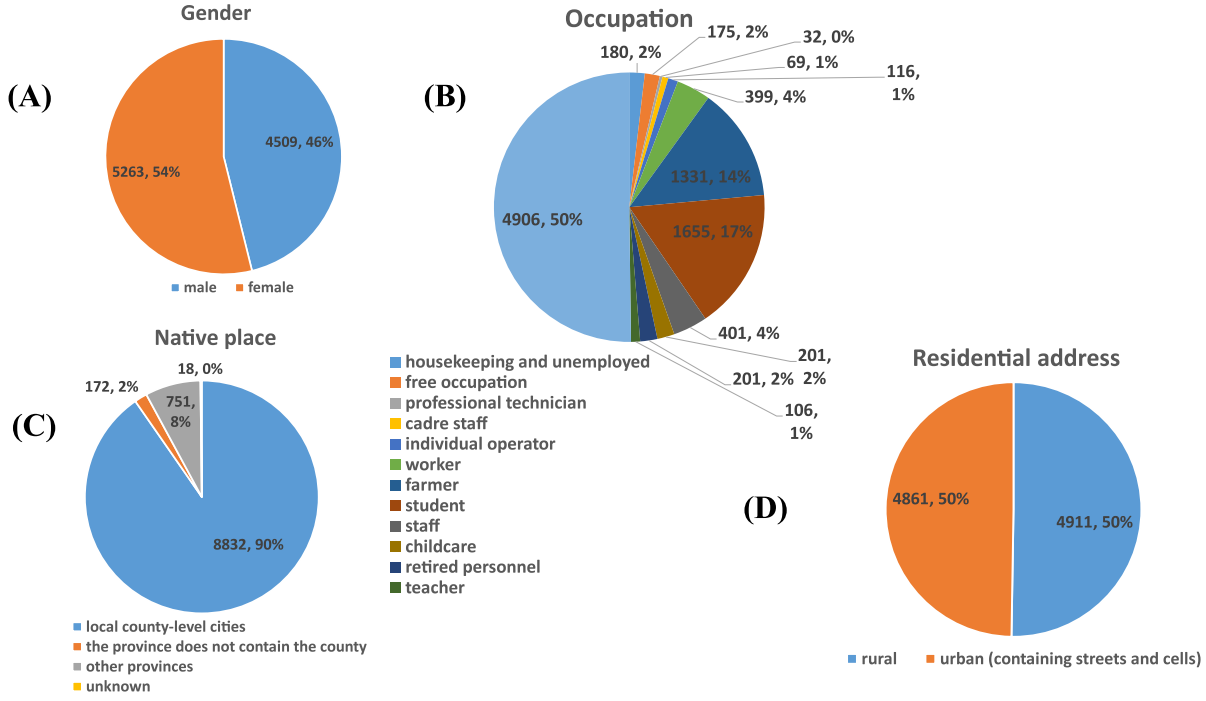

Fig. 3. Distribution of gender, occupation, native place and residential address.

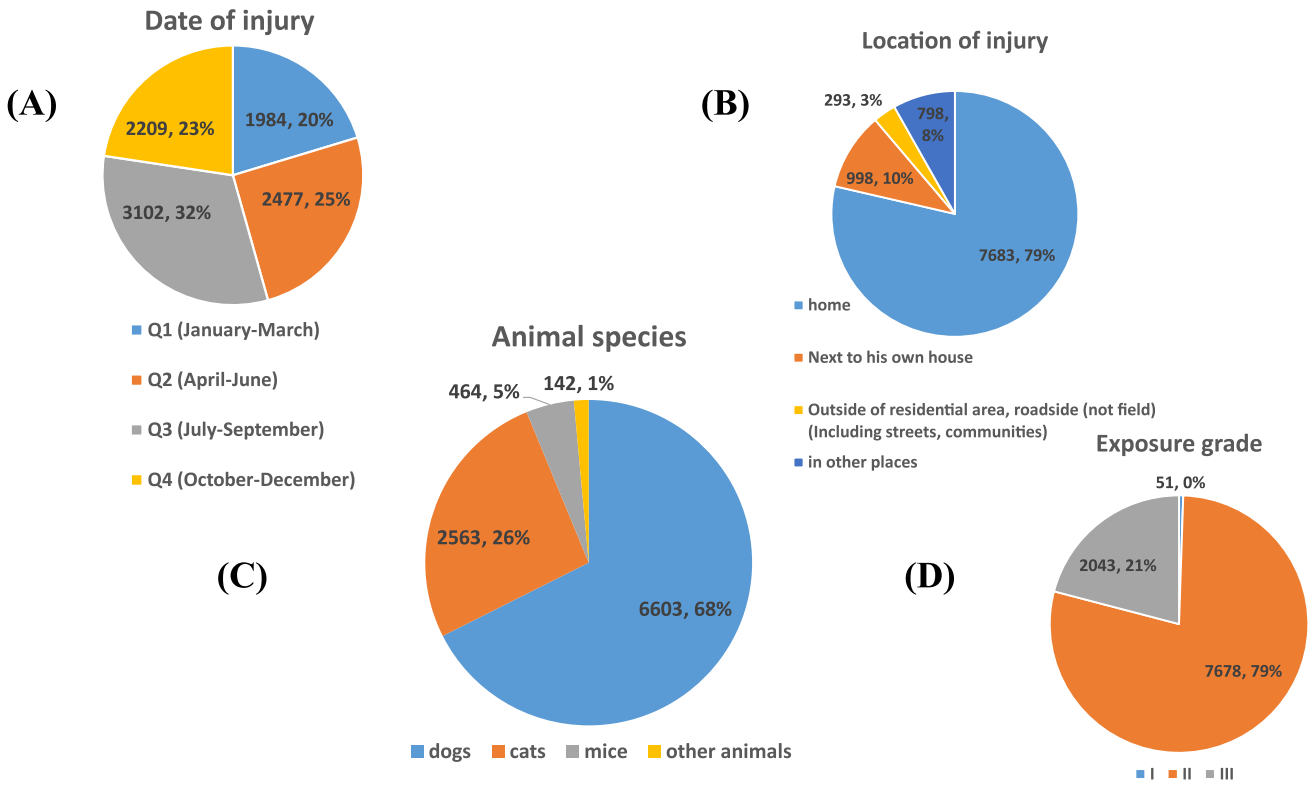

Fig. 4. Distribution of date of getting injured, place of getting injured, animal species and exposure grade.

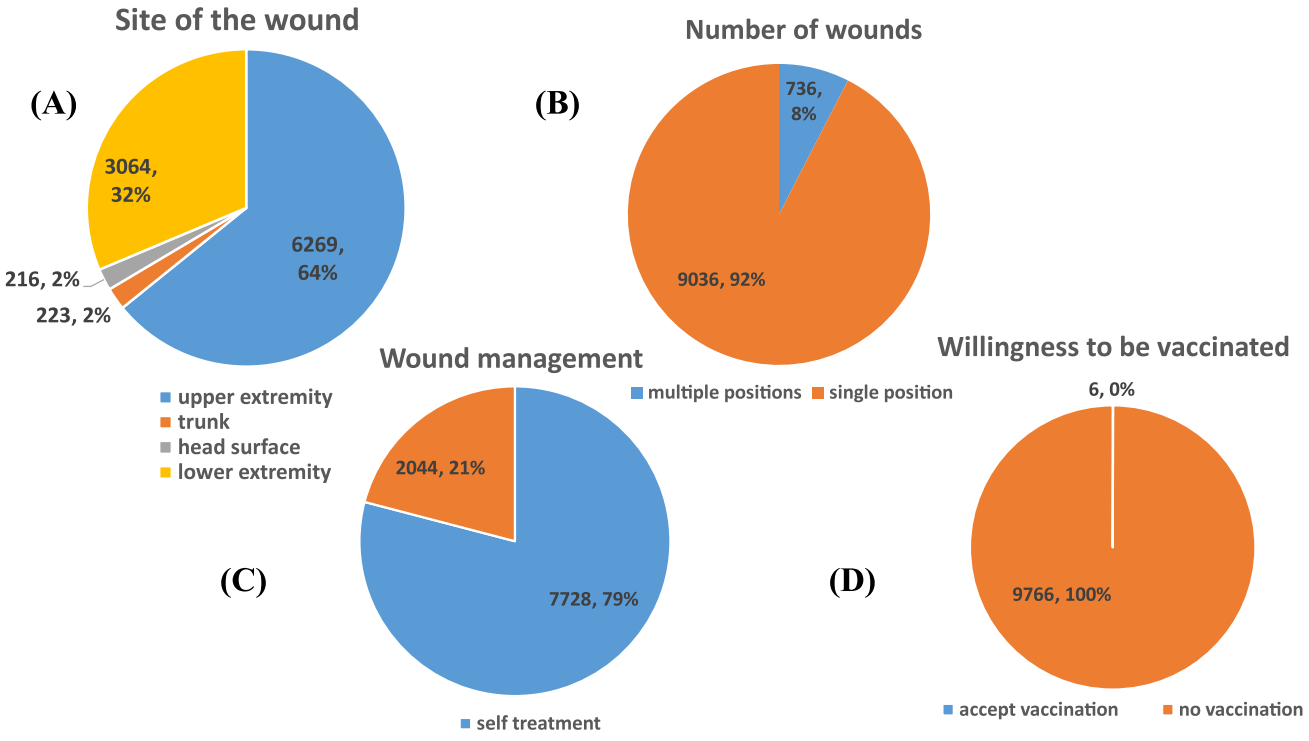

Fig. 5. Distribution of wound site, number of wounds, wound management and whether to be vaccinated.

age of 44 are more likely to get bites or scratches on their lower extremities. However, the difference was not significant among patients aged 75–89, 45–59 and 60–74.

The chance of getting bitten by a dog was closely associated with age. Older people were more likely to get bitten by a dog, compared with that by other animals ($P<0.0001$) (Table 3). Comparisons were made among 4 age groups (Fig. 7). The corrected P values (which were 0.0083 and 0.0017) were used in the analysis. The results showed that there were significant differences in the probability of getting bitten or scratched by a dog among patients aged 0–44, 45–59, 60–74 and 75–89. It suggests

Table 2
Incidence of bites or scratches on lower extremities in patients of different ages.

Age	Bitten or scratched on the lower extremity	Bitten or scratched on other parts of the body	Total	Proportion of patients getting bitten or scratched on the lower extremity
0–44	1457	4719	6176	23.59%
45–59	862	1202	2064	41.76%
60–74	562	566	1128	49.82%
75–89	176	200	376	46.81%

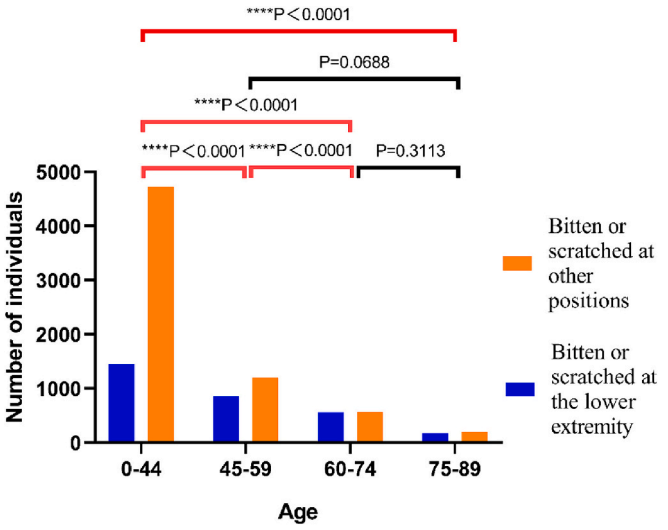

Fig. 6. Incidence of bites or scratches on the lower extremity in patients of different ages. People aged 44 or above are more likely to have animal bites or scratches on their lower extremities than those younger than 44. However, there was no significant difference in the probability of lower extremity injury among people aged 75–89, 45–59 and 60–74.

Table 3
Incidence of dog bites or scratches in patients of different ages.

	Dog bites or scratches	Bites or scratches from animals other than dogs	Total	Proportion of dogs bites or scratches
0–44	3749	2427	6176	60.70%
45–59	1582	482	2064	76.65%
60–74	916	212	1128	81.21%
75–89	331	45	376	88.03%

that dogs are more prone to biting or scratching people of older age.

3.3. The sites of dog and cat bites and scratches are different

A significant association was observed between the dog bite and the lower extremity wound (P<0.0001) (Table 4, Fig. 8). It suggests that dogs tend to bite the lower extremity. However, studies have shown that when people play with cats, more protection should be given to upper extremities (P<0.0001) (Table 5, Fig. 9).

3.4. Injuries to upper extremities require attention in the home setting

The current study showed a significant increase in upper extremity wounds at home, compared with those in other environments (Table 6). Specifically, 83.19% (n = 5215) of upper extremity bites and scratches occurred in the home setting, and 70.45% (n = 2468) were found in other environments (P<0.0001) (Fig. 10). Therefore, more protection should be given to upper limbs when there are animals at home.

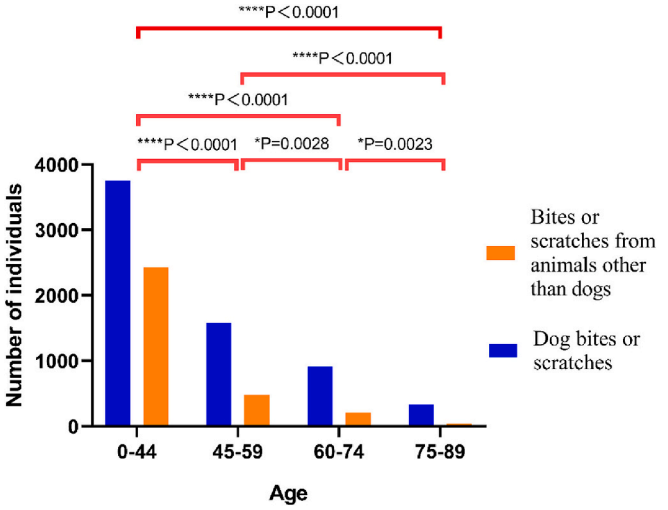

Fig. 7. Incidence of dog bites or scratches in patients of different ages. Compared with younger people, older people had an increased chance of being bitten by dogs.

Table 4
Odds of dog bites or scratches on lower extremities.

	Dog bites or scratches	Bites or scratches from animals other than dogs	Total	Proportion of dog bites or scratches
On the lower extremity	2581	483	3064	84.24%
On other body parts	4022	2686	6708	59.96%
P value	<0.0001			

3.5. There were significant correlations between exposure grade, wound treatment and number of wounds

Multiple wounds were significantly associated with exposure grade III (P<0.0001) (Table 7, Fig. 11(A)). It indicates that patients with multiple wounds are most likely defined as exposure grade III.

Multiple wounds and the outpatient of medical institutions were significantly associated. It suggests that patients with multiple wounds tend to seek treatment at the outpatient of medical institutions (P<0.0001) (Table 8, Figure11(B)). The outpatient of medical institutions was associated with exposure grade III (Table 9, Fig. 11(C)). It indicates that people classified as exposure grade III will seek treatment in the outpatient of medical facilities. At the same time, exposure grade II was strongly associated with self-treatment (P<0.0001) (Tables 10, 11 (D)). It demonstrates that a majority of patients of exposure grade II manage wounds by themselves.

Exposure grade II was strongly associated with single wound (P<0.0001) (Table 11, Fig. 11(E)). It means that most patients of exposure grade II have single wound, which conforms to the reality. Single injury was strongly associated with self-treatment (P<0.0001) (Table 12, Fig. 11(F)). It suggests that most patients with single injury handle wounds by themselves, which shows that people's ability to treat wounds by themselves has improved.

4. Discussion

Multiple epidemiologic and clinical features were associated with the outcome. In the present study, it was found that the incidence of rabies in farmers was still high [13.62% (n = 1331)], but the incidence was even higher in students [16.93% (n = 1665)]. This finding might be attributed to the decline in the number of farmers due to the gradual

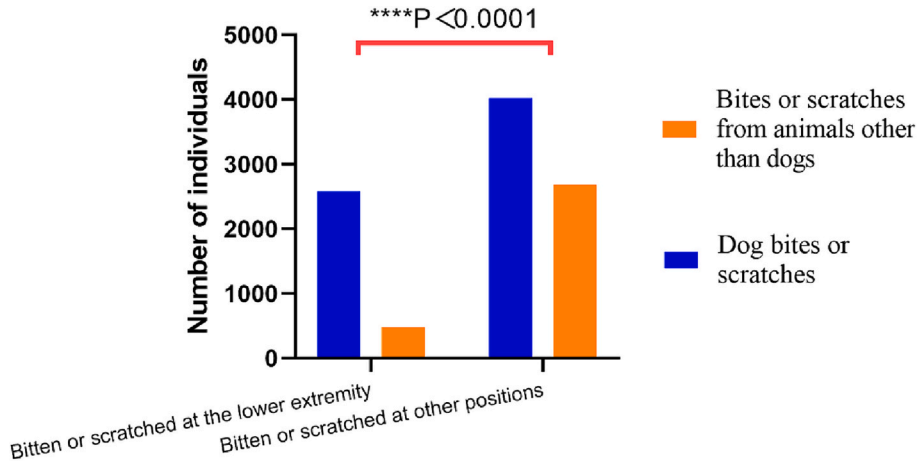

Fig. 8. Odds of dog bites or scratches on lower extremities. Dogs were more likely to bite or scratch lower extremities.

Table 5
Odds of cat bites or scratches on upper extremities.

	Cat bites or scratches	Bites or scratches from animals other than cats	Total	Proportion of cat bites or scratches
On the upper extremity	1998	4271	6269	31.87%
On other body parts	565	2938	3503	16.13%
P value	<0.0001			

urbanization of coastal cities in China. There were 46.14% (n = 4509) male cases and 53.85% (n = 5263) female cases, indicating that more females got bitten than males. In addition, students had a relatively poor understanding of rabies, so corresponding knowledge should be strengthened. The numbers of rural and urban cases were close [50.26% (n = 4911) and 49.74% (n = 4861), respectively].

Age, season, wound site and animal species are important factors. Most rabies cases occurred in the third quarter between 2018 and 2022, followed by those in the second quarter. There were many factors leading to exposure in summer. Besides, in summer the canine went into estrus and the level of skin exposure to canines was high. Therefore, prevention and awareness should be enhanced in summer and autumn, which will help reduce seasonal exposure of at-risk populations. The age of onset of the advanced age groups was significantly higher than that of the low age group [14]. In addition, there was a high prevalence of rabies at home, and 78.62% (n = 7683) of bites took place at home. Thus, it is necessary to increase protection against pet bites at home. Besides, the present study also showed that most patients were bitten by dogs and cats. Although there are reports of reservoir host animals such as bats, dogs, cats and other carnivores that harbor the rabies virus, rodents are rarely infected with rabies. There was no evidence of rabies caused by rodent bites [9,15,16]. In real life, after being bitten by the mouse, we will get vaccinated against rabies.

More attention should be paid to pet bites at home. About 64.0% (n = 6272) of the patients were bitten on upper limbs and 31.3% (n = 3072) on lower limbs. In general, patients were ignorant of dog or cat

Table 6
Chances of getting bitten or scratched on the upper extremity at home.

	Getting bitten or scratched at home	Getting bitten or scratched at other places	Total	Proportion of getting bitten or scratched at home
On the upper extremity	5215	1054	6269	83.19%
On other body parts	2468	1035	3503	70.45%
P value	<0.0001			

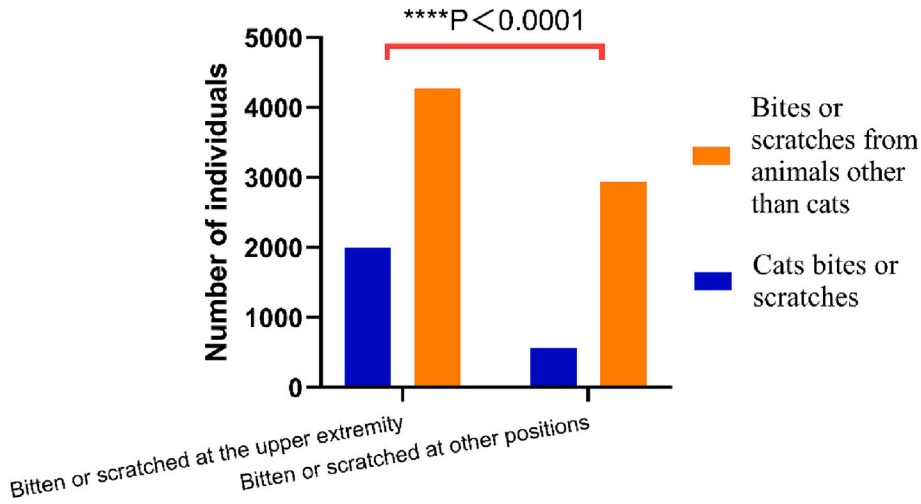

Fig. 9. Odds of cat bites or scratches on upper extremities. Cats were more likely to bite or scratch upper limbs.

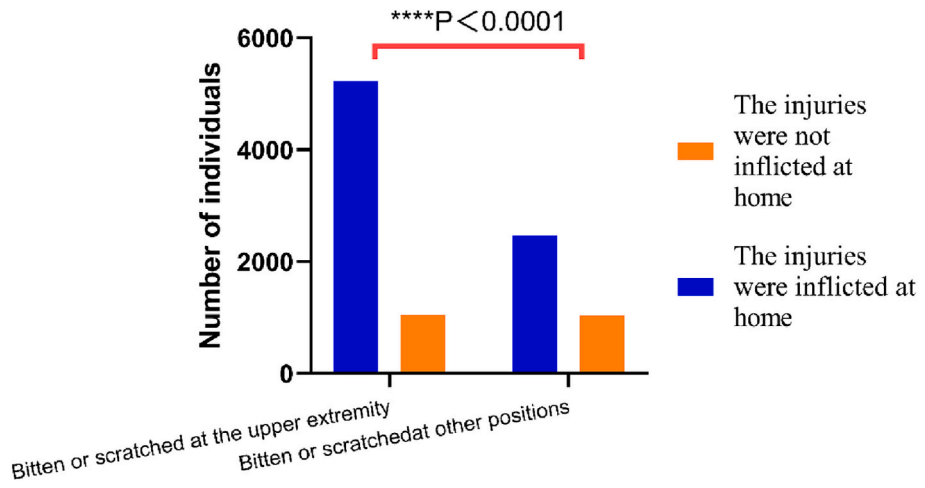

Fig. 10. Chance of getting bitten or scratched on the upper extremity at home. People should pay more attention to protecting their upper extremities from animal bites or scratches at home.

Table 7
Correlation between exposure grade III and multiple wounds.

Exposure grade	Patients with multiple wounds	Patients with single wound	Total	Proportion of patients with multiple wounds
Grade III	378	1665	2043	18.50%
Not-grade III	358	7371	7729	4.63%
P value	<0.0001			

bites on lower limbs. The bite on upper extremities occurs only when one is engaged in relatively intimate play with a cat or dog. It suggests that an increasing number of people are getting bitten on the upper extremity by the pet harboring the rabies virus. Since such a large number of people are bitten at home, we should attach greater importance to preventing the bite by a pet dog or pet cat.

Increased self-medication capacity in people with less severe injuries is a trend. About 7.53% (n = 736) of the rabies cases had multiple wounds, and 92.47% (n = 9036) had single wound. This finding illustrates the predominance of minor injuries. About 79.09% (n = 7728) of the patients handled the wounds by themselves, and 20.91% (n = 2044) sought treatment in the outpatient of medical institutions. It indicates that the ability to deal with wounds by ourselves is improving.

Standardized prevention is the key. 99.94% of 9772 individuals received the rabies vaccine, which showed greatly improved awareness of protection against rabies. Post-exposure prophylaxis refers to the prophylactic treatment within a certain period of time after exposure to a pathogen, such as a virus. Post-exposure prophylaxis can help prevent infection or the development of disease caused by that pathogen. Standardized post-exposure prophylaxis disposal can 100% prevent the morbidity. Cases of disposal failure are relatively rare, and the failure is mainly resulted from inadequate or non-standard disposal. Besides, patients with immune function defects also cannot effectively respond to

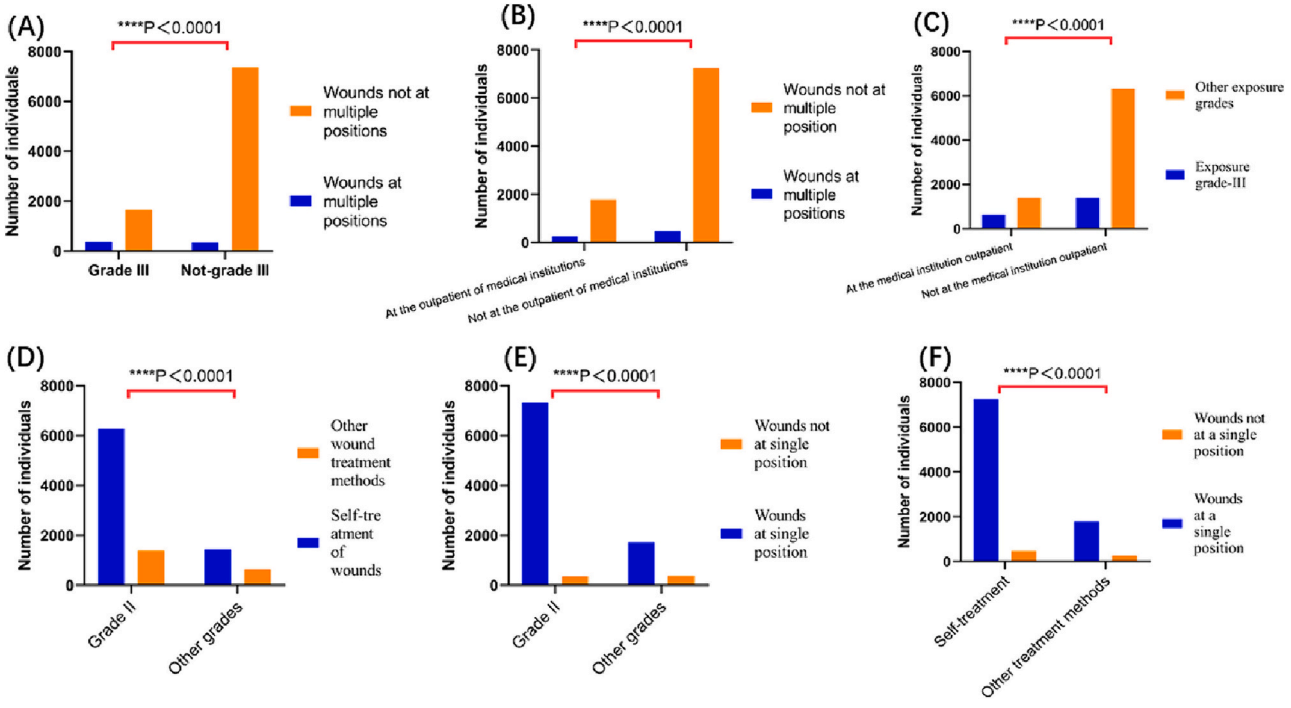

Fig. 11. Correlation analysis among exposure grade, wound treatment and number of wounds.

Table 8
Correlation between the outpatient of medical institutions and multiple wounds.

Wound management	Patients with multiple wounds	Patients with single wound	Total	Proportion of patients with multiple wounds
At the outpatient of medical institutions	260	1784	2044	12.72%
Self-treatment	476	7252	7728	6.16%
P value	<0.0001			

Table 9
Correlation between the outpatient of medical institutions and exposure grade III.

Wound management	Exposure grade III	Other exposure grades	Total	Proportion of patients of exposure grade III
At the medical institution outpatient	640	1404	2044	31.31%
Self-treatment	1403	6325	7728	18.15%
P value	<0.0001			

Table 10
Correlation between exposure grade II and self-treatment.

Exposure grade	Self-treatment	Other treatment methods	Total	Proportion of patients treating wounds by themselves
Grade II	6285	1393	7678	81.86%
Other grades	1443	651	2094	68.91%
P value	<0.0001			

Table 11
Correlation between exposure grade II and single wound.

Exposure grade	Single wound	Multiple wounds	Total	Proportion of patients with single wound
Grade II	7320	358	7678	95.34%
Other grades	1716	378	2094	81.95%
P value	<0.0001			

Table 12
Correlation between self-treatment and single wound.

Wound management	Single wound	Multiple wounds	Total	Proportion of patients with single wound
Self-treatment	7252	476	7728	93.84%
Other treatment methods	1784	260	2044	87.28%
P value	<0.0001			

the disposal [17]. The post-exposure prophylaxis procedure consists of prompt local treatment of the wound, prompt rabies vaccination, and, if necessary, early passive immunization against rabies.

5. Conclusions

The elderly are vulnerable to animal bites or scratches. They should pay more attention to dog bites or scratches on lower limbs than younger people. Among the animals studied in this paper, dogs are more likely to bite or scratch lower limbs, while cats prefer to attack upper limbs. When we have a pet in the house, our upper extremities are more likely to get bitten or scratched. Therefore, we need to be careful not to get bitten by pet animals. Moreover, our ability to treat wounds caused by animals by ourselves has improved. It is a good method that everyone gets vaccinated against rabies. At last, prevention and management measures for rabies infection caused by pet dog or cat bites or scratches should be strengthened.

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Ethics approval

This study was approved by the Institutional Ethics Committee of Wenling Hospital of Traditional Chinese Medicine.

Declaration of competing interest

Authors declare that there is no conflict of interest associated with this manuscript.

Data availability

Data will be made available on request.

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None.

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