Epidemiological Patterns, Trends of Animal Bites and Factors Associated with Delays in Initiating Post-Exposure Prophylaxis for Rabies Prevention in Hurand, Iran: A Cross-Sectional Study

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ABSTRACT
Background and objectives: Animal bites account for tens of millions of injuries annually. The present study aimed at identifying the epidemiological patterns of animal bites and factors affecting the delay of post-exposure prophylaxis for the injured patients in Hurand, northwestern Iran.

Methods: In this cross-sectional study, data were collected from medical records of animal bite victims who were referred to the rabies center of Hurand between 2014 and 2017. The epidemiological pattern of animal bites and factors affecting delayed initiation of post-exposure prophylaxis was investigated using the Poisson regression.

Results: The majority of animal bites occurred in males and people aged 5-15 years. Moreover, most injuries were caused by dog bite. The most commonly affected organs were the lower limbs. The risk ratio of delay in vaccination for men was 0.88 compared with women. Delay in post-exposure prophylaxis was more common among rural residents and those bitten by cats.

Conclusion: According to the results, males, rural residents and people aged under 15 years of age are most vulnerable to animal bites. Designing a comprehensive educational program for these target groups seems essential for reducing animal bites. In addition, to prevent delays in vaccination, factors such as sex, animal type, location of events and the extent of bites should be considered.

Keywords: Rabies; Delay of vaccine; Post-exposure prophylaxis; Animal bite

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INTRODUCTION
Animal attacks are still a major health issue worldwide. Animal bite is the main source of transmission of rabies to humans, which has not yet been controlled in most parts of the world (1). Approximately 85-90% of human animal-bite injuries are caused by dogs, 5-10% by cats and 2-3% by humans and rodents (2). In low-income countries, several studies have demonstrated that dogs account for 76-94% of animal-bite injuries, resulting in a high prevalence of rabies and higher fatality rates due to poor access to anti-rabies post-exposure treatment (3, 4).

According to the Center for Disease Control (CDC), around 4.5 million people worldwide are bitten by animals every year, which often require post-exposure prophylaxis (PEP) (5).

Through the involvement of the central nervous system, rabies leads to encephalitis with a fatality rate of 100% which means more than 60,000 deaths in the world annually (6). According to the estimation made by the World Health Organization (WHO), more than 15 million people take prophylaxis annually for the prevention of this disease (7). "Zero human rabies death by 2030" is the joint project of the WHO, the Food and Drug Administration and the Global Union of Rabies Control to eliminate rabies by 2030 (8). An animal bite can lead to infections, post-traumatic stress disorder, disfiguring injuries requiring reconstructive surgery and rarely death (9, 10).

Nearly 95% of the deaths from rabies occur in Asia and Africa. Rabies are mostly related to bats in the US and to dogs in Europe, Asia and Africa (11). According to the WHO, 31,000 deaths occur annually in Asia because of human rabies which accounts for about 56% of total global rabies deaths (12). The rabies virus is endemic in both wild and domestic animals of Iran (13). The main route of transmission is through rabid dog bites, which account for 96% of human rabies cases (14). According to the CDC, the prevalence of animal bites in Iran was 173.2 per 100,000 people in 2005 (15). Rabies is prevalent in almost all 31 provinces of the country (16). This imposes a great financial burden on the country’s health system (17). Pre-exposure prophylaxis (PrEP) or PEP vaccination is the only treatment available for the disease; however, it inflicts a great economic cost to the health system of the countries (1). Annually, the overall economic costs of human rabies has been estimated to be 8.6 billion USD (95% CIs 2.9–21.5 billion), with the largest proportion of costs caused by premature death in Asia and Africa (18).

The first step in disease control is epidemiological surveillance (19), which could provide useful information for planning and evaluating public health interventions (20). Factors such as type of incidence, place of residence and distance from health center affect PEP (21). A review of online sources indicated that most cities in Iran have a similar epidemiological pattern of animal bites (22). The present study aimed at identifying the epidemiological patterns of animal bites and the factors affecting the delay of PEP among injured people in Hurand (northwestern Iran) between 2014 and 2017.

MATERIALS AND METHODS
This cross-sectional study was conducted to investigate the animal bite patterns among the cases referred to the rabies Center of Hurand (also known as Horand) between 2014 and 2017. All animal-related injuries were included. Incomplete data were excluded from the final analysis. It is important to note that trained staff completes the checklist of disease surveillance information throughout the country in the same way. According to the census of population 2021, Hurand has 20000 inhabitants in 5038 families. Data were extracted from patients’ records at the health facilities and the Ministry of Health. Animal bite injuries and human deaths due to suspected rabies were checked by clinicians at health facilities. We used a standardized data extraction form to collect the following information: age, sex, occupation, place of residence, year, type of bite (domestic/wild), damaged organ, history of an animal bite, size of bite (large or small), time pattern of the incidence (time, season) and the pattern of services provided.

The qualitative variables were expressed in frequency and percentage and quantitative variables were expressed as mean and standard deviation. The subjects were classified into different age groups. The Poisson regression model was also adopted to estimate the delay in time and to determine associated risk factors. In this model, it is assumed that the dependent variable has a Poisson distribution, and it is equally assumed that its arithmetic logarithm
can be modeled linearly as an uncertain parameter. A p-value of less than 0.05 indicated lack of equivalence between mean and variance. The variables that had a meaningful level of less than 0.1 in the univariate model entered the multivariate model with the Enter method. Statistical analysis was performed by the statistical package of STATA version 15 (STATA Corp, College Station, TX, USA). Graphs were created using Prism software, version 6.0 (GraphPad, CA, USA).

RESULTS

Overall, 293 people bitten by animals have been referred to the Hurand vaccination center between 2014 and 2017. Most of the injured were men 232 (79.2%) and aged 5-15 years 94 (32.1%). The mean age of the injured patients was 28.82 ± 20.07 years (range 4-87 years). Moreover, 83.2% of the injuries were superficial, while 16.7% were deep (Table 1). Most injuries were due to dog bite. In terms of the occupational distribution of victims, most injuries occurred among students, followed by ranchers and farmers. Most bites occurred during 6-12 am and 12-18 pm. Most injuries affected the lower limbs (68.6%), followed by shoulder and hand (23.7%).

As shown in (figure 1), animal bites were more common among rural residents compared with urban residents. The data also revealed a steady rise in the number of animal bites in rural areas since 2014.

| Table 1. Frequency distribution of animal bite cases by in Hurand, Iran |
|--------------------------|--------------------------|--------------------------|
| Variables                | Sub-groups   | Frequency (percent) |
| **Age groups (years)**   |             |                        |
| <5                       | 9 (3.1)      |                         |
| 5-15                     | 94 (32.1)    |                         |
| 16-30                    | 84 (28.7)    |                         |
| 31-45                    | 43 (14.7)    |                         |
| 46-60                    | 39 (13.3)    |                         |
| >60                      | 24 (8.2)     |                         |
| **Gender**               |             |                        |
| Male                     | 232 (79.2)   |                         |
| Female                   | 61 (20.8)    |                         |
| **Season of bite**       |             |                        |
| Spring                   | 83 (28.3)    |                         |
| Summer                   | 64 (21.8)    |                         |
| Fall                     | 69 (23.5)    |                         |
| Winter                   | 77 (26.3)    |                         |
| **Injury status**        |             |                        |
| Deep                     | 49 (16.7)    |                         |
| Superficial              | 244 (83.2)   |                         |
| **Number of injuries**   |             |                        |
| One                      | 176 (60.0)   |                         |
| Two                      | 77 (26.3)    |                         |
| Three                    | 28 (9.6)     |                         |
| ≥ Four                   | 12 (4.1)     |                         |
As shown in (figure 1), PEP delay was significantly more common among residents in rural areas.

![Figure 1](image1.png)

**Figure 1.** Number of animal bite cases reported from urban and rural areas of Hurand between 2014 and 2017.

The incidence of animal bites has risen since 2015, reaching 21.3 per 1000 people in 2016, but in 2017, the corresponding value declined to 19.1 per 1000 people.

Based on the multivariate regression analysis, a p-value for the goodness of fit test after the Poisson was found to be (1.0), which indicates the equivalence between the mean and variance of the multivariate model. In the single-variable analysis, the risk ratio for men compared with women was 0.88 (95% confidence interval: 0.79, 0.97). In order to analyze the type of animal bites, to avoid data sparseness, wolf and donkey bites were merged under the ‘other group’. In comparison to dog bites (0.18), cat bites had a delay of more than one day before vaccination. However, 34.4% of the bites by other animals were managed quicker than the bites by dogs.

Compared to villagers, residents in urban areas experienced 10% less delay in referring to vaccination. Moreover, cases with extensive injuries were managed more quickly compared with the reference group with a risk ratio of 1.17 (Table 2).

![Figure 2](image2.png)

**Figure 2.** Number of patients reporting delay of PEP based on place of residence.
### Table 2. Estimation of risk ratio at 95% confidence level based on the Poisson regression model to predict vaccination delay

<table>
<thead>
<tr>
<th>Variables</th>
<th>Subgroups</th>
<th>Univariate Model</th>
<th>Multi variable</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Incidence rate</td>
<td>Incidence rate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ratios</td>
<td>ratios</td>
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<tr>
<td>Gender</td>
<td>Female</td>
<td>Ref</td>
<td>Ref</td>
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<tr>
<td></td>
<td>Male</td>
<td>0.88</td>
<td>0.79 - 0.97</td>
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<tr>
<td>Animal type</td>
<td>Dog</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td></td>
<td>Cat</td>
<td>0.82</td>
<td>0.78 - 0.86</td>
</tr>
<tr>
<td></td>
<td>Others</td>
<td>1.34</td>
<td>1.08 – 1.66</td>
</tr>
<tr>
<td>Location of animal attack</td>
<td>Village</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td></td>
<td>City</td>
<td>0.90</td>
<td>0.82 – 0.99</td>
</tr>
<tr>
<td>Extension of the bite</td>
<td>Minor</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td></td>
<td>Extensive</td>
<td>1.17</td>
<td>1.07 – 1.27</td>
</tr>
</tbody>
</table>

### DISCUSSION

This study demonstrates that animal-bite injuries remain an important cause of morbidity and referral to health facilities in Hurand, Iran. Since the proportion of households with dogs is increasing in Iran, it is important for healthcare providers and families to be aware of dog-bite injuries. This is important as bite-related injuries are the main mode of transmission of rabies to humans (18). The risk ratio of delay in the vaccination program for men compared with women was 0.88. In comparison to dog bites, 0.18 of the bites by cats had a delay of more than one day for vaccination.

Our findings indicate that the number of animal bites has increased in Hurand, Iran. In a study by Babazadeh et al., in Chaldoran, the average incidence of animal bites was reported to be 541 cases per 100,000 people between 2008 and 2014 (22). In a study by Amiri et al. in 2007, the incidence of animal bites was 146 cases per 100,000 (23). A possible explanation for this might be that the sensitivity of the health system in detecting animal bites has increased. Another possible explanation for this is that people’s awareness about animal bites have improved over the years. Inconsistent with our findings, a study in the United States reported no significant difference in the incidence of dog-bites between 1994 and 2003 (24).

In this study, people aged 5 to 15 years were most vulnerable to animal bites. In the study carried out by Babazadeh et al. (22), the frequency of animal bites among people aged 10-19 years and 20-29 years was 30% and 21.3%, respectively. In the Golestan Province, most bites occurred in people aged 26-35 years (25). However, in the Lorestan Province, the prevalence of animal bite was highest among those aged between 10 and 29 years (26). A previous report in the United States showed that dog-bite injury rate was highest among children aged between 5 and 9. Another study also indicated that the rate decreased with age (27). In South Korea, most dogs bites were reported among school-aged children (7–12 years), followed by adults over 18 years of age (28). It appears that the high frequency of animal bite injuries in teenagers and young adults is because of near contact with animals and provoking aggressive behavior in animals.

In our study, 86% of the bites were related to dogs, which is similar to the rate reported by Babazadeh et al. (22). Annually, approximately 4.5 million people are bitten by dogs in the United States, 25% of which require some form of medical care (24).
Similar to previous studies (19, 29), we found that students, rancher and farmers are more vulnerable to animal bites. Students generally have less perception of risk, especially when dealing with animal, which could justify the higher rate of animal bites among them. However, the increased prevalence of animal bites among rancher and farmers may be due to their frequent contact with animals.

Consistent with results of previous studies (22, 29), we found that animal bites were more common in males than in females. A study demonstrated that animal bites were more common among female teenagers and adults and male children aged 12 years or younger (28). A study in Italy also reported a significant difference in the incidence of animal bite between male (66%) and female (34%) adults (30).

In the present study, the majority of animal bites occurred in rural areas, which is in agreement with results of previous studies in Iran (26, 31, 32). This may be due to the fact that villagers are generally more exposed to wild animals.

Based on the results, animal bites mostly affected the foot, which is consistent with the findings of other studies (33, 34). We also found that the delay in PEP was less frequent for men than for women, which is in line with results of previous study (32). This could be related to the dependence of women on men in order to visit the clinic. In addition, cases bitten by cats experienced more delay in PEP compared with those injured by dogs. This may be related to the greater extent of injury caused by dog bites compared with cat bites (35).

**Limitation**

This study was based on routinely collected from the health center records. It is important to stress that, this study describes patients that sought care in health facilities, and therefore it missed a critical population that did not seek medical attention.

**CONCLUSION**

According to the results, males, rural residents and people aged under 15 years of age are most vulnerable to animal bites. Designing a comprehensive educational program for these target groups seems essential for reducing animal bites. It is also recommended to develop prevention strategies consisting of educational programs on dog behavior and enhancing dog control programs. Patients injured with animal bite should be informed and followed up to expedite the PEP process. The epidemiologic characteristics of dog-bite injuries and factors affecting delay of PEP could vary at the regional or national level, so region-specific studies may be beneficial.

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**DECLARATION**

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**Ethics approvals and consent to participate**

The study protocol was approved by the Ethics Committee of Tabriz University of Medical Sciences (ethics code: IR.TBZMED.REC.1398.134).

**Conflicts of interest**

The authors declare that there is no conflict of interest.

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