

## Original Article

# Animal Bite and Deficiencies in Rabies Post-Exposure Prophylaxis in Tehran, Iran

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## Abstract

**Background:** Rabies post-exposure prophylaxis (PEP) is an effective measure if administered immediately. We evaluated the primary health care provided after animal bite and determined the deviations from rabies PEP protocol.

**Methods:** This 6-year population-based cross-sectional study was conducted in Tehran, the capital of Iran, from April 2006 to March 2012. The study population included people who referred to health centers of Tehran, seeking PEP. The data were extracted from rabies registry databases using a checklist of items according to the context of the health records. All statistical analyses were performed at a significance level of 0.05 using Stata software, version 11.

**Results:** Of 22,766 cases of animal bite, 84.5% were men, 31.9% were aged 21–30 years, and 66.3% lived in urban areas. Most cases were the result of a dog bite (81.7%), mostly at midday (29.9%), and more frequently in spring (27.9%) and summer (27.7). Legs (45.6%) and hands (43.4%) were the most common sites of animal bite. The PEP was associated with a variety of shortcomings as follows. A majority of cases who had indication of receiving a 5-dose vaccination schedule had received only three doses. Most of the cases with a wound in the head and neck and many of cases with deep wounds had not received immunoglobulin. A number of cases needed to receive one-mL dose of vaccine while they had received 0.5-mL doses.

**Conclusions:** According to our results, rabies PEP is not well monitored and the preventive measures are associated with some insufficiencies and deviations from the national PEP protocol which must be taken into consideration by public health authorities to ensure that rabies surveillance is efficient.

**Keywords:** Animal bite, Iran, post-exposure prophylaxis, rabies

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## Introduction

Rabies is a zoonotic viral disease that is transmitted to humans from animals. Rabies causes acute inflammation of the brain in humans and other warm-blooded animals.<sup>1,2</sup> The time period between contracting the disease and the initiation of symptoms is usually one to three months<sup>1</sup>; this period is dependent on the distance between the wound and the central nervous system.<sup>3</sup>

Rabies is a preventable disease as long as rabies post-exposure prophylaxis (PEP) is started immediately after exposure to animal bite. Nonetheless, over 60,000 people die of rabies worldwide every year, the majority of which occurs in Asia and Africa.<sup>1</sup> The disease infects domestic and wild animals. Dogs are the source of the vast majority of human rabies deaths worldwide. Bats are the source of most human rabies deaths in America, and recently in Australia and Western Europe.<sup>1,4</sup> Rabies may also spread through exposure to infected foxes, raccoons, and jackals.<sup>1,2</sup> Domestic farm animals can be infected by the virus and can transmit the

disease to humans.<sup>5</sup>

After a typical human infection by bite, the virus replicates in the bitten muscle and gains access to the peripheral nervous system. The virus then travels toward the central nervous system.<sup>6</sup> During this phase, the virus is hardly detectable within the host, but immunization can prevent symptomatic rabies. When the virus reaches the brain, the majority of clinical symptoms manifest as acute encephalitis. Once the symptoms of the disease develop, treatment is almost never effective and the probability of mortality is over 99%.<sup>7</sup>

PEP can prevent the disease if administered immediately, generally within a maximum of 10 days of infection.<sup>8</sup> However, multiple deep transdermal bites or wounds in the head and neck, particularly in endemic regions, need immediate vaccination and immunoglobulin. Irrigation of the wound as soon as possible with soap and water for approximately five minutes appears to be effective in reducing the number of viral particles.<sup>1,2</sup> Annually, about 29 million people in the world receive a PEP to prevent rabies disease at an estimated cost of US\$ 2.1 billion.<sup>1</sup> PEP is a cost-effective measure for preventing the disease if administered immediately.<sup>9</sup> Any failure of PEP may lead to rabies disease and death.

Rabies surveillance is rarely monitored and reported,<sup>10</sup> particularly in developing countries. A local study in Iran indicated that only 37.2% of the cases received timely PEP within the first six hours.<sup>11</sup> A case-series on 16 human rabies deaths in Iran indicated that the majority of cases did not receive full doses of vaccine and some of them did not receive immunoglobulin.<sup>12</sup> Another epidemiological studies conducted in western Iran reported that over 81% of the people who were bitten by animals did not complete

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the vaccination schedule.<sup>13</sup> Despite the importance of PEP, evidence from different parts of Iran shows a deviation from the standards defined by the national guideline for control and prevention rabies in Iran.<sup>14</sup> To date, PEP has not been properly investigated in Iran. The only information comes from small, unrepresentative samples of local data. Therefore, we evaluated the primary health care provided after animal bite and determined the deviations from rabies PEP protocol.

## Materials and Methods

The Research Committee of Hamadan University of Medical Sciences approved this study. This 6-year population-based cross-sectional study was conducted in Tehran Province, the capital of Iran, from April 2006 to March 2012. The study population included people who had referred to rural and urban health centers affiliated with 'Tehran', 'Shahid Beheshti', and 'Iran' Medical Universities seeking primary health care due to animal bites. During the study period, 22,766 cases of animal bite were reported by the three universities.

The data were extracted from the three health network databases in Tehran using a checklist of items according to the context of the health records. The checklist included data on demographic characteristics (age, sex, area of residence), a history of animal bite, the type of involved animals, the clinical condition of the involved animals, the clinical characteristics of the wounds, and the number of vaccination doses and immunoglobulin.

An animal bite is a wound caused by the teeth of an animal. The injury can damage skin, nerves, bone, muscle, blood vessels, and joints.<sup>15,16</sup> In the Islamic Republic of Iran, any case of animal bite should receive a PEP according to the World Health Organization recommendations.<sup>14,17</sup> The PEP consists of local treatment of the wound (washing the wound promptly with soap and water for approximately five minutes), followed by rabies vaccination (with or without rabies immunoglobulin). Vaccination is initiated immediately after animal bite. Treatment may be discontinued (after the third dose) if the animal involved remains healthy throughout an observation period of 10 days; or if the animal is killed and found to be negative for rabies by laboratory examination. The indication for rabies vaccination depends on the type of contact with the rabid animal. Minor scratches or abrasions without bleeding need immediate vaccination. Patients affected by animal bite and referred to health centers within 48 hours receive intramuscular doses of 0.5 mL, while those who refer to health centers after 48 hours, have to receive intramuscular doses of 1 mL, given as five doses over four weeks.<sup>14</sup> One dose of the vaccine should be administered on days 0, 3, 7, 14, and 30. All intramuscular injections must be given into the deltoid muscle for adults or into the anterolateral area of the thigh muscle for small children. Vaccine should never be administered in the gluteal region.<sup>17</sup> Single or multiple deep transdermal bites or wounds in the head and neck need immediate vaccination and administration of rabies immunoglobulin (RIG). Human RIG is given in a single dose of 20 IU per kg of body weight. Immunoglobulin is administered with the first dose (zero day) of vaccine at the same time, but in a different part of the body. For cases who have previously undergone complete pre-exposure immunization or PEP, two intramuscular doses of vaccine separated by three days are sufficient. Immunoglobulin is not necessary in such cases. Administration of RIG should be infiltrated into the depth of the wound and around the wound as

much as anatomically feasible. Any remainder should be injected at an intramuscular site distant from that of vaccine inoculation e.g. into the opposite deltoid muscle or into the opposite anterior thigh muscle.<sup>17</sup>

All statistical analyses were performed at a significance level of 0.05 using Stata software, version 11 (StataCorp, College Station, TX, USA).

## Results

The characteristics of the cases are given in Table 1. Of 22,766 cases of animal bite, 84.51% were men, 31.93% were aged 21 to 30 years, and 66.27% were residents of urban areas. Most cases were the result of a dog bite (81.71%). Bites occurred most often in early morning (27.17%) and at midday (29.87%). Bites happened more frequently in spring (27.87%) and summer (27.74%). Legs (45.62%) and hands (43.36%) were the most common sites of the animal bite.

Shortcomings of PEP of animal bite in term of the vaccination dose are given in Table 2. According to the guideline, vaccination may be discontinued after the third dose if the animal involved remains healthy for a 10-day observation period or if the animal is killed and found to be negative for rabies by laboratory examination; otherwise, five doses of vaccine must be administered. However, 21.06% of the cases needed to receive five doses of vaccine rather than three doses. Furthermore, all cases of animal bite inflicted by a wolf, fox, jackal, donkey, cow, or animals other than dogs or cats have to receive five doses of vaccine while the majority of such cases had received only three doses of rabies vaccine.

Shortcomings of PEP of animal bite in term of RIG administration are given in Table 3. The majority (61.19%) of the cases with a wound in the head and neck had not received immunoglobulin. Furthermore, all cases with deep wounds needed to receive the vaccine as well as RIG, but most of such cases had not received immunoglobulin.

Shortcomings of PEP of animal bite in term of admission time and vaccination dose are given in Table 4. All patients affected by animal bite and referred to health centers after 48 hours had to receive doses of 1 mL while 21.46% of such cases had received vaccination doses of 0.5 mL.

## Discussion

Based on our findings, the PEP of animal bite was associated with some deficiencies and deviation from the national guideline, including prescription of three doses of vaccine rather than a five-dose schedule, not receiving RIG while it was indicated, and receiving doses of 0.5 mL whereas doses of 1 mL needed to be prescribed. These deficiencies in PEP may increase the risk of rabies in patients affected by animal bite and may result in irreversible disease and death. A study conducted by Christian, *et al.*<sup>10</sup> to describe the epidemiology of PEP and its associated shortage in the USA reported that PEP is loosely monitored and a precise estimate of PEP use was unknown. Of course, incomplete immunization and delay time is a major problem even for routine vaccination.<sup>18</sup>

We indicated that most cases were the result of a dog bite. The most important global source of rabies in humans is from uncontrolled rabies in dogs. Previous epidemiological studies conducted in other parts of Iran reported that the majority of animal bites in

**Table 1.** Descriptive analysis of the study population.

Variable	Count	Percentage
<b>Age group (yr)</b>		
<10	2,050	9.08
11–20	4,145	18.37
21–30	7,206	31.93
31–40	3,741	16.58
41–50	2,624	11.63
51–60	1,689	7.48
61–70	783	3.47
>70	332	1.47
<b>Sex</b>		
Female	3,521	15.49
Male	19,216	84.51
<b>Region</b>		
Urban	14,921	66.27
Rural	7,596	33.73
<b>Time (o'clock)</b>		
Morning (5–10)	3,062	27.17
Midday (11–15)	3,366	29.87
Evening 16–19)	2,681	23.79
Night (20–4)	2,161	19.17
<b>Season</b>		
Spring	6,336	27.87
Summer	6,307	27.74
Winter	4,864	21.39
Autumn	5,229	23.00
<b>Animal</b>		
Dog	18,157	81.71
Cat	2,964	13.34
Wolf	39	0.18
Fox	69	0.31
Jackal	8	0.04
Donkey	67	0.30
Cow	30	0.14
Others	886	3.99
<b>Organ</b>		
Head & neck	448	2.06
Legs	9,916	45.62
Hands	9,424	43.36
Trunk	511	2.35
Hand & foot	854	3.93
Multiple organs	581	2.67
<b>Severity</b>		
Surface	11,683	79.01
Deep	3,104	20.99

**Table 2.** Shortcomings of post-exposure prophylaxis of animal bite in term of vaccination dose.

Vaccination schedule	3-dose		5-dose	
	Number	Percentage	Number	Percentage
<b>Animal observation</b>				
Observed	6773	75.14	2241	24.86
Escaped	289	21.06	1083	78.94
<b>Type of animal</b>				
Dog	13975	77.21	4126	22.79
Cat	1404	47.48	1553	52.52
Wolf	8	20.51	31	79.49
Fox	10	14.49	59	85.51
Jackal	0	0.00	8	100.00
Donkey	20	29.85	47	70.15
Cow	4	13.33	26	86.67
Others	287	32.54	595	67.46

**Table 3.** Shortcomings of post-exposure prophylaxis of animal bite in term of anti-rabies immunoglobulin (Ig) injection.

Variables	Ig injected		Ig not injected	
	Number	Percentage	Number	Percentage
<b>Superficial wounds</b>				
Head and neck	85	38.81	134	61.19
Legs	676	12.79	4,611	87.21
Arms	803	16.73	3,996	83.27
Trunk	65	22.73	221	77.27
Arms and legs	60	18.69	261	81.31
Multiple organs	73	36.32	128	63.68
<b>Deep wounds</b>				
Head and neck	41	62.12	25	37.88
Legs	692	59.35	474	40.65
Arms	794	63.47	457	36.53
Trunk	52	74.29	18	25.71
Arms and legs	181	74.49	62	25.51
Multiple organs	138	79.31	36	20.69

**Table 4.** Shortcomings of post-exposure prophylaxis of animal bite in term of admission time and vaccination dose.

Admission time (hr)	Vaccination dose					
	0.5 mL		1 mL		Unknown	
<48	6,702	38.47	4,314	24.76	6,407	36.77
>48	188	21.46	495	56.51	193	22.03
Unknown	757	16.95	395	8.84	3,315	74.21

Iran is the result of a dog bite.<sup>11,13,19</sup> Exposure to rabid dogs is still the cause of over 90% of human exposure to rabies and over 99% of human deaths worldwide.<sup>1,2</sup> However, in the USA, wild carnivores and bats are the principal rabies hosts.<sup>2,20</sup>

This study had a number of limitations. Evaluation of rabies surveillance system requires reliable sources of data. We used data recorded in the databases of three universities in Tehran. The quality and accuracy of the data depends primarily on the quality of the recorded death certification while we were unable to verify the accuracy of the recorded data, thus information bias is probable. Furthermore, the Pasteur Institute, which is a referral center, was the fourth center in Tehran that provides 24-hour rabies post-exposure services. We tried to access the data recorded in this center but we were unable due to bureaucratic barriers. This is the main limitation of this study that may raise the possibility of selection bias and underestimating the results. Despite its limitations, the current study could clearly reveal some deviations from the national rabies PEP protocol in Iran. Furthermore, our study was conducted in the megacity of Tehran which hosts 20% of the Iranian population. We retrieved 22,766 cases of animal bite. Thus, the body of evidence identified allows a robust conclusion regarding the objective of the study for evaluating the shortcomings of rabies surveillance in Iran.

In conclusions, according to our results, rabies PEP is not well monitored and the preventive measures are associated with a number of insufficiencies and deviations from the national PEP protocol that need to be taken into consideration by public health authorities to ensure that rabies surveillance is efficient. Periodical education of public health professionals with respect to rabies PEP and systematic monitoring of rabies surveillance are suggested.

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## Conflict of interest statement

The authors declare that they have no conflicts of interest.

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