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Epidemiology of acute animal bite and the direct cost of rabies vaccination

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ABSTRACT

Objective: To describe the epidemiological aspects of animal bites and to calculate the financial burden resulting from rabies vaccination in Chalderan City.

Methods: In this cross-sectional study, records of all victims of animal bites in a seven-year period were reviewed. Studied variables included demographic information of victims, biters' profile, time and place patterns, clinical aspects of the victims and the cost of vaccination.

Results: Most of bites were observed in men in the age group of 10–19 years old, at rural areas and occupational group of farmers. The vast majority of animal bites happened by dogs and domestic animals. The average age of victims with head and neck injuries was lower than that of victims with injuries in the lower extremities, shoulders and hands ($P = 0.001$). The cost of vaccination was 11 665 dollars with three doses of rabies vaccine and 849 dollars for five doses, and the 12 514 dollars cumulative frequency in the studied period. Based on the results of trend test, the incidence of animal bites was increased significantly during the study period ($P = 0.02$).

Conclusions: The results of this study showed that due to the increasing incidence of animal bites and the financial burden resulting from animal bite vaccination, it is necessary to design and implement preventive measures in order to reduce the animal bites.

1. Introduction

Rabies is recognized as the most important viral zoonoses nowadays, due to the global distribution, high incidence, human and veterinary costs, and its mortality, which imposes high

economic costs annually in various countries^[1,2]. Rabies is one of the consequences of a bite that has high virulence and case fatality rate^[3,4]. It is an acute viral illness that causes encephalomyelitis in humans, all mammals and warm-blooded animals. The disease is common in domestic and wild animals in most provinces of Iran^[5,6]. Dogs play the most important role in the transmission of rabies to humans^[6]. By proper vaccination coverage for at least 70% of dogs and cats population, an effective barrier will be created for the transmission of the disease to humans^[7].

The main sources of rabies in the northern regions of Iran are dogs and foxes, and in the western and northwestern regions of Iran are wolves^[8,9]. In areas where rabies is endemic, children aged 5–15 years old are about 40% of people exposed to dog bites^[10,11]. In the world, the death rate due to rabies in children under 15 years

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The study was performed according to the Helsinki Declaration. The study protocol was reviewed and approved by the Ethics Committee of Tabriz University of Medical Sciences. Identity of all bitten persons kept confidential.

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old results in the loss of about 1.74 million disability adjusted life years^[12]. Asia carries 96.5% of the disease burden in developing countries, with annual expenditures of about 560 million dollar mainly for the treatment-prevention^[13].

Increased annual incidence of animal bites results in increased costs for taking care of victims, such as the rabies vaccine and serum^[14]. In Iran, billions of rials are annually spent to prevent human rabies, and there is no other contagious disease in the country that costs as much as rabies^[15]. However, its global cost is estimated more than a billion dollars a year^[15,16]. In addition to the financial costs of prevention and treatment of animal bites, the mental and social consequences caused by animal bites and scars can greatly affect the life of victims and their family^[17]. Wide geographical distribution, ecological diversity and interdependence of the major risk factors of rabies with wildlife species, as well as differences in health-related behaviors and knowledge of the population, necessitate the need to conduct researches separately in different regions of the country^[18].

There were some quotes about high incidence of animal bite in Chalderan County. So this study was conducted with the aim of describing the epidemiology of animal bites, identifying people at risk, seasonal and temporal patterns of animal bites, and calculating the financial burden of vaccination of victims. Results of the study will help us to design the intervention programs in order to prevent and reduce cases of animal bites and reduce its burden on health care system.

2. Materials and methods

This cross-sectional study examined the patterns of animal bite in a seven-year period from March 21st, 2008 to March 20th, 2014 longitudinally in Chalderan City, West Azerbaijan province, Iran. The seven-year period of the study was selected due to the availability of data. The health center in this city had two units for the prevention of rabies, which provided health care and treatment services for all victims of animal bites. Data on the bitten subjects were extracted from rabies records.

2.1. Study site

In the study site, people usually did not keep pet dogs with them at the home. The dogs were typically used as guard at the house yard or with the sheep herds. No national vaccination program was run in the country for dogs and other pets. In urban areas, most people did not keep pet dogs and most dogs in these areas were stray dogs.

2.2. Target population

All cases of animal bites in all age and sex groups referred to the rabies prevention units and their data were fully recorded in the files.

2.3. Animal bitten subjects

The subjects of this study included person who referred to rabies units due to fear of contracting rabies and/or other diseases from animal bites.

All the cases of animal bites referred to the health centers in the study period were included in the study (census).

2.4. Studied variables

Age, gender, occupation, residential information in urban or rural and location of the injury in urban or rural, type of biting animal, biter's situation after 10 days of bite by domestic, wild or escaped ones, injury site, the extent of the wound (large or small), time patterns of injury (hour, month, season, year), patterns of health services provided for the victims: the number of vaccination, and vaccination costs in terms of the number of rabies vaccine were assessed.

2.5. Code of ethics

The study protocol was reviewed and approved by the Ethics Committee of Tabriz University of Medical Sciences. Identity information of all bitten persons kept confidential.

2.6. Data analysis

Data were analyzed by SPSS software version 20. Descriptive characteristics of the participants were presented with statistics such as mean \pm SD. And in case of lack of normality, the median and inter-quartile range and qualitative variables were presented with the relative frequency.

2.7. Statistical analysis

To investigate the possible correlations between the qualitative variables, the *Chi*-square test was used. In case of low sample size, Fisher's exact test was used. To examine the equality of the means of quantitative variables, the independent samples *t*-test was applied with equal variances assumed. To examine the equality of means of categories of qualitative variables the One-way ANOVA test was used. The Cochran–Armitage test for trend was also used to examine the incidence trend of bites during the seven-year study period. In all statistical tests, the *P*-value less than 0.05 was considered as significant.

3. Results

3.1. Demographic characteristics of victims

In total, during the study period, 1724 bitten subjects with an average age of (21.00 \pm 14.56) were registered and there was a statistically significant difference between the mean age of men (20.52 \pm 14.72) and women (22.20 \pm 14.11) (*P* = 0.03). In terms of gender distribution, 1241 (72%) cases of the victims were male. Male to female ratio was 2.56.

Most of the victims of animal bite in terms of occupation were farmers with 494 cases (28.7%), students with 435 cases (25.2%) and housewives with 332 cases (19.3%). The most involved age group for men was 10–19 years old and for women was 20–29 years old (Figure 1).

3.2. Spatial patterns

The residential status of 288 cases (16.6%) were living in urban areas and 1437 (83.4%) in rural areas. In terms of the location of bites, 409 cases (23.7%) happened in urban areas and 1234 cases (71.5%) in rural areas and the location of 81 bites

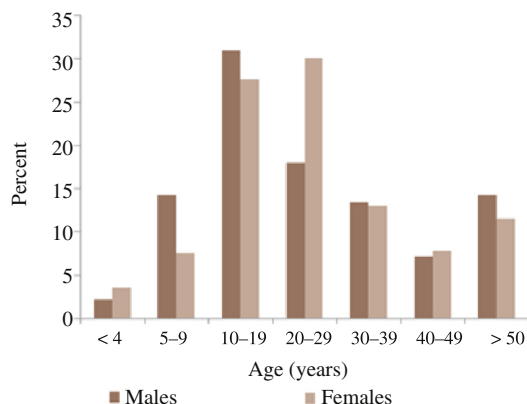


Figure 1. Distribution of age groups by gender of animal bitten victims referred to the prevention centers of rabies in Chalderan city (2008–2014).

(4.8%) were not registered. There was a statistically significant difference between the spatial status of animal bites ($P = 0.003$).

3.3. Temporal patterns

Most of the cases of animal bites happened in the summer with 566 cases (32.8%) and the least in the winter with 322 cases (18.7%). July with 230 cases (13.3%) and August with 176 cases (10.2%) were the months with the highest rate of animal bites. The lowest rate happened in January with 98 cases (5.7%). The highest proportion of bites was happened in the afternoon (12–18 p.m.) and the lowest in the morning (6–12 a.m.).

3.4. Cases of human bites

Most bites occurred by pet dogs in 1642 cases (95.2%). Other categories were 44 cases by stray dogs (2.6%), 21 cases by cats (1.2%), 5 cases by wolves (0.3%), 2 cases by foxes (0.1%) and 10 cases by other animals (0.6%), respectively.

In terms of the bitten organ, lower extremity had the highest frequency with 1337 cases (77.6%), shoulders and hands with 280 cases (16.2%), chest with 66 cases (3.8%) and head and neck 41 cases (2.4%), respectively.

The average age of victims with head and neck injuries was 27.25 ± 19.11 , and significantly lower than the lower extremities injury with 32.79 ± 16.88 and shoulders and arms (38.83 ± 18.77) ($P = 0.001$).

In terms of the extent of the wound, 1568 injuries (90.9%) had small lesions and 156 injuries (9.1%) had large lesions.

About 1293 (75%) of animal bites took place with protections such as clothes, and 431 cases (25%) without any protection.

3.5. Cases of rabies

During the study period, no case of human rabies was reported. Four cases of rabies in animals were discovered: three dogs and one sheep. All 4 cases of rabies in animals were observed in rural areas.

3.6. Cost of vaccination

The direct cost of rabies vaccination of the animal bite victims was calculated for the prevention and treatment. The costs included the injection of lyophilized rabies vaccine without

considering the costs of keeping, transporting, human resources costs, and the costs of syringes.

The price of each vial of lyophilized rabies vaccine in the Islamic Republic of Iran equaled 217000 rials (7 dollars), which meant that for every animal bite victims, three doses of rabies vaccine costed 651000 rials (21 dollars), and five doses of rabies vaccine costed 1085000 rials (36 dollars). The direct costs of total vaccination for all the victims with three and five doses of rabies vaccine were presented in Table 1.

Table 1

Costs of rabies vaccination for animal bite victims referred to prevention and treatment centers in Chalderan city, Iran (2008–2014).

Number of vaccines	Number (relative frequency)	Costs (rials)	Costs (dollar)	Cumulative frequency price (dollar)
3 times	1607 (93.2%)	1046157000	11665	11665
5 times	117 (6.8%)	25740000	849	12514

In this study, 156 individuals received rabies serum. Given the cost of 1.95 million rials (65 dollars) for each vial of 300 IU serum, the total cost of serum therapy was calculated. According to the national instructions of Iran, 300 IU of rabies serum is needed for each 15 kg of the victim's weight. Considering that the mean weight of the victims was 60 kg, in average, four vials of 300 IU were used for the victim. Thus, the cost was 7.8 million rials (260 dollars) for each victim and 1.2168 billion rials (40560 dollars) for the total of 156 victims.

Figure 2 shows the patterns of incidence rate of animal bites in Chalderan City. In this study, the incidence of animal bite cases in per hundred thousand inhabitants during 2008–2014 was an average of 541 cases (Figure 2). As 481 cases happened in 2008 and have also been fluctuated over the years, but had an overall upward trend, though it reached 609 cases in 2014. The results of the Cochran–Armitage test for trend also confirmed the increasing trend of animal bites in Chalderan City ($P = 0.02$).

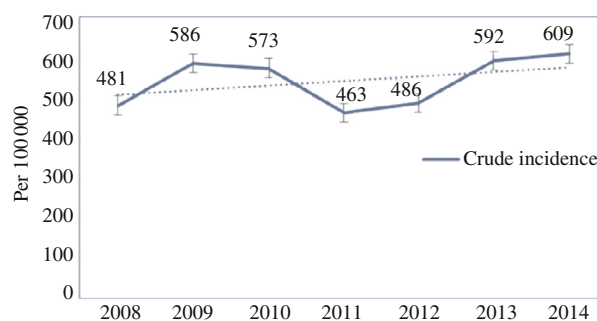


Figure 2. The patterns of incidence rate of animal bites in Chalderan City during 2008–2014.

4. Discussion

The incidence of animal bites during the seven-year study period was an average of 541 per 100000 populations, which was higher than that of studies conducted in other areas of the country^[19]. This indicated that the animal bite is one of the most important public health problems in Chalderan City.

Findings of the study showed that the incidence of animal bites in the study period had an increasing trend. In the study of Fayaz et al. in Iran, during the two periods of 1993–1994 and 2008–

2009, the number of persons bitten by animals suspected to rabies was increased 1.5 times^[20]. In the study of Nikbakht *et al.* in Babol, north of Iran, on victims under 18 years old, the results showed that the incidence of animal bites during the four-year period (2010–2014) had an increasing trend per 100 000 people between 82.5 and 123.1 ($P = 0.001$)^[21]. In another study performed in Rafsanjan City, central of Iran, the incidence of animal bites in 2003, 2004 and 2005 was estimated at 180 cases, 195 cases and 241 cases per 100 000 people, respectively^[22]. Also, the results of the present study were in line with the studies on animal bites in the northern provinces of Iran^[19,23].

Based on the findings of this study, the majority of bites had happened to men. This is consistent with most of the studies in the country^[19,20,24,25]. It seems that the high frequency of injuries in men is due to their higher presence outside for the occupational and non-occupational activities or due to their audacity and more contacts^[19].

Results of this study showed that the majority of the bites occurred in rural areas. This finding is consistent with the findings of previous studies in the country. So that 65.9% of the bites in Babol^[21] and 64.5% in Ilam^[18] and in other studies conducted in Iran, a high proportion of bites occurred in rural areas^[9,26,27]. High frequency of animal bites in rural areas might be due to the routine works of the residents as farmers and keeping the dogs as guards.

In this study, most cases of animal bite victims were in the age group of 10–19 years old in men and 20–29 years old in women. In the study of Fayaz *et al.*, 33.46% of people bitten by animals suspected of rabies were in age group 21–30 years old, and 15.65% in age group 11–20 years old^[20]. In other studies performed by Babaeian-moghaddam *et al.* (2013), age group 21–30 years old^[28] and in the study performed by Zohrevandi *et al.* (2012), age group 20–29 years old^[24] were the most bitten people by animals. It seems that the high frequency of animal bites in age group of 10–19 years old in men in this study is due to the conditions related to jobs such as farming and animal husbandry mostly in the rural areas.

According to the findings of this study, the majority of the bites were in the lower extremities and the average age of victims with head and neck injuries was lower than that of victims with injuries of lower extremities, shoulders and hands injuries. Height is the most important determinant factor in children with upper extremities bites^[29]. In this study, like the study by Zohrevandi, the victims with head injuries were younger than the victims with injuries to the rest of the body^[24]. In a study in Babol, the average age of the victims with head and neck injuries (25.72 ± 21.02) was lower compared to the victims with injuries to lower extremities (33.79 ± 16.45) and victims with injuries to two or more organs (37.83 ± 17.88)^[19]. These results are in agreement with other previous studies^[26,30,31].

According to the results of this study, most of the bites occurred in the summer and spring seasons. In the studies in Makoo, northwest of Iran^[6], most cases of animal bites occurred in the spring and in Ilam, west of Iran^[18] most cases were reported in the winter, which are different from findings of this study. The difference might be due to the climatic differences over the different regions of the country.

In most of the studies inside and outside the country, the majority of the animal bites cases were related to dogs^[24,32]. But in the present study, almost all of the victims were bitten by dogs (97.8%). Epidemiological studies done in other parts of world represented that a high percentage of animal bites is the result

of a dog bite^[33,34]. Considering the role of the cats in bites reported in other studies in the country^[18], it seems that an under-reporting taken place about the bites by the cat, because people may not think a bite by cats can be dangerous. Since over 95% of the bites occurred by pet dogs, educating people on how to behave animals to prevent aggressive situation in them, may reduce the incidence of animal bites. Other studies also recommended vaccination of pets and reduction of the population of stray dogs^[6] for controlling the rabies.

In this study, the number of diagnosed cases of rabies included three dogs and one sheep. In the study of Bahonar *et al.* in Ilam, west of Iran, most cases of rabies were observed in cattle (33.3%)^[18]. The study of Esfandiari in the northern region of Iran, also reported the highest registered number of rabies cases in the cattle^[23]. According to the report of rabies center of the Pasteur Institute of Iran, in 2002 and 2003, the cows constitute 56.3% and 52.4% of all rabies cases in the country^[8]. The number of positive cases of rabies in dogs, wolves, foxes and jackals approved by the Pasteur Institute in 2003 was 32.4% of total cases^[35].

The results of this study showed that a high price was spent on vaccinate the victims of animal bites against rabies (Table 1) and in providing them with immunoglobulin. However, this study only considered the cost of rabies vaccines and the immunoglobulin. If a broader viewpoint was taken including the direct medical costs such as the costs of wages for health care personnel, provision of supplies and consumables *etc.*, direct non-medical costs such as commuting costs to the health center for vaccination, indirect costs such as absenteeism from work due to animal bites, and intangible costs such as pain and suffering caused by animal bite injury, the total costs caused by animal bites will be much more. This shows a heavy financial burden of animal bites, which indicates the need for appropriate policies to reduce animal bite.

As the results of the study showed, the majority of victims received 3-times rabies vaccine. It might be due to that the majority of patients who had indication of receiving a 5-dose vaccination schedule had received only three doses^[36]. A study conducted by Hoseini *et al.* who described the epidemiology of post-exposure prophylaxis and its associated shortage in the USA, reported that post-exposure prophylaxis is loosely monitored and a precise estimate of post-exposure prophylaxis use was unknown^[37].

Based on these results, only limited number of victims received rabies immunoglobulin, which was in consistent with the study by Hossain in Bangladesh. It showed that a negligible number of patients received rabies immunoglobulin^[33].

This study revealed a relatively high incidence of animal bites in Chalderan City, and thus a heavy burden of rabies vaccination. The bites are mostly caused by domestic dogs in rural areas on farmers. The reduction efforts must be concentrated on controlling the dogs and on providing training programs to groups at risk and the dogs' owners. The increasing trend of animal bites was observed in this study and therefore the increasing cost of the vaccination can help the managers and policymakers to predict and provide resources for the next years.

However, the incidence of animal bites may be underestimated in this study, because some of the victims refuse to refer to health centers for vaccinations, especially for small injuries. Also due to the retrospective study design, information bias may occur by poorly documentation and incomplete information recorded in the registries.

Conflict of interest statement

The authors report no conflict of interest.

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