

Factors associated with delay in post-exposure prophylaxis in bitten people

Salman Khazaei¹, Shahab Rezaeian², Mokhtar Soheylizad³, Behzad Gholamaliee⁴

Received: 22 July 2013

Accepted: 3 March 2014

Published: 29 December 2014

Abstract

Background: Although the incidence of animal bite is increasing in Iran, there is no sufficient knowledge about delayed Post-Exposure Prophylaxis (PEP). Hence, the aim of this study was to evaluate delayed PEP and its associated factors in bitten people.

Methods: This cross-sectional study was conducted in Tuyserkhan district of Hamadan Province (West of Iran) from February 2011 to February 2012 and included 425 cases of animal bites recorded in the Rabies Treatment Center (RTC) using the census method. The associations between delayed PEP and each of the potential risk factors were investigated using Chi-square test.

Results: Of 425 registered cases, 71.8% were male and 81.2% were from rural areas. The mean age of the subjects was 32.4 years (± 21.3). Dogs were the most frequent source of exposure (69.4%), and the most common bitten part of the body was legs (49.4%). With respect to the wounds, 16.2% of the cases had deep injuries. Overall, 37.2% of the cases received timely PEP (less than 6 hours).

Delayed PEP was associated with sex ($p=0.001$), type of animal ($p=0.020$), injury status ($p<0.001$), place of residence ($p=0.006$) and distance from RTC ($p<0.001$).

Conclusion: Although all victims of animal bite injuries suspected to be rabid, they received complete PEP. However, delayed time of PEP was still very high. The factors associated with delayed PEP may help health care workers to prevent adverse disease outcomes. Furthermore, considering the results of this study, it is highly recommended that proper attention and emphasis be given to public educational programs on dog behavior, dog-child interaction, the risk of dog bites and bite wound management for the general population, particularly children.

Keywords: Post-Exposure Prophylaxis, Vaccination, Animal bites, Rabies.

Cite this article as: Khazaei S, Rezaeian Sh, Soheylizad M, Gholamaliee B. Factors associated with delay in post-exposure prophylaxis in bitten people. *Med J Islam Repub Iran* 2014 (29 December). Vol. 28:158.

Introduction

One of the most zoonotic diseases, a disease transmitted to humans from animals, is rabies which is caused by a virus in the Rhabdovirus family that affects wild and domestic mammals. Because rabies is a vaccine-preventable disease, the estimated 55,000 annual human deaths caused by this disease worldwide is unacceptable and inexcusable (1). Rabies is present in all continents with the exception of Antarctica, but

more than 95% of human deaths occur in developing countries in Asia and Africa where the disease is endemic in domestic dog populations (1).

Other studies conducted in different parts of Iran have shown that the incidence of animal bites in our country has been increasing in recent years. For example, a study to clarify the epidemiological features of rabies in Ilam province (West of Iran) reported that the incidence of animal

1. MSc in Epidemiology, Department of Biostatistics and Epidemiology, School of Public Health, Hamadan University of Medical Sciences, Hamadan, Iran. s_khazaei@yahoo.com

2. (Corresponding author) MSc, PhD Student, Health Promotion Research Center, Zahedan University of Medical Sciences, Zahedan, Iran. shahab.rezayan@gmail.com

3. MSc Student in Health Education, Department of Public Health, School of Public Health, Hamadan University of Medical Sciences, Hamadan, Iran. soheilyzad@gmail.com

4. MSc Student in Health Education, Department of Public Health, School of Public Health, Hamadan University of Medical Sciences, Hamadan, Iran. bhzdgholami80@yahoo.com

bites has increased from 34 per 100,000 in 1999 to 98 per 100,000 in 2008 (2). Another report from Rafsanjan (Southeast of Iran) also showed that the incidence of animal bites increased from 180 per 100,000 in 2003 to 241 per 100,000 in 2005 (3). The same situation has been reported from Birjand in Southern Khorasan province (East of Iran) (4). However, in one of the districts of Golestan province where the highest rate of animal bite have been reported, the rate of animal bite had a descending trend from 2005 to 2009 (5).

According to the WHO report, to prevent this disease, more than 15 million people receive a post-exposure vaccination every year worldwide (1). In reality, the post exposure prophylaxis (PEP) is the most critical life-saving intervention essential for the prevention of rabies in humans after exposure (6). Although the cost-effectiveness of PEP has been well established (7), the post-exposure prophylaxis of the individual cases is not desirable yet (8, 9). Therefore, the present study, which to the best of our knowledge is the first of its kind, was conducted to evaluate delayed PEP and its associated factors in bitten people.

Methods

This retrospective cross-sectional study was conducted in Tuyserkan district of Hamadan province (West of Iran) and included 425 cases of animal bites recorded from February 2011 to February 2012 (for duration of one year and using the census method) in the Rabies Treatment Center (RTC). The individuals who were not the residents of the district were excluded from the analysis.

In Tuyserkan district, health care services are offered by different health networks including one hospital, 16 rural health centers, 3 urban health centers and 62 health houses. It is noteworthy to mention that over 50% of the Tuyserkan population is rural.

Information on demographic and clinical characteristics including sex, age, place of residence (rural, urban), type of biting ani-

mal (dog, cat, domestic or wild animal), injury status (deep, superficial), date and season of bite, distance from the Rabies Treatment Center (less than 30 kilometers, over 30 kilometers), bite site (leg, hand, body, head or face) were obtained using a checklist.

Statistical Methods

The follow up of each bitten subject was calculated from the date of the biting incident to the date of admission to the Rabies Treatment Center. This period divided into 3 times: on time (0-6 hours), delayed time (7-48 hours) and more than 48 hours. Duration of delayed post exposure prophylaxis during the bite period was assessed using Kaplan-Meier hazard function. Chi-square test (or Fisher's Exact Test) was used for data analysis at the 5% significance level to determine whether any factors were associated with delays in post exposure prophylaxis delivery, using the statistical software Stata 11 (StataCorp, College Station, TX, USA).

Results

The incidence rate of animal bite was 423 per 100,000 people. Of the victims, 71.8% were male (male/female ratio was 2.5:1); and 81.2% were from rural areas. The mean age of the subjects was 32.4 years (95%CI: 30.4, 34.4), and the highest proportion of them (34.1%) fell in the 0-to-20-year age range. Domestic dogs were involved in 59.1% of the exposures, and the most common bitten part of the body was legs (49.4%). The distribution of demographic and clinical characteristics of the bitten subjects is shown in Table 1.

With respect to the wound status, 16.2% of the cases had deep injuries and 83.8% had superficial injuries. Overall, 37.2% of the cases received timely PEP (less than 6 hours), and the mean time delay from the injury to the initial management was 33.3 hours (95%CI: 26.7, 39.8). The mean delay for females was 45.3 hours (95%CI: 29.8, 60.8) and it was 28.5 hours for males (95%CI: 21.8, 35.2) ($p=0.023$).

Table 1. Distribution of demographic and clinical characteristics of bitten subjects in Tuyserkan district, 2012

Variable	No. (%)	On time (%) (0-6 hr)	Delay		p
			Less than 48 hr (7-48 hr)	More than 48 hr	
Gender					
Male	305(71.8)	122(40.0)	151(49.5)	32(10.5)	0.010
Female	120(28.2)	36(30.0)	59(49.2)	25(20.8)	
Residency					
Urban	80(18.8)	43(53.8)	29(36.2)	8(10.0)	0.006
Main village	269(63.3)	93(34.6)	142(52.8)	34(12.6)	
Satellite village	76(17.9)	22(28.9)	39(51.3)	15(19.8)	
Age groups(Year)					
<10	76(17.9)	31(40.8)	36(47.4)	9(11.8)	0.643
11-20	69(16.2)	19(27.5)	43(62.3)	7(10.2)	
21-30	86(20.2)	35(40.7)	42(48.8)	9(10.5)	
31-40	55(13.0)	21(38.2)	25(45.5)	9(16.3)	
41-50	44(10.3)	17(38.6)	20(45.5)	7(15.9)	
+51	95(22.4)	35(36.9)	44(46.3)	16(16.8)	
Distance from the RTC					
Less than 30 km	207(48.7)	98(47.3)	86(41.6)	23(11.1)	<0.001
More than 30 km	218(51.3)	60(27.5)	124(56.9)	34(15.6)	
Season of bite					
Spring	115(27.1)	42(36.5)	59(51.3)	14(12.2)	0.224
Summer	102(24.0)	46(45.1)	41(40.2)	15(14.7)	
Fall	99(23.3)	36(36.4)	54(54.5)	9(9.1)	
Winter	109(25.6)	34(31.2)	56(51.4)	19(17.4)	
Injury status					
Deep	69(16.2)	51(73.9)	16(23.2)	2(2.9)	<0.001
Superficial	356(83.8)	107(30.1)	194(54.5)	55(14.4)	
Bite site					
Leg	210(49.4)	76(36.2)	107(51.0)	27(12.8)	0.081
Hand	170(40.0)	61(35.9)	85(50.0)	24(14.1)	
Body	25(5.9)	8(32)	15(60.0)	2(8.0)	
Head & Face	20(4.7)	13(65.0)	3(15.0)	4(20.0)	
Type of biting animal					
Domestic Dog	251(59.1)	102(40.6)	123(49.0)	26(10.4)	0.020
Stray Dog	44(10.3)	17(38.6)	22(50.0)	5(11.4)	
Cat	89(20.9)	21(23.6)	47(52.8)	21(23.6)	
Other	41(9.7)	18(43.9)	18(43.9)	5(12.2)	

According to the results of Table 1, delayed PEP was associated with sex ($p=0.001$), type of animal ($p=0.020$), injury status ($p<0.001$), place of residence ($p=0.006$) and distance from RTC ($p<0.001$). No statistically significant relation was found between delayed PEP and age, season of bite and site of injury. Fig. 1 shows delay time of PEP according to various factors.

Discussion

The main finding of this study was estimating the rate of timely PEP in bitten people; and it was found that 37.2% of the patients have received timely PEP. We found only one similar study conducted on the Iranian population, but it was written in Farsi (10). It should be noted that our find-

ings are consistent with those of previous epidemiological studies in other regions which stated that the PEP of the individual cases is not desirable yet (8, 9). In fact, this study is one of the first studies to assess the factors associated with delayed PEP in Iran. These findings suggest that there are important relationships between sex, type of animal, injury status, place of residence and distance from RTC and delayed PEP.

Although there are no global estimates of animal bite incidence, the WHO reported that dogs are responsible for over 90% of the reported cases of rabies (11). Animal bites are one of the most important public health problems in some countries of the world. In the present study, 69.4% of our cases were victims of dog bites while 59.1% were of domestic dogs. These data

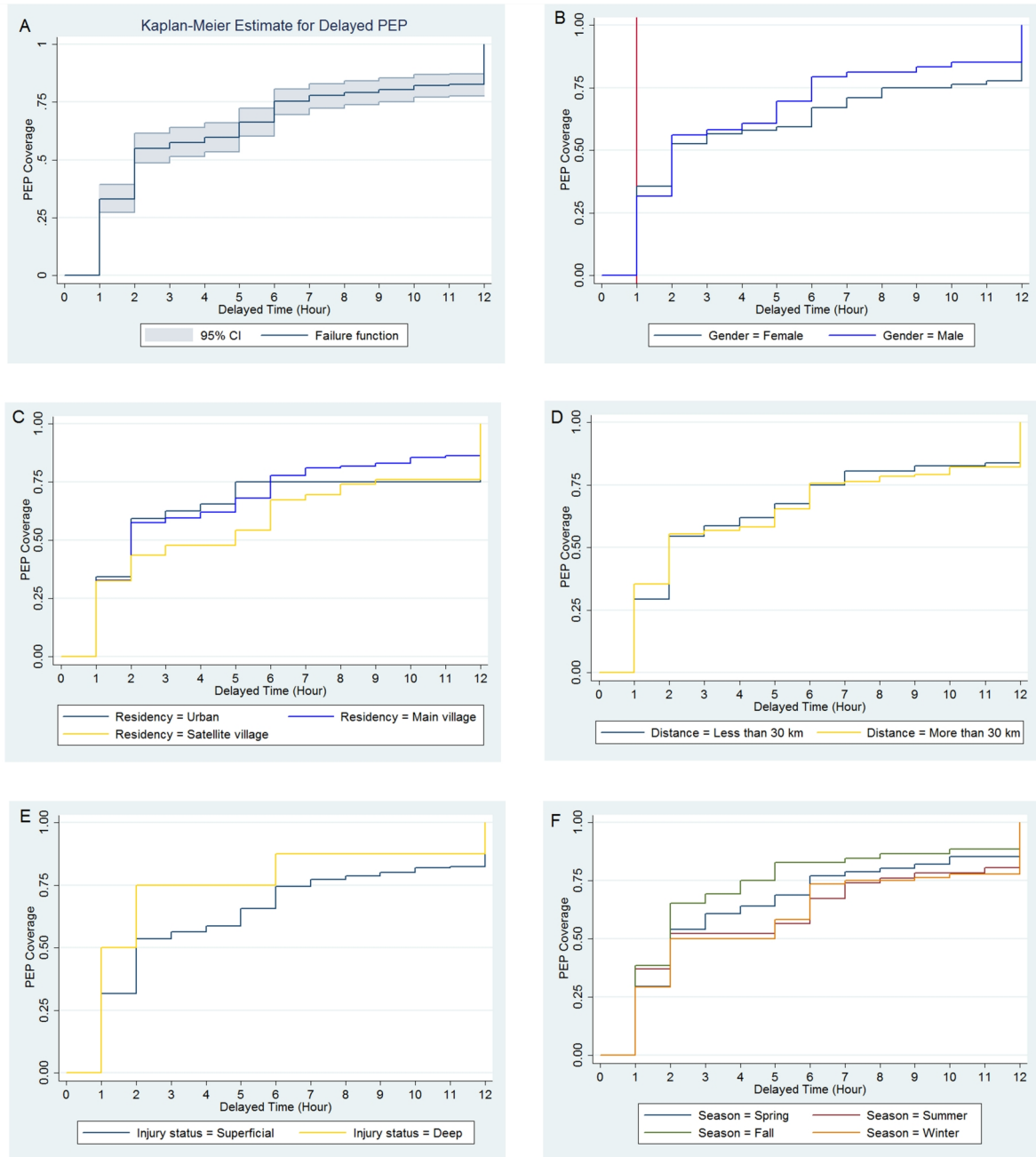


Fig. 1. Delayed Post-Exposure Prophylaxis according to various factors; Each time unit is equal to six hours.

are in agreement with those reported in the literatures which confirm that the most animal bites are from dogs (2-4, 10). The same findings have been reported from other country (12-14). There was also a significant correlation between delayed PEP and type of biting animal. In concordance with a similar study (10), the delay time was longer among those subjects who were bitten by a domestic dog. Meanwhile, domestic dogs play a principal role as a reservoir and transmitter of urban rabies to humans

(15). In addition, an epidemiological study of animal bites which analyzed 192 records of rabies cases in India revealed that dog bites caused maximum mortality. The authors have also reported that the failure to seek timely and appropriate treatment led to development of rabies (14).

The risk factors for human animal bites identified in our study are very similar to those of other studies conducted elsewhere (3, 16). For example, animal bite injuries were more common in subjects aged 0-20

years and more common in males. A previous study conducted by Tenzin et al. to understand the use and distribution of human rabies post exposure prophylaxis vaccine in Bhutan also showed that PEP was provided more often to younger age groups and males (59%) (17). In addition, Riahi et al. (10) reported that 86% of the bite victims were male and 44.6% of them aged 10-29 years. They have also shown a significant difference between PEP and age (10). The higher incidence of disease and bites in males and also in children is considered a behavioral risk because of their extreme curiosity, lack of inhibition, limited knowledge and experience about dog behavior and inability to protect themselves from an attack (13, 16). However, it is also believed that children do not report minor bites or scratches to their parents, which increases the risk of rabies infection.

According to our finding, a significant relationship was observed between delayed PEP and distance from RTC and place of residence. On the other hand, the distance from the RTC was more than thirty kilometers for the majority of the cases (51.3%), and up to 72.5% of them did not receive timely PEP. Our results suggest that the population investigated may not be aware of the risks of rabies transmission as revealed previously (13, 18). Hampson et al. in a study to assess risk factors associated with rabies exposure reported that 20% of rabies-exposed individuals did not seek medical treatment and were not documented in official records, and only 65% of the identified rabies exposures received PEP. The authors also showed that those who live furthest from the health facilities and are in lower socioeconomic classes undergo longer delays before receiving PEP which increases the risk of developing rabies (19). Another study showed that the mean time in receiving PEP was significantly more in those having low educational level, living at rural areas and living at a distance more than 5 kilometers from the vaccination centre (20).

A significant correlation was found be-

tween delayed PEP and injury status. The delay time was shorter among those victims who had deep lesion. In the present study, 16.2% of the wounds were deep. Similarly, studies performed in Rafsanjan (Southeast of Iran) and Turkey showed that 15% and 17% of the wounds were deep, respectively (3, 21). In a similar study to determine the epidemiology and causes of delays in receiving treatment for rabies and animal bites in Tabas (East of Iran), it was revealed that 27.9% of the wounds were deep, but they did not find a significant relationship between PEP and injury status (10). In another study on the rabies post-exposure management of travelers from New Zealand, it was found that 85.2% of the animal exposures were graded as WHO category III (assessing as carrying a risk of developing rabies require PEP) and only 25% of the subjects received PEP consistent with WHO guidelines (22). It should be mentioned that we did not have any information on rabies in the public population or the health workers in the region of study. There is a very critical need to improved awareness and understanding of dog bite management among health care providers to prevent rabies deaths (23).

In this research, we were unable to collect other variables such as educational level or socio-economic status due to the retrospective design of the study, and this was considered as a limitation of this study.

Conclusion

In conclusion, this study has provided important information about human animal bites, its risk factors and the key aspects of health services that could be targeted to improve the treatment of patients reporting animal-bite injuries. For instance, many bite victims had to travel to the Rabies Treatment Center to obtain PEP, which prolonged delays before PEP delivery, increased the risk of disease and imposed considerable costs on victims and their families. Although all the victims of animal bite injuries were suspected to be rabid, they received complete PEP, but the de-

layed time of PEP was still very high. The presence of large numbers of stray dogs is also a public health concern in our district. Intervention measures should include public educational programs on dog behavior, dog-child interaction, the risk of dog bites and bite wound management (e.g., washing with soap and water), particularly for children.

Acknowledgments

We would like to express our deep gratitude to the vice-chancellor of the Research and Technology of Hamadan University of Medical Sciences for the financial support of this study and we would also like to thank the health expert of the Rabies Treatment Center in Hamadan University of Medical Sciences who collaborated in data collection. The authors declare that there is no conflict of interest.

References

1. World Health Organization. Rabies. Geneva: WHO; 2013; Available from: <http://www.who.int/mediacentre/factsheets/fs099/en/>.
2. Sabouri Ghannad M, Roshanaei G, Rostampour F, Fallahi A. An epidemiologic study of animal bites in Ilam Province, Iran. *Arch Iran Med*. 2012;15(6):356-60.
3. Sheikholeslami NZ, Rezaeian M, Salem Z. Epidemiology of animal bites in Rafsanjan, southeast of Islamic Republic of Iran, 2003–05. *East Mediterr Health J*. 2009;15(2):455-7.
4. Bijari B, Sharifzade GR, Abbasi A, Salehi S. Epidemiological survey of animal bites in east of Iran. *Iran J Clin Infect Dis*. 2011;6(2):90-2.
5. Charkazi A, Behnampour N, Fathi M, Esmaeili A, Shahnazi H, Heshmati H. Epidemiology of animal bite in Aq Qala city, northern of Iran. *J Edu Health Promot*. 2013;2:13.
6. Quiambao BP, Dy-Tioco HZ, Dizon RM, Crisostomo ME, Teuwen DE. Rabies post-exposure prophylaxis with purified equine rabies immunoglobulin: one-year follow-up of patients with laboratory-confirmed category III rabies exposure in the Philippines. *Vaccine*. 2009; 27(51): 7162-6.
7. Hampson K, Cleaveland S, Briggs D. Evaluation of Cost-Effective Strategies for Rabies Post-Exposure Vaccination in Low-Income Countries. *PLoS Negl Trop Dis*. 2011;5(3):e982.
8. Wasay M, Malik A, Fahim A, Yousuf A, Chawla R, Daniel H, et al. Knowledge and attitudes about tetanus and rabies: a population-based survey from Karachi, Pakistan. *J Pak Med Assoc*. 2012; 62(4): 378-82.
9. Yin CP, Zhou H, Wu H, Tao XY, Rayner S, Wang SM, et al. Analysis on factors related to rabies epidemic in China from 2007-2011. *Virolog Sin*. 2012; 27(2):132-43.
10. Riahi M, Latifi A, Bakhtiyari M, Yavari P, Khezeli M, Hatami H, et al. Epidemiologic Survey of Animal Bites and Causes of Delay in Getting Preventive Treatment in Tabas during 2005-2010. *TB*. 2012;34(1):20-31. (Persian).
11. Organization WH. Animal bites. Geneva: WHO; 2013; Available from: <http://www.who.int/mediacentre/factsheets/fs373/en/>.
12. Quiambao BP, Dytioco HZ, Dizon RM, Crisostomo ME, Laot TM, Teuwen DE. Rabies Post-Exposure Prophylaxis in the Philippines: Health Status of Patients Having Received Purified Equine F(ab')₂ Fragment Rabies Immunoglobulin (Favirab). *PLoS Negl Trop Dis*. 2008;2(5):e243.
13. Si H, Guo ZM, Hao YT, Liu YG, Zhang DM, Rao SQ, et al. Rabies trend in China (1990–2007) and post-exposure prophylaxis in the Guangdong province. *BMC Infect Dis*. 2008;8:113. doi: 10.1186/471-2334-8-113.
14. Ichhpujani RL, Mala C, Veena M, Singh J, Bhardwaj M, Bhattacharya D, et al. Epidemiology of animal bites and rabies cases in India. A multicentric study. *J Commun Dis*. 2008;40(1):27-36.
15. Tang X, Luo M, Zhang S, Fooks AR, Hu R, Tu C. Pivotal role of dogs in rabies transmission, China. *Emerg Infect Dis*. 2005;11(12):1970-2.
16. Rezaeinasab M, Rad I, Bahonar AR, Rashidi H, Fayaz A, Simani S, et al. The prevalence of rabies and animal bites during 1994 to 2003 in Kerman province, southeast of Iran. *Iran J Vet res*. 2007; 8(4):343-50.
17. Tenzin, Dhand NK, Ward MP. Human rabies post exposure prophylaxis in Bhutan, 2005–2008: Trends and risk factors. *Vaccine*. 2011; 29(24):4094–101.
18. Zhang YZ, Xiong CL, Xiao DL, Jiang RJ, Wang ZX, Zhang LZ, et al. Human rabies in China. *Emerg Infect Dis*. 2005;11(12):1983-4.
19. Hampson K, Dobson A, Kaare M, Dushoff J, Magoto M, Sindoya E, et al. Rabies Exposures, Post-Exposure Prophylaxis and Deaths in a Region of Endemic Canine Rabies. *PLoS Negl Trop Dis*. 2008;2(11):e339. doi:10.1371/journal.pntd.0000339.
20. Tiwari RR, Kulkarni PN, Ingole S. Animal bites: Factors for delay in post exposure prophylaxis. *Indian J Med Sci*. 2000; 54:233-7.
21. Sengoz G, Yasar KK, Karabela SN, Yildirim F, Vardarman FT, Nazlican O. Evaluation of cases admitted to a center in Istanbul, Turkey in 2003 for rabies vaccination and three rabies cases followed up in the last 15 years. *Jpn J Infect Dis*. 2006;

59(4):254-7.

22. Shaw MT, O'Brien B, Leggat PA. Rabies postexposure management of travelers presenting to travel health clinics in Auckland and Hamilton, New Zealand. *J Travel Med.* 2009;16(1):13-7.

23. Salahuddin N, Jamali S, Ibraheem K, Sardar

S. Awareness about rabies post exposure prophylaxis in Pakistan among patients and health care workers: results from an Asian Rabies Expert Bureau study. *J Coll Physicians Surg Pak.* 2011; 21(8):491-4.