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Animal Health

Dog bites and human rabies: epidemiological analysis of post exposure prophylaxis in Bhutan

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ABSTRACT

The study objective was to describe the epidemiology of dog bites and the use of anti-rabies vaccine as Post-Exposure Prophylaxis (PEP) in Bhutan over a period of four years (2009–2012). Dog-bite and PEP-treatment data of 18,813 patients were retrieved from 34 health centres and subjected to descriptive analysis. Multivariable logistic regression analysis was performed to identify the risk factors for in-complete course of PEP. Dog-bite incidents in humans were found to be higher in males than females ($p \leq 0.001$) and more common in children than adults ($p \leq 0.001$). Males (n=10,924; 59.19%) received more PEP courses than females (n=7,849; 41.81%) across all age groups ($p \leq 0.001$). The median age of both dog-bite and PEP-treatment recipients was 20 years (range <1 to 93 years) and the modal age was 6 years. Children, particularly those of 5–14 years age group were exposed to animal bites and also received more PEP treatments than people in other age groups. Rabies PEP treatment was provided throughout the year and the number of cases increased significantly ($p \leq 0.001$) from less than 1500 cases in 2009 to over 7000 cases in 2012. Of the18,813 patients that received PEP, 57.12% (n=10,746) received an in-complete course (less than 5 doses). Multivariable logistics regression analysis indicated that males and adult age group of patients were less likely to complete PEP than females and children. Patients with animal bite injury were less likely to complete PEP than non-bite exposure, indicating risk of rabies infection if exposure animal is rabid. Patients who reported to medical centers in rabies endemic areas (south Bhutan) were more likely to complete PEP course than in rabies free interior Bhutan. The study provides valuable information on the epidemiology of dog bites and PEP treatment in humans for informed policy decision on dog population management, public health risk, communication to reduce dog-bite incidents, and expenditure on PEP treatment in Bhutan.

INTRODUCTION

Dog-bites in humans are a common problem and have been well documented in developed (e.g., Overall and Love 2001; Keuster et al. 2006; Gilchrist et al. 2008; Rosado et al. 2009) as well as in developing countries (Fevre et al. 2005; Sudarshan et al. 2006; Hossain et al. 2011; Tenzin et al. 2011a), but most cases are believed to be not reported or under-reported, especially in developing countries. Although, only a very small proportion of dog-bites results in the death of the victim (e.g., Sacks et al. 1996; Sacks et al. 2000; Raghavan et al. 2008) they cause psychological trauma and post-traumatic stress (Peters et al. 2004; Keuster et al. 2006;) and in some cases, cause severe injuries requiring reconstructive surgeries (Wolf 1998; Gilchrist et al. 2008). Dog bites also result in great monetary expense for treatment including emergency hospitalization and treatment with anti-rabies post-exposure prophylaxis vaccine (PEP) (Chomel et al. 1992; Weiss et al. 1998; Quinlan and Sacks 1999). Globally more than 59,000 people die of rabies each year, particularly in Asia and Africa as a result of a dog bites (Knobel et al. 2005; WHO 2010, 2013; Hampson et al. 2015). Approximately, 20 million people receive PEP treatment annually after dog bite injuries, at an estimated cost of $1.5 billion (WHO 2010, 2013). Thus, dog bites and risk of rabies infection is an issue of considerable public health importance in the world.

In Bhutan, dog bites are common and is a public health problem, but the number of human deaths resulting from rabid dog bites is small; 17 deaths were recorded between 2006 and 2016, equating to a cumulative incidence of 0.23 per 10,000 population) (Tenzin et al. 2011b; Tenzin et al. 2012a). Until 2013, the dog bite patients were treated with the human diploid cell vaccine (HDCV) administered as a standard 5-dose (1ml each) Essen intramuscular regimen on days 0, 3, 7, 14 and 28 (WHO 2010; Tenzin et al. 2011b, Tenzin et al. 2012a). Currently, it is being administered as intradermal regimen (0.1ml on each right and left deltoid region) on days 0, 3, 7 and 28 (MoH 2014). The vaccine is provided free of charge to patients by the Ministry of Health and the eligibility for PEP treatment is assessed and determined by the clinic staff on consultation with the patients (MoH 2014). However, the cost of PEP treatment is escalating every year (Tenzin et al. 2012a). The Ministry of Health spent an average of Nu.1615 per full course of PEP per person (Essen regimen) on vaccine alone (direct cost only) and the total annual expense on PEP treatments is approximately Nu.5.85 million (Tenzin et al. 2012a). A periodic assessment of the pattern of dog bites and the use of anti-rabies vaccine is necessary to assist the public

health policy decision making in improving the efficiency and effectiveness of prevention and control programs including dog population management. In this study, we describe the epidemiology of dog bites in humans and the use of PEP treatment for rabies in Bhutan for the period between January 2009 and December 2012.

MATERIALS AND METHOD

Data source

In Bhutan, health care is provided free of cost to its people through 32 hospitals, 192 Basic Health Units (BHU), 48 indigenous medicine units, and 550 outreach clinics distributed in 20 *dzongkhags* (districts) and 205 *gewogs* (blocks). Hospitals are located in urban areas whereas the BHU are located within the village communities, except for a few located in urban areas. Animal-bite victims that visit the hospitals/BHU to seek medical care are given first-aid and PEP treatment for rabies if necessary after careful assessment by the clinical staff. These hospitals and BHU collect basic information on patients treated including name, date of visit to the hospitals/BHUs for medical advice and PEP, age, sex, resident address, type of exposure, reasons for PEP and date of PEP injection (day 0, 3, 7, 14 and 28 for intramuscular Essen regimen and day 0, 3, 7, and 28 for intradermal regimen) (MoH 2014). For this study, we retrieved four years' data (January 2009-December 2012) on dog bites and PEP treatment from 34 medical centres (26 hospitals and 8 BHUs) in Bhutan, during which time the Essen regimen – Intramuscular injection of rabies vaccine was followed in the country. The study was approved by the Research Ethics Board of Health, Bhutan (REBH/Approval/2012/028).

Data analysis

Stata, version 13.1 (Stata 2013) and Epi Info™ version 7.1.2.0 (Centers for Disease Control and Prevention (CDC), Atlanta, GA, USA) were used for data management and analyses. Chi-square tests were used to compare the difference in proportions of dog bites and PEP recipients between gender, age groups, season and years. The observed frequencies of PEP for various age groups were compared with expected frequencies calculated from the Bhutan census data of 2005. For comparison of genders, seasonal and annual differences, equal expected frequencies were assumed between groups (Tenzin et al. 2011b).

A complete course of rabies PEP (Essen regimen) is five doses (WHO 2010), but many patients received an incomplete course of treatment (i.e. <5 doses). Logistic regression analysis was performed to identify possible risk factors for incomplete PEP as the outcome variable (incomplete vs complete). The risk factors investigated included gender and age group of the patients, type of exposure (animal-bite vs non-bite), area of PEP (rabies outbreak or endemic area vs rabies free areas), and season based on the available data retrieved from the treatment records (Tenzin et al. 2011b). The contingency tables were constructed between explanatory variables and the outcome, and unadjusted odds ratios (ORs) and the corresponding 95% confidence intervals and P-values calculated. Variables associated with the outcome ($p<0.25$) were selected for multivariable logistic regression model. The goodness of fit of the model and model selection was assessed by examining changes in the model coefficients and using Akaike information criteria (AIC). No confounding effect of the variables was evident in the final model.

RESULTS

From a total of 18,957 cases data collected from 34 health centres in Bhutan, 43 cases were excluded from analyses (25 cases of pre-exposure prophylaxis and 18 cases of booster PEP doses). Of the 18,914 remaining cases, 18,813 (99.47%) were given various courses of rabies PEP treatment and included in the analyses reported in this paper.

Mode of contact and type of exposure

The patients that had a history of both animal-bite and non-bite incidents were presented to the health centres for PEP treatment. The majority (n=15,163; 80.60%) of patients that received PEP treatment had been bitten by various animal species and the remaining 19.40 % (n=3,650) were treated for other reasons (Table 1). The reason for PEP treatment was not recorded in the treatment register for 2,286 cases (12.15%), which we assumed to be due to dog bites. Of the total animal-bite cases, 88.67% (n=13,445) were bitten by dogs. The non-bite incidents mainly included touching and feeding of suspected or confirmed rabid animals, contact with suspected or confirmed rabid animals by owners during zoo sanitary measures and also consumption of meat and dairy products derived from rabies suspected or rabid animals (Table 1).

Dog bites and PEP

Of the total number of patients reporting animal-bite incidents that received PEP treatment (n=15,163; 80.60%), the majority were bitten by dogs (n=13,445; 88.67%) or cats (n=1,327; 8.75%) (Tables 1 and 2).

Gender and age of dog bite patients

Of the 13,445 patients reported with dog-bites, more were male (n=8,075; 60.18%) than female (n=5,343; 39.82%) ($p\leq0.001$) (Figure 1). The median age of patients bitten by dogs was 20 years (range >0 to 93) and the mode age was 6 years. The majority of the PEP treatment administered to patients bitten by dogs was reported in children, especially within the age group of 5–14 years. Figure 1 illustrates the age and sex distribution of dog bites indicating males are at higher risk of experiencing dog bites than females across all age groups.

Monthly pattern and distribution of dog bites

Dog bites were reported throughout the year with increasing cases in the spring season. The difference between the observed and expected cases was significant across all seasons ($p\leq0.001$). The number of patients presenting to health centres for PEP treatment following dog bites has also increased over the years (2009: 958; 2010: 2,500; 2011: 4,858; and 2012: 5,129), and found higher in the interior of Bhutan where rabies had not occurred for >20 years (65.04%, n=8,745) when comapred to rabies risk areas in south Bhutan (34.96%, n=4,700 (Table 2).

Gender distribution of PEP recipients

A total of 18,773 patients (99.79%, 18,773/18,813) had complete information for gender. Of these, 58.19% (n=10,924) were male and 41.81% (n=7,849) female. The number of rabies PEP recipients was significantly higher in males than in females during the study period ($p\leq0.001$) (Figure 2).

Age of PEP recipients

Of the 18,813 patients that received PEP, age data was available for 18,247 patients (96.99%). The median age of patients that received PEP was 20 years (range <1 to 93 years) and the modal age was 6 years. The observed and the expected frequencies of PEP recipients differed significantly across age groups ($p\leq0.001$).

Table 1 Details of various reasons for receiving rabies post exposure prophylaxis (PEP) by people in Bhutan, January 2009–December 2012.

Reasons for Rabies PEP vaccination	Number of people that received rabies PEP vaccine	Percentage of PEP given
1. Dog bite	13,445	71.47
2. Cat bite	1,327	7.05
3. Rat bite	171	0.91
4. Other animal bite (monkey, bear, goat, pig, horse, insect, rabbit)	220	1.17
5. Consumption of animal products (diary and meat derived from rabies suspected/confirmed animals)	868	4.61
6. Contact with rabies suspected/confirmed animals (through handling during zoo sanitary measures)	418	2.22
7. Contact with rabid patient (close relatives/others)	78	0.41
8. Reasons not recorded in the treatment register (but most cases may be due to dog bites)	2,286	12.15
Total	18,813	100

Note: PEP due to animal bite (n=15,163, 80.6%); other reasons (n=3,650, 19.4%).

Table 2 Total number of people reported to various medical centres for rabies PEP (N_1), dog bites cases reported for PEP (N_2) and estimated total doses of anti-rabies vaccine used (N_3) in Bhutan, January 2009-December 2012.

Hospital name	N_1 (%)	N_2 (%)	N_3 (%)
Rabies risk areas			
Gelephu RRH*	2834 (15.06)	1591 (11.83)	10803 (16.31)
Phuntsholing Hospital	2790 (14.83)	1301 (9.68)	12305 (18.57)
Samtse Hospital	955 (5.08)	604 (4.49)	2926 (4.41)
Sarpang Hospital	737 (3.92)	414 (3.08)	3082 (4.65)
Gomtu Hospital	387 (2.06)	128 (0.95)	1733 (2.62)
Lhamoizingkha BHU	301 (1.60)	2 (0.01)	1285 (1.94)
S/Jongkhar Hospital	227 (1.21)	222 (1.65)	759 (1.14)
Nganglam BHU	223 (1.19)	2 (0.01)	717 (1.08)
Sibsoo Hospital	199 (1.06)	11 (0.08)	661 (1.00)
Non-rabies risk areas			
JDWNRH*	3611 (19.19)	3586 (26.67)	10542 (15.91)
Paro Hospital	934 (4.96)	892 (6.63)	3290 (4.97)
Bajo Hospital	529 (2.81)	466 (3.47)	1661 (2.51)
Dechencholing BHU	506 (2.69)	489 (3.64)	1312 (1.98)
Tsirang Hospital	506 (2.69)	479 (3.56)	797 (1.20)
Gidakom Hospital	457 (2.43)	455 (3.38)	1513 (2.28)
Bali BHU	321 (1.71)	255 (1.9)	1026 (1.60)
Mongar RRH	282 (1.50)	256 (1.9)	994 (1.50)
Bumthang Hospital	255 (1.36)	2 (0.01)	784 (1.18)
Kanglung BHU	255 (1.36)	181 (1.35)	975 (1.47)
Chukha BHU	243 (1.29)	242 (1.8)	879 (1.33)
Gedu Hospital	241 (1.28)	183 (1.36)	971 (1.46)
Ranjung BHU	217 (1.15)	206 (1.53)	727 (1.09)
Trashigang Hospital	216 (1.15)	186 (1.38)	768 (1.16)
Trongsa Hospital	197 (1.05)	196 (1.46)	694 (1.04)
Dagana BHU	194 (1.03)	32 (0.24)	690 (1.04)
Lhuentse Hospital	168 (0.89)	156 (1.16)	522 (0.78)
Punakha Hospital	167 (0.89)	167 (1.24)	340 (0.51)
Pemagatshel Hospital	166 (0.88)	142 (1.06)	706 (1.06)
Tsimalakha Hospital	157 (0.83)	156 (1.16)	778 (1.74)
Dagapela Hospital	135 (0.72)	84 (0.62)	475 (0.72)
Trashiyangtse Hospital	111 (0.59)	96 (0.71)	380 (0.57)
Riserboo Hospital	108 (0.57)	108 (0.8)	468 (0.71)
Zhemgang BHU	94 (0.50)	76 (0.57)	372 (0.56)
Yebilaptsa Hospital	90 (0.48)	79 (0.59)	268 (0.40)
Total	18,313	13,445	66,239

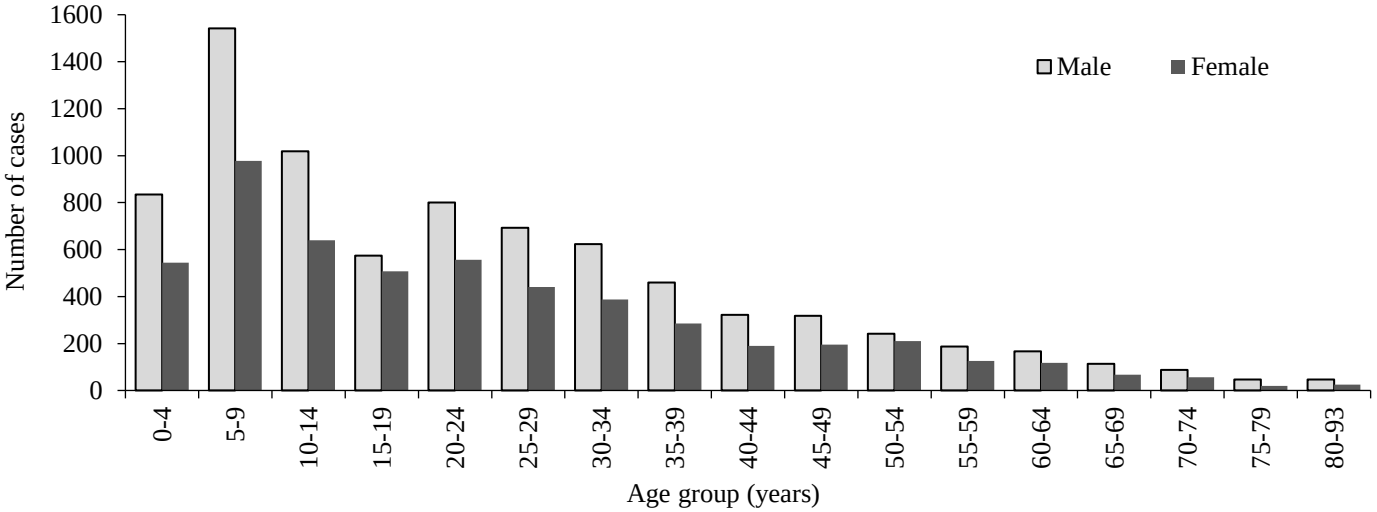

Figure 1 Number of reported cases of dog bite in humans, by age and gender, between January 2009 and December 2012 in Bhutan (n=13,445).

The maximum number of PEP recipients were in the 5–9-year-old age group (n=3,228; 17.18%) followed by the 10–14 year-old (n=2,283; 12.15%) age group. When the population at risk was taken into account for analyses, the incidence of treatment was still higher in children below 14 years of age, followed by adults 20–64 years old. Figures 2 and 3 illustrate the distribution of rabies PEP by age and gender between 2009 and 2012 in Bhutan, in which the proportion of PEP recipients was numerically higher in males than in females in all age groups.

Seasonal and annual trend of PEP

Rabies PEP was given throughout the year with more cases reported during spring, summer and autumn months compared with winter months ($p \leq 0.001$). The number of people that received PEP increased from less than 1,500 patients in 2009 to more than 7,000 patients in 2012 ($p \leq 0.001$) (2009: 1,385; 2010: 3,963; 2011: 6,421 and 2012: 7,044), but there was missing data from two sampled hospitals during 2009 and the data presented here likely underestimates the true number of cases in 2009.

Geographical distribution of PEP event

Of the 18,813 patients that received PEP, 8,653 (46%) patients reported for treatment in rabies risk areas where rabies outbreaks in animals occurred sporadically, whilst 10,160 (54%) cases reported for treatment in areas in which rabies has not been reported in animals or humans for more than 20 years (interior rabies free Bhutan); $p \leq 0.001$). Table 2 show the number of PEP cases for each health centre reported between January 2009 and December 2012. Of the five hospitals that reported the highest number of cases, three were located in rabies-risk areas in southern Bhutan (Gelephu, Phuentsholing and Samtse) whereas two were located in the interior of Bhutan where rabies had not been reported for more than 20 years (Thimphu and Paro).

Rabies PEP course

Of the 18,813 patients receiving rabies PEP, 8,067 (42.88%) patients received a standard 5-dose intramuscular injection (Essen regimen) on days 0, 3, 7, 14 and 28 whilst 10,746 (57.12%) patients received an incomplete course (less than 5 doses) of treatment (Tables 3 and 4). Over 66,000 doses of rabies vaccines have been used to treat people against rabies in the country during January 2009-December 2012 (Tables 2 and 3).

Risk factors for incomplete PEP course

Six variables were unconditionally associated ($p \leq 0.05$) with incomplete PEP treatment—sex, age, type of exposure (animal bite versus non-bite), area (rabies-risk/endemic versus rabies-free area), and season (Table 5). The final multivariable model indicated that males and adults (>20 years of age) are less likely to complete PEP treatment than females and children (Table 6). Patients with animal-bite injuries are less likely to complete

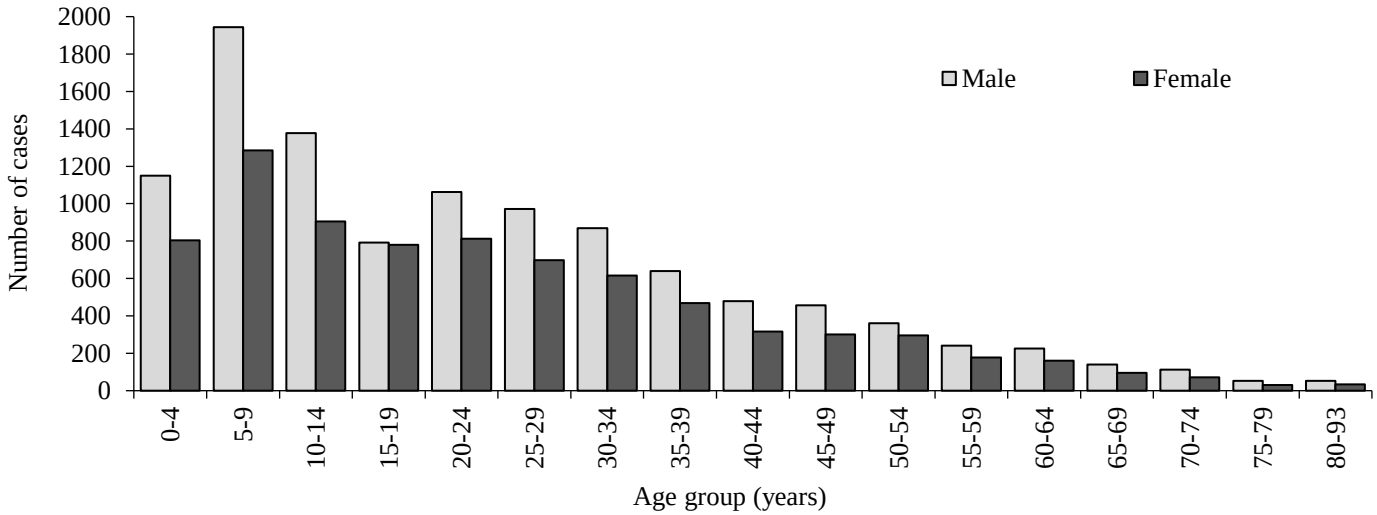

Figure 2 Number of people that received rabies post-exposure prophylaxis (PEP) by age and gender in Bhutan, January 2009-December 2012 (n=18,813).

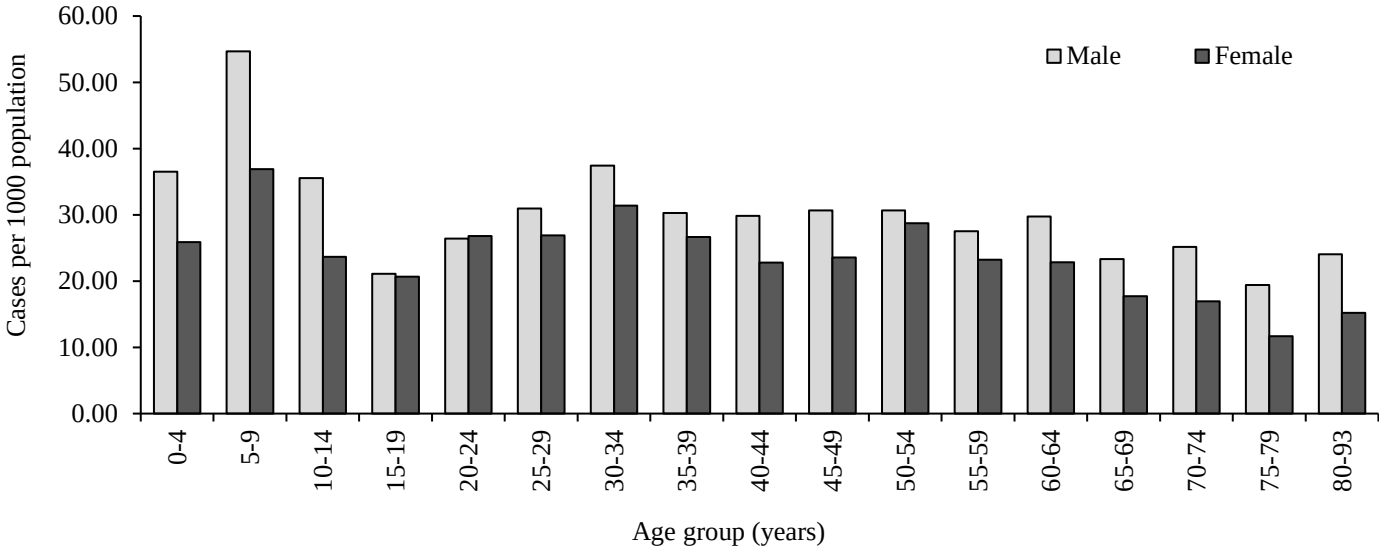

Figure 3 Number of cases per 1000 population that received rabies post-exposure prophylaxis (PEP), by age and gender, between January 2009 and December 2012 in Bhutan (n=18,813).

PEP treatment than non-bite patients, and patients in rabies risk or outbreak areas (south Bhutan) are more likely to complete treatment than patients from interior part of Bhutan that have not reported rabies for more than 20 years. Patients presenting to hospitals for PEP during spring and summers months are more likely to receive a complete course of treatment than patients presenting during winter months (Table 5 and 6). The proportion of patients that completed PEP was lower in 2009, 2011, 2012 (less than 47%), and was 57% in 2010.

Table 3 Number of patients reported for PEP and number of human anti-rabies vaccine (ARV) doses given from January 2009 to December 2012.

Number of ARV doses given	Number of cases (%)	Total doses given*
1	3009 (15.99)	3009
2	2254 (11.98)	4508
3	3545 (18.84)	10635
4	1938 (10.30	7752
5	8067 (42.88)	40335
Total	18,813	66,239

Interpretation: Of the total 18,813 patients, 3009 people received only single dose of ARV, 2254 received only two doses of ARV and so on.
* Total doses given is the product of number of ARV doses given and the number of cases. Approximately 66,239 doses of human anti-rabies vaccine were used between 2009 and 2012 in the sampled medical centres.

Table 4 Total number of PEP (ARV doses) given at various days of the Essen regimen (intramuscular injection) to people in Bhutan, January 2009–December 2012.

Day of PEP course	PEP received N (%)	PEP not received N (%)	Total
0	18,216 (96.83)	597 (3.17)	18,318
3	15,279 (81.22)	3,534 (18.78)	18,318
7	13,678 (72.71)	5,135 (27.29)	18,318
14	10,259 (54.53)	8,554 (45.47)	18,318
28	8,807 (46.81)	10,006 (53.19)	18,318

Interpretation: Of the total 18,813 patients reported to medical centres for PEP treatment, 18,216 received PEP on Day 0 and 597 did not receive PEP; on Day 3, 15,279 patients received PEP and 3,534 did not receive PEP and so on, indicating lack of patient's compliance to complete the course of PEP using the Essen regimen.

DISCUSSION

The first study on the pattern of human rabies exposure and use of rabies PEP in Bhutan is described by Tenzin et al. (2011b). In this study, we described the epidemiology of dog bites and use of PEP using hospital-based data from 2009 to 2012. The overall prevalence of PEP was higher among children up to 14 years of age than in older children and adults, which is in agreement with the previous study in Bhutan (Tenzin et al. 2011b) and also studies conducted elsewhere in the world (e.g., WHO 2010; Helmick 1983; Pancharoen et al. 2001; Blanton et al. 2010). This was likely due to the higher prevalence of dog-bite incidents amongst children than adults, which is also similar to the previous studies findings and other reports (Sudarshan et al. 2006; Tenzin et al. 2011a; Tenzin et al. 2011b; Khokhar et al. 2003; O'Bell et al. 2006). These findings are consistent with evidence that children are at higher risk of dog bites as well as rabies infection. Globally, more than 60% of human deaths due to rabies are reported in children below 16 years of age (WHO 2010; Knobel et al. 2005). The PEP was provided throughout the year with more use during the spring, summer and autumn seasons than in the winter months. This may be due to similar seasonal variation in the incidence of dog bites and occurrence of sporadic outbreaks of rabies. In Bhutan, children go to school in the spring, summer and autumn months and dog bites in children may either be more common or more likely to be reported to the hospitals for treatment in those months because of good supervision in the schools.

In developed countries, most dog-bite incidents have been reported during the spring and summer months because of more interaction between pets (Keuster et al. 2006; Schalamon et al. 2006). The study result indicates that the number of PEP cases have consistently increased over the years; from 1,500 cases recorded in 2009 (although there was some missing data in two hospitals in 2009) to more than 7,000 cases recorded in 2012. A similar trend of increasing prevalence of dog bites and PEP over time was also observed in the previous study (Tenzin et al. 2011b). The increase in use of PEP over time may be associated with an increase in the incidence of dog bites or with increased awareness of people about the importance of reporting to hospital for treatment after being bitten, even

Table 5 Contingency table for explanatory variables with "incomplete" rabies post-exposure prophylaxis in Bhutan and odd ratios based on univariable logistic regression analysis, January 2009–December 2012.

Variables & categories	Complete	Incomplete	*b*	SE(*b*)	OR (95% CI)	P-value*
Sex						
Male	4536	6388	-	-	1.00	-
Female	3518	4331	-0.135	0.029	0.87 (0.82-0.93)	<0.001
Age group						
0-9 years	2352	2855	-	-	1.00	-
10-19 years	1725	2133	0.019	0.043	1.02 (0.94-1.11)	0.665
20-29 years	1437	2115	0.193	0.044	1.21 (1.11-1.31)	<0.001
30-39 years	1094	1500	0.122	0.049	1.13 (1.03-1.24)	0.012
40-93 years	1459	2143	0.191	0.044	1.21 (1.11-1.32)	<0.001
Type of exposure						
Animal bite	6037	9126	-	-	1.00	-
Non-bite	2030	1620	-0.639	0.037	0.53 (0.49-0.57)	< 0.001
Area of PEP						
Rabies risk areas	5168	3969	-	-	1.00	
Rabies free areas	2899	6777	1.113	0.031	3.04 (2.87-3.23)	<0.001
Seasons of PEP						
Autumn (Sep-Nov)	2231	2936	-	-	1.00	
Spring (Mar-May)	2232	2631	-0.110	0.040	0.90 (0.83-0.97)	0.006
Summer (Jun-Aug)	2080	2659	-0.029	0.041	0.97 (0.89-1.05)	0.474
Winter (Dec-Feb)	1524	2520	0.228	0.043	1.26 (1.16-1.37)	<0.001
Year of PEP						
2009	647	738	-	-	1.00	-
2010	2274	1689	-0.429	0.063	0.65 (0.58-0.74)	<0.001
2011	2735	3686	0.167	0.060	1.18 (1.05-1.33)	0.005
2012	2411	4633	0.522	0.059	1.68 (1.49-1.89)	<0.001

LR Chi 2 P <0.001, Likelihood ratio test, p < 0.001; * Likelihood ratio test p-value

Table 6 Final multivariable model for incomplete rabies post-exposure prophylaxis course in Bhutan, January 2009–December 2012.

Variables and categories	*b*	SE (*b*)	OR (95% CI)	P-value*
Sex				
Male	-	-	1.00	-
Female	-0.107	0.032	0.90 (0.84-0.96)	0.0007
Age group				
0-9 years	-	-	1.00	-
10-19 years	0.052	0.045	1.05 (0.96-1.15)	0.2512
20-29 years	0.177	0.047	1.19 (1.09-1.31)	0.0002
30-39 years	0.124	0.051	1.13 (1.02-1.25)	0.0158
40-93 years	0.159	0.046	1.17 (1.07-1.28)	0.0006
Type of exposure				
Animal bite	-	-	1.00	-
Non-bite	-0.102	0.042	0.90 (0.83-0.93)	0.015
Area of PEP				
Rabies risk area	-	-	1.00	
Rabies free area	1.038	0.033	2.82 (2.65-3.01)	<0.001
Season of PEP				
Autumn (Sep-Nov)	-	-	1.00	-
Spring (Mar-May)	-0.183	0.043	0.83 (0.76-0.91)	<0.001
Summer (Jun-Aug)	-0.113	0.043	0.89 (0.82-0.97)	0.008
Winter (Dec-Feb)	0.200	0.046	1.22 (1.12-1.33)	<0.001
Year of PEP				
2009	-	-	1.00	-
2010	-0.479	0.066	0.62 (0.54-0.70)	<0.001
2011	-0.009	0.062	0.99 (0.88-1.12)	0.882
2012	0.330	0.062	1.39 (1.23-1.57)	<0.001

LR Chi 2 P <0.001, Likelihood ratio test, p < 0.001; * Likelihood ratio test p-value

though the incidence of outbreaks of rabies in Bhutan over that period remained the same (Tenzin et al. 2011b; Tenzin et al. 2012b). In this study dog bites accounted for 88.7% of animal-bite incidents and 71.5% of dog-bite victims that reported to hospitals were given PEP. The high incidence of dog bites in Bhutan is directly related to the presence of large numbers of free-roaming/stray dogs, particularly in urban areas that have relatively high human population density and food resources for dogs. This study also indicates that a large amount of PEP was administered to cases whose risk of exposure to rabies was extremely low in areas where the occurrence of rabies had not been reported for more than two decades in the interior Bhutan. However, because rabies is a fatal disease and sporadic cases have been reported in southern Bhutan, clinic staff would have approved PEP if the biting animal was not available for observation as most bite incidents occur from stray dogs. Also, because the PEP is provided free of charge, there may have been pressure from the victims to receive treatment as a precautionary measure rather than due to risk of true exposure (McCombie 1989; Tenzin et al. 2011b). However, the incidence of PEP given to people that had not been bitten by an animal (non-bite incidents) but had contact with an animal suspected of having or that had rabies (e.g., through handling during zoo sanitary measures), contact with a rabid human patient, or who had consumed dairy products or meat derived from an animal suspected of having rabies was 50% lower than that previously reported for the period 2005–2008 (Tenzin et al. 2011b). This reduction of unnecessary PEP may be due to implementation of revised national rabies PEP guideline, greater training and awareness of clinic staff about this guideline, and also due to increase awareness of people about avoiding unnecessary contact. Exposure not related to an animal bite and subsequent report to medical centres for PEP is more common at the time of rabies outbreaks in cattle, after consumption of dairy products derived from rabid cattle which is due to lack of awareness on rabies. Therefore, there is a need to educate the general public regularly on the risk of rabies transmission to avoid unnecessary contact and to reduce expenditure on PEP. Regarding the pattern of PEP events in the country, 35% of PEP was provided in the medical centres in southern Bhutan. This may be because the national PEP guideline for rabies prophylaxis recommend that any dog-bite cases in southern Bhutan should be given PEP, irrespective of whether the biting dog is pet or stray, because of the high risk of rabies infection in the south bordering areas. For instance, all human rabies cases reported in the past 20 years occurred in southern Bhutan following rabid-dog bites and failure to seek medical treatment. However, it was observed that large amount of ARV doses was used in hospitals located in interior Bhutan, despite there being no history of rabies in these areas for more than two decades. The high cases of PEP events in interior Bhutan may be due to large number of stray dogs associated with high incidence of dog bites. Also, the revised national guideline for rabies prophylaxis in human in Bhutan advise administration of PEP to victims of any animal bite because of endemic situation of rabies in south Bhutan.

The PEP regimen used in Bhutan during this study period requires administration of 5 intramuscular doses of anti-rabies vaccination (Essen regimen) which requires 5 visits by the patients to medical centres to complete a full course (on days 0, 3, 7, 14 and 28) (WHO 2010). For adequate immunization and protection, patient compliance to complete the course is critical, particularly if they have been bitten by a confirmed rabid animal. In this study, we found that 57.12% of patients received an incomplete vaccine course (<5-dose course) and 3, 18 and 27% did not receive PEP on days 0, 3 and 7 respectively which are most critical period for protection against the rabies. The percentage of patients that received an incomplete course of treatment was 17% higher in this study than in the previous study conducted from 2005 to 2008 (Tenzin et al. 2011b). However, the majority of the patients that received an incomplete course of treatment were in the interior of Bhutan where the risk of rabies infection – even if they were left untreated – was very low. Male and adult patients were less likely to complete a full course of treatment compared to females and children. Our study also shows that people who had animal bites are less likely to complete a full course of treatment than people seeking treatment for non-bite exposure, posing risk of rabies if the biting dogs are indeed infected with rabies virus. Nevertheless, it is also possible that PEP treatment must have been discontinued on days 14 and 28 if the biting dog was available for observation and proved not to be rabid, especially in the case of pet dog bites. This approach was recommended by the Ministry of Health in 2011 in an effort to reduce expenditure on PEP (WHO 2010). However, there were no reliable data in the records analysed in this study about the type of dog (pet vs. stray) that caused the bite incidents and also the circumstances of bites (provoke vs. non-provoke bite) and the health status of biting animals (rabid vs. non-rabid animal bite). Failure to complete a full course of PEP treatment is a common problem in developing countries due to poor patient compliance and the long duration of treatment requirement (5 visit to the hospital). In majority of the cases, the patients were not able to afford payment for the treatment unless it is provided free of cost (Knobel et al. 2005, Hampson et al. 2015). In Bhutan, health care is provided free of cost by the government, including rabies PEP, resulting in substantial cost. To reduce the expense of PEP, the medical centres in Bhutan have introduced the intra-dermal method of treatment in 2013 that have been used successfully in other countries where rabies is endemic, thus reducing the PEP cost by about 60% (Gongal et al. 2011; WHO 2013).

CONCLUSIONS

The results from this study indicate that dog bites and the associated high use of PEP are a public health problem in Bhutan and the study findings provide useful information for public health policy discussion and development. One of the important findings include the higher risk of dog bites and greater likelihood of completion of a full course of PEP treatment in children than in adults. Although, many factors associated with incomplete PEP treatment were identified in this study, we also believe there may be other reasons that resulted in failure to comply with the PEP course which could be identified by further case-tracing study and questionnaire interviews to better inform policy decisions. We also recommend that the quality of data about dog bites and PEP maintained in medical centres be improved to provide better data on the type of dog-bite exposures (pet *vs.* stray), site and severity of bite wound, circumstances of bite, health status of biting animals, time elapsed between time of bite and report to medical centres for treatment. Nevertheless, the available data indicate the social and economic impact of dog bites and PEP both for the people and the government. Therefore, to control rabies effectively both in dogs and humans and to reduce hazards resulting from dog bites including costs of treatment, it is important for animal health and public health sectors and other relevant agencies to strengthen and collaborate towards elimination of rabies in the country using One Health approach.

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