

Determinants of Rabies Post-Exposure Prophylaxis Completion in Sarawak

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Abstract:

Objective: Rabies remains persistent in Sarawak despite efforts to control its spread. This study investigates the determinants of rabies post-exposure prophylaxis (PEP) completion among individuals in Sarawak that have been exposed to potential rabies transmission through animal bites.

Material and Methods: A retrospective cohort study, using a universal sampling approach was employed, utilizing data from the Sarawak i-Bite System. Binary logistic regression was used to identify significant variables: a p-value<0.05 was considered as statistically significant.

Results: The mean age of people having experienced animal bites was 38.1 (S.D.=22.4) years. Most were male (51.6%) and of Chinese ethnicity (37.2%). The predominant sites of animal bites were the upper (53%) and lower limbs (39.5%).

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Category 3 bite injuries and bites from fully confined pets were the most frequently reported (68.9% and 43.9%, respectively). In total 56.5% of the study population had a complete rabies vaccine regimen as post-exposure prophylaxis, while 5.4% had incomplete vaccinations, and 38% received no vaccination. The majority received treatment at government hospitals (59.1%). The significant determinants of rabies post-exposure prophylaxis completion in Sarawak were the Iban ethnicity (odds ratio (OR)=2.9, 95% confidence interval (CI):1.08–2.44, p-value=0.02), grade 3 bite (OR=3.9, 95% CI=1.86–4.68, p-value<0.001), pet mixed with stray (OR=2.41, 95% CI=1.32–2.33, p-value<0.001), stray animals (OR=2.41, 95% CI=1.78–3.25, p-value,0.001) and treated in a government hospital (OR=0.63, 95% CI=0.47–0.83, p-value<0.001).

Conclusion: This study reported that only 56.5% of patients completed the rabies PEP series. The important determinants of PEP completion status were found to be the Iban ethnicity, bite severity, category of animal, and place of treatment. These findings offer valuable insights to assist the Sarawak State Health Department in prioritizing strategies to enhance the compliance rate, with the ultimate goal of eliminating dog-mediated Rabies deaths by 2030.

Keywords: predictors, post-exposure prophylaxis, rabies, Sarawak

Introduction

Rabies, caused by the Lyssavirus, is a zoonotic disease found in more than 150 countries globally, leading to approximately 59,000 human fatalities each year. The majority of these deaths (96%) occur in Asia (59.6%) and Africa (36.4%). Additionally, it contributes to approximately 3.7 million disability-adjusted life years (DALYs) annually. Delay in seeking Rabie prophylaxis, incorrect wound care, undiscovered wounds, direct nerve inoculation, lack of compliance with immunisation regimens, poor quality rabies vaccine, and improper administration of Rabies Immunoglobulin (RIG) are essential factors leading to Rabies mortality. Globally, 20 million people are estimated to receive post-exposure prophylaxis (PEP) for suspected rabies exposure yearly¹. However, in canine-endemic nations is required as to why some patients begin and finish the regimen while others do not. Studies have found that age group, gender, level of education, types of animals, and locality of residence are related to treatment-seeking behaviors for animal attacks and obtaining vaccinations^{2–11}. Moreover, fewer statistics are available for RIG, given that only a tiny percentage (2–4%) of the population has access to it¹².

Sarawak is one of the largest states in Malaysia, located in the region of East Malaysia, northwest of Borneo Island. It is bordered by Sabah to the northeast, Kalimantan to the South, and Brunei to the north¹³. The residents of Sarawak are comprised of multiple ethnicities consisting of six major ethnicities; including Iban, Chinese, Malay, Bidayuh, Melanau, Orang Ulu, as well as a number of minor ethnic; such as Kedayan, Penan, Murut, and many more. Administratively, Sarawak is further divided into twelve divisions. In Sarawak, the people keep dogs not only as pets but also as companions in their daily lives and cultural traditions. Their dogs act as protectors, hunters, and companions to their owners on hunting expeditions, especially for those living in remote areas nestled in rainforest areas. Some ethnic groups, like the Penan, live closely with their dogs, allowing them to lounge in their house or courtyard.

Malaysia recorded the first case of Rabies in 1924, which was widespread in states neighboring Thailand. The disease then spread southward, and by 1952, a major outbreak occurred in central peninsular Malaysia, leading to the introduction of the Rabies Control Program. Rabies was promptly controlled, in which the epidemic ended in

1954, and sporadic cases occasionally occurred until 1998¹⁴. After a 15-year hiatus of zero rabies cases, Malaysia was declared free from rabies in 2013. However, this status was held only briefly before rabies cases were redetected again in 2015, in northern Peninsular Malaysia¹⁵. In July 2017, the East Malaysia region recorded the first rabies case suspected to have originated from West Kalimantan, and a rabies outbreak was declared in Sarawak.

The rabies outbreak was declared a Level 2 Disaster in January 2019. Thus, every government entity has been authorised to combine resources and focus its efforts on controlling rabies. As of 24th July 2023, there were 68 confirmed human rabies cases, with 61 fatalities recorded during the ongoing outbreak; with all 12 divisions in Sarawak declared as rabies areas. In animal surveillance from 2017 until 2021, as high as 30.18% of animal rabies were found to be positive in dogs and cats^{15,16}.

The administration of rabies PEP soon after exposure is an effective prevention strategy. The regime and doses of PEP depend on the types of vaccine. In Sarawak, the Purified Vero Cell Rabies Vaccine (PVRV) is used¹⁴. There are two types of vaccine regimes, which include a 4-dose Essen regimen (1-1-1-0); given at one site 0.5 ml intramuscularly at days 0,3,7, and day 14-28, and the Institute Pasteur du Cambodge (IPC) regime (2-2-2-0-0); given at 2 sites (0.1ml per site) intradermally at days 0, 3 and 7. Generally, the PEP is given to those that have category 2 and 3 exposure. A completed PEP can provide 99% protection against human rabies, while incomplete vaccination will not give effective protection, where the disease is 100% fatal once symptoms occur¹⁷.

In 2019, 32 Post Bite Clinics were offering Rabies PEP in Sarawak, and the number increased to 62 centers on 13th June 2023. However, the surveillance data of Post Bite Clinic and adherence to the PEP protocol still need to be improved¹⁶. While Sarawak has proved its ability to give PEP, there has yet to be a formal assessment of patients' adherence to the PEP treatment. This research aimed to

identify the epidemiologic features of patients in Sarawak that had defaulted rabies post-exposure prophylaxis treatment in animal bite cases.

Material and Methods

This retrospective cohort study was conducted from 1st June 2023 to 31st July 2023, in Sarawak and employed a universal

Sampling approach

All animal bite patients in Sarawak registered in the i-Bite system who sought treatment after exposure in any healthcare facility, from 1st June 2023 to 31st July 2023, were included in this study. Inclusion criteria consisted of patients with a history of animal bite exposure while staying in Sarawak during the period of research registered in the i-Bite system. Exclusion criteria were made for, (i) cases with repeated exposure to animal bites within the study timeframe and (ii) patients that received the vaccine series or follow-up outside Sarawak.

This study utilises the i-Bite system, an online registry developed by the Sarawak State Health Department, functioning as a surveillance database. The i-Bite system has been used in Sarawak as of April 2021, as a digital platform for notification, record keeping of case investigation, care plan, and monitoring of vaccination of animal bite cases from all health facilities in Sarawak. The data available in the system includes, data on place of treatment, number of bites, body part bitten, place of initial wound care, initial wound washing done, grade of bite, immunocompromised status, history of rabies vaccination, types and category of animal, animal vaccination status, number of PEP doses given, date of bite and date of treatment. This database is accessible for download by the i-Bite administrator at the Crisis Preparedness and Response Centre (CPRC) Sarawak. It contains numerous information; such as

animal-related factors, exposure factors (site of exposure and injury), and treatment given.

In this study, completed PEP was defined as: animal bite patients that received at least 3 doses of vaccine. Meanwhile, incomplete PEP was defined as: animal bite patients that received no vaccine and those whom received 1 to 2 doses of vaccine. The grade of the bite was divided into three categories, based on the WHO classification of animal bites¹⁸. Category 1 refers to exposure only involving touching or feeding animals and licks on intact skin. Category 2 refers to exposure involving nibbling uncovered skin with minor scratches or abrasion without bleeding. Whereas, Category 3 refers to exposure involving single or multiple transdermal bites or scratches, with contamination of mucous membranes or broken skin that is exposed to animal saliva from licking.

Statistical analysis

Data analysis was conducted using Statistic Package for the Social Sciences (SPSS) version 28 software. Descriptive statistics were used to summarise subject characteristics and socio-demographic information. The normality distribution was determined based on the result of the histogram, skewness, kurtosis, and Shapiro-Wilk test. This study considered several independent variables; including age group, gender, race, bite location, grade of bite, category animal, vaccine doses, and place of treatment. The dependent variable was the postexposure prophylaxis status; categorized as either complete or incomplete. Complete PEP status was defined as any patient that completed the recommended vaccination; including those whom received the vaccine later than the prescribed date of vaccination. Incomplete PEP status was defined as animal bite patients that discontinued the vaccination at any point during the recommended course (except those whom discontinued vaccination after 3 doses wherein the dog remains healthy and alive for at least 10 days after exposure.

Binary logistic regression was performed to determine the relationship between the predictors and outcome variables while controlling for the confounding factors. A p -value <0.05 was considered statistically significant.

Ethical approval

This study entailed the retrieval of secondary data from the i-Bite system, an online registry established by the Sarawak State Health Department. Permission to access and utilise this data was previously obtained from the Sarawak State Health Department. A unique code number distinguished each individual case. The information was collected based on a preformed checklist, and only the relevant data were extracted and used for this study. No direct human interviews were conducted in this study. Ethical approval was approved by the Sarawak State Health Department from the National Medical Research Registry (NMRR) Ethical Board.

Results

A total of 1,275 patients had sought treatment for animal bites during the study period. The average age of individuals experiencing these incidents was 38 (S.D.=22.4) years. Males reported a higher proportion of injured individuals, at 51.6%, compared to females; at 48.4%. Among the ethnic groups, individuals of Chinese ethnicity had the highest incidence of animal bites (37.2%), followed by Iban (25.2%), and other ethnic groups combined: accounting for 24.9%. Predominantly, animal bites occurred on the upper (53%) and lower limbs (39.5%), with a smaller percentage involving other body parts. There were 27 cases (2.1%) that had injuries on multiple body parts. Category 3 bite injuries were the most common (68.9%), followed by Category 2 (23.4%) then Category 1 injuries (7.8%). Bites from fully confined pets were most frequently reported (43.9%), while incidents involving stray animals and pets that mingled with strays had similar occurrence rates at 28.3% and 27.8%, respectively. Within our study population, 56.5%

of patients received the complete rabies vaccination as part of their post-exposure prophylaxis. In comparison, 5.4% did not complete their vaccinations, and 38% did not receive any vaccination at all. The majority of the patients sought treatment at government hospitals (59.1%) and government health clinics (28.5%), while a smaller proportion received care in private healthcare settings.

Table 1 Characteristics of patients attending the post-bite clinic in Sarawak, June 2023–July 2023 (n=1275)

Characteristics	n (%)
Age in years	
≤15	235 (18.4)
16–30	312 (24.5)
31–45	222 (17.4)
46–60	244 (19.1)
≥61	262 (20.5)
Mean=38.1 years, min=0, max=103 years, S.D=22.4	
Gender	
Male	658 (51.6)
Female	617 (48.4)
Race	
Malay	163 (12.8)
Chinese	474 (37.2)
Iban	321 (25.2)
Others	317 (24.9)
Bite location	
Head & face	34 (2.7)
Torso & abdomen	11 (0.9)
Upper limb	676 (53.0)
Back	24 (1.9)
Lower limb	503 (39.5)
Multiple parts	27 (2.1)
Grade of bite	
Category 1	99 (7.8)
Category 2	298 (23.4)
Category 3	878 (68.9)
Category of animal	
Stray	361 (28.3)
Pet-mixed with stray	354 (27.8)
Pet fully confined	560 (43.9)
Vaccine Doses	
No vaccine given ^a	485 (38.0)
1–2 doses given ^a	69 (5.4)
At least 3 doses given ^b	721 (56.5)
Place of treatment	
Government clinic	363 (28.5)
Government hospital	753 (59.1)
Private GP	52 (4.1)
Private hospital	107 (8.4)

GP=General Practitioner

^aIncomplete PEP, ^bCompleted PEP

Table 2 shows the PEP completion status of the patients in this study; based on the age group, gender, race, location and grade of bite, category of bite, and place of treatment (n=1,275)

Variable	PEP status	
	Incomplete	Completed
	n (%)	n (%)
Age group		
≤15	93 (7.3)	142 (11.1)
16–30	133 (10.4)	179 (14.0)
31–45	90 (7.1)	132 (10.4)
46–60	106 (8.3)	138 (10.8)
≥61	122 (9.6)	140 (11.0)
Gender		
Male	285 (22.4)	373 (29.3)
Female	259 (20.3)	358 (28.1)
Race		
Malay	76 (6.0)	87 (6.8)
Chinese	202 (15.8)	272 (21.3)
Iban	119 (9.3)	202 (15.8)
Others	147 (11.5)	170 (13.3)
Location of bite*		
Head & face	16 (1.3)	18 (1.4)
Torso & abdomen	6 (0.5)	5 (0.4)
Upper limb	307 (24.1)	369 (28.9)
Back	13 (1.0)	11 (0.9)
Lower limb	190 (14.9)	313 (24.5)
Multiple parts	12 (0.9)	15 (1.2)
Grade of bite		
Category 1	63 (4.9)	36 (2.8)
Category 2	158 (12.4)	140 (11.0)
Category 3	323 (25.3)	555 (43.5)
Category of animal		
Pet fully confined	295 (23.1)	260 (20.4)
Pet-mixed with stray	135 (10.6)	224 (17.6)
Stray	114 (8.9)	247 (19.4)
Place of treatment		
Government clinic	127 (10.0)	236 (18.5)
Government hospital	352 (27.6)	401 (31.5)
Private GP	26 (2.0)	26 (2.0)
Private hospital	39 (3.1)	68 (5.3)

PEP=post-exposure prophylaxis GP=general practitioner

Determinants of vaccine completion status

Binomial logistic regression was used to determine the factors associated with the PEP, which was divided into incomplete and completed, and included five predictor

variables: age group, part of body bitten, risk stratifications, category of animal, and category of bitten category. The chi-square test of independence was statistically significant $X^2(20)=115$, p -value<0.001, indicating the predictor variables collectively explain a significant portion of the variance in a vaccine given. Analysis revealed that certain factors; such as being of Iban ethnicity in comparison to Malay (AOR=1.62, 95% confidence interval (CI): 1.08, 2.44; p -value<0.05), category 3 bite as opposed to category

1 (AOR=2.96, 95% CI: 1.86, 4.68; p -value<0.001) and the animal category, specifically, pets mixed with strays (AOR=1.76, 95% CI: 1.33, 2.35; p -value<0.001) and stray versus pet (AOR=2.32, 95% CI: 1.73, 3.12; p -value<0.001) as well as receiving treatment at a government hospital instead of a government clinic (AOR=0.64, 95% CI: 0.48, 0.84; p -value<0.001), were associated with significant predictors of PEP completion status (Table 3).

Table 3 Determinant of Post-exposure prophylaxis completion status (n=1275)

Variable	Crude (OR)	Adjusted OR	95% CI	p-value*
Age group (years)				
16-30-<15	0.88	0.88	0.61-1.28	0.50
31-45-<15	0.96	0.95	0.63-1.42	0.80
46-60-<15	0.85	0.88	0.59-1.31	0.54
>61-<15	0.75	0.75	0.51-1.10	0.15
Gender				
Female-male	1.06	1.16	0.91-1.48	0.23
Race				
Chinese-Malay	1.18	1.39	0.93-2.07	0.11
Iban-Malay*	1.48	1.62	1.08-2.44	0.02
Others-Malay	1.01	1.25	0.83-1.88	0.29
Location of bite				
Torso and abdomen – head and face	0.74	1.08	0.26-4.49	0.91
Upper limb-head and face	1.07	1.28	0.62-2.66	0.51
Back-head and face	0.75	0.84	0.27-2.57	0.75
Lower limb-head and face	1.46	1.67	0.79-3.51	0.18
Multiple part-head and face	1.11	1.04	0.36-3.00	0.94
Grade of bite				
2-1	1.55	1.56	0.94-2.54	0.09
3-1**	3.00	2.96	1.86-4.68	0.00
Category of animal**				
Pet mixed with stray-pet	1.88	1.75	1.32-2.33	0.00
Stray-pet	2.46	2.41	1.78-3.25	0.00
Place of treatment				
Government hospital-government clinic**	0.61	0.63	0.47-0.83	0.00
Private GP-government clinic	0.54	0.79	0.42-1.50	0.48
Private hospital-government clinic	0.94	1.02	0.62-1.66	0.94

AOR=adjusted Odds ratio, LL=lower limit of 95% confidence interval, UL=upper limit of 95% confidence interval

** p -value<0.001; * p -value<0.05

Discussion

This study examined the factors that may influence compliance and adherence to rabies post-exposure prophylactic vaccination among animal bite cases in Sarawak. Several factors, such as ethnicity, bite severity, animal condition and place of treatment, were found to be associated with vaccine compliance. Among the ethnic groups studied, the Iban bite victims were found to be more readily compliant with vaccination. The significant link between the completion of rabies PEP and Iban ethnicity in Sarawak presents an intriguing aspect in understanding health-seeking behavior among the major ethnicities within this state. One of the possible reasons that may contribute to this finding is the intensified approach of rabies management in Sarawak over the past few years. This includes a number of public education campaigns and awareness campaigns to raise awareness regarding rabies disease and its prevention. The awareness campaign is not only done through social media, but also utilises local community events, educational materials in the local language, and engaging the longhouses community leaders to reach out to the local audiences more effectively^{19,20}. Effective and rigorous health education may be able to influence the local community's perceptions of the disease, leading to better health-seeking behavior, and thus, better compliance with rabies PEP²¹. In addition, a local study that looks into the determinants of healthy lifestyle practices among Sarawakians showed that health literacy and knowledge of disease directly influence lifestyle practices; irrespective of ethnicity²².

Consistent with the findings in similar studies, a higher proportion of males, accounting for 51.6% of cases, experienced animal bites compared to their female counterparts at 48.4%, respectively^{2,7,23}. This pattern may be attributed to the difference in occupational exposure; such as males being more likely to work outdoors in the agricultural and construction sectors²⁴. In this study, it was observed that the highest incidence of reported animal bites occurred

among individuals in the working-age demographic; aged between 20 and 65 years. This aligns with findings from Vietnam, wherein 64% of cases involved individuals aged 25 years or older: as documented in a previous study². In contrast, studies conducted in other countries, such as in Iran and France, have reported a higher susceptibility to animal bites among younger individuals, especially those under 30 years of age, with prevalence rates ranging from 53.5% to 65%. This variance in age distribution in this study is believed to be due to the underreporting of minor injuries in children, which may result in their being unregistered in the system^{23,25}.

However, interestingly, this study found that there is no significant difference between age groups and genders in adherence to rabies PEP completion in Sarawak. One of the possible factors contributing to these findings is the access to healthcare and rabies PEP vaccines that are free of charge regardless of the population's age or gender²⁶. The rabies PEP vaccine is provided free of charge at both government and public health facilities. It is available in both urban and rural areas, helping to reduce disparities across different age groups and genders. Furthermore, factors related to health literacy and awareness may also influence adherence to rabies PEP completion²⁷. Individuals that are well informed on the importance of completing PEP are more likely to adhere to the regime, regardless of their gender or age.

As anticipated, individuals with more severe bite injuries were more likely to seek medical treatment, with 68.9% of patients presenting category 3 bites, as opposed to 23.4% in category 2 bites and 7.8% with category 1 bites. This is similar to the findings in Vietnam, wherein 93.6% of reported animal bites were Category 2 & 3 combined. This underscores the direct correlation between the severity of the injury and the likelihood of completion of vaccination^{2,18}.

Notably, our research revealed a higher incidence of animal bites originating from fully confined pets, as opposed

to stray pets and pets mixed with strays²⁵. As fully confined pets mainly live in homes or cages there are more frequent intimate interactions between pets and humans, which increases the potential for bites. Additionally, there appears to be a lesser degree of vigilance concerning diseases that can result in incomplete (PEP)²⁸. Additionally, there could be a lack of awareness of the disease fatality and the effectiveness of PEP following bites. Inadequate counseling on the importance of adhering to complete vaccination schedules could also contribute to PEP incompleteness indicated in this study²⁹.

Given the persisting issue of incomplete PEP reported among patients bitten by both fully confined pets, strays, and pets mixed with strays, it is important to educate both pet owners and the public about this issue; as pets constitute one of the main reservoirs of diseases. Furthermore, healthcare providers attending to such cases must ensure the delivery of thorough counseling to address barriers hindering PEP completeness³⁰.

Patients receiving post-exposure rabies prophylaxis at a government hospital may be more likely than those receiving treatment at a government clinic to complete the rabies vaccination series. This could be attributed to factors; such as geographical location, accessibility to healthcare facilities, treatment quality, and effectiveness of communication and follow-up systems available in the area. These combined elements may facilitate a higher vaccine completion rate at the center^{31,32}.

To achieve rabies elimination by 2030, we need to cooperate strongly with the Department of Veterinary Service and other relevant agencies. This collaboration should focus on raising public awareness and promoting rabies vaccination as a fundamental health measure. Data sharing is important to improve rabies surveillance, which in turn may aid in educating animal bite patients to adhere to rabies PEP, and improve the clinician's ability to evaluate exposure incidents. Sarawak should continue to disseminate

public announcements through diverse communication platforms concerning the ongoing rabies endemic until the outbreak is officially declared over. Other socio-demographic differences between ethnic groups; such as economic and educational background, remain to be explored in terms of their effect on vaccine compliance.

Limitation

The main limitation encountered in this study is related to the data's quality, as it relied on secondary data sources. Thus, there was limited control over data collection and record keeping, resulting in several data inconsistencies and missing values that were identified in this study. Additionally, this study's investigation focused only on selected patient and animal-related factors to PEP status completion. To gain a comprehensive understanding of rabies PEP adherence behavior, future research should engage the community to identify their awareness levels and barriers in seeking treatment for animal bites.

Conclusion

This study reported that only 56.5% of patients completed the rabies PEP series. The important determinants of PEP completion status were found to be the Iban ethnicity, bite severity, animal condition, and place of treatment; which were found to be associated with vaccine compliance. These findings offer valuable insights that can assist the Sarawak State Health Department in prioritizing strategies to enhance the compliance rate, aligning with the ultimate goal of eliminating dog-mediated rabies deaths by 2030.

Conflict of interest

There are no potential conflicts of interest to declare.

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