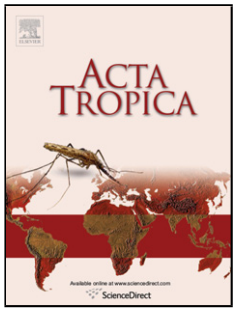

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A PROSPECTIVE STUDY ON THE INCIDENCE OF DOG BITES AND MANAGEMENT IN A RURAL CAMBODIAN, RABIES-ENDEMIC SETTING

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Highlights

- We undertook 6-months prospective surveillance of dog bites in 1779 persons in four rural Cambodian villages.
- We found the overall incidence of dog bites to be the highest published, at nearly 5 bites per 100 person-years.
- Some were repeat bite victims, and extremely few had referred for post-exposure management.
- All of the biting dogs were owner dogs.
- Adapted control policies for prevention education, canine population control and vaccination are urgently needed.

Abstract

Rabies circulates intensely in Cambodia, mainly affecting rural populations. We conducted a prospective study to estimate the baseline incidence of potentially infective dog bites in rural villages of Siem Reap province, Cambodia. The study was conducted in a convenience sample of 844 families totaling 1,779 persons in four villages. The study collected data in a total of 802.3 person-years.

Trained village health workers (VHW) exhaustively documented consecutive dog bites at the end of each month. Between May 15th and November 15th, 2011, a total of 40 attacks (43 bites; 1.07 bites per attack) were notified by 39 persons (50% female; one suffered two distinct incidents) to VHW. The all-age attack rate for bites over this 6-month period was 2.3% (CI95%: 1.7% - 3.1%), with a global incidence rate estimated at 4.84 bites/100 person-years (CI95%: 3.5 – 6.6). The mean age in bite victims was 20.8 ± 18.9 years (median 12.5; interquartile range 6-36; range 1 - 63). The dog was identified in 39 (97.5%) of cases, being the household dog in 9 (22.5%) of cases. Bites were classified as severe (WHO Category III - broken skin with bleeding) in 33 (82.5%) of cases with a severe dog bites incidence estimated at 4/100 person-years (CI95%: 2.8 – 5.6). The bites involved the hand or face in 1 (2.5%) case each (both Category III). In 20 incidents (50%), only rice was applied to the wounds. There were no suspected or confirmed human rabies deaths during the study period but one dog died after biting (2 others were lost to follow-up and 14 were put

down by their owner). Our study documented an extremely high incidence of dog bites in of rural Cambodian adults and children. Adapted control policies for canine vaccination are urgently needed.

Keywords: Rabies; Cambodia; Asia; Dog bite; rural; incidence; prospective

Introduction

Dog bite injuries are a major public health issue worldwide. Dogs' attacks and consecutive wounds can lead to permanent disfigurement, post traumatic trauma, and sometimes death by direct traumas or rabies virus inoculation [1,2]. They also cause an economic burden for the victims. Research studies show that efforts to raise awareness among communities [3,4] or individuals [5], policy makers [6] and health care professionals [7] are effective in preventing dog bites and improving aggressive dogs' ownership practices and legislation [8–10]. In developing countries, a series of factors are likely to increase dog bite incidence and bites seriousness: dogs are often not confined and dog population is uncontrolled [11]. The rural areas of developing countries are characterized by the uneven distribution of health infrastructures with often long distance to travel to and from these health care facilities [12], the scarcity of human resources, the poor quality of services and the difficulty of payment [13].

In 2012, the population of Cambodia was 14.86 million people, with 80% living in rural areas [14]. Cambodia remains one of the poorest countries of Southeast Asia, ranked 136 out of 187 on the Human Development Index [15] and the illiteracy rate is one of the World's highest, at 63%. Despite increasing economic growth, 2.8 million of people are still considered very poor (earning less than $1.25 per day). Life expectancy is 71 years, and 40% of children under the age of 5 are malnourished [16]. Dogs play an important role in Cambodian families as house or farm guards, as companions but also increasingly as a source of protein and therefore a source of income. In Cambodia, the dog-to-human ratio is the highest in the region according to a study conducted by the Institut Pasteur du Cambodge (IPC) in 2007: 1 dog to 3.1 humans (95%CI 1:3.0–1:3.2) in rural areas, with 75 % of the families having at least one dog [17]. This suggests that interactions between humans and dogs are intense and that dog attacks are frequent.

IPC hosts the largest rabies prevention center (rpc@ipc), providing post exposure prophylaxis (PEP) to over 21,000 bite victims each year [18]. The dog bite incidence in Phnom Penh, the capital

city, was estimated in 2007 at around 591/100,000 population [17]. This estimation is one of the highest published worldwide, and we suspected bite incidence in rural areas to be even higher [19–22]. Although 80 % of the Cambodian population lives in rural areas there are no precise data on rural dog bite incidence. A KAP study in Phnom Penh and in Kandal, a periurban province, found a yet higher annual incidence estimated retrospectively at 1,120/100,000 population per year [23]. Knowing that animal bites are the most common exposure to rabies and that 99% of human cases are caused by dogs [24] improved estimates of dog bites incidence in rural areas are crucial to better evaluate the risk of rabies in the population.

Material and Method

1. Area description

Siem Reap province, with an area of 10 300 km2 and a population of 900,000 inhabitants is located in the northwestern part of the country. It is among the poorest provinces of Cambodia. The villages where the study took place are located in the rural areas in three different districts, 30 to 60 km from the city of Siem Reap. The poverty rate in these districts ranges from 36% to 45 %. Villages are surrounded with paddy fields and are usually organized around one main road with farms alongside and paths leading to other houses. Houses are not fenced and animals are free to circulate inside and outside the houses.

2. Villages' selection

The villages' selection was facilitated because AVSF, partner of the study, had former experience in this area and contacts were already established. Villages were selected according to key person's acceptance and willingness to participate. We selected the four villages in distinct locations, spaced out one from each other from at least 30 km (Figure 1).

3. Sample size calculation

The results of this study were intended as baseline data for a cluster randomized vaccine trial. Sample size was determined in the frame of this trial, for a power of 80% and an α risk of 5% [25]. A minimum of 80 households per village had to be randomly selected. The lists of village

households were provided by the Village chiefs.

4. Questionnaire design and data collection by teams of villagers

The longitudinal survey lasted six months between the 15th of May to the 15th of November. With approval and support from the National Veterinary Research Institute, local authorities in each village were informed of the purpose of the study and provided permission to conduct the study. Consent was obtained from the head of each household. The participation was voluntary and confidential. Only households from which consent was obtained were kept in the survey.

Study participants were asked each month if someone had been attacked in their household since the last visit. An attack could be composed of several dog bites. If so, a questionnaire tested in the field prior to the study was completed. One questionnaire referred to a single attack and a single member of the family, but may describe several wounds. The questionnaires were completed in Khmer by four trained volunteer villagers in each village (Village Teams, VT). One questionnaire required 10 to 15 minutes for completion. For each bite event, the questionnaire documented information on the victim (age, sex, initials), on the biting dog (its status as owner or ownerless dog, location of bite occurrence, status regarding rabies suspicion, current state of the dog, cause of the attack), the injury (number of bites, anatomic location and severity, using the WHO Grading I-III [26]), wound management (basic rinsing, disinfection, rabies vaccine/tetanus vaccine, other, and cost of the treatment).

Each volunteer followed 20 to 22 households and received a small financial compensation on a monthly basis. Each month, the research team staff visited the VT, collected and checked the relevance of the questionnaires and answered potential questions from VT. In case of doubt on the answers, the attack victim was contacted directly by the research team for clarification. After 6 months, a meeting with participants provided feedback and a discussion session was organized.

5. Data analysis

Bite reports were recorded in Excel (Microsoft Corp., Redmond, Washington, USA) Statistical computations were done using R software (R Core Team (2013). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria). Chi-squared tests were performed to compare the anatomical location of bites in several age categories. Association with gender, village of origin and age were determined by univariate and multivariate

Poisson regression. Incidence calculation and comparison of attack incidence between villages and according to each variable were undertaken. Annualized incidence rates of attack were expressed per total number of person-years of risk. Rates' 95% confidence intervals were computed under Poisson law.

RESULTS

The population per village ranged from 507 inhabitants to 1,713 inhabitants for a total population of 4,512 inhabitants in the four villages. In all, 1,679 persons in 344 households agreed to participate to the study. The majority of the households were followed for 6 months (90.4%), some were followed only for 4 months (4.6%) and for 2 months (4.9%). Our data corresponds to the follow-up of 802.3 person-years (p-y), 409 p-y in women and 393.3 p-y in men. The mean age of the cohort was 24.9 ± 17.5 years (median 22; IQR 11-36; range 0 - 87).

Epidemiology of dog bites

There were 40 dog attacks which caused 43 bites (Table 1). The attacks incidence was estimated at 5 attacks/100 person-years (CI95%: 3.5 - 6.6). Of these, 82.5 % were severe (WHO Category III) with an estimated incidence of 4.1 attacks/100 person-years (CI95%: 2.8 -5.8). There were no fatal injuries.

Results per age group are shown in Table 2.There was a significant association between age groups and attack incidence with the most severely affected being children aged 1 to 5 years old (coef. = 1.08, p=0.007) and children aged 6 to 12 (coef= 0.76, p=0.04). There was no significant association between attack incidence and gender.

High heterogeneity in attack incidence among villages was also observed as shown in Table 2. The bite incidence per village, adjusted by age categories, was significantly lower in Boeng Mealea villlage (IRR= 0.49, p= 0.001) and lower in Tagoun village (IRR= 0.37, p= 0.001).

There was a significant difference in anatomical site of bites according to age. As shown in Table 3, children below ten were more likely to be bitten on the head, and less likely to be bitten at the lower limbs level. Overall, 58.8% of injuries were located on the head or upper limb for children aged below 10, against 7.7% for people over 10 years old ($\chi^2 = 10.9$, df = 1, $p<0.001$).

All attacking dogs were owner dogs. Only 52.5 % of dogs were available for monitoring after the interview: 35% were killed after the attack; one dog died after the attack and the remaining

escaped. The proportion of available dogs is significantly higher for provoked than for unprovoked attacks (Table 4).

There were more attacks documented in May, June and July than during the other months, as 65% of bites occurred during these 2.5 months. Only 1 attack was reported in August.

Injuries management and cost

Fifty percent of the attack victims of severe attacks rinsed their wound with water, 33 % used soap. 6% applied disinfectant on the wound. Twenty-two (75%) used a "traditional treatment", applying rice alone or with salt or herbs for 80%. Three people with only minor scratches also resorted to traditional treatment. Twelve people (36 % of Category III exposures) including five children under 10 years old received another treatment (pills, or injections). Among these, the average transportation cost was 0.9 USD (median=0.0, range: 0 -7.5 USD; IQR 0.0-1.46 USD). The average treatment cost was 7.6 USD (median=0.625 USD, Range= 0 - 45 USD; IQR 0.0 - 4.5 USD). Four people (12%) said they received at least one injection of rabies PEP in private clinics of district towns, although the real quality of the products could not be confirmed. They received respectively 1, 2, 3 and 5 injections each. No human deaths, whether of suspected rabies or otherwise, were reported during the study period.

DISCUSSION

To our knowledge, this prospective community-based survey on dog bite incidence is the first to be carried out in Cambodia and more generally in Southeast Asia. Our study documented an extremely high incidence of dog attacks with bite in a Cambodian rural population, at approximately 5 attacks per 100 person-years (95% CI [3.6-6.8]), far greater than the 3.5/100 p-y reported in Guatemala [27], 2.2 /100 p-y in Belgium [28], 1.7 reported in India [22], 1.5 in the USA [29] or 0.8 in Bhutan [30].

In context such as Cambodia where rabies circulates in dogs and where dog is the main reservoir of virus [31], the estimation of dog bite incidence is a precious proxy used for rabies incidence estimation [32]. It is a basic measure, fundamental as preliminary data and as a monitoring tool for controlling the effectiveness of mitigating measures implemented at country level [33]. Most studies conducted worldwide on dog bites incidence were hospital or school-based [34–38]. Very

little has been published on community-based calculations of dog bite incidence. Some of them are retrospective studies, and may lead to an important memory bias [39,40].

In our study, over 80 % of the wounds were WHO Category III (punctured skin and blood effusion) [26], contrasting with the results of a Netherland computer-assisted community-based survey which found most wounds to be superficial [41]. Our study also shows the vulnerability of children: nearly 60% of victims with severe dog bites are aged below 17, confirming data from a hospital-based study in Thailand [42]. In our study, the most at-risk age group are children aged 1-5 years, with an overall attack incidence of 11.84/100 p-y (95% CI [5.42- 22.48]), and up to more than 20/100 p-y, in one of the villages (Oleu village, which raises many dogs). To our knowledge, no higher incidence has been reported thus far in the literature.

Due to their height, children also present the most serious wounds and the most-at risk injuries in terms of rabies inoculation: they are significantly more often located on the head, face, and upper limb location compared to adults, contrary to what was shown in Guatemala [27] but similarly to findings of a study in Austria [43].

Regarding wound management, only eight persons among the 33 victims with Category III exposure visited a doctor or a medical center. This confirms that access to medical facilities and timely and adequate rabies PEP remains extremely challenging for rural populations. One-third of the victims with Category III exposures underwent appropriate basic management (including washing wound with soap), and half used only water. This is lower than the percentages found in a study (66%) conducted in eight Asian countries [44] or India [45] which found that herbal or indigenous treatment were used by a majority of victims, as in our study.

The proportion of dogs killed by the owner after the bite event prevented us from calculating a severe rabid dog bite incidence. Putting the dog down is an obvious way to prevent the community from rabies and bite recurrence, reflecting the widespread fear of bites and rabies in Cambodian communities, even after a provoked attack. It also reflects the fact that dog meat is increasingly consumed or sold in Cambodia [44]. By contrast with studies in India [20], or Thailand [46], no stray dog was the cause of attacks, and no presence of stray dogs was reported by the Village Teams. Most attacks occurred in private places, involved the household dog, and most victims had provoked the dog before being attacked (by disturbing it while eating, or feeding puppies…). These data suggest that most attacks could be avoided by educating children and parents, raising

awareness on dog ownership responsibility and children supervision. As no wildlife species except bats have been identified as a rabies reservoir in Southeast Asia, these preliminary results suggest that owner dog vaccination would effectively eliminate rabies in owner dog populations and reduce dog bite incidence [33].

The association of bites with socio-economic status was raised by Indian studies [21]. In the three villages with the highest bite incidence, dog raising and trade is a non-negligible activity, according to the village team. This activity is still not well documented to date in Cambodia.
The high proportion of bites occurring between May and July suggests the existence of bite seasonality. This is particularly important for the organization of an eventual future dog vaccination campaign in the choice of the month it should be done [47]. The correspondence with heat in females for example was mentioned by the village teams. Whereas in constant conditions dogs don't show any reproduction seasonality, the increase of feeding resources available during one season could result in a grouped induction of heat in females when animals are under nourished. The role of other external factors could be investigated: seasonal increases in farmer families' work load leading to a decrease of children supervision, seasonal migratory phenomena which could facilitate dog fights, etc. This should be confirmed on a bigger study group and for at least one year duration.

Finally, bite incidence is one of the parameters used for rabies incidence estimation, using a model first developed in Tanzania and adapted to other settings [30,48]. These models are based on three main measures: bite incidence; the proportion of biting dogs positive for rabies; and the probabilities of contracting rabies after a dog bite according to anatomical site. Thus far, this model has used hospital-based data, for reasons of availability and convenience. In a setting like Cambodia where rabies is endemic, where people have a very limited access to health facilities and where scarce resources exist for out-of-pocket medical expenses [18], such a methodology might lead to a highly biased estimate of rabies incidence. Using this method, IPC epidemiologists estimated method rabies incidence in Phnom Penh [17]. Data from the rural areas, however, are missing to get a more accurate estimation of rabies incidence in Cambodia and to better understand rabies epidemiology in the Kingdom. This is what we proposed to initiate through this study. In such settings, the model should be based on community-based data. The incidence estimated by the present study is significantly higher than that estimated by modeling based on Phnom Penh

data [17]. This may be due to the fact that the incidence may be higher in rural areas, especially at those times of the year. It may also be that a study conducted on a smaller geographic area may provide specific estimates ta the local level. It is also very likely that since 2007 the Cambodian population has grown and so has the canine population. Furthermore, dogs are increasingly raised for sale or butchering in Cambodia and neighboring Vietnam, an industry which was very limited some years ago. To our knowledge, our prospective study is one of the very few conducted in rural communities, and the only one carried out in Southeast Asia. The estimated bite incidence in our study is higher than all published figures to date [31]. Further community-based studies including dog heads analyses, combined with the present data, would allow building a relevant model for rabies estimation in rural areas and reevaluating the rabies burden in Cambodia. This could help mobilize national policymakers to propose community interventions for the control and the elimination of canine - and therefore human - rabies in Cambodia as they strive to meet their commitment to eliminate canine-mediated rabies by 2030 [49].

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Figure 1: Map of study area, localization of the four study villages in Siem Reap province, Cambodia.

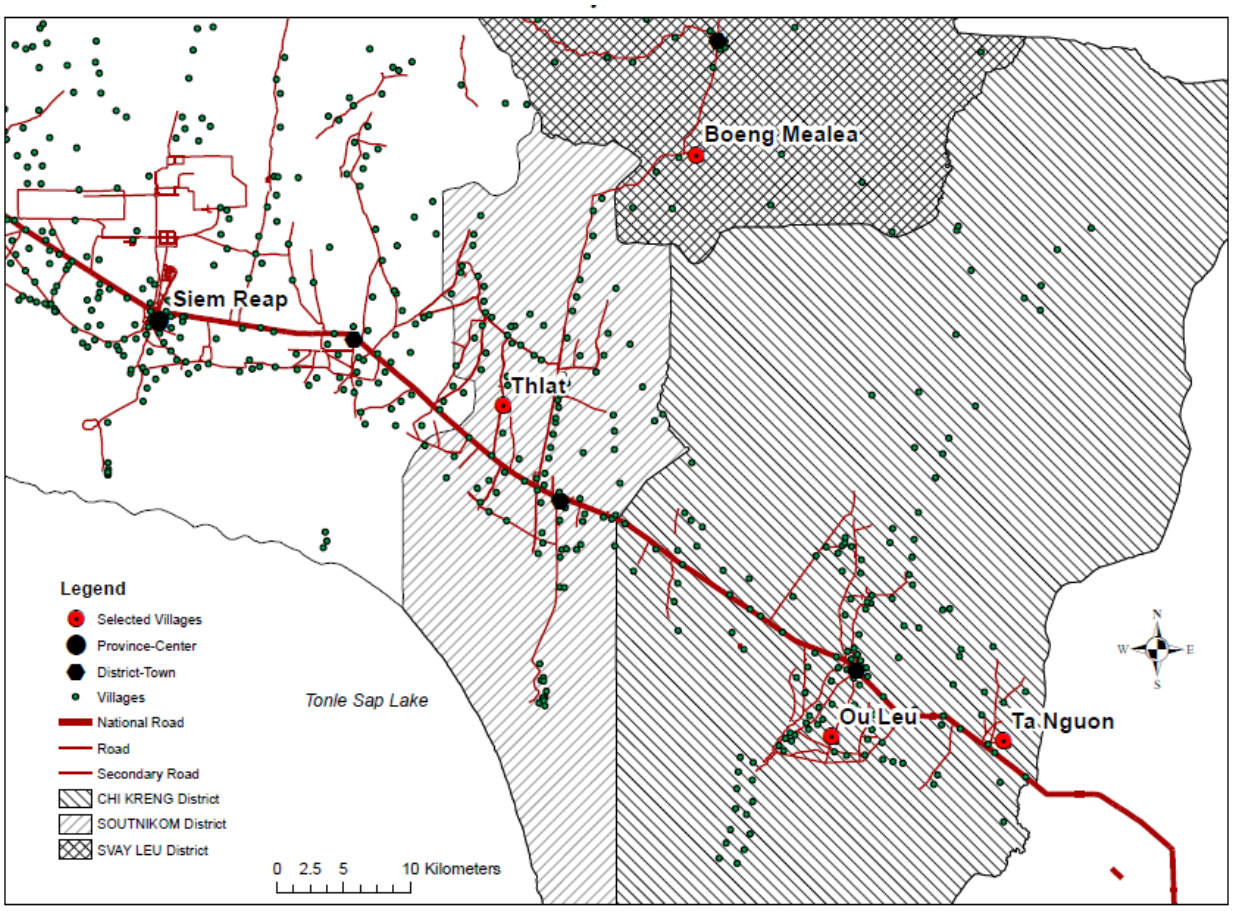

Table 1: Attacks and severe attacks incidence per age categories.

	Number of attacks	Number of severe attacks	Number of pers.year	Attacks incidence 95% CI		Severe attacks incidence 95% CI	
< 1 year old	0	0	15.5	0.0	[0- 24.8]	0.0	[0- 24.8]
1 to 5 years old	9	9	76.0	11.8	[5.4- 22.5]	11.8	[5.4- 22.5]
6 to 12 years old	10	8	126.2	7.9	[3.8- 14.6]	6.3	[2.7- 12.5]
13 to 17 years old	3	2	88.3	3.4	[0.7-9.9]	2.3	[0.3- 8.2]
≥ 18 years old	18	14	496.3	3.7	[2.2- 5.8]	2.9	[1.6- 4.8]
Global	40	33	802.3	5	[3.5 - 6.6]	4.1	[2.8 -5.8]

Table 2. Poisson regression of adjusted incidence risk ratio of attacks.

	IRR	**95% CI**	**p**
Age category (>18 years old)			
>18 years old	1		
13-18 years old	1.14	[0.71-1.83]	0.58
6-12 years old	3.31	[2.37-4.62]	0.001
1-5 years old	2.47	[2.60-3.77]	0.001
Village			
Oleu	1		
Thlat	1.02	[0.47-2.21]	0.96
Boeng Mealea	0.49	[0.39-0.62]	0.001
Tagoun	0.37	[0.30-0.46]	0.001

Table 3. Anatomical site of dog bites, by age (≤ or > 10 years old) and gender.

	≤ 10 years old	> 10 years old	p	Female	Male	p	Total
Anatomical location of wounds							
Lower limb (%)	7 (41.2)	23 (92.3)	< **0.001**	14 (63.6)	16 (81)	0.552	30 (72.1)
Upper limb (%)	4 (29.4)	2 (7.7)	0.143	4 (22.7)	2 (9.5)	0.448	6 (16.3)
Head (%)	4 (29.4)	0 (0)	**0.014**	2 (13.6)	2 (9.5)	1	4 (11.6)
Attack place							
private place (%)	12 (80)	17 (68)	0.65	15 (71.4)	14 (73.7)	1	29 (72.5)
public place (%)	3 (20)	8 (32)	0.65	6 (28.6)	5 (26.3)	1	11 (27.5)
Dog							
- dog of the house (%)	3 (20)	5 (20)	1	5 (23.8)	3 (15.8)	0.81	8 (20)
- other owner dog (%)	12 (80)	19 (76)	1	16 (76.2)	15 (78.9)	1	31 (77.5)
- stray dog (%)	0 (0)	0 (0)	1	0 (0)	0 (0)	1	0 (0)
- unidentified (%)	0 (0)	1 (4)	1	0 (0)	1 (5.3)	0.96	1(2.5)
Attack circumstances							
- provoked (%)	9 (60)	8 (32)	0.16	12 (57.1)	11 (57.9)	1	23 (57.5)
-unprovoked (%)	6 (40)	17 (68)	0.16	9 (42.9)	8 (42.1)	1	17 (42.5)

Table 4. Dog management after attack

Dog management	Global	Provoked attack	Unprovoked attack
- killed	14 (35)	3 (17.6)	11 (47.8)
- died by itself	1(2.5)	1 (5.9)	0 (0.0)
- escaped	2(5)	0 (0.0)	2 (8.7)
- observed, normal	21(52.5)	13 (76.5)	8 (34.8)
- don't know	2 (5)	0 (0.0)	2 (8.7)