

Prophylactic treatment abandonment in people bitten by suspected rabid animals, El Salvador, 2013-2017

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ABSTRACT

Introduction: Around the world 60,000 people die from rabies each year. The main form of exposure to rabies is by the bite of animals infected with the virus. More than 20,000 cases of rabies-transmitting animal bites are reported each year, in El Salvador, a country located in Central America. People exposed should be managed with rabies prophylaxis. **Objective:** To determine the abandonment of post-exposure prophylaxis (PEP) cumulative incidence (CI) in humans bitten by suspected rabid animals in El Salvador from 2013 to 2017. **Methodology:** This is an ecological study based on the cases of bites by suspected rabid animals reported between 2013 and 2017 in the public health system of El Salvador. Descriptive and correlation analysis was performed using Statistical Package for the Social Sciences (SPSS) version 24. The municipality CI, expressed per 100,000 inhabitants. **Results:** The national CI of abandonment PEP in humans bitten by suspected rabid animals was $25.6 \times 100,000$ inhabitants. Simple bivariate correlation analysis shows that the departments with the highest CI of bites caused by cats, wild animals, and bites on the neck ($R^2 = 0.99$ $P < 0.05$) are mostly associated with dropping out of the PEP. **Conclusion:** In El Salvador, the abandonment CI of PEP is lower than other countries, however, bites by rabid suspected animal are frequent, this represents a public health problem due to the presence of the rabies virus in wild animals and the high lethality of the disease. Municipalities where head bites are common are the most related to the abandonment of PEP.

Keywords: El Salvador, human bite, patient abandonment, post-exposure prophylaxis, rabies

Introduction

Cases of bites from animals suspected of being rabid are a burden on primary care, mainly in low income countries.^[1] Around 60,000 people die from rabies each year worldwide, most of them occur in Africa and Asia where the access to health attention is limited.^[1,2] Rabies is a viral zoonosis considered a neglected tropical disease, prevalent in developing countries and, associated with poverty and lack of adequate sanitary conditions.^[1] Rabies is an infectious disease with the highest case-fatality ratio; once clinical signs appear, the disease is almost inevitably fatal.^[3]

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Rabies deaths are responsible for 3.7 million disability-adjusted life years each year.^[4] Between January 2015 and September 2021, 11 countries from Latin America reported cases of rabies (Argentina, Bolivia, Brazil, Colombia, Cuba, Dominican Republic, Guatemala, Haiti, Mexico, Peru, and Venezuela).^[5] However, the number of cases and human deaths have decreased by about 98%, since a regional program for the control of rabies in dogs was implemented in 1983.^[4,6]

The main form of exposure to rabies is by the biting of animals infected with the virus.^[1] According to the World Health Organization (WHO), 99% of rabies cases are related to dog bites.^[1,7] Between 2013 and 2016, the Global Alliance for Rabies Control reported a total of 10 deaths from rabies related to dog bites and 23 due to rabies in other species in Latin America.^[4]

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In El Salvador, rabies is controlled in domestic animals through vaccination, but it is considered as a health hazard because the virus is present in the environment through wild animals, the rabies virus has been isolated from hematophagous and insectivorous bat, and elimination of bat rabies is not feasible.^[4] Human rabies is currently under control, an average of ten cases per year was reported between 1980 and 1998, with a reduction of approximately three cases per year between 1999 and 2008, no more cases have been recorded since then.^[7] Between 2005 and 2017, more than 20,000 cases of rabies-transmitting animal bites per year were reported, while canine and feline rabies cases remain under control and have been reduced by up to 90%.^[7]

The Ministry of Health of El Salvador carries out different preventive measures that consist of domestic animal vaccination and the management of animal bite cases.^[8] Every person who suffers an injury due to rabies transmitting animals has access to primary care, where it is treated immediately, to identify the conditions in which the aggression occurred, to evaluate wound characteristics, and to know the health condition of the aggressor animal. Severe wounds require rabies post-exposure prophylaxis (PEP), that consists of homologous rabies serum plus four doses of cell culture rabies vaccine, the abandonment of PEP represents a risk to develop human rabies, for this reason the aim of this study is to determine the abandonment of PEP cumulative incidence (CI) in humans bitten by suspected rabid animals in El Salvador between 2013 and 2017.

Methodology

This is an ecological study carried out in El Salvador, a country located in Central America, it has 21,041 km² and is divided into 262 municipalities. El Salvador borders Guatemala to the west, Honduras to the north and east, the Gulf of Fonseca to the southeast and the Pacific Ocean to the south. This study was approved by National Institute of Health Ethics Committee (CEINS Spanish acronym) on September 27, 2018.

The database used in this study includes people exposed to rabies through bites from suspected rabies animals from all over the country recorded in the Statistical System of Service Production (Secretaría de Educación Pública [SEPS] Spanish acronym) from the Ministry of Health from El Salvador between January 1, 2013 and December 31, 2017. The database includes 109,932 cases of suspected rabid animal bites. The variables included in the analysis were municipality, years, anatomical bite site, bite severity, and PEP. All variables in the database were grouped by municipality. According to the Salvadoran technical guidelines for prevention and control of rabies,^[9] the following anatomical bite sites considered as severe were: “head, face, neck, genitals, hands, fingertips, multi-site, popliteal fossa, mucous membranes and chiropter bite” and as mild were the following, “upper limb, lower limb, trunk and foot.” The vaccination schedule suspended due to medical indication is considered as a complete treatment.

A descriptive analysis was performed using the Statistical Package for Social Sciences (SPSS) version 24. The total number of bites, minor and severe bites, and the number of PEPs started and completed were distributed over time by month. Municipality CI, expressed per 100,000 inhabitants, was calculated using the population projection proposed by Dirección General de Estadística y Censos (DIGESTYC Spanish acronym).^[10] A simple correlation analysis was performed to determine in a bivariate way the relationship of the independent variables (anatomical bite site) with the dependent variable (abandonment of PEP). The SPSS Automatic Linear Modeling component of the program was used to determine the variables that contribute to the prediction of the dependent variable through the Step Analysis Method. Once these variables were determined, the linear regression module was run to obtain the coefficients of the model.

In addition, the spatial distribution of the municipality CIs of bites by animals suspected of being rabid was carried out. The municipality CIs were classified by Jenks Natural Breaks analysis, which identifies the best group with similar values and the differences between classes. Three groups of homogeneous values were created, then a grayscale was created to represent each group. Finally, a choropleth map was created through the Quantam Geographical Information System (QGIS) 3.0 program.

Results

Between 2013 and 2017, 109,932 cases of bites from animals suspected of being rabid were recorded, of which almost a quarter (24%) occurred in 2013 [Table 1]. Mild bites showed a decrease between 2013 and 2017, but severe bites showed a similar number of cases registered each year during the study period. Overall, 27.4% of bites were severe, of this, almost half (46.2%) were on hands and 24% were facial [Table 1].

The majority of bites were caused by dogs (89.6%), 8.1% by cats, and the rest by chiropter (0.9%), wild animals (1%), and other unspecified animals (0.4%). A total of 33,060 bitten people were managed with vaccination, of which, 63% finished the PEPs treatment, 32% was referred to another establishment for further vaccination and 5% abandoned treatment [Table 1].

Overall, cases of bites from animals suspected of having rabies decreased from 2,239 in January 2013 to 1,578 in December 2017. The mild and severe bites have a similar pattern between months. The pattern of decrease in severe bite is less than mild bites or total bites. The amount of post-exposure treatments started is higher than the amount of treatment finished. On an average 127 persons dropped out of the PEP each month [Figure 1].

The national CI of bites by animals suspected of being rabid between 2013 and 2017 was $1,720.6 \times 100,000$ inhabitants. The severe bite CI was $471.6 \times 100,000$ inhabitants. All municipalities reported cases of bites by suspected rabid animals, but 80 municipalities showed a higher CI than the national CI. The most affected municipality was Perquin, with a CI of $7,132.7 \times 100,000$

Table 1: Types of bite and exit condition of bitten patients per year, El Salvador, 2013-2017

Variable	2013		2014		2015		2016		2017		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
Total bites	26,464	24	22,630	20.6	20,422	18.6	20,491	18.6	19,925	18.1	109,932	100
Bite severity												
Mild bites	19,629	74.2	16,965	75.0	14,692	71.9	14,617	71.3	13,900	69.8	79,803	72.6
Severe bites	6,835	25.8	5,665	25	5,730	28.1	5,874	28.7	6,025	30.2	30,129	27.4
Mild bites												
Upper extremities bite	4,940	25.2	4,420	26.1	3,814	26.0	4,048	27.7	3,969	28.6	21,191	26.6
Lower extremities bite	12,368	63.0	10,707	63.1	9,338	63.6	9,006	61.6	8,419	60.6	49,838	62.5
Trunk bite	1,314	6.7	984	5.8	788	5.4	796	5.4	767	5.5	4,649	5.8
Foot bite	1,007	5.1	854	5.0	752	5.1	767	5.2	745	5.4	4,125	5.2
Severe bites												
Head bite	339	5.0	231	4.1	244	4.3	263	4.5	297	4.9	1,374	4.6
Face bite	1,612	23.6	1,382	24.4	1,464	25.5	1,441	24.5	1,343	22.3	7,242	24.0
Neck bite	90	1.3	63	1.1	65	1.1	69	1.2	53	0.9	340	1.1
Bite in the genitals	131	1.9	122	2.2	106	1.8	122	2.1	104	1.7	585	1.9
Hand bite	3,261	47.7	2,564	45.3	2,550	44.5	2,611	44.5	2,919	48.4	13,905	46.2
Bite on the tip of the toes	177	2.6	305	5.4	300	5.2	321	5.5	260	4.3	1,363	4.5
Multi-site bite	691	10.1	542	9.6	519	9.1	610	10.4	612	10.2	2,974	9.9
Bite in the popliteal fossa	339	5.0	281	5.0	304	5.3	285	4.9	271	4.5	1,480	4.9
Bite in the mucous membranes	87	1.3	68	1.2	98	1.7	59	1.0	53	0.9	365	1.2
Chiropter bite in another part of the body	108	1.6	107	1.9	80	1.4	93	1.6	113	1.9	501	1.7
Exit condition												
PEP ended	6,563	63.2	3,717	57.9	3,654	58.6	5,088	69.6	13,398	93.8	20,835	63.0
Abandonment of treatment	227	2.2	149	2.3	127	2.0	244	3.3	891	6.2	1,638	5.0
Referral to another facility to continue treatment	3,595	34.6	2,552	39.8	2,457	39.4	1,983	27.1	ND	ND	10,587	32.0

ND: No data

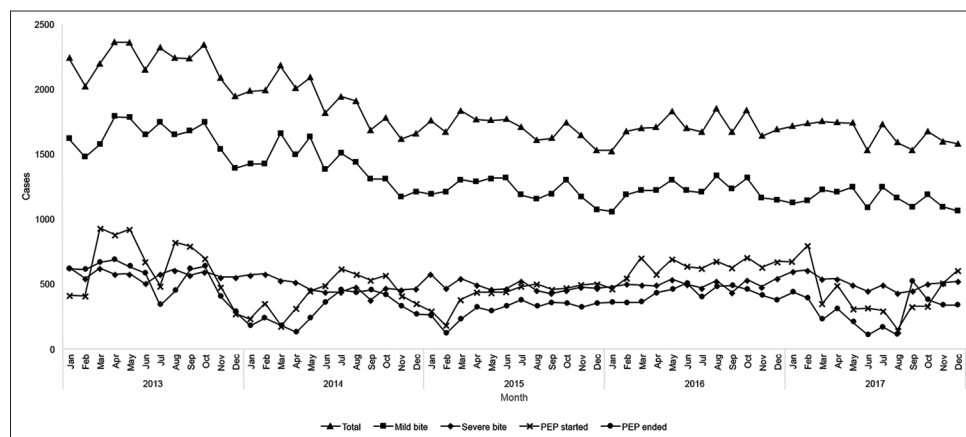


Figure 1: Distribution of cases of mild and severe bites, start and ended PEP per month in El Salvador between 2013 and 2017

inhabitants and the least affected was San Luis de la Reina, with a CI of $211.7 \times 100,000$ inhabitants [Table 2].

The spatial analysis shows ten municipalities with the highest CI of bites by rabies transmitting animals. Most of them are grouped in the eastern zone, in Perquin, Pasaquina, and Nueva Guadalupe municipalities. In the north is Azacualpa municipality with a high CI and in the west side Nahuilingo while San Salvador, which is located in the center of the country [Figure 2 and Table 2].

The national CI of complete and abandonment PEP in humans bitten by suspected rabid animals were $507.4 \times 100,000$ inhabitants

and $25.6 \times 100,000$ inhabitants, respectively. The average PEP compliance municipality CI is $296.6 \times 100,000$ inhabitants (SD $145 \times 100,000$), 22% of municipalities have a complete PEP CI higher than the average CI. The average treatment abandonment municipality CI is $13.8 \times 100,000$ inhabitants (SD $79.2 \times 100,000$ inhabitants). The average abandonment CI is exceeded in 23% of municipalities.

The municipalities with the highest PEP compliance CI [Table 2] are not the same municipalities with the highest CI of bite. Panchimalco ($13,193.2 \times 100,000$ inhabitants), El Congo ($12,624 \times 100,000$ inhabitants), and Acajutla ($1,617.5 \times 100,000$

inhabitants) have the highest PEP ended, however Acajutla has the highest PEP abandonment CI (1,259.7 × 100,000 inhabitants), followed by Bolívar (159.2 × 100,000 inhabitants) and Perquin (82.3 × 100,000 inhabitants). The municipality of Las Flores has a zero PEP compliance CI and an abandonment CI of 75.6 × 100,000 inhabitants, like the municipality of Arcatao, has a zero PEP compliance CI and an abandonment CI of 36 × 100,000 inhabitants.

Simple bivariate correlation analysis shows that the PEP abandonment CI is related to the CI of bites caused by cats, wild animals, and the CI of bites caused on the neck ($R^2 = 0.99$) [Table 3]. The linear regression model applied selected three independent variables (bite CI caused by cats, wild animals, and the CI of bites caused on the neck). The correlation between the real values of abandonment and the predicted values according to the linear regression model is dispersed.

$$Y(X_1, X_2, X_3) = 1.888 - 4.786(X_1) + 0.260(X_2) + 1.993(X_3)$$

Table 2: Municipalities with the highest CI of bites, compliance, and PEP abandonment, El Salvador, 2013-2017

Municipality	Municipality CI of bite*	PEP ended CI*	Abandonment PEP CI*
Perquin	7,132.7	219.5	82.3
Pasaquina	6,172.5	0.0	0
Azacualpa	5,738.9	0.0	0
Nahuilingo	4,504.3	299.7	8.8
San Salvador	4,404	1,042.9	50.5
Nueva Guadalupe	3,976.4	412.0	0
Mercedes de la Ceiba	3,617.5	471.8	0
Dulce Nombre de Maria	3,401.8	64.6	0
San Emigdio	3,371	132.2	0
Aguilares	3,313.2	702.4	33.9

*All CI are expressed per 100,000 inhabitants.

The correlation coefficient (r) for the CI of bites caused by cats, wild animals and the CI of bites located on the neck, and PEP abandonment CI was 0.99, was statistically significant ($P < 0.05$), although it means that the departments with the highest CI of bites caused by cats, wild animals, and bites caused on the neck are mostly associated with dropping out of the PEP.

Discussion

This study shows that the departments that show a high CI of bites caused by cats, wild animals, and bites on the neck are more related to a high CI of PEP abandonment. El Salvador has a surveillance, prevention, and treatment plan for rabies-transmitting animal bites. In other countries PEP is the second most expensive treatment, however in El Salvador it is free.^[11,12] The abandonment of the treatment in El Salvador could be related to ignorance of risks, irrational fear of needles,^[13,14] and cultural and religious beliefs.^[15]

Ignorance of the risk of developing rabies may be related to the lack of educational interventions by primary care physicians, who are the first to care for the victims of rabies-transmitting animal bites.^[16] However, healthcare providers make mistakes when they misclassify a wound or fail to educate patients properly^[17] or because they do not have the time to carry out the education task.^[15] In El Salvador, physicians have to attend a large number of patients in a short period of time, which contributes to the failure of measures to promote adherence.

The PEP abandonment CI in people who were bitten by rabies-transmitting animals in El Salvador is lower than that reported in other countries where rabies deaths are involved,^[18-20] however, it does not represent the absence of the risk of rabies cases.

Bites on the head and neck are considered as serious bites^[8] and are more frequent in children^[21] as the short stature makes it easier for the animal to cause the bite in this area. This type of bite requires intervention, antibiotics,^[22] and PEP. Although

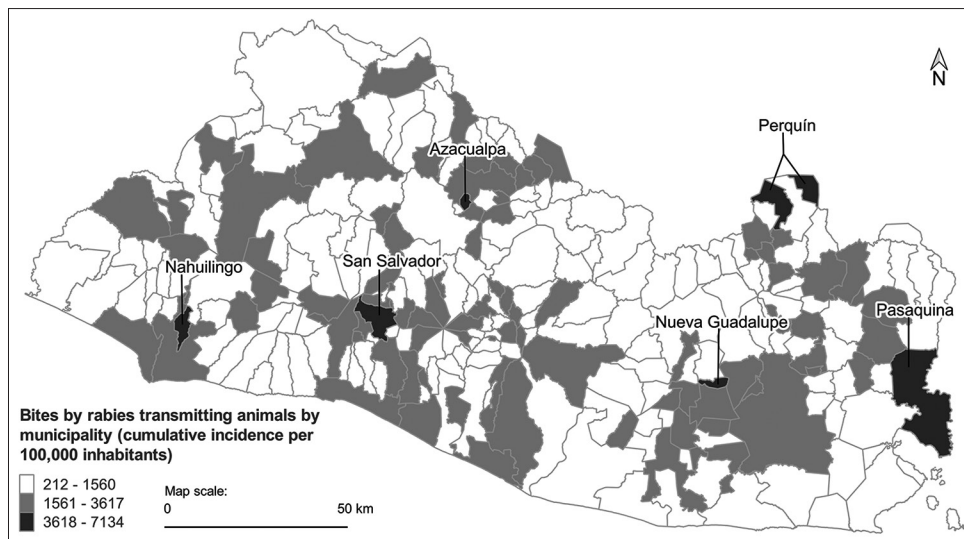


Figure 2: Bites by rabies transmitting animals by municipality (CI per 100,000 inhabitants)

Table 3: Animal causing the bite per year, El Salvador, 2013-2017

Variable	2013		2014		2015		2016		2017		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
Dog	23,868	90.2	20,436	90.3	18,371	90.0	18,264	89.1	17,520	87.9	98,459	89.6
Cat	1,874	7.1	1,679	7.4	1,608	7.9	1,818	8.9	1,975	9.9	8,954	8.1
Chiropter	300	1.1	194	0.9	203	1.0	158	0.8	152	0.8	1,007	0.9
Wild animals	286	1.1	249	1.1	161	0.8	184	0.9	207	1.0	1,087	1.0
Other animals	136	0.5	72	0.3	79	0.4	67	0.3	71	0.4	425	0.4

the frequency of most reported mild bites decreased over time. This may be because people who suffer minor injuries caused by a bite do not seek treatment as they believe the injury does not pose a risk.^[23,24] A 10-year study in Iran shows that most people with mild bites do not seek medical attention.^[25] However, even if the bite is classified as mild, the victim should seek medical help because of the risk of becoming infected with the rabies virus and the severity involved.^[3,4,26]

The cases registered in El Salvador per year is similar to the number of cases reported in other countries.^[11,27,28] A 5-year study in Bangladesh reported 149,439 cases of rabies transmitting animal bites.^[28] The CI of bites by animals suspected of being rabid registered in El Salvador is higher than that reported in other countries, for example, the one shown in a 10-year study in a region of Iran larger than El Salvador reported a CI of cases of bite by rabies transmitting animals of $223.23 \times 100,000$ inhabitants.^[29] Another 5-year study, conducted in a province of Iran, reached to $195 \times 100,000$ inhabitants in 2014.^[30] In general, cases of rabies transmitting animal bites show an upward trend, however, in the last 3 years, the percentages of reported cases remain constant. The upward trend may be influenced by the increase in cases between 2013 and 2014.

The CI identified in this study reaches similar values to those of other infectious diseases, for example, the maximum CI of rabies transmitting animal bites exceeds the rate of diarrhea and gastroenteritis in El Salvador.^[31] In addition, a 9-year investigation conducted in an area of Eastern Europe reports an CI of $470.9 \times 100,000$ inhabitants, lower than that found in this study.^[32]

Even though severe bites represented a small quantity, there is a tendency of increase, that could be related to increasing consultations, that allow primary care physician to identify a real diagnosis that is classified correctly. Some studies have shown that serious injuries occur more frequently at home, mainly in animal owners,^[14,25,33] who do not seek medical attention because they believe the injury is not serious or because the animal may be euthanized,^[4] risking a bite injury that involves not only the possibility of rabies infection but also local bacterial infection and anatomical lesions that may result in amputation.^[21]

The bites recorded in El Salvador have been caused mainly by dogs and cats. Similar findings were obtained in Brazil,^[11] Senegal,^[14] Bhutan,^[1] and the west region of Cameroon.^[12] In El Salvador, the density of dogs is 59.6 dogs per km², which

is considered an overpopulation of dogs compared with other studies^[34] that report about 14 dogs per km². This represents an increased risk of rabies transmitting animal bites^[35] and an overload for the public health system.

In El Salvador, raising dogs as guardians dogs is not common in urban areas;^[36] but dogs act aggressively against strangers or to protect its territory or its owners.^[37] However, other studies have described that the prolonged time of animals away from home or the fear of strangers^[38] are the main risk factors for animals attacking people. Other risk factors described are the breed of the animal, age under 14 years old, or keeping it chained.^[39] In addition, the implementation of effective vaccination campaigns against feline and canine anti-rabies has very profitable results.^[40]

Some factors are related to the incubation period such the proximity of innervation to the wound and its depth because of the amount of virus inoculated.^[41] In relation to this, Salvadoran technical guidelines for the prevention and control of rabies indicate that lesions must be treated according to the characteristics of the aggressor animal, how the aggression occurred, and the location of the wound, and not only by the size of the wound, therefore, lesions occurring in the popliteal region, on the hands, fingers and face should be classified as severe and treated as immediate with homologous anti-rabies serum and cell-culture-derived vaccines.^[42] According to the anatomical site, most of the recorded bites occurred in the lower extremities, followed by the upper extremities and the face.^[43]

The spatial distribution of the CI of bites by rabies transmitting animals shows that the municipalities with the highest CI of rabies transmitting animal population are those with a high rurality index^[44] like other studies have described.^[30]

The data presented in this study should be treated with caution, as they only include the cases registered in the public health system; it is likely that by including the cases registered in other services the prevalence of rabies transmitting animal bites may increase. Although there have been no reports of human rabies in El Salvador since 2009, injuries caused by rabies transmitting animals are frequent. Gender and age are also not included in the analysis, but some studies have identified that males and children^[45,46] are the most common victims of bites.^[28] The design of this study does not allow establishing an individual relationship between the variables that influence treatment abandonment, therefore the relationship found in department with the highest

CI of head bites and treatment abandonment should be taken as a first approach to the problem.

An important strategy is to monitor the interaction of children and dogs to avoid defensive behavior of animals due to the provocation of minors or aggressive behavior due to the stress generated.^[47] Some studies also show that changes in animal behavior should be identified to avoid situations that may generate anxiety or insecurity in animals, such as confinement, provocation by children and health problems, which may lead to aggressive behavior in the animal.^[48] Although this is established in the law for the protection and promotion of the welfare of companion animals in El Salvador,^[49] it is necessary to strengthen compliance with this law. Other specific studies that educate the population about the risks of suffering a biting effect is that they consult in a timely manner and receive adequate treatment.^[48] Finally, canine and feline density control is another strategy for rabies prevention,^[50] otherwise, the canine birth rate may be higher than the mortality rate, as shown in a study conducted in the north of the Australian Peninsula.^[51] Surgical sterilization is the most commonly used technique, which also helps to maintain better control of anti-rabies vaccination, however, this procedure is only performed by non-governmental or private institutions.^[51]

Conclusion

In El Salvador, the abandonment CI of PEP is lower than other countries, however, bites by rabid suspected animal are frequent, this represents a public health problem due to the rabies virus that is present in wild animals and the high lethality of the disease. Which implies that those who drop out the PEP may die. The municipalities with the highest frequency of head bites are related to the abandonment of PEP. The highest abandonment CI occurs especially in the municipalities of Acajutla and Bolívar. In the recent years, the number of serious bites has increased.

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Conflicts of interest

There are no conflicts of interest.

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