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Cutaneous Leishmaniasis Associated With the Level of Poverty of the Andean Rural Population: A Five-Year Single-Center Study

Jeel Moya-Salazar [1,2]*, Israel A Pasco [3], Betsy Cañari [2], Hans Contreras-Pulache [2**]

[1] Hospital Nacional Docente Madre Niño San Bartolomé, Lima, PERU
[2] Faculties of Health Science, Universidad Norbert Wiener, Lima, PERU
[3] Hospital General Celendin, Cajamarca, PERU
*Corresponding Author: jeel.moya@gmail.com
**Corresponding Author: hans.contreras@uwiener.edu.pe

ARTICLE INFO	ABSTRACT
	Introduction: Leishmaniasis is a disease that dramatically afflicts American populations as it is related to socioeconomic factors such as poverty. We aimed to determine the incidence of Leishmaniasis associated with poverty level among patients admitted to the Celendin Regional Hospital in Cajamarca, Peru. **Materials and Methods:** This single-center, retrospective study included 250 peri-urban and rural patients (mean 29.3±20 years) diagnosed with leishmaniasis during 2015-2020. A collection card was used to extract the clinical, and epidemiological information. We used the 2013 Fondo de Cooperación para el Desarrollo Social (FONCODES) to estimate the level of poverty in Cajamarca. **Results:** Of total, 156 (37.6%) were positive for cutaneous leishmaniasis and the most common lesions were the upper limbs (110 [44%]) and the head (24 [9.6%]). The most frequent place origin of patients weres Celendín (54 [21.6%]), Huasmin (58 [23.2%]), and Utco (13 [5.2%]) district. The highest incidence rate of Leishmaniasis was found in the districts of Utco (0.93 × 1000 inhabitants) and Huasmin (0.41 × 1000 inhabitants). We found that the poverty rate (p = 0.002) and extreme poverty rate (p = 0.001) were positively associated with the incidence of Leishmaniasis. The most affected age group were those <18 years-old (61 [62.2%]) (p = 0.029). **Conclusions:** We determined a significant association between poverty and leishmaniasis cases in the Peruvian Andean population. **Keywords:** cutaneous leishmaniasis, poverty, environmental, economics, Peru

INTRODUCTION

Leishmaniasis is a zoonotic and anthroponotic disease caused by the protozoa of the *Leishmania* genus, which has three main forms: cutaneous, mucocutaneous, and visceral, the latter being highly fatal in 95% of cases; for this reason, this disease is considered a severe Public Health problem worldwide [1].

This disease, which is subject to emergencies and re-emergencies, is affected by social determinants and is transmitted by the bite of an infected hematophagous dipteran of the genus *Phlebotomus* (Europe, Africa, and Asia) and *Lutzomyia* (America) [2]. According to the World Health Organization (WHO), Leishmaniasis has a worldwide distribution affecting specific regions mainly in populations with drastic risk factors such as migration, malnutrition, socioeconomic determinants, climate change, and urbanization [3].

The social and economic disparities have caused 70-75% of cases to occur in 10 countries worldwide. In the Americas, 96% of cutaneous leishmaniasis cases are concentrated in Brazil and during the last 18 years 1,028,054 cases (2001-2019) of cutaneous and visceral leishmaniasis have been reported in 17/18 countries. After Brazil and Colombia, Peru has been the country with the highest infections for 2019 with 5,349 cases despite its trend in the reduction in cases [4].

For Peru, the National Center for Epidemiology, Prevention, and Control of Diseases has shown for the last five years that cases have decreased from 5,999 for 2015 to 4,688 for 2020, with an average of 7,264 cases per year, of which more than 94% were cutaneous leishmaniasis [5,6]. This reduction is due to latent government effort, the detection, surveillance, and control systems of Leishmaniasis are also subject to the health support of each Peruvian region, which is why cities such as Junin, Pasco, and Cajamarca (regions of the Andes), and Amazonas, Ucayali, and Loreto (regions of the Peruvian jungle) are those that concentrate the highest incidence of cases since they present high-indicators of poverty and sanitary difficulties that reduce the effectiveness of the strategies of control [7,8].

In this context, where the pathology of poverty allows the recrudescence of Leishmaniasis, it is necessary to understand, which epidemic areas have greater cases, where the spread of the disease is larger, which previously free areas are presenting emergency cases, and what causes could be attributable (i.e.,

migration, climate change, tourism, military activities, occupations, etc.). The literature is not yet clear on how poverty indicators are related to the maintenance and increase of cases in endemic and free areas in Peru.

The objective of this study was to determine the incidence of Leishmaniasis associated with poverty level among rural Andean patients admitted to the Celendin Regional Hospital in Cajamarca, Peru.

MATERIALS AND METHODS

Design and Patients

A five-year, single-center, retrospective study was designed (2015-2020) with a non-probabilistic sampling. We included the medical records of all patients diagnosed with leishmaniasis treated at the Celendin Regional Hospital, in Cajamarca (2750 meters above sea level). Said diagnosis was using the epidemiologic history, suggestive clinical manifestations (ulcerative skin lesions with raised edges, nodular or in plaques or at the mucosal level), and the microscopic evaluation of the parasites obtained directly from the lesions of the patients following the recommendations of the Ministry of Health of Peru [9]. The detected patient samples were sent to the Cajamarca reference laboratory for serum confirmation by direct agglutination test. Patients with no skin or mucocutaneous lesions were excluded

Characteristics of Patients

The patients were from all peri-urban and rural localities derived from primary care networks (**Figure 1**). A collection card was used to extract the clinical (time, place, and number of injuries), and epidemiological (age group, gender, place of origin, and date of diagnosis) information. We used the 2013

Fondo de Cooperación para el Desarrollo Social (FONCODES) to estimate the level of poverty in Cajamarca [8].

Data Collection and Analysis

Data were independently verified by two researchers. Initially, we used a univariate analysis (absolute and relative frequencies, median and standard deviations (SD) according to the variables). We calculated the global incidence of cutaneous leishmaniasis by district as previously described [10]. The non-parametric Spearman and simple lineal regression test was used to analyze the association between the poverty index and the place of origin of patients with leishmaniasis, considering a p-value <0.05 and 95% confidence interval as significant. Data analysis was conducted on IBM SPSS v23.0 (Armonk, US).

Ethical Aspects

To comply with the ethical guidelines, this study has the approval of the heads of the Hospital services, for carrying out the study and access to patient data. This research has been registered and approved by the Ethics Committee at Universidad Norbert Wiener.

RESULTS

The 250 patients included in the study had an average age of 30.4±23 years (95% CI 27.6 to 33.3), and most of them were male (154 [61.6%]). The 96 (45.6%) women (31.1±25.2 years, 95% CI 26 to 36.1) had no difference in age from men (30±21.6 years, 95% CI 26.6 to 33.4) (p = 0.804). We found an association between the place of origin (p = 0.043, rho = 0.451), the area of injury and results (p = 0.046, rho = 0.469) and sex (p = 0.041, rho = 0.522) with the positive results of Leishmaniasis (**Figure 1**).

(A)	(B)

Figure 1. Skin lesions on the upper limb (A) and head (B) of patients with Leishmaniasis from Celendin, Cajamarca
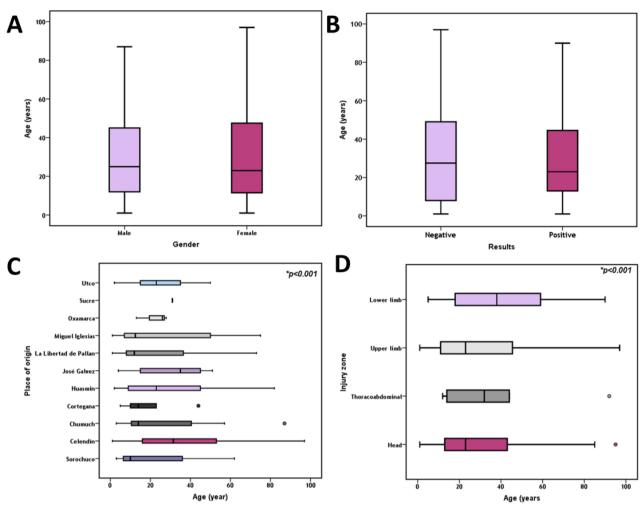
Figure 2. Distribution of the characteristics of rural Andean populations with Leishmaniasis by age. A. Gender. B. Laboratory results. C. Place of origin. D. Injury zone. *p <0.001 (significant)

Of the 250 patients enrolled in the 5 years of the study, 156 (37.6%) were positive for leishmaniasis, with an average age of 29.3±20 years (95%CI 26.2 to 32.5). We found differences between the ages and the place of origin of the participants (p <0.001). All cases correspond to cutaneous leishmaniasis, and the most common lesions were the upper limbs (110 [44%]) and the head (24 [9.6%]) (**Figure 2**).

The most frequent origin of patients with Leishmaniasis was the district of Celendín (54 [21.6%]), Huasmin (58 [23.2%]), Utco (13 [5.2%]), La Libertad de Pallan (7 [2.8%]), and others (24 [15.4%]). The highest incidence rate of Leishmaniasis was found in the districts of Utco (0.93 × 1000 inhabitants) and Huasmin (0.41 × 1000 inhabitants) (**Figure 3**).

Celendín presents an average poverty rate of 69.7% (range 45 to 88.7%) and an extreme poverty rate of 36.8% (range 13.2 to 56%). We found that the poverty rate (p = 0.002) and extreme poverty rate (p = 0.001) were positively associated with the incidence of cases in Celendín district. Excluding Celendín, all the districts have a 100% rurality rate, and the districts in the first poverty quintile had the highest Leishmaniasis incidence rates (p = 0.035).

The number of patients per year in 2015 (12 [7.7%]) increased towards 2018 (45 [28.8%]) and 2020 (22 [14.1%]). (**Figure 4**) The most affected age group were those <18 years-old (61 [62.2%]), followed those between 41 to 60 years-old (33

[13.2%]), and from 18 to 30 (32 [12.8%]) years old (p = 0.029) (**Table 1**).

DISCUSSION

This study determined for the first time the association between the poverty rate and the incidence of leishmaniasis among rural Andean patients of Peru, where the districts of Celendín, Huasmin, and Utco accumulated half of the cases. The clinical alterations of this disease were preferably skin lesions in the upper limbs and affected 3 out of 10 patients during the five years of the study.

Leishmaniasis is a millenary ill in the Americas, specifically in Peru; in fact, many pre-Columbian cultures such as the Mochicas (330 B.C. to 500 A.C.) and Chimú (900-1400 A.C.) have represented in their anthropomorphic ceremonial objects the deformations, destructive and disfiguring sequelae of leishmaniasis, mainly in the nose and mouth [11,12]. Since then, Leishmaniasis has been living in humid places, affecting the populations in the Andes and jungles of South American countries, mainly those with inadequate economic and sanitary conditions.

In this retrospective study, we determined that the increase in cases of leishmaniasis among the Andean rural population was related to poverty and extreme poverty rates, showing that
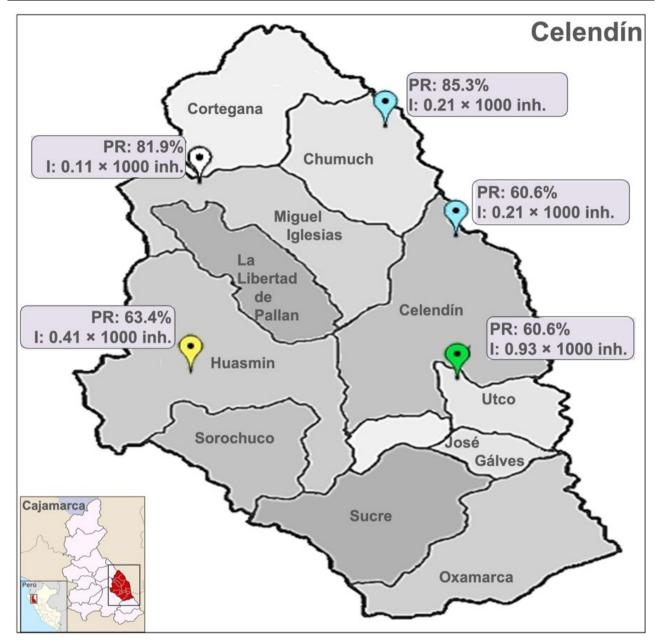
Figure 3. Georeferencing of rural Andean populations with Leishmaniasis in Celendin, Cajamarca-Peru. The estimated incidence (I) per 100 inhabitants (inh) and the poverty rate (PR) for each district are shown. The highest incidence is shown within the purple boxes for each district. Other smaller incidence rates were for La Libertad de Pallan (I = 0.08 × 1000 inh., PR = 45%), Jorge Gálvez (I = 0.07 × 1000 inh., PR: 62.3%), Cortegana (I = 0.05 × 1000 inh., PR = 76.8%), Oxamarca (I = 0.03 × 1000 inh., PR = 66.3%) and Sorochuco (I = 0.02 × 1000 inh., PR = 75.4%)

the highest incidence rate was 0.93×1000 inhabitants (with an increase of 21% in cases between 2015 and 2020). This increase in cases may be due to poor control and surveillance of the disease, as has been seen in other low-settings countries [13]. Previous studies in South American countries [14-16] have also shown a link between leishmaniasis and poverty, which is consistent with our findings in the weakest districts of Celendín. Therefore, poverty is considered to be a key risk factor for the persistence and increase of leishmaniasis.

Clearly, a disproportionality has been seen in the cases of leishmaniasis in communities with poverty or extreme poverty worldwide, to the point of being considered one of the main determinants of the disease [17]. In this sense, our findings have also shown that communities with higher rates of poverty (such as Utco and Huasmin) have a higher incidence of leishmaniasis with an Indian report [18]. However, our results

do not agree with that stated by El Omari et al. [13] in the Moroccan population, where poverty was not associated with cases of cutaneous leishmaniasis. The difference with this study is basically at the population level, since they evaluated a large number of urban inhabitants where the deficiencies that promote the infectious cycle of leishmania are not completely linked.

As these municipalities are in the first quintile of poverty and most have a 100% rurality rate according to the FONCODES report, the Ministry of Health of Peru has increased the health centers and stands for the care of the Andean population. However, this universalization of health programs has not been efficient in meeting the costs and needs of the prevention of leishmaniasis [19]. It is likely that the diagnosis already implied a community and family financial pressure on already limited resources, so families invest their active income (land,

Table 1. Demographic and clinical characteristics of the Andean population with Leishmaniasis in Peru, Data in n (%)

Characteristics	Leishmaniasis	
	Negative	Positive
Total	94(37.6)	156(62.4)
Age group		
<18	37(14.8)	61(24.4)
18-30	14(5.6)	32(12.8)
31-40	13(5.2)	20(8)
41-60	13(5.2)	33(13.2)
>60	18 (7.2)	11(4.4)
Gender		
Male	51(20.4)	103(41.2)
Female	43(17.2)	53(21.2)
Place of origin		
Celendin	43(17.2)	54(21.6)
Huasmin	18(7.2)	58(23.2)
Utco	5(2)	13(5.2)
La libertad de Pallan	13(5.2)	7(2.8)
Chumuch	4(1.6)	7(2.8)
Miguel Iglesias	4(1.6)	6(2.4)
Cortegana	1(0.4)	4(1.6)
José Gálves	3(1.2)	2(0.8)
Oxamarca	1(0.4)	2(0.8)
Chorochuco	1(0.4)	2(0.8)
Piobamba	0	1(0.4)
Sucre	1(0.4)	0 (0)
Injury zone		
Upper extremities	62(24.8)	110(44)
Head	13(5.2)	24(9.6)
Lower extremities	16(6.4)	19(7.6)
Thoracoabdominal	3(1.2)	3(1.2)

livestock, housing) or acquire informal loans to cover the costs of diagnosis and treatment of leishmaniasis.

These communities also have in common a set of interrelated risk factors that prevent their control and prevention, these range from malnutrition and limited control of reservoirs to the urbanization of areas, ecological changes, and global warming [15,17,20]. A Just as climate change is displacing the areas of distribution and frequency of vector-borne diseases, it is also showing a roadmap for the identification of potential risk areas, as has been seen in Colombia [21].

Climate change may also be responsible for the movement and settlement of new *Leishmania* species in endemic communities such as in communities without previous cases, for example, the introduction of *Leishmania (Leishmania) lainsoni* and *Leishmania (L.) equatoriensis* in Colombia, and *Leishmania* (L.) *amazonensis* in the province of Huánuco, Peru [22,23].

Peru is a country particularly vulnerable to climate change and infectious diseases can change its infection dynamics as we previously demonstrated [24]. This mobilization of species affected by human activities (socio-economical changes, social conflicts, heterogeneous agricultural zones, etc.) as well as by environmental determinants (sea level, coverage of forest, etc.) may be gradually altered by climate change. Thus, this set of determinants could explain the increase in the number of cases in Celendín from 7.7% in 2015 to 14.1% in 2020 (**Figure 4**).

An important finding of our study is the age group most frequently affected by Leishmaniasis (<18 years, 62%). This illness of infants, children, and adolescents are nothing new in Peru, in fact, the oldest case in the world has been reported in a 6-year-old mummy from 2000 B.C. and annually >15% of cases happen in the Americas [25,26]. Pediatric leishmaniasis is highly prevalent in endemic areas and can present intermittent fever, anorexia, weight loss, hepatosplenomegaly, among others [27]. Infants and children present greater risks of contagion in rural communities since livestock activities of the parents leads to greater exposure of this group may occur due peri and intra-domiciliary transmission [28]. Further research is necessary in view of the large proportion of children and infants with Leishmaniasis.

All the cases of Leishmaniasis in the Andean population evaluated were skin alterations (known as "uta"). In Peru,
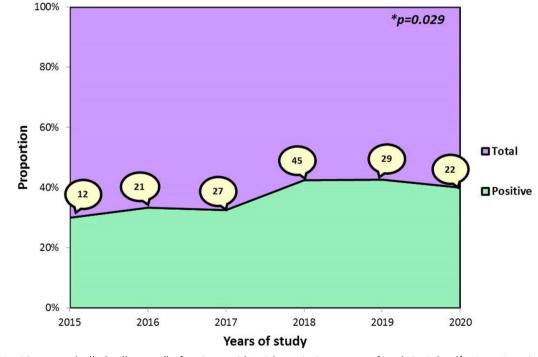

Figure 4. Positive cases (called yellow oval) of patients with Leishmaniasis per year of study in Celendín, Peru. Data in %, *p <0.05 (significant)

around 6% of cases are mucocutaneous alterations, which could explain why we did not report any cases of visceral or mucocutaneous leishmaniasis [23]. As in other reports, the most exposed areas such as the upper limbs and the head were the ones that had the largest areas with uta (ulcerative lesion of the thick granulomatous tissue with raised edges that can become over-infected) [1,7,27].

To the best of our knowledge, this is the first work that associated the poverty rate and incidence of cases at the district level in Peruvian Andes. However, our study faces some limitations: first, the FONCODES poverty report from 2013 was used. Although this is a recent report, the determinants of poverty may have undergone some changes in recent years. Second, in this study, we did not determine the species of *Leishmania* that affected the study population. By 2020, five species of *Leishmania* have been reported in Peru, eight species in Ecuador, and nine in Colombia [22,23,30]. however, it is possible that these species may fluctuate between communities as they are subject to environmental, social, and economic changes. Third, the *Leishmania* vector also spreads the rod-shaped bacterium that causes Bartonella disease. The Andean population of the province of Cajamarca may have cases of coinfection by both pathogens as it is one of the main provinces with Bartonellosis in Peru.

In conclusion, we determined an association between poverty and leishmaniasis cases in the Peruvian Andean population, increasing the incidence of cases according to the poverty rate. These populations developed in their entirety with cutaneous leishmaniasis (Uta) on exposed body parts, and the main affected age group is <18 years.

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