

Prevalence and Risk Factors for Human Cystic Echinococcosis in the Cusco Region of the Peruvian Highlands Diagnosed Using Focused Abdominal Ultrasound

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Abstract. Latin America is among the highly endemic regions for cystic echinococcosis (CE). In Peru, an estimated 1,139 disability-adjusted life years are lost annually from surgical treatment of CE. This is comparable with the combined total for Argentina, Brazil, Uruguay, and Chile. The prevalence of human infection has been investigated in the central Peruvian Andes, but there are no community-based screening data from other regions of Peru. We carried out a population survey in January 2015 using abdominal ultrasound to estimate the prevalence of abdominal CE in the Canas and Canchis provinces, in the Cusco region of Peru. Among 1,351 subjects screened, 41 (3%) had CE. There was significant variation between communities with similar socioeconomic features in a small geographical area. A history of CE was reported by 4.1% of the screened subjects, among whom 30.3% still had CE on ultrasound. Among patients reporting previous CE treatment, 14.9% had CE in active stages. Limited education, community of residence, and knowing people with CE in the community were associated with CE. These results demonstrate a significant burden of CE in the region and suggest the need for further investigations, control activities, and optimization of clinical management for CE in this area.

INTRODUCTION

Cystic echinococcosis (CE) is a neglected parasitic zoonosis distributed worldwide. It is particularly prevalent in livestock-raising regions. The lifecycle of the tapeworm *Echinococcus granulosus* s.l. requires dogs as definitive hosts and ungulates (especially sheep) as intermediate hosts. Humans are accidental intermediate hosts, who are infected by ingestion of tapeworm eggs from the feces of parasitized dogs. Larvae released from the eggs can invade and develop in the intermediate host, forming expanding fluid-filled cysts or hydatids. Dogs and other canids harbor the tapeworm form, acquired by feeding on raw viscera containing hydatid cysts.

CE has a profound health and economic impact in endemic communities. The global burden of CE has been estimated at 1.2 million persons infected and 1–3.6 million disability-adjusted life years (DALYs) lost annually.^{1,2} No global data on case fatality rates have been published; however, limited country-level data suggest that CE may cause significant mortality. In Chile, the reported mortality was 8.5 deaths per 10⁵ inhabitants in the Aysen and La Araucania regions.³ Costs associated with human infection globally, including those for treatment and lost wages, have been estimated to exceed 750 million U.S. dollars. Furthermore, costs associated with livestock production losses may be over 2 billion dollars annually.¹ Notwithstanding these figures, CE has been relatively neglected even compared with “neglected tropical diseases.”

Human CE affects mainly poor communities and its diagnosis and treatment require significant resources. The real prevalence of infection and quantification of disease burden are difficult to assess. Uneven distribution of the infection, limited availability of imaging studies in rural endemic areas, and the lack of effective disease reporting systems likely lead to significant underestimation of the true prevalence. Long-term, well-coordinated programs involving both human and veterinary health services are needed to interrupt transmission. However, most resource-limited countries lack effective control programs and instead focus is on treatment of individual human cases. However, cost-effective multidisciplinary control strategies could help prevent CE and reduce unnecessary treatment costs.

Latin America is among the regions of the world with the highest prevalence of CE. The annual economic burden of CE in Peru is estimated to be \$6.3 million per year.⁴ That includes \$2.4 million for human infection (one-third is for surgical treatment and two-thirds due to lost productivity) and \$3.8 million from livestock production losses. The estimated number of DALYs associated with surgical cases in Peru is 1,139 per year, comparable with the total estimated for Argentina, Brazil, Uruguay, and Chile combined.⁴ Moreover, the number of DALYs associated with surgical cases in Peru is comparable to that of other important infections including malaria and leishmaniasis.⁴ Even so, these figures may not account for the full impact of decreased human productivity (including preoperative and convalescent periods) and underdiagnosis.⁴

Population surveys in rural communities found a prevalence of human infection up to 9.3% in the central Peruvian Andes.^{5–9} The prevalence of infection was reported as 38–87% in sheep and 32–46% in dogs.^{6,8} While community-based data have not

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been reported from other regions of Peru, surgery for CE is common in the highlands and causes a significant burden to the system.^{10,11} Herein, we present the results of an ultrasound survey of the prevalence of abdominal CE in four districts of the Canas and Canchis provinces, in the Cusco region of Peru.

METHODS

We performed a secondary analysis of data obtained during a screening campaign for CE using abdominal ultrasonography in the Canas and Canchis provinces of the Cusco region in Peru. The campaign was performed during 2 weeks in January 2015. The surveys were performed in the town of Sicuani and adjacent rural communities of Marangani, Ocobamba (aka Occobamba), and Langui (Figure 1). All the communities are situated at an elevation between 3,550 and 4,200 m. The only formal slaughterhouse in the area is located in Sicuani and serves mostly cattle owners. Most sheep and alpaca are slaughtered at home or at informal abattoirs. Sheep, cattle, and alpaca farming are major economic activities in the region. An estimated 18–36% of the population is below the threshold for poverty.¹²

The survey was performed through a collaboration involving the Peruvian Ministry of Health, the Universidad Peruana Cayetano Heredia, and the University of Texas Medical Branch Collaborative Research Center in Cusco. The screening campaign was advertised through the local health center's outreach programs and on the radio in Quechua and Spanish languages. Although male and female subjects older than 18 years were the targets of the survey, children brought by parents responding to the advertisement were also examined. All volunteers who appeared at the screening centers and were able to tolerate the supine

position were enrolled. Information on demographics, medical history including prior diagnosis of CE, and risk factors for echinococcal infection was gathered from participants. All underwent an abdominal ultrasound examination in the supine and lateral decubitus positions using Medison, Mindray, and Sonosite portable ultrasound machines with convex probes. Four expert sonographers (Francesca Tamarozzi, Maria Teresa Giordani, Amy Hou, and Freddy Vilca) performed the examinations and used the World Health Organization Informal Working Group on Echinococcosis (WHO-IWGE)-standardized ultrasound classification of echinococcal cysts to characterize their findings.¹³ All lesions were reviewed by at least two of the sonographers for consensus on diagnosis and stage classification.

The study protocol was approved by the institutional review boards of Universidad Peruana Cayetano Heredia and Mount Auburn Hospital. No identifiable information was retrieved, and subjects were not contacted in any way as part of the present study. All subjects diagnosed with CE, suspected lesions, or lesions deserving further assessment were registered by personnel from the Peruvian Ministry of Health, included in the Comprehensive Health Insurance program, and linked to health care by social services.

Data were stored and analyzed using the Statistical Package for the Social Sciences (SPSS v.18.0, IBM, Armonk, NY). Mean (\pm standard deviation), medians with interquartile ranges (IQRs), and frequencies were used to describe the distribution of the variables. Student's *t* and χ^2 tests were used to compare variables. Backward logistic regression analysis was used to model the presence of echinococcal cysts and factors associated with infection. Clinically relevant variables and variables with a $P < 0.10$ were input into the model and then excluded using the likelihood-ratio method. The analysis was conducted using the presence of CE by ultrasonography as the dependent variable. Subjects with cystic lesion ([CL], according to the WHO-IWGE classification) were not considered as having CE (due to lack of opportunity to rule-out the disease by serological testing) and were excluded from the bivariate and logistic regression analyses. Similarly, subjects who reported having CE in the past but had a normal ultrasound were excluded from the bivariate and logistic regression analyses of factors associated with CE, as their prior CE diagnoses were not verifiable. Subjects with active and inactive CE were considered as having CE for the analysis. Statistical tests were considered significant if $P < 0.05$.

RESULTS

A total of 1,351 subjects underwent focused abdominal ultrasound screening for CE. The median age of the participants was 38 years (IQR = 21.7–50) and 70.6% (954/1,351) were female. Most subjects were screened in Sicuani (57.2%, 773/1,351) and Marangani (22.2%, 300/1,351) in Canchis Province. Most of the participants were born in Canchis (74.5%, 1,007/1,351) and still resided in that province (90.8%, 1,227/1,351). One in six subjects (15.5%, 210/1,351) had very limited education and another one-third (32.9%, 444/1,351) had only completed elementary school. The three most common occupations were homemaker (25.2%, 341/1,351), student (24.6%, 333/1,351), and farmer (21.2%, 286/1,351) (Table 1). The median number of family

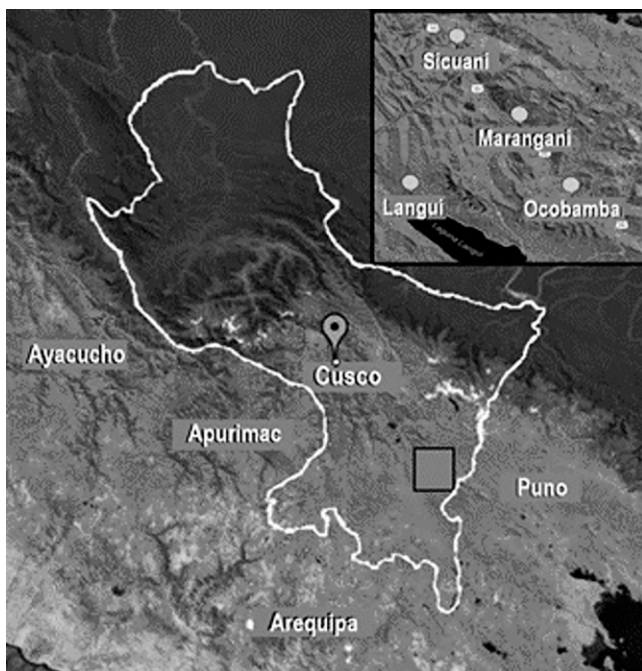


FIGURE 1. Map of the southern highlands of Peru showing the Cusco region and the communities where the cystic echinococcosis screening was performed (inset). Source: Google maps 2016.

members living in the same household was four persons (IQR = 2–5). Most subjects were involved in raising, slaughtering, and/or selling sheep (70.6%, 953/1,349) and cattle (66.2%, 893/1,349) at some point in their lifetime. Only 5.6% (75/1,351) noted contact with alpacas and llamas. Almost all subjects (93.8%, 1,266/1,349) had contact with stray or family-owned dogs. Twenty-six percent (26.8%, 362/1,350) of the subjects reported having at least one (22.5%, 304/1,350) or more than one (4.2%, 58/1,350) family member with CE. Among 192 subjects who reported the relationship to these family members, direct consanguinity was present in 57.8% (111/192). Also, 21.7% (293/1,351) people reported knowing at least one (15.5%, 210/1,351) or more than one (6.1%, 83/1,351) person with CE in their neighborhood or at work.

The focused abdominal ultrasound screening found at least one cyst in 3.7% (51/1,351) of the subjects of which 3.0% (41/1,351) were considered to have CE and 0.7% (10/1,351) to have undifferentiated cysts (CLs or residual lesions/cavities after previous surgery for CE, with no pathognomonic signs of relapse) (Table 1). The highest prevalence of CE was reported in Sicuani (4.1%). No CE cases were diagnosed in Langui (Table 1).

The total number of cysts found was 74 with 62 classified as CE and 12 as undifferentiated cysts (nine CLs and three postsurgical residual lesions) (Table 2). The median number of CE cysts per subject was 1 (IQR = 1–2) with a range of 1–5 cysts. The median diameter of CE cysts was 5.5 cm (IQR = 3.2–9.4) with a range of 0.5–16 cm. CE cysts were commonly located in the liver (88.7%, 55/62) and 65.6% involved the right hepatic lobe. Extrahepatic cysts were located in the spleen (4.8%, 3/62), lung (1.6%, 1/62), and kidney (1.6%, 1/62). In two subjects, the location of one of the cysts was not recorded. The 12 undifferentiated cysts were located in the liver. There were similar numbers of active (27/55, 49%) and inactive (28/55, 51%) liver cysts. The most common active stage was CE1 (55.5%, 15/27) and the most common inactive stage was CE4 (60.7%, 17/28). No CE3A cysts were identified (Table 2).

There were 35 CE liver cysts among subjects without previous treatment of CE; 19/35 (54.3%) were inactive cysts (CE4 and CE5) and 16/35 (45.7%) were active cysts (CE1, CE2, and CE3B). Active CE presented at a younger age

TABLE 2

Classification and location of the cystic lesions found by abdominal ultrasonography

Cystic lesions identified by ultrasonography (N = 74)			
Cystic echinococcosis* (N = 62)		Undifferentiated cysts (N = 12)	
Liver	55 (88.7%)	CL	9 (75.0%)
Active		Residual lesions	3 (25.0%)
	CE1 15 (27.3%)		
	CE2 5 (9.1)		
	CE3B 7 (12.7%)		
Inactive			
	CE4 17 (30.9%)		
	CE5 11 (20.0%)		
Spleen	3 (4.8%)		
Lung	1 (1.6%)		
Kidney	1 (1.6%)		
Unspecified	2 (3.2%)		

CE = cystic echinococcosis; CL = cystic lesion.
*No CE3A cysts were diagnosed.

than inactive CE (35.5 years [\pm 19.7] versus 49.7 years [\pm 12.9], $P = 0.01$) (Figure 2).

A history of CE was reported by 4.1% (56/1,351) of the subjects. Liver CE (37.5%, 21/56) and lung CE (33.9%, 19/56) were the most common locations. Seven percent (7.1%, 4/56) reported a history of both liver and lung CE. One each reported kidney CE or lung and kidney CE. Seven (12.5%) subjects reported abdominal CE without a specific location and three (5.3%) subjects did not provide a location. Fifty of the 56 subjects with a history of CE provided information regarding previous treatment. Most subjects (74%, 37/50) received only surgical intervention, 14% (7/50) received medical treatment, 6% (3/50) received surgical intervention combined with medical treatment, and 6% (3/50) did not receive any treatment. One-third (33.9%, 19/56) of the subjects with a history of CE still had CLs during the focused abdominal ultrasound screening. Thirty percent (30.3%, 17/56) of these were classified as CE and 3.6% (2/56) were classified as CL/residual cavities. Of the 17 with CE, nine had active CE, six had inactive CE, and two had missing information on staging. Of the nine patients with active CE, prior therapy included surgery alone (five), surgery and medical treatment (two), and no treatment (two).

TABLE 1

Study population characteristics and comparison of the characteristic of uninfected subjects and subjects with CE or CL/residual lesions

Characteristic	Population (N = 1,351)	CE negative (N = 1,263)	CE positive (N = 41)	P value	CL/residual lesion (N = 10)	P value	
Age (years)	Mean (\pm SD)	37 (18.9)	37.09 (19.0)	39.1 (20.2)	0.48	50.2 (16.4)	0.03
Sex	Female	954 (70.6)	898 (71.1)	28 (68.3)	0.69	7 (70.0)	1.00
	Male	397 (29.4)	365 (28.9)	13 (31.7)		3 (30.0)	
Community	Sicuani	773 (57.2)	706 (55.9)	32 (78.0)	< 0.01	5 (50.0)	0.44
	Marangani	300 (22.2)	283 (22.4)	8 (19.5)		5 (50.0)	
	Occobamba	180 (13.3)	178 (14.1)	1 (2.4)		0 (0)	
	Langui	98 (7.3)	96 (7.6)	0 (0)		0 (0)	
Occupation*	Entrepreneur	115 (8.9)	110 (9.1)	3 (7.7)	0.39	0 (0)	0.63
	Farmer	286 (22.0)	268 (22.1)	7 (17.9)		3 (37.5)	
	Homemaker	341 (26.3)	321 (26.4)	9 (23.1)		2 (25.0)	
	Student	333 (25.6)	311 (25.6)	12 (30.8)		1 (12.5)	
	Other	223 (17.2)	205 (16.9)	8 (20.5)		2 (25.0)	
Education*	None	210 (15.7)	197 (15.8)	9 (22.0)	0.51	2 (20.0)	0.61
	Elementary and up	1,127 (84.3)	1,052 (84.2)	32 (78.0)		8 (80.0)	

CE = cystic echinococcosis; CL = cystic lesion; SD = standard deviation.

*Percentages may not sum up to 100% and subjects categories may not sum up to total population number because the information was incomplete for some subjects. Subjects reporting previous CE and with normal ultrasound were excluded from the comparisons (N = 37).

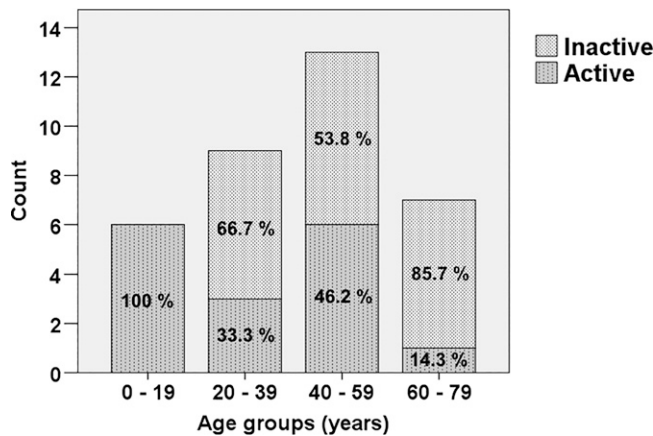


FIGURE 2. Number of active and inactive liver cystic echinococcosis cysts among subjects without previous treatment of CE distributed by age groups.

More CE cases were diagnosed in Sicuani (32/41, 78.0%) compared with the other three communities (9/41, 22.0%) ($P = 0.01$). No association with prevalence of CE was found according to age, sex, occupation, or education (Table 1). CE was associated with having raised alpaca (odds ratio [OR] = 2.47, 95% confidence interval [CI] = 0.94–6.5, $P = 0.05$), but not with having raised sheep ($P = 0.89$) or cattle ($P = 0.36$), or contact with dogs ($P = 0.73$). Subjects who knew someone with CE in their neighborhood or at work were more likely to be infected (OR = 2.22, 95% CI = 1.02–4.71, $P = 0.02$). Those who had a blood relative with CE were more likely to be infected but the difference was not statistically significant (OR = 2.20, 95% CI = 0.80–5.74, $P = 0.11$). The variables “being from Sicuani,” “having less than 5 years of education,” and “knowing someone with CE in the neighborhood or at work” were selected as predictors of CE diagnosis by focused screening ultrasound in the backward logistic regression model (Table 3).

DISCUSSION

CE is endemic in South America but data on prevalence and burden are limited. Estimates of prevalence are hampered by uneven distribution of transmission, the high proportion of asymptomatic cases, and the large number of symptomatic patients without access to health-care services. Our results show that CE is common in the Cusco region. Risk factors included lack of education, knowing others with CE, and location.

We found that the communities in close geographical proximity and with similar socioeconomic features varied in CE prevalence, ranging from none in Langui to over 4% in

Marangani and Sicuani, located 14 and 18 km away, respectively. Fewer people were examined in Langui compared with other communities, which might increase the risk of sampling error. However, other factors we did not explore (e.g., livestock density and dog population) may explain the differences. Active cyst stages including CE1 were found among youths and the adult population, indicating ongoing transmission of CE at all ages. Thus, control programs should include all ages and aim for measurable results in a relatively short timeframe. Indeed, Beard described a reduction in human CE cases 3–5 years after implementation of control activities in Tasmania in all age groups.¹⁴

The majority (54.3%) of liver CE cysts found in patients never treated previously were inactive. This indicates that many CE cysts spontaneously degenerate into inactive forms.^{15,16} The fact that inactive cysts were not found in the younger population but increased with age suggests that this process happens over several years. This is in line with results from previous reports. Cross-sectional studies conducted in Argentina,¹⁷ China,¹⁸ and Morocco,¹⁹ found that spontaneous inactivation of CE cysts occurred in 5%, 18.9%, and 53.4% of cases, respectively. Additionally, Guarnera and others¹⁷ reported that the mean age of subjects with untreated inactive CE cysts was higher (53–64 years) than that of subjects with active CE cysts (21–45 years). Chebly and others¹⁹ found that the risk of having active cysts significantly decreased with age. These results are also supported by the longitudinal study of untreated patients conducted by Larrieu and others in Argentina,²⁰ demonstrating that 20% of cysts showed spontaneous involution over 4 years of follow-up. There is a need for a stage-specific management of CE cysts, and inactive cysts should be just monitored over time unless symptomatic.¹³ This approach would avoid overtreatment. By contrast, there was a high rate of active liver CE infection in patients previously treated with surgery alone. This approach is not currently recommended and suggests a need for training of local physicians on optimal stage-specific clinical management of CE that includes concomitant medical treatment.¹³

We found that social conditions such as education and community of residence were significantly associated with CE infection. By contrast, exposures previously linked to transmission (e.g., contact with dogs) were not a significant risk factor. The latter may be in part due to the nearly ubiquitous contact with dogs. We noted similar results in Morocco,¹⁹ where environmental contamination was identified as the main factor responsible for CE transmission in the Mid Atlas Mountains. The association with having contact with a person with CE in the neighborhood or at work is also consistent with environmental contamination.

TABLE 3
Backward logistic regression analysis of factors associated with having a CE diagnosed by focused screening ultrasound

	Adjusted OR	95% CI	P value
Knowing someone with CE in the neighborhood or at work	2.28	1.03–5.66	0.04
Being from Sicuani	2.78	1.22–6.36	0.01
Having less than 5 years of education	2.46	1.10–5.50	0.02

CE = cystic echinococcosis; CI = confidence interval; OR = odds ratio. Variables entered in the model: sex, age, community, education, having raised alpacas, consanguinity with a family member with CE, knowing someone with CE in the neighborhood or at work. Hosmer and Lemeshow test: $\chi^2 = 2.83$, $df = 3$, $P = 0.41$.

Consanguinity as a risk factor might be due to either environmental exposure or genetic susceptibility. The bivariate analysis showed an association between CE and raising alpaca. This has not been reported in other studies and can represent a marker for environmental cofactors. However, CE prevalence maybe as high in alpaca as in sheep in the Peruvian highlands and alpacas may be a key intermediate host in the transmission cycle.⁴

Our studies in Canas and Canchis focused on ultrasound screening for abdominal CE. We were able to detect a few lung cysts located in the lower lobes and close to the surface, but ultrasound is not a sensitive method to detect lung cysts. Thus, our data cannot accurately assess the prevalence or risk factors for lung CE. Another limitation of this study is the lack of serologic data. Some of the CL cases might have been confirmed as CE by serologic tests. Thus, our estimates of prevalence of abdominal CE may also be low. Furthermore, the lack of serologic testing may have biased our assessment of the spectrum of infection.²⁰

In conclusion, we demonstrated a high prevalence of CE in the Cusco region of Peru. This pilot study shows that population-based screening was readily accepted by the population and useful for assessing prevalence. The high prevalence of disease and evidence of ongoing transmission suggests further need for disease control. Preliminary data suggest clustering and perhaps transmission from environmental contamination. We also noted evidence that current clinical management is suboptimal, suggesting a need for further education of the medical community regarding current management recommendations.

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