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Spatio-temporal clusters of incident human brucellosis cases in Ecuador

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ABSTRACT

This study aimed to determine whether variations in the incidence of reported cases of human brucellosis in Ecuador were clustered in space and time. In addition, the effects of cattle and small ruminant population density and other socio-economic factors on the incidence were investigated. Significant space–time clusters were found in the northern and southern highlands and parts of Ecuadorian Amazonia. Customs of people, cattle, goat and sheep population density appeared to influence the incidence of brucellosis. In this study, the incidence of reported cases of human brucellosis was found to be higher in the highlands (sierra) and in municipalities near Peru and Colombia. The results of this study highlight the need for prevention and control measures aimed at abating the incidence of brucellosis among livestock and humans.

1. Introduction

Brucellosis is one of the world's major zoonoses (Pappas et al., 2005). Four *Brucella* species are mainly responsible for the disease: *Brucella abortus* typically found in cattle; *Brucella melitensis* in goats and sheep; *Brucella suis* in swine; and *Brucella canis* in dogs (Fosgate et al., 2002; Sauret and Vilissova, 2002). Even though these four species of *Brucella* can infect humans; *B. melitensis* has been mentioned as the most pathogenic and frequent in humans (Lucero et al., 2008). Humans contract the disease through consumption of infected and unpasteurized milk and milk products, through direct contact with infected tissues such as placenta and through inhalation of infected aerosolized particles (Pappas et al., 2005). Human brucellosis is associated with chronic debilitating infections and is often characterized by fever of unknown origin, a less specific symptom (Sauret and Vilissova, 2002; Almuneef et al., 2004; Martins et al., 2009).

Brucellosis in cattle and in small ruminants remains a significant animal health problem in many countries (Sauret and Vilissova, 2002; Anonymous, 2005; D'Orazi et al., 2007; Martins et al., 2009). The disease mainly affects reproduction and fertility in females, thereby reducing survival of newborns, and reducing milk yield (Sewell and Brocklesby, 1990; Zinsstag et al., 2005). In industrialized countries, effective control measures are implemented for eradication, including intensive national surveillance systems in animals and removal of infected livestock (Pappas et al., 2005; Lithg-Pereira et al., 2004; Yamamoto et al., 2008; Lee et al., 2009). However, developing countries rarely have national programs to prevent, control, monitor and eradicate brucellosis in animal populations.

Ecuador, with nearly 5 million cattle, 1.2 million sheep, 1.7 million pigs, and 0.15 million goats has no structured

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system for livestock disease management. Slaughterhouses and National Veterinary Service reports frequently include foot and mouth disease cases, distomatosis, metritis, and mastitis in cattle, goats, sheep and pigs that are slaughtered (Anonymous, 2008a). The seroprevalence of bovine brucellosis was officially estimated to range from 1.92% to 10.62% among the provinces in the highlands (Sierra) and from 4.12% to 10.62% among provinces in the Coast (Torres, 2008). The seroprevalence of bovine brucellosis was estimated to be 2.17% and 9.42% using the Rose Bengal Test (RBT) and indirect Enzyme-linked immunosorbent assay (iELISA), respectively in Santo Domingo (Pichincha) and 1.08% and 9.73% respectively in El Carmen (Manabí) (Angulo and Tufiño, 2005). Furthermore, in Ecuador, an average of 12 hospitalized human brucellosis cases are reported through the National Office of Statistics every year (Anonymous, 2006).

A Study carried out among farmers in Peru (bordering country of Ecuador) have estimated a brucellosis seroprevalence to be between 1.5% and 4.5% in humans (Mendoza-Núñez et al., 2008), and a pilot study conducted in the northern part of Ecuador estimated a true prevalence between 24% and 48% in cattle (Ron-Roman, 2003). In both studies, the consumption of unpasteurized milk and milk products, permanent contact with animals, and the occupation of the people were the main factors found to be associated with brucellosis seropositivity among humans. The identification of the municipality and time period with an elevated risk of the infection may contribute to our understanding of the underlying risk factors for the disease. For example, the results of comparing and contrasting clusters with information on the population density of livestock or on the ethnic groups in the population may be used to explain observed clusters (Fosgate et al., 2002; DeChello and Sheehan, 2007).

The aim of this study was to determine the spatio-temporal distribution of incident human brucellosis cases in the continental Ecuadorian territory using municipality level data on reported cases of human brucellosis between 1996 and 2008. This will enable the identification of areas with a high incidence of the disease and also to assess the effects of important risk factors such as ethnicity and cattle, sheep and goat population densities on the space–time distribution of the disease.

2. Materials and methods

2.1. Study region and data

The study unit was the municipality. In Ecuador, after the province, the municipality is the second level of political administration. Information on the number of incident human cases of brucellosis and total human population between 1996 and 2008 for each municipality was provided by the National Office of Statistics (Anonymous, 2006). It was assumed that all cases originated at patients municipality of residence. Brucellosis cases were identified based on presumptive clinical diagnosis. The map showing the political division of the country at municipality level was provided by the agricultural office of geographical information systems (Anonymous, 2007). Since the data were aggregated at the municipality level, each record was designed to contain the total number of reported human cases, the population, the year and the coordinates of the centroid of each municipality. In addition, the number of cattle, goats, sheep, and swine population by municipality were collected for each year. Information was also available for some potential municipality level risk factors for the presence of human brucellosis: climatic zone (tropical or highlands), percentage of farms with technical assistance (fraction of the number of farms which were visited by veterinarians or agronomist), number of people in the municipality, percentage of indigenous people in each municipality, percentage of grazing land in the municipality, proportion of farms with artificial irrigation in the municipality, percentage of households with tubing water, percebtage of people living in extreme poverty and literacy level in the municipality (Anonymous, 2008b).

The study was reviewed and approved by the ethical committee of the Biomedical Center of the Central University of Ecuador (COBI/CBM/UCE).

2.2. Zero-inflated Poisson regression model

The data used for this study are reported cases of incident human brucellosis based on hospital records of clinically diagnosed patients and risk factors at municipality level were obtained from national databases. For most of the municipalities, no human brucellosis cases were reported. Therefore, use of the Poisson and negative binomial regression models on this type of data may lead to biased estimations as they do not take account of the overabundance of zeros. To overcome these drawbacks, zero-inflated Poisson (ZIP) models first proposed by Lambert (Lambert, 1992) can be used. The ZIP model accounts for excess zeros by distinguishing between two types of zeros namely structural and random. For the data at hand, structural (true) zeros arose in municipalities where individuals were not predisposed to brucellosis for example not consuming unpasteurized milk products or not involved in occupations that increase their risk of acquiring brucellosis. Random (false) zeros on the other hand are believed to have arisen from confusing brucellosis symptoms with those of other health problems, not seeking treatment due to lack of hospitals or because individuals though subject to activities that expose them to the infection are not infected. To determine which of the ZIP and zero-inflated negative binomial models (ZINB) models best fits the observed data, both models were fit to the data with no covariates and the expected counts were obtained. The model with the fitted counts closest to the observed counts was selected as the most appropriate model to start with (Zaninotto and Falaschetti, 2011).

To assess the influence of the selected risk factors (Section 2.1) on the incidence of reported cases of incident human brucellosis, the ZIP (or ZINB) model models the non-zero counts and those that can be expected under a Poisson model using a Poisson distribution (or Negative Binomial distribution) and the zero counts using a logistic regression model to model the probability of a municipality being in the structural zero group (Long and Freese, 2001). A man-