

Brucellosis in Household Members of *Brucella* Patients Residing in a Large Urban Setting in Peru

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Abstract. During home visits and using a point-of-care test for brucellosis, we screened the household members of adult patients found to have brucellosis by investigation at the Hospital Nacional Daniel Alcides Carrión in Callao, Peru. A total of 206 household members of 43 patients were screened, and 15 (7.3%) household members in 10 (23.3%) households tested seropositive. Brucellosis was diagnosed in 14 of them, all but 4 presenting with acute or subacute uncomplicated disease. Regardless of attempts to control brucellosis in Peru, the disease continues to be reasonably common among household members of brucellosis patients. Household members presumably remain the single most important identifiable risk group in an urban setting, and screening them provides an effective means for their early diagnosis. Although contact with livestock was rare, the consumption of unpasteurized dairy products was reported by almost all patients with brucellosis, their household members, and hospitalized non-brucellosis patients.

INTRODUCTION

Despite efforts to control brucellosis through the vaccination of goats and pasteurization of milk, the disease remains an important public health problem in parts of coastal Peru.¹ Brucellosis is a zoonosis with four different species being considered infectious to humans.² Of these, *Brucella melitensis*, transmitted by small ruminants, is by far the most important species in Peru.

Brucellosis generally presents as an acute or subacute febrile illness with protean clinical manifestations.^{3,4} To the unaware patient, the acute phase of the disease may be experienced as an innocent febrile illness that does not need consultation with a physician. However, brucellosis should be treated promptly because the infection may persist, and the patient may develop severe complications.⁵ Because of its non-specific clinical presentations, the diagnosis of brucellosis requires confirmation by laboratory testing.^{6,7}

In Peru, most cases of brucellosis are reported from Callao, the harbor city of Lima. In urban areas, brucellosis is mostly acquired through the consumption of contaminated dairy products that have not been pasteurized.^{8–12} In Peru, fresh goat cheese is an important ingredient of “Papa a la Huancaína,” a popular local dish, and in Callao, goat cheese is imported from neighboring provinces where brucellosis is known to be endemic.

In 1954, Spink¹³ noticed that family members of patients with brucellosis were at risk of acquiring the disease. This observation was confirmed by studies in Israel and Saudi Arabia.^{14–16} About two decades ago, Gotuzzo and others¹⁷ in Peru studied the clinical presentations of brucellosis among household members of patients with brucellar arthritis and found that most of the cases in household members were

diagnosed in the early stages of the disease. To determine the need for and use of active surveillance for brucellosis in urban Peru, we screened the household members of patients who were hospitalized with brucellosis at the major public hospital of Callao. A simple and rapid point-of-care test, the *Brucella* IgM/IgG immunochromatographic lateral flow assay, was used for testing during home visits.¹⁸ The sensitivity and specificity of this assay for culture confirmed brucellosis is > 96%, even when used in endemic areas.^{18–20} This point-of-care test uses a drop of whole blood collected by finger prick and is ideal for the rapid screening of risk groups.^{21,22}

MATERIALS AND METHODS

Of the 289 patients with clinical suspicion of brucellosis that were hospitalized between December 2005 and December 2006 at the Hospital Nacional Daniel Alcides Carrión (HNDAC), 54 tested positive in the Rose Bengal test (RB), of whom 45 were diagnosed with brucellosis. Home visits were made to test the household members of these patients for the presence of antibodies against *Brucella*. Individuals were considered household members if they consumed at least five meals per week in the same house as the patient. Permission was obtained to visit the homes of 43 patients, and a total of 206 household members were enrolled in the study. The average number of individuals enrolled per household was 4.8 (range, 1–10). Home visits were made within 3 days to 2 weeks after the diagnosis was confirmed. In a few cases, additional visits were needed to see all household members. Household members were screened on the spot for the presence of *Brucella*-specific antibodies by testing a drop of finger prick blood in the *Brucella* IgM/IgG flow assay. Those with a positive test result were referred to the Infectious Disease Clinic of HNDAC for further medical examination, laboratory testing, and treatment. During the home visit household members were interviewed using a structured questionnaire to collect demographic, epidemiologic, clinical, and risk factor data. To compare the risk behavior all 45 hospitalized pa-

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tients diagnosed with brucellosis, a control group of 40 patients initially hospitalized with a clinical suspicion of brucellosis that was later excluded were also interviewed using the same questionnaire.

The *Brucella* IgM/IgG flow assay was performed by application of ~10 μ L whole blood collected by finger prick to the sample application pad of the plastic assay device. A 50- μ L glass capillary containing heparin was used to transfer the blood sample, and application of the blood was immediately followed by the application of 130 μ L running fluid. Results were read after 10 minutes. The result was considered positive if two colored bands appeared in the assay window of the device, one at the test zone and one at the control zone, and the result was regarded as negative if only one colored band positioned in the control zone was observed. Positive results were subjectively rated 1+ to 4+ depending on the staining intensity of the line in the test zone as follows: 1+, weak staining; 2+, moderately strong staining; 3+, strong staining; 4+, very strong staining.¹⁸

The RB for screening and the tube agglutination test (TAT) for serologic confirmation of brucellosis were performed using antigens obtained from the Peruvian National Institutes of Health.^{23,24} The TAT was considered consistent with brucellosis for titers \geq 1:200.²⁵ Blood culture for brucellosis was performed on 5 mL venous blood according to the Ruiz-Castañeda method.²⁶

Permission to visit the houses of the patients was obtained from the patient, approval to interview household members was obtained from household heads, and consent for participation in the study was obtained from each individual. Children and adolescents < 18 years of age were excluded from the hospital-based part of the study. However, household members > 5 years of age were included when screening household members. All household members suspected of having brucellosis received appropriate medical evaluation and care. However, children and adolescents < 18 years of age who tested positive during household visits were, after referral for further medical examination, considered hospitalized and, following the approved protocol, excluded from the study. Laboratory testing in these patients was done at the discretion of the responsible physician. Sample collection, testing, and data collection were performed by qualified staff.

RESULTS

Fifteen (7.3%) household members of patients diagnosed with brucellosis in 10 (23.3%) households within a total of 51 household members tested seropositive in the *Brucella* IgM/IgG flow assay (Table 1). Twelve individuals tested positive at the first visit. The other three individuals presented with complaints at the hospital between 2 weeks and 4 months later and showed seroconversion on testing. Fourteen seropositive household contacts were diagnosed with brucellosis, and one was diagnosed with bronchitis. The patient with bronchitis was culture negative for brucellosis and treated for a lung infection. In one household, five members were diagnosed with brucellosis. A relative of the family with five cases presented with brucellosis at the hospital during the course of the study. This relative had eaten a single meal together with this family, and it is suspected that at this occasion several members of the household were infected. Three household members diagnosed with brucellosis were children, and according

TABLE 1

Laboratory test results for household members of patients with brucellosis

Group and assay (no. tested)	No. (%)
Households (<i>N</i> = 43)	
No. households with a member who tested seropositive in the <i>Brucella</i> IgM/IgG flow assay	10 (23.3)
Household members (<i>N</i> =206)	
<i>Brucella</i> IgM flow assay positive	9 (4.4)
<i>Brucella</i> IgG flow assay positive	9 (4.4)
<i>Brucella</i> IgM and/or IgG flow assay positive	15 (7.3)
Adult household members diagnosed with brucellosis (<i>N</i> =9)*	
RB positive	9 (100)
TAT positive	6 (66.7)
Blood culture positive	4 (44.4)
<i>Brucella</i> IgM flow assay positive	5 (55.6)
<i>Brucella</i> IgG flow assay positive	7 (77.8)
<i>Brucella</i> IgM and/or IgG flow assay positive	9 (100)

* Results of RB, TAT, and blood culture are presented for the adult patients treated at the HNDAC; results were not available for two adult household members with brucellosis who preferred medical treatment elsewhere and for the three children.

to the approved research protocol, their laboratory test results were not available for the study. Two seropositive adults preferred further medical care at another hospital, and for these patients, confirmatory laboratory testing was not performed at HNDAC. Four seropositive household contacts had a positive blood culture for *B. melitensis*, and the serum samples from all nine adults that were tested agglutinated in the TAT, although in three culture negative patients at a low titer (< 1:200).

Seven of the 11 adult patients identified by screening household contacts had acute brucellosis and 3 had subacute brucellosis. The disease status of the other patient could not be defined with certainty. One of the patients with subacute brucellosis had articular manifestations that could be caused by brucellosis. All other patients were diagnosed with uncomplicated brucellosis. Two of the household members with a positive blood culture for *B. melitensis* never presented with clinically evident disease. The 14 household members with brucellosis came from nine households, and of the 9 index cases, 6 were diagnosed with acute brucellosis, 2 had subacute brucellosis, and 1 was a case of persistent brucellosis. Four of the index cases presented with complications, including two with hepatic disease, one with skeletal complaints, and one with hematologic and skeletal involvement. Complications are common in patients with brucellosis diagnosed at HNDAC, and 18 (40%) of the hospitalized patients with brucellosis presented with complications, which included hepatic (52.1%), articular (30.4%), dermatologic (4.3%), hematologic (4.3%), and genitourinary involvement (4.3%). Four patients had two complications affecting different organ systems. At the time of the home visit, the mean duration (22 days) of the symptoms and signs of the household members diagnosed with brucellosis was similar to that of the index cases.

All patients with brucellosis, 80.1% of their household members, and 97.9% of the patients with an illness other than brucellosis mentioned the consumption of fresh dairy products. Fresh dairy products consumed by household members of patients with brucellosis included cheese (66.5%), "Papa a la Huancaína" (51.5%), cow's milk (13.1%), goat cheese (7.3%), and goat's milk (1%). The consumption of the different products was fairly similar to that consumed by patients hospitalized with brucellosis at HNDAC (cheese, 79.6%;

“Papa a la Huancaína,” 53.7%; cow’s milk, 20.4%; goat cheese, 16.7%; goat’s milk, 1.7%) and by the patients with an illness other than brucellosis (cheese, 89.7%; “Papa a la Huancaína,” 46.2%; cow’s milk, 12.8%; goat cheese, 12.8%). As expected for an urban area, contact with livestock was rare, with only one brucellosis patient and one patient with an illness other than brucellosis reporting superficial contact with cattle.

DISCUSSION

The intake of contaminated dairy products is the prime mode of transmission and the major risk factor for acquiring brucellosis in urban areas. Therefore, household members of patients with the disease logically seem to be at an increased risk for acquiring it. Screening household members of patients from Callao allowed the identification of one or more patients with the disease in almost one quarter of the households visited, and after excluding the exceptional case of the household with five seropositive individuals, we estimate that the attack rate among the household members is ~4.8%. In two separate studies investigating the presence of brucellosis among Saudi Arabian household members of *Brucella* patients, 10.9% and 12.4% of them were diagnosed with the disease.^{15,16} These studies showed the effectiveness of screening individuals sharing risk factors. Screening risk groups may also help to diagnose the disease at an early stage. A study performed in Israel among Bedouin families showed that several seropositive asymptomatic household members of patients with brucellosis developed brucellosis during follow-up.¹⁴ In this study, only one (7.1%) of the patients identified by screening household members developed a complication, which is in contrast with the 40% of the patients hospitalized with brucellosis who presented with one or more complications. It must be noted, however, that culture of tissue biopsies was not attempted, and no definite proof was obtained that the observed complications were caused by brucellosis. In an earlier study performed in Lima, the attack rate of brucellosis among household members of patients with osteoarticular involvement was 50.9% within the first 4 months after the diagnosis of the index case, and whereas all index cases suffered from severe disease, the majority of the cases identified during the survey had mild disease.¹⁷ The latter study was performed two decades ago, and only households with at least two patients with brucellosis were included in the study. Since then, screening household members still seems beneficial, although the epidemiology of brucellosis may have changed considerably because of increased vaccination of goats and pasteurization of milk. Several studies have indicated the existence of genetic factors that may affect susceptibility to brucellosis.^{27–31} Such factors could contribute to a high attack rate in family members exposed to the pathogen.

All patients with brucellosis, many of their household members, and almost all hospitalized patients that did not have brucellosis mentioned the consumption of fresh dairy products purchased at local shops and markets. This seems to indicate that the majority of the population of Callao is at risk of acquiring the disease but that this risk is small. The prevalence of brucellosis in Callao has dropped considerably in recent years, most likely as a result of vaccination of livestock and the establishment of formal dairy plants where milk is pasteurized. However, it is suspected that unvaccinated goat

herds are kept in the vicinity of Callao and some even within the city limits at backyard farms. Most supermarkets in Lima and Callao sell pasteurized dairy products, but at smaller shops and markets, the origin and quality of the unlabeled products may be unclear. Shop owners may obtain their products directly or indirectly from farmers outside Callao, and occasionally, a batch of milk or cheese may be derived from an infected herd and prepared for consumption without pasteurization. In Peru, most human cases of brucellosis are caused by infection with *B. melitensis*, and because few people consume goat’s milk, the ingestion of fresh goat’s cheese is the most likely cause of disease.

Two of the seropositive household members were bacteremic while completely asymptomatic. Such cases have been rarely reported. One such case was described by Spink and Anderson³² in 1950. Recently, Celebi and others³³ identified two asymptomatic household members with bacteremia for *B. melitensis* biovar 3 by screening the family members of a patient with brucellosis. Interestingly, the pathogen could be isolated from the breast milk of one of these asymptomatic individuals. A study using polymerase chain reaction also found evidence for the presence of the pathogen in the blood of occupational exposed individuals who were asymptomatic, but this observation was not supported by blood culture.³⁴ The incubation period in brucellosis is ~10 weeks.³⁵ This relatively long incubation period may explain why such cases are found by screening risk groups.

In conclusion, despite efforts to control brucellosis in Peru, the disease still seems to be fairly common among household members of patients with brucellosis. Household members presumably remain the single most important identifiable risk group in an urban setting, and screening them provides an effective means for their early diagnosis. Testing household members can be done in settings like this with relatively little effort using the *Brucella* IgM/IgG flow assay. However, the cost benefit of screening should be considered and prioritized in relation with other urgent health problems. Finally, because early termination of control measures may result in the quick re-emergence of the infection, it is recommended to make efforts to identify remaining foci of transmission and to take appropriate actions to eliminate them.³⁶

Received September 20, 2007. Accepted for publication January 3, 2008.

Acknowledgments: The authors acknowledge the dedicated efforts of the other members of the “Brucellosis Working Group in Callao” in realizing this work; Laura Castañeda-Castañeda, Jenny Manrique, Nancy Cordova, Pilar Tuesta, Pilar Osorio, and Zósimo Yausen from the Hospital Nacional Daniel Alcides Carrión, Callao, Peru, and Melissa Méndez and Milagros Zavaleta from the Departments of Microbiology and Pathology, Universidad Peruana Cayetano Heredia, Lima, Peru. The authors thank Gavin Jackson and Coosje Tuijn for editing the manuscript. Approval for the study was obtained from the Institutional Review Boards of HNDAC and of Asociación Benéfica Proyecto en Informática, Salud, Medicina y Agricultura (A.B. PRISMA), a non-governmental organization based in Lima.

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a work prepared by a military service member or employee of the US government as part of that person's official duties. The authors declare to have no competing interests in the publication of this report.

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