Reviewer's report

Title: Health-seeking behaviour and clinical characteristics of human brucellosis cases in Arusha and Manyara regions, Tanzania

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Reviewer: Pablo C Baldi

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General

This paper describes the clinical presentation and epidemiology of human brucellosis in a region of Tanzania. The major contribution of the paper is the epidemiological analysis of the factors associated with the delay for seeking medical care and for receiving medical care. According to the authors, however, one of the goals of the study is “to determine whether clinical criteria for diagnosis can be identified using the clinical features”. While the clinical features of the cases may be briefly mentioned, the search for clinical markers of human brucellosis is nonsense. Hundreds of studies in different settings have clearly documented that brucellosis clinical findings are non-specific and that clinical features cannot be used as an isolated criterion for diagnosis. Another drawback of the paper is that the diagnosis of human brucellosis is ill-defined. Brucella was not identified by blood cultures and the serological diagnosis relied on a screening test (RBPT) and a “confirmatory” test whose validity is not supported with references.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

*) The most questionable aspect of the paper is the attempt to identify clinical features that help to the definitive diagnosis of brucellosis. As the authors themselves state in the Introduction, “the multiple and non-specific features of brucellosis contribute to difficulties in the diagnosis of brucellosis…”. Clinical aspects of brucellosis have been described in different settings since the first formal report of the disease, more than 100 years ago. From these reports it is clear that clinical manifestations of brucellosis are similar to those of many febrile illnesses. This subject has been extensively documented in the literature and new attempts to find differential clinical markers seem unjustified. Authors should delete from the article any mention to the search for differential signs and symptoms of the disease (including Table 7).

*) Another flaw of the paper are the criteria used to confirm Brucella infection. Brucellosis cases were defined as those presenting suspicious signs and symptoms, a positive RBPT and a positive c-ELISA. The reasons for including only these tests in the serological diagnosis of brucellosis are not given. Literature supporting the sufficiency of these tests for confirmation of brucellosis should be cited. No mention is made to attempts to confirm the infection through blood cultures.

*) Materials and Methods, Suspect and cases enrolment. "Detailed data …were colleted by the practitioners and blood sampling for the RBPT and hospital tests was conducted". It is not clear whether such “hospital tests” are other brucellosis tests. Authors should clearly indicate whether hospital diagnosis of brucellosis included only RBPT.

*) Results, Brucellosis Cases. It is said that 1586 samples from suspected brucellosis cases were sent to the VLA to be analyzed by c-ELISA. Do these 1586 samples represent the “brucellosis seropositives” mentioned in Materials and Methods?

*) Results, Brucellosis Cases. Has the c-ELISA been validated as a “confirmatory test”? Is so, authors should cite the relevant reference.

*) Results, Brucellosis Cases. The paragraph after Table 1 contains percentages and numbers in parentheses that represent a “proportion”, but it is not said which proportion. The paragraph makes reference to Table 2 and seems to repeat the data already presented in that Table. If so, Table 2 should be deleted. It must be noted, however, that numbers in the Table and in the paragraph are slightly different.

*) Results, Factors responsible for patient delay. While the association of several factors with patient delay
was explored, authors did not consider the potential contribution of presentation symptoms. This factor should be also analyzed, since affected patients are probably more likely to visit the physician when symptoms are more severe.

*) Results, Factor responsible for patient delay. In Table 5, age appears as a factor significantly associated with patient delay (likelihood ratio \( p \leq 0.001 \)). However, the odds ratio is very close to 1 (1.02), which suggests no association between age and patient delay. Authors should perhaps check the statistical significance of this variable.

*) Results, Hospital diagnoses of the cases….(page 15). It is said that 166 patients with positive screening serology for brucellosis were treated. However, only 98 patients had confirmed brucellosis. Why was treatment initiated without confirmation of brucellosis? Which was the antimicrobial regimen used? Was it the same for all patients?

*) Discussion, first paragraph. "There were proportionally more cases of brucellosis recorded in hospitals located in pastoral than in hospitals located in agropastoral areas". This conclusion can be misleading, since it suggests a relationship between these occupations and brucellosis. However, this proportion may be also influenced by differences between regions in the percentage of patients that seek medical care.

*) Discussion, second paragraph. It is said that patients that delayed visit to the hospital “only presented to hospital when symptoms worsened”. This is not shown in the Results. Therefore, this information should be added or, otherwise, this commentary should be deleted.

*) Discussion, page 17. The association between business and brucellosis is intriguing. Authors comment that “data on types of businesses cases were doing were not collected…” Nevertheless, authors could explain better what do they mean by “business”. Do they mean “trade” or “selling goods”? This could help to understand the relationship with brucellosis.

*) Discussion, page 18. "As a result of false negative results, 22 (54%) brucellosis cases were not diagnosed …". The occurrence of false negatives is rare in acute brucellosis. Authors should comment whether these missing diagnoses were acute or chronic brucellosis cases.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

*) In the Abstract, Results section, the number of confirmed brucellosis cases is wrong. Therefore, \( n=1586 \) should be replaced by \( n=98 \).

*) Results, Patient delay and treatment delay. It is said that “system delay was a result of false negative results …on their first visit to hospitals” Which serological tests had been used in those cases?

*) Results, Factors responsible for patient delay. In Table 5 there are two rows of values (coefficient, OR, etc.) for Tribe and Economic status, while the other variables have only one row. The reason for this difference is not explained in the text.

*) Determination of the persistence of antibodies to Brucella using the RBPT. Why was c-ELISA not included in the follow-up?

Discretionary Revisions (which the author can choose to ignore)

Which journal?: Not appropriate for BMC Medicine: an article whose findings are important to those with closely related interests and more suited to BMC Public Health

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Quality of written English: Acceptable

Statistical review: Yes
Declaration of competing interests:

I declare that I have no competing interests.