

Sero-prevalence and risk factors of human brucellosis among febrile patients visited health institutes at Awra and Gulina district, Afar Region, Ethiopia

Biruk Zerfu (✉ Biruk.zerfu@aaau.edu.et)

Addis Ababa University <https://orcid.org/0000-0002-2406-5971>

Sintayehu Mehari

Addis Ababa University

Kassu Desta

Addis ababa University

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Abstract

Background: Brucellosis is an important neglected bacterial zoonotic disease that affects animals and humans for decades. The aim of this study was to determine the sero-prevalence and risk factors of human brucellosis among febrile patients visited health institutes at Awra and Gulina district of Afar region Ethiopia.

Methods: A purposive cross-sectional study was conducted among 444 febrile patients visiting two health institutes in Awra and Gulina district of Afar region from February to May 2019. A 3-5ml blood samples were collected, thick and thin blood films were examined microscopically for malaria; serum was separated and tested antibody of *Brucella* using Rose Bengal Plate Test (RBPT) and positives ones were further subjected to ELISA. Data were entered using EpiData3.1 and analyses were performed using StataSE 14.

Results: A total of 444 febrile individuals (59.5% female) of age ranging from 2-83 years (mean= 26.1, SD = ± 11.8) participated in this study. The overall sero-prevalence of brucellosis was 31.5 % and 15.8% by RBPT and ELISA, respectively and 4.3% of the patients were positive for *P. falciparum*. Being male (AOR=2.41, 95%CI: 1.36 – 4.26, $p < 0.002$), drinking raw milk (AOR=15.42, 95%CI: 5.17 - 45.95, $p < 0.001$) and touching aborted fetus/discharges without protectives (AOR= 3.70, 95%CI: 1.61 - 8.50, $p = 0.02$) were independently associated with brucellosis among febrile patients.

Conclusion: Human brucellosis is highly prevalent in pastoralist patients presenting with fever in this study area. Consumption of raw milk and contamination with aborted or discharge of animals are major risk factors. Hence, brucellosis should be considered as an important public health problem in this study area.

Background

Brucellosis is a neglected bacterial zoonotic disease that has been affecting animals and humans for years [1]. The annual global human brucellosis case reports are about half a million [2]. The poor surveillance systems in developing countries like Ethiopia have led to underestimation of the true burden of the cases of brucellosis [3]. Several developed countries eradicated brucellosis as but it remains endemic in areas like northern and eastern Africa, India, central Asia, Mexico and central and southern America [4]. In Sub-Saharan Africa, animal brucellosis ranges from 10.2 to 25.7% [5]. Human beings can acquire the infection and can have a potential threat of re-emergence in several countries with an increasing incidence of infection in cattle [5].

Brucellosis is an occupational hazard for veterinarians, laboratory workers, slaughterhouse workers and farmers which can be acquired through either contact with infected animals, their tissues or animal products. The bacteria enter human through wounds or abrasion of skins/mucous membranes during contact with infected animals, and during consumption of raw or unpasteurized milk and dairy products of such milk [6]. Brucellosis in human is manifested mainly by intermittent or irregular fever, headache,

weakness, profuse sweating, chills, arthralgia, depression, weight loss, hepatomegaly and splenomegaly[7] and rarely arthritis, spondylitis, osteomyelitis, epididymitis and orchitis, but in severe cases neuro brucellosis, liver abscesses and endocarditis have been reported [8].

Since human brucellosis has wide clinical feature presentations, it mimics many communicable and non-communicable diseases like malaria, typhoid fever, typhus, rheumatic fever, joint diseases and others. These features pose a diagnostic difficulty for brucellosis especially in developing countries like Ethiopia because, they adhere mostly on apparent clinical signs and symptoms as diagnostic indicators to rule out diseases. In Ethiopia, determination of risk factors and health intervention of human brucellosis is not yet undertaken routinely due to lack of effective and appropriate diagnostic facilities [9, 10].

On the other hand, 75% of the Ethiopia's landmark is favorable for malaria transmission that has left about 68% of the total population at risk of malaria [11]. However, Ethiopia scaled up malaria intervention programs towards elimination that has achieved 40% reduction of malaria cases and increased capacity of case confirmation of presumed malaria diagnosis from 54% in 2013 to 87% in 2017 [12]. But the intervention has left abandoned those diseases with clinical features similar to malaria like brucellosis as undiagnosed and untreated. The current study area is a pastoral and agro-pastoral that rears camel, sheep, goat and cattle. Some studies have showed that animal brucellosis is highly distributed and the livelihood of the population is very close to animals that create potential risk factors to acquire brucellosis [13–15]. Nevertheless, human brucellosis has been rarely surveyed either as misdiagnosed or abandoned at all due to similarity of signs and symptoms presumably with malaria or unfamiliarity of health care workers with the disease and its epidemiology in this area [16, 17]. The aim of this study was to determine the sero-prevalence and risk factors of human brucellosis among febrile patients visiting health institutes in Awra and Gulina District of Afar region, Ethiopia

Methods

Study setting and population

The study was conducted in Kelwani primary hospital and Derayitu health center of Awra and Gulina district of Afar Region which is found in the north eastern part of Ethiopia. The majority of the communities are pastoralists whose livelihoods depend on livestock, specifically camels, cattle and small ruminants while few are practicing agro-pastoralist and growing crops by irrigation of Awash river.

Study design and sample size determination

A health institution based cross-sectional study design was used to determine sero-prevalence and risk factors of brucellosis among febrile patients visiting health institutes of Awra and Gulina district of Afar region, Ethiopia from February to May 2019. The finding of previous community based sero-prevalence of brucellosis (4.4%) in other pastoral area of the community of the region was used to estimate the sample size [17]. Based on this information, the calculated sample size, at 95% confidence level, 5% degree of accuracy and with 10% compensation for refusal, was 444 respondents.

Study participants, sample and data collection

All patients older than two years who had fever and measured axial body temperature ≥ 37.5 °C during data collection period, willing to provide written consent/assent for participation, was recruited to the study. A total 444 respondents were interviewed in their local language (Afar language) using a structured questionnaire to collect socio-demographic characteristics, sex, age, educational status, marital status, occupational status, residential address (urban/rural), potential risk factors: milk source (large ruminants, small ruminates or camels), ways of milk consumption either raw or boiled, experience of milk consumption from aborted animals, exposure to aborted fetus/ materials of animal without protective equipment, and the clinical features they felt along the onset of days of the features. A 3–5 ml of venous blood was collected from each febrile patients using plain vacutainer tube. Thin and thick blood smears were prepared immediately from each blood samples for the diagnosis of malaria. The remaining sample was kept at room temperature for 30 minutes to facilitate clotting and centrifuged at 3000 rpm for 5 minutes to get clear serum. All sera were separated in a labeled 1.8 ml Cryotubes, transported to Addis Ababa Federal police laboratory in a cold box and stored at 4 °C until testing.

Blood examination for malaria

Malaria was detected from Giemsa stained blood films following the guideline of Ethiopian Ministry of Health for the diagnosis of malaria and identification of *Plasmodium* species at the health institute [18].

Blood examination for brucellosis:

Two types of serological tests were used to determine sero-prevalence of brucellosis.

The sera were screened using Rose Bengal Plate Test (RBPT) and positive reactors were further subjected to ELISA. All sera and RBPT reagent and controls were taken out from refrigerator and kept at room temperature for 30 minutes to screen for anti-*Brucella* antibodies in Addis Ababa Federal police laboratory. As previously described [19], the smooth, attenuated stained *Brucella* antigen suspension was mixed with positive and negative controls and serum on circular test card. If specific antibody to *Brucella* antigen is present in the serum, it reacts with the antigen suspension to produce visible agglutination after shaking on a low speed shaker for four minutes. No agglutination indicates absence of specific antibodies to *Brucella* antigens. All sera positive for *Brucella* antibody using RBPT were transported to Armeaur Hansen Research Institute (AHRI) to confirm the anti-*Brucella* antibodies by IgG ELISA. According to manufacturer's guideline (Demeditec *Brucella abortus* IgG ELISA DEBRU01, Germany), qualitative anti-*Brucella* IgG ELISA was determined based on the principle of the spectrophotometric enzyme immunoassay at the wave length of 450 nm. The calculated absorption for the patient sera were compared with the value of the cut-off standard. If the value of the sample was higher than the cut-off standard, it was considered as positive whereas below the cut-off standard, the result was considered negative.

Data analysis

Descriptive analysis was used to summarize the data in the forms of frequencies and percentages. Pearson Chi² test was used for testing relationships between brucellosis and malaria infection with each demographic characteristic of study participants. Univariate logistic regression analyses were conducted to establish the association of the putative risk factors with brucellosis and odds ratio at 95% confidence intervals (CI) was considered. All risk factors significant at univariate analysis were considered for multivariate logistic regression analysis to determine the independent association between risk factors and brucellosis at 95% CI. P-value below 0.05 was considered statistical significance.

Ethical Consideration

This study received ethical clearance from the Ethical Review Board of Department of Medical Laboratory Science, College of Health Sciences, Addis Ababa University (DRERC/410/19/MLS). Permission was obtained from Derayitu Health center and Kelwani Primary Hospital. Participants' information sheet, which contains the objective of the study, inclusion/exclusion criteria, the required data and methods of data collection as well as informed consent/assent document, were prepared in Amharic the national language of the country. Then, the elements of participants' information sheet initially were orally translated to the local language (Afar Language) and described to each of the study participants or parents in case of children under 18 years by trained local health personnel. Informed consent was obtained from the participants and/or assent in children aged between 12 and 18 years. Blood sample was collected under aseptic condition by experienced laboratory technicians. Study participants who were found positive for malaria were treated according to malaria treatment guideline and the rest were treated with different antibiotics accordingly as per clinician presumptive diagnosis.

Results

Socio-demographic characteristics

A total of 444 febrile individuals (female, 59.5%), with age range of 2 to 83 (mean = 26.1, SD = ±11.8) years participated in the study, with the majority, 241 (54.3%) of the participants between 15–29 years old. Among 444 febrile study participants, 249 (56.1%) were agro- and/or pastoralists 201 (45.3%) were illiterate, 313 (70.5%) married, and 347 (78.1%) were rural residents. The clinical features were fever 444 (100%), headache 340 (76.6%), vomiting 139 (31.1%), general malaise 128 (28.6%), joint pain 125(28.2%) and general weakness 118 (26.6%) and the duration of the reported illness ranged from 1 to 30 days, with most of the patients 289 (65.1%) felt the illness for the duration of 1-3 days (Table 1).

Laboratory results

Of all (444) tested sera for brucellosis, the sero-prevalence of brucellosis was found 31.5% (140) by RBPT. From the entire sero-positive (140), 50 % (70) were found positive by ELISA. The combined sero-prevalence was 15.8% (70/444). Brucellosis was frequently detected in males than females (37.8% vs.27.3%, $X^2 = 5.47$, $p = 0.019$), among illiterate than compared to those with primary school and above

(20.4% vs. 11.9%, $X^2 = 6.21$; $p = 0.045$) and among rural residents than among urban residents (33.7% vs. 23.7%, $X^2 = 3.52$, $p = 0.041$) (Table 2).

Among all patients (444) tested for malaria, 4.3% (19) were found positive for *P. falciparum* by microscopic detection of Giemsa stained thick and thin blood films and therefore, were classified as malaria infected. Malaria cases were more common among males than females (7.2% vs. 2.3%, $X^2 = 6.14$, $p = 0.01$) and non-married than married (7.6% vs. 2.9%, $X^2 = 5.10$, $p = 0.02$). The frequency of *P. falciparum* malaria was high in the age group between 2-14 years (10.3%, $X^2 = 7.66$, $p = 0.05$) (Table 3).

Potential risk factors for brucellosis

At univariate logistic regression analysis, drinking raw milk (COR=27.71, 95%CI: 3.59 - 213.68, $p = 0.001$), drinking milk from aborted animal (COR = 2.87, 95% CI: 1.49 - 5.54, $p = 0.002$) and touching aborted fetus/discharges without protective equipment (COR = 2.82, 95%CI: 1.16 - 6.86, $p = 0.022$), were significantly associated with the occurrence of human brucellosis among these febrile patients (Table 4).

Multivariate logistic regression analysis model was built in to measure the relationship between sero-positivity for brucellosis and independent variables. All socio-demographic factors and potential risk factors that showed p -values < 0.05 in the univariate analysis were considered in the final multivariable logistic regression model. Being male (AOR=2.41, 95%CI: 1.36 – 4.26, $p < 0.002$), drinking raw milk (AOR=15.42, 95%CI: 5.17 - 45.95, $p < 0.001$) and touching aborted fetus/discharges without protective (AOR= 3.70, 95%CI: 1.61 - 8.50, $p = 0.02$) were associated with higher odds of having brucellosis infection among febrile patients (Table 5).

Discussion

This institution-based cross-sectional study identified 31.5% (140/444) positive by screening test (RBPT) for brucellosis, of which 50% (70/140) of them were confirmed positive by ELISA. Hence, the overall combined sero-prevalence of brucellosis was found 15.8% (70/444) and the prevalence of malaria was 4.3% (19/444) among febrile study patients. This study showed that there is high prevalence of brucellosis than malaria among febrile individuals of this pastoral area which demanding a public health consideration of neglected zoonotic brucellosis.

The prevalence of *P. falciparum*, was 4.3% and *P. vivax* was not detected. The result is lower than the previous health institution based studies carried out before full implementation of the intervention programs in Ethiopia such as in 2013 (51.5%) [20], in 2015(17%) [21], in 2016 (43.8%)[22]. This significant reduction of malaria prevalence may be the impact of scaling up of malaria intervention programs towards elimination introduced since 2016 in the country [23]. Malaria infection was found common among male and young children which is most likely due to the fact that as observed males traditionally move from home for a short or long time camping along livestock for grazing and naïve immunity of young children for malaria parasites. Even if the prevalence of malaria was found relatively

low due to the prevention and control measures employed by the country towards to eliminate from the country [23], sustainable devotion of control and prevention need to be enhanced by addressing all infection. Because there would be a possibility of resurgence of malaria epidemic and this identified *P. falciparum* which is the most severe of malaria may impact the health of the community in this study area.

The prevalence of human brucellosis is felt within the livestock prevalence range (10.2–25.7%) of lower- and middle-income countries [5]. This finding showed that the source of human brucellosis is most likely animals which are infected and served as reservoirs in this study area. The result is in agreement with the findings from febrile individuals of different Sub-Saharan African countries like Tanzania (15.4%), Northern Uganda (18.7%), and Northeastern Kenya (13.7%) [24–26]. This result revealed that human brucellosis is a febrile illness and highly circulating among sub-Saharan African countries including Ethiopia. The result was higher than the 2016 Ethiopian domestic animal brucellosis estimate, 5.3% in goats, 2.9% in cattle and camel and 2.7% in sheep but it was concurrent with the human estimates of pastoral area (17.4%) and higher than the human estimates of sedentary area (3.1%) [32]. The confirmatory finding of this study was lower than health facility based studies in Borena (34.9%) South Ethiopia and Metema (29.4%) North Ethiopia [27], but it is quite higher than many previous findings of health facility based studies of febrile individuals in other part of the country, southwestern Ethiopia, 1–3.6% [21, 28] and 2.15% in central Ethiopia [29]. The possible explanation for the difference in the seroprevalence could be due to difference in the sampling design schemes used, the number of samples, exposure to *Brucella* species and type of diagnostic tests used.

The study identified residential area and sex as important risk factors for human brucellosis. Rural residents and being male who lived in this area were about three and half and five and half times more likely to be sero-positive for brucellosis compared to urban residents and females, respectively. This finding is in agreement with other studies in Uganda and Egypt [24, 30], which might be due to male individuals having frequent contact with animal than females.

This study also identified consumption of raw milk and contacts with aborted fetus/discharges without protective equipment to be associated with brucellosis, which is in line with other couple of study findings in Uganda [24, 31]. This finding is supported by WHO report which revealed contact with infected materials such as aborted fetus, placenta, urine, manure and carcass has been reported to cause human brucellosis in 60–70% of cases [2]. The traditional habits of consumption of unpasteurized milk and fresh cheese and contamination of animal discharge are particularly common among remote areas like this study area which requires attention to create awareness on possible risk of acquiring *brucella* and other zoonotic infections.

This study has a few limitations. First, since it was a purposive cross-sectional study, we recruited only febrile individuals that visited health facilities that left behind apparently healthy chronic patients and during self-reporting there would be recall bias by the participants for possible factors associated to the occurrence of brucellosis in humans that weaken the inference of the finding. The other limitation is the

test being based on serological tests; the reported sero-prevalence of brucellosis could be difficult to differentiate from previous infection.

Conclusion

Human brucellosis is high among pastoral patients presenting with febrile illness in Ethiopia. Consumption of raw milk and exposure to animal discharge could lead to significant risk of infection with *Brucella*. Brucellosis presents clinical features indistinguishable from other febrile illness like malaria, and highly accurate diagnostic tools like ELISA are crucial for proper febrile disease management. The community based investigations that could address asymptomatic brucellosis, studies designed to identify the circulating *Brucella* species and drug profile, and study that can study similarity and difference of the species among humans and animals need to be introduced in this study area.

Abbreviations

AHRI

Armeaur Hansen Research Institute

AOR

Adjusted Odds Ratio

COR

Crude Odds Ratio

ELISA

Enzyme Linked Immunosorbent Assay

RBPT

Rose Bengal Plate Test

WHO

World Health Organization

Declarations

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Author's Contributions

BZ participated in the study conception, design, data collection, laboratory work, data analysis, data interpretation and manuscript writing. SM participated in its laboratory work, collection, data analysis, data interpretation and manuscript writing. KD participated in its design, data analysis, data interpretation and manuscript writing.

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Availability of data and materials

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Ethics declarations

Ethical approval and consent to participate

The study obtained ethical clearance from Ethical and Review Committee of Department of Medical Laboratory Science, College of Health Science, Addis Ababa University (DRERC/410/19/MLS). Permission to conduct the study was also obtained from Derayitu Health center and Kelwani primary Hospital. Written informed consent was obtained from each of the study participants and from their parent or guardian for those who were less than 18 years.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

Competing interests

The authors have no conflict of interests concerning the work reported in this paper

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Tables

Table 1: The socio- demographic characteristics of the study participants (No = 444)

Factors		No (%)
Sex	Male	180(40.5)
	Female	264(59.5)
Age	2-14	58(13.1)
	15-29	241(54.3)
	30-44	111(25.0)
	≥ 45	34(7.6)
Educational status	Illiterate	201(45.3)
	Primary school and above	243(54.7)
Marital status	Married	313(70.5)
	Non married	131(29.5)
Residents	Urban	97(21.9)
	Rural	347(78.1)
Occupation	Agro- /Pastoralist	249(56.1))
	Others*	195(43.9)
Clinical features	Fever	444(100.0)
	Headache	340(76.6)
	General weakness	118(26.6)
	Vomiting	139(31.1)
	Malaise	127(28.6)
	Joint pain	125(28.2)
Onset days of febrile	1-3 days	289(65.1)
	More than 3 days	155(34.9)

*Daily laborer, Governmental workers and students

Table 2: Demographic characteristics and distribution of brucellosis among study respondents (No =444)

Factors		No tested	No RBPT ⁺ ve (%)	No ELISA ⁺ ve (%)	Sero ⁺ ve at over all (%)	χ^2 ; P value
Sex	Male	180	68(37.8)	42(61.8)	42(23.3)	13.05; <0.001
	Female	264	72(27.3)	28(38.9)	28(10.6)	
Age	2-14	58	18(31.0)	7(38.9)	7(12.1)	3.58; 0.311
	15-29	241	77(32.0)	37(48.1)	37(15.4)	
	30-44	111	34(30.6)	17(50.0)	17(15.3)	
	≥ 45	34	11(32.4)	9(81.8)	9(26.5)	
Educational status	Illiterate	201	71(35.3)	41(57.8)	41(20.4)	6.21; 0.045
	Primary school and above	243	69(28.4)	29(40.0)	29(11.9)	
Marital status	Married	313	99(31.9)	52(52.3)	52(16.6)	0.57; 0.449
	Non married	131	41(31.3)	18(43.9)	18(13.7)	
Residents	Urban	97	23(23.7)	9(39.1)	9(9.3)	3.93; 0.047
	Rural	347	117(33.7)	61(52.1)	61(17.6)	
Occupation	Agro- /Pastoralist	249	86(34.5)	46(53.5)	46(18.5)	3.13; 0.077
	Others	195	54(27.7)	24(44.4)	24(12.5)	

Table 3: Socio- demographic characteristics and malaria among febrile study respondents (No =444)

Factors		No tested	No +ve (%)	X ² ; p value
Sex	Male	180	13(7.2)	6.40; 0.01
	Female	264	6(2.3)	
Age	2-14	58	6(10.3)	7.66; 0.05
	15-29	241	12(4.0)	
	30-44	111	0(0.0)	
	≥ 45	34	1(2.9)	
Educational status	Illiterate	201	7 (3.5)	0.57; 0.45
	Primary school and above	243	12 (4.9)	
Marital status	Married	313	9(2.9)	5.10; 0.02
	Non married	131	10(7.6)	
Residents	Urban	97	5(5.2)	0.23; 0.63
	Rural	347	14(4.0)	
Occupation	Agro- / Pastoralist	249	8(3.2)	1.57; 0.21
	Others	195	11(5.6)	

Table 4: Univariate analyses of potential risk factors for brucellosis of the study patients (No = 444)

Factors		No tested	No ⁺ ve at overall (%)	**COR(95% CI)	P value
Milk from large ruminant	No	332	49(14.7)	1	0.419
	Yes	112	21(18.7)	0.78(0.42;1.42)	
Milk from small ruminant	No	168	18(10.7)	1	0.725
	Yes	276	52(18.8)	1.12(0.57;2.23)	
Milk from camel	No	214	29(13.5)	1	0.144
	Yes	230	41(17.8)	0.64(0.35;1.17)	
Drinking raw milk	No	96	1(1.0)	1	0.001
	Yes	348	69(19.8)	27.71(3.59;213.68)	
Drinking of boiled milk	No	248	38(15.3)	1	0.222
	Yes	198	32(16.02)	0.70(0.40;1.24)	
Drinking milk from aborted animal	No	393	54(13.7)	1	0.002
	Yes	51	16(31.3)	2.87(1.49; 5.54)	
Touching of aborted materials/fetus	No	391	51(13.0)	1	0.022
	Yes	53	19(35.8)	2.82(1.16;6.86)	

**COR-Crude odds ratio, CI-Confident interval

Table 5: Multivariable analysis of risk factors for occurrence of brucellosis of the study patients

Factors		Adjusted OR(95% CI)	P value
Sex	Female	1	
	Male	2.41(1.36;4.26)	0.002
Educational status	Illiterate	1	
	Primary school and above	0.76 (0.40; 1.44)	0.399
Resident	Urban	1	
	Rural	1.19 (.53;2.64)	0.678
Drinking of raw milk	No	1	
	Yes	17.79 (2.41;131.32)	0.005
Drinking milk from aborted animal	No	1	
	Yes	0.76 (0.28;2.02)	0.577
Touching of aborted materials/fetus	No	1	
	Yes	2.50 (1.01;6.18)	0.048

Supplementary Files

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