



High brucella infection in patients with febrile illness in Sokoto, Nigeria: A study in malaria and typhoid endemic region

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Abstract

Brucellosis being a disease of zoonotic importance poses great danger to human health. Several studies here in Nigeria have shown brucellosis to be endemic in animals. However, there is dearth of information of the situation in humans. This study attempts to find out the prevalence of brucella infection in patients with febrile illness in Sokoto, Nigeria. The study was conducted to establish the presence and prevalence of *Brucella abortus* and *Brucella melitensis* antibodies in the sera of patients being tested for malaria parasites and for the Widal reaction. The study also involve sera screening of families of Nomadic Fulani pastoralists and veterinarians to see if they are at greater risk of brucella infection in Sokoto state of Nigeria. Sera samples were collected from patients in the acute febrile illness referred to the diagnostic laboratories at both the Usmanu Danfodiyo University Teaching Hospital (UDUTH) Sokoto and Sokoto Specialist Hospital. A total of 655 samples for malaria parasites and typhoid salmonella's tests and 50 apparently healthy volunteers (Livestock breeders and veterinarians) were tested for malaria/typhoid and *Brucella abortus* and *Brucella melitensis* using Rose Bengal plate test, serum Agglutination test and Competitive Elisa test. Out of the 705 samples screened (655 hospital patients and 50 apparently healthy persons), 312 (44%) had malaria parasite, 215 (30%) indicates enteric fever infection while 102 (14.4%) were seropositive to brucella infection. Twenty nine subjects showed mixed infection of brucella and malaria. Twelve persons showed brucella and enteric fever while another 12 had malaria and enteric fever. There was no association between gender or age and human brucella infection. The study has found out that a lot of febrile illness that are due to brucellosis are misdiagnosed or completely missed out. The implication is that the diseases will eventually become endemic in human with all its attendant consequences. Based on the findings, it is recommended that apart from malaria and enteric fever that is endemic in tropical regions, tests for brucella infection should be included in doctor's request to the laboratory.

Keywords: Brucella, Infection, Malaria, Typhoid, Patient, Sokoto

Introduction

In Nigeria, most patients presenting at hospitals with febrile illness tend to be clinically diagnosed as malaria or enteric fever, largely because of the high endemic nature of these two infections. Requests for confirmatory tests routinely submitted to Diagnostic Laboratories ask for malaria parasites and (or typhoid salmonellae (the Widal test). Generally, no requests are made for brucellosis. Human brucellosis is marked by non-specific recurring fever, headache, chills, joint pains, undue fatigue, anorexia, night sweats, among others (Alausa, 1979). Clinical diagnosis of brucellosis is difficult in malaria and enteric fever endemic regions, as the clinical picture mimics this more common acute febrile illness. In spite of high potential risk of human

exposures to infected animals and animal products, in most major hospitals brucellosis is never mentioned in differential diagnosis of human patients.

There are few reports of clinical brucellosis in Nigeria (Falade, 1974). Much of the published work on human brucella infections are based on sero-survey of occupational high risk groups such as livestock herders, farmers, butchers and other abattoir workers, and veterinarians (Adekolu, 1989; Ocholi *et al.*, 1993; Njoku, 1985; Atsanda and Agbede, 2001). Our observations (Junaidu *et al.*, 2008) in the course of epidemiological surveillance of brucellosis in Sokoto State, suggest that the magnitude of human brucella infections may be greater than is appreciated and that some patients responding poorly to malaria and typhoid treatment may be cases of brucellosis.

In an effort to assess this problem, we carried out a collaborative screening of patients with febrile illness presenting at two major hospitals in Sokoto State. The objective was to establish the presence and prevalence of *Brucella (abortus and melitensis)* antibodies in the sera of patients being tested for malaria parasites or the Widal reaction. We also conducted sero-screening of families of nomadic Fulani pastoralists (Livestock breeders) and Veterinarians to see if they are at greater risk of brucellar infection.

Materials and Methods

Sokoto State is located in the arid, northwestern border of Nigeria between Longitude 11°30 and 13°50 East and Latitude 4° and 6° North. Sokoto is the second largest livestock producing State in Nigeria. The indigenous populations are primarily farm families, mostly co-habit with various farm animals or are engaged in animal-related occupations. Much of the cow milk produced by Fulani herds is hawked fresh and raw or in the traditionally fermented form (“nono”). Consumption of fresh milk and local milk products is virtually habitual. As many as 80 to 100 herds of cattle, 8-10 camels and several sheep and goats are slaughtered daily at the Sokoto Municipal abattoir.

Commercial *Brucella abortus* antigens for Rose Bengal Plate Test (RBPT) and Serum Agglutination Test (SAT) as well as *Br. Melitensis* antigens were purchased from the Veterinary Laboratory Agency, Weybridge, United Kingdom. The antigens were stored and used in accordance with the instructions. Competitive Elisa Kit (COMELISA 400^R) for the detection of antibodies in serum for *Brucella* infection was also procured from the Weybridge Veterinary Laboratories.

Blood samples were collected from patients with acute febrile illness referred to the Diagnostic laboratories at the Usmanu Danfodiyo University Teaching Hospital and Specialist Hospital, Sokoto. The patients were tested for malaria parasites and the typhoid salmonellae at the diagnostic laboratories. Duplicates of serum samples for the Widal Test were taken in bijoux bottles to Veterinary Public Health Laboratory for brucella sero-screening. A total of 655 patients' sera were tested. Blood/serum samples were also collected from 50 apparently healthy volunteers (informed consent) livestock breeders and Veterinarians. All through the study, the strict confidentiality of the patient's identity and records was maintained. The samples were tested for malaria, and brucella antibodies.

Each centrifuged serum sample was screened for *Brucella abortus* and *Br. Melitensis* antibodies using the Bengal Plate Test, as described by Alton *et al* (1975). All sera showing positive reaction to *Br. abortus*

RBPT were re-tested by the SAT according to the method of Morgan (1967). Samples with four-fold titres (1:80) and above were confirmed *Br. abortus* positive.

By systematic (1 in 3) random selection, 30 of the serum samples positive for *Br. abortus* SAT as well as the 10 samples positive for *Br. melitensis* were subjected to the Competitive Elisa Test (COMELISA). Following the preparation and reconstitution of the reagents (dilution buffer, wash solution, stopping solution, positive and negative controls, conjugate solution, and substrate chromogen solution), the sera was tested in accordance with the procedures outlined for COMELISA 400.

Results

Out of the total 705 samples screened (655 hospitals patients presenting with acute febrile illness and 50 apparently healthy persons), 312(44%) had malaria parasites while 215(30%) indicated enteric fever infection (Positive Widal tests). One hundred and two (14.4%) were seropositive to *Brucella* infection. Twenty-nine subjects showed mixed infection of brucellar and malaria, twelve sera showed brucella and enteric fever, while another 12 had malaria and enteric fever (Table 1).

Among the 655 hospital febrile cases, 82(12.5%) indicated presence of brucella antibodies and out of these, 72 showed positive reaction to brucella abortus RBPT, while 10 were positive to *Br. melitensis* (Table 2). The *Br. abortus* SAT titres ranged from 1:40 (14 patients), high-risk persons, 20(40%) were positive to *Br. abortus* RBPT (Table 2). Nineteen of the 40 livestock breeders/herders examined showed positive brucella infection, while one (1) out of the ten (10) Veterinarians tested positive.

Table 3 shows the sex and age distribution of brucella infection among the 705 subjects. Although 68(66.5%) of the 102 Brucellar positive persons are males, considering the populations of the sexes screened, there was no significant difference in the proportions of male (16%) and female (17%) infected ($X^2 = 0.0091$, $P=0.0215$).

Similarly, 54 percent of the 102 positive brucella infections occurred in persons 18 years and above, and only 6 percent in the 0-10 years age band. However, there was no significant difference in the age-specific infection rate.

Discussion

Malaria and enteric fever (typhoid fever) has remained very common endemic diseases in Sokoto state in particular and Nigeria in general. Generally, at all levels of healthcare delivery system (Primary,

Table 1: Diagnostic Laboratory Results of Patients with Acute Febrile illness and Apparently Healthy High-risk Persons

Infection Status	Specific Infection	With Malaria	With Enteric Fever	With Brucella	Total
Malaria	271	-	12	29	312(44%)
Enteric Fever	191	12	-	12	215(30%)
Brucella infection	61	29	12	-	102(14.4%)
None of the above infection	-	-	-	-	64(11.6%)
Total					705(100%)

Table 2: Prevalence of Human Brucella Infection in Sokoto, Nigeria-risk Persons

		No. of sera Tested	<i>Br. abortus</i>		<i>Br. melitensis</i>	Prevalence
			RBPT	SAT		
Hospital patients with acute febrile illness	University Teaching Hospital	397	42	39	6	48
Enteric Fever	Specialist Hospital	258	30	27	4	
Sub-total	-	655	72(11%)	66	109(1.5%)	82(12.5%)
Occupational High-risk apparently healthy persons	Livestock breeders/herders	40	19	18	-	19
	Veterinarians	10	1	1	-	1
Sub-total	-	50	20	19	-	20(40%)
Grand Total	-	705	92	79	10	102(14.4%)

Table 3: Sex and Age Distribution of Human Brucella Infection

Status	Sex			Age			Total
	Male	Female	Total	0-10yrs	11-17yrs	18yrs and above	
Infected	68(66.5)	34(33.5%)	102	6(7%)	40(39%)	56(54%)	102
Non-infected	403	196	603	41	272	290	603
Total	475	230	705	47	312	346	705

* $\chi^2 = 0.0091$, $P = 0.0215$

secondary and tertiary levels), deferential diagnosis of febrile illness exclude brucellosis and some common zoonotic diseases. Virtually in almost all hospitals and clinics malaria and typhoid are the only differentials considered in the cases of febrile illness.

Although malaria and enteric (typhoid) fever remained the two most common infections recorded among the hospital patients presenting with acute febrile illness, representing 44% and 30% respectively, of the individuals tested, this study reveals that as much as 12.5% of the 655 patients were seropositive to Brucella infection. This large proportion of brucella infections would have been misdiagnosed or missed out, since tests for brucella are not requested, considered or routinely carried out in Diagnostic Laboratories. Our study confirms the high seroprevalence of brucellosis among occupational at-risk populations. Prevalence rates ranging from 28 to 57% have been reported in other studies in Nigeria (Falade 1974; Adekolu, 1989; Ocholi et al., 1993, Njoku 1995, Atsanda and Agbede, 2001). We recorded 40 percent among just 50 high-risk persons.

Brucella abortus is the primary cause of human brucella infection in Sokoto as shown by the study; only 10 cases out of the 82 sero-positive individuals had *Brucella melitensis* infection. This finding seems to be in contrast to reports in parts of Africa especially in the Southeastern and Mediterranean regions where *Br. melitensis* (from goats) is the predominant species affecting man. The low prevalence of *Br. melitensis* may be explained by the fact that although goats population is high in Sokoto State, subsists essentially by free-range for ageing animal-human contact is in frequent; goat meat is not favoured by the indigenous population, much of the goat reared are transported for sale in the Southern Nigeria, and drinking of goat milk is unpopular.

We found no association between gender or age and human brucella infection. Infection seems more associated with potential or relative risk of exposure. Persons routinely engaged in cattle-related occupations (breeding and herding) hand milking of cows, traditional processing of cow milk to produce "nono" by the women, abattoir workers and meat handlers; field veterinary practitioners; regular consumers of

fresh milk and milk products (Yoghurt and “Nono”) especially by farm families and middle class public servants, etc. are more likely to be infected. We noted that 61 (59%) of the 102 brucella infected hospital febrile cases are fulltime housewives and public servants. Thirty-five (34%) are from farm families who probably were exposed to newborn calves aborted fetuses, and placenta tissues and fluid; or were engaged in on-farm consumption of home produced milk and milk products.

Conclusions

It is inexplicable that brucellosis is not considered in differential clinical diagnosis of acute febrile illness. Through coordinated eradication programme, animal brucellosis is virtually absent in advanced countries and human infection is uncommon. Expatriate doctors from these countries may not be sufficiently aware of the recognition of human brucellosis in Africa and other tropical regions. Indigenous and foreign physicians and other health workers in these regions need to become more aware of the comparatively high prevalence of the human infection. Apart from malaria and enteric fever endemic in the tropical regions tests for brucella infection should be included in the doctors’ requests submitted to diagnostic laboratories. Under the primary healthcare, major hospitals and laboratories need to procure and have in stock commercial standardized brucella febrile antigens for routine sera-screening of referred patients, the same way most hospital now have Widal Test Kits for detection of antibodies to typhoid salmonellae. There is also the need for the intensification of collaboration between health care providers (the medical doctors, Veterinarians, laboratory technologist etc) to address the issue of zoonotic diseases which are not well captured in our health care delivery system.

There is need for Public health education through the media on the public health significance of

brucellosis in particular and zoonosis in general. Vaccination against brucellosis should also be carried out regularly by the government and farmers to protect both animals and human health. Also farmers whose animals tested positive should be paid compensation to avoid consumption of infected animals.

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