

## ORIGINAL ARTICLE

## SEROPREVALENCE OF BRUCELLOSIS AMONG PATIENTS PRESENTING WITH NON – SPECIFIC SYMPTOMS AT AYUB TEACHING HOSPITAL ABBOTTABAD

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**Background:** Brucellosis is one of the prevalent zoonotic diseases worldwide. It not only adds to the global burden of disease but also has huge economic impact. Clinical features of human brucellosis are usually vague. This study was carried out to find out the frequency of brucellosis among patients presenting with nonspecific symptoms in hospital setting and to find out risk factors. **Methods:** Study was carried out in outpatient Medicine Department of Ayub Teaching Hospital Abbottabad for the period of 3 months. Patients presenting with nonspecific symptoms of fever, body aches, myalgias, arthralgia, headache, backache, malaise and insomnia of either gender between the ages of 18–60 years were included in the study through consecutive sampling technique. Blood Samples from patients were sent for screening Brucella antibodies by serum agglutination method. Antibodies were checked for both Brucella abortus and mellitensis. **Results:** total 70 patients were recruited in the study. Out of these 49 (70%) were found positive for Brucella. These positive Brucella patients were mostly 42 (85.71%) female and majority 35 (71.4%) were in the age group of 21–40 years. In both male and female patients' majority were positive for both species of Brucella. Nonspecific symptoms included Aches, Pains and Myalgia in all the patients with additional symptoms of Malaise in 13 (18.6%), headache 10 (14.3%) and insomnia and fever in 9 (12.9%) each. Majority of the enrolled patients 53 (75.71) gave negative history of using boiled/pasteurized milk in their daily consumption while 17 (24.3%) patients suggested use of boiled/pasteurized milk. **Conclusion:** A high frequency of human brucellosis was found among patients presenting with nonspecific symptoms, therefore it is recommended that such patients should be screened for brucellosis.

**Keywords:** Brucellosis; Brucella abortus; Brucella mellitensis; Nonspecific symptoms; Zoonosis

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### INTRODUCTION

Brucellosis is confirmed to be one of the significant and prevailing global zoonotic infection according to World Health Organization.<sup>1</sup> Despite the fact that it has been eradicated in many developed countries, it is still endemic in middle East, Africa, Mediterranean, parts of Asia and Latin America.<sup>2</sup> Estimated 500,000 new human cases are reported annually worldwide with prevalence rate of 10/100,000.<sup>3</sup>

Brucellosis affects domestic animals like cows, goats, dogs etc except cats.<sup>3</sup> Species pathogenic to humans are Brucella abortus found in cows, Brucella mellitensis in goats, sheep and camels, Brucella suis in pigs and Brucella canis in dogs. Among the species Brucella mellitensis causes severe illness while Brucella abortus is least invasive and causes mild illness. Brucella mellitensis is the most common cause of brucellosis worldwide.<sup>4</sup> Transmission to humans occurs from infected animals either through direct contact or consumption of contaminated food and milk. As Brucella is readily killed by boiling or pasteurization, food borne exposure is limited to unpasteurized milk and dairy

products.<sup>5</sup> Clinical features of brucellosis are usually nonspecific. Common symptoms are fever, malaise, chills, fatigue, night sweats, headache, myalgia, arthralgia, anorexia and weight loss. It can also manifest as localized disease affecting nervous system, gastrointestinal, genitourinary, cardiovascular, musculoskeletal and integumentary system. Peripheral arthritis, sacroilitis and spondylitis are most frequent complications. Endocarditis though rare is the cause of mortality in 5% of human brucellosis.<sup>6</sup> The diagnosis of human brucellosis can be confirmed by blood culture and antibody titers with serum agglutination test (SAT).<sup>3</sup> A titre of 1:80 or above was considered positive.

Brucella although is rarely fatal but because of this debilitating and disabling disease there is not only huge impact on human health and well-being but it also contributes towards the global burden of disease. This disease also has huge economic impact in terms of losses in animal production both locally and at national level.<sup>7</sup> In Pakistan estimated prevalence is about 7%.<sup>8</sup>

Very scant data are available on the prevalence of human brucellosis in Pakistan. The objective of this study was to determine the frequency of brucellosis among patients presenting with nonspecific symptoms in outpatient department of Ayub Teaching Hospital Abbottabad and to describe patient characteristics that might help clinicians to suspect brucellosis in such patients. Patients with nonspecific symptoms often get neglected and are treated empirically resulting in inaccurate treatment and under reporting of this disease.

**MATERIAL AND METHODS**

This descriptive study was conducted in Out Patient Department of Medicine, Ayub Teaching Hospital Abbottabad for a period of 3 months from 1<sup>st</sup> to 30<sup>th</sup> November 2017. Patients presenting with nonspecific symptoms were recruited through consecutive sampling technique. Symptoms included fever, body aches and pains, myalgias, malaise, insomnia, anorexia, backache, headache and arthralgia. Patients of both sexes were included in the study. Patients below 18 years and above 60 years were excluded from the study.

Patients with chronic medical disorders like diabetes, hypertension, autoimmune disorders and chronic arthritis etc were also excluded from the study. Informed consent was taken from all the patients. Detailed history and examination was recorded on predesigned Performa. Variables included were age, gender, address, occupation, symptoms, duration of symptoms, use of pasteurized milk, clinical findings and *Brucella* status. Samples from patients were sent for screening *Brucella* antibodies by serum agglutination method. Antibodies were checked for both *Brucella abortus* and *mellitensis*. A titre of 1:80 or above was considered positive. Statistical analysis was performed by using SPSS version 16. Values were expressed as Mean±SD and percentages. Significance of difference was determined by using chi square test. Value of  $p < 0.05$  was considered as statistically significant.

**RESULTS**

This study enrolled 70 patients with nonspecific symptoms to assess the frequency of *Brucella*. Majority of these patients were female 58 (83%). Mean age of the enrolled patients was 31.05±9.31 years. The age of the patients ranged between 18-60 years with most of the patients 50(71.4%) belonging to the age group between 21–40 years.

Majority of the patients who presented to Ayub Teaching Hospital with nonspecific symptoms hailed from Mansehra 28 (40%) followed by Battagram 17 (24.3%). Maximum number of *Brucella*

positive patients were from district Mansehra 22 (44.90%) of the total brucella positive cases followed by 10 (20.4%) from Abbottabad and Battagram each. No statistical difference was found between *Brucella* positivity and geographical location ( $p$  value > 0.05). Majority 56 (80%) of the patients from these districts were house wives.

Of the total 70 enrolled patients, *Brucella* was positive in 49 patients while 21 patients showed negative results for *Brucella* giving frequency of 70%. These positive *Brucella* patients were mostly 42 (85.71%) female and majority 35 (71.4%) were in the age group of 21–40 years (Table-1).

Nonspecific symptoms included Aches, Pains and Myalgia in all the patients with additional symptoms of Malaise in 13 (18.6%), headache 10 (14.3%) and insomnia and fever in 9 (12.9%) each (Table-2).

Most of the patients 37 (52.9%) were suffering from these symptoms for less than 6 months when they first presented to OPD followed by 22 (31.4%) patients who reported between 1–2 years after the onset of the symptoms (Table-3) , however no significant difference was found between duration of symptoms and *Brucella* positivity.

Majority of the enrolled patients 53 (75.71) gave negative history of using boiled/pasteurized milk in their daily consumption while 17 (24.3%) patients suggested use of boiled/pasteurized milk. Of the 49 patients with positive *Brucella* results, 12 (16.32%) had *Brucella abortis*, 2 (4.08%) had *Brucella Mellitensis* and rest 39 (79.59%) *Brucella* positive patients had both *Brucella abortis* and *Mellitensis* positive results. In both male and female *Brucella* positive patients, the commonest results were presence of both species of *Brucella abortis* and *mellitensis* 6 (50%) and 22 (56.9%) respectively (Table-4).

The results did not reveal any significant association either between gender and *Brucella* positivity ( $p=0.261$ ) or age group and *Brucella* positivity ( $p=0.790$ ). However, significant association ( $p=0.001$ ) was found between non-consumption of boiled/pasteurized milk and *Brucella* positivity (Table-5).

**Table-1: Age and *Brucella* status**

Age group	Brucella Status		Total
	Brucella Positive	Brucella Negative	
upto 20 years	7	2	9
	77.8%	22.2%	100.0%
	35	15	50
21-40 years	70.0%	30.0%	100.0%
41-60 years	7	4	11
	63.6%	36.4%	100.0%
	49	21	70
Total	70.0%	30.0%	100.0%

**Table-2: Frequency of nonspecific symptoms**

	Frequency	Percent
Aches, Pains Myalgia, Fever	9	12.9
Aches, Pain Myalgia, Malaise	13	18.6
Aches, pain Myalgia, Insomnia	9	12.9
Aches, pain Myalgia, headache	10	14.3
Aches, Pains Myalgia,	29	41.4
Total	70	100.0

**Table-3: Duration of symptoms**

Duration	Frequency	Percent
<6months	37	52.9
6–12 months	5	7.1
1–2 years	22	31.4
>2 years	5	7.1
off & on	1	1.4
Total	70	100.0

**Table-4: Frequency of brucellosis among male and female patients**

Gender		Frequency	Percent
Male	Brucella negative	5	41.7
	Brucella abortus Positive	1	8.3
	Brucella abortus and Brucella mellitensis Positive	6	50.0
	Total	12	100.0
Female	Brucella negative	16	27.6
	Brucella abortus Positive	7	12.1
	Brucella mellitensis Positive	2	3.4
	Brucella abortus and Brucella mellitensis Positive	33	56.9
	Total	58	100.0

**Table-5: Association of brucellosis with use of unpasteurized milk**

Use of Pasteurized Milk		Brucella status		Total	p-value
		Brucella Positive	Brucella Negative		
No		17	0	17	0.002
		100.0%	.0%	100.0%	
Yes		32	21	53	
		60.4%	39.6%	100.0%	
Total		49	21	70	
		70.0%	30.0%	100.0%	

**DISCUSSION**

Brucellosis is an infectious disease that affects both humans and animals. It is a systemic disease presenting with fever and nonspecific symptoms like malaise, anorexia, headache, arthralgia and backache with clinical findings of hepatosplenomegaly and lymphadenopathy.<sup>9</sup>

This study was conducted to find out the frequency of brucellosis in patients presenting with nonspecific symptoms. Total 70 patients were recruited out of which 49 were found to be positive for Brucella giving frequency of 70%. A study conducted in Pakistan in 2012 among patients presenting with febrile illness and pyrexia of unknown origin reported prevalence of brucellosis 70% which is same as in the present study study.<sup>10</sup> Another hospital based study conducted in Khyber

Pakhtunkhwa reported prevalence of brucellosis ranging from 27.04 to 32.90% among different occupational groups.<sup>8</sup> A study from Bangladesh reported seroprevalence of brucellosis in patients with prolonged fever of 2%.<sup>11</sup> Hospital based study from Kenya indicated prevalence rate of 13.7% in febrile patients.<sup>12</sup> A study from Saudi Arabia reported frequency of 26.92% among patients who presented with fever and nonspecific symptoms.<sup>3</sup> We found higher frequency of brucellosis as compared to other regional and international studies. This may be due to that fact that majority of the patients in this study belonged to rural areas of Mansehra, Batagram and Abbottabad districts where domestic livestock like cows and goats are common and socioeconomic conditions and literacy rates are low.

No clinically significant difference was found between gender and seropositivity of Brucella, but majority of the positive patients were female. This may be due to the fact that majority of patients were female. However, studies conducted in Saudi Arabia<sup>3,13</sup> and Uganda<sup>14</sup> observed higher rates in males. This may be due to the cultural differences of these regions where males are more exposed as compared to the females, while females' patients in our study were housewives who are equally exposed as they work directly with livestock and in fields alongside their males.

No significant difference was observed between age and brucellosis. Majority of Brucella positive individuals belonged to age group 21–40 years. Most of the studies showed higher prevalence in the age group 20–60 years.<sup>11,15,3,16,15</sup> Our results are in line with these studies. However, few studies showed increased prevalence among age above 60 years.<sup>17,18</sup> Higher prevalence in younger age group is because of the fact that young people are more involved in working with livestock and also exposed to other occupational risks.

Regarding non-specific symptoms all patients had aches, pains and myalgias. Additional symptoms were malaise (18.6%), headache (14.3%), and insomnia (12.9%) and fever (12.9%). General symptoms of brucellosis are often vague. A systemic review and meta-analysis on clinical manifestation of human brucellosis documented various symptoms in patients of brucellosis. Fever was the commonest (78%) followed by malaise (71%), arthralgia (65%), sweats (54%), myalgias (47%), backache (45%) and headache (28%).<sup>7</sup> A study conducted in Iran also reported fatigue, myalgia and fever as the most common complaints of patients with brucellosis.<sup>19</sup> Ali Ismael *et al* from Saudi Arabia reported that 85% of Brucella positive patients had fever, while 78% presented with arthralgia, 35% had headache and 28% presented with anorexia.<sup>3</sup> Study from

Bangladesh revealed significant association with a positive serological test for *Brucella* and arthralgia and backache ( $p < 0.05$ ).<sup>11</sup> Another study from Azerbaijan also showed that after fever the most common symptoms in *Brucella* positive patients were sweats, fatigue, rigors, arthralgia and myalgias.<sup>20</sup> All these studies show that the frequency of nonspecific symptoms is higher in patients who have brucellosis strengthening the findings of this study. Clinical management of patients with such symptoms are often done empirically, resulting in inadequate treatment of patients. Clinicians should have high index of suspicion for brucellosis in patients with nonspecific symptoms and fever of unknown origin. Proper social and exposure history should be taken and laboratory investigations should be sent for timely diagnosis and treatment.

We tested patients for two species of *Brucella*, *Brucella abortus* and *mellitensis*. Patients who tested positive for both species were highest (79.59%), followed by *Brucella abortus* positive (16.32%) and *Brucella mellitensis* positive (4.08%). Another study from Pakistan in 2014 also showed similar results with highest seropositivity for both *Brucella abortus* and *mellitensis* (78.40%), followed by *Brucella mellitensis* (14.37%) and *Brucella abortus* (13.17%).<sup>8</sup> Studies from Bangladesh and Kenya reported *Brucella abortus* seropositivity only in their subjects.<sup>11,12</sup> *Brucella mellitensis* seropositivity was found in all subjects in a study conducted in Iran.<sup>9</sup> Hussein Ageely *et al* from Saudi Arabia reported that *Brucella mellitensis* is the main cause of human brucellosis followed by *Brucella abortus*.<sup>4</sup> Cattles are the principle host for *Brucella abortus* while *Brucella mellitensis* is hosted mainly by sheep, goats and buffalo. The difference between species seropositivity from other countries is mainly because of traditional livestock differences where sheep and goat are more commonly herded. Our study population from rural areas commonly have both cattles and buffalos as domestic animals that is why majority of patients were positive for both species. Although no vaccination is available for humans, vaccination of livestock by reducing brucellosis in animals can reduce human cases. We found significant difference between *Brucella* positivity and use of unpasteurized milk ( $p = 0.001$ ). Use of unpasteurized milk is a recognized risk factor for transmission of brucellosis to humans and our findings are similar to the other studies conducted.<sup>4,12,14,21,22</sup> Raising awareness regarding importance of consuming only pasteurized or treated milk and dairy products can reduce the frequency of human brucellosis.

Human brucellosis has significant impact on human health and wellbeing. It is a neglected

zoonotic disease which not only causes disabling disease in humans but also has economic impact in term of livestock productivity. Systemic review published in 2016 proposed based on its review and weights from the 2004 global burden of disease study, a disability weight of 0.150 for chronic and 0.190 for acute brucellosis.<sup>7</sup> Our study has the limitation that it was based on a relatively small sample size so the results should be interpreted carefully. Also, sample was based on patients attending the tertiary care hospital and thus may not be the true representative of the population to which these patients belonged to. Further research is required based on population studies to find out the true prevalence of this debilitating but under reported disease. Despite the limitations of study quite high frequency was detected in patients with nonspecific symptoms. It is recommended that patients with such symptoms should be screened for brucellosis so that timely and adequate treatment can be provided to avoid long term disability.

## CONCLUSION

We found high frequency of human Brucellosis among patients presenting with nonspecific symptoms. Clinicians should screen patients for brucellosis who present with nonspecific symptoms for timely diagnosis and proper treatment of this disease.

## RECOMMENDATIONS

Pakistan is an agricultural country with majority of the population living in rural areas and depending on livestock production, it is imperative that human brucellosis should be notified properly and timely so that livestock and human contacts can be screened. Being a zoonotic disease addressing Brucellosis in animals can be the most efficient method of controlling human disease. It is recommended that frequent sampling from suspected livestock and vaccination should be carried out by veterinary clinic and agricultural offices. Public awareness campaigns should be organized by health authorities especially in rural areas to educate people about Brucellosis, its risk factors, modes of human transmission and how to prevent it. Consumption of unpasteurised milk and its products should be particularly discouraged.

## AUTHORS' CONTRIBUTION

SM: Data collection. IS: Literature search and write-up. AR & MZH: Proof reading

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