RESEARCH PAPER

Serological Evidence Of Brucella Infection In Acute Febrile Illness Patients At A Tertiary Care Centre: A Prospective Study

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Abstract

Background: Brucellosis is a zoonotic disease, a global health concern that remains underdiagnosed in humans due to its non-specific clinical presentations. India, is particularly vulnerable to brucellosis due to its high-density livestock farming. This study aimed to estimate the seroprevalence of brucellosis in individuals presenting with non-specific clinical symptoms.

Materials and Methods: This prospective follow up study was conducted in departments of microbiology, lhmc and associated hospitals and department of medicine in lhmc from april 2024 to august 2025. A total of 132 serum samples were collected from individuals suffering from acute febrile illness for brucellosis testing. Detection of anti-brucella igm antibodies in serum samples was performed by commercially available elisa kit according to the manufacturer's instruction.

Results: Out of 132 subjects, 18 cases were caused by brucella spp (13.6%) detected by igm elisa. In brucella positive patients most commonly presenting feature along with fever were myalgia (66.75%), headache (61.1%), malaise (61.1%). While most common presenting sign were joint tenderness (27.7%), skin rash (22.2%), and jaundice (16.7%). Laboratory parameter shows raised crp (100%), leukocytosis (72.2%), and raised haematocrit (77.8%). Majority of brucella positive patients (50%) were in age group 18-25 years, median hospitalization was 10 days. Out of 18 brucella positive 4 were on monodrug therapy and 14 were on multidrug therapy. All patients discharged after full recovery no mortality seen.

Conclusion: This study demonstrates a significant seroprevalence of brucellosis among both symptomatic and asymptomatic individuals. Owing to its non-specific clinical presentation, routine serological screening is essential, particularly in high-risk populations. Furthermore, adopting a one health approach that integrates human and animal health surveillance is vital for effective prevention and control of the disease.

Keywords: Na

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INTRODUCTION

Acute febrile illness is a common presentation in clinical settings across the globe, with a wide range of bacterial, viral, parasitic, and fungal infections being implicated. Globally, AFI encompasses a range of infectious diseases such as typhoid fever, leptospirosis, brucellosis, scrub typhus, rickettsial infection[1].

Brucellosis is one more significant however disregarded zoonotic illness with a worldwide distribution. It contributes significantly to economic losses for animal handlers. Long ago in his publication epidemics Hippocrates described brucellosis type syndrome in humans living in the Mediterranean littoral. After centuries, in 1886, British physician David Bruce with Greek physician Mistokles Zammit discovered the causative organism Micrococcus melitensis, of brucellosis and would identify milk product of goat as the source of infection for military troops on the island of Malta [2]. Even after centuries, it is still a serious issue for human beings. It occurs in humans as an acute, sub-acute or chronic illness which develops from direct or indirect contact with animals

or by consumptions of unpasteurized milk, milk products or meat of infected animals[3, 4]. The most common route of transmission occurs when humans consume raw milk or cheese made from infected animals [5]. It is also known as undulant fever, Mediterranean fever or Malta fever [6].

Brucellosis is caused by Brucella spp., made out of seven terrestrial species and something like two marine species. Terrestrial Brucella spp., include *B. abortus*, *B. melitensis*, B. *Suis, B. ovis, B. canis, B. neotomae*, and a newfound species category, *B. microti* [2, 6, 7]. Among all the Brucella species, *B. melitensis* is mostly responsible for human brucellosis and prevalent in Southeast Asian countries including India[3]. Human brucellosis can be caused by any of the four significant species. *B. abortus, B. melitensis*, *B. suis*, and *B. Canis.* In India, where dairy cattle raising is normal, *B. abortus* and *B. melitensis* are known to cause AFL.

All around the world, 500,000 cases are accounted for each year, with 2.4 billion individuals at risk. All age groups are affected. The detailed typical predominance pace of brucellosis in high risk populations is found to be 8.5% in India[8]. India has the largest livestock population in the world approximately 535.82 million, still productivity of the livestock sector is very low in India as compared to developed countries of the world[9]. Brucellosis lacks pathognomonic clinical signs; its diagnosis requires laboratory tests[10]. The symptoms of systemic brucellosis are most of the time non-specific, including fever, exhaustion, perspiring, muscle pain, joint pain, back pain, and loss of appetite[5].

Over the years several serological tests have been developed for detection and surveillance of brucellosis. In which there is rose Bengal test (RBT), ELISA, complement fixation(CFT), fluorescence polarization assay (FPA) and serum agglutination test (SAT)[10].Overall brucellosis is diagnosed by blood and bone marrow culture or serological tests. The Brucella Serum agglutination test (SAT) is utilized regardless of its lower sensitivity and specificity, 23 PCR tests might be more sensitive and specific for diagnosing human brucellosis than blood culture or conventional serological tests.

AIMS AND OBJECTIVE

1. To estimate the seroprevlance of *Brucella* responsible for acute febrile illness in adults admitted in a tertiary care hospital by serological tests.
2. To correlate with clinical profile, morbidity and mortality in adults patients with acute febrile illness.

MATERIALS AND METHODS

This Prospective follow up study was conducted in Departments of Microbiology, LHMC and Associated Hospitals and Department of Medicine in LHMC from April 2024 to August 2025.

Study population: Patients admitted with acute febrile illness in the ward of the medicine department and emergency department in LHMC.

Inclusion criteria

• Adult patients of more than 18 years of age

Patients with fever of 2 weeks or shorter in duration with body temperature of more than 38 °C who are admitted in the hospital as per definition[11, 12].

• The cause of illness is undiagnosed after medical history and physical examination.

Exclusion criteria.

1. Fever due to any other causes like connective tissue disease, malignancy, immunocompromised condition. llness.

STUDY METHODOLOGY

The information regarding age, gender, presenting symptoms on admission, co-morbidities, and lab results was collected using structured questionnaires and appropriate treatment provided according to bacterial etiology. Patients were followed twice weekly till discharge/ death. 3 ml of blood was collected in a plain vial and transported to the lab at the earliest. Serum was separated and aliquoted and stored at – 70 degree Celsius till further testing.

2. SAMPLE PROCESSING:

Detection of anti-*Brucella* IgM antibodies in serum samples was performed by commercially available ELISA kit according to the manufacturer's instructions.

Ig M ELISA for Brucella species

PRINCIPLE OF THE ASSAY

The assay is based on an enzyme-linked immunosorbent assay (ELISA) format. Microtiter wells are pre-coated with Brucella antigens. Patient samples and controls are added, allowing specific IgM antibodies to bind. After washing, HRP-conjugated anti-human IgM binds to the captured antibodies. Addition of tetramethylbenzidine (TMB) substrate results in a blue color, which turns yellow upon stopping the reaction. The color intensity, measured spectrophotometrically, is proportional to the amount of specific IgM antibodies in the sample.

RESULTS

This study was conducted in the Department of Microbiology, Lady Hardinge Medical College, New Delhi between April 2024 and August 2025. A total of 132 adult patients with acute febrile illness admitted in Smt. Sucheta Kriplani Hospital were enrolled in this study.

Table 1: Age and sex distribution of study subjects (n=132)

Age Group (in years)	Sex distribution		Total
	Male	Female	
18-25	16(28.1%)	41(71.9%)	57(43%)
26-35	11(24.4%)	34(75.6%)	45(34.1%)
36-45	8(57.1%)	6(42.9%)	14(10.6%)
46-55	7(87.5%)	1(12.5%)	8(6.1%)
56 and above	2(25%)	6(75%)	8(6.1%)
Total	44(33.3%)	88(66.7%)	132

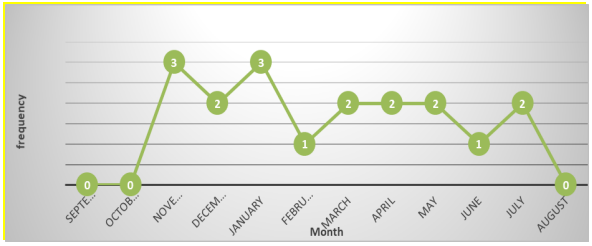
Out of 132 subjects, 18 cases were caused by *Brucella spp* (13.6%) detected by IgM ELISA.

Table 2: Age group-wise distribution of *Brucella* species in AFI cases

Age group (in years)	*Brucella spp* n (%)
18-25	9(50%)
26-35	7(38.9%)
36-45	1(5.6%)
46-55	1(5.6%)
56 and above	0
Total	18

Majority of *Brucella spp* were detected in 18-25 years of age group followed by 26-35 years of age group.

Fig 1: Month-wise distribution of AFI cases positive for *Brucella* spp



Brucella spp were detected from AFI cases throughout the year with maximum cases reported in November and January.

Table 3: Clinical symptoms in AFI cases positive for *Brucella* spp (n=18)

Symptoms	Frequency	percentage	P value
Fever	18	100	2.2×10^{-10}
Vomiting	8	44.4	0.74
Abdominal pain	6	33.3	0.09
Myalgia	12	66.7	0.09
Arthalgia	5	27.7	0.04
Headache	11	61.1	0.32
dizziness	2	11.1	5.23×10^{-6}
Malaise	11	61.1	0.32
Anorexia	10	55.5	0.27

p value calculated by fisher exact test., p value < 0.05 is significant

Most common symptoms associated with fever were myalgia (66.7%) followed by headache and malaise (61.1%).

Table 4: Clinical signs in AFI cases positive for *Brucella* spp (n=18)

Signs	Frequency	Percentage	P value
Skin rash	4	22.2%	0.0022
Jaundice	3	16.7%	0.00015
Hepatomegaly	1	5.6%	0.012
Splenomegaly	1	5.6%	4.8×10^{-5}
Joint tenderness	5	27.7%	0.003
Low urine output	1	5.6%	7.1×10^{-8}

p value calculated by fisher exact test., p value < 0.05 is significant

Commonest signs were joint tenderness (27.7%) and skin rash (22.2%) followed by jaundice (16.7%).

Table 5: Laboratory parameters of AFI cases with *Brucella* infections (n=18)

Parameters	Frequency	Percentage
Thrombocytopenia	2	11.1%
Raised hematocrit	14	77.8%
Leucopenia	0	0
Leucocytosis	13	72.2%
Elevated ALT	3	16.6 %
Elevated AST	3	16.6%

Elevated ALP	2	11.1%
Raised CRP	18	100%

Hematocrit was raised in 77.8% of cases. Liver enzymes were deranged in 16.6 % of cases while all cases showed raised CRP levels.

Table 6: Clinical outcome of patients positive for *Brucella spp* (n=18)

Category	**Characteristics**	
Severity	**Fever (High grade)**	06
	Hospitalization days, Median (range)	10 days (5-14 days)
	Complications	0
Therapy	**Single drug**	4
	Multiple drug	14
Outcomes	**Recovered**	18
	Death	0
	Lost to follow up	0

Six out of 18 patients had high grade fever with no complications. All 18 patients were fully recovered at the time of discharge.

DISCUSSION

Out of 132 patients, 66.6% were female and 33.3% were male. In enrolled patients maximum patients (43.2%) lie in age group 18-25 years reflecting adult population predominance. The mean age of patients were 31.7 years and median age was 26 years. Previously one study was conducted in the same tertiary hospital by Gautam et al shows the same pattern with female predominance[13]. Similar finding was also seen in various study done for AFI in which most of the affected person lie in age group 20-30 years with median age 26 years [14-16].

Out of the 132 patients evaluated, human brucellosis seroprevalence by IgM was 13.6 %. Globally, human brucellosis prevalence in endemic regions exhibit a wide range from 2-70% depending on the degree of livestock infection, preventive health infrastructure and at-risk practices [17-20]. *Bruella* spp were detected from AFI cases throughout the year with maximum cases reported in November (16.6%) and January (16.6%). When we compared these findings regionally (north India), our findings closely aligned with results from a hospital based study in Punjab (2025) where the seroprevalence rate was 17.5% among symptomatic individuals[17]. While a large-scale population survey in Orissa (2022) documented a prevalence of 16.65% among rural adults involved in animal husbandry [18]. In Rajasthan, another study was performed which reflected 9.3% prevalence[19]. Majority of Brucella IgM ELISA positivity case in current study were in adults (18-25 years) with female predominance. Similar finding was reported by others studies also[21, 22].

Fever was the universal presenting symptoms in all *Brucella* positive patients along with other frequently associated symptoms, myalgia (66.7%), weakness and headache (61%) vomiting (44%) and some other non-specific complaints. Commonest sign seen in affected patients were joint tenderness (27.7%) and skin rash (22.2%) followed by jaundice (16.7%). Singh et al reported same clinical finding in their study which shows fever (72%) joint pain (43%) and myalgia (57%) that closely resembles with other acute or chronic illness which makes it difficult to be diagnosed [1, 23, 24]. Less frequently observed symptoms were skin rash, jaundice, dizziness and low urine output in our study.

Laboratory finding frequently include elevated inflammatory markers (raised CRP in 100% patients) deranged liver enzyme (elevated ALT and AST in 16.6%) and some cases cytopenias (thrombocytopenia in 11.1%).While leukocytosis seen in 72.2% and raised hematocrit in 77.8% cases. Pericheria et al reported similar types of laboratory finding with predominant feature raised CRP (80%) and leukocytosis (74%) [25].

Median hospital stay for *Brucella* positive patients was 10 days with range of 5-14 days[25]. Out of 18 patients 4 patients were on monotherapy (doxycycline) and 14 were on multidrug therapy (doxycycline + rifampicin/streptomycin/gentamycin). No any further complication was seen in *Brucella* positive patients during their hospital stay and discharge from hospital after full recovery. There was no cases of any mortality in our study.

Human brucellosis remains underdiagnosed in India, often missed due to its nonspecific symptoms, closely resembling with other AFI causes like typhoid, dengue, lack of physicians awareness and non-availability of routine test done for brucellosis[24]. Current study emphasize the necessity for heightened clinical suspicion, especially in patients with long duration fever and relevant exposure history and advocate for the inclusion of routine test for brucellosis which may increase the case finding in Delhi region and take a look for awareness regarding brucellosis.

CONCLUSION

Acute febrile illness, causes considerable morbidity and mortality and economic burden to developing countries. Similar clinical presentation makes confusion in distinguishing between different causative organisms of AFI. Routine diagnostic methods are still incapable of identifying the exact cause due to their certain limitation and time of detection is also more.

Most of the tertiary hospital are dependent on routine diagnostic. Routinely *Brucella* screening should be done in suspected cases so that we can decrease the burden and improve clinical outcomes in adult AFI.

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