ORIGINAL RESEARCH

Assessment of Clinical Manifestations and Treatment Outcomes in Patients with Brucella Endocarditis

[1]Dr. Ramanpreet Kaur Mongra, [2]Dr. Utpal Goswami

[1]Assistant Professor, Department of Microbiology, ICARE Institute of Medical Sciences and Research and Dr. Bidhan Chandra Roy Hospital, Haldia (IIMSAR & BCRHH), West Bengal, India
[2]Associate Professor, Head of Department, Department of Pathology, ICARE Institute of Medical Sciences and Research and Dr. Bidhan Chandra Roy Hospital, Haldia (IIMSAR & BCRHH), West Bengal, India

Corresponding Author: Dr. Utpal Goswami
Associate Professor, Head of Department, Department of Pathology, ICARE Institute of Medical Sciences and Research and Dr. Bidhan Chandra Roy Hospital, Haldia (IIMSAR & BCRHH), West Bengal, India
Email: ukdgowami@gmail.com

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ABSTRACT
Background: Human brucellosis, a zoonotic disease, can be transmitted through the consumption of unpasteurized milk and dairy products from infected sources, inhalation of aerosols, and direct contact with contaminated animal parts. The present study was conducted to assess clinical profile, and outcomes of Brucella endocarditis. **Materials & Methods:** 56 patients with infective endocarditis (IE) of both genders were selected. Brucella species were isolated and identified from blood cultures using the automated Bact/Alert culture media and VITEK 2 system (Biomerieux, USA). To detect antibody titres, the Standard Agglutination Test (SAT), which measures total agglutinating antibodies {Immunoglobulin M (IgM) and Immunoglobulin G (IgG)}, was employed. **Results:** Out of 56 patients, 30 were males and 26 were females. Valve involved was aortic in 21, mitral in 20, both in 8 and prosthetic in 7. Vegetation size was <1 cm in 34 and >1 cm in 22. Complications were perforation in 4, abscess and SOV aneurysm in 1 and systemic embolization in 2. Management done was medical in 37 and urgent surgery in 19. Antibiotic used was Rifampicin+ Doxycycline in 12 and Rifampicin+ Doxycycline+ gentamycin in 44. Outcome was survived 50 and died 6. The difference was significant (P< 0.05). **Conclusion:** Brucella endocarditis is often marked by large vegetations and can result in paravalvular and embolic complications. The findings of this study highlight that valve involvement, vegetation size, presence of complications, treatment modality, and antibiotic regimen are key determinants of clinical outcome in Brucella endocarditis.

Keywords: Brucellosis, Infective endocarditis, Rifampicin, Doxycycline, Gentamycin.

INTRODUCTION

Human brucellosis, a zoonotic disease, can be transmitted through the consumption of unpasteurized milk and dairy products from infected sources, inhalation of aerosols, and direct contact with contaminated animal parts.[1] The causative agent is a gram-negative intracellular bacillus from the genus Brucella, resulting in chronic granulomatous infection affecting multiple organs. The bacteria typically develop in the lymph nodes of the area and enter the blood circulation via the ductus thoracicus. Brucellosis has been reported in countries worldwide, with the highest concentration of cases occurring in Central Asia and the Mediterranean region.[2,3]

Cardiovascular manifestations of brucellosis, which occur in approximately 2% of infections, include Infective Endocarditis (IE), myocarditis, and pericarditis. IE is the primary contributor to mortality in brucellosis, responsible for 70-80% of deaths.[4] Due to its nature as a slow-growing and fastidious organism, along with the constraints of serological tests, diagnosing brucellosis presents considerable difficulties and is frequently overlooked. Brucella endocarditis

occurs with a prevalence of 1.3-1.7%.[5] In India, the available data consists solely of case reports and case series. In India, there has been no assessment of haematological parameters and treatment outcomes. The management of brucella endocarditis includes medical and surgical treatment based on the severity of valve involvement and complications.[6]

AIM & OBJECTIVES

The present study was conducted to assess clinical profile, and outcomes of Brucella endocarditis.

MATERIALS AND METHODS

Study Design

This was a prospective observational study aimed at evaluating the clinical profile, treatment modalities, and outcomes of patients diagnosed with Brucella endocarditis.

Study Population

A total of 56 patients (both male and female) with confirmed infective endocarditis (IE) were enrolled in the study. All participants provided written informed consent prior to inclusion.

Study Place

The study was conducted in the Department of Microbiology in collaboration with Department of Pathology, ICARE Institute of Medical Sciences and Research and Dr. Bidhan Chandra Roy Hospital, Haldia (IIMSAR & BCRHH), West Bengal, India, equipped with facilities for microbiological diagnostics, echocardiography, and cardiothoracic surgery.

Study Duration

The study was carried out over a period of one years, from December 2020 to November 2021.

Inclusion Criteria

- Patients aged ≥18 years.
- Clinical diagnosis of infective endocarditis based on modified Duke's criteria.
- Blood culture positive for Brucella species.
- Willingness to participate and provide written informed consent.

Exclusion Criteria

- Patients with culture-negative endocarditis.
- Patients with endocarditis due to organisms other than Brucella.
- Patients with immunocompromised states (e.g., HIV/AIDS, chemotherapy).
- Patients not consenting to participate.

Ethical Considerations

The study protocol was reviewed and approved by the Institutional Ethics Committee. Informed consent was obtained from all patients prior to data collection. All procedures were carried out in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments.

Study Procedure

1. Data Collection: Demographic data including age, gender, and clinical symptoms were recorded at baseline.
2. Microbiological Analysis:
   - Blood cultures were collected aseptically and processed using Bact/Alert culture media system.
   - Identification and antimicrobial susceptibility were performed using the VITEK 2 system (BioMérieux, USA).
3. Serological Testing:
   - Standard Agglutination Test (SAT) was used to detect anti-Brucella antibodies, measuring total IgM and IgG titres.
4. Clinical Evaluation:
   - Symptoms such as fever, dyspnoea, weight loss, and night sweats were recorded.
   - Dyspnoea was assessed using the New York Heart Association (NYHA) classification.
   - Anaemia was defined as Hb <12 g/dL (females) and <13 g/dL (males).
   - Thrombocytopenia was defined as platelet count <1.5 lakh/mm³.
   - Liver enzyme elevation was defined as ALT/AST >2× the upper limit of normal.
5. Echocardiography: All patients underwent transthoracic and/or transesophageal echocardiography to confirm vegetations and valve involvement.
6. Treatment:
   - Antibiotic regimens and dosages were documented. Treatment included combinations of doxycycline, rifampicin, aminoglycosides, and/or ceftriaxone.
   - Some patients underwent cardiac surgery based on the extent of valve destruction, abscess formation, or heart failure. Specific surgical techniques were tailored to individual valve pathology.

Surgical Technique

Surgical interventions included valve repair or replacement, performed via open heart surgery under cardiopulmonary bypass. Indications included severe valvular regurgitation, large vegetations (>10 mm), recurrent embolic events, or persistent bacteraemia despite adequate antibiotic therapy.

Outcome Measures

- Primary outcomes: Mortality and relapse rates.
- Secondary outcomes: Clinical improvement, echocardiographic resolution, normalization of hematologic and liver parameters.
- Outcomes were followed for a minimum of 3–6 months post-treatment.

Statistical Analysis

- Data were compiled and analyzed using SPSS (version 20.0, USA).
- Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables as frequencies and percentages.
- Chi-square test or Fisher's exact test was used for categorical comparisons.
- Student's t-test or Mann-Whitney U test was used for continuous variables, depending on normality of data.
- P-value <0.05 was considered statistically significant.

RESULTS

Table 1: Gender wise distribution of Patients

Total- 56		
Gender	**Males**	**Females**
Number	30 (53.57%)	26 (46.43)

Table 1 shows that out of 56 patients, 30 were males and 26 were females.

Table 2: Assessment of Clinical and Treatment Parameters in Patients with Brucella Endocarditis

Parameters	Variables	Number	P value
Valve involved	Aortic	21	0.03
	Mitral	20	
	Both	8	
	Prosthetic	7	
Vegetation size	<1 cm	34	0.05
	>1 cm	22	
Complications	Perforation	4	0.05
	Abscess and SOV aneurysm	1	
	Systemic embolisation	2	
Management	Medical	37	0.01
	Urgent surgery	19	
Antibiotic used	Rifampicin+ Doxycycline	12	0.05
	Rifampicin+ Doxycycline+ gentamycin	44	
Outcome	Survived	50	0.01
	Death	6	

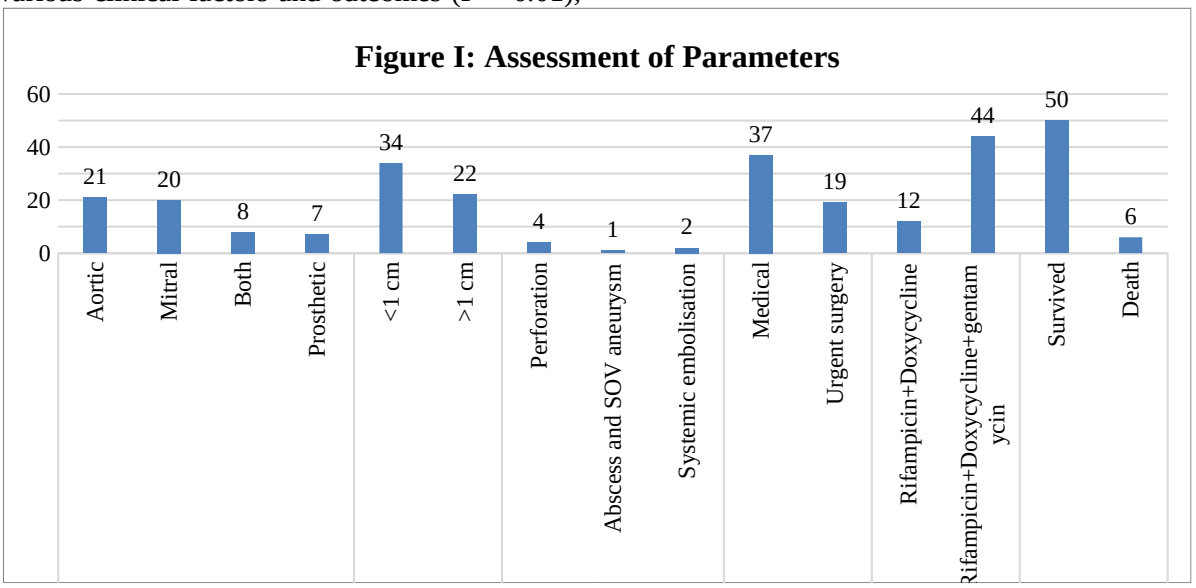
Table 2, figure I show that Aortic valve involvement was observed in 21 patients, mitral valve in 20 patients, both valves (aortic + mitral) in 8 cases, and prosthetic valve endocarditis was noted in 7 patients. A statistically significant association was found between the type of valve involved and Brucella endocarditis (P = 0.03), suggesting the pattern of valve involvement may influence clinical course or outcomes. Vegetation size was <1 cm in 34 and >1 cm in 22 patients. The vegetation size was significantly associated with the disease course **(**P = 0.05), possibly influencing complications or management approach. Complications such as perforation were seen in 4 patients, abscess and Sinus of Valsalva (SOV) aneurysm in 1 patient, and systemic embolisation in 2 patients. Overall, the presence of complications showed statistical significance (P = 0.05), indicating that they may affect prognosis. Medical management alone was effective in 37 patients, while urgent surgical intervention was required in 19 patients.

The mode of management had a highly significant impact on outcomes (P = 0.01), underlining the importance of timely surgical decisions in selected cases. Regarding antibiotic therapy, Rifampicin + Doxycycline was administered to 12 patients, whereas Rifampicin + Doxycycline + Gentamicin was used in 44 patients. The 'difference in antibiotic regimens was statistically significant (P = 0.05), suggesting that triple therapy may be associated

with better outcomes. In terms of outcomes, survival was recorded in 50 patients, while death occurred in 6 patients.

A significant association was observed between various clinical factors and outcomes (P = 0.01), highlighting the importance of early diagnosis, appropriate antibiotic therapy, and timely surgical intervention.

Figure I: Assessment of Parameters



DISCUSSION

Brucellosis is a highly contagious zoonosis caused by bacteria of the genus Brucella and affecting mammals. Human Brucellosis is caused by ingestion of unpasteurized or undercooked food product from infected animals, or close contact with them.[7] The present study was conducted to assess clinical profile, and outcomes of Brucella endocarditis.

The gender distribution in our study showed a slight male predominance, with 30 males (53.57%) **and** 26 females (46.43%) among the 56 patients. In our study, the male-to-female ratio of 1.15:1 reflects this trend, although the difference is not markedly disproportionate. **Al Dahouk et al. (2011)** note that males, particularly those working in agriculture or animal husbandry, are more commonly affected by Brucella infections, leading to a higher incidence of complications such as endocarditis.[8]

Previous research has suggested that females may have a better overall prognosis compared to males when affected by infectious diseases, due to immune system differences, although these findings are not always consistent across studies. For example, **Zhang et al. (2019)** reported that while males tend to have higher rates of infection, females may experience less severe outcomes.[9] However, our study did not find significant differences in survival or mortality based on gender, aligning with studies that have failed to establish a gender-specific impact on Brucella endocarditis outcomes.[10]

Brucella endocarditis (BE) is a rare but severe complication of systemic brucellosis, accounting for up to 80% of brucellosis-related deaths despite constituting less than 2% of all brucella infections.[11]

In our study, the aortic valve was the most frequently affected (30%), followed by the mitral valve (29%), both valves (11%), and prosthetic valves (10%). This distribution is consistent with prior studies which also report aortic valve predilection in BE due to its higher pressure gradients and greater susceptibility to endothelial damage.[12,13] The statistically significant association between the type of valve involved and disease occurrence (P = 0.03) suggests that aortic involvement may be linked with a more aggressive clinical course, a finding echoed by Raju et al., who noted worse outcomes in aortic valve BE due to rapid hemodynamic deterioration.[14]

Vegetation size, a key prognostic factor in endocarditis, showed statistical significance in our study (P = 0.05). Patients with vegetations >1 cm had higher complication rates, including perforation (n = 4), Sinus of Valsalva (SOV) aneurysm (n = 1), and systemic embolisation (n = 2). Large vegetations have been previously associated with systemic emboli and valvular destruction in infective endocarditis, including BE.[15,16]

Management of BE remains challenging and often requires a combination of prolonged antibiotic therapy and surgical intervention. In our cohort, medical management alone was successful in 37 patients, while urgent surgery was required in 19 cases. The mode of treatment showed a highly significant association with outcomes (P = 0.01). These findings align with recommendations by the European Society of Cardiology and other studies that emphasize early surgical intervention in patients with heart failure, large vegetations, or uncontrolled infection .[8,10] Delayed surgery may contribute to complications, thus underscoring the need for timely surgical decisions.

The choice of antibiotics plays a crucial role in treatment success. In our study, dual therapy (**Rifampicin + Doxycycline**) was administered in 12 patients, while triple therapy (**Rifampicin + Doxycycline + Gentamicin**) was used in 44 patients. Triple therapy showed a statistically significant association with better outcomes (P = 0.05). Similar results have been reported in multiple studies advocating the use of aminoglycoside-containing regimens for at least 6 weeks to improve bactericidal activity and minimize relapse rates.[17,18]

Despite the complexity of BE, our study recorded a survival rate of 89%, with 6 deaths (11%), which is comparable to more recent literature that cites improved outcomes with early surgical and medical intervention.[19] The overall association between various clinical and treatment parameters and patient outcomes was statistically significant (P = 0.01), reinforcing the importance of integrated, early, and individualized care in BE.

Jia et al[12] analyzed the clinical characteristics and treatment outcomes of 590 patients with brucellosis. The clinical characteristics, laboratory findings, complications and prognosis of 590 patients infected with brucellosis were retrospectively analyzed. These patients had a mean age of 44.24 ± 15.83 years with 60.5% having a history of close contacting with cattle and sheep. Of them, 53.6% (316 /590) were in acute phase and 21.5% were in chronic phase. Agglutination test showed 98.5% positive with 34% blood culture positive of *Brucella*. The major symptoms were fatigue (91%), hyperhidrosis (88.1%), fever (86.9%), and joint pain (81%) with 29.8% having enlarged liver, 26.1% having enlarged spleen and 23.2% having osteoarticular complications. Combination of doxycycline plus rifampicin for 12 weeks was an effective regimen for patients without complications. The 3-drug regimen (doxycycline+ rifampicin+ levofloxacin) for 12 weeks was recommended for these with complications. There were 6 patients died (1.02%) with overall relapse rate of 5.98%.

LIMITATIONS OF THE STUDY

- Single-centre study limits generalizability to broader populations.
- Small sample size (n=56) may affect statistical power and limit subgroup analysis.
- Absence of long-term follow-up data for assessing late complications or relapses beyond the initial study period.
- Lack of control group for direct comparison with other aetiologies of endocarditis.
- Surgical decisions were based on clinician discretion, introducing potential selection bias.

CONCLUSION

Authors found that Brucella endocarditis is often marked by large vegetations and can result in paravalvular and embolic complications. The gender distribution in our study showed a male predominance, which is consistent with the epidemiology of Brucellosis and its complications, particularly in **high-risk occupations**, the findings emphasize the need for targeted interventions to reduce the burden of Brucellosis, particularly among males in endemic areas. The findings of this study highlight that valve involvement, vegetation size, presence of complications, treatment modality, and antibiotic regimen are key determinants of clinical outcome in Brucella endocarditis. Early recognition and aggressive management strategies—including prolonged combination antibiotic therapy and timely surgery—are essential to reduce morbidity and mortality in this potentially fatal disease.

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