

**HUMAN BRUCELLOSIS; A PHYSICIAN'S EXPERIENCE OVER 12 YEARS**Mallikarjuna Shetty\*<sup>1</sup>, Adiraju Krishna Prasad<sup>2</sup> and Nageswar Rao Modugu<sup>3</sup><sup>1</sup>Associate Professor, The Department of General Medicine, Nizam's Institute of Medical Sciences – Hyderabad.<sup>2,3</sup>Professor, The Department of General Medicine, Nizam's Institute of Medical Sciences – Hyderabad.**\*Corresponding Author: Dr. Mallikarjuna Shetty**

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**ABSTRACT**

**Introduction;** Brucellosis is the commonest zoonosis all over the world. with varied presentation involving multiple organs with misdiagnosis and treatment. **Aim:** To study the clinical features, laboratory investigations, complications and treatment outcome in patients with Brucellosis. **Material and methods:** We retrospectively collected data from case records of patients with Brucellosis over 2005 to 2016 (12 years) and the parameters studied were Age, symptoms, signs, investigations specially Blood and bonemarrow serology for brucellosis along with blood and bonemarrow cultures for brucellosis along with treatment outcome. **Results:** Total number of patients were 13 with Male to female ratio of 6:7, and mean age was 43.15 years, the commonest occupation was house wife and the symptom was fever in 100% with average duration of 96.3 days, followed by joint pains in 61%, with hepatosplenomegaly in 7.6% patients. Pallor was present in 15.2% patients with average ESR of 103.66mm1st hour, Obstructive hepatopathy in 46% patients, Brucella serology positivity in blood was seen in all patients except 1, with titres of 1:160 in 46% 1:320 in 7.6%, 1:640 and 1:1280 in 15.2% patients, Bonemarrow positive serology for Brucella was seen in 10 patients with titres of 1:160 in 7.6%, 1:320 in 15.2%, 1:640 in 23%, 1:1280 in 23% patients. And 30.76% patients had grown Brucella on blood culture and 23% had grown Brucella by bonemarrow culture. All the patient responded to the treatment, except 1 patient mortality due to multiorgan involvement. **Conclusion:** Brucellosis still remains a challenging disease for physicians with different presentations. Its important to diagnose and treat early to prevent morbidity and mortality.

**KEYWORDS:** Blood serology, Bone marrow culture, Doxycycline, Fever, Rifampicin, Streptomycin.**INTRODUCTION**

Human Brucellosis is one of the commonest zoonotic disease in the world.<sup>[1]</sup> It affects domestic and wild mammals, and it is transmitted to humans through ingestion of unpasteurised milk, chesses other dairy products or by direct contact with infected animals.<sup>[2]</sup> It mimics many diseases both infectious and non-infectious conditions causing difficulty in diagnosis.<sup>[3]</sup> The disease may occur in acute, sub-acute or chronic forms with incubation period ranging from 1-3 weeks to several months<sup>[4]</sup>, Due to wide spectrum of clinical manifestations and no specific clinical signs, early diagnosis of human brucellosis is difficult.<sup>[5]</sup> So, the laboratory diagnosis along with history and clinical signs is performed.<sup>[5]</sup> Since there are few studies on clinical spectrum and also by physicians and paucity of data which made us to look into the clinical profile, laboratory test and treatment of Brucellosis.

**MATERIAL AND METHODS**

Case records of admitted patients with diagnosis of Brucellosis, to Nizams Institute of Medical sciences hospital which is a multispecialty, tertiary care referral

hospital were collected over a period of 12 years (2005-2016).

**Inclusion criteria was**

- 1) All patients diagnosed patients with Brucellosis
- 2) Age above 12 years. were included.

Exclusion criteria was. Patients Age below 12 years were excluded.

Information from case sheets of all patients recruited for analysis was reviewed. In the history, demographic details, symptoms with the duration, loss of appetite and weight were noted. The risk factors information tabulated were septicemia and immunocompromised status of patient. Occupational history was also noted.

Clinical findings specifically noted were presence of temperature, enlargement of Liver, Spleen, Lymph node enlargement, joint enlargement with tenderness, skin rash, and pleural effusion.

The investigation reports of Hemogram, chest radiograph, abdominal ultrasonography (carried with

MYLAB60 model, eSaote company from Ahmedabad), Contrast Enhanced Computed Tomography (CECT) of neck chest, abdomen (carried with Philips Brilliance 16 model, 16 slice CT, PHILIPS company from Netherlands), Mantoux test, HIV ELISA, Brucella Latex agglutination test Electrocardiogram, trans-thoracic Echocardiogram, Blood cultures (incubated for more than 6 weeks BACT TALert 3D automated blood culture system Biomeriest), Urine cultures, Bone Marrow study with cultures were ever done were documented.

The treatment details of medical management like Antibiotics dose and duration of therapy were documented.

The above data from all patients was tabulated and analyzed retrospectively. The reports of CECT chest, Bone marrow study, FNAC/ biopsy of Lymph node, Brucella latex agglutination test and Brucella culture reports were also collected (wherever they were carried out depending on clinical profile).

Diagnosis of Brucellosis was made on clinical features with Brucella latex agglutination test showing antibody

titre of 1:160 or more on serology with Blood cultures or Bone marrow cultures showing growth of Brucella organism.

The study was retrospective audit with no patient direct identifiers, hence consent was not taken. Hospital ethics committee was informed of the study.

## RESULTS

Total 13 patients data were collected, with age ranging from 18 to 75 years and mean age being 43.15 years, with Male to Female ratio of 6:7. Among them 7 were housewife, 3 farmers, 1 student, 1 veterinary doctor and 1 government worker.

Main clinical feature (Table-1) was fever in 100% patients with average duration of 96.3 days, Joint pain was seen in 8 patients, mainly involving wrist joint in 8, hand joints in 5, sacroiliac joint in 4, elbow joint in 2, 1 in knee joint, 1 in ankle joint and 1 in feet joint. Cough was present in 3 patients, vomiting in 3 patients, loose motions in 1 patient, altered sensorium in 1 patient, loss of appetite in 4 patients and loss of weight in 5 patients.

**Table: 1 Shows Clinical findings.**

Demographic data	Numbers (%)
Age	18-75 years ,mean age=43.15 years
Male; female ratio	6:7(46%:54%)
Occupation	Housewife 7(54%), Farmers3(23%), veterinary doctor1 (7.6%), Socialworker1(7.6%),Government worker1(7.6%)
Symptoms Fever	13 (100%)Average 96.3 days
Joint pains	Wrist joint 8 (61%), Elbow joint 2(15.2%), Sacroiliac joint 4 (30.7%), Hands joint 5 (38.4%), Knee joint 1(7.6%), Ankle joint 1(7.6%), Feet joints1(7.6%)
cough	3(23%)
Vomiting	3(23%)
Loose Motions	1(7.6%)
Altered sensorium	1(7.6%)
Loss of weight	5(38.4%)
Loss of appetite	4(30.7%)
Signs	
pallor	2 (15.2%),E tender noduls1,SCH 1,
Lymph node enlargement	2 (15.2%) cervical
HepatoSpleenomagley	1(7.6%)
Erythematous rash	1(7.6%)
Erythematous tender nodule	1(7.6%)
Subcutaneous hemoraghe	1(7.6%)

The clinical signs noted were pallor in 2 patients, tender erythematous nodule in 1 patient, Erythematous rash in 1 patient, Subconjunctival hemoraghe in 1 patient and 2 patients had cervical lymphadenopathy. 1 patient had hepatosplenomegaly on abdomen examination. 1 patient had right upper lobe consolidation.

Investigation showed mean hemoglobin of 9.6gm/dl, 3 patients had leukocytosis among them 2 had polymorpholeucocytosis, 3 patients had leucopenia, and other 7 had normal leucocyte count. The average ESR was 103.66mm1st hour, and liver function test showed obstructive hepatopathy in 6 patients. On ultrasound

abdomen examination 5 patients had hepatomegaly, 4 patients had splenomegaly, 1 patient had benign prostatic hypertrophy, 1 patient had gallstone, 2 patients had pleural effusion when their chest radiography's were normal, in 1 patient who had undergone computer tomography of the chest showed right upper lobe consolidation. In 1 patient Cerebral spinal fluid showed feature of meningitis.

Microbiological investigations (Table-2) like Brucella latex agglutination test showed by blood serology rise of 1:160 in 6 patients, 1:320 in 1 patient, 1:640 in 2 patients, 1:640 in 2 patients, 1:1280 in 2 patients. Bone marrow serology for Brucella showed 1:160 in 1 patient, 1:320 in 2 patients, 1:640 in 3 patients, 1:1280 in 3 patients. 4 patients had grown Brucella on Blood culture, but 3 patients had grown Brucella on bone marrow culture.

**Table: 2 Microbiology laboratory findings.**

Blood Serology positive	Numbers (%)
Blood agglutination 1:160	6(46%)
Blood agglutination 1:320	1(7.6%)
Blood agglutination 1:640	2(15.2%)
Blood agglutination 1:1280	2(15.2%)
Blood serology negative	1(7.6%)
Bone marrow serology positive	
Bone marrow aspiration 1:160	2(15.2%)
Bone marrow aspiration 1:320	2(15.2%)
Bone marrow aspiration 1:640	3(23%)
Bone marrow aspiration 1:1280	3(23%)
Bone marrow serology negative	1(7.6%)
Blood culture positive for Brucellosis	4(30.76%)
Bone marrow culture positive for Brucellosis	3(23%)

Bone marrow study showed 2 patients having reactive marrow and 2 having granulomatous marrow. 1 patient had normal marrow.

Treatment (Table-3) was given with Streptomycin plus doxycycline in 4 patients for 8 weeks but 2 patients required treatment with doxycycline plus rifampicin for 4 more months, 1 patient required it for 8 months and 1

patient was given for 6 weeks. 5 patients received rifampicin plus doxycycline for 8 weeks. 1 patient received doxycycline for 1 week, 2 patients received cotrimoxazole plus doxycycline for 6 weeks, and 1 patient received streptomycin plus doxycycline plus rifampicin for 6 weeks. All the patients were treated till serology became negative.

**Table 3: shows treatment given with duration.**

Drugs given	Numbers	duration	Extended with duration in months
Streptomycin plus Doxycycline	4	8 weeks	2 patients for 4 months, 1 patient for 8 months
Rifampicin plus Doxycycline	5	8 weeks	
Doxycycline	1	1 week	
Cotrimoxazole plus doxycycline	2	6 weeks	
Streptomycin plus doxycycline plus Rifampicin	1	6 weeks	

1 patient had associated hypertension, 1 patient had diabetes mellitus, 3 patients had coronary artery disease, 1 patient had bronchial asthma, 1 patient vitamin B12 deficiency and 3 patients had history of alcohol consumption.

1 patient died due to multiorgan dysfunction ARDS, AKI, and DIC Hepatopathy with shock.

### STATISTICAL ANALYSIS

Microsoft office 2007 was used for the statistical analysis. Descriptive statistics like mean and percentages were used to interpret the data.

### DISCUSSION

Brucellosis is often neglected Zoonotic disease in India, with protean manifestation causing difficulty in diagnosis.<sup>[6]</sup> In our study, we had total 13 patients of brucellosis over a period of 12 years, Vishwanth et al<sup>[7]</sup> reported 68 patients over a period of 5 years, Koshi et

al<sup>[8]</sup> reported 10 cases. But highest number of patient reported from India was by Mantur et al<sup>[6]</sup> were 792 patients and Turan et al<sup>[9]</sup> from Turkey reported 1028 patients over 10 years period.

The age of our patients ranged from 18 to 75 years, it was similar to Vishwanth et al<sup>[7]</sup> who had age ranging from 9 to 75 years. The mean age was 43.15 years. Turan et al<sup>[9]</sup> reported mean age of  $33.7 \pm 16.34$  years, it was around 50 years in Vishwanth et al.<sup>[7]</sup> The majority of our patients occupation was house wife in 53%. 28% were farmers and 1 patient 7.6% was Veterinary doctor but 1(7.6%) was social worker and 1(7.6%) was government worker. Turan et al<sup>[9]</sup> reported 42.3% and Vishwanth et al<sup>[7]</sup> reported 64.7% gave history of contact with live stocks.

Most of our patients were female 53.84% to male 46% with ratio of 6:7, turan et al reported 52.4% female to 47% male similar occurrences but in Vishwanth et al<sup>[7]</sup> 68% were male patients.

The main presenting feature was fever in 100% of our patients. Similarly, seen in Vishwanth et al<sup>[7]</sup> but Mantur et al<sup>[6]</sup> (2008) had in 78.9% and Turan et al<sup>[9]</sup> in 72.2% patient. Next symptom was joint pains in 61% of the patients which is less than Turan et al<sup>[9]</sup> 73.7% and Kokuglu et al<sup>[10]</sup> 77.5% but Mantur et al<sup>[6]</sup> and Vishwanth et al<sup>[7]</sup> had around 23%. The Commonest joint pain was seen in wrist joint in 60% patients followed by shoulder joint in 30%. elbow joint, sacroiliac joint in 14.6%. Ankle joint, Knee joint feet in 7.6% whereas hand joints were involved in 38% patients. Turan et al<sup>[9]</sup> reported in 14.3%. 23% patients had cough in our study which is less than seen by Turan et al<sup>[9]</sup> in 2% and Mantur et al<sup>[6]</sup> in 3.5% patient. The next symptom was vomitings in 23% patients but Mantur et al<sup>[6]</sup> reported 3.2% loose motion was present in 7.6% and loss of weight was seen in 38.46%. Similarly reported by Turan et al<sup>[9]</sup> in 42.44% patients. But loss of appetite was present in 30.76% patients in our study which is less than Turan et al<sup>[9]</sup> 49% and in Mantur et al<sup>[6]</sup> it was only 3.2%.

In our study, 15.2% patients had pallor but Vishwanth et al<sup>[7]</sup> had 57.3% Mantur et al<sup>[6]</sup> had 1.7% patients H.Roushan et al<sup>[11]</sup> had 15.7% patients. 7.6% patients had skin erythematous rash and 7.6% patients had erythematous nodule but Turan et al<sup>[9]</sup> had in 2.4% and Mantur et al<sup>[6]</sup> in 1.3% patients. 7.6% of patient had hepatosplenomegaly which is similarly seen in Turan et al<sup>[9]</sup> 10% and in Vishwanth et al<sup>[7]</sup> it was 28%. Lymphadenopathy was seen in 15.2% patients in our study which is more than Turan et al<sup>[9]</sup> had 2.4% Mantur et al<sup>[6]</sup> had 2.9% may be because the number in our study was small.

The mean Hemoglobin in our study was 9.6gm/dl (70%) which is more than reported by Vishwanth et al<sup>[7]</sup> 57.3% and Turan et al<sup>[9]</sup> 40.3%, 23% patients in our study had leucocytosis and 23% had leucopenia but Vishwanth et al<sup>[7]</sup> had 14.7% patient with leucocytosis as well as

leucopenia but Turan et al<sup>[9]</sup> had 10.9% patients having leucopenia and 9% patients having leucocytosis. Elevated ESR was seen in all (100%) patients, with average of 103.66 mm/1<sup>st</sup> hour but Vishwanth et al<sup>[7]</sup> reported in 80.8% and Turan et al<sup>[9]</sup> in 19.6% patients. In our study, we had Meningitis in 7.6% patients, Renal failure in 7.6% patient and even Vishwanth et al<sup>[7]</sup> had Meningitis in 4% patients. Turan et al<sup>[9]</sup> in 5.6% patients. 7.6% patient had consolidation of lung diagnosed by CECT chest. Turan et al<sup>[9]</sup> had in 2.7% patients.

Brucellosis was diagnosed by serology in blood, bone marrow and by culturing blood/bone marrow. A titre for serology 1:160 above was considered as diagnostic of brucellosis similarly taken by vishwanath et al.<sup>[7]</sup> In our study, we had 46% patient positivity with blood serology of 1:160 titres and 7.6% with 1:320 titres, 15.2% with 1:640 & 1:1280 titres. Total it was positive by serology in 93.4% patients and 7.6% was negative by both blood and bone marrow serology.

Turan et al<sup>[9]</sup> showed 94.1% but Mantur et al<sup>[6]</sup> showed 84% positivity by serology we had 30.76% patients had grown Brucella in blood culture and 23% patients had grown Brucella in bone marrow cultures. Vishwanth et al<sup>[7]</sup> reported 4% positive in bone marrow culture. Turan et al<sup>[9]</sup> in 2.5% by bone marrow culture and 11.4% by blood cultures. 1 patient (7.6%) was negative by serology of Blood and Bone marrow, but had grown Brucella on Bone marrow culture.

Treatment given in our patient were streptomycin plus doxycycline in 4 patient (30.76%), among them 2 patients required treatment with doxycycline plus rifampicin for 4 more month as they had not responded, 1 required it for 8 months, 1 patient was given for 6 weeks but Turan et al<sup>[9]</sup> and vishwanth et al<sup>[7]</sup> gave similar treatment with similar response.

In our study, 5 patients 30.76% had received rifampicin plus doxycycline for 8 weeks but turan et al<sup>[9]</sup> used in 20% patients all responded like in our study. 1 patient (7.6%) received streptomycin plus doxycycline for 6 weeks, 1 patient (7.6%) received only doxycycline for 1 week. 2 (15%) patients received cotrimoxazole plus doxycycline for 6 weeks. 1 patient (7.6%) was treated with streptomycin plus doxycycline plus rifampicin for 6 weeks. Similar use of 3 drugs but different Drugs Were given in Turan et al<sup>[9]</sup> study who used streptomycin plus doxycycline plus rifampicin in 5.7% patients and doxycycline plus rifampicin plus ceftriaxone in 5% patients. All the patients were treated till serology became negative and improved clinically.

1 patient (7.6%) had hypertension, diabetes mellitus, bronchial asthma, 3 patients were alcoholics and 1 patient had vitamin B12 deficiency. 1 patient (7.6%) died due to multi organ dysfunction which is similarly reported by vishwanth et al.<sup>[7]</sup>

**CONCLUSION**

Brucellosis is still a challenging disease for physicians to diagnose and to treat it as there is no proper diagnostic and treatment guidelines. We recommend Doxycycline plus Rifampicin as the first choice still culture reports come.

**Limitations**

Main limitations in our study was the small number of patients . being a retrospective study.and use of different antibiotic regimes.

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My wife Keerthi, my daughter Saanvi,my patients

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