



## Paediatric Brucellosis: A case series from a tertiary care center in Karnataka.

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**ABSTRACT** Brucellosis is an emerging zoonotic disease, but it may be overlooked and misdiagnosed, due to its protean & varied presentation, the absence of awareness and lack of experience among health care providers coupled with limited laboratory facilities. The disease causes diminution of manpower and is of great public health significance. We present a case series and retrospective analysis of seven children admitted to a tertiary care hospital of coastal Karnataka with a diagnosis of Brucellosis. Their epidemiological characteristics, contact history, clinical features and laboratory parameters were studied. This report aims to create awareness about the disease and highlight the importance of its consideration as a differential diagnosis of Pyrexia of unknown origin.

**KEYWORDS :** Brucellosis, Paediatrics, Zoonosis

**Abbreviations:** AST- Aspartate transaminase, ALT- Alanine transaminase, ESR- Erythrocyte sedimentation rate, HSCRP- Highly sensitive C-reactive protein, Hb- Hemoglobin, L- Lymphocyte, PLT- Platelet, TLC- Total leukocyte count.

### Introduction:

Brucellosis is caused by a gram-negative, non-spore bearing, and nonmotile coccobacillus. Humans are accidental hosts and acquire the disease from direct contact with an infected animal or consumption of infected unpasteurized dairy products or raw meat, the latter being the major cause of brucellosis in children.<sup>1</sup> Other modes of transmission are contamination of skin abrasions, inhalation of aerosols from animal manure or bacterial culture media and rarely person to person transmission.<sup>2,3</sup> It is also an occupational hazard among people working with livestock and lab personnel handling the infective material. It has versatile and wide clinical presentation, ranging from non-specific fever to multisystem involvement like Arthritis, Osteomyelitis, Meningitis, Pneumonia, Endocarditis, Hepatic/Splenic abscess, Pancytopenia, Epididymo-orchitis, and Nephritis.<sup>3-6</sup> However, one should have a high degree of suspicion in a child presenting with pyrexia and joint pains which remain its most common manifestation.<sup>7</sup>

### Case series:

A retrospective analysis of Brucellosis diagnosed cases admitted to the Paediatric department in a tertiary care center in coastal Karnataka, India from January 2015 to June 2016 was performed. The diagnosis was made by the presence of significant antibody titer ( $\geq 1:160$ ) demonstrated by standard tube agglutination test, or isolation of Brucella species from blood (BACTEC) coupled with clinical features suggestive of Brucellosis. Positive culture though considered as gold

standard, it has a limitation of low yield.<sup>3</sup>

A total of 7 diagnosed cases of Brucellosis were identified. Clinical features and investigation parameters of the study population are represented in Table 1 and 2 respectively.

**Table 1: Epidemiological and clinical features of the study population**

Patient No	Age(y ears)	Sex	Loca lity	Complaints	Contact history	Organo megal y
1	11	M	Rural	Fever, Myalgia	Cattle at home	Hepatomegal y
2	17	M	Rural	Fever, Arthralgia, Headache, vomiting	Cattle at home, Consumption of unpasteurized milk	Absent
3	10	M	Urban	Fever, cough, weight loss	Not significant	Hepato-splenomegal y
4	10	M	Urban	Fever, Right hip pain	Consumption of beef and mutton	Absent
5	16	M	Rural	Fever, Arthralgia	Cattle at home	Hepato-splenomegal y
6	5	F	Rural	Fever, weight faltering	Cattle at home, H/O brucellosis in father	Hepatomegal y
7	14	M	Rural	Fever, Arthralgia, Headache, Anorexia	Not significant	Hepatomegal y

**Table 2: Laboratory parameters of the study population**

Patient No	Hb (g%)	TLC (/mm <sup>3</sup> )	L (%)	PLT (/mm <sup>3</sup> )	Creatinine (mg/dL)	AST (U/L)	ALT (U/L)	ESR (mm/hr)	HSCRP (mg/L)	Serology Titre	Blood Culture
1	9.9	7600	56	3.8lakh	0.5	137	71	36	82	1:320	Brucella
2	14.4	6000	46	2.2 lakh	0.8	38	27	62	34	1:1280	Brucella
3	8.6	4800	67	90000	0.3	123	145	90	36	1:320	Brucella
4	10	9600	64	3.3 lakh	0.3	26	13	68	8	1:320	Brucella
5	9.2	3400	70	1.1lakh	0.5	35	19	56	64	1:640	Brucella
6	10.1	8500	56	4 lakh	0.2	172	68	48	56	1:320	Brucella
7	9.3	1700	52	86000	0.1	148	56	51	94	1:640	Sterile

-Age appropriate reference range was considered for all laboratory parameters. HSCR value >40mg/L was taken as a positive value.

-Abbreviations used in table are- Hb- Hemoglobin, TLC- Total leukocyte count, L- Lymphocyte, PLT- Platelet, AST- Aspartate transaminase, ALT- Alanine transaminase, ESR- Erythrocyte sedimentation rate, HSCR- Highly sensitive C-reactive protein

All children were treated as per standard protocol with Doxycycline + Rifampicin (>8years) or Cotrimoxazole + Rifampicin (<8 years) for 6 weeks.<sup>1</sup> All children became asymptomatic by the end of therapy (6 weeks) and as seroconversion usually takes longer time<sup>8</sup>, antibody titer was not repeated. Guidelines suggest the use of aminoglycoside antibiotic and prolonged course of doxycycline in complicated scenarios (Meningitis, Osteomyelitis, and Endocarditis).<sup>1</sup> However, none of the cases in present study had any organ system involvement at presentation except for organomegaly (which reflects tropism of the organism for the reticuloendothelial system).

### Results and Discussion:

There were six males and one female. The mean age of presentation was 12 years, and the majority were from the rural area (n=5). In a study, Brucellosis in children by Ayazi P et al<sup>9</sup>, male to female ratio was 1.6:1 with 57% of the children from the rural area. In a case series by Mohan D K et al<sup>10</sup>, 6/10 were males and 8/10 were from rural area. In another case series reported by Luk S<sup>11</sup>, 4/6 were men. In the current study, significant and positive contact history with animals or their products was present in 5 children. There was a positive family history in a child where one of the parent was admitted and diagnosed to have brucellosis, a week prior to child's admission. In the study by Ayazi P et al<sup>9</sup>, 65% of the study population had a history of consumption of unpasteurized milk or milk products, 33% had contact with cattle and 25% had a family history of Brucellosis.

In our study, all the children presented with fever. Arthralgia was present in four children, where one child had single joint involvement (right hip joint), whereas others had multiple joint involvement (mainly knees and hip joint). No child had involvement of sacroiliac joint. Fever with joint involvement was the most common presentation in other similar studies as well.<sup>9,11</sup> Serology was positive for all children and Brucella was isolated from blood of six children in the present study. Other investigations showed anemia (n=6), normal total leukocyte count (n=5), relative lymphocytosis (n=7), thrombocytopenia (n=3), deranged liver enzymes (n=4), elevated ESR (n=7) relative to elevated highly sensitive CRP (n=4). Brucellosis was considered as a provisional working diagnosis in only one child (who had a family member with brucellosis). In other children, it was considered only after ruling out other conditions with appropriate investigations when clinically indicated (like Malarial parasite quantitative buffy coat, Widal, Weil-Felix, Serology for scrub typhus, Leptospira, Mantoux, chest Xray, Rheumatoid factor, urine analysis). The laboratory profile was similar in other studies except for few differences. Anemia was seen only in 19% of subjects in Ayazi P et al<sup>9</sup>, deranged creatinine was observed in 4/10 individuals in the case series by Mohan D K et al<sup>10</sup> (none had deranged creatinine in our study), and in the case series by Luk S<sup>11</sup>, CRP was elevated relative to ESR.

### Conclusion:

Brucellosis is chronic granulomatous zoonosis with worldwide existence and is especially prevalent in Mediterranean region, Persian Gulf, India, and parts of Mexico and Central and South America.<sup>12</sup> In India, though it is said to account for a loss of about 30 million man-days per year, the actual magnitude of the disease seems to be much more (almost 25 times higher the reported incidence) due to underreporting or misdiagnosis.<sup>13</sup> As this report is a hospital-based retrospective clinical study, it also cannot measure real incidence and prevalence of the disease. However, the purpose of this case series is to create awareness among the health care providers regarding the disease and its varied presentation. The disease poses a diagnostic challenge, as it is often under-diagnosed due to lack of suspicion and diagnostic facilities despite cattle farming (an important risk factor) being one of the main occupation in rural India. Many children with prolonged pyrexia and failure to thrive are empirically treated with anti-tubercular therapy. It may be worth investigating such children for Brucellosis, as this zoonotic disease can manifest in many & any manner. History of exposure is pivotal for clinching the diagnosis. Additional clues include anemia, normal total leukocyte count with relative lymphocytosis, elevated acute phase reactants (ESR and CRP)

and deranged liver enzymes. As the sensitivity of blood culture is inferior when compared to serology, the disease may be missed particularly when the index of suspicion is low. Newer investigations like ELISA and PCR may be reserved for special circumstances like chronic brucellosis, complicated cases, and re-infection. However, management of Brucellosis is not as difficult as establishing the diagnosis. If compliance to the therapy is ensured, the prognosis is excellent with negligible relapse rate. Emphasis should also be laid on prevention of the disease by means of pasteurization of milk and dairy products, maintaining personal hygiene and practicing protective strategies when involved in animal rearing or handling infective laboratory products and eradication of organism from domestic animals.

-Financial source & other competing interest – None

-Acknowledgement - None

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