

Clinico-Demographic Profile Treatment Outcomes and Rare Presentations of Childhood Brucellosis: A Hospital Based Prospective Study from North India

Aasiya Unjum^{1*}, Zul Edain Hassan¹, Aijaz Ahmed Bhat²

¹Department of Pediatrics, Sher-I-Kashmir Institute of Medical Sciences SKIMS Soura, Srinagar, India; ²Department of Internal Medicine, Sher-I-Kashmir Institute of Medical Sciences SKIMS Soura, Srinagar, India

ABSTRACT

Objective: To describe the clinical and demographic profile, treatment outcomes and rare presentations of brucellosis in children in Kashmir, highlight the risk factors associated with acquisition of brucellosis in childhood and suggest measures to prevent animal to human transmission of disease in this age group.

Design and setting: Hospital based prospective study conducted in Department of Pediatrics Sher I Kashmir Institute Of Medical Sciences, Soura Srinagar over a period of two years from January 2018 to January 2020.

Participants: Children in the age group of 1 to 18 years with a history of Pyrexia of unknown origin or with a history of contact with animals or history of consumption of unpasteurized milk were included in the study.

Methods: A total of 1500 patients were screened for brucellosis out of which 15 (0.6%) patients with either a positive blood culture or Serum Agglutination Test (SAT) titre more than or equal to 1:160 were enrolled in the study. Informed written consent was obtained from the parents/guardians of all these children and their history and clinical examination was recorded in a preset proforma.

Results: Our study revealed a prevalence of 0.6 % in children. Males (60%) outnumbered females. 70% of the cases of brucellosis belonged to rural population. Consumption of unpasteurized milk was found to be an important risk factor for acquiring brucellosis in children. 60% of the children had consumed unpasteurized cow's milk.

Mean age of children was 10.5 (\pm 4.2) years and 50% of the children were in the age group of 11 to 18 years. Most common presenting complaints were prolonged fever (73.3%), arthralgias and myalgias (26.6%). Hepatosplenomegaly was present in 05 (33.3%) patients. Low back pain was present in 03 (20%). Abdominal pain was present in 02 (13.3%) and Rash was present in 02 (13.3%). Few patients in our study had rare presentations. These included Arthritis (n=01), Meningitis (n=01), Liver abscess (n=01), Epididymo orchitis (n=01) and Thrombocytopenia causing GI bleed (n=01).

10 (66.6%) patients in our study had a raised ESR and 04 (26.6%) patients had transaminitis. CBC showed Anemia in 06 (40%) patients, relative lymphocytosis in 05 (33.3%), leukopenia in 03 (20%), Thrombocytopenia in 01 (6.6%) and Pancytopenia in 01 (6.6%).

All patients were followed up for six months after the completion of therapy. Relapse was reported in one patient within two weeks of completion of therapy. None of the patients in our study died.

Conclusion: In conclusion brucellosis typically presents as a prolonged indolent disease with varied presentations in endemic regions. It may be overlooked and misdiagnosed due to its versatile presentations and overlap with tuberculosis and other such diseases. A high index of suspicion is needed for its diagnosis Prompt initiation and completion of therapy are important factors determining its outcome in children.

Keywords: brucellosis; Zoonosis; Children; Rare presentations

Correspondence to: Unjum A, Department of Pediatrics; Sher-I-Kashmir Institute of Medical Sciences SKIMS Soura, Srinagar, India, Email: thepediatrician138@gmail.com

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INTRODUCTION

Brucellosis (also known as undulant fever, Mediterranean fever or Malta fever) is a zoonotic infection transmitted to humans from infected animals (cattle, sheep, goats, camels, pigs, Buffalo, Dogs) [1] by ingestion of food products such as unpasteurized dairy products or by contact with tissue or fluids of the infected animals [2].

Brucellosis is endemic in many parts of the world and is especially prevalent in Mediterranean basin, Persian Gulf, Indian subcontinent and parts of Mexico and Central and South America [3].

Brucella melitensis is the most prevalent species causing human brucellosis and is most often carried by sheep, goats, camels and buffalo [4].

Childhood brucellosis accounts for 10 to 30 % of the cases of Human brucellosis [5].

MATERIALS AND METHODS

This was a hospital based prospective study conducted in Department of Paediatrics Sher I Kashmir Institute of Medical Sciences Soura Srinagar over a period of two years from January 2018 to January 2020. Children in the age group of 1 to 18 years were included in the study. This study was done to find out the prevalence of childhood brucellosis in Kashmir where there is a general perception that brucellosis is only seldom encountered in children.

Inclusion criteria

- 1) Patients admitted with the diagnosis of PUO (pyrexia of unknown origin) after excluding other causes.
- 2) Children having predisposing conditions for brucellosis like ingestion of raw/unpasteurized milk and contact with infected livestock.

Patients who met the inclusion criteria were screened for brucellosis by the standard agglutination test (SAT) and Blood Culture (BACTEC).

Single SAT titre of more than or equal to 1:160 was taken as positive.

Patients who grew *Brucella* on Blood Culture or had a SAT titre of more than or equal to 1:160 were enrolled in the study.

Informed written consent was obtained from the parent/guardian of the children and information regarding clinical features, demographic profile, risk factors for brucellosis and treatment given was recorded in a preset proforma.

Patients were followed up for a period of 6 months for outcome assessment.

RESULTS

Study participants

A total of 1500 patients were screened for brucellosis out of which 15 (0.6%) patients had either a positive blood culture or SAT titre more than 1:160. All these 15 patients were diagnosed as having brucellosis.

Blood culture was positive in 08 (53%) patients and SAT was positive in 07 (46.6%) patients. All blood cultures grew *Brucella melitensis*. Mean age of children was 10.5 (\pm 4.2) years. 50% of the children were in the age group of 11 to 18 years. Males (60%) outnumbered females. Majority (75%) of children in our study belonged to rural areas (Table 1).

Table 1: Demographic profile of children with brucellosis.

Age in years	Mean : 10.5 \pm 4.2
1 to 5	02
6 to 10	06
11 to 18	08
Area of residence	
Rural	11
Urban	04
Gender	
Males	09
Females	06

Most common presenting complaints were prolonged fever (73.3%), arthralgias and myalgias (26.6%). Hepatosplenomegaly was present in 05 (33.3%) patients. 02 (13.3%) patients had hepatomegaly alone and 01 (6.6%) had splenomegaly alone. Low back pain was present in 03 (20%). Abdominal pain was present in 02 (13.3%) and Rash was present in 02 (13.3%).

Few patients in our study developed rare complications. These included Arthritis (n=01), Meningitis (n=01), Liver abscess (n=01), Epididymo orchitis (n=01) and Thrombocytopenia causing GI bleed (n=01) (Table 2).

Table 2: Clinical features of children with brucellosis.

Clinical features of children	Percentage
Fever	11 (73.3%)
Arthralgias and Myalgias	04 (26.6%)
Low back pain	03 (20%)
Hepatosplenomegaly	05 (33.3%)
Hepatomegaly alone	02 (13.3%)
Splenomegaly alone	01 (6.6%)
Liver abscess	01 (6.6%)
Abdominal pain	02 (13.3%)
Arthritis	01 (6.6%)
Meningitis	01 (6.6%)
Epididymo orchitis	01 (6.6%)
Rash	02 (13.3%)

Majority of patients in our study had an uncomplicated course. Rare presentations of brucellosis in our study described below.

Brucellar liver abscess in a patient with chronic granulomatous disease (Cgd)

One patient in our study presented with fever, hepatomegaly and abdominal pain was diagnosed as having liver abscess. His 2D echo was normal. This patient was initially started on IV ceftriaxone, Vancomycin and clindamycin but remained febrile even after 1 week of treatment.

Blood Culture in this patient grew *Brucella melitensis* and he ultimately responded to anti *Brucella* regime consisting of doxycycline, gentamycin and rifampicin. Serial Usgs done over the next 6 months showed a gradual reduction in the size of the abscess with no further recurrence of fever and abdominal pain. This patient was diagnosed earlier with Chronic Granulomatous Disease.

Osteoarticular Brucellosis

Another patient presented with a 10 days history of fever, pain and swelling of the Right knee joint for 3 days. USG of the knee joint showed joint effusion with thickened synovium. Synovial Fluid analysis showed a TLC of 500/mm³ with lymphocytic pleocytosis. He was provisionally diagnosed as septic arthritis and was empirically started on IV ceftriaxone and vancomycin but since he continued to have fever and joint swelling even after 7 days of IV antibiotic therapy an alternative diagnosis was sought. His montoux test came out positive. CB NAAT,

Gram Stain and ZN stain of the synovial fluid was negative. His initial blood and synovial fluid cultures were sterile. He was empirically started on CAT 1 ATT regimen and discharged on DOTS. But he returned with persistent fever and joint swelling after 3 weeks.

His diagnosis was reviewed as his synovial fluid grew *Brucella melitensis* and his SAT showed a titre of 1:640.

He was started on doxycycline and rifampicin for 6 months and surgical drainage was also done. On serial follow up his knee joint showed mild deformation on X ray images but with good function.

Brucellar meningitis

Another child presented with 6 days history of fever headache and vomiting with altered sensorium for 3 days. This patient presented to the ED with active convulsions (GTCS). His serum electrolytes and blood Gas analysis was normal, serum calcium level was 9 mg/dl. A provisional diagnosis of viral encephalitis/Bacterial meningitis was made and investigated. CSF showed TLC of 300 mm³ with neutrophilic predominance. CSF protein was 500 mg/dl and CSF sugar was 20 mg/dl. Blood glucose level done simultaneously was 80 mg/dl.

His CSF culture was sterile and blood culture grew *Brucella melitensis*. He was initially started on IV ceftriaxone and Vancomycin which were later changed to Doxycycline, Gentamycin and Rifampicin.

The patient was finally discharged after 2 weeks. This patient recovered with no residual abnormalities on follow up.

Epididymo orchitis

An adolescent boy was diagnosed with *Brucellar* epididymo orchitis. This patient had presented to us with fever and chills for 1 week and bilateral testicular pain and abdominal pain for 3 days. There was no history of dysuria or penile discharge. Urine analysis was normal. USG of the testis showed acute bilateral epididymitis. He was started on I/V ceftriaxone and discharged. 7 days later he came back with ongoing testicular pain. Physical examination revealed a swollen Right hemiscrotum. Testicular USG with Doppler showed an enlarged heterogenous hyperaemic epididymis and testis consistent with epididymo orchitis. His tubercular work up was negative. The history was reviewed and the boy was found to be shepherd and had close contact with sheep. This prompted us to send a *Brucella* blood culture and SAT for *Brucella*. Blood culture was negative but the SAT titre was 1:640 and the patient responded to anti *Brucellar* regime. He was discharged home on doxycycline and rifampicin for 6 months. He also received gentamicin for 2 weeks.

Two patients in our study had dermatological manifestations. Out of these one patient had a petechial rash and one had maculopapular eruptions.

Thrombocytopenia presenting as upper GI bleed

One patient had isolated thrombocytopenia with a platelet count of 5000 mm³. This patient presented to us with Upper GI bleed and received IV pulse methylprednisolone for five days. Later a history of ingestion of unpasteurized goat milk was revealed by the parents and blood culture grew *Brucella melitensis*. His platelet count increased to 50,000 two days after starting Co trimoxazole and gentamycin and it returned to normal 5 days after starting the therapy.

10 (66.6%) patients in our study had a raised ESR and 04 (26.6%) patients had transaminitis. CBC showed Anemia in 06 (40%) patients, relative lymphocytosis in 05 (33.3%), leukopenia

in 03 (20%), Thrombocytopenia in 01 (6.6%) and Pancytopenia in 01 (6.6%) (Tables 3 and 4).

Table 3: Laboratory findings of the patients who tested positive for brucellosis.

Laboratory findings of the patients	Percentage
Pancytopenia	01 (6.6%)
Thrombocytopenia	01 (6.6%)
Anemia	06 (40%)
Leukopenia	03 (20%)
Relative lymphocytosis	05 (33.3%)
Elevated Alanine Amino transferase	02 (13.3%)

Table 4: Antibiotic susceptibility of *Brucella melitensis* on blood culture.

Antibiotic	Susceptibility of brucella
Doxycycline	13/15
Aminoglycosides	15/15
Co trimoxazole	12/15
Rifampicin	10/15

Around 60% of the patients in our study had a history of consumption of raw milk and close animal contact.

All patients were followed up for six months after the completion of therapy. Relapse was reported in one patient within two weeks of completion of therapy. Likely cause being noncompliance to drugs. None of the patients in our study died.

DISCUSSION

This was a hospital based prospective study carried out to ascertain the prevalence of brucellosis in children in Kashmir province and to describe its clinical profile and generate awareness for brucellosis in the community especially the rural community to prevent animal to human disease transmission.

Our study revealed a prevalence of 0.6% in children which is comparable to a study carried out by Kadri et al. [6].

On the contrary another study from India that was carried out in Ludhiana by Yohannes et al. found a high prevalence of 26.66% [7].

In our study more than 70% of the cases of brucellosis belonged to rural population. Likely cause for this could be an increased exposure to infected livestock in children belonging to rural population.

Consumption of unpasteurized milk was found to be an important risk factor for acquiring brucellosis in children. 60% of the children had consumed unpasteurized cow's milk and majority of these patients were in the age group of 6 to 10 years and belonged to rural areas. These results signify the need for creating a public awareness among the residents of rural areas about the disease. As in these areas people own cattle and have easy access to raw milk taken from cows. They tend to feed children with raw cow's milk as it is a cheap source of nutrition for them. These results were analogous to those reported by Satish, et al. [8].

In our study maximum number of patients affected was adolescents between the age group of 11 to 18 years. This could be due to increased occupational exposure to livestock in this age group.

Most of the cases in our study had an uncomplicated course and responded well to anti *Brucellar* regime. Only 04 patients developed brucellosis related complications. Most common symptoms were Fever, Myalgias, arthralgias and low backpain.

These patients showed prompt response to therapy and were treated successfully.

It's worthwhile to mention here that there is likelihood of missed diagnosis and under reporting cases of brucellosis by physicians causing an extended debilitating disease. In our study brucellosis had unusual presentations like meningitis, arthritis, epididymis orchitic, Liver abscess, rash, pancytopenia, anemia and isolated thrombocytopenia. So brucellosis should be considered in differential diagnosis of all such patients.

Similar results were also reported by mantur et al. [9] and Sindhu et al. [10].

brucellosis presenting as liver abscess is very rare in children. There has been just one case report of a child presenting with *Brucellar* liver abscess in literature [11].

Brucella melitensis was the sole isolate from all patients in our study and was consistent with previous reports [12].

Only one patient in our study was reported to have a relapse within two weeks of discontinuation of therapy and the likely cause for relapse was a poor compliance to drugs. This highlights the need to enlighten the parents about the importance of sticking to the long drug regimen.

CONCLUSION

In conclusion brucellosis typically presents as a prolonged indolent disease with varied presentations in endemic regions. It may be overlooked and misdiagnosed due to its versatile presentations and overlap with tuberculosis.

Early diagnosis and prompt initiation of treatment are associated with favourable response and outcome.

Majority of patients recover without complications. Prevention of brucellosis depends on effective eradication of the organism from livestock. Pasteurization of milk and dairy products for human consumption remains an important aspect of prevention.

No vaccine currently exists for use in children and therefore education of the public continues to have a prominent role in prevention of brucellosis.

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