
Original Article

Evaluation of Clinical Findings and Treatment of Childhood Brucellosis in Zahedan

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ABSTRACT

Background and Aim: Human brucellosis caused by organisms of the genus *Brucella*, continues to be a major public health problem worldwide. The aim of the study was to evaluate the clinical features and treatment in children with Brucellosis.

Materials and Methods: We retrospectively evaluated the records of 45 children with brucellosis.

Results: In this study there were 31 males (68.8%) and 11 females (24.4%). Only 16.3% (8/42) of the patients were less than 5 years, 24% (12/42) were older than 5 years but ≤10 years and 59.7% (22/42) were older than 10 years but ≤15 years. Twenty eight of the children lived in rural areas and the remaining lived in urban areas. Ingestion of unpasteurized milk was reported in 24 (53.3%), contact with animal in 15 (33.3%), while 19 (42.2%) appeared to have no history of exposure to either. The most common symptom in 32 children was high grade fever reaching 39.5 °C, four had chills; intermittent and night fever was observed in 10 children. Sweating was complained in 76.4%; and arthralgia or arthritis involved mainly the knees and hips in 30 (83%) children. Sacroileitis was seen in 2 children (4.8%). Antibiotic treatment lasted for 28 days on average. There were no complications or relapses, except one and the final outcomes were excellent.

Conclusion: In the present study we attempted to evaluate the clinical and laboratory findings, treatment modalities and final outcome of brucellosis in children. It seems that better socioeconomic conditions and standards of living results in milder illness with no complications and better response to treatment.

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INTRODUCTION

Human brucellosis caused by organisms of the genus *Brucella*, continues to be a major public health problem worldwide (1). Humans are accidental hosts and acquire this zoonotic disease

from direct contact with an infected animal or consumption of products of an animal (2-4). Dr. Bruce first described the symptoms of brucellosis in himself as “gastric remittent fever”.

Brucellosis has many synonyms derived from the geographical regions in which disease occurs e.g. Mediterranean fever, Malta fever, Gibraltar

fever, Cyprus fever; from the remittent character of the fever *e.g.* undulant fever; or from its resemblance to malaria and typhoid *e.g.* typhomalarial fever, intermittent typhoid (5).

Because of improved sanitation, brucellosis has become rare in industrialized countries (6). It is an important infection of human in many parts of world such as Latin America, southern Europe, Africa and Asia (7). The disease is endemic especially in countries of the Mediterranean basin and the Persian Gulf (1). Brucellosis is a common infection of children of Iran (8).

The major reservoirs of the disease include goat and sheep (*Brucella melitensis*, *B. melitensis*), swine (*Brucella suis*, *B. suis*), cattle (*Brucella abortus*, *B. abortus*) and dogs (*Brucella canis*, *B. canis*) (4); although much of brucellosis in children is food-borne and is associated with consumption of unpasteurized milk products (1). Many countries have eradicated *B. abortus* from cattle; in some areas *B. melitensis* and *B. suis* have emerged as causes of this infection in cattle, leading to human infections. Currently *B. melitensis* remains the principal cause of human brucellosis worldwide. The recent isolation of distinct strains of *Brucella* from marine mammals as well as humans is an indicator of an emerging zoonotic disease (9,10).

Brucellosis in endemic and non-endemic regions remains a diagnostic puzzle due to misleading non-specific manifestations and increasing unusual presentations. Fewer than 10% of human cases of brucellosis may be clinically recognized and treated or reported. Brucellosis is a systemic disease that can involve any organ or system of the body (1).

The aim of this study was to evaluate the clinical and laboratory findings, treatment and final outcomes of childhood brucellosis in eastern part of Iran. This is of interest because there are no similar reports from other parts of world with demographic characteristic different from those of Iran and this study allowed us to compare the findings from these different areas.

MATERIALS AND METHODS

Records of the preceding 7 years of 45 children (age ranging from 1 to 15 years) with brucellosis from our Department of pediatrics were studied retrospectively. All met the standard and case definition of this descriptive study. Criteria for case inclusion included a compatible clinical picture with either a positive blood culture for brucella organism or a brucella antibody titer 1/160 and /or rising titer. Cases not fulfilling the above mentioned criteria were excluded. Relapse was defined as recurrence of symptoms within six months of the initial diagnosis with persistent high titer and/or rising titer. Cure was defined as no recurrence of symptoms within 6 month of the initial diagnosis.

Initial laboratory investigations included complete blood cell count and the agglutination test using Rose Bengal plate, which has the compatibility to detect antibodies of IgM and IgG classes against 3 brucella species (*B. melitensis*, *B. abortus* and *B. suis*). Brucella species titer was measured using Wrights test with proper dilution of sera to avoid the Prozone phenomenon. Diphasis blood culture medium (Hemoline, BioMerieux, France) was incubated for at least 4 weeks. Data were statistically analyzed by X^2 test, Mann Whitney U test, and unpaired t-test for comparison analysis. Statistical analysis was performed by application of SPSS statistical package.

RESULTS

Records of 45 children were reviewed; 31 males (68.8%) and 11 females (24.4%). Only 16.3% (8/42) of the patients were <5years. Meanwhile 24% (12/42) were older the 5 years but ≤ 10 years and 59.7% (22/42) were older than 10 years but ≤ 15 years. Twenty eight of the children were living in rural areas and the remaining living in urban areas. Ingestion of

unpasteurized milk was reported in 24 (53.3%) children and animal contact in 15 (33.3%), while 19 (42.2%) children appeared to have no history of exposure to either. Also 22 (48.8%) patients had positive family history of brucellosis.

The disease was acute and sub-acute in 97.1% and chronic in 2.9% of the cases. High fever reaching 39.5°C was the most common symptom observed in 32 children, 4 had chills and intermittent and night fever was observed in 10 children. Sweating in 76.4% and arthralgia or arthritis involving mainly the knee and hips was observed in 30 (83%) children. Sacroileitis was seen in 2 children (4.8%).

On physical examination hepatomegaly was found in 26 (59%) children; splenomegaly confirmed by ultra sonography was detected in 24 (38%) patients. Lymphadenopathy involved the cervical lymph nodes. Table 1 demonstrates symptoms observed in the patients.

Varying combination of Rifampin, Cotrimoxazole, Tetracycline and Gentamycin resulted in a prompt pyrexial response (mean 4.2 days) and lower response in arthropathy and hepato and splenomegaly. The mean duration of treatment was 28 days. Relapse was related to poor compliance of single drug or a shorter duration of chemotherapy. No complication- especially no occurrence of CNS or cardiac disease- was detected during treatment of the children.

Table 1. Incidence of clinical symptoms in 42 children with brucellosis

Symptom	No. of patients (%)
Fever	14 (32%)
Sweating	34 (76.4%)
Weakness	9 (20%)
Myalgia	7 (16%)
Anorexia	7 (16%)
Weight loss	3 (6%)
Cough	3 (6%)
Headache	1 (2.2%)

DISCUSSION

Although the patients in our study (no. 42) appeared to be exposed to risk factors (milk ingestion, animal contact and positive family history) we believe that these patients must have had some sort of exposure. Milk and dairy products appear to have an associated relationship with brucellosis.

Other report have also suggested that consumption of raw milk or dairy products is the main source of infection in children (11,12), whereas control of the disease in domestic animals and pasteurization of milk have led to the scarcity of childhood cases in UK and US (13,14). *B. abortus* and not *B. melitensis*, as expected, was the main pathogen isolated in the blood cultures. In Middle east countries such as Jordan, Iraq and Palestine and in South Africa infection with *B. melitensis* predominates (15,16). *B. abortus* is more common in developed regions than *B. melitensis* and often leads to unapparent or mild illness (17).

The clinical manifestations in our series seem to be similar to those reported by other countries (11,12,16,17). Arthralgia was the most common presenting symptom followed by fever (as found by others) and occurred more often in children than in adults (74% versus 52%) ($p < 0.05$) shown in a study conducted in Gaza Strip (18). In a prospective study in Iran, fever (72%) was the most common clinical feature encountered followed by sweating, arthralgia (50%) and hepatosplenomegaly (32%) (8); while in a study in Saudi Arabia fever was present in 100% of patients and arthralgia in 25% (19).

The most constant finding on physical examination was hepatomegaly, followed by splenomegaly and lymphadenopathy. Young patients more often have positive blood cultures and lower antibodies titers than do older ones. These findings probably indicate that young children have reduced defense against brucella pathogens compared to older children, which

frequently leads to bacteremia. Although none the patients, even those with positive blood cultures, had complications we conclude that brucellosis in young children may be more severe, and requires particular attention because the risk of complications due to bacteremia is increased. However, further confirmation of these findings is necessary, as we were not able to find other studies that could support our results (11,12,18,20).

Treatment of childhood brucellosis is controversial and is currently dependent on the inclusion of an aminoglycosidic antibiotic. It is evident from other researches that therapy with a single antibiotic is not as effective in brucellosis as when appropriate combinations are used (21). Our study showed that Gentamycin in combination had much more satisfactory results than streptomycin in combination. However, Lubani et al in Kuwait demonstrated that Gentamycin in combination had satisfactory results in treatment of brucellosis (22).

A multi center prospective study carried out by Cisneros et al on antimicrobial therapy for brucellosis concluded that the combination of Doxycycline and Streptomycin was an effective treatment for the types of brucellosis included in their study (23). Armin Sh. et al found that the combination of Cotrimoxazole plus Rifampicin, Cotrimoxazole plus Streptomycin and Cotrimoxazole plus Rifampicin and Gentamycin were effective (8). In our study other combinations excluding Gentamycin and Streptomycin (Cotrimoxazole and Rifampicin, Tetracycline and Cotrimoxazole) had better results than Gentamycin in combination which supports the recommendation of Armin Sh. that the combination of Rifampicin and Cotrimoxazole as the preferred regimen for children (8). Patients were treated with diverse therapeutic regimens and the treatments duration varied. Since the study is a retrospective one, the mean duration of therapy was about 4 weeks that was

proposed by the World Health Organization (WHO) in 1986 to be the regimen of choice for brucellosis.

CONCLUSION

In the present study we attempted to evaluate the clinical and laboratory findings, treatment modalities and final outcome of brucellosis in children. It seems that better socioeconomic conditions and standards of living results in milder illness with no complications and better response to treatment.

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