

Epidemiology, Clinical Presentation, and Treatment Outcome of Brucellosis Among Children

Manijeh Khalili ¹; Batool Sharifi-Mood ²; Maliheh Metanat ^{2,*}; Masoud Salehi ²

¹Children and Adolescents Health Research Center, Zahedan University of Medical Sciences, Aliebn-E-Abitaleb Hospital, Zahedan, IR Iran

²Infectious Diseases and Tropical Medicine Research Center, Zahedan University of Medical Sciences, Boo-Ali Hospital, Zahedan, IR Iran

*Corresponding author: Maliheh Metanat, Infectious Diseases and Tropical Medicine Research Center, Zahedan University of Medical Sciences, Boo-Ali Hospital, Zahedan, IR Iran. Tel: +98-5413228101-2, Fax: +98-541 3236722, E-mail: malihemetanat@yahoo.com

Received: June 27, 2014; Revised: June 29, 2014; Accepted: July 25, 2014

Background: Brucellosis is a systemic infection with a various clinical manifestations ranging from asymptomatic infection to serious and fatal diseases. In endemic area, one-third of all cases of human brucellosis have been reported in children.

Objectives: This study aimed to evaluate epidemiology, clinical presentation, and treatment outcome of brucellosis among children in Zahedan City.

Patients and Methods: During 36 months, from December 2008 through October 2011, we evaluated all patients younger than 19 years old who were referred to Infectious Diseases Clinic in Boo-Ali Hospital (Zahedan City, southeastern Iran). The patients were referred because of fever, myalgia, and arthralgia, chronic low-back pain, bone pain, and other signs or symptoms consistent with brucellosis and had a positive results for serology test. Titers > 1:80 were considered as positive results.

Results: Among 32 patients with brucellosis (24 male and 8 female; age range, 7-19 years), 83% had chronic bone pain. Fever was reported in 39% and the least frequent complication was osteomyelitis (3%). Patients were treated medically and all the patients survived.

Conclusions: Our study showed that the clinical manifestations and complication in children with brucellosis are similar to that in the adults; however, treatment can be different according to age of patients. In endemic areas, every patient with low-back pain in any age group should be evaluate for brucellosis.

Keywords: Brucellosis; Epidemiology; Child; Complication; Outcome

1. Background

Brucellosis is a highly contagious zoonosis caused by small, gram-negative coccobacilli, namely, *Brucella* species. Ingestion of unpasteurized dairy products such as milk and cheese or undercooked meat can infect human (1-3). In addition, infection can be transmitted to humans through contact with fluids from infected animals such as cattle, sheep, camel, or other infected animals. The bacteria can enter the body through the eyes and inhalation of infected droplets (3, 4). The main source of infection in children is consumption of unpasteurized dairy products and adults boys are more commonly infected than girls are. Transmission from mother to child is rare but possible. Disease presents with flu-like syndrome or persistent bone pain, weakness, and headaches. Other common symptoms and signs include fever, arthralgia, sweating, and arthritis, especially monoarthritis, and the most commonly affected joints are hip and knee (2-6). Like tuberculosis, clinical presentation varies and all organs may be involve during the course of the disease. Serologic tests are the most important methods of diagnosis. Standard agglutination test (SAT) with titers > 1:80 and the 2-mercaptoethanol (2ME) test with titers $\geq 1:40$ are suggestive of active infection (2, 3, 5-7). Drugs that are

used for treatment in children are similar to those used in adults; however, doxycycline and quinolones are not recommended in children younger than eight years of age because of osteoarticular side effects. Children older than eight years of age can be treated with doxycycline for 45 days or eight weeks plus gentamicin for seven or five days or streptomycin for 14 days (6-8). There are many studies concerning childhood brucellosis; some of them have evaluated epidemiology and clinical syndromes and some of the reports have explained treatment of diseases in children (6-11).

2. Objectives

Sistan-and-Baluchistan Province is an endemic area for brucellosis and there was no published data about childhood brucellosis; therefore, we decide to evaluate epidemiology, clinical presentation, and treatment outcome of brucellosis among children in Zahedan City, the capital of Sistan-and-Baluchistan Province in southeastern Iran.

3. Patients and Methods:

From December 2008 through October 2011, we eval-

ated all patients younger than 19 years old who were referred to Infectious Diseases Clinic in Boo-Ali Hospital (Zahedan City, southeastern Iran) because of fever, myalgia, arthralgia, chronic low-back pain, bone pain, and other signs or symptoms consistent with brucellosis that had positive results in serologic test. The STA titers $> 1:80$ and 2ME test titers $\geq 1:40$ were considered as positive results. Blood samples of the admitted patients were inoculated aseptically into the bottles containing brain-heart infusion broth and were incubated at 37°C for three weeks. A structured checklist was prepared to record demographic data, clinical presentations, laboratory results, drugs regimen, and clinical outcome.

4. Results

Among 32 children and adolescents with brucellosis (24 male, 8 female; age range, 7-19 years), 83% had chronic bone pain and other frequent signs and symptoms were consecutively headache (55%), weakness (45%), arthralgia (41%), fever (39%), gastrointestinal disorders such as abdominal pain and nausea (21%), and bone complication (spondylodiscitis) (3%). Patients who were younger than eight years (three cases) were treated with gentamicin for five days plus cotrimoxazole for six weeks and children older than eight years were treated with gentamicin for five days plus cotrimoxazole for six weeks or doxycycline with STM. Drug regimen in patient with spondylodiscitis consisted of cotrimoxazole plus rifampin and streptomycin for three months.

5. Discussion

Brucellosis is a highly contagious disease of livestock, which is characterized by abortions or reproductive failure (1-3). Infected and untreated animals can shed the causative bacteria and lead into significant economic burden through reduced productions in livestock. Brucellosis in humans is often related to the consumption of unpasteurized milk and soft cheese made from the milk of infected animals, especially goats. If they left untreated, the disease in humans can become chronic and patient would be faced with serious complication such as spondylodiscitis, sacroiliitis, endocarditis, meningoencephalitis, granulomatous hepatitis, uveitis, optic neuritis, pancytopenia, and chronic anemia (1-5). Diagnosis is made on the basis of achieved serologic tests results through STA, 2ME assay, enzyme-linked immunosorbent assay, or blood and bone marrow cultures. Histopathologic evidence of granulomatous hepatitis on hepatic biopsy and radiologic findings in infected bone or vertebrae can help to diagnose brucellosis (2, 5-8). Our study showed that routes of transmission, diagnostic tests, and complication in children were similar to those observed in adults, but drug regimen can be different because some drugs have serious side effects in children younger than eight years of age. As adults, disease is more frequent in males and females are less involved. There are

many reports about clinical presentations and complications in children (6-14). In Ulug et al. study, demographic data were similar to that of our study and clinical presentation such as fever, malaise, lack of appetite, and arthralgia were the most common clinical symptoms and hematologic problems were the main complications (7). Our patients had not important hematologic disorders but mild anemia was found in 33% of patients. In Issa and Jamal report, arthralgia (78%), fever (75%), and sweating (60%) were consecutively the most common clinical presentations and the most frequent complications were limping (75%) and arthritis (54%), consecutively (6). In an Iranian study in 2013 on 34 children with brucellosis, arthritis, splenomegaly, hepatomegaly, lymphadenopathy, skin rashes, and fever were the major clinical finding and similar to our report, anemia (53%) was the most common laboratory abnormality (8). El-Koumi et al. found that among 60 children with brucellosis, sweating (68%), bone aches (62%), and chills (55%) were consecutively the most common clinical manifestations and arthritis (32%) was the major complication in the studied population. The main laboratory abnormalities included anemia (43%) and pancytopenia (18%) (10). Brucellosis is a chronic disease and as seen in many reports as well as in our study, anemia is a common complication; however, brucellosis can cause lymphoproliferative disorders and malignant diseases. In these malignant presentations (acute lymphoblastic leukemia), complete remission from all problems would be achieved after receiving brucellosis treatment (15). Most studies have reported that males are more susceptible than females; however, in Buzgan et al. report on 1028 patients, 539 (52.4%) were female and 489 (47.6%) were male and the most frequent complication was osteoarticular involvement (25%) (12). In that study, the overall relapse rate was 4.7% and the highest relapse rate was found in the patients with osteoarticular involvement. Our patients had no relapse but osteoarticular involvement was seen in one case. Although death has been reported due to serious complication, we had no mortality among our patients.

We conclude that human brucellosis may lead to serious morbidities and mortality and it continues to be a major health problem in developing countries such as Iran. Based on our results, the clinical manifestations, diagnostic methods, and complication in children with brucellosis are similar to that of adults but treatment can be different according to age of patients. In endemic area, every patient with low-back pain, headache, arthralgia, and fever in any age group should be evaluated for brucellosis.

References

1. Bosilkovski M, Dimzova M, Grozdanovski K. Natural history of brucellosis in an endemic region in different time periods. *Acta Clin Croat*. 2009;48(1):41-6.
2. Mantur BG, Amarnath SK, Shinde RS. Review of clinical and laboratory features of human brucellosis. *Indian J Med Microbiol*. 2007;25(3):188-202.

3. Pappas G, Papadimitriou P, Akritidis N, Christou L, Tsianos EV. The new global map of human brucellosis. *Lancet Infect Dis*. 2006;6(2):91-9.
4. Colmenero JD, Reguera JM, Martos F, Sanchez-De-Mora D, Delgado M, Causse M, et al. Complications associated with Brucella melitensis infection: a study of 530 cases. *Medicine (Baltimore)*. 1996;75(4):195-211.
5. Kassiri H, Amani H, Lotfi M. Epidemiological, laboratory, diagnostic and public health aspects of human brucellosis in western Iran. *Asian Pac J Trop Biomed*. 2013;3(8):589-94.
6. Issa H, Jamal M. Brucellosis in children in south Jordan. *East Mediterr Health J*. 1999;5(5):895-902.
7. Ulug M, Yaman Y, Yapici F, Can-Ulug N. Clinical and laboratory features, complications and treatment outcome of brucellosis in childhood and review of the literature. *Turk J Pediatr*. 2011;53(4):413-24.
8. Fanni F, Shahbaznejad L, Pourakbari B, Mahmoudi S, Mamishi S. Clinical manifestations, laboratory findings, and therapeutic regimen in hospitalized children with brucellosis in an Iranian Referral Children Medical Centre. *J Health Popul Nutr*. 2013;31(2):218-22.
9. al-Eissa YA, Assuhaimi SA, al-Fawaz IM, Higgy KE, al-Nasser MN, al-Mobaireek KF. Pancytopenia in children with brucellosis: clinical manifestations and bone marrow findings. *Acta Haematol*. 1993;89(3):132-6.
10. El-Koumi MA, Afify M, Al-Zahrani SH. A prospective study of brucellosis in children: relative frequency of pancytopenia. *Mediterr J Hematol Infect Dis*. 2013;5(1).
11. Islek A, Sayar E, Yilmaz A, Gunseren F, Artan R. Relapsing brucellosis after liver transplantation in a child: what is the appropriate regimen and duration of therapy? *Transplantation*. 2013;96(2):e6-7.
12. Buzgan T, Karahocagil MK, Irmak H, Baran AI, Karsen H, Evrigen O, et al. Clinical manifestations and complications in 1028 cases of brucellosis: a retrospective evaluation and review of the literature. *Int J Infect Dis*. 2010;14(6):e469-78.
13. Aysha MH, Shayib MA. Pancytopenia and other haematological findings in brucellosis. *Scand J Haematol*. 1986;36(4):335-8.
14. Yildirmak Y, Palanduz A, Telhan I, Arapoglu M, Kayaalp N. Bone marrow hypoplasia during Brucella infection. *J Pediatr Hematol Oncol*. 2003;25(1):63-4.
15. Eser B, Altuntas F, Soyuer I, Er O, Canoz O, Coskun HS, et al. Acute lymphoblastic leukemia associated with brucellosis in two patients with fever and pancytopenia. *Yonsei Med J*. 2006;47(5):741-4.