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Original Article

Epidemiological, Clinical and Laboratory Features of Brucellosis: A Retrospective Evaluation of 175 Children

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ABSTRACT

***Background**: Human brucellosis, a multi-organ system disease which may mimic other conditions, has a low incidence in childhood and the diagnosis may be easily missed. Brucellosis has become a major medical problem in some provinces of Iran. This study aimed to examine the epidemiology, clinical, and laboratory features, and treatment outcome of Brucellosis.*

***Materials and Methods**: We retrieved and reviewed the records charts of all patients admitted to pediatric infectious diseases, Ghods Hospital from March 1995 to March 2004 with a clinical diagnosis of brucellosis whose brucella agglutination titer was 1:160 or greater in department. Information on age, gender, history of using unpasteurized milk or milk products, presenting symptoms and physical signs were extracted from the patients' files. We also noted the result of routine laboratory tests, treatment given and outcome of treatment.*

***Results**: Children under 12 years constituted the total brucellosis admissions. One hundred and seventy-five patients (107 males, 68 females with a M/F ratio of 1.6:1) had a diagnostic label of brucellosis and a brucella titer of 1:160. Eighty-seven patients (50%) were 1-6 years old, 86 (49%) were 7-12, while 2 patients were under 1. One hundred (57%) patients were from rural areas and 75 (43%) from cities. The admission for the disease was in summer in 76 patients (43%), followed by spring in 52(30%), winter in 24 (14%) and autumn (13%). One hundred and fourteen (65%) had history of using unpasteurized milk or milk products. The most frequent symptoms were arthralgia (79%) and fever (78%). The most common physical findings were fever (51%) and arthritis (26%). Of patients, 157 cases (89.5%) had acute and 17 (9%) had chronic disease. Normal white blood cell count was found in 123 cases (71%), anemia in 33 (19%), increased erythrocyte sedimentation rate (ESR) in 92 (53%), positive C-reactive protein (CRP) in 85 (48%) and positive radiological changes in 20 (11%). The most common antibiotics used were cotrimoxazole + gentamycin in 83 (47.5%) and cotrimoxazole + rifampin in 72 (41%) cases.*

***Conclusion**: Brucellosis presents in various ways and should be included in the differential diagnosis of arthritis in endemic countries. As symptoms, signs and first-line laboratory findings are not characteristic, agglutination tests, and if possible, blood culture should be performed in any child with prolonged fever. Treatment is effective, but prevention of the disease by educating high risk families is indicated.*

***Keywords:** Brucellosis, Epidemiology, Clinical Features, Children*

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INTRODUCTION

Brucellosis is a zoonotic infection, transmitted to human primarily by consumption of unpasteurized milk and milk products. Other modes of transmission in endemic areas are less common (1).

Although human brucellosis is endemic in many areas of the world (500,000 new cases annually), the number of reported infections in some countries has dropped remarkably as a result of mandatory milk pasteurization, slaughter of infected animals, and an aggressive vaccination program (2).

The clinical presentation of brucellosis is non-specific and heterogeneous in its course and severity, and in humans it presents as a multisystem disease involving many organs and tissues (3).

2. Acute brucellosis: Acute infection presents with high fever, malaise, headache, sweats, and arthralgia (duration<one month).

3. Chronic brucellosis: the chronic form of brucellosis occurs after a year of illness and usually requires bone marrow biopsy to be diagnosed.

Brucella organisms are able to survive and even multiply within the cells of the mononuclear-phagocytic system; thus, explaining the tendency of the disease to have a prolonged clinical course with relapses and the difficulty in treatment (1,4). The absolute diagnosis of brucellosis requires isolation of the bacterium from blood or tissue sample. The sensitivity of blood culture varies, depending on the individual laboratory practices and how actively the obtaining of cultures is pursued. The percentage of cases with positive cultures ranges from 15% to 70% (4, 5).

Bone marrow cultures are considered the gold standard for the diagnosis of brucellosis, since the relatively high concentration of brucella in reticuloendothelial system makes it easier to detect the organism.

Furthermore, bacterial elimination from the bone marrow is equivalent to microbial eradication (4). However, harvesting bone marrow for culture remains an invasive, painful technique, and results have been universally reproducible (4).

There are two broad categories of serologic methods for diagnosing brucellosis: Those based on antibody production against lipopolysaccharide and those based on antibody production against other bacterial antigens. Developed by Bruce, the serum agglutination test remains the most popular diagnostic tool for the disease. Titer above 1:160 is considered diagnostic in conjunction with a compatible clinical presentation (4).

In addition to above mentioned diagnostic tests, a new dipstick test, offers a rapid and reliable diagnostic alternative in acute brucellosis (6).

Although pasteurization of milk and milk products is developing in Iran, but childhood brucellosis continues to be common in Iran and knowledge about the disease as well as possible changes in its clinical course, complications and outcome remain of interest.

The aim of this study was to evaluate the clinical and laboratory findings, treatment modalities, complication and final outcomes of brucellosis in children in Ghazvin, Iran. This is of interest because there are similar reports from other parts of the country with demographic and epidemiological characteristics different from those of Ghazvin, and this study allowed us to compare the findings in different areas (7-9).

MATERIALS AND METHODS

This study was performed on 175 children less than 12 years of age with brucellosis whom were treated in the department of pediatric infectious diseases, Ghazvin Medical University from March 1995 to March 2004. Signs, symptoms, laboratory findings, treatment modalities, complications and final outcomes were retrospectively analyzed.

Laboratory diagnosis of brucellosis was based on standard tube agglutination methods. Titer 1:160 or greater, using continuous serum dilutions was estimated as a positive result (10). The information on age, gender, place of residence (urban or rural), season of admission, history of consumption of unpasteurized milk or milk products, history of brucellosis in family members and history of animal exposure were collected from the medical records of patients.

Information on clinical symptoms (arthralgia, fever, anorexia, weakness, sweating, nausea and vomiting, gastroenteritis, cough and weight loss) was obtained as well.

In addition to the above-mentioned data, the information on clinical signs (fever, arthritis, splenomegaly, hepatomegaly, lymphadenopathy and limitation of motion) was collected from the medical records.

Information on laboratory findings [Hb, ESR, CRP, Tube agglutination test, 2-mercaptoethaml (2ME)] and radiological data etc, were considered as well.

RESULTS

From March 1995 to March 2004, there were 175 patients (age ≤12 years) diagnosed with brucellosis at our hospital. All were non-bacteremic cases (reports on brucella bacteremia are scarce) (11) and were diagnosed based on symptoms suggestive of brucellosis and a serological titer of 1:160 or greater.

Analysis of the seasonal distribution of hospitalization revealed that 76 patient (43%) were admitted during summer, while 52 (30%) were admitted during spring**,** 24 patients (14%) in winter and 23 (13%) in autumn.

Among 175 patients with brucellosis, 61% were males and 39% were females. Duration of symptoms prior to hospitalization was detected in 175 patients among which 144 (82%) had a duration less than or equal to one month, and 31 (18%) had duration longer than one month.

One-hundred fourteen (65%) had a history of consumption of unpasteurized milk or milk products, and 58 (33%) had a history of contact with an infected cattle. Family members of 44 (25%) patients had a history of brucellosis. The disease was acute in 89.5% and the remaining had a past history of brucellosis.

The presenting symptoms and signs of 175 patients are shown in Tables 1 and 2.

Table 1. Frequency of presenting symptoms

Symptoms	No. of patients	%
Arthralgia/Arthritis	138	79
Fever	137	78
Excessive sweating	77	44
Weakness	71	40
Anorexia	50	28
Chills	41	23
Abdominal pain	36	20
Headache	34	19
Nausea and vomiting	28	16
Cough	27	15
Weight loss	25	14
Gastroenteritis	19	11

The most frequent symptom was arthralgia (79%), (Table 1). The most common physical finding was fever (51%). (Table 2), and the most common joints involved were knee (31%), followed by many joints (22.5%) and hip (18%).

Table 2. Frequency of signs

Sign	No. of patients	%
Fever	90	51
Arthritis	46	26
Splenomegaly	35	20
Hepatomegaly	25	16
Lymphadenopathy	21	12

Of 175 patients, the initial Wright seroagglutination titer was equal to 1:640 in 53

patients (30%), 1:1280 in 29 (16.5%), 1:320 in 29 (16.5%) and 1:2560 in 18 patients (10%).

The hemoglobin values were within the normal limit in 142 patients (81%) and the remaining had anemia (19%).White blood cell (WBC) counts were within the normal limit in 123 patients (71%), and 29 patients (16.5%) had leukocytosis.

Erythrocyte sedimentation rate (ESR) was within the normal limit in 92(53%) patients and 80(45%) transmitted had moderate to severe elevation.

C - reactive protein (CRP) showed mild to severe elevation in 85 patients (48%), 38 patients (22%) had normal CRP, and there was no record in the remaining.

Initial agglutinating antibody titer was 1:640 in 53 patients (30%), 1:1280 and 1:320 in 29 (16.5%) and 29 (16.5%) patients respectively.

The highest initial agglutinating titer was 1:2560 in 18 patients (10%). 2-ME titer was 1:320, 1:80, 1:160, 1:640 and 1:1280 in 26(15%), 24(14%), 21(12%), 15(8.5%) and 15(8.5) patients respectively.

Osteoarthicular investigations revealed radiological changes in 20 patients (11%).

Treatment regimens used in 175 patients consisted of combinations of two drugs: co-trimoxazole plus gentamycin (47.5%), co-trimoxazole plus rifampin (41%) and other combinations (11.5%).

DISCUSSION

Childhood brucellosis continues to be an important public health problem in our country, although a trend toward an overall decrease of the prevalence of disease is suggested (8, 9).

The annual incidence of brucellosis cases presenting to our hospital has declined with time as well, but there are still reports of childhood brucellosis in provinces of Iran (8, 9). Therefore, evaluation of the clinical features and laboratory findings of brucellosis in children remains of great importance.

In our patients there was an obvious preponderance of males, and this is in accordance with other studies performed in Iran as well as in other countries (11-14).

The scarcity of subjects younger than 1 year of age as found in our series (only 2 cases) and others, may be explained by the fact that brucellosis is less transmitted through milk than dairy solids and breast-feeding may have anti-brucella activity in addition to preventing exposure to contaminated milk (1, 17). Brucellosis may also present as an asymptomatic/ nonspecific milder self-limited course in this age group (1, 18). The disease occurred mainly in the school age group (50%) which was compatible with other studies (12).

The prevalence of disease was the highest in summer (43%) which was in accordance with other studies (8, 19).

In agreement with other studies, the majority of patients (65%) had a history of consumption unpasteruized milk or milk products (8, 12, 13, and 19).

More than 58 percent of patients had a history of close contact with animal which was in accordance with other studies (12).

Family members of 44 percent of patients had a history of brucellosis. Reposts on brucellosis of family members, however, are scarce.

Duration of illness prior to diagnosis was less than 1 month in 82 percent of patients which was in agreement with other studies (12, 20).

The clinical manifestations in our series seem to be similar to those reported by others in Iran as well as in other countries (3, 8, 9, 13, 20, 21).

A combination of fever and arthralgia or arthritis was very common and of particular value for the diagnosis. In agreement with other studies, it was found that arthritis or arthralgia involves most commonly the knee and hip joints (3, 5, 12, 21, 22). None of the children had involvement of the sacroiliac joint, as was found in a previous study but unlike others (1, 22).

Patients were treated with combinations of two agents: co-trimoxazole plus gentamycin (47.5%), co-trimoxazole plus rifampin (41%) and other combinations (11.5%).

CONLCUSION

We emphasize that eradication of this worldwide disease can be achieved only by aggressive preventive measures starting with eliminating the infected animals; vaccinating newborn animals; education; and enforcement of control measures.

REFERENCES

1. Gottesman G, Vanunu D, Maayan MC, Lang R, Uziel Y, Sagi H, Wolach B. Childhood brucellosis in Israel. ***Pediatr Infect Dis J*** 1996; 15(7):610-5.
2. Troy, Stephanie B. Brucellosis in San Diego. ***Medicine***. 2005 vol. 84(3), PP 174-184.
3. Giannakopoulos I, Nikolakopoulou NM, Eliopoulou M, Ellina A, Kolonitsiou F, Papanastasiou DA. Presentation of childhood brucellosis in Western Greece. ***Jpn J Infect Dis*** 2006; 59(3):160-3.
4. Georgios Pappas. Brucellosis. ***NEJM*** 2006. Vol PP. 2325-36.
5. Memish Z, Mah MW, Al Mahmoud S, Al Shaalan M, Khan MY. Brucella bacteraemia: clinical and laboratory observations in 160 patients. ***J Infect*** 2000; 40(1):59-63.
6. Casao MA, Smits HL, Navarro E, Solera J. Clinical utility of a dipstick assay in patients with brucellosis: correlation with the period of evolution of the disease. ***Clin Microbiol Infect*** 2003; 9(4):301-5.
7. Roushan, Mohammad Reza Hassanjani. Efficacy of cotrimoxazole and rifampin for 6 to 8 weeks of therapy in childhood brucellosis. ***The pediatr Infec Dis J*** 2006; V.25 (6), PP. 544-5.
8. Salari MH, Khalili MB, Hassanpour GR. Selected epidemiological features of human brucellosis in Yazd, Islamic Republic of Iran: 1993-1998. ***East Mediterr Health J*** 2003; 9(5-6):1054-60.
9. Roushan, Mohammad Reza Hassanjani, Childhood brucellosis in Babol, IRAN. ***Tropical doctor***, V.35, No, 35, Oct. 2005, PP. 229-231(3).
10. Behrman R.E. Nelson textbook of pediatrics. 17th ed. Philadelphia: WB Saunders; 2004: 939-41.
11. Almuneef M, Memish ZA, Al Shaalan M, Al Banyan E, Al-Alola S, Balkhy HH. Brucella melitensis bacteremia in children: review of 62 cases. ***J Chemother*** 2003; 15(1):76-80.
12. Mantur BG, Akki AS, Mangalgi SS, Patil SV, Gobbur RH, Peerapur BV. Childhood brucellosis--a microbiological, epidemiological and clinical study. ***J Trop Pediatr*** 2004; 50(3):153-7.
13. Shaalan MA, Memish ZA, Mahmoud SA, Alomari A, Khan MY, Almuneef M, Alalola S. Brucellosis in children: clinical observations in 115 cases. ***Int J Infect Dis*** 2002; 6(3):182-6.
14. Tsolia M, Drakonaki S, Messaritaki A, Farmakakis T, Kostaki M, Tsapra H, Karpathios T. Clinical features, complications and treatment outcome of childhood brucellosis in central Greece. ***J Infect*** 2002; 44(4):257-62.
15. Street L Jr, Grant WW, Alva JD. Brucellosis in childhood. ***Pediatrics*** 1975; 55(3):416-21.
16. Sabbaghian H. Fresh white cheese as a source of Brucella infection. ***Public Health*** 1975; 89(4):165-9.
17. Awad R. Human brucellosis in the gaza strip, Palestine. ***Eastn Mediterr Health*** 1998, vol 4(2): P: 225-33.

18. Gedalia A, Watemberg N, Rothschild M. [Childhood brucellosis in the Negev]. ***Harefuah*** 1990; 119(10):313-5.
19. Benjamin B, Annobil SH. Childhood brucellosis in southwestern Saudi Arabia: a 5-year experience. ***J Trop Pediatr*** 1992; 38(4):167-72.
20. al-Eissa YA, Kambal AM, al-Nasser MN, al-Habib SA, al-Fawaz IM, al-Zamil FA. Childhood brucellosis: a study of 102 cases. ***Pediatr Infect Dis J*** 1990; 9(2):74-9.
21. Joint food and agriculture organization (1986). FAO/WHO expert committee on brucellosis (sixth report). WHO technical report series. No. 740. P. 56-57. World health organization, Geneva.