Evaluation of epidemiologic, clinical, and paraclinical features of children with brucellosis hospitalized in two teaching hospital related to Mazandaran University of Medical Sciences, Iran, during the years 2010-2016

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Abstract

Original Article

BACKGROUND: The clinical manifestations of brucellosis are very diverse. This study was conducted to investigate the epidemiological, laboratory, and clinical characteristics in pediatrics patients with brucellosis.
METHODS: In this descriptive cross-sectional study, the population included patients under age of 18 years who were hospitalized with a diagnosis of brucellosis in Razi hospital, Qaemshahr City, and Bu-ali Sina hospital, Sari City, Iran, during the years 2010-2016. Twenty seven patients with a mean age of 12.5 years including 9 girls and 18 boys had inclusion criteria and entered to study. Most patients (70.3%) were in the age range of 12-18 years.
RESULTS: Twenty one patients (77.8%) consumed unpasteurized dairy products and 10 patients (37%) had direct contact with livestock. Most of the initial complaints were fever in 13 cases (48.1%), joint pain in 12 cases (44.4%), and limbs pain in 5 cases (18.5%). The most common clinical findings were arthritis (14.8%) and splenomegaly (7.4%). In laboratory findings, 11.1% had leukopenia, 48.1% had anemia, 3.7% had thrombocytopenia, 29.6% had a moderate increase in erythrocyte sedimentation rate (ESR), 25.9% had high increase in ESR, and 18.5% had leukocytosis. Clinical signs and laboratory parameters in the study included chills and fever, joints and limbs pain, arthritis, splenomegaly, increase in ESR, anemia, leukocytosis, and leukopenia.
CONCLUSION: In patients with fever and skeletal or joints pain, brucellosis should be considered as a possible disease, and initial diagnostic measures should be taken, especially in children. Signs and symptoms of brucellosis are various and nonspecific. Educating the high risk families plays an important role in management of disease.
KEYWORDS: Brucellosis, Pediatrics, Epidemiology, Clinical Medicine

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Introduction

Brucellosis is a common disease between humans and animals (the most common disease, commonly seen in wild and domestic animals). Although brucellosis is eradicated in some countries and is controlled in some others, it remains a threat to human health in areas such as Mexico, South and Central

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America, the Mediterranean region, the Arabian Peninsula, Iran, and the Indian subcontinent. Today, 8 species of brucellosis have been identified of which four species have moderate to severe pathogenicity: Brucella melitensis (B. melitensis), Brucella abortus, Brucella canis, and Brucella suis. B. melitensis is the main cause of human brucellosis in Iran. In endemic areas, especially when B. melitensis is common, children over 25% of cases develop human brucellosis.[1]

This bacterium is transmitted from animal to human through the use of contaminated food, direct contact with an infected animal, or aerosol inhaling. Brucella can enter the human body through skin damage, mucous membranes, conjunctiva, as well as respiratory and digestive tract. The main route for oral transmission is the unpasteurized milk. Workers at slaughterhouses, farmers and shepherds, veterinarians and microbiologists are at the risk of brucellosis contamination.[2] The etiologic agent of the disease is a gram-negative coccobacilli that is mobile, without spore production and oxidative metabolism, and does not grow in normal culture media. Brucella attacks both phagocytic and non-phagocytic cells (that is unique in this regard), and can survive in the intracellular environment and escape the immune system.[3]

Brucella can be inserted into the lymph system, the kidneys, spleen, breast tissue, or joints; it can give local or systemic involvement and cause a wide range of clinical symptoms. Almost all body systems can be involved in the disease.[2] Fever and chills, and joint pain are major symptoms of brucellosis in children. Sweating, anorexia, weight loss, low back pain, headache and general weakness are also symptoms of brucellosis, especially in children. The risk of brucellosis should be considered when confronting with these symptoms, especially in hyperendemic areas. The disease incubation period is one to three weeks, but it can also be several months.

Brucellosis symptoms can range from a subclinical infection to a chronic disease. If clinical symptoms take more than 12 months, it is considered to be chronic, mostly due to the presence of deep infectious sites such as areas of pus in the bones, joints, liver, spleen, and kidneys.[4,5]

The most common focal manifestations are musculoskeletal pain, septic arthritis, and knee, hip, sacroiliac, shoulder, sternocellular joints involvement in the form of monoarthritis or polyarthritis.[6] Objective criteria are useful for assessing the probability of brucellosis, including clinical signs and serologic tests. The best way to treat brucellosis is prevention and proper use of dairy products and other animal products.[6]

In clinical examinations, fever and lymphadenopathy are more common symptoms. Arthritis is the most common localized complication of brucellosis. In children, single-knee joint as well as sacroiliac and hip joints involvement are more common.[4,5] Peripheral blood tests usually do not recognize the disease or even may be misleading. The number of white blood cells (WBC) usually affects the lymphocytosis. In general, Wright's titer increases in most patients with acute brucellosis within 1-2 weeks, and changes in serum will occur in almost all patients within three weeks after the onset of the disease. The change in the Wright test head is considered to be valuable and significant when increased by a factor of four or more, and when the initial titer is at least 1/40 or greater, and then increases to 1/160 or more, in other words, the titer 1/160 is considered positive. Most referrals have a headline greater than or equal to 1/160 in non-endemic regions and a headline of 1/320 in endemic regions, but in Iran's protocol for brucellosis, the titer 1/80 for Coombs Wright test and 1/40 for 2 mercaptoethanol (2 ME) are considered positive.[7]

Considering the prevalence of brucellosis in

Iran and its endemic as well as different clinical manifestations, it is possible to study the incidence of the disease with clinical and laboratory manifestations in this regions; early diagnosis and treatment of the disease can reduce its complications, especially among children. Considering the above issues, this research was conducted to study the epidemiological characteristics, clinical signs, and laboratory findings in patients. Finally, the statistics can be compared with the results of other studies in Iran and other parts of the world.

Materials and Methods

The aim of this case study was to evaluate patients with positive clinical signs of brucellosis and Wright titer equal to or greater than 1/80 who were hospitalized in infectious or pediatric wards of Razi hospital in Qaemshahr City, and Bou-ali Sina hospital in Sari City, Iran, two teaching hospital related to Mazandaran University of Medical Sciences, during the years 2010-2016. The study population was patients under the age of 18 with diagnosis of brucellosis whose records were available in the hospitals.

The exclusion criteria were lack of confirmation of Brucellosis. For data collection, information form was used and the variables like gender, clinical symptoms, and hematologic findings such as WBC, platelets (PLT), hemoglobin (Hb), red blood cells (RBC), etc were extracted from the files. Anemia was a decrease in hemoglobin rate to below 11.5 g/dl. Leukopenia was associated with a decrease in WBC to less than 4,500 µg/µl, while leukocytosis was in the form of an increase in WBC more than 10,000 µg/µl; thrombocytopenia included a decrease in the number of PLT to less than 150,000 µg/µl. Aspartate aminotransferase (AST) outside the range of 5 to 40 units per liter of serum, alanine transaminase (ALT) outside the range of 7 to 56 units per liter, and alkaline phosphatase (ALP) greater than or equal to 350 units per liter of serum were reported abnormal. The normal erythrocyte sedimentation rate (ESR) value was 25 mm/hour, according to that the patients were divided into three groups: patients with ESR in the range of 0-25, patients with ESR in the range of 25-50 (average increase), and patients with ESR value above 50 mm/hour which indicated a sharp increase.

After collecting information, the data were entered into SPSS software (version 17, SPSS Inc., Chicago, IL, USA) and analyzed using descriptive statistics. Generally, on the basis of clinical evidence based on laboratory tests and according to Wright's national protocol, titer of 1/80 and 2 ME with a titer of 1/40 were considered positive, and the patients should be examined for clinical, epidemiological, and laboratory characteristics.

Results

The range of patients' age was between 13 to 17 years and the average age was 12.5 years. 4 cases (14.8%) in the age group of 0-6 years, 4 cases (14.8%) in the group of 6-12 years , and 19 cases (70.3%) in the group of 12-18 years old, diagnosed with brucellosis were selected for the study. Of the 27 patients under study, 18 cases (66.7%) were boys and 9 cases (33.3%) were girls. Of the total patients, 16 cases (59.3%) were rural residents and 11 cases (40.7%) were urban residents. The number of visits in different seasons was as 8 cases (29.6%) in the spring, 12 cases (44.4%) in the summer, 4 cases (14.8%) in the fall, and 3 cases (11.1%) in the winter. 21 cases (77.8%) had a history of local and non-pasteurized dairy consumption, while 6 people (22.2%) did not have history of local dairy consumption.

According to the information obtained from the questionnaire, 10 cases (37%) had a history of direct contact with the livestock, while 17 cases (63%) did not have such a record. Among the main complaints mentioned in the

questionnaire (fever, chills, stroke, lameness, limb pain, joint pain, headache, and swelling), the most common complaint was fever. 13 patients (48.1%) reported fever as their main problem, while in 4 cases (14.8%) chills, in 12 cases (44.4%) joint pain, in 4 cases (14.8%) limping, in 5 cases (18.5%) limb pain, in 1 case (3.7%) headache, and in 1 patient (3.7%) joint swelling were the main complaints of the patients.

The most common symptom was fever, which included 22 cases (81.5%) of the patients. Chills was observed in 10 cases (37%), sweating in 12 cases (44.4%), headache in 5 cases (18.5%), nausea in 7 cases (25.9%), vomiting in 4 cases (14.8%), abdominal pain in 2 cases (7.4%), anorexia in (10%), weight loss in 9 cases (33.3%), myalgia in 12 cases (44.4%), arthralgia in 18 cases (66.7%), low back pain in 4 cases (14.8%), weakness and lethargy in 7 cases (25.9%), and limping in 8 cases (29.6%). Other findings were as arthritis in 4 cases (14.8%), splenomegaly in 2 cases (7.4%), hepatomegaly in 1 case (3.7%), and lymphadenopathy in 1 case (3.7%). There was no orchitis in any of the patients.

Anemia was observed in 48% of patients (hemoglobin < 11.5 g/dl). Moreover, 11% of patients had leukopenia (WBC < 4500 per μl) and 18.5% of patients had leukocytosis. Platelets (PTL) was within the normal range (150,000-400,000 per μl) in most patients (88.8%). The highest ESR values were within the range of 0-25 mm/hour, which was defined in the normal range. Subsequently, ESR was increased by 33.3% (25-50mm/hour). According to liver function tests, AST was in the abnormal range in 22.2% of the cases, ALT was abnormal in 14.4% of patients, and ALP increased in 40.7% of cases. The liver can be involved in brucellosis as the largest organ of the reticuloendothelial system, but most cases of hepatitis are subclinical and will not interfere with laboratory tests. In the case of liver biopsy, in these cases, hepatitis is reported in most patients.

Discussion

This study was carried out to determine the epidemiological, clinical and laboratory characteristics of brucellosis in children admitted in two teaching hospital related to Mazandaran University of Medical Sciences during the years 2010-2016. In terms of gender distribution, 66.7% were boys and 33.3% were girls, which could be due to more occupational or non-occupational exposure, which is higher in boys at that age, and has been the same in other studies; considering the fact that boys have more contact with animals compared to girls and also use more unsafe foods.[8,9]

The majority of patients in this study were in the age group of 12-18 years, and the average age was 12.5 years. This contrasts with the study of Fanni et al., with nearly half of the patients aged 2 to 5 years.[10] Moreover, in the study of Tanir et al. in Turkey,[12] and Giannakopoulos et al. in Greece,[8] only 18% of patients were under the age of 5 years; due to the fact that in the present study most of the children were living in rural areas and had inevitable contacts with the livestock, which increased the possibility of pediatric exposure at this age, while in Fanni et al. study, most children were infected through contaminated dairy products,[10] which is more likely to be used at lower ages and infancy period.

In this study, 40.7% and 59.3% of patients were urban and rural residents, respectively; which shows that dairy pasteurization in rural areas is still not well. In addition, 77.8% had a history of local dairy consumption, while 22.2% had no history of using non-pasteurized dairy products. However, it was found that other ways of transmitting disease from animals to humans included inhalation of aerosols and contamination through scratches and cuts in the surface of the skin. However, the high percentage of local dairy use in this study and other studies suggests that

consumption of contaminated dairy products is still the main route for transmission of disease. In the study by Aghaali et al., only 29% had local dairy consumption.[11] According to the results most patients (63%) of the present study did not have contact with the livestock. This indicates that although contact with the livestock is a risk factor, in its absence, other symptoms and findings, especially in endemic areas, should be noted. In the study by Aghaali et al., livestock exposure was found in only 17% of patients.[11]

Most cases of disease were observed in the spring and summer seasons, which could be due to traveling to the rural areas in these seasons, and also due to the consumption of local dairy products.[12] However, in adults, the incidence of this disease in spring and winter is higher, due to the coincidence with breastfeeding.[13-17] In this case, the result of this study is similar to that of others. In endemic areas, family history of brucellosis, the use of non-pasteurized dairy products or contact with pets may lead physicians to research and detect brucellosis in obese children.

In this study, none of the patients had a positive family history of brucellosis; but in the study of pediatric brucellosis in northeastern Iran in 2012, 91.6% had a history of brucellosis in the family.[13] The most common complaint was fever (48.1%), followed by joint pain (44.4%). Therefore, in each patient, joint treatment should be considered, especially in endemic brucellosis areas, except for one of the main differential diagnoses. In a study by Armin et al., all children diagnosed with brucellosis during 1996-2005 were studied in one of the largest children's hospitals in Tehran, Iran; similar to other studies, fever and arthralgia were the most common complaints. The most common clinical signs and symptoms were fever (81.5%), arthralgia (66.7%), sweating and myalgia (44.4%), weight loss and appetite decrease (37% and 33.3%), followed by lameness (29.6%), anxiety and

nausea (25.9%), headache (18.5%), back pain and vomiting both (14.8%), and abdominal pain (7.4%).[16] In other studies, more common symptoms such as sweating, headache, abdominal pain and weight loss were reported.[12,18-22]

Arthritis was most commonly found in the present study (14.8%). After that, splenomegaly with 7.4%, and hepatomegaly and lymphadenopathy with 3.7% were mostly observed. In the study of Fanni et al.[10] and Sawadkohi et al.[23] the most common findings were arthritis and splenomegaly. Brucella species involve the reticuloendothelial system, and organomyelagia is often found in the examination, but this wide range of reports may be due to the experience of examiners, the quality of the physical examination, and the duration of the disease.[9]

In the present study, skin rash and orchitis were not observed in any of the patients, while in the study of Fanni et al., maculopupular rash was found in patients.[10] In laboratory studies of the present research anemia was seen as the most common laboratory finding in 48% of patients, which includes one-third of the patients. In the study of Fanni et al. anemia, leukopenia, and thrombocytopenia were the most common laboratory findings.[10] In addition, 11% of patients had leukopenia (WBC < 4500 per μl) and 18.5% had leukocytosis (18.5%); in most patients (70%) WBC was within the normal range (4500-10000 μl) and the majority of patients (88.8%) had platelet count in the normal range (150,000-400,000). In the study of Fanni et al., only one case had leukocytosis, 33% had leukopenia and 12% had thrombocytopenia.[10]

The highest ESR values were in the abnormal range, 29.6% increase in average and 25.9% increase in severity. In terms of AST liver function tests, 22.2% of cases were in abnormal range, 14.8% of cases were abnormal in terms of ALT, and 40.7% had ALP increase. In another study by Yoldas et al., ALT has

been reported above 200 IU/l in 90 brucellosis cases, and in 1 case AST has been reported above 200 IU/l, with 40% AST above 40 IU/l and 34% ALT over 40 IU/l.[9]

Many of the patients who referred to the hospital's clinic and diagnosed with brucellosis were not admitted to hospital and were treated out patiently, and therefore excluded from this study. Moreover, the time was relatively limited. Other limitations were the incompleteness of files and their illegibility, especially in laboratory information and inquiries. Indications and clinical symptoms in this study included fever and chills, joint pain, limb pain, lameness, as well as arthritis and splenomegaly. Besides, Hb and ESR values were within the abnormal range (often increasing by definition), and leukocytosis was the most common site of sacrum involvement.

Conclusion

Due to the endemic nature of Mazandaran area in terms of brucellosis, familiarity with those signs and findings of the disease that are more prevalent will be useful in faster diagnosis and treatment. Moreover, in any illness with fever and nonspecific symptoms such as sweating, weight and appetite loss, weakness and lethargy as well as skeletal complaints, it is important to consider brucellosis as an important differential diagnosis.

Conflict of Interests

Authors have no conflict of interests.

Acknowledgments

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