

## Epidemiology, Clinical Manifestations, Laboratory Findings and Outcome of Brucellosis in Hospitalized Children in Northwest of Iran

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| ARTICLE INFO  | ABSTRACT   |
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| <p><i>Article type:</i><br/>Original article</p> <hr/> <p><i>Article History:</i><br/>Received: 19-Sep-2018<br/>Accepted: 04-Feb-2019</p> <hr/> <p><i>Key words:</i><br/>Brucellosis<br/>Children<br/>Infection</p>   | <p><b>Introduction:</b> Brucellosis is a zoonotic disease, which is associated with great economic and general health concerns. This is an endemic disease in Iran, and thus this study aimed to investigate its epidemiology and trend over a ten-year period in children hospitalized in northwest Iran</p> <p><b>Materials and Methods:</b> A retrospective study was conducted on children hospitalized with brucellosis diagnosis in the Children's Hospital. Information of the patients, such as type of living place, age, history of consuming unpasteurized dairy products, family history of brucellosis in the past year, type of contact patterns with livestock, clinical symptoms, Wright's test, 2-mercaptoethanol test, Coombs Wright test and treatment failure, was collected</p> <p><b>Results:</b> Over a ten-year period, 59 medical records were extracted, out of which 21 subjects (35.6%) were female and 38 (64.4%) male. The mean age of involvement was 80.5 months. In addition, 16.9% and 22% of patients had a history of contact with livestock, and 22% had a history of consuming unpasteurized dairy products. Moreover, 78.6% of patients had Wright's test titers of <math>\geq 1:160</math> and 91.8% had Coombs test titers of <math>\geq 1:160</math>. Blood culture results of 19 patients were available, out of which 21.1% were culture-positive</p> <p><b>Conclusion:</b> Epidemiological studies assessing important risk factors for the spread of brucellosis in different regions across the world are very effective in disease control. Moreover, the results revealed that the serological tests can be used to diagnose brucellosis. To the best of our knowledge, this is the first report about epidemiology of children brucellosis in northwest Iran</p> |
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### Introduction

Brucellosis is a zoonotic disease that can be transmitted through contact with secretions of infected animals (e.g. sheep, goat, and cat) to human. It may be caused by consumption of such

unpasteurized dairy products as milk and cheese (1, 2). Brucellosis is associated with great economic and general health concerns. It is indeed an occupational disease among those in contact

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with infected animals or tissues (specifically dairy farmers, veterinarians, and slaughterhouse workers) (3,4). Brucellosis, as a very important disease for every society, is endemic in many geographical regions including Iran (5-7), Northeast Africa, Southeast Asia, and Central Asia, and affects all age and sex groups (8, 9). It is more prevalent among young people. The disease is caused by a gram-negative bacilli called 'Brucella,' which is killed through pasteurization and boiling (10,11). *Brucella abortus*, *B. suis*, *B. melitensis*, and *B. canis* are able to cause brucellosis in humans (12,13). Among these bacteria, *B. melitensis* causes most cases of human brucellosis (12,14). *Brucella abortus* can result in acute brucellosis, whereas *B. suis* does not lead to human infection (15). The annual incidence rate of brucellosis in Mediterranean and Middle East regions is between 1 and 78 per 100,000 general population (16, 17). Brucellosis is endemic in Iran. Cultures of blood or bone marrow in Castañeda setting, as well as serology (Wright's test) are brucellosis diagnostic methods. The prevalence of brucellosis in men is higher than in women (18-19). Incubation period ranges from 1 to 4 weeks, and sometime to 1 month (20, 21). Brucellosis is a systemic infection with a broad clinical spectrum, ranging from asymptomatic disease to severe and/or fatal illness (22). Its main manifestation is acute febrile illness with or without signs of localization. Clinical manifestations of brucellosis depend on various factors such as the size of the infected area, source of infection, patient's age, duration of the disease, and type of brucellosis infection (23). Among other symptoms are night sweats, arthralgia, malaise, back pain, weight loss with muscle weakness, headache and fatigue (24). Hepatomegaly, splenomegaly, and lymphadenopathy can be diagnosed through clinical examinations. Epidemiological studies assessing important risk factors for the spread of brucellosis in different regions of the country are very effective in disease control and prevention.

Several studies have been recently conducted on the epidemiology of brucellosis in different areas of Iran. Given the lack of a similar study in northwest Iran on children living in highly endemic regions, this study aimed to investigate the epidemiology of brucellosis and its trend over a ten-year period. The main objective of the study was to assess the epidemiology and clinical manifestations of brucellosis in children.

## Methods

This retrospective descriptive analytic study was conducted on 1-month to 14-year-old children diagnosed with brucellosis who were hospitalized in Tabriz Children's Hospital, Tabriz University of Medical Sciences from 23 August 2007 to 22 August 2016. Patients' data were collected using questionnaires with items consisting of the month and year of report, county, type of living place, age, history of using unpasteurized dairy products, family history of brucellosis, type of contact with livestock, clinical symptoms, Wright's test, 2ME test, Coombs Wright test, onset date of symptoms, diagnosis date, and treatment failure. After data collection, the pre-processing stage was initiated and measures, such as the removal of additional fields, unifying data unit and format, and data combination and analysis using SPSS 21 were taken.

## Results

In total, 59 out of 63 children under the age of 14 years, who were hospitalized in Tabriz Children's Hospital from 2007 to 2016, had medical records. Among these patients, 21 subjects were female (35.6%) and 38 were male (64.4%). The involvement age was 80.5 months, on average, ranging from 15 months to 166 months. Among the patients, 66.1% and 33.9% were from rural and urban areas, respectively. Furthermore, the age-based incidence of the disease is presented in Figure 1. Accordingly,

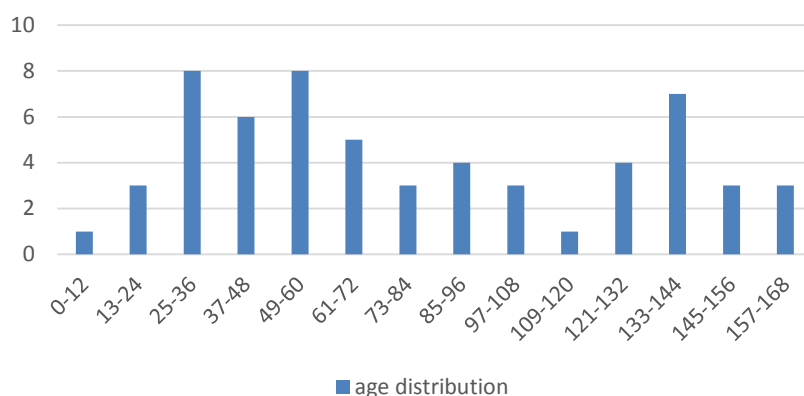


Figure 1. Age distribution of hospitalized children with brucellosis (months)

patients aged 25-36 months and 49-60 months had the highest frequency (11.59%), followed by 0-5 years (44.06%), 6-10 years (27.11%), and 11-14 years (23.72%). In addition, 16.9% and 22% of patients had history of contact with livestock, and 22% had history of consuming unpasteurized dairy products. According to the reports, 26.7%, 10.2%, 33.9%, 3.4%, 22%, and 16.9% of patients suffered from monoarticular arthritis, back pain, abdominal pain, skin rash, splenomegaly, and hepatomegaly, respectively (Table 1). In addition, 78.6% of patients had Wright's test titers of  $\geq 1:160$  and 91.8% had Coombs test titers of  $\geq 1:160$ . Blood culture data of 19 patients was available, out of which 4 patients (21.1%) were culture-positive. Findings from laboratory data showed that 16.9%, 37.3%, 27.1%, and 18.6% of patients came for clinical visit in spring, summer, fall and winter, respectively (Table 2). The highest rates of clinical visit were observed on 23 August to 22 September and 21 January to 18 February. The lowest rate was observed on 19 February to 20 March.

**Table 1.** Clinical manifestation of hospitalized children with brucellosis

| clinical manifestation  | No | percent |
|-------------------------|----|---------|
| Fever                   | 29 | 49.2%   |
| Arthralgia              | 41 | 69.5%   |
| Monoarticular arthritis | 37 | 62.7%   |
| Backache                | 6  | 10.2%   |
| Abdominal discomfort    | 20 | 33.9%   |
| Skin rash               | 2  | 3.4%    |
| Splenomegaly            | 13 | 22%     |
| hepatomegaly            | 10 | 16.9%   |

**Table 2.** Laboratory findings of hospitalized children with brucellosis

| Parameter  | Value  |
|------------|--|
| WBC        | 8281 $\pm$ 3349 /mm <sup>3</sup>                 |
| Neutrophil | 45.7 $\pm$ 14.6%                                 |
| Lymphocyte | 46.3 $\pm$ 14.5%                                 |
| Eosinophil | 1.29 $\pm$ 1.52%                                 |
| Hb         | 11.46 $\pm$ 1.46 mg/dl                           |
| PLT        | 310 $\pm$ 121 ( $\times 10^3$ /mm <sup>3</sup> ) |
| ESR        | 33 $\pm$ 21 mm/hr                                |
| ALKP       | 592 $\pm$ 911                                    |
| AST        | 51 $\pm$ 26                                      |
| ALT        | 30 $\pm$ 19                                      |

## Discussion

Although brucellosis is less prevalent in developed countries, it exists in Eastern Mediterranean countries (25). The results of this epidemiological study were obtained based on clinical symptoms and involvement age of hospitalized children under the age of 14 from 23 August 2007 to 22 August 2016. Among the patients, 66.1% and 33.9% were from rural and urban areas, respectively. However, a study conducted in central Iran showed that the majority of infections occurred in urban areas (26); however, another study conducted in

northeast Iran showed that 90.6% of patients were from rural areas (27). A similar study on children suggested rural regions as brucellosis-endemic areas.

Similar to the study conducted in central Iran, the highest frequency of involvement was observed among patients aged 0-5 years (44.06%); whereas, the highest frequency in Turkey (28) and Greece (29) was observed among children aged 11-15 years, probably due to having a direct contact with livestock in rural areas.

The most prevalent symptoms in children under investigation were arthralgia (69.5%), followed by mononuclear arthritis (62.5%), and fever (49.5%). The least common symptom was skin rash (3.4%). A similar study in Iran reported fever, muscle pain, and shivering as the most common symptoms (30).

In the present study, 64.4% and 35.6% of patients were male and female, respectively. A study conducted on adults in this region showed that 54.9% and 45.1% of patients were male and female, respectively (25). Some similar studies on children suggested that the prevalence of brucellosis were higher in males than in females (28, 31, and 32), which can be due to direct contact with animals and consumption of unhealthy foods.

According to obtained data, 16.9%, 37.3%, 27.1%, and 18.6% of patients came for clinical visit in spring, summer, fall and winter, respectively. The highest rates of clinical visit were observed on 23 August to 22 September and 21 January to 18 February

Serological diagnosis of brucellosis with tube agglutination test dates back to more than 100 years; however, it may be associated with false positive reactions due to cross-reactive induction by pathogenic microorganisms, such as *Vibrio cholerae*, *Francisella tularensis*, and *Yersinia* spp. It is one of the most common tests with very high sensitivity, but lower specificity. Usually, brucellosis titer 1:160 is taken as positive; however, brucellosis titer 1:180 is considered positive in endemic areas. This test was positive in 56-95% of patients with brucellosis. In our study, 78.6% of patients had Wright's test titers of  $\geq 1:160$  and 91.8% had Coombs test titers of  $\geq 1:160$ . Unfortunately, of one-third of patients undergoing blood culture, only 21.1% were culture-positive, which is one of the limitations of the study. In this study, one patient was diagnosed with neurobrucellosis, based on cerebrospinal fluid Wright's test (33). Since the chance of positive culture is low due to the history of using antibiotics and given that blood and CSF cultures are time-consuming, risky, and aggressive procedures, therefore the serological tests can be really helpful in brucellosis. According to the findings of the present study, titer of 1:180 can be

regarded as a diagnostic titer in suspected cases of brucellosis with clinical symptoms, specifically in endemic regions. To the best of our knowledge, this is the first report showing the epidemiology, clinical and laboratory findings of brucellosis among children in northwest of Iran.

## Conclusion

Since brucellosis was more prevalent among 2-5 year-old children in this study, it is necessary to take preventive measures and provide necessary trainings, specifically for parents, on avoiding the use of unpasteurized dairy products, livestock vaccination, and accurate evaluation of disease symptoms for early visit to healthcare centers. Furthermore, when the blood and/or CSF cultures are not available, serological tests can be used to diagnose brucellosis.

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## Conflicts of Interest

None.

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