

## ORIGINAL ARTICLE

**Brucellosis in a 12-Year-Old Boy in Saudi Arabia: A Case Report for Literature Review**FAHAD AL JARBOA<sup>1</sup>, SALEH ALMANEA<sup>2</sup>, BADER ALDEBASI<sup>1</sup><sup>1</sup>King Abdullah International Medical Research Center, Ministry of National Guard, King Saud bin-Abdulaziz University for Health Science, Ministry of National Guard – Health Affairs, Riyadh, Saudi Arabia.<sup>2</sup>Prince Mohammed bin Abdulaziz Hospital, Riyadh, Saudi Arabia.

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**ABSTRACT**

Brucellosis is a type of an infection caused by bacteria that affects humans and animals and usually affects the former by drinking unpasteurized milk. This study deals with a clinical case of human Brucellosis. Sudden onset of left hip pain with no history of past trauma, recent URTI, or any other abnormal symptom was examined, and left joint effusion was found. On further investigation, ESR was determined to be 41, and high levels of antibody against Brucella were revealed after the serum agglutination test. Methods to prevent the prevalence of this disease by implementing various measures and creating awareness have also been made.

**Keywords:** Brucellosis, trauma, zoonotic diseases**INTRODUCTION**

**Background:** Brucellosis is a bacterial infectious disease that affects animals and humans. It was first discovered in Malta 1850s (1). Usually, human infection occurs due to the consumption of unpasteurized milk from infected animals with Brucella Melitensis (2). The most common animals that have an infection of Brucella Melitensis or B. Melitensis are the goats and sheep (3). Nonspecific symptoms of Brucellosis appear within two weeks to three months. Symptoms vary from person to person. In some cases, Brucellosis becomes chronic, and its symptoms persist for years. In most cases, symptoms might include chills, fever, sweat, loss of appetite, weakness, fatigue, headache, joint, muscle, and back pain (4, 5).

Brucellosis can be found in Latin America, the Middle East, Asia, and the Balkans (6, 7). WHO listed Brucellosis as one of the seven neglected endemic zoonoses (8). About half a million new human cases are annually reported worldwide (9). In Saudi Arabia, human Brucellosis is one of the concerned zoonotic diseases since livestock importation is important to the country, especially during the Hajj season. According to a study done by Aloufi et al. 2016, data collected between 2004-2012 from a national registry showed the incidence rate was constant with a significant reduction of IR in 2012 compared to the year 2004 (10). Although children are not commonly infected with Brucellosis, the number of reports from endemic areas showed a high percentage of pediatric patients (20-30% of affected patients) (11).

**CASE DETAILS**

This case involved a 12-year-old healthy Saudi boy who made complaints of sudden onset of left hip pain for three days. The pain was progressive, increased with time and activity, and was relieved by rest. No exposure to radiation, other joint involvement, history of trauma, fever, recent URTI, weight loss, sweating or malaise, vomiting or diarrhea, abnormal bowel motion, urinary symptom, or any other similar problem was found. Parents were not sure of recent raw milk ingestion while he was traveling. The patient's general condition was stable other than his limping pain. His vital signs: (BP- 116/75mmHg, HR-96, RR-22, T-37.1°C) and his growth, good weight, and height for age. Hip exam: limping gait, no swelling, erythema, or sign of bruising. There is point tenderness midline of the inguinal area but not related to bony prominence. Other systemic exams were unremarkable. Hip ultrasound showed left joint effusion in the anterior recess, which caused the separation of a layer of capsule measuring about 0.5cm and not drainable. The surrounding soft tissue and muscle appeared normal, the benign-looking lymph node was noted in the left inguinal area measuring 0.5cm, both testes were normal, and the other hip was completely normal. The initial investigation was done, and CBC was normal, but ESR was 41. Renal and liver profiles, as well as urine analysis, were found to be normal. (6)

Thus, there was suspicion of Brucellosis before the serum agglutination test was performed. The test revealed the presence of a high antibody level against Brucella. was (1:12080) where Blood culture showed gram-negative Coccobacilli. After 14 days, the same test was repeated, and the result was the same; there was a high level of antibodies against Brucella. After the serum agglutination test, a diagnosis of Brucellosis was made. A combination of Rifampicine p. o. once a day and Doxycycline p.o. twice a day for six consecutive weeks before full recovery. (6)

**DISCUSSION**

The most frequently reported acquired infection is Brucellosis, particularly those caused by B. melitensis. About 20% - 30% of affected cases are pediatrics and commonly obtained infection from raw milk ingestion. The patient consumed unpasteurized raw milk, and transmission was believed to occur mainly via ingestion (11). In Saudi Arabia, Brucellosis is considered an endemic, and in 2011, MOH reported an incidence of 18/per 100,000 population/year. (3) The overall seroprevalence rate, 15%, was in Saudi Arabia. It was also found that 10% was in children aged 0-14 years. (12). The reasons behind the high prevalence of Brucella infection in Saudi Arabia are the techniques of animal raising for camels and sheep, the old beliefs that ingesting raw milk has greater benefits, and also many animals in Saudi Arabia were imported from territories with a high rate of Brucellosis like in Africa.

In addition, raising together different animal herds, mixing with each other just like the sheep and cattle, lack of public awareness and knowledge of the seriousness of Brucellosis as a human disease, and the resistance to slaughtering the infected animals are factors contributing to the high prevalence of Brucella infection.

In Saudi Arabia, animals have a high prevalence of Brucella, 8% in camels, 18% in cattle, 6.5% in sheep, and 9.7% in goats (13,14)

Brucella spp. (3) are small, rod-shaped (coccobacillus), gram-negative, non-motile, non-spore-forming bacterial organisms. (3) A zoonotic disease caused by the consumption of raw unpasteurized milk from infected animals or with the close contact of their secretions. Different reservoirs for different Brucella spp in animals are known to cause human disease. (2) (See Table 1)

Table 1: Virulence of different species of Brucella

Species	Animal Host	Virulence
Brucella melitensis	Goat, Sheep, Camels	++++
Brucella Abortus	Cows, other Bovidae animals, and Camels	+++
Brucella Canis	Dogs	+
Brucella Suis	Pigs	+

Table 2: Drugs used for Brucellosis and their dosages

Drug	Dosages
Rifampicin	20 mg/kg/day in two divided doses (max.600 mg)
Doxycycline	5 mg/kg/day in two divided doses (max.(0) 200 mg) (only for children more than 8 years of age)
TMO/SMX	10 mg of trimethoprim/kg/day (max. 480mg)
Gentamicin	(0) 5-7.5 mg/kg/day IM or IV either as a single dose or three divided doses
Streptomycin	15 mg/kg IM or IV once daily (max. (0) 1g/day) (only for children more than 8 years of age)
Ciprofloxacin	30 mg/kg/day in two divided doses (max. 1.5g)

Table 3: Treatment for Brucellosis (0)

Drugs	Dosages
Rifampicin	20 mg/kg/day in two divided doses. (max 600 mg)
Doxycycline	5 mg/kg/day in two divided doses (max. 200 mg) (only for children more than 8 years old of age)
TMP/SMX	10 mg of trimethoprim / kg/day (max. 480 mg)
Gentamicin	(0) 5-7.5mg/kg/day IM or IV either as a single or three divided doses
Streptomycin	15 mg/kg IM or IV once daily (max. 1 g/day) (only for children more than 8 years of age)
Ciprofloxacin	30 mg/kg/day in two divided doses (max. 1.5 g)

Table 4: Regimes for different manifestations of Brucellosis) (2)

Diseases	Therapy 8 years old children	Therapy 8 years old children	Comment and Duration of Therapy
Common Diseases: Acute Brucellosis, Brucella Arthritis, Brucella Osteomyelitis Brucella Bacteremia	Rifampicin and septria Or rifampicin for 45 days and gentamicin for 7 days	Doxycycline and Rifampicin OR Doxycycline for 45 days and streptomycin for 14 days OR doxycycline for 45 days and gentamicin for 7 days	Hospitalized patients add gentamicin for 5-7 days, duration of Therapy 6 weeks
Serious Illness Brucella Endocarditis	Rifampicin, Septra and Ciprofloxacin	Doxycycline, Septra and Rifampicin	Gentamicin for the initial two weeks Surgical intervention is indicated. Duration of Therapy is 3-9 months
Neurobrucellosis	Rifampicin, Septra and Ciprofloxacin	Doxycycline, Septra and Rifampicin	Gentamicin for the initial two weeks. Ceftriaxone has shown some efficacy and it is usually used in the initial Therapy for 2-4 weeks. Duration of therapy is 3-6 months up to one year in complicated cases.

Brucella melitensis is the most prevalent species in Saudi Arabia and neighboring countries, causing 70%-90% of Brucella infection cases.

Brucella abortus is the next common disease-causing pathogen, and the other species rarely cause the disease. Consumption of unpasteurized raw milk and other dairy products, especially soft cheese, butter, and cream, leads to the transmission of the organism to humans. But hard cheese, sour milk, and yogurt are unlikely to transmit Brucellosis due to propionic and lactic fermentation. Other transmission causes are direct contact with infected animal secretions and their products, such as placenta or aborted materials. In addition, transmission to humans can also be by air, aerosolized materials through open wounds or mucus membranes, whether in animal areas or laboratory when dealing with blood and other infected cultures. Direct contact with Brucella-contaminated soil, animal feces, and dust is also associated with a higher risk of acquiring infection. (15)

In our case, the patient showed only pain in the hip joint. However, most children infected with Brucellosis presented acute and sub-acute symptomatology in 2-4 weeks. (16, 17) Symptoms of Brucella infection are very inconsistent due to the variable pathogenicity of different strains. B. abortus causes milder disease with mild symptoms or focal lesions. On the other hand, B. melitensis is associated with a high rate of Bacteremia, short incubation periods, and noticeable symptoms (11, 15). 76% of infected patients have the onset of their symptoms within two weeks. Fever and joint pain are the most common signs presented. Monoarthritis was more common than polyarthritis, creating confusion with pyogenic arthritis in children; therefore, awareness about this entity should prompt the investigation of the disease, and doctors should have a high index of suspicion for Brucella arthritis.

The hip and knee joints are the most affected areas by this disease. On the other hand, in adults, the sacroiliac joint and the axial skeleton are rarely affected (17). Brucella osteomyelitis is rare in children. (3) As per studies, only 1-2% of children infected with Brucella have osteomyelitis (11, 18).

(0) Neurobrucellosis seldom affects children and is reported in only 0.5-1% of children with Brucella infection. (2) Presentation of neurobrucellosis is variable having; meningitis and meningoencephalitis are the most common. It also includes polyradiculopathy, myelitis, and psychiatric disorders, with

depression being the most common. CNS manifestations are rare and include brain abscess, hydrocephalus, pseudotumor cerebri, Guillain Barre Syndrome, cranial nerve palsy, cerebral venous sinus thrombosis, subdural and epidural collection, and stroke (19). (3) Clinical manifestations of Neurobrucellosis include fever and malaise, frank meningitis, cranial nerve neuropathy, hearing loss, visual disturbance, chronic vomiting, altered sensorium, coma, and various neurological focal motor deficits. (6) The recovery of this disease once infected is typical, and sequelae are uncommon.

Acute symptoms of human brucella infection include undulating fever, myalgia, and other clinical manifestations such as splenomegaly, hepatomegaly, and spondylitis (18). The most devastating complication from systemic Brucellosis, although it rarely happens, is Infective Endocarditis which which require surgical intervention. Spleen, liver, and pulmonary abscesses can also develop. Enlargement of lymph nodes is found in 10-20% of cases, and enlargement of the spleen and liver in 20-30% of cases. Rare conditions include deep vein thrombosis, leukocytoclastic vasculitis, nephritis, and meningitis. Eye manifestations of Brucellosis include optic neuritis, uveitis, and papilledema (20). The most common hematologic findings are Leukopenia, thrombocytopenia, and anemia (21). RBPT is a rapid, less costly, and effective serological test compared to serum agglutination, complement fixation, comb, indirect immunofluorescent antibody, and enzyme-linkedenzyme-linked immunosorbent assay (ELISA). RBPT can be performed with minimum equipment, and the naked eye can read the results. Although the sensitivity and specificity are unclear, the results are still reliable. In our study, we performed serum agglutination test as the first serology test for diagnosis. This test was recognized as the most commonly used test that is able to detect antibodies against B. Abortus, B. Suis, and B. Melitensis but not B. Canis (18). Rifampicin 450 mg/day (p.o.) and Doxycycline 100 mg, twice a day (p.o.) are standard treatments for human Brucellosis to be taken in six weeks. (7) But the standard treatment may be changed depending on the age or pregnancy status of the patient (22). (6) No statistical difference was noticed in the type of combination therapy in the early clinical response of human Brucella Infection. The recommended treatments are as follows: A combination therapy of trimethoprim-sulfamethoxazole and aminoglycoside (23, 24) or a combination of rifampicin and trimethoprim-sulfamethoxazole for 45 days are recommended for children

younger than eight years old (25). For 8 years old and above, a combination of doxycycline and rifampicin or rifampicin and gentamicin could be used. Another regime of treatment is a combination of ciprofloxacin and rifampicin for 30 days, had shown to be effective and has the advantage of a short duration of treatment (26).

Brucella infection management relies on using antibiotic that has the ability to act intracellularly and in acidic media, using a combined therapy and antimicrobials for a long duration according to the extent of the system involved. The limited number of antibiotics that can be prescribed to treat Brucella infection includes rifampicin, doxycycline, trimethoprim-sulfamethoxazole, streptomycin, gentamicin, and ciprofloxacin (see table 2). Successful results of treatment for children are a combination of Rifampicin and TMP/SMX for children below eight years old or Doxycycline and TMP/SMX or rifampicin for children above eight years old. The combination of these drugs showed the highest success rate and must be prescribed in children older than eight years old to avoid the staining of the teeth in younger children. For serious infections such as neurobrucellosis and Endocarditis, a large number of drugs for about 3 to 5 are needed for a long duration and usually take three to twelve months (see table 3).

## CONCLUSION

In the Kingdom of Saudi Arabia, Brucella infection still affects the health of the people and causes economic losses as well. Decreasing Brucella infection to zero is the main point of our recommendations. However, Brucella Infection is difficult to control in Saudi Arabia due to a high number of animals imported every year from other countries, especially during the Hajj season. Then, in addition, there are a large number of uncontrolled animal movements across the countries' borders. Decreasing the prevalence of Brucella infection among humans and infection sources is the main goal. Some preventive measures are (1) Implementing a government surveillance program for Brucella Infection: (i) Creating a clear case definition to catch all cases. This case definition should be more sensitive to make sure that health providers capture all suspected cases of Brucellosis; (ii) Organize the flow of reported data from health centers, laboratories, and the IDD at MOH so that it is smooth and fast; (iii) Provides all health centers with the qualified laboratory personnel and equipment to capture all Brucellosis samples; and (iv) Take samples frequently from susceptible livestock especially those in potentially epidemic areas; (2) Enforcing animal importation protocols; (3) Enforcing compulsory vaccinations of all susceptible animals in veterinary clinics and agricultural offices; (4) Increasing public education and awareness, especially the high-risk group like shepherds, those working at slaughterhouses and those working in laboratories. Rural Health Centers should give importance to activities or programs that will increase health awareness among people. Brucellosis causes were found mostly among uneducated people or those who had not completed secondary school (27); (5) Increasing the biosafety level in laboratories to level 3, as laboratory workers are at high risk. Brucella Infection is one of the diseases to be considered a laboratory-acquired infection. Even for the centers not located in potentially epidemic areas, they should increase their precautionary measures or biosafety level since not all laboratory personnel possesses the knowledge and familiarity in dealing with brucella samples and the disease's clinical manifestations (28). Motivating researchers to conduct more studies about Brucella infection in Saudi Arabia since most published articles do not cover the main distribution and determinant factors of Brucella infection transmission in the kingdom in recent years. Then, most of the published papers rely on the serology of the disease in humans and animals, which could lead to the disease's underestimation. Connecting human health with that of animals and the environment with the goal of building a healthy and safe environment for all is the One Health approach concept. Creating collaborations between veterinarians, medical personnel, and other environmental disciplines is also one of the

goals of the "One Health Approach" and also the prevention of potential disease outbreaks. Giving vaccinations to susceptible animals against Brucella infection has decreased cases of Brucella infections among humans, decreased animal losses, and improved the economy, but we still have to be vigilant; Brucellosis still deserves attention and resources to be totally eradicated.

**Acknowledgements:** We thank the participant and his parents for being a part of this case report. We appreciate their cooperation.(22)

**Conflicts of Interest:** The authors declare that they have no competing interests.

**Funding:** Not funded

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