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ORIGINAL ARTICLE

Evaluation of the Demographical, Clinical, Laboratory Findings and Treatments of Pediatric Patients with Brucellosis Diagnosis in the Pediatrics Department of the Faculty of Medicine at Sivas Cumhuriyet University Between 2009 and 2019

2009-2019 Yılları Arasında Sivas Cumhuriyet Üniversitesi Tıp Fakültesi Çocuk Kliniği'nde Bruselloz Saptanan Çocuk Hastaların Demografik, Klinik, Laboratuvar Bulguları ve Tedavilerinin Değerlendirilmesi

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ABSTRACT

Purpose: The purpose of the present study is to evaluate the demographical and clinical characteristics, laboratory findings, all symptoms, treatments received, durations of hospital stay and prognosis after treatment of the pediatric patients with brucellosis diagnosis followed-up in the Pediatrics Department of the Research and Application Hospital of Sivas Cumhuriyet University.
Materials and Methods: In this study, 51 patients within the age group 0 and 18, who were diagnosed with brucellosis and admitted to the Pediatrics Department of Research and Application Hospital of Sivas Cumhuriyet University between January 1st, 2009 and December 31st, 2019, were included. The files of the patients were analyzed retrospectively. The diagnosis was made in all patients with the presence of history, clinical symptoms and findings by the positivity (≥1/160) of the Standard Tube Agglutination Test (STA) and/or by the growth of Brucella species in the blood culture. The time the patients who were included in the study admitted to the hospital, their ages, gender, place of residence, intake of raw milk and dairy products, contact history with farm animals, time elapsed until diagnosis, Brucella history in the other members of the family, the properties of their houses, the number of people living in the house, social insurance, physical examination findings, laboratory findings, all symptoms of the patient, treatments received, duration of hospital stay, complications and prognosis after treatment were examined and recorded.
Findings: 41 of the patients (80.4%) were males and 10 of them (19.6%) were females. The ages of the patients were between 2 and 17, and the average age was 10.9±4.10. The time it took between the patients' onset of complaints and the diagnosis of brucellosis varied between 1 and 30 days, and the average number of days was 10. The most frequent complaint was fever which was seen in 39 (76.5 %) patients. The second most frequent complaint was joint pain observed in 34 (66.7 %) patients. 15 (29.4 %) of the patients presented with fever and 12 (23.5 %) patients had joint swelling. Statistically significant difference was observed between the Erythrocyte Sedimentation Rates (ESH), C-Reactive Protein (CRP) values before and after the treatment (p=0.001, p=0.002). Before the treatment, Platelets (PLT), Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) were significantly high (p=0.010, p=0.000, p=0.000).
Conclusion: Because Turkey is an endemic zone for Brucellosis, Brucellosis must be considered for every child with complaints of long-lasting fever, perspiration and joint pain. Both clinical and serological evaluations of the family members of the patient with brucellosis diagnosis might be needed. This would enable the early diagnosis and treatments of probable cases. Diagnosis and treatment of the disease in the early stage, awareness-raising in public against consuming raw milk and/or dairy products in places where animal breeding is prevalent, especially in the rural areas, training of the public and the health personnel on the causes of Brucellosis transmission and the methods of protection from Brucellosis would be the precautions to be protected from this infection and would lead to a reduction in the development of complications.

Key words: Brucellosis, fever, joint pain, child, STA

ÖZ

Amaç: Bu araştırmada Sivas Cumhuriyet Üniversitesi Araştırma ve Uygulama Hastahanesi Çocuk Sağlığı ve Hastalıkları Kliniğinde izlenen Brusellozis tanısı almış çocuk hastaların demografik ve klinik özellikleri, laboratuvar bulguları, hastanın tüm belirtileri, aldığı tedaviler, yatış süresi, komplikasyonları, tedavi sonrası prognozunun değerlendirilmesi amaçlanmıştır.
Gereç ve Yöntemler: Bu çalışmaya Sivas Cumhuriyet Üniversitesi Araştırma ve Uygulama Hastahanesi Çocuk Sağlığı ve Hastalıkları Kliniği'ne 01.01.2009-31.12.2019 tarihleri arasında başvuran 0-18 yaş grubu, Brusellozis tanısı alan 51 hasta alındı. Hastaların dosyaları geriye dönük olarak incelendi. Tüm olgularda tanı; öykü, klinik belirti ve bulguların varlığında Standart Tüp Aglütinasyon Testi (STA)'nin pozitif (≥1/160) olması ve/veya kan kültüründe Brusella türlerinin saptanmasına göre konulmuştur. Araştırmaya alınan hastaların hastahaneye başvuru tarihleri, yaşları, cinsiyetleri, yaşadıkları yer, çiğ süt ve süt ürünü kullanımı, çiftlik hayvanları ile temas öyküsü, tanıya kadar geçen süre, ailede diğer bireylerde Brusella öyküsü, yaşanılan konutun özellikleri, evde yaşayan kişi sayısı, sosyal güvence, fizik muayene bulguları, laboratuvar bulguları, hastanın tüm belirtileri, aldığı tedaviler, yatış süresi, komplikasyonları, tedavi sonrası prognozu incelenip kaydedildi.
Bulgular: Hastaların 41 'i (%80,4) erkek, 10' u (%19,6) kızdı. Hastaların yaşları 2-17 yaş arasındaydı ve yaş ortalaması 10,9±4,10'du. Hastaların yakınmalarının başlaması ile Bruselloz tanısı almaları arasındaki süre 1 gün ile 30 gün arasında değişiyordu ve ortalama 10 gündü. En sık şikayet 39 (%76,5) hastada görülen ateş idi. İkinci sık olarak görülen şikayet 34 (%66,7) hastada olan eklem ağrısıydı. 15 (%29,4) hastanın başvuru anındaki fizik muayenesinde ateşi mevcuttu. 12 (%23,5) hastanın eklem şişliği vardı. Tedavi öncesi ve tedavi sonrası Eritrosit Sedimentasyon Hızı (ESH), C-Reaktif Protein (CRP) değerleri istatistiksel olarak anlamlı fark saptandı (p=0,001, p=0,002). Tedavi öncesi Trombosit (PLT),Aspartat Aminotransferaz (AST) ve Alanin Aminotransferaz (ALT) değerleri anlamlı derecede yüksek idi (p=0,010, p=0,000, p=0,000).
Sonuç: Türkiye'nin Bruselloz açısından endemik bölge olmasından dolayı uzun süren ateş, terleme, eklem ağrısı şikayetleri olan her çocukta Bruselloz da düşünülmelidir. Bruselloz tanısı alan hastanın aile üyelerinin hem klinik hem serolojik olarak değerlendirilmesi gerekebilir. Bu durum olası olguların da erken tanı ve tedavilerinin yapılmasına olanak sağlayacaktır. Hastalığın erken dönemde tanınması ve tedavi edilmesi, hayvancılığın yaygın olduğu yerlerde, özellikle kırsal kesimde; halkın çiğ süt ve/veya süt ürünlerinin kullanılmaması konusunda bilinçlendirilmesi, Bruselloz'un bulaşma yolları ve korunma yöntemleri açısından halkın ve sağlık personelinin eğitimi, Bruselloz'dan korunmada önlem olacak ve komplikasyon gelişiminde azalma sağlayacaktır.

Anahtar Kelimeler: Bruselloz, ateş, eklem ağrısı, çocuk, STA

Introduction

Brucellosis is one of the zoonotic diseases that can be transmitted to humans through direct contact with an animal infected with Brucella bacteria or through infected milk and dairy products. It can be seen frequently in many societies and is known for its complications all over the world (1-3). Brucellosis, an animal disease endemic in Turkey, is transmitted to humans through the contact with meat and milk of animals such as sheep, goats, buffalo, cattle, and pigs, dairy products prepared from uncooked contaminated milk, body fluids such as urine and open wounds in humans with infection. It is a systemic disease that could become chronic and affect many organ systems such as the musculoskeletal, gastrointestinal, cardiovascular, genitourinary, and central nervous systems (4-7). Veterinarians, shepherds, farmers, laboratory workers, slaughterhouse workers are risky occupational groups regarding brucellosis (8-13).

Brucella melitensis (B.melitensis) is a common cause of acute brucellosis in humans (14). B. abortus infects cattle; it can also be transmitted with animals such as water buffalo, horses, deer, camel, and sheep (15). B. suis infects pigs, while B. canis infects dogs (16,17).

Although the disease's incubation period varies from one week to one month, it is usually 2-3 weeks. Although the onset of symptoms can be sudden, they can also occur insidiously. According to the duration of symptoms, the disease is divided into acute, subacute, and chronic stages. The acute, subacute, and chronic stages are symptoms lasting < 8 weeks, 8 - 52 weeks, and > 52 weeks, respectively (9,18-20). The most common complaints of patients with brucellosis who apply to hospitals are fever, chills, headache, low back pain, loss of appetite, weakness, sweating, and joint pain. Patients may be misdiagnosed because the most common symptoms are general signs of infection. Patients may present to the physician with acute, subacute, or tuberculosis-like chronic symptoms. Fever occurs in patients with symptoms such as fatigue, myalgia, and arthralgia (19, 21-23). Anamnesis, physical examination, laboratory findings, and radiological findings are essential for the diagnosis of brucellosis. In laboratory findings, the leukocyte count is usually normal or decreased. Hematological disorders such as lymphomonocytosis, thrombocytopenia, hemolytic anemia, diffuse intravascular coagulation, and pancytopenia may be observed in some cases (24-27). Isolation of bacteria in culture is the gold standard within 5-7 days. The definitive diagnosis is established with the growth of the agent in blood and bone marrow cultures (28). When the disease cannot be identified by blood culture, the diagnosis is put made serological methods (29). The most widely used and easy serological test is the serum tube agglutination test (STA). In the STA test, agglutination at ≥1/160 dilutions or a 4-fold increase in titer within three weeks is considered significant (11,26,30,31).

In this study, we aimed to evaluate the demographic and clinical characteristics, symptoms, laboratory findings, treatments, length of hospital stay, complications, and post-treatment prognosis of pediatric patients diagnosed with brucellosis and followed up at Sivas Cumhuriyet University Research and Practice Hospital, Pediatrics Clinic.

Materials and Methods

51 patients aged 0-18 years, diagnosed with brucellosis at Sivas Cumhuriyet University Research and Practice Hospital, Pediatric Clinics between 01.01.2009-31.12.2019 were included in this study. Patients' files were reviewed retrospectively. The diagnosis was based on history, physical examination, positive STA (≥1/160), and/or detection of brucella in blood culture.

Date of hospital admission, age, and gender of patient, place, and characteristics of residence (city center, rural area, etc.), use of raw milk and dairy products, history of contact with farm animals, duration of symptoms until diagnosis, brucellosis family history, the number of people living in the house, physical examination findings, laboratory findings, the treatments, the length of hospitalization, complications, and the prognosis after the treatment were examined and recorded. Exclusion criteria were malignancies, collagen tissue diseases, other viral diseases including Crimean-Congo hemorrhagic fever; periodic fever syndromes, other chronic infections such as tuberculosis, and syndromes such as fibromyalgia.

Approval for the study was obtained from the Ethics Committee of Sivas Cumhuriyet University Faculty of Medicine (Decision No: 2020-01/20 and Date: 15.01.2020).

In the complete blood count, leukocyte, lymphocyte, neutrophil, thrombocyte, and hemoglobin values were evaluated according to the normal values for age. Normal platelet count is 150-450x109/liters. Platelet count <150x109/L and >450x109/L were evaluated for thrombocytopenia and thrombocytosis, respectively. Diagnosis of anemia was made in line with the guidelines of The National Health and Nutrition Examination Survey (NHANES-III). Leukopenia and neutropenia were defined as a total leukocyte count <4.000/μL and <1500/μL, respectively.

The normal values for C-Reactive Protein (CRP) measured in the Biochemistry Laboratory of Cumhuriyet University Faculty of Medicine Research and Application Hospital are 0-8 mg/L, for Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT) 0-40/UL and Erythrocyte Sedimentation Rate (ESR) between 0-20 mm/hour.

SPSS Windows Version 22 package program was used for statistical analysis in the research. Our study data were loaded on the SPSS 22.0 program, and as the data did not follow the normal distribution in evaluating

the data, the Wilcoxon test was used to compare the two measurement values obtained at different times in the same individuals, the Chi-Square Test and Fisher Exact Test were used in evaluating the data obtained by counting in 2x2 and multi-eyed designs. Our data were expressed as arithmetic mean, median, standard deviation, number of individuals, and % (percentage) in the tables, and the error level was taken as 0.05.

Results

Of the patients, 41 (80.4%) were male, and 10 (19.6%) were female. The ages of the patients were between 2-17 years, and the mean age was 10.9 ± 4.10 years.

Forty-two patients (82.4%) lived in rural areas, 9 (17.6%) in the city. Forty-five patients (88.2%) lived in cottage type detached houses and 6 (11.8%) in flats. Of the 9 patients living in the city, 3 lived in the suburbs and cottages, while 6 in the city centers and apartment-type houses. When we evaluate the number of individuals living in the family, 2-4 people were living in the houses of 16 (31.4%) patients, 5-7 people living in the houses of 25 patients (49%), and 8 or more people living in the houses of 10 patients (19.6%). 27 (52.9%) patients had a history of active brucella infection in their families or close environment. There was a history of consumption of raw milk and/or dairy products in 43 (84.3%) patients. In 43 (84.3%) patients, there was a history of contact with farm animals such as sheep, goats, and cattle. The time between the onset of the patient's symptoms and the diagnosis of brucellosis ranged from 1 day to 30 days, with an average of 10 days. Since, all of our patients (100%) were in the acute stage, we did not have any patients admitted in subacute or chronic phase. While 12 (23.5%) of the patients were treated as outpatients, 39 (76.5%) were hospitalized and treated. The hospitalization period of the inpatients was between 3 days and 21 days, and the median length of stay was 7 days.

The most common complaint was fever in 39 (76.5%) patients. The second most common complaint was joint pain in 34 (66.7%) patients. The joint swelling and redness were observed in 12 patients (23.5%) and 1 patient(2%), respectively. The knee joint was involved in 17 (33.3%), the hip joint in 14 (27.5%), the ankle in 3 (5.9%), and the elbow in 1 (2%) patients (Table 1). Other complaints are summarized in Table 1.

Table 1: Application complaints of children with a diagnosis of Brucellosis

Complaint	n (%)
Fever	39 (76.5)
Joint pain	34 (66.7)
Night sweat	24 (47.1)
Malaise	17 (33.3)
Loss of appetite	17 (33.3)
Joint swelling	12 (23.5)
Cough	10 (19.6)
Weight loss	9 (17.6)
Abdominal pain	5 (9.8)
Low back pain	5 (9.8)
Headache	4 (7.8)
Joint redness	1 (2.0)

In the physical examination of the patients, fever was present in 15 patients (29.4%) at the time of admission. Twelve patients (23.5%) had joint swelling, 9 (17.6%) had limitations of joint motion, 8 (15.7%) had increased joint temperature. While cervical lymphadenopathy was present in 3 (5.9%), and hepatosplenomegaly in 4 (7.8%) patients.

At the time of diagnosis, 3 patients (6.0%) had leukopenia, 5 (10.0%) thrombocytopenia, 3 (6.0%) neutropenia, 2 (4.0%) lymphopenia, 2 (4.0%) thrombocytosis, 2 (4.0%) lymphocytosis and 1 (2.0%) leukocytosis. The number of patients with normal leukocytes was 46 (92.0%) and with normal platelets was 43 (86.0%). Anemia was detected in 15 (30.0%), and pancytopenia in 1 (2.0%) patients. While leukocytosis, leukopenia, thrombocytopenia and pancytopenia were not observed in patients after treatment, thrombocytosis in 3 (6.8%), anemia in 4 (9.1%), lymphopenia in 1 (2.3%), neutropenia in 1 (2.3%), and lymphocytosis in 2 (4.5%) patients.

STA values were measured in all 51 patients at the time of admission (before treatment). Considering the STA values before treatment; 12 (23.5%) patients had 1/160, 17 (33.3%) 1/320, 12 (23.5%) 1/640, 6 (11.8%) 1/1280, 3 (5%) 1/2560, and 1 (2.0%) had 1/10240.

The mean ESR and CRP values of the patients before and after treatment were compared. The mean ESR values measured in 49 patients before and after treatment were 21.67±19.31 mm/h and 6.90±8.36 m/h (p=0.001), respectively. CRP values measured in 47 patients before and after treatment were 25.90 ± 26.42 mg/L and 3.26 ± 2.69 mg/L (p=0.002), respectively.

A statistically significant difference was found between the rates of ESR and CRP values before and after treatment (Table 2).

Pre-treatment ESR values were normal in 28 (57.1%) patients (<20 mm/h), and >20 mm/h in 21 (42.9%) patients. The CRP value was normal in 13 (27.7%) patients, and high (>8 mg/L) in 34 (72.3%) patients. Post-treatment ESR value was normal in 28 (93.3%) patients and >20 mm/h in 2 (6.7%) patients. Post-treatment CRP value normal in 29 (87.9%) patients, and > 8 mg/L in 4 (12.1%) patients.

Thirty-five (68.6%) patients received Doxycycline and Rifampicin, 3 (5.9%) Gentamicin and Rifampicin, 4 (7.8%) Doxycycline, Gentamicin and Rifampicin, 1 (2.0%) Gentamicin and Doxycycline, 7 (13.7%) Cotrimaxazole and Rifampicin, and 1 (2.0%) Cotrimaxazole, Rifampicin and Gentamicin. Three patients under the age of 8 treated with Gentamicin and Rifampicin received dual therapy because they were allergic to Cotrimaxazol.

While thrombocytosis was observed in 2 (4.0%) patients before treatment, thrombocytopenia in 5 (10.0%) patients. After treatment, was found thrombocytopenia was not observed in any patient, and thrombocytosis in 3 (6.8%). Before treatment, ALT was seen within normal reference values (<40 U/L) in 33 (66.0%) and >40 U/L in 17 (34.0%) patients. AST was within normal reference values (less than 40 U/L) in 29 (58.0%), and >40 U/L in 23 (46.0%) patients. In 15 (30.0%) patients, both AST and ALT were >40 U/L, which is the reference value. While ALT was within normal within reference values (less than 40 U/L) in 39 (95.1%) patients after treatment, it was high in 2 (4.9%) patients. While AST was within normal reference values (<40 U/L) in 40 (97.6%) it was high in 1 (2.4%) patients. In 1 (2.4%) patient, both AST and ALT values were > 40 U/L.

The mean AST, ALT and PLT values of the patients before and after treatment were compared. The mean PLT value measured in 50 patients before treatment was 251.20 ± 102.30 x109/L, it was 282.18 ± 83.73 x109/L (p=0.010). The mean AST value measured in 50 patients before in 44 patients after treatment was 60.14 ± 81.46 U/L, and it was 26.04 ± 7.22 U/L (p=0.000). The mean ALT value measured in 50 patients before treatment was 46.46 ± 49.70 U/L, and in it was 18.75 ± 11.72 U/L (p=0.000).

Pre-treatment PLT, in 41 patients after treatment AST and ALT values were significantly higher.

Table 2: Comparison of ESR and CRP values before and after treatment in children with brucellosis

	Pre-treatment	Post-treatment	P
ESR (mm/h)			
Mean±Standart Deviation	21.67 ± 19.31	6.90 ± 8.36	
	18	2.29	**0.001**
Median	1-102	1-39	
Range (Min-Max)			
CRP (mg/dl)			
Mean±Standart Deviation	25.90 ± 26.42	3.26 ± 2.69	
	18.90	5	**0.002**
Median	1-118	1-12,8	
Range (Min-Max)			

Discussion

The main source of transmission of brucellosis in the world and our country is still raw milk and/or raw milk products. In studies by Issa et al. and Logan et al. raw milk and/or dairy products were consumed by 58.2% and 76.0% of patients, respectively (32, 33). In brucellosis studies performed in Anatolia, it was reported that although the people knew about the disease and its transmission routes, they continued to consume dairy products they prepared without boiling them enough or at all, and this practice could not be prevented (34,35). In a study by Kaya et al. that evaluated 75 cases of brucellosis, brucellosis was transmitted to 68.0% of patients from they determined that uncooked milk and dairy products (35). In a study by Helvacı et al. this rate was 82.5% (36). In our study, using raw milk and/or raw milk products was established in 84.3% of the cases, and this finding was consistent with the rates in the studies.

Brucellosis is more common in people dealing with livestock because it is a disease transmitted from animals to humans, and the incidence of brucellosis is higher in males than females, especially in the Middle East and Mediterranean countries, since males deal with livestock more than females (33,36). In a study by Tanır et al. on brucellosis, 70.0% of male patients were diagnosed with brucellosis (37). In a study conducted in Iran in 2014, 71.7% of the patients were male (38), and it was 80.4% in our study.

Brucellosis is more common in rural areas where animal husbandry is intense, and there is usually direct or indirect animal contact in these cases (33). In the study of Abuhandan et al., Brucellosis is more common in rural areas where animal husbandry is intense, and there is usually direct or indirect animal contact in these cases (33). In the study of Abuhandan et al. and Kara et al., 76.8% and 75.5% of the patients were reported to live in rural areas (39,40), respectively. In the study of Sasan et al. and Çiftdoğan et al., the rates of contact with farm animals were 76.0% and 26.3%, respectively (41.42). In our study, the rate of living in rural areas and the rate of contact with farm animals were 82.4%, and 84.3%, respectively, and these rates are compatible with the literature.

Brucellosis could occur at any age (9). In studies involving only the pediatric age group, the age range was 6 months-16 years (40). In our study, the age range was between 2-17 years, and these values are consistent with the age range in studies conducted on children.

Brucellosis can be seen more frequently in people who share the same socioeconomic conditions, have a history of eating and drinking the same milk and dairy products, and have a contact history with the same sick animals (43). Brucellosis is detected in different individuals from the same family in regions where the disease is endemic (33). In a study by Ataman et al., a history of active brucellosis in the family or the immediate environment was present in 45.5% of the cases (44). In the Edremit district of Van, 5 of 12

members of a family dealing with animal husbandry were diagnosed with brucellosis (45). In our study, a history of active brucellosis in a family or immediate environment was present in 52.9% of the cases, and this finding is consistent with the literature. That's why the immediate environment of pediatric patients diagnosed with brucellosis should be evaluated both clinically and with laboratory studies regarding brucella. This is important in the control of the disease. This way, asymptomatic cases could be detected early and complications prevented.

Brucellosis usually can be progresses with various non-specific signs and symptoms such as fever, chills, night sweats, weakness, and arthralgia, easily confused with many diseases (9-10). When the studies of Çelebi et al., Shaalan et al., and Shalev et al. examined, the most common symptoms are fever, are sweating, and fatigue (46-48). In our study, fever was the most common symptom with a rate of 76.5%, sweating 47.1%, and fatigue 33.3%.

Osteoarticular involvement is the most common physical examination finding in brucellosis. In our country, osteoarticular involvement in pediatric cases is between 28-83% (49-51). In our study, 12 (23.5%) patients had joint swelling. While the limitation of joint motion was present in 9 (17.6%) patients, increased temperature in the joint in 8 (15.7%). So, joint complaints were present in 29 occurred (56.8%) patients.

Although the leukocyte count is normal in brucellosis, either leukopenia or leukocytosis could also be seen (8,9). Hematological abnormalities such as anemia, thrombocytopenia, and pancytopenia may be seen in brucellosis, but their diagnostic values are not high. These abnormalities are mild or moderate and could be improved with treatment (52). In studies, the rate of leukopenia was 3.0-54.3%, leukocytosis 1.9-14.2%, anemia 28.9-62.5% thrombocytopenia 1.9-35.0% and thrombocytosis 1.3-62.5% (53-55). In our study, the rate of leukopenia was 6.0%, leukocytosis 2.0%, thrombocytopenia 10.0%, and thrombocytosis 2.0% and consistent with the literature. Although it is a bacterial it is disease, leukocyte value may not guide the diagnosis of brucellosis. As seen in 46 (92.0%) of our cases, normal leukocyte value is an important point to consider when evaluating patients.

ESR and CRP positivity are guiding in the diagnosis of brucellosis. In the literature, elevated ESR and CRP were 38.0-56.8% and 50.0-87.2%, respectively (53.54). In our study, we detected high levels of ESR (42.9%) and CRP (72.3%), and these rates are consistent with the literature.

The liver is the largest organ of the reticuloendothelial system and in brucellosis, it is often involved. So, a slight elevation in liver enzymes is expected (56). In studies in the literature, elevated transaminase levels were found (18.3-55.0%) (35.53). In our study, high transaminase levels were present in 30.0% of patients, and this finding is consistent with the literature.

The most widely used and easy serological test is the STA test. In the STA test, agglutination was considered significant at dilutions of ≥1/160 (11,26,30,31). In a study, there were 13.9% patients with a pre-treatment STA value of 1/160, 62.7% with 1/320, 18.6% with 1/640, and 2.32% with >1/640 (55). In our study, there were 23.5% patients with a pre-treatment STA value of 1/160, 33.3% with 1/320, 23.5% with 1/640, and 11.8% with 1/1280.

The treatment in brucellosis is dual, in some cases, triple combined antibiotic therapy, as recommended by the World Health Organization (WHO). Monotherapy is insufficient due to the rapid development of resistance, intracellular proliferation of bacteria, and relapses, leading to treatment failure (9,57). In 1986, WHO made some changes in the treatment of the disease. WHO recommended doxycycline, a long-acting tetracycline derivative, 200 mg/day (100 mg with 12-hour intervals) and rifampicin (single dose 600-900 mg/day) for 6 weeks (9,57,58). This treatment protocol for brucellosis is the same way since 1986 (59). Tetracyclines are not suitable for use in children aged ≤8 years, as they cause developmental disorders and bone deformities in addition to permanent discoloration of the teeth. Cotrimoxazole (10 mg/kg/day) + rifampicin (20 mg/kg/day) combination for 4-6 weeks and gentamicin (5-7 mg/kg/day, 5 days) are used in children aged ≤8 years. Combination treatment with doxycycline (doxycycline + rifampicin) is appropriate in children >8 years (60). In our study, 35 (68.6%) patients were treated with doxycycline + rifampicin, 3 (5.9%) with gentamicin + rifampicin, 4 (7.8%) with doxycycline + gentamicin + rifampicin, 1 (2.0%) with gentamicin + doxycycline, 7 (13.7%) with cotrimoxazole + rifampicin, and 1 (2.0%) with cotrimoxazole + rifampicin + gentamicin. The heterogenous treatment options in our clinic was because our patients were selected over a long period of 10 years, and the current treatment options were different during these periods, and the clinicians treating them were different.

In conclusion, brucellosis is a zoonotic infectious disease that may involve many organ systems and present with different clinical manifestations in our country. Since Turkey is an endemic region, brucellosis should be considered in every patient with prolonged fever, sweating, joint pain, and weakness, especially in children living in rural areas and consuming raw, poorly boiled milk and dairy products. Family members of the patient with brucellosis should be evaluated both clinically and serologically. Early diagnosis and treatment of the disease, increasing public awareness to avoid raw milk and/or dairy product consumption in rural areas where animal husbandry is prevalent, education of the public health personnel regarding transmission routes and prevention methods of brucellosis are helpful to prevent the disease and reduce the risk of complications.

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