HAYDARPAŞA NUMUNE MEDICAL JOURNAL

DOI: 10.14744/hnhj.2022.10327
Haydarpasa Numune Med J 2023;63(4):515–521

ORIGINAL ARTICLE

Evaluation of Epidemiological, Clinical, and Laboratory Characteristics of Brucellosis Patients Followed the Children Infectious Diseases Policyclinic as Retrospective

Muhammed Yaşar Kılınç[1], Derya Arslan[2], Özge Metin[3], Murat Konak[4]

[1]Department of Neonatology, Kanuni Sultan Suleyman Training and Research Hospital, Istanbul, Türkiye
[2]Department of Pediatric Cardiology, Konya Training and Research Hospital, Konya, Türkiye
[3]Department of Pediatric Infection, Necmettin Erbakan University, Konya, Türkiye
[4]Department of Neonatology, Selcuk University, Konya, Türkiye

Abstract

Introduction: In our study, it was aimed to assess clinical and epidemiological features, laboratory findings, applied treatments, and complications of patients who were referred retrospectively to Konya Training and Research Hospital Pediatric's Infectious Disease Clinic.

Methods: This study was conducted on 50 patients diagnosed with brucellosis who applied to the Pediatric Infectious Diseases outpatient clinic between December 2014 and July 2016.

Results: In our study, 46% of the patients were female and 54% were male, and the median age was 10.3±3.2 years (min: 5-max: 18 years). It was observed that patients were referred most frequently in the spring and summer seasons. Eighty percent of the patients had a history of eating raw milk cheese, and 52% had an animal contact history. Brucellosis history in the family environment and immediate surroundings was found in 44% of the patients. According to frequency order, referral complaints of our patients were 70% arthralgia, 64% fatigue, 60% anorexia, and 50% fever. Arthralgia was the most common physical examination finding (40%). Serum agglutination titer at the rate of 88%, serum immunocapture test at the rate of 96%, enzyme-linked immunosorbent assay at the rate of %88 were found positive, and the agent culture rate of blood culture, which was taken from 34% of the patients, was found to be 35%. As complications, patients were monitored by the reason of 8% pancytopenia, 8% hepatitis, and 12% osteoarticular involvement. At the follow-up between 7 and 14 days of treatment, serum immunocapture agglutination titers decreased. There were no patients in whom drug side effects, abnormality of laboratory findings, or relapse were observed.

Discussion and Conclusion: Brusellosis, which is endemic for our country, should be considered in patients with fever, arthralgia/arthritis, and hepatosplenomegaly; family history, occupation with stock farming, raw milk, and milk product consumption should be questioned; and tests for this disease should be wanted.

Keywords: Arthralgia; brusellosis; hepatosplenomegaly; immunocapture agglutination; serum agglutination.

Brucellosis develops due to microorganisms from the Brucella family (gram-negative coccobacillus), and it continues to be an important public health problem worldwide[1]. Brucellosis is among the diseases that must be reported in our country, and the seroprevalence of brucellosis varies between 2 and 6%[2]. Humans are inciden-

Correspondence: Murat Konak, M.D. Department of Neonatology, Selcuk University, Konya, Türkiye
Phone: +90 532 581 28 62 **E-mail:** drmkonak@hotmail.com
Submitted Date: 15.06.2021 **Revised Date:** 15.03.2022 **Accepted Date:** 06.05.2022
Haydarpaşa Numune Medical Journal

tal hosts and contract zoonotic disease by direct contact with an infected animal or by consuming the products of infected animals. The majority of brucellosis in children is of food origin and is associated with the consumption of unpasteurized dairy products. Brucellosis is a systemic disease that can be difficult to diagnose in children without animal or food exposure. Non-specific symptoms may present acutely or insidiously and usually begin 2–4 weeks after inoculation. Although the clinical presentation may be variable, the triad of fever, arthralgia or arthritis, and hepatosplenomegaly can be seen in most patients. Some patients may present with a fever of unknown origin. Common symptoms in children are loss of appetite, fatigue, and growth retardation. The fever pattern can be very variable, and almost any organ or tissue may be involved. Routine laboratory tests are not helpful; thrombocytopenia, neutropenia, anemia, or pancytopenia may occur. A diagnosis is made by demonstrating microorganisms in the blood, bone marrow, or other tissues. In cases where positive culture results cannot be obtained, various serological tests are applied in the diagnosis of brucellosis. The key role of long-term treatment with agents with intracellular killing properties in eradicating the infection is clear. If it is not treated timely and effectively, chronicity, complications, and relapses may occur. There is no vaccine for use in children to prevent the disease, and therefore, education in society has a prominent role in the prevention of the disease[1].

In this study, it was aimed to retrospectively evaluate the epidemiological, clinical, and laboratory characteristics of pediatric patients diagnosed with brucellosis in our clinic and to examine them together with other studies on childhood brucellosis.

Materials and Methods

The records of 50 brucellosis cases who were followed up in the outpatient clinic or hospitalized in our service between December 2014 and July 2016 were evaluated retrospectively.

Patients' gender, age, place of residence, time until diagnosis, history of living with active brucellosis in the family and close environment, presence of similar complaints in the family at the time of diagnosis, consumption of raw milk and dairy products, history of consumption of fresh cheese, dealing with livestock, cattle, or sheep farm animals, contact with admission complaints, and duration of complaints were obtained from files. According to the period of complaints, brucellosis is divided into three forms. Acute brucellosis is defined as cases with a complaint duration of <2 months. Subacute brucellosis is a case that lasts from 2 months to a year. Patients with chronic brucellosis disease symptoms longer than 1 year are defined. The patients were classified as rural by their living area which is located outside towns and cities. Other patients who live in city or town were defined as urban area. Physical examination and laboratory findings, tests used in diagnosis, treatment regimen, duration, complications, and relapse development were evaluated.

Statistical analyses were performed using the "SPSS for Windows 16.0" package program (SPSS 'Statistical Package of Socil Sciences 2, Inc. Chicago, IL). If the data obtained with the measurement were normally distributed, the mean and standard deviation were shown; if not, the median value was shown, and the categorical data (sex, disease, etiological group, etc.) were shown according to their frequency (percentage). Exact chi-square test analysis was used for statistical evaluations. A value of 0.05 was taken as the level of significance (p); $p<0.05$ was considered statistically significant.

Results

Fifty patients were included in the study. Twenty-three (46%) of the patients were female, and 27 (54%) were male. The patients were between 5 and 18 years of age, with a mean age of 10.3±3.2 years. The number of patients admitted from the rural area was 42 (84%) and 8 (16%) from the urban area (Fig. 1). The patients from the Central Anatolia Region (92%) applied most frequently (Fig. 2). The transmission route of infection was detected in 45 (90%) patients; 40 (80%) patients had a history of eating cheese from raw milk; and 26 patients (52%) had animal contact. It was observed that the symptoms started in the summer

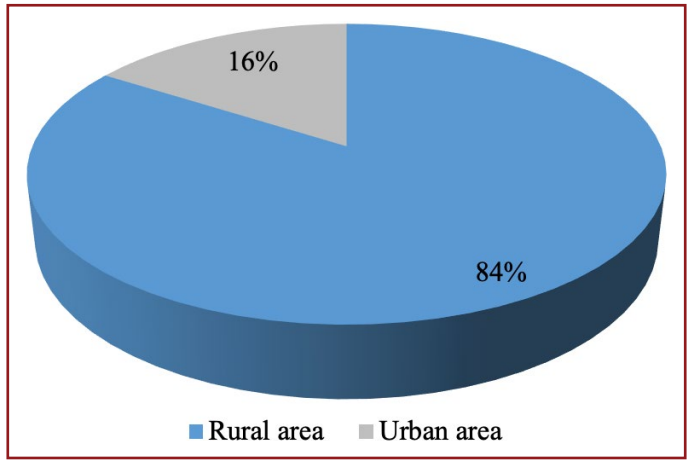

Figure 1. Rural-urban region distribution.

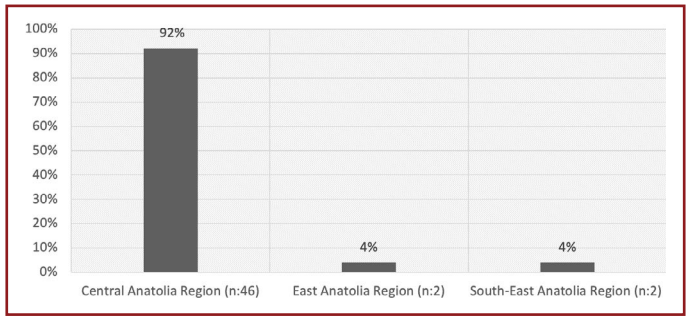

Figure 2. Distribution of patients according to the geographical regions they applied to.

in 24 (48%) patients, in the spring in 15 (30%) patients, in the autumn in 6 (12%) patients, and in the winter in 3 (6%) patients. A family history of brucellosis was present in 22 (44%) patients. The distribution of patients according to risk factors is shown in Table 1.

Thirty-four (84%) of the patients first applied to our hospital, and 16 (16%) patients were referred from other centers. The number of inpatients was 9 (18%), and the number of outpatients was 41 (82%). The mean time between the onset of symptoms and admission to the hospital ranged from 26.5±14.3 days. When classified as the clinical form, 44 (88%) patients had acute and 6 (12%) patients had subacute brucellosis. In order of frequency, 35 (70%) patients presented with arthralgia, 32 (64%) patients with fatigue, 30 (60%) patients with anorexia, and 25 (50%) patients with fever. Arthritis was the most common physical examination finding in 20 (40%) patients. The complaints and physical examination findings of the patients are shown in Table 2.

In our study, increased erythrocyte sedimentation rate (ESR) was detected in 13 (26%) patients and elevated C-reactive protein (CRP) in 11 (22%) patients. Serum aspartate aminotransferase (AST) levels were found in 15 (30%) patients, and alanine aminotransferase (ALT) levels were above 50 IU/L in 16 (32%) patients. Anemia was observed in 9 (18%), leukopenia in 6 (12%), anemia and leukopenia concomitant in 2 (4%), pancytopenia in 4 (8%), thrombocytopenia in 6 (12%), and lymphomonocytosis in 25 (50%) patients. The highest, lowest, and mean values of the non-specific Brucella infection laboratory tests of the patients are shown in Table 3.

Table 1. Distribution of patients according to risk factors

Risk factors	Number of Cases (%)
Raw milk and dairy products consumption history	40 (80)
History of contact with farm animals	26 (52)
History of brucellosis in the family or in the immediate environment	22 (44)
History of miscarriage in animals	6 (12)

Table 2. Application complaints and physical examination findings of the patients

Clinic	Number of Cases	Ratio (%)
Arthralgia	35	70
Hip	20	47
Knee	9	18
Knee and hip	2	4
Ankle	2	4
Wrists and knees (mobile)	2	4
Weakness	32	64
Anorexia	30	60
Fever	25	50
Abdominal pain	6	12
Night sweats	4	8
Weight loss	2	4
Myalgia	2	4
Arthritis	2	4
Nausea-vomiting	1	2
Headache	1	2
Physical Examination		
Arthritis	20	40
Fever	17	34
Splenomegaly	14	28
Hepatosplenomegaly	8	16
Hepatomegaly	6	12
Cardiac murmur	3	6
Lymphadenopathy	2	4
Monoarthritis	2	4
Atypical walk	2	4
Rash	1	2
Neck stiffness and altered consciousness	1	2

Table 3. Mean, minimum, maximum values of laboratory findings

Laboratuvary findings	Mean	SD	Minimum	Maximum
White Blood Cells(/mm^3)	6955	1820	3610	9000
Hb (gr/dL)	11	1.5	9	15
Platalet (/mm^3)	225000	60300	106000	386000
ESH (mm/sa)	20	12.6	2	51
CRP (mg/dL)	10	14.6	2	86
AST (U/l)	16	225	16	225
ALT (U/l)	35	53	8	295
Hematocrit (%)	35	6.8	29	45

SD: Standard Deviation.

Table 4. Treatment regimens

Treatment Regimen	Number of cases	Ratio %
Doxycycline + Rifampicin	26	52
Doxycycline+ Rifampicin+Gentamicin	10	20
Co-trimoxazole + Rifampicin	14	28

Brucella spp. was found in 6 (35%) blood cultures taken from 17 (34%) patients who were positive. In our cases, the positivity rate of the serum immunocapture agglutination test (96%) was higher than the serum agglutination test (88%). Brucella IgM and/or IgG (ELISA) tests were negative in 6 (12%) of 50 patients. Since blood cultures were taken from only 17 of the patients, blood culture, which is considered the gold standard diagnostic test, could not be compared with other tests. Organ and/or system involvement was present in 16 (32%) of the patients. Liver involvement was detected in 4 (8%), hematological involvement in 6 (12%), and musculoskeletal involvement in 6 (12%) patients.

The duration of treatment was 6 weeks in 44 (88%) patients. The treatment duration of 6 (12%) patients with musculoskeletal involvement due to brucellosis varied between 8 and 12 weeks. Doxycycline, rifampicin, and gentamicin were given to 4 patients with pancytopenia and 6 patients with musculoskeletal involvement. The treatment regimens are shown in Table 4. 7–14 days of treatment in the follow-up of the patients. It was observed that serum immunocapture agglutination titers decreased between days. The patients were included in the outpatient follow-up program for 6 months after the treatment. When the treatment was completed, serological tests were not repeated because all patients had no complaints. No adverse reaction to brucellosis treatment was observed in any patient.

Discussion

Brucellosis is the most common zoonosis worldwide, caused by Brucella bacteria[3]. According to the data of the Ministry of Health, the annual morbidity rate of brucellosis in our country is 20 per 100,000, and the annual mortality rate is 0.01 per million[4]. It is more common in the eastern and southeastern Anatolia regions, where animal husbandry is common[5]. In our study, patients from the Central Anatolia Region (92%) applied most frequently. Children older than 5 years constitute the majority of childhood brucellosis cases[6]. In this study, the largest patient group was the 8–15 age group (50%), similar to other published pediatric brucellosis series[7-11]. In our study, the rate of boys was found to be higher (54%) in children, and it was found to be consistent with the pediatric brucellosis series reported in the literature[8-11]. The youngest patient in our study was a 5-year-old, 1-month-old male patient, and the mean age was 10.3, similar to other studies performed in our country[12-15]. According to the study of Konca et al.,[16] 61.7% of the patients, and according to the study of Abuhandan et al.[17] 76.8% were patients living in rural areas. In our study, there were patients living most frequently in rural areas. Although the disease can be seen in all months of the year in Türkiye, it is more common during the calving period of sheep and in the spring and summer months when cheese production increases[14]. According to the study of Uluğ et al.,[18] patients applied mostly in the spring and summer months. In the study of Tartar,[19] 81.4% of the cases occurred in the spring and summer months. In our study, the most frequent application was seen in the summer and spring months. The most common mode of transmission of the disease is through the consumption of raw milk and dairy products[20]. In the study of Tanir et al.,[6] consumption of unboiled milk was 71.1%, livestock 45.6%, and family history 15.6%. In the study conducted by Gül et al.[21] on 1110 pediatric brucellosis patients, 30.2% had a history of animal husbandry. In the study conducted by Helvacı et al.,[22] 82.5% of the patients had a history of using open milk, and 50.9% of them had a history of dealing with livestock. In our study, the transmission route of infection was detected in 90% of the patients, and the most common was the history of eating cheese from raw milk and animal contact. 23% of the patients who had contact with animals had a history of abortion in the farm animals they came into contact with. A history of brucellosis in the family and in the immediate environment was present in 44% of the patients. 40% of patients diagnosed during screening due to family history were asymptomatic. The high prevalence within the family can be explained by the contact of the family members with the same sick animals and consuming the same dairy products. For this reason, clinical and serological examination of family members of patients diagnosed with brucellosis is an important approach for early diagnosis and treatment of possible new cases, and it is a situation that should be considered, especially in countries such as Türkiye where the disease is endemic.

Brucellosis can be seen in acute, subacute, and chronic forms, as well as relapse. 50% of childhood brucellosis is acute, the rest is subacute or subclinical[15]. Similar to other studies, in our study, the number of acute patients was higher; 88% had acute and 12% had subacute brucellosis[14,23-25]. There was no case of chronic brucellosis. Only 2% of patients were diagnosed with relapsed brucellosis. The mean time between the onset of symptoms and ad-

mission to the hospital ranged from 26.5±14.3 days.

In most of the pediatric brucellosis series, fever (55.3–95%) was reported as the most common complaint, and arthralgia (74–85.6%) was the second most common complaint[26]. In our study, the complaints of our patients were arthralgia, malaise, anorexia, and fever, in order of frequency. Although brucellosis causes many nonspecific somatic complaints, it presents with very few physical examination findings. Except for arthritis and fever, the most frequently reported physical examination findings in children were hepatomegaly 13–60%, splenomegaly 9.6–55%, and lymphadenopathy 1.7–67%[26]. In our study, arthritis was found to be the most common physical examination finding. In pediatric brucellosis series, knee joint involvement was reported as 9.6–47%, hip joint involvement as 7.5–34.7%, and joint involvement of the knee and hip joint as 3.2% in only one study[26]. In our series, the most common joint involvements were hip and knee. In our study, the most common reasons for admission after arthralgia were fatigue in 64% of patients and anorexia in 60% of patients. Fatigue and anorexia are nonspecific symptoms and may require investigation for brucellosis in patients who cannot be attributed to any cause and apply from an endemic region of brucellosis. In our series, 50% of the patients presented with the complaint of fever, and 34% of the patients had fever on admission. Infectious diseases, especially tuberculosis and brucellosis, are among the leading causes of fever of unknown origin in our country[27]. It is seen that brucellosis was detected at a rate of 6–56% in studies conducted by various centers in our country in which the etiology of fever of unknown origin was investigated[28-30]. In our country, especially in endemic regions, brucellosis draws attention as a disease that should be considered primarily in patients with fever of unknown origin.

Laboratory findings in brucellosis are variable, and hematological disorders such as leukopenia, anemia, thrombocytopenia, and lymphomonocytosis can be seen in 25–50% of the cases, but these findings are not diagnostic[31]. ESR varies and is not very helpful in diagnosis. Most of the time, a slight to moderate increase is observed[32]. Anemia in brucellosis can be seen as mild hypochromic and microcytic. Anemia varies between 44 and 74%[33,34]. Pancytopenia has been reported at varying rates, such as 3–21%[35]. In many studies, a 26–57% increase in transaminases has been found in brucellosis, and it has been reported that this increase is usually 2–4 times and rarely exceeds 10 times[36,37]. In our study, similar to the literature, elevated ESR, CRP, AST, and ALT levels were found. In our study, anemia was seen in 18% of patients, leukopenia in 12%, anemia and leukopenia in 4%, pancytopenia in 8%, thrombocytopenia in 12%, and lymphomonocytosis in 50% of patients.

The diagnosis of brucellosis is made by detecting positivity in serological tests and/or producing the agent in culture. In our country, the Wright test is most frequently applied[38]. In various studies, the rate of production of the agent in blood cultures in children with brucellosis has been reported between 23.5% and 59.7%[7,8,39,40]. In the study of Aydın,[41] the sensitivity and specificity of the serum agglutination test were reported as 88.9% and 76.5%, and in the study of Güzelant et al.,[42] the sensitivity and specificity of the serum agglutination test were reported as 94% and 96%, respectively. Özdemir et al.[43] reported that the detection of positivity and a high titer in the Brucellacapt test was higher than in the serum agglutination test. Ardic et al.[44] found the positive detection rate to be 80% in the serum agglutination test and 87% in the Brucellacapt test when titers of 1/160 and above were considered positive. In our study, the positivity rate of the serum immunocapture agglutination test (96%) was found to be higher than the serum agglutination test (88%). Brucella IgM and/or IgG (ELISA) tests were negative in 12% of patients. The ELISA test was positive in 4% of the patients in whom both serum immunocapture agglutination tests and serum agglutination tests were negative.

Since Brucella is an intracellular pathogen, the administration of drugs that can only act intracellularly at an appropriate time provides success[45]. The generally accepted duration of treatment in children is 6 weeks[46]. In the literature, relapse rates have been reported as 5–12% after 6 weeks of treatment[47]. Bayindir et al.[48] and Ranjbar et al.[49] found relapse rates between 9.3% and 19% with dual antibiotic therapy. In our study, the duration of treatment was 6 weeks for 88% of the patients. The treatment duration of 12% of patients with musculoskeletal involvement ranged from 8 to 12 weeks. No case of relapsed brucellosis was observed after treatment.

Conclusion

Brucellosis is the most common zoonotic disease in our country. Most brucellosis in children is associated with the consumption of unpasteurized dairy products and animal exposure. Risk factors should be questioned by patients. Brucellosis is a systemic disease that can be difficult to diagnose in children without animal or food exposure. It should be kept in mind that brucellosis may present with non-specific symptoms.

Ethics Committee Approval: This study was approved by Selçuk University Ethics Committee (Date: 15/03/2016, Number: 2016/88).

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: M.Y.K., D.A.; Design: D.A., Ö.M.; Data Collection or Processing: D.A., Ö.M.; Analysis or Interpretation: M.Y.K., Ö.M.; Literature Search: M.K.; Writing: M.Y.K., M.K.

Acknowledgment: We would like to thank you for your support to Dr. Çelebi Kocaoğlu.

Conflict of Interest: None declared.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Schutze GE, Jacobs RF. Brucella. In: Behrman RE, Kliegman RM, Jenson HB, editors. Nelson textbook of pediatrics. 17th ed. Philadelphia: WB Saunders; 2013. p.980–2.
2. Doğanay M, Alp Mese E. Bruselloz. In: Willke Topçu A, Söyletir G, Doğanay M, editors. Enfeksiyon Hastalıkları ve mikrobiyolojisi. 3. baskı. Istanbul: Nobel Tıp Kitabevleri; 2008. p.897–909.
3. Pappas G, Papadimitriou P, Akritidis N, Christou L, Tsianos EV. The new global map of human brucellosis. Lancet Infect Dis 2006;6:91–9.
4. T.C. Sağlık Bakanlığı. Temel sağlık hizmetleri genel müdürlüğü, 2006. Çalışma Yıllığı. Available at: http://www.saglik.gov.tr/TR/dosya/1-64856/h/ web2006.rar. Accessed Sep 3, 2023.
5. Buzgan T, Karahocagil MK, Irmak H, Baran AI, Karsen H, Evirgen O, et al. Clinical manifestations and complications in 1028 cases of brucellosis: A retrospective evaluation and review of the literature. Int J Infect Dis 2010;14:e469–78.
6. Tanir G, Tufekci SB, Tuygun N. Presentation, complications, and treatment outcome of brucellosis in Turkish children. Pediatr Int 2009;51:114–9.
7. Mantur BG, Akki AS, Mangalgi SS, Patil SV, Gobbur RH, Peerapur BV. Childhood brucellosis - a microbiological, epidemiological and clinical study. J Trop Pediatr 2004;50:153–7.
8. Shaalan MA, Memish ZA, Mahmoud SA, Alomari A, Khan MY, Almuneef M, et al. Brucellosis in children: Clinical observations in 115 cases. Int J Infect Dis 2002;6:182–6.
9. Tsolia M, Drakonaki S, Messaritaki A, Farmakakis T, Kostaki M, Tsapra H, et al. Clinical features, complications and treatment outcome of childhood brucellosis in central Greece. J Infect 2002;44:257–62.
10. Giannakopoulos I, Nikolakopoulou NM, Eliopoulou M, Ellina A, Kolonitsiou F, Papanastasiou DA. Presentation of childhood brucellosis in Western Greece. Jpn J Infect Dis 2006;59:160–3.
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;15:76–80.
12. Kara SS, Aslan MH, Volkan B, Özel M, Fettah A. Retrospective evaluation of 94 pediatric patients with brucellosis diagnosis. Kocatepe Tıp Derg [Article in Turkish] 2016;17:60–5.
13. Çataklı T, Kılıç N, Dallar Y. Thirty-three patient with brucellosis evaluated retrospectively. Ege Tıp Derg [Article in Turkish] 2011;50:39–42.
14. Öncel EK, Özsürekci Y, Cengiz AB, Kara A, Ceyhan M, Çelik M, et al. Çocukluk çağında bruselloz: Hacettepe Üniversitesi deneyimi. Cocuk Sagligi Hastaliklari Derg [Article in Turkish] 2011;54:135–41.
15. Çelebi S, Hacımustafaoğlu M, Demirtaş F, Salı E, Gül Ü, Özel M. Brucellosis in childhood. J Pediatr Inf [Article in Turkish] 2011;5:59–62.
16. Konca Ç, Tutanç M, Güneş A, Taş MA. Childhood Brucellosis in Southeastern Region of Türkiye: A retrospective analysis. İzmir Dr. Behçet Uz Çocuk Hast Derg [Article in Turkish] 2013;3:54–9.
17. Abuhandan M, Güzel B, Çakmak A, Çiçek A. Pediatric brucellosis: A retrospective evaluation of 82. J Pediatr Inf [Article in Turkish] 2012;6:74–8.
18. Uluğ M, Uluğ NC. Evaluation of 78 Cases with Brucellosis. Klimik Derg [Article in Turkish] 2010;23:89–94.
19. Tartar AS. Brucellosis: Retrospective evaluation of cases. F Ü Sağ Bil Tıp Derg [Article in Turkish] 2014;28:111–5.
20. Logan LK, Jacobs NM, McAuley JB, Weinstein RA, Anderson EJ. A multicenter retrospective study of childhood brucellosis in Chicago, Illinois from 1986 to 2008. Int J Infect Dis 2011;15:e812–7.
21. Gül S, Satilmiş OK, Ozturk B, Gökçe MI, Kuscu F. Seroprevalence of brucellosis among children in the Middle Anatolia Region of Türkiye. J Health Popul Nutr 2014;32:577–9.
22. Helvacı M, Dinçer A, Barışık V. The retrospective evaluation of 57 cases with brucellosis in childhood. Tepecik Eğit Hast Derg [Article in Turkish] 2011;21:135–8.
23. Bayoğlu DS, Calhan D, Gürbüz T, Önal ZE, Akıcı N, Nuhoğlu Ç. Evaluation of children who are followed and treated with the diagnosis of brucellosis. Haydarpaşa Numune Tıp Derg [Article in Turkish] 2014;54:156–60.
24. Işıkay S, Yılmaz K, Işıkay N, Balcı O, Özarslan K, Yılmaz F, et al. Evaluation of 21 cases with Brucellosis. Turkiye Klinikleri J Med Sci [Article in Turkish] 2013;33:785–9.
25. Sarı E, Sarı Özgen İ, Say A, Güven F, Ulutaş AP. The evaluation of brucellosis in children in an endemic region of Türkiye, Van. Gaziantep Med J [Article in Turkish] 2013;19:1–4.
26. Postgraduate education course brucellosis: Epidemiological, microbiological, clinical and therapeutic aspects. 6-7 May 2010, Kuşadası - Türkiye.
27. Erten N, Saka B, Ozturk G, Karan MA, Tascioglu C, Dilmener M, et al. Fever of unknown origin: A report of 57 cases. Int J Clin Pract 2005;59:958–60.
28. Ciftçi E, Ince E, Doğru U. Pyrexia of unknown origin in children: A review of 102 patients from Türkiye. Ann Trop Paediatr 2003;23:259–63.
29. Yüce A. Türkiye'de Brusellozun durumu. In: XXXI. Türk Mikrobiyoloji Kongresi, 19-23 Sep 2004, Kufladası - Aydın, Kongre Kitabı. İstanbul: Türk Mikrobiyoloji Cemiyeti & Klinik Mikrobiyoloji ve infeksiyon Hastalıkları Derneği 2004:119–22.
30. Ergönül O, Willke A, Azap A, Tekeli E. Revised definition of fever of unknown origin: Limitations and opportunities. J In-

fect 2005;50:1–5.
31. Kaya S. 44 The evaluation of 44 patients with brucellosis. Bruselloz olgusunun değerlendirilmesi. Klimik Derg 2007;20:17–9.
32. Edward JY. Brucella species principles and practice of infectious diseases 7th ed. Philadelphia:Chuchill Livingstone; 2009. p. 2386–93.
33. Navarro-Martínez A, Solera J, Corredoira J, Beato JL, Martínez-Alfaro E, Atiénzar M, et al. Epididymoorchitis due to brucella mellitensis: A retrospective study of 59 patients. Clin Infect Dis 2001;33:2017–22.
34. Karakukcu M, Patiroglu T, Ozdemir MA, Gunes T, Gumus H, Karakukcu C. Pancytopenia, a rare hematologic manifestation of brucellosis in children. J Pediatr Hematol Oncol 2004;26:803–6.
35. Young EJ. Brucella Species. In: Mandell GL, Bennet JE, Dolin R, editors. Principles and practice of infectious diseases 5th ed. New York: Churchill Livingstone Inc.; 2000. p. 2386–93.
36. Bayraktar M, Bayraktar N, Bayındır Y, Durmaz R. Evaluation of serum levels of C-reactive protein, ıron and ferritin in diagnosis and monitoring of brucellosis. Ankem Derg [Article in Turkish] 2005;19:61–3.
37. Ayaz C, Geyik MF, Mendes H. Brusellozlu 145 hastanın değerlendirilmesi. X. 15-19 Oct 2001, Türk Klinik Mikrobiyoloji ve İnfeksiyon Hastalıkları Kongresi, Adana, s.356.
38. Yılmaz K, Bayraktaroğlu Z, Sivaslı E, Güler E, Bolat A, Kılınç M. Clinical and laboratory evaluation of children with brucellosis. Çocuk Derg [Article in Turkish] 2004;4:102–6.
39. Issa H, Jamal M. Brucellosis in Children in South Jordan. East Med Health J 1999;5:895–902.
40. Gür A, Geyik MF, Dikici B, Nas K, Cevik R, Sarac J, et al. Complications of brucellosis in different age groups: A study of 283 cases in southeastern Anatolia of Türkiye. Yonsei Med J. 2003;44:33–44.
41. Aydın L. The investigation of brucellosis by serological tests (rose bengal plate, modified rose bengal plate, serum agglutination, rivanol agglutination, 2-mercaphtoethanol aglutination and ELISA) in patients with complaints of fever and joint pain in health centers in Konya. Master's thesis. Konya: Selçuk Üniversitesi; 2009.
42. Güzelant A, Kurtoğlu MG, Kaya M, Keşli R, Terzi Y, Baysal B. Comparison of the brucellacapt with other serological tests used for the diagnosis of brucellosis. Selçuk Tıp Derg [Article in Turkish] 2009;25:125–31.
43. Özdemir M, Doğan B, Baysal B. A new method in the diagnosis of brucellozis: Immuncapture agglutination test. Genel Tıp Derg [Article in Turkish] 2007:17:9–13.
44. Ardic N, Ozyurt M, Sezer O, Erdemoglu A, Haznedaroglu T. Comparison of Coombs' and immunocapture-agglutination tests in the diagnosis of brucellosis. Chin Med J Engl 2005;118:252–4.
45. Brucellosis. In: Pickering LK, editor. 2009 Red book: Report of the committee on ınfectious diseases. 28th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2009. p. 237–9.
46. Roushan MR, Mohraz M, Janmohammadi N, Hajiahmadi M. Efficacy of cotrimoxazole and rifampin for 6 or 8 weeks of therapy in childhood brucellosis. Pediatr Infect Dis J 2006;25:544–5.
47. Hall WH. Modern chemotherapy for brucellosis in humans. Rev Infect Dis 1990;12:1060–99.
48. Bayindir Y, Sonmez E, Aladag A, Buyukberber N. Comparison of five antimicrobial regimens for the treatment of brucellar spondylitis: a prospective, randomized study. J Chemother 2003;15:466–71.
49. Ranjbar M, Keramat F, Mamani M, Kia AR, Khalilian FO, Hashemi SH, et al. Comparison between doxycycline-rifampin-amikacin and doxycycline-rifampin regimens in the treatment of brucellosis. Int J Infect Dis 2007;11:152–6.