



Investigation of Brucella Knee Prosthetic Joint Infections by Pool Analysis Method

Brucella Diz Protetik Eklem Enfeksiyonlarının Havuz Analizi Yöntemiyle İncelenmesi

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ABSTRACT

Aim: Brucellosis is a zoonotic disease seen globally. It is endemic in many development countries. Although it is rare sometimes prosthetic joint infections may occur, even cases were reported from non-endemic countries. With this study, we aimed to shed light on clinical diagnosis and treatment management by examining prosthetic infections due to brucella in the literature with the pool analyze method.

Material and Method: To find the published series, four databases (Scopus, Google Scholar, PubMed, and the Web of Science database) were searched. The study was conducted using key words ['Brucella' or 'Brucella spp.' and 'knee' and 'infection' and 'prosthetic joint' or 'knee arthroplasty' or 'loosening' or 'arthroplasty']. Only studies published in English language or with English abstracts were included.

Results: 27 publications and 28 reported cases were identified of patients with brucella knee prosthetic joint infections. The cases were reported from 14 different countries. The average age of the patients for whom data were provided was 65.59±8.42 years. 13 of the cases were female and 14 were male, in one publication did not have gender information. Eating unpasteurized dairy products (50%) was the common risk factor. Systemic symptoms and fever were reported 53.57% of the cases.

Conclusion: Successful results are observed with 2-stage revision arthroplasty and at least dual antibiotic therapy in prosthetic infections due to Brucella. In addition, it is beneficial that the cement used is antibiotic proof. The use of long-term combined antibiotics is important in the success of treatment.

Keywords: Brucella, knee prosthesis, prosthesis infection, revision arthroplasty

ÖZ

Amaç: Bruselloz tüm dünyada görülen zoonotik bir hastalıktır. Gelişmekte olan birçok ülkede endemiktir. Nadir de olsa bazen protez eklem enfeksiyonları oluşabilmekle birlikte, endemik olmayan ülkelerden bile vakalar bildirilmiştir. Bu çalışma ile literatürdeki brusellaya bağlı protezik enfeksiyonları havuz analizi yöntemi ile inceleyerek klinik tanı ve tedavi yönetimine ışık tutmayı amaçladık.

Gereç ve Yöntem: Yayınlanan seriyi bulmak için dört veritabanı (Scopus, Google Scholar, PubMed ve Web of Science veritabanı) tarandı. Çalışma, anahtar kelimeler ['Brucella' veya 'Brucella spp.' ve 'diz' ve 'enfeksiyon' ve 'protez eklem' veya 'diz artroplastisi' veya 'gevşetme' veya 'artroplasti'] kullanılarak yapıldı. Yalnızca İngilizce dilinde veya İngilizce özetleri ile yayınlanan çalışmalar dahil edilmiştir.

Bulgular: Brusella diz protezi eklem enfeksiyonu olan hastalarda 27 yayın ve bildirilen 28 vaka tespit edilmiştir. Vakalar 14 farklı ülkeden bildirildi. Verileri sağlanan hastaların yaş ortalaması 65,59±8.42 yıl idi. Olguların 13'ü kadın, 14'ü erkekti, bir yayında cinsiyet bilgisi yoktu. Pastörize edilmemiş süt ürünleri (%50) yemek ortak risk faktörüydü. Olguların %53,57'sinde sistemik semptomlar ve ateş bildirilmiştir.

Sonuç: Brucella'ya bağlı protezik enfeksiyonlarda 2 aşamalı revizyon artroplastisi ve en az ikili antibiyotik tedavisi ile başarılı sonuçlar gözlenmektedir. Ayrıca kullanılan çimentonun antibiyotik geçirmez olmasında fayda vardır. Tedavinin başarısında uzun süreli kombine antibiyotik kullanımı önemlidir.

Anahtar Kelimeler: Brucella, diz protezi, protez enfeksiyonu, revizyon artroplastisi

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INTRODUCTION

Brucellosis is a zoonotic disease seen globally. It is endemic in many development countries. Especially Mediterranean countries (Portugal, Spain, Southern France, Italy, Greece, Turkey, North Africa), Middle East, Eastern European countries are endemic regions for this disease. It is known that it is transmitted to humans as a result of contact with small-bovine animals (such as sheep, goats and cattle) or by consuming infected meat, milk, dairy products (1,2).

This disease can affect many organs with the capability of Brucella bacteria cause bacteremia, and may be accompanied by focal symptoms (3). Often reported focal complications are hematological, osteoarticular, genitourinary, neurologic, cardiovascular, gastrointestinal and ocular involvements (4). Bone and joint involvement of the disease is a frequent and the incidence of this involvement ranges from 10% to 85% (5).

Although it is rare sometimes prosthetic joint infections may occur, even cases were reported from non-endemic countries. Brucella knee prosthetic joint infection was first described in the year 1991 by Agarwal et al (6).

In this study we aimed to investigate the clinical features of published Brucella knee prosthetic joint infection cases by using pool analysis method.

MATERIAL AND METHOD

To find the published series, four databases (Scopus, Google Scholar, PubMed and the Web of Science database) were searched. As the data from congress books were heterogeneous, they were not included in the study. Pediatric series, evaluation of any other than the knee joint articles and without data not available for search criteria were excluded. Due to the limited data available on this topic, case reports or case series were included.

The study was conducted using key words ['Brucella' or 'Brucella spp.' and 'knee' and 'infection' and 'prosthetic joint' or 'knee arthroplasty' or 'loosening' or 'arthroplasty']. Only studies published in English language or with English abstracts were included. Two independent reviewers separately completed the search, and the results were duplicated two times by each reviewer. Each case was evaluated separately. All data were analyzed with SPSS for Windows, version 23.00.

All published cases were evaluated as similar features. The following data categories were extracted from articles: year, country, age, gender, risk factors, symptoms, physical examination findings, laboratory/radiological findings, diagnostic criteria, treatments, and outcomes.

RESULTS

As a result of the search with the defined keywords, 27 publications and 28 reported cases were identified of patients with brucella knee prosthetic joint infections (Figure 1).

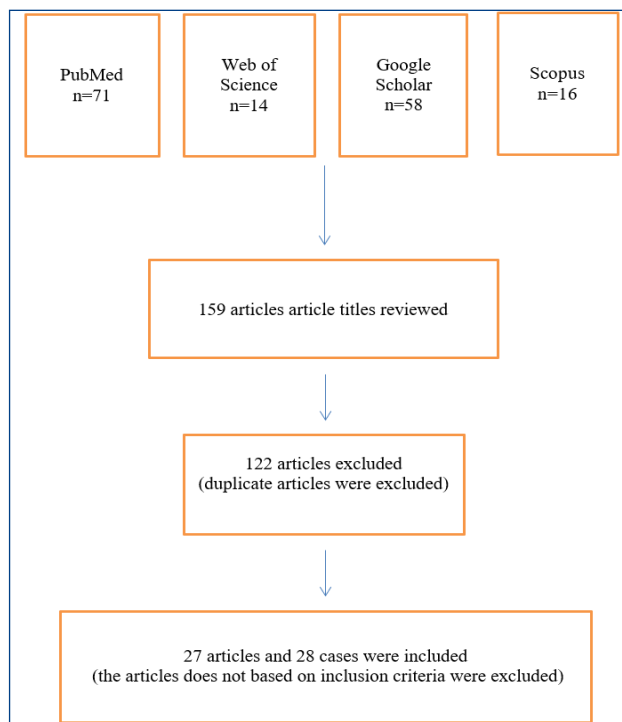


Figure 1. The flowchart details the method of retrieval of published articles.

The cases were reported from 14 different countries (Turkey:5, Iran:4, Israel:3, Italy:3, Greece:2, Saudi Arabia:2, Spain:2, Canada:1, Germany:1, Lebanon:1, Oman:1, Portugal:1, Switzerland:1, United Kingdom:1). In addition, the cases reported from Switzerland and Germany was originating from Turkey and the case reported from United Kingdom was originating from Thailand. Three of the cases were not from endemic areas. In the year 2016, maximum number of cases reported per year (n=4) (Figure 2).

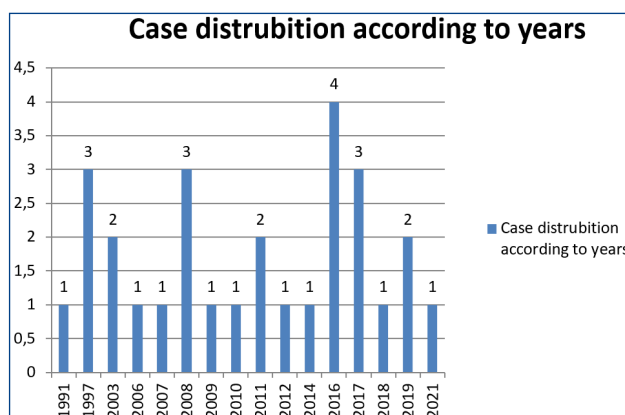


Figure 2. Distribution of the reported cases according to year

The average age of the patients for whom data were provided was 65.59 ± 8.42 years. 13 of the cases were female and 14 were male, in one publication did not have gender information. Eating unpasteurized dairy products (50%) was the common risk factor. Systemic symptoms and fever were reported 53.57% of the cases. **Table 1**; It summarizes the gender, comorbid disease, symptom, and risk factor status of 28 patients.

	n =28	%
Gender (male)	14	50
Comorbidities		
Arthrosis	2	7.14
Hemophilia	1	3.57
Idiopathic local osteonecrosis	1	3.57
Psoriatic arthritis	1	3.57
Diabetes mellitus	1	3.57
None	1	3.57
Juvenile rheumatoid arthritis	1	3.57
No information	20	71.42
Risk factors (* more than one risk factor)		
Unpasteurized dairy products	14	50
Shepherd	1	3.57
Consumed raw meat	2	7.14
Contact with goat	2	7.14
No information	5	17.85
None	1	3.57
Previously brucella infection	1	3.57
Working in a restaurant as a kitchen assistant	1	3.57
Travelling to the endemic areas	3	10.71
Other brucellar infection		
Systemic symptoms	15	53.57
None	13	46.42

Table 2 summarizes data on joint infection findings, clinical serological tests, cultures, x-ray findings, treatment modalities, and relapse.

DISCUSSION

Brucella is a zoonotic bacterium that usually causes systemic infection and affects osteoarticular tissues in 10-85% of patients (7). Although prosthetic joint infections have been discussed in detail in the literature, there are not enough publications in the literature about septic arthritis after knee arthroplasty caused by Brucella (8). Difficulties are also experienced in diagnosis and treatment due to the lack of clinical experience in non-endemic areas. In this publication, we wanted to contribute to the literature by analyzing the cases reported so far.

Brucella is transmitted frequently through consumption of contaminated food and beverage, through inhalation, and due to skin wounds (9). Among these, consumption of unpasteurized dairy products in 14 of 28 cases, as stated in our study, caused knee prosthesis infection due to brucella.

Table 2. Clinical laboratory radiological summaries of reported cases by using pooled analyses method.

Joint infection symptoms/ findings		
Pain	24	85.71
Swelling	12	42.85
Limitation in the knee joint movements	8	28.57
Warmth	7	25
Tenderness	3	10.71
Redness	4	14.28
Effusion	4	14.28
Loosening	18	64.28
Fever	15	53.57
Brucella subtype isolated from cultures		
Brucella melitensis	15	53.57
Brucella spp.	2	7.14
Brucella suis	1	3.57
Laboratory tests performed*		
Blood cultures	6	21.42
Aspiration culture fluid cultures	20	71.42
Serological testes	23	82.14
Cultures taken from the sinus tract discharge	2	7.14
Tissue culture	20	71.42
Histopathological examination	1	3.57
Brucella spp. isolation cite		
Aspiration culture	5	17.85
Tissue culture	7	25
Blood culture	1	3.57
Aspiration culture in blood culture bottles	2	7.14
Serological test result		
Positive	22	78.57
Negative	1	3.57
No Information	5	17.85
Radiological tests performed*		
X ray	10	35.71
Computed tomography	1	3.57
Three-phase scintigraphy	1	3.57
Bone scanning	5	17.85
Treatment		
Only medical	8	28.57
Medical+surgical	20	34.48
Removal of the previous prosthesis	15	53.57
Given therapies*(more than 1 antibiotics)		
Streptomycin	4	14.28
Rifampisin	28	100
Doxycycline/ tetracycline	27	96.42
Cotrimoxazole (trimethoprim sulfamethoxazole)	3	10.71
Gentamicin	5	17.85
Levofloxacin	1	3.57
Combinations therapies		
2 antibiotics regimen	16	57.14
3 antibiotics regimen	12	42.85
Surgical procedure (Total: 20)		
1 stage revision	2	7.14
2 stage revision	14	50
DAIR (Debridement, antibiotics, and implant retention) procedure	1	3.57
No Information	3	10.71
Outcome		
Cured	26	92.86
Relapse	2	7.14



Serological test positivity and tissue and joint fluid culture positivity were significant in the diagnosis, serological test positivity was found to be 78.57%. The symptoms are nonspecific, culture from joint fluid, serological tests, and a history of Brucella infection are important in diagnosis (10). In the cases, the mean erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels were high, while the white blood cell level was normal on average. All the information here is compiled from the publications listed in Table 3 (6, 9, 12, 14-16, 18-23, 25-40).

Table 3. Brucella knee prosthetic joint infection cases included in the present study.

1st author	Publication country, Year
Agarwal S	Saudi Arabia, 1991
Atay T	Turkey, 2008
Balkhair A	Oman, 2019
Çetin ES	Turkey, 2008
Dauty M	Portugal, 2009
Erdogan H	Turkey, 2010
Flury D	Switzerland, 2017
Hamdi A	Saudi Arabia, 2019
Hashemi SH	Iran, 2007
Iglesias G	Spain, 1997
Jabalamelı M	Iran, 2016
Jabalamelı M	Iran, 2021
Karaaslan F	Turkey, 2014
Kasim RA	Lebanon, 2004
Kim SJ	Republic of Korea, 2017
Klassov Y	Israel, 2016
Lewis JM	United Kingdom, 2016
Maalouf P	Lebanon, 2018
Malizos KN	Greece, 1997
Marbach F	Italy, 2007
Marchese M	Italy, 2006
Mortazavi SMJ	Iran, 2017
Ortega-Andreu M	Spain, 2002
Ortı A	Spain, 1997
Oner M	Turkey, 2012
Papastergiou SG	Greece, 2011
Ruiz-Iban MA	Spain, 2006
Sazegari MA	Iran, 2016
Tassinari E	Italy, 2008
Tena D	Spain, 2007
Turvey S	Canada, 2017
Walsh J	Ireland, 2019
Weil Y	Israel, 2003
Wünschel M	Germany, 2011
Total	28

In most of the cases, the authors recommended at least 6 weeks of treatment (10-13). High relapse rates have been reported with monotherapy in the treatment of Brucella knee infections. Rifampin, doxycycline, ciprofloxacin, trimethoprim-sulfamethoxazole, and aminoglycosides are effective in the treatment of brucellosis. Long-term antibiotherapy is recommended in

the treatment of prosthetic infections due to Brucellosis, and the recommended combinations are Doxycycline-Streptomycin, Rifampicin-Doxycycline, Rifampicin-Cotrimoxazole, and the duration of treatment varies between 6 months and 26 months (14-21). It is important for the success of the treatment to determine a common approach by acting together with orthopedists, infectious diseases specialists and microbiologists in treatment. While the authors thought that brucella-related knee prosthesis infections without radiological loosening could be treated with double or triple antibiotic therapy without surgery, they considered that two-stage revision surgery should be performed in cases where there is radiological loosening (20, 22).

In the reported cases, Weil et al. Recurrence was observed in a patient who was treated with tetracycline twice by their patients (10, 22). In 2016, Klassove et al. added trimethoprim-sulfamethoxazole as the third antibiotherapy in their patients who could not achieve the desired results with two-stage revision surgery and rifampin and doxycycline, and they achieved success after 6 months of triple antibiotic therapy (18, 23). In studies, the use of bone cement with antibiotics reduced the infection rate. and it has been shown to prevent recurrence (10, 24).

CONCLUSION

Successful results are observed with 2-stage revision arthroplasty and at least dual antibiotic therapy in prosthetic infections due to Brucella. In addition, it is beneficial that the cement used is antibiotic proof. The use of long-term combined antibiotics is important in the success of treatment. Care should be taken after traveling to endemic regions, and care should be taken about the consumption of non-pasteurized dairy products. New studies on this subject, which has very few publications in the literature, will guide us in terms of appropriate treatment.

ETHICAL DECLARATIONS

Ethics Committee Approval: This study data were obtained digitally, ethics committee approval is not required.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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