

Brucellosis: An Outpatient Non-Probability Retrospective Study of 199 Patients

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How to cite this paper: Al Ramahi, J.W. (2024) Brucellosis: An Outpatient Non-Probability Retrospective Study of 199 Patients. *Advances in Infectious Diseases*, 14, 549-562. <https://doi.org/10.4236/aid.2024.143040>

Received: July 21, 2024

Accepted: August 30, 2024

Published: September 2, 2024

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Abstract

Background: A descriptive study of the characteristics of brucellosis patients in Jordan and antimicrobial therapy. **Methods:** In an outpatient study, records were reviewed between July 2016 and April 2024 and electronically saved. Brucella diagnosis was based on epidemiological factors, risk factors, the standard tube agglutination test (STA), and blood or tissue cultures. Records were uploaded into a spreadsheet and imported into the R-Program. A 2-sample Kruskal-Wallis rank sum tested the equality of proportions between two treatment regimens for all available and spondylodiscitis, $P < 0.05$ was considered significant. **Results:** Two hundred patients with Brucellosis were analyzed; males 106 (53%) with a mean age of 46.8 years, and females 94 (47%) with a mean age of 48.1 years. Patients from Jordan were 159 (79.9%), and the Arabian Peninsula 25 (12.6%). Brucellosis was a non-focal presentation in 121 (60.50%) patients, spondylodiscitis in 64 (32.0%), and sacroiliitis in 7 (3.5%). Spondylodiscitis involved lumbar 48 (75.0%), thoracic 11 (17.20%), and cervical 5 (7.8%). STA was a common diagnostic method (188, 94%). Risk factors included cheese 80 (47.3%), cattle, small ruminants, and she-camel milk 37 (21.89%), dairy products 28 (16.57%), meat 9 (05.33%), and working with cattle 10 (05.92%). ESR was highest in spondylodiscitis (mean of 54.5). Imaging studies commonly requested were MRI and Bone scans. Doxycycline/Rifampin were mostly prescribed antimicrobials. **Conclusion:** There is no clear guidance on brucella treatment. In endemic areas, brucella is still a concern. Population education must be a priority. Support for randomized trials addressing antimicrobials and durations is extremely needed.

Keywords

Brucella Spondylodiscitis, Brucella Sacroiliitis, Brucellosis in Jordan, Brucella Treatment, Quinolones in Brucellosis

1. Introduction

Brucella is a zoonotic infection, a seroprevalence study in Jordan demonstrated 6.7% of the screened individuals tested positive in 2022 [1], while in the same year, a seroprevalence of 10% was detected in Jordan among the Syrian refugees. With the new Millennium, the incidence of brucella reached high levels in the country; in 2012 it reached a low prevalence of 1/10,000 population, a setback in 2017 caused to reach up to 4.6/10,000, it was associated with the Syrian civil war, population movement, and crossing the borders with their cattle was blamed [2] [3].

Though the Brucella genus contains many species, in Jordan a molecular study of 630 specimens was analyzed by a whole genome multilocus sequence typing (wgMLST) and demonstrated that the commonly diagnosed species in animals and humans are *B. melitensis* and *B. abortus*, [4] [5] with no data on the antimicrobial susceptibility. Infection is transmitted to humans through several mechanisms all of which are based on drinking unboiled milk, eating dairy products, improperly cooked or uncooked meat, contact with sheep, goats, the Arabian she-dromedary, cattle, taking care of them, and contact with their hemolymph in slaughterhouses [6]. A large Brucella outbreak occurred in China while a Bio-pharmaceutical plant was producing the Brucella vaccine, failure of proper sanitization allowed the contaminated waste in the form of aerosol to be leaked into the air with the direction of the wind, and more than 10,000 individuals were infected [7] [8]. Other transmission methods were laboratory and sexual transmission, though the sexual was not well documented [9] [10], Brucella infection causes several clinical presentations including the non-focal form, spondylodiscitis, sacroiliitis, arthritis, epididymoorchitis, and the uncommonly diagnosed osteomyelitis, infective endocarditis, and neurobrucellosis [11] [12]. It may be considered in the differential diagnosis of fever of unknown origin [13], and rarely reported as thyroiditis [14].

This study describes several clinical aspects of the commonly diagnosed presentations, risk factors, laboratory and imaging workup, and the treatment regimen in non-focal and spondylodiscitis making an effort to gain confidence in the antimicrobials' treatment approach of the various clinical syndromes, particularly randomized controlled studies are either infrequent or underpowered.

2. Materials and Methods

2.1. Settings

This is a retrospective single-center outpatient study in Amman, Jordan, it accepts exclusively infectious disease cases. The patients were recruited between July 2016 and April 2024 and mostly were referred from the country, in addition to walk-ins, a cross-sectional convenience non-probability sampling was collected from the author's clinic outpatient files. For a few admitted patients, their records were reviewed and kept electronically as Microsoft Word and saved into the Brucella folder over the years as an Excel spreadsheet (MS Corporation).

2.2. Included Patients

Records of the patients managed as outpatients were reviewed, a few patients were earlier admitted for evaluation as fever, diagnosed as brucellosis, treated, and discharged to return to the clinic. The diagnosis of Brucella was based on the history including epidemiological factors, risk factors, the standard (micro)tube agglutination test (STA) with a cut limit of 1/160, and blood or tissue cultures. Patients were included if they were referred while they were not on treatment, treatment started elsewhere, patients presented by the end of therapy, finished their treatment, and came for continued care or opinion and advice on the next step in their management.

2.3. Definitions

Non-focal brucellosis: fever syndrome, aches, pains, loss of energy with sweating without focal anatomical disease. Improvement: Disappearance of all symptoms related to brucella infection, and/or negative STA a year after end of therapy. Partial improvement: Persistent milder symptoms with no objective evidence for disease activity. No improvement: Fever and subjective feelings of aches and pains not explained by other conditions, and a positive STA a year after treatment with no re-exposure to one of the risk factors. In the case of spondylodiscitis local back bulge or signs of infection/inflammation or new weakness in the lower extremities, and signs of fever, or systemic symptoms related to brucellosis and a positive STA a year after the end of therapy with no re-exposure to one of the risk factors, other focal disease showing new symptoms and evidence of clinical disease activity. Neurobrucellosis: earlier studies defined neurobrucellosis based on four diagnostic criteria which include: 1) Signs and symptoms suggestive of neurobrucellosis, including a severe and persistent headache that interferes with the patient's normal activity, insomnia, confusion, depression, behavior change, incontinence, and neck stiffness, 2) any neurological finding in an examination, 3) a positive finding of Brucella spp. in the cerebrospinal fluid (CSF), and or a positive titer of antibodies targeting brucella in the CSF, lymphocytosis with high protein levels and low glucose levels in CSF, 4) and imaging findings (either cranial magnetic resonance imaging or computed tomography) peculiar to neurobrucellosis [15] [16].

2.4. Statistical Analysis

The patients' records were uploaded into a spreadsheet through Google Forms and then to an MS-excel, sheet, and a comma-separated variables (CSV delimited) spreadsheet was generated and then imported into R (*R version 4.2.3 (2023-03-15 ucrt. Shortstop Beagle)*), and R studio [17]. A descriptive data analysis including frequency, rates, means, standard deviations, and the range for some variables. Due to the small count of some table cells, analysis for the difference in outcome between the two antimicrobials regimens was calculated by the 2-sample Kruskal-Wallis rank sum test for equality of proportions with continuity correction to detect significance in the difference, which was considered for $P < 0.05$.

3. Results

Two hundred patients were treated and considered for analysis, including all clinical presentations (**Table 1**). There were 106 (53%) males with a mean age of 46.8 years, (SD = 20.8, and range of 3 - 86), and 93 (47%) females with a mean age of 48.1 years (SD = 20.6, and range of 3 - 85). The patients came from Jordan 158 (79.8%), the Arabian Peninsula 25 (12.6%), and 15 (7.5%) from other Arabian countries. The commonest diagnoses were: non-focal presentation diagnosed in 121 (60.5%) patients, spondylodiscitis in 64 (32.0%), sacroiliitis in 7 (3.5%), osteomyelitis/arthritis 5 (2.5%), and epididymoorchitis 2(1.0%). Among the 64 patients with spondylodiscitis, the commonest sites were: lumbar 48 (75.0%), thoracic 11 (17.2%), and cervical 5 (7.8%). Diagnostic methods were utilized in all patients (N = 200), the commonest was STA in 188 (94%) of patients, blood cultures growing brucella species in 10 (5.0%), ELISA 1 (0.5%), and one patient had lumbar bone biopsy culture grew *Brucella* 1 (0.5%), and her brucella STA was negative. Risk factors associated with Brucellosis in 164 patients were: white cheese in 80 (47.3%), sheep/goat/cow/she-camel milk in 37 (21.89%), different formulations of dairy products in 28 (16.57%), work with cattle 10 (5.92%), and improperly cooked (Kabab) or raw meat (Kubbeh) in 9 (5.33%) of patients.

ESR had a mean of 46.0 (SD 20.3, range 1 - 137). The highest mean ESR was in spondylodiscitis 52.4 (27.9, 2.0 - 137), sacroiliitis 43.3 (10.0, 28.0 - 60), non-focal brucellosis 43.7 (14.5, 1 - 105), and epididymoorchitis 40 (8.47, 34 - 46). Other laboratory tests showed normal ALT in 179/188 (95.2%) of patients. The patient's white blood cells had normal counts of 189/193 (94.5%). Imaging studies were mostly MRI, which was requested 59 times (69.41%), and Tc-HDP Bone Scan in 22 (25.88%), followed by CT scan in 3 (3.53%) patients, and one plain (1.18%).

A history of a recent family brucellosis in the index case was reported in 24/196 (12.96%) patients. A follow-up brucella test-of-cure after one year was negative in 35/35 (100%) of those who returned to the clinic for a final checkup, however, 18 (52.94%) of them needed further 2ME-STA test due to the absence of symptoms and the STA was $\geq 1/160$ before deciding on retreatment, and all were negative. One had a negative Tc-HDP Bone Scan after one year of treatment for Spondylodiscitis (self-requested).

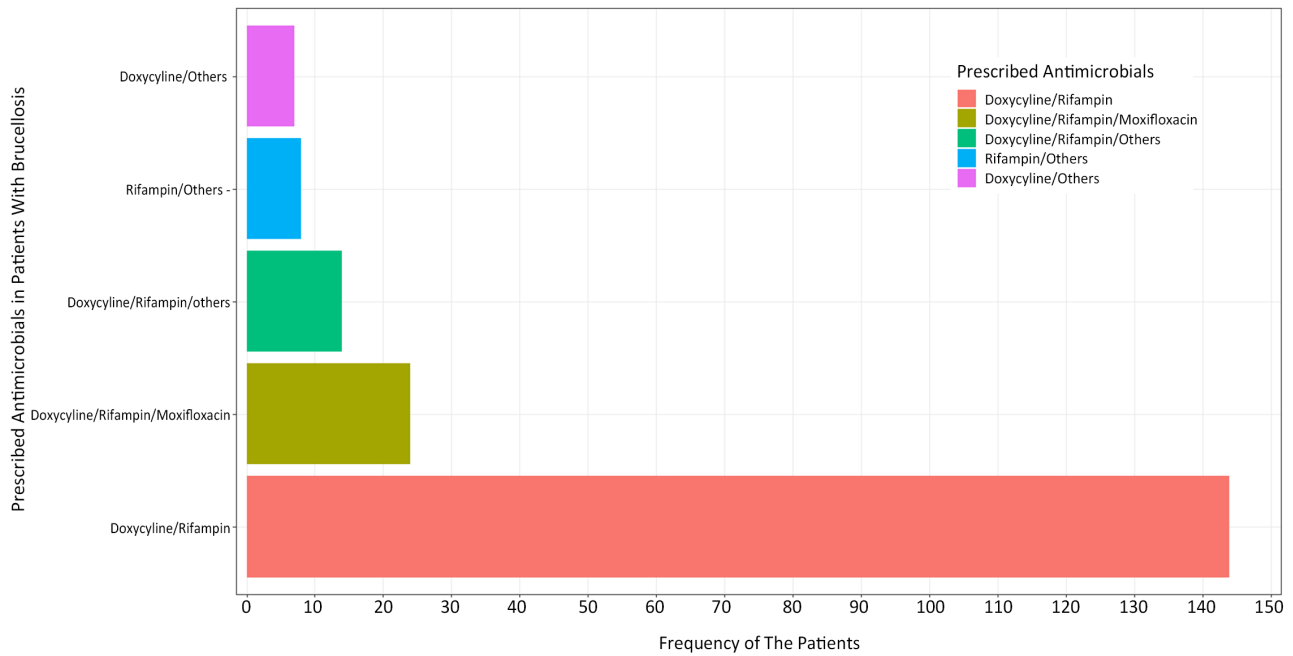
Data on antimicrobial therapy was available in 197 patients (**Figure 1**) with various *Brucella* clinical presentations: Doxycycline/Rifampin were the commonest prescribed regimens 143 (72.6%), and combined with Moxifloxacin in 24 (12.2%) of patients. Or combined with another agent 14 (7.1%) including a fluoroquinolone, TMP/SMX. Streptomycin, and a β -lactam replaced Doxycycline/rifampin in 8 (4.1%). Doxycycline/Rifampin were commonly prescribed antimicrobials, followed by an addition of fluoroquinolones, especially Moxifloxacin (**Figure 1**). The Sites for *Brucella* clinical presentations, their Frequency, and their Distribution Based on Antimicrobial Treatment showed that Doxycy-

cline/Rifampin led the way in spondylodiscitis, sacroiliitis, and other clinical presentations (Figure 2).

Table 1. Characteristics of 200 patients with brucellosis referred to the infectious diseases clinic (July 2016 - April 2024).

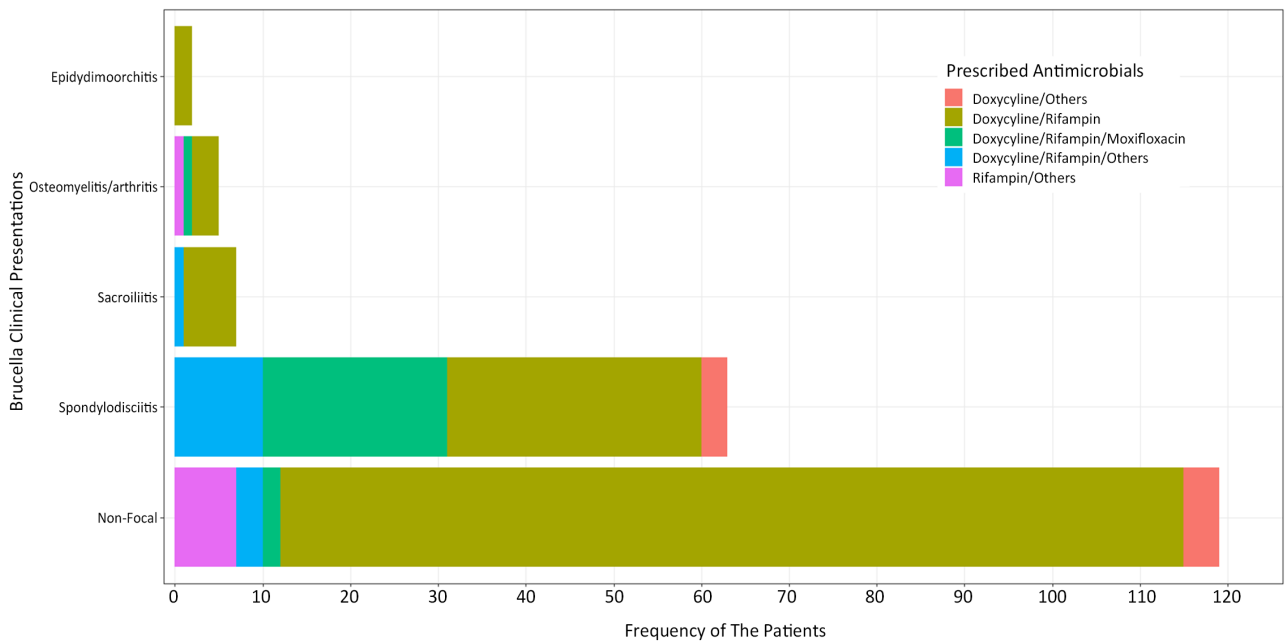
Characteristics	Total (N)	Categories	Frequency N (%)
Age (Mean, SD, Range)			
Male	199	46.8 (20.8, 3 - 86)	106 (53.0)
Female		47.9 (20.6, 3 - 85)	93 (47.0)
Country*	189	Jordan	158 (79.8)
		Arabian Peninsula	25 (12.6)
		Other Arabian Countries	15 (7.6)
Diagnosis	189	Non-focal**	121 (60.8)
		*Spondylodiscitis	64 (32.2)
		Sacroiliitis	7 (3.5)
		Osteomyelitis/arthriti	5 (2.5)
		Epididymo-orchiti	2 (1.0)
Spondylodisciti	64	Lumbosacral	48 (75.0)
		Thoracic	11 (17.2)
		Cervical	5 (7.8)
Diagnostic method	199	STA	187 (93.97)
		Blood culture	10 (5.03)
		Bone culture	1 (0.5)
		ELISA	1 (0.5)
Risk factors	168	White cheese	84 (50.0)
		Milk	37 (22.02)
		Dairy Products	28 (16.67)
		Works with cattle	10 (05.95)
		Meat (Lamb and Kubbeh)	9 (05.36)
ESR, Mean (SD, Range)	199	All Patients	46.0 (20.3, 1 - 137)
		Spondylodisciti	52.4 (27.9, 2.0 - 137)
		Sacroiliiti	43.3 (10.0, 28.0 - 60)
		Non-focal	43.7 (14.5, 1 - 105)
		Osteomyeliti/Arthriti	25.4 (17.9, 4 - 46)
ALT serum level	187	Normal	178 (95.2)
		Elevated	9 (4.8)
WBC count	192	Normal	188 (97.92)
		Elevated	1 (0.52)
		Low count	3 (1.56)
Imaging	85	MRI	59 (69.41)
		*Tc-HDP Bone Scan	22 (25.88)
		CT scan	3 (3.53)
		Plain roentgenography	1 (1.18)
Family history of Brucella	196	Yes	25(12.76)
		No	171 (87.24)
One-year follow-up (negative STA test)	35	STA	17 (48.57)
		STA + 2-ME [@]	18 (51.43)

SD: Standard deviation. *Other Arabian Countries: Sudan, Iraq, Palestine. SD: Standard Deviation. **Non-focal presentation: fever, sweating, and protean symptoms without focal lesions. *STA: Standard tube agglutination. #Goats, sheep, cows, and She-camel. @2-ME: 2-Mercaptoethanol with STA. ESR: Erythrocyte sedimentation Rate. ^s ^{99m}Tc-HDP Bone Scan: Technetium bone scan.



Others; Trimethoprim-Sulphamethoxazole, beta-lactams, streptomycin, and other quinolones.

Figure 1. Prescribed antimicrobial therapy for 197 patients with brucellosis and all clinical presentations.



Others; Trimethoprim-Sulphamethoxazole, beta-lactams, streptomycin, and other quinolones. A regimen containing TMP/SMX was prescribed for a pregnant woman and 3 pediatric patients with rifampin. *One patient with neuro-brucellosis received Ceftriaxone 2 grams twice daily for 3 weeks with oral Doxycycline/Rifampin 100 mg twice daily and oral Rifampin 600 mg once daily for six months.

Figure 2. The sites of brucella infections, their percent, and their unique distribution based on antimicrobial treatment.

4. Outcomes

Patient outcomes (Table 2) were monitored at three different time intervals 6,

Table 2. The treatment outcomes for patients by the durations six, twelve, and twenty-six weeks of treatment and follow-ups with various clinical diagnoses.

Treatment Duration and Sites of Infection	Total N	Improved n (%)	Partial improvement n (%)	No Improvement n (%)
Six weeks of treatment and follow-up	N = 15	146	10	2
Non-focal	85	80 (94.1)	4 (4.7)	1 (1.2)
Spondylodiscitis	59	53 (89.8)	5 (8.5)	1 (1.7)
Sacroiliitis	7	6 (85.7)	1 (14.3)	0.0
Osteomyelitis and arthritis	4	4 (100)	0.0	0.0
epididymo-orchitis	2	2 (100)	0.0	0.0
Twelve weeks of treatment and follow-up	N = 57	n = 57	0.0	0.0
Non-focal	22	22 (100)	0.0	0.0
Spondylodiscitis	29	29 (100)	0.0	0.0
Sacroiliitis	4	4 (100)	0.0	0.0
Osteomyelitis/arthritis	2	2 (100)	0.0	0.0
Twenty-six weeks of follow-up	N = 50	n = 50	0.0	0.0
Non-focal	17	17(100)	0.0	0.0
Spondylodiscitis	27	27 (100)	0.0	0.0
Sacroiliitis	4	4 (100)	0.0	0.0
Osteomyelitis/Arthritis	1	1 (100)	0.0	0.0
Epididymo-orchitis [#]	1	1(100)	0.0	0.0
One year follow-up for STA	35			
STA				
Non-focal	8	0.0	0.0	0.0
Spondylodiscitis	8	0.0	0.0	0.0
Sacroiliitis	1	0.0	0.0	0.0
STA + 2-ME				
Non-focal	8	0.0	0.0	0.0
Spondylodiscitis	7	0.0	0.0	0.0
Sacroiliitis	3	0.0	0.0	0.0

[#]One patient with osteomyelitis and epididymoorchitis (the same one).

12, and 26 weeks for the available patients. After six weeks of treatment for non-focal brucellosis, 85 patients returned to the clinic, improvement was noted in 80 (94.1%), partially improved 4 (4.7%), and no improvement in 1 (1.2%), on week 12, the patients (N = 22) returned to the clinic for follow-up, and the patients (N = 17) returned to the clinic on week 26 and reported 100% improvement. Other sites of infection showed improvement in all i.e. osteomyelitis 3, and epididymo-orchitis 2. After six weeks of treatment, and among 59 patients with spondylodiscitis improvement was demonstrated in 53 (89.8%), partial improvement in 5 (8.5%), and no improvement in 1 (1.7%), seven patients with sacroiliitis were available, 6 (85.7%) patients improved, and 1 (14.3%) partially improved. All patients who returned to the clinic on week 12 showed 100% improvement on follow-up (non-focal 22, spondylodiscitis 29, and sacroiliitis 4), also 100% improvement occurred in patients on week 26 of follow-up (non-focal 17, spondylodiscitis 27, and sacroiliitis 4). Analysis for all patients treated with doxycycline/rifampin or adding moxifloxacin were not statistically different (P =

0.728). A nested analysis for the difference in treating Spondylodiscitis with either doxycycline/rifampin or adding moxifloxacin to the regimen showed no difference in the outcome ($P = 0.190$) by Kruskal-Wallis rank sum test (**Table 3**).

Table 3. The statistical difference between treating patients with brucella spondylodiscitis by week six with doxycycline/rifampin alone or adding moxifloxacin.

Commonly Prescribed Medication	All Patients		P*	Nested for Spondylodiscitis		P*
	Improved	Partial (Not) Improved		Improved	Partial (Not) Improved	
Doxycycline, Rifampin	105	8	0.73	24	3	0.19
Doxycycline, Rifampin, & Moxifloxacin	19	1 (1)		17	1(1)	

*Kruskal-Wallis rank sum test, 2-sample test for equality of proportions with continuity correction, P-value was rounded Kruskal-Wallis rank sum test was used here, some cells are less than five.

5. Discussion

Jordan shares the eastern Mediterranean countries with the high rates of *Brucella*. *Brucella melitensis* rates accounted for almost 50% of the cases, *Brucella abortus* 37%, and the remaining 13% were undefined *Brucella* species [18]. *Brucella* causes a spectrum of clinical presentations, a non-focal clinical presentation accounted for 61% (121 patients), higher than in a previous study where it caught 49.7%, but a decade later 2003 - 2005 it became even less at 33.3%, giving way to the increasing rate of the focal forms [19]. Focal brucellosis causes an array of clinical presentations, it causes a devastating disease like what is reported in the current study: spondylodiscitis, sacroiliitis, osteomyelitis and arthritis, and epididymoorchitis.

Spondylodiscitis is the most frequent focal disease secondary to *Brucella* infection and was 32% in our patients. Earlier studies pointed out that the incidence of spondylodiscitis in *Brucella* patients reached up to 60%, this high rate may be due to delayed diagnosis in areas with low endemicity. Spine involvement mostly affects the lumbosacral spine (75%) followed by thoracic (15.6%) and (7.8%) in the cervical spine almost similar to other reports on spondylodiscitis, and *Brucella* spondylodiscitis [19]-[22]. Clinically, STA, and imaging studies diagnosed seven patients (3.5 %) with sacroiliitis, which were narratively sensitive and specific procedures for diagnosing brucella sacroiliitis, and should not be missed given the careful attention to the patient history [23]. Although sacroiliitis is readily diagnosed in countries with high *Brucella* prevalence, it may be missed and a delay in diagnosis in low-prevalence countries occurs possibly due to the several differential diagnoses of sacroiliitis [24] [25]. The rates of sacroiliitis in China at 2% were close to what this study cites at 3.5% [26], unlike what was reported from Iran cited as high as 13.6% [27].

Despite the well-known risk factors for brucella infection, brucella is still endemic in some parts of the world, including our region. Regional social and po-

litical instability and the local norms and traditions in handling milk and its products are tightly tied with the burden of brucellosis, frequently milk is collected from unvaccinated animals away from the local authorities' supervision [28]. Usually, brucellosis increases sharply in Jordan during spring after delivery of the small ruminants. People become at risk when exposed to milk processing and tasting its products before sterilization, like white cheese and Shanina (similar to buttermilk). Cattle and she-camel milk occasionally cause limited outbreaks in Jordan [29]. A few of our patients consume raw minced beef or lamb (raw Kubbeh), in addition to working and raising small ruminants [30].

Not all laboratory values have thrown light on their significance in brucellosis; white blood cell count was almost normal in all patients denoting its lack of importance as a diagnostic tool [31], brucella affects the liver as part of the reticuloendothelial system infection, in our patients ALT was elevated in 9 patients (4.8%) as transaminitis, with no serious sequelae. Similar to what was observed in studies from Türkiye, where liver involvement was a benign process [32] [33].

In high-prevalence areas, *Brucella* endemicity is expected to correlate well with a family history of the index case, they usually share the same risk factors in some socioeconomic classes. In Jordan and as reported from Türkiye milk products are the leading risk factors, especially white cheese during its preparation. However, in this study, a family history of brucellosis was not helpful, only 24 patients (12.69%) gave a family history of brucellosis, patients tend to hide an infection in the other family members especially if they commercially raise small ruminant herds, dromedary, or own a local dairy factory to save the family business [34]. Despite the frequent denial, obtaining a family history of brucellosis in endemic areas, and elsewhere, is crucial and evident in patients with non-specific protean symptoms like fever, arthralgias, myalgias, back pains, and hepatosplenomegaly [35].

Some patients after being treated properly in endemic areas believe that they suffer from recurrent brucellosis yearly in the same season, frequently it is a reinfection and not a relapse, because people do not quit their practices while dealing with collecting and processing milk, the dairy products, and animal husbandry. We did not observe relapses in the 6-week return of 156 patient visits, and up to 6 months, though the number of return-to-clinic patients was less.

A Spanish study conducted on 167 patients in 1995 - 1999 found a 1.37% relapse rate after 45 days of Doxycycline/Rifampin compared with a 30-day treatment duration where relapse was very high around 12.3% [36]. Furthermore, our patients were referred to an infectious disease clinic, and were supposed to have selection bias towards more complicated cases, we did not observe in the 35 returned-to-the-clinic patients a relapse, or a phone call from others, as usually they do for complaints. An important follow-up obligation for treated patients is to ensure an absent regression to resume risk factors, and to request an STA test (± 2 -ME) a year after the end of treatment before declaring a relapse or reinfection. A year after the end of treatment, 35 (17.5%) patients were tested and fi-

nally all were negative: 17 (48.57%) patients had negative initial STA, and 18 (51.43%) patients had a positive STA but all converted to negative with the addition of 2-mercaptoethanol [37] [38]. An important concept to be disseminated at large and in endemic areas is that human immunity to a new infection does not occur, and a protective human vaccine is not available in the foreseeable future [39]-[41].

WHO treatment options for non-Focal adult brucellosis include doxycycline 100 mg twice a day for 45 days, plus streptomycin 1 g daily for 15 days. An alternative regimen is doxycycline at 100 mg, twice a day, plus rifampicin at 15 mg/kg/day, combined for 45 days. However, the US-CDC recommends a combined regimen of doxycycline/Rifampin for ≥ 6 weeks for the treatment of uncomplicated (non-focal) infections [42] [43]. The clinic practice in Jordan for more than three decades is to prescribe a regimen of Doxycycline/Rifampin similar to what is being recommended by the US-CDC. Streptomycin is too toxic to be a regular option in the presence of a highly effective oral regimen devoid of serious chronic side effects. In a prospective randomized trial in 1985 by J Ariza *et al*, Doxycycline/Rifampin was compared versus tetracycline hydrochloride /Streptomycin, defervescence rates were similar for both, relapse occurred in both regimens and was higher with the Doxycycline/Rifampin ($P = 0.024$), however, both were prescribed only for 30 days duration [44], another randomized controlled trial on the treatment of Brucellosis with Doxycycline/Rifampin or Doxycycline/Streptomycin for 45 days with around 16 months mean follow-up, both were efficacious in most patients with brucellosis but Doxycycline/ Rifampin might be less effective in spondylodiscitis [45]. Our experience showed improvement at six weeks of follow-up, and all return-to-clinic patients improved by the 12th and 26th weeks and the one-year return for STA test (Table 2). A nested analysis for treating spondylodiscitis with Doxycycline/Rifampin versus adding a fluoroquinolone (here moxifloxacin) in the first four weeks to the regimen did not add more recovery benefit by week six ($P = 0.317$). The Seven patients with sacroiliitis were treated with Doxycycline/Rifampin for 12 weeks except one with an added undefined antimicrobial agent, all showed improvement, and none of the patients returned with persistent symptoms or relapse. Hitherto, the literature is not decisive on the treatment of sacroiliitis and the duration, some regimens contain doxycycline/Rifampin with an aminoglycoside [27].

Doxycycline/Rifampin were the backbones for the other focal Brucellosis in this study and were a few in count, two osteomyelitis/arthritis patients were treated with the addition of moxifloxacin, one with Rifampin and TMP/SMX. The treatment of epididymoorchitis was for six weeks with Doxycycline/Rifampin. Even though there is no consensus or trials on this issue, it is tempting to use ceftriaxone initially for its adequate CSF levels, combined with a prolonged treatment period with Doxycycline/Rifampin, possibly 4 - 6 months [14] [46].

In conclusion, *Brucella* infection is still endemic in our region, and it is not lessening with the ongoing geopolitical unrest and refugee movement across borders. Brucellosis may have several clinical presentations and its consideration

in the differential diagnosis as focal and non-focal disease should be suspected in approaching patients presenting with or without protean symptoms. Despite the well-described risk factors, control over the spread of infection is far from near, as the social tradition is deeply rooted in small local vendors' preparation of milk products, away from officials' attention. An objective definition and guidance in diagnosing relapses versus reinfection needed to be clarified, to utilize STA with the 2-ME test to ensure cure or not after a year of the end of therapy. In our opinion, Doxycycline/Rifampin is still the main corner in the treatment of adult forms of brucellosis, streptomycin should be avoided for its toxicity and lack of well-documented studies to address streptomycin containing regimen clear superiority over doxycycline/Rifampin.

Acknowledgment

Thanks to the medical secretary (Hala Wadi) for uploading data from the medical files making this study possible.

Authors' contributions

The corresponding author designed the included data and worked with R-program for statistical analysis.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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