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Research Article

Prevalence and Determinants of Focal Brucellosis in a Tertiary Healthcare Center in Taif, Saudi Arabia (2020-2023)

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Abstract

Background: The most commonly described complication of brucellosis in humans is the infection of bones and joints, which is predominantly reported in all ages and both sexes in high-risk regions. Thus, implementing early management and diagnostic modalities to identify high risk group for developing such complications is of vital importance. **Objectives:** To determine prevalence of focal-complicated-brucellosis and identify risk factors associated with focal disease. **Material and methods:** A retrospective chart-review study was conducted at the Infectious Disease Clinic, Alhada Military Hospital; Taif, Saudi Arabia included all Brucellosis cases diagnosed between 2020 and 2023. Data were collected from patient files based on ICD codes, positive culture of Brucella species or serology (titre 1:160 or more), and clinical manifestations suggestive of brucellosis. **Results:** A total of 146 patients with confirmed Brucellosis were included in the study. Their age ranged between 15 and 86 years with a mean±SD of 53.0±17.2 years. Almost two-thirds (64.4%) were males. Intake of unpasteurized milk products was the commonest reported mode of brucellas transmission (80.7%). The median (interquartile range) of Charlson Index was 2 (0-3). Slightly less than half (48.6%) of cases had focal brucellosis. With each increase in age by one year, there was an increase in the risk of developing focal brucellosis by 2% (adjusted odds ratio "aOR": 1.02, 95% confidence interval "CI": 1.001-1.04, p=0.037. Charlson Index was not significantly associated with development of focal brucellosis, after controlling for the effect of confounders. **Conclusion:** Focal brucellosis is a common status of patients with brucellosis. It is more likely to affect older patients. Thus, close monitoring of those patients is of vital importance.

Keywords: Brucellosis; Focal; Prevalence; Associated factors; Saudi Arabia

Introduction

Brucellosis is a zoonotic infection caused by the bacterial genus Brucella. The bacteria are transmitted from animals to humans by ingestion through infected food products, direct contact with an infected animal, or inhalation of aerosols. Brucella organisms, which are small aerobic intracellular coccobacilli are traditionally classified according to their preferred animal host, and four species, each comprising several biovars, are recognized in humans: *B. melitensis* (goats, sheep and camel), *B. abortus* (cattle), *B. suis* (pigs) and *B. canis* (dogs). The organisms may survive in unpasteurized white soft goat cheese for up to 8 weeks and die within 60-90 days in cheese that has undergone lactic acid fermentation. Freezing dairy products or meat does not destroy the organisms, but they are killed by pasteurization and boiling. The organisms are shed in animal urine, stool, and products of

conception, and remain viable in soil for 40 days or more [1,2].

The global burden of human brucellosis remains enormous. The organism causes more than 500,000 infections per year worldwide. The distribution of brucellosis is worldwide, but a high prevalence in certain geographical areas in the Mediterranean region, Indian subcontinent, Mexico, and Central and South America is well recognized. *B. melitensis* is the most common cause of brucellosis in the world [3]. Saudi Arabia has an infection rate of about 70 per 100,000 people [4]. An annual global incidence of more than 500,000 and more than 10/100,000 of the population in some affected countries [1].

The incubation period of brucellosis is about 1 to 3 weeks but may extend up to several months. Brucellosis should be considered in any patient whose place of residence or dietary, travel, or occupational history suggests a risk for the infection and who is experiencing any of the various known neurologic or non-neurologic complications of brucellosis. Classification of brucellosis as acute, subacute, chronic, serological, bacteraemic or mixed types serves no purpose in diagnosis and management. The term 'active brucellosis with/ without localization' is recommended [1].

The most commonly described complication of brucellosis in humans is the infection of bones and joints, which is predominantly reported in all ages and sexes in high-risk regions, such as the Middle East, Asia, South and Central America, and Africa. It is estimated that prevalence of osteoarticular brucellosis with estimates ranging from 27% in low-risk regions to 36% in high-risk regions [3].

Genitourinary, neuropsychiatric [5], cardiovascular [5-7], pulmonary [8] and skin soft tissue involvement [9] are also well recognized complication of the disease [5,7]. Due to large number of cases presented to our clinic, we planned to do retrospective analysis of these cases in order to determine the prevalence of focal (complicated) disease in order to try to implement early management and diagnostic modalities to detect the diagnosis earlier and to try to identify high risk group for such endemic disease whom at higher risk to develop complications.

Material and Methods

A retrospective chart-review study was conducted at the Infectious Disease Clinic, Al-Hada Military Hospital; Taif, Saudi Arabia included all Brucellosis cases diagnosed between 2020 and 2023. Al Hada Armed Forces Hospital is a tertiary care academic hospital with a bed capacity of 371 beds and provides diagnostic and therapeutic services to local patients from Taif City and adjacent suburbs and considered as a regional referral center for critically ill and complex patients. Data were collected from patient files based on ICD codes, positive culture of Brucella species or serology (titer 1:160 or more), and clinical manifestations titer suggestive of brucellosis such as fever, sweats, malaise, and muscle pain or focal manifestation.

A checklist was prepared to collect data extracted from patients` file including demographic data (patient`s age, gender), and clinical data (focal or non-focal disease, site of the focal disease, Charlson index, complications). Ethical approval was obtained from the regional Research and Ethics Committee at Al-Hada Armed Forces hospital.

Data entry and statistical analysis

Data entry and statistical analysis were performed using the Statistical Package for Social Sciences (SPSS), version 28. Data were described using frequency and percentage for categorical variables while mean, median, standard deviation and interquartile range were used for numerical variables. Univariate analysis was done utilizing independent two sample t-test, Mann-Whitney test and Chi-square test. Multivariate analysis expressed as adjusted odds ratio (aOR) and 95% Confidence Interval (CI) was done to control for the effect of confounding. P-value ≤0.5 was considered statistically significant.

Results

A total of 146 patients with confirmed Brucellosis were included in the study. Their age ranged between 15 and 86 years with a mean±SD of 53.0±17.2 years. Almost two-thirds (64.4%) were males (Table 1).

Variables	Description
Age (years)	
Range	15-86
Mean ± SD	53.0 ± 17.2
Gender (N; %)	
Male	94; 64.4%
Female	52; 35.9%
SD: Standard Deviation	

Table 1: Age and gender distribution of 146 cases of Brucellosis, Al-Hada Armed Forces hospital (Taif): 2020-2023.

Intake of unpasteurized milk products was the commonest reported mode of brucellas transmission (29%), while contact with animals and both were reported by 11% and 8.3% of patients, respectively whereas 51.7 of patients reported no clear source of infection. Co-morbidity was observed among 61.6% of patients. The median (interquartile range) of Charlson Index was 2 (0-3) (Table 2).

Variables	Frequency	Percentage
Mode of transmission (n=145)		
No clear source	75	51.7
Intake of unpasteurized milk products	42	29
Contact with animals	16	11
Both	12	8.3
Co-morbid diseases		
No	56	38.4
Yes	90	61.6
Charlson Index (n=145)		
Median	2	
Interquartile range	0-3	

Table 2: Clinical characteristics of 146 cases of Brucellosis, Al-Hada Armed Forces hospital (Taif): 2020-2023.

Slightly less than half (48.6%) of cases had focal brucellosis as displayed in Figure 1. Regarding systems involved with focal brucellosis, joints ranked first (40.8%), followed by bones (36.6%) and genitourinary tract (15.5%) (Figure 2) while regarding focus site among patients with focal brucellosis, the most frequently reported was lumber spine (23.9%), followed by knee joint (22.5%) and epididimo-orchitis (15.5%) (Figure 3).

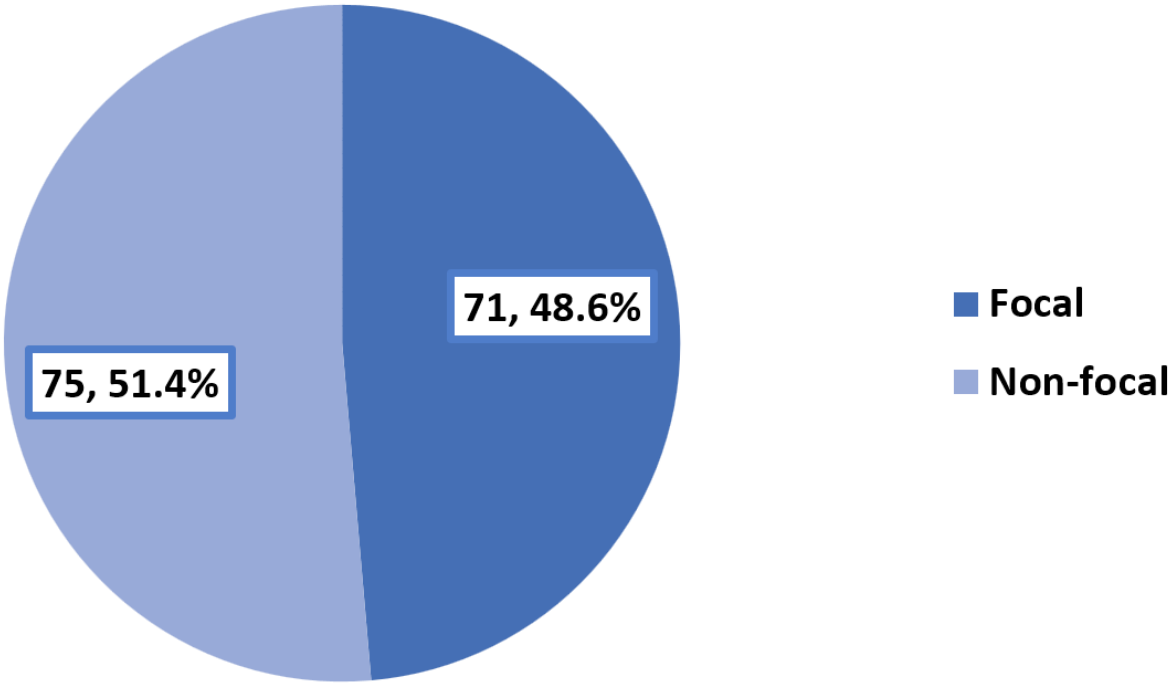

Figure 1: Prevalence of focal type among patients diagnosed with Brucellosis, Al-Hada Armed Forces hospital (Taif): 2020-2023.

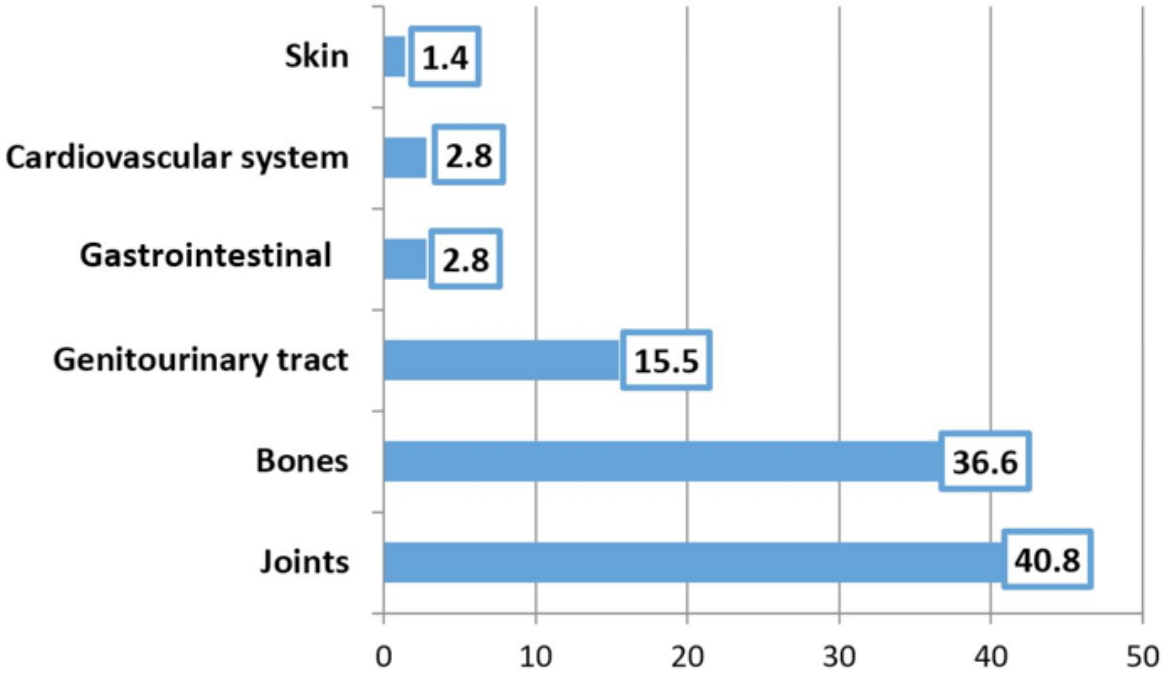

Figure 2: Systems involved with focal brucellosis (n=71).

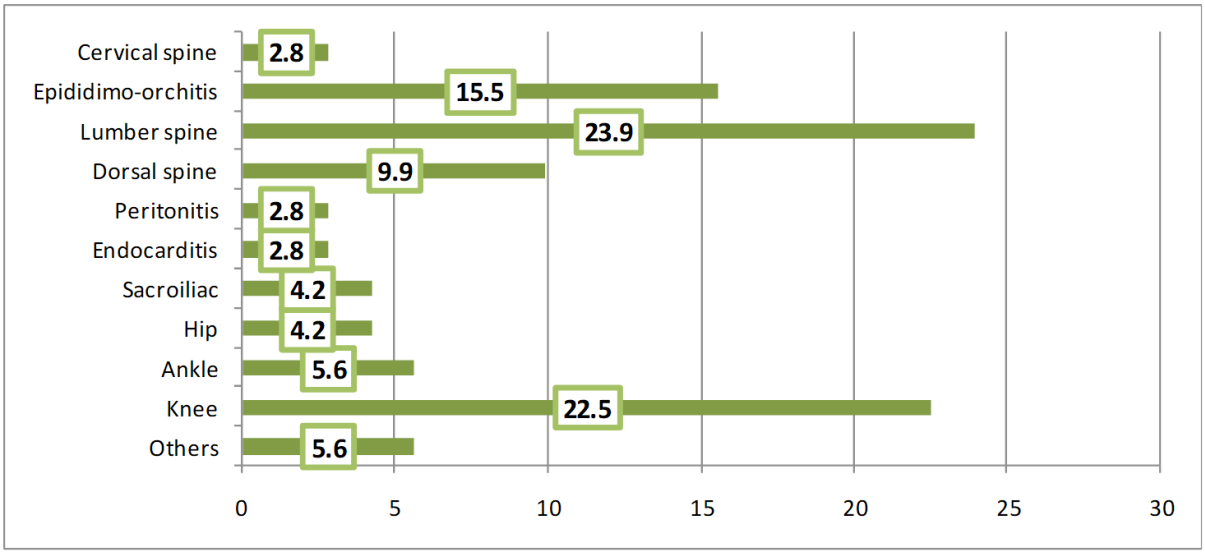

Figure 3: Focus site among patients with focal brucellosis (n=71).

The age of patients with focal brucellosis was significantly higher than that of those without focal brucellosis (56.0±16.9 vs. 50.1±17.1), p=0.040. The highest rate of focal brucellosis was observed among patients who reported both of intakes of unpasteurized milk products and contact with animals as mode of brucella transmission (75%) whereas the lowest one was observed among those who reported only contract with animals (31.2%). However, the difference was borderline insignificant, p=0.051. The Charlson Index score was significantly higher among patients with focal brucellosis compared to their peers (mean ranks were 81.24 and 65.31, respectively (p=0.019). Patients` gender and mode of brucella transmission were not significantly associated with focal brucellosis (Table 3).

	Focal brucellosis		p-value
	No N=75 N (%)	Yes N=71 N (%)	
Age (years) Mean ± SD	50.1±17.1	56.0±16.9	0.040*
Gender			
Male (n=94)	43 (45.7	51 (54.3)	
Female (n=52)	32 (61.5)	20 (38.5)	0.067**
Mode of transmission (n=145)	**N=75**	**N=70**	
No clear source (n=75)	43 (57.3)	32 (42.7)	
Intake of unpasteurized milk products (n=42)	18 (42.9)	24 (57.1)	
Contact with animals (n=16)	11 (68.8)	5 (31.2)	
Both (n=12)	3 (25.0)	9 (75.0)	0.051**
Co-morbid diseases			
No (n=56)	24 (42.9)	32 (57.1)	
Yes (n=90)	51 (56.7)	39 (43.3)	0.105**
Charlson Index (n=145)	N=75	N=70	
Median	1	2	
Interquartile range	0-3	0-4	
Mean rank	65.31	81.24	0.019•
*Independent two sample t-test; **Chi-square test; •Mann-Whitney test			

Table 3: Factors associated with focal brucellosis: Univariate analysis.

With each increase in age by one year, there was an increase in the risk of developing focal brucellosis by 2% (adjusted odds ratio "aOR": 1.02, 95% confidence interval "CI": 1.001-1.04, p=0.037. Charlson Index was not significantly associated with development of focal brucellosis, after controlling for the effect of confounders (Table 4).

	B	**SE**	**AOR**	**95% CI**	**p-value**
Age	0.021	0.010	1.02	1.001-1.04	0.037
B: Slope ; AOR: Adjusted odds ratio; CI: Confidence interval; SE: Standard deviation. Mode of transmission and Charlson Index were not significant and not included in the final logistic regression model					

Table 4: Predictors of focal brucellosis: Multivariate logistic regression analysis.

Discussion

This study aimed to address some of the factors (demographic and clinical) possibly associated with focal (complicated) brucellosis in order to offer reference for physicians helping them for early diagnosis and prompt management of such cases.

In accordance with others [10], the present study showed that almost half of patients with brucellosis developed complications (i.e. focal brucellosis). Other studies reported rate of focal brucellosis ranged between 21.4% and 90% [11-13].

The present study revealed in univariate analysis that older patients, patients who reported both of intakes of unpasteurized milk products and contact with animals as mode of brucella transmission and those with higher Charlson Index score were more likely to develop focal brucellosis while in multivariate analysis only, patient`s age was a significant predictor for the development of focal brucellosis. In a similar study conducted in China [10], the significant predictors for the development of focal brucellosis were co-morbidity, higher c-reactive protein (CRP) ">10 mg/L" and higher erythrocyte sedimentation rate (ESR).

In the current study, concerning systems involved with focal brucellosis, joints ranked first (40.8%), followed by bones (36.6%) and genitourinary tract (15.5%) while regarding focus site, the most frequently reported was lumber spine (23.9%), followed by knee joint (22.5%) and epididimo-orchitis (15.5%). In Qatar, osteoarticular involvement; namely spine (8.4%) and peripheral joint (3.2%) ranked first, followed by epididimo-orchitis (6.6%) while neurobrucellosis and infective endocarditis were observed among minority of cases [11]. In China, osteoarticular (77%), hematologic (2-53%), and genitourinary systems (2-20%) were commonly involved [14]. In a more recent Chinese study, also osteoarticular involvement ranked first [10]. Thus, focal brucellosis should be included in the differential diagnosis of osteoarthropathy and orchitis; particularly in endemic areas.

In accordance with our findings, other studies indicated more affection of spine and large joints with osteoarticular brucella complications [10,15-17]. Many studies showed an association between delayed diagnosis and development of complications in patients with brucellosis [7,18,19]. Unfortunately, we did not include this important issue in the present study due to its lacking in the patients` records.

Also, some similar studies reported as association between CRP (cut-off of 5.4 mg/L) and ESR (cut-off of 25 mm/h) levels and development of focal involvement in brucellosis [7,10,17,19]. However, in the current study due to unavailability in all patients` recorded, these parameters were not investigated.

Limitations

Important limitations should be addressed in this study. First, being a single healthcare setting study could impact the generalizability of its findings over other healthcare settings in Taif and in Saudi Arabia in general. Second, many other important possible risk factors for the development of focal brucellosis were not included in the present study such as delayed diagnosis and laboratory parameters including ESR and CRP levels. Finally, depending on data collected from patients` files is considered a limitation as it was incomplete in some important aspects. Despite of those limitations, the study is considered unique in its nature in Saudi Arabia, up to our best knowledge and also it investigated an important issue in our region.

Conclusions

Focal brucellosis is a common status of patients with brucellosis. It is more likely to affect older patients. Thus, close monitoring of those patients is of vital importance. Additionally, early treatment should be given to prevent the onset of adverse complications. Further multi-centric study including more investigated risk factors is needed.

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