

# Early predictors of *Brucella* epididymo-orchitis

Abdullah Alarbid, Shady Mohamed Salem<sup>1</sup>, Turkey Alenezi, Abdullah Alenezzi, Khaled Alali, Feras Ajrawi, Faisal Alhajry

Department of Urology, Farwaniya Hospital Kuwait, Al Farwaniyah, <sup>1</sup>Department of Urology, Menofia University, Menofia, Egypt

## Abstract

**Introduction:** Epididymo-orchitis (EO) is a common urological condition. In endemic areas, EO may be the presenting picture of brucellosis. Early suspicion and proper diagnosis is necessary for patient recovery.

**Objective:** The aim of our study is to identify early predictors of *Brucella* EO.

**Patients and Methods:** We retrospectively collected the data of all patients who were treated at the Urology Unit, Farwaniya Hospital, with acute EO above the age of 12 years between April 2017 and February 2019. Data from electronic and hardcopy files were gathered and analyzed. The diagnosis of acute EO was based on clinical, laboratory, and radiological findings. A total of 120 patients under the diagnosis of EO, epididymitis, and orchitis were reviewed. Thirty-one patients were tested for *Brucella* based on the history of animal contact, ingestion of unpasteurized dairy products, or persistent fever for more than 48 h. of those patients, 11 tested positive for *Brucella* orchitis.

**Results:** A comparison between *Brucella*-positive and *Brucella*-negative patients regarding age, presence of fever, complete blood count (CBC) parameters, pyuria, and abscess formation was made. In the *Brucella* group, 72% of the patients had a history of animal contact compared to 33% in non-*Brucella* group ( $P = 0.006$ ). When comparing CBC parameters in the two groups, *Brucella* group had statistically significant lower total leukocytic count and neutrophil count (mean  $\pm$  standard deviation [SD])  $13.07 \pm 4.22$ ,  $6.4 \pm 9.98$  versus *Brucella* negative group  $17.35 \pm 5.28$ ,  $7.8 \pm 10.53$ , and  $P$  values were 0.037 and 0.004, respectively. *Brucella* group showed lymphocytosis (mean  $\pm$  SD)  $25.95 \pm 9.78$  versus non-*Brucella* group  $13.22 \pm 8.05$  and  $P < 0.01$ .

**Conclusion:** *Brucella* orchitis constituted 9% of the orchitis patients treated in our hospital. Patients with a history of animal contact, EO with lymphocytosis, and relative neutropenia should raise the suspicion for *Brucella* orchitis in endemic areas.

**Keywords:** Brucellosis, epididymitis, epididymo-orchitis, orchitis

**Address for correspondence:** Dr. Shady Mohamed Salem, Area 5, Bahrin St. Building 69, Salmia, Kuwait.

E-mail: sh\_dy@yahoo.com

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## INTRODUCTION

Epididymo-orchitis (EO) is a common urologic emergency, and it accounts for 600,000 cases of emergency and clinic visits every year in the United States.<sup>[1]</sup> EO has bimodal age incidence and is usually related either to urinary pathogens

or sexually transmitted pathogens; however, the causative agent is not identifiable in up to 46% of cases.<sup>[2]</sup> As a high incidence of epididymitis and orchitis, the uncommon forms are not unusual in clinical practice, with mumps orchitis, Tuberculosis (T.B) epididymitis, and *Brucella* orchitis are best known unusual variants.<sup>[3]</sup>

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Human brucellosis is the most prevalent zoonotic disease.<sup>[4]</sup> Brucellosis, also known as Mediterranean or Malta fever, is an endemic zoonosis in several parts of the world such as Southern Europe, the Middle East, and Southern America. It is commonly encountered in many developing countries, where it affects more than 500,000 new cases yearly.<sup>[5]</sup> Brucellosis is transmitted through direct and indirect animal contact, contaminated raw milk products, or direct contact with infected tissues. Brucellosis is a multisystemic disease with several various organ or body system involvements genitourinary. Genitourinary complications of brucellosis include EO, prostatitis, cystitis, pyelonephritis, and renal and testicular abscess.<sup>[6]</sup>

Brucellar EO is the most common urogenital complication of brucellosis, and it occurs in 2%–20% of cases. It requires early identification and proper treatment, as it may lead to serious complications such as necrotizing orchitis, testicular abscess, infarction, atrophy, and suppurative necrosis.<sup>[7]</sup>

The management of *Brucella* orchitis requires some significant laboratory investigations such as CBC, urine routine, urine culture, *Brucella* antigen test, and radiological imaging such as testis Doppler ultrasound. Treatment requires the involvement of infectious diseases specialist and usually consists of doxycycline plus rifampin for 6 weeks and may be repeated; surgical intervention is required in case of abscess formation.<sup>[8]</sup>

## Objective

The aim of our study is to identify possible early predictors of *Brucella* EO.

## PATIENTS AND METHODS

This is a retrospective study; data were collected from patients' files and electronic patients' records. The study design was reviewed and approved by the hospital ethical committee.

We retrospectively collected the data of all patients who were treated for acute EO above the age of 12 years in the urology unit at Farwaniya Hospital between April 2017 and February 2019. The diagnosis of acute EO was based on clinical, laboratory, and radiological findings. Patients with incomplete records were excluded from the study.

We identified a total of 120 patients (with complete records) under the diagnosis of EO, epididymitis, and orchitis. Patients who met any of the following criteria were tested for brucellosis history of animal contact, ingestion of unpasteurized dairy products, or had a persistent fever for more than 48 h.

Thirty-one patients met one or more of those criteria and were tested for *Brucella* using *Brucella* antigen test (a test would be considered positive if titer was 1/160 or higher) and *Brucella* blood culture. Of the 31 patients tested, 11 were positive. Then, we compared epidemiological, clinical, and laboratory data between the two groups aiming of identifying possible early identifiers of *Brucella* orchitis, and the data were collected, tabulated, and analyzed using Stata 12.0 software (Stata Corporation, College Station, TX, USA). We used Chi-square test and Mann–Whitney test when appropriate, and  $P < 0.05$  as statistically significant results.

## RESULTS

We identified 120 patients with full records diagnosed as EO; 31 out of 120, around 25.8%, met one or more of the criteria for testing for *Brucella*, and 11 out of the 31 tested were positive, 9.2% of the whole cohort. We divided patients who underwent *Brucella* test into *Brucella* group, they were 11 patients whose test was positive, and non-*Brucella* group, they were 20 patients whose test was negative. Following that, we compared the clinical picture and laboratory results at the presentation [Table 1]. There was no statistical difference between the two groups, with a mean age of  $32.5 \pm 8.9$  years in *Brucella* group and  $32.9 \pm 15.5$  in *Brucella* negative.

Ten patients (90.9%) in *Brucella* group had a persistent fever for more than 2 days compared to 13 (65%) patients

**Table 1: Clinical and laboratory parameters**

Variable	<i>Brucella</i> positive (11)	Non- <i>Brucella</i> (20)	<i>P</i>
Age (years), mean±SD	32.5±8.9	32.9±15.5	0.7256
Persistent fever >2 days (%)			
Negative	1 (9.1)	7 (35)	0.203
Positive	10 (90.9)	13 (65)	
Pyuria (>5 WBC/HPF) in urine routine (%)			
Negative	11 (100)	13 (65)	0.033
Positive	0 (0)	7 (35)	
Pyuria (%)			
Negative	11 (100.0)	13 (65.0)	0.033
Positive	0 (0.0)	7 (35.0)	
History of animal contact (%)			
No	3 (27.27)	16 (80.00)	0.007
Yes	8 (72.72)	4 (20.00)	
CBC parameters, mean±SD			
WBC count	13.07±4.22	17.35±5.28	0.037
Neutrophils	6.4±9.98	7.8±10.53	0.004
Lymphocytes	25.95±9.78	13.22±8.05	0.0003
Neutrophil-to-leukocyte ratio	2.89±1.29	8.15±4.44	0.0003
MPV	9.15±0.88	9.87±1.21	0.13
RDW	12.71±2.70	13.01±1.57	0.91

SD: Standard deviation, WBC: White blood cell, HPF: High-power field, CBC: Complete blood count, MPV: Mean platelet volume, RDW: Red cell distribution width

in non-*Brucella* group, with no statistically significant difference. Pyuria was not detected in any of the *Brucella* groups and was present in 7 (35%) in non-*Brucella* group, and the difference was statistically significant with  $P = 0.03$ .

History of animal contact was found in 8 (73.7%) patients of the *Brucella* group and 4 (20%) patients of the non-*Brucella* group; the difference was statistically significant with  $P = 0.007$ .

Regarding laboratory parameters, total leukocytic count was higher in non-*Brucella* group with  $17.35^3 \pm 5.28^3$  white blood cells (WBCs)/high-power field (HPF), whereas  $13.07^3 \pm 4.22^3$  WBCs/HPF in *Brucella* group with  $P = 0.03$ . Neutrophil counts were lower and lymphocyte counts were higher in the *Brucella* group compared to non-*Brucella* group reading  $6.4^3 \pm 9.98^3$  and  $25.95^3 \pm 9.78^3$  WBCs/HPF versus  $7.8^3 \pm 10.53^3$  and  $13.22^3 \pm 8.05^3$  WBCs/HPF, respectively. Furthermore, there were statistically significant differences in  $P = 0.004$  and  $0.0003$ , respectively. Furthermore, neutrophil-to-total leukocytic (relative neutropenia) count ratio was lower in the brucellosis group ( $2.89 \pm 1.29$ ), whereas in the non-*Brucella* group, it was  $8.15 \pm 4.44$ ; there was a highly significant difference with  $P = 0.0003$ .

After starting of proper management, no patient developed abscess in the *Brucella* group and one patient in the non-*Brucella* group.

## DISCUSSION

Several studies examined the incidence of EO in *Brucella* patients with incidence ranging from 2% to 20%. Celen *et al.* reported 27 (18.8%) cases of EO among 143 male patients treated for brucellosis. Papatsoris *et al.* reported 25 cases of EO (2.5%) among 995 males diagnosed with *Brucella*. The big difference may be attributed to the difference in the clinical diagnostic criteria of EO.<sup>[9,10]</sup>

In our study, we examined the incidence of *Brucella* among patients who presented with EO. Similar approach was done by Papatsoris *et al.*, as they reported 17 *Brucella* EO out of 158 (11%) patients with EO in Greece.<sup>[9]</sup>

Several reports showed excellent outcome of *Brucella* epididymo orchitis (BEO) when identified early and treated properly. Treatment of BEO is different than the standard treatment of standard epididymo orchitis (EO). The key to good outcome are identification and involvement of infectious disease specialists. The use of doxycycline and rifampicin for 6–12 weeks is considered the standard treatment.<sup>[11,12]</sup>

Several reports have tried to establish early predictors of *Brucella* EO. Animal contact and consumption of unpasteurized milk are obvious risk factors; in our study, 8 (73%) out of 11 *Brucella* EO reported animal contact. Similar results were reported by Bosilkovski *et al.*, 74% of the 34 cases with *Brucella* EO have direct animal contact.<sup>[11]</sup>

In our study, we have reported leukocytosis in both groups; however, the rise in leukocytic count was lower in *Brucella* group, with a mean WBCs count of  $13.07^3 \pm 4.22^3$  WBCs/HPF versus  $17.35^3 \pm 5.28^3$  WBCs/HPF in non-*Brucella* group. Colmenero *et al.* have reported even lower leukocytic count of  $7.30 \pm 2.57$  WBCs/HPF in their report of 48 cases of *Brucella* orchitis.<sup>[8]</sup>

In general, brucellosis is associated with relative neutropenia and relative lymphocytosis.<sup>[13,14]</sup> In our study, we found lower neutrophil counts and higher lymphocyte counts in the *Brucella* group compared to the non-*Brucella* group reading  $6.43 \pm 9.983$  and  $25.953 \pm 9.783$  WBCs/HPF versus  $7.83 \pm 10.533$  and  $13.223 \pm 8.053$  WBCs/HPF, respectively. Similar results were reported by Cift and Yucel, they compared 20 cases with *Brucella* EO to 50 cases with non-*Brucella* EO. Lower neutrophil count and higher lymphocyte count in *Brucella* orchitis were statistically significant in their cohort.<sup>[15]</sup>

## CONCLUSION

In endemic areas, *Brucella* orchitis as the first presentation of brucellosis is not uncommon. The history of animal contact is an important clue. In addition, relative neutropenia and lymphocytosis should raise the attention of possible brucellosis.

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## Conflicts of interest

There are no conflicts of interest.

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