

## ORIGINAL RESEARCH

# Clinical characteristics, management, and treatment outcomes of epididymo-orchitis among patients in a referral hospital in Southern Saudi Arabia

Abdullah Ayed<sup>1,†</sup>, Raed Alwadai<sup>2</sup>, Shahzada K. Sohail<sup>3</sup>, Syeda F. Rizvi<sup>3</sup>, Najim Z. Alshahrani<sup>4</sup>, Omar B. Ahmed<sup>5</sup>, Mutasim E. Ibrahim<sup>6,\*</sup>,†

<sup>1</sup>Department of Surgery, College of Medicine, University of Bisha, 67614 Bisha, Saudi Arabia

<sup>2</sup>Department of Urology, King Abdullah Hospital, Ministry of Health, 67714 Bisha, Saudi Arabia

<sup>3</sup>Department of Pathology, College of Medicine, University of Bisha, 67614 Bisha, Saudi Arabia

<sup>4</sup>Department of Family and Community Medicine, Faculty of Medicine, University of Jeddah, 21589 Jeddah, Saudi Arabia

<sup>5</sup>Department of Environmental and Health Research, The Custodian of the Two Holy Mosques Institute for Hajj and Umrah Research, Umm Al-Qura University, 21955 Makkah, Saudi Arabia

<sup>6</sup>Department of Microbiology and Clinical Parasitology, College of Medicine, University of Bisha, 67614 Bisha, Saudi Arabia

\*Correspondence  
meibrahim@ub.edu.sa  
(Mutasim E. Ibrahim)

† These authors contributed equally.

## Abstract

Epididymo-orchitis (EO) is a common genitourinary clinical syndrome in men, and delayed investigation and improper management can lead to complications. This study aimed to analyze clinical and laboratory findings and treatment outcomes in EO patients. We conducted a retrospective record-based study at King Abdullah Hospital in southern Saudi Arabia from 2018 to 2022, reviewing data from 63 EO patients who had a median age of 34 years (range: 16–82 years). The results showed that the most common complaints were scrotal pain and swelling (54%), followed by testicular pain (44.4%). Scrotal ultrasonography showed increased vascularity in both testes and epididymis in 49 patients (77.8%), while 14 patients (22.2%) had epididymal involvement alone. Reactive hydrocele was observed in 15 patients (23.8%), abscesses in seven (11.1%), and hypoechoic lesions in three (3.8%). Anti-*Brucella* antibody titers ( $\geq 1:80$ ) were detected in 22 cases, and 14.3% had positive urine cultures. Of the patients, 87.3% responded well to the initial treatment course, while four (6.3%) were cured after a second course of treatment. EO complications occurred in three cases (4.8%), and one patient (1.6%) succumbed to septicemia. Of the 15 patients treated with ceftriaxone and ciprofloxacin, one required orchiectomy due to non-response. Relapse occurred in one of the 10 patients treated with triple therapy (doxycycline, rifampicin and gentamicin). Among the nine patients treated with ceftriaxone and co-trimoxazole, one did not respond, developed a testicular abscess, and underwent incision and drainage. In conclusion, our study highlights that most cases of EO can be effectively resolved with appropriate antibiotic therapy, particularly combinations containing cefuroxime and/or ciprofloxacin. Clinicians in *Brucella*-endemic regions should consider the possibility of brucellosis as an underlying cause of EO.

## Keywords

Epididymo-orchitis; Management; Treatment outcomes; Complication; Saudi Arabia

## 1. Introduction

Epididymo-orchitis (EO) is a prevalent genitourinary clinical syndrome in men, characterized by inflammation affecting both the epididymis and the corresponding testis, leading to pain and swelling [1, 2]. This inflammation typically arises as a result of infection spreading from the bladder, urethra, prostate, ejaculatory duct and vas deferens [3]. EO can affect individuals of all age groups and represents the most common cause of acute scrotal pain in outpatient healthcare settings [1]. In the United States, the reported annual incidence of EO reaches 600,000 cases, with 250 cases per 10,000 men reported in the United Kingdom [4, 5]. Notably, data from the US reveals that EO ranks as the fifth most frequent urological diagnosis among patients aged between 18 and 50 years attending outpatient facilities [6].

The inflammatory responses associated with EO typically arise from infectious agents or non-infectious factors, such as genitourinary trauma, iatrogenic bladder or urethral instrumentation, amiodarone usage, vasculitis and autoimmune disorders [1, 2]. Sexually transmitted pathogens are the predominant infectious agents responsible for EO in men under the age of 35, while Gram-negative bacteria are more commonly implicated in older men [5]. However, it is important to note that the diagnostic assessment and treatment approach may vary depending on the patient's age [1].

EO is the most frequent complication of *Brucella* infection, with prevalence rates ranging from 1.4% to 25% among affected males [7]. The incidence of human brucellosis has become a significant public health concern in Saudi Arabia, leading to the implementation of various control measures since 1983 [8]. Presently, the hyperendemic nature of bru-

cellosis remains a significant epidemiological challenge in the country, particularly in rural areas [9–12]. Numerous studies have detailed the clinical features and risk factors associated with brucellosis in the southern region of Saudi Arabia [13–15]. Notably, it has been observed that EO is the most common genitourinary complication of brucellosis in endemic regions [2, 16, 17]. A prior investigation conducted in a tertiary care hospital in Riyadh reported EO in 1.6% of patients with brucellosis [18]. Additional studies in Saudi Arabia have documented complications of brucellosis, including testicular abscess [17] and non-caseating granulomatous EO, with a focus on necrosis [19]. Therefore, healthcare practitioners encountering EO cases in endemic areas should be vigilant regarding the potential association with brucellosis [18]. The differential diagnosis of an inflamed scrotum, a common urological emergency, remains a clinical challenge [2, 19, 20]. Nevertheless, it is crucial to highlight that delayed investigation and inappropriate management of EO can lead to various complications, including testicular abscess, atrophy, necrotizing orchitis, testicular infarction, atrophy and male infertility [2, 18].

Given these above considerations, in this present study, we aim to analyze the clinical and laboratory findings and treatment outcomes in patients diagnosed with EO at a referral hospital in southern Saudi Arabia.

## 2. Materials and methods

### 2.1 Study design and setting

A retrospective record-based study was conducted at King Abdullah Hospital (KAH) in the Bisha Province, Aseer region, southern Saudi Arabia, based on treated cases from 2018 to 2022. KAH is the main referral hospital in the province, catering to numerous patients referred from various primary and secondary healthcare centers in the northern Aseer region.

### 2.2 Patients and data

We included adult male inpatients at KAH who presented with acute scrotal pain, swelling and tender enlarged testicles. Eligible patients diagnosed with EO between January 2018 and December 2022 were identified using electronic patient records from the urology department. Their general information, medical history, physical examination findings, comorbidities, complete blood count (CBC) results, routine urinalysis and culture, serological tests for brucellosis and radiological findings were retrieved from patient medical records and hospital databases. All data were gathered anonymously to maintain patient confidentiality.

### 2.3 Diagnosis of epididymitis or epididymo-orchitis

The diagnosis of EO was based on clinical assessment involving scrotal redness and/or swelling, testicular pain, tenderness and the presence of an enlarged, tender testicle and/or epididymis during physical examination [3, 20]. In addition, scrotal ultrasonographic examination and laboratory tests were conducted for confirmation [3, 20], which included CBC, anti-

*Brucella* antibody titers, and routine urinalysis with culture, following established protocols [1, 2]. *Brucella* infection was diagnosed serologically using the standard tube agglutination test [21].

### 2.4 Treatment and follow-up

The patients were treated with single or combinations of antibiotic drugs from various classes following established recommendations [4]. Treatment choices were guided by clinical presentation, drug tolerability, potential side effects and the presence of complications. The drug regimens included intravenous ceftriaxone (2 g per day) for four weeks, intravenous amikacin (1 g daily), and intramuscular gentamicin (240 mg daily) for seven days, along with oral antibiotics administered for a minimum of six weeks: doxycycline (100 mg twice daily), rifampicin (600 mg once daily), ciprofloxacin (500 mg twice daily), and co-trimoxazole (80/400 or 160/800 twice daily). After discharge, the patients underwent routine control visits at three-week intervals and were monitored for six months. Clinical cure was determined by the complete resolution of all disease-related clinical signs and symptoms.

### 2.5 Statistical analysis

The data were analyzed using IBM SPSS version 27.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were employed, with categorical variables presented as frequencies, proportions and counts and continuous variables expressed as either mean  $\pm$  standard deviation or median with interquartile range (IQR).

## 3. Results

Data was collected from 63 EO-diagnosed patients (Table 1). Their median age was 34 years (range 16–82 years), most were Saudi nationals (77.8%,  $n = 49$ ), and approximately half were young adults and adults (54%,  $n = 34$ ). Their median hospital stay was 7 days (IQR = 4 to 10 days), with 38 patients (60.3%) staying for 7 days or less, while 25 patients (39.7%) had admissions exceeding seven days. Among the patients, 55% were smokers, 34.9% had a history of animal contact, 25.4% had comorbidities, and 7.9% reported consuming raw milk.

### 3.1 Clinical findings

Of the 63 patients, 15 (23.8%) presented with fever, eight (12.7%) had a prior history of urinary tract infection (UTI), and two (3.4%) had undergone catheterization. Scrotal pain and swelling were the predominant complaints, reported by 54% ( $n = 34$ ) of patients, followed by testicular pain in 44.4% ( $n = 28$ ). These symptoms were either on the right side, left side or bilaterally (Table 1). Additionally, one patient exhibited symptoms of sepsis, which was subsequently confirmed through a blood culture, identifying *Klebsiella pneumoniae* as the causative agent.

**TABLE 1. Baseline characteristics of the patients.**

Characteristics	Frequency, n (%)
<b>Age Group</b>	
Youth (15–24 years)	12 (19.0)
Young adults (25–44 years)	34 (54.0)
Adults (45–64 years)	15 (23.8)
Elder ( $\geq 65$ years)	2 (3.2)
<b>Nationality</b>	
Saudi	49 (77.8)
Non-Saudi	14 (22.2)
Consuming raw dairy products	5 (7.9)
History of contact with animals	22 (34.9)
Smoking	35 (55.6)
Fever	15 (23.8)
<b>Symptoms</b>	
Left scrotal pain and swelling	21 (33.3)
Left testicular pain	15 (23.8)
Left scrotal swelling	4 (6.3)
Right testicular pain	13 (20.6)
Right scrotal pain and swelling	7 (11.1)
Bilateral scrotal pain and swelling	2 (3.2)
Bilateral epididymo-orchitis	1 (1.6)
<b>Chronic Disease</b>	
Diabetes mellitus	13 (20.6)
Hypertension	8 (12.7)
Ischemic heart disease	5 (7.9)
Chronic kidney disease	2 (3.2)
Chronic obstructive pulmonary disease	1 (1.6)
History of urinary tract infection	8 (12.7)
*History of STD	1 (1.6)
History of urethral stricture	1 (1.6)
History of catheterization	2 (3.2)
<b>Site of epididymo-orchitis</b>	
Left	37 (58.7)
Right	23 (36.5)
Bilateral	3 (4.8)

Abbreviations: STD: Sexual transmitted disease; \*: Due to *Neisseria gonorrhoea* infection.

### 3.2 Laboratory and radiological findings

Table 2 presents the results of admission laboratory tests for the patients. The average values from the complete blood count indicated an elevated total leukocyte count (TLC; median = 12, IQR (9–17)), an increased neutrophil count (median = 9.96, IQR (5.85–12.02)), and a normal platelet count (median = 274, IQR (230–330)). Anti-*Brucella* antibody titers ( $\geq 1:80$ ) were detected in 22 cases (34.9%), with six of them showing positive blood cultures for *Brucella* species. Brucellosis was diagnosed in 11 of the 63 patients (17.5%) based on clinical symptoms,

with titers of  $\geq 160$  and/or positive blood cultures.

Routine urinalysis yielded abnormal findings in 13 cases (20.6%), while positive cultures were observed in 9 cases (14.3%). Among these, urine cultures were positive for 9 patients (14.3%), with *Klebsiella pneumoniae* identified in 6 cases and *Escherichia coli* in 3 cases.

Scrotal ultrasonography was performed for differential diagnosis of potential testicular abscesses and masses (Figs. 1,2). Increased vascularity was evident in both testes and epididymis in 49 patients (77.8%) (Fig. 1A), while 14 patients (22.2%) had increased vascularity in the epididymis alone (Fig. 1B).

**TABLE 2. Laboratory parameters for patients diagnosed with epididymo-orchitis.**

Parameters	Frequency, n (%)
Routine urine test	
Normal findings	50 (79.4)
Abnormal findings	13 (20.6)
Only WBC	6 (9.5)
WBC, RBC, protein and nitrate	3 (4.8)
Only RBC	2 (3.2)
Leucocyte and red blood cells	1 (1.6)
WBC, RBC and protein	1 (1.6)
Positive urine culture	9 (14.3)
<i>Escherichia coli</i>	6 (9.5)
<i>Klebsiella pneumoniae</i>	3 (4.8)
Complete blood count	
Increased total leucocyte count	42 (66.7)
Neutrophilia	41 (65.1)
Platelets count	
Increased	0 (0.0)
Normal	62 (98.3)
Decreased	1 (1.6)
Positive anti- <i>Brucella</i> antibody titer	22 (34.9)
1/80	2
1/160	1
1/320	8
1/640	6
1/1280	5
Blood culture	
* <i>Brucella</i> species	6/22 (27.3)
** <i>Klebsiella pneumoniae</i>	1

\*: Isolated from patients with positive anti-*Brucella* antibodies; \*\*: Isolated from a patient with sepsis. WBC: white blood cells; RBC: red blood cells.

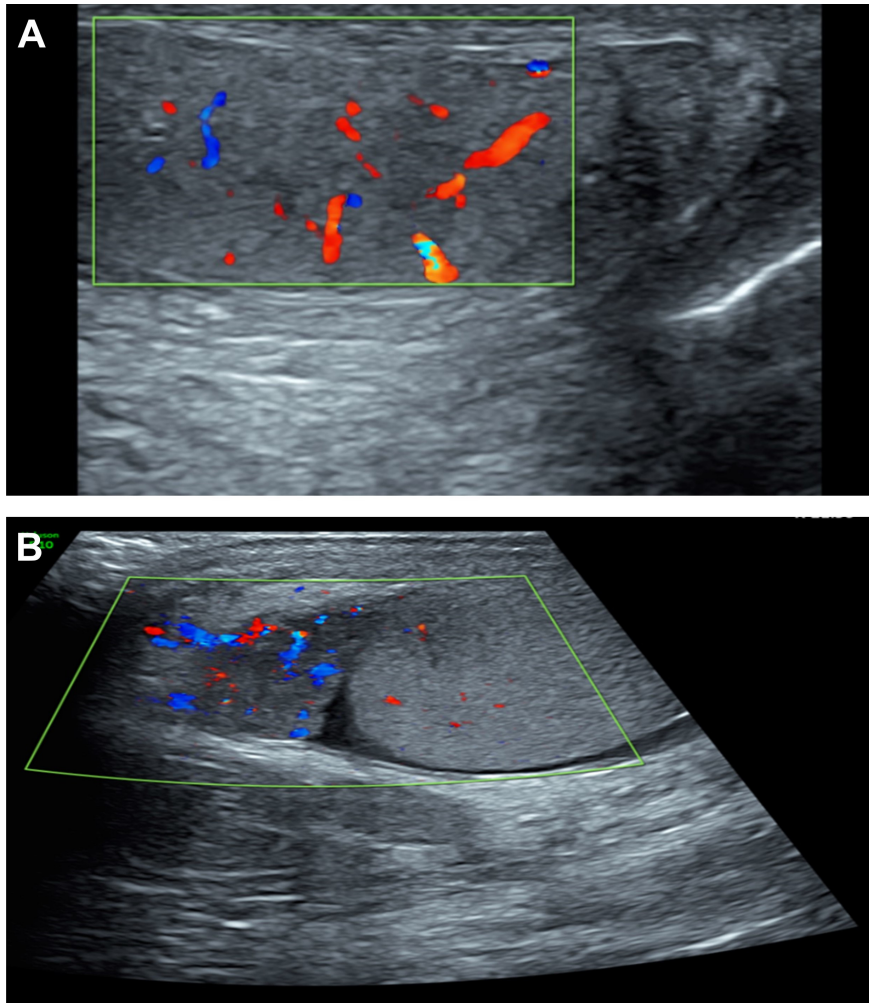
Complications of EO included reactive hydrocele in 15 patients (23.8%) and abscess formation in seven patients (11.1%) (3 testicular, 3 scrotal and 1 epididymal). Notably, one patient with a scrotal abscess subsequently developed *K. pneumoniae* sepsis. Additional complications comprised hypoechoic lesions in three patients (3.8%) (Fig. 2), epididymal thickening in two patients (3.1%), and one case of Fournier gangrene.

### 3.3 Treatment and outcomes

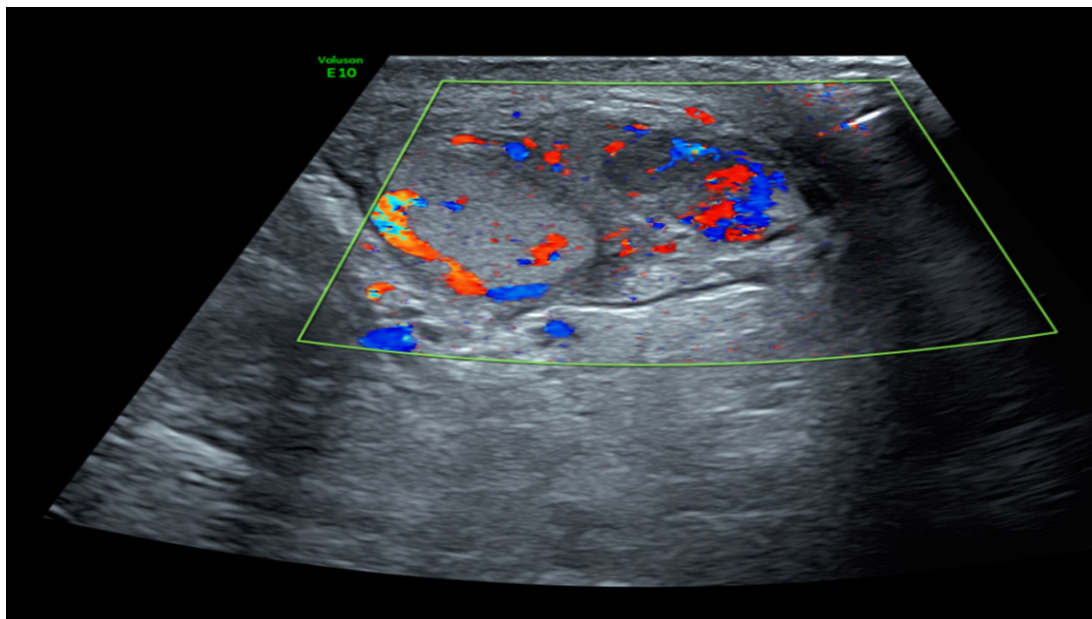
Fig. 3 shows the various treatment regimens administered to the 63 EO patients. Empirical treatment was given to 48 patients, while those with positive urine culture results (n = 9) received treatment based on culture and sensitivity reports. Of the total, 55 patients (87.3%) responded favorably to the initial treatment course, and four patients (6.3%) achieved a cure following the second course. Additionally, EO complications were observed in three cases (4.8%), and one patient (1.6%) succumbed to septicemia. Among the 15 patients (23.8%)

treated with a combination of ceftriaxone and ciprofloxacin, one patient did not respond to treatment and required orchiectomy due to a testicular abscess. Among the 10 patients (15.9%) treated with triple therapy (doxycycline, rifampicin and gentamicin), one experienced relapse after 6 months of completing treatment, characterized by the recurrence of EO symptoms in the absence of reinfection. Of the nine patients (14.3%) treated with ceftriaxone and co-trimoxazole, one did not respond to treatment, developed a testicular abscess, and underwent incision and drainage. Two patients (3.2%) did not respond to ceftriaxone monotherapy; therefore, one was switched to ciprofloxacin, and the other received a combination of ciprofloxacin and rifampicin. Levofloxacin monotherapy was modified to amikacin and amoxicillin/clavulanate in one patient (1.6%), and ciprofloxacin was replaced with amikacin in another. Overall, these changes led to complete resolutions, with all local symptoms disappearing and no clinical signs observed at six months.

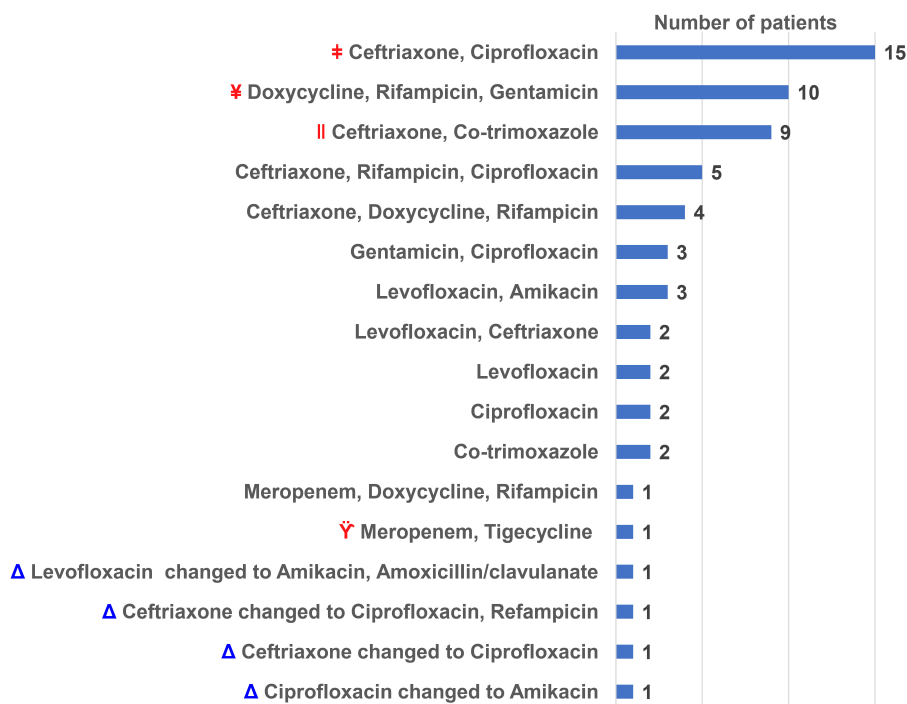
One patient (1.6%) succumbed to sepsis following treatment



**FIGURE 1. Representative scrotal ultrasonography image of a patient with epididymo-orchitis.** (A) Increased vascularity in both epididymis and testes, as observed in 77.8% of the patients. (B) Increased vascularity in the epididymis, as detected in 22.2% of the patients.



**FIGURE 2. Scrotal ultrasonography showed left epididymitis with the hypoechoic lesion as a complication of epididymo-orchitis in three (3.6%) of the 63 investigated patients.**



**FIGURE 3. The antibiotic regimens used for treating patients with epididymo-orchitis.** ‡: Not improved, underwent orchietomy (n = 1 patient); ¥: Relapse (n = 1 patient); ||: Not improved, undergone abscess drainage procedure (n = 1 patient); Ÿ: Developed sepsis and died (n = 1 patient); Δ: Improved after the second course of treatment (n = 4 patients).

with a combination of meropenem and tigecycline. This particular patient presented with fever lasting more than 7 days, along with lower urinary tract symptoms, left scrotal pain and swelling. He had multiple comorbidities, including diabetes, hypertension, ischemic heart disease and chronic renal failure requiring hemodialysis. Initial laboratory tests indicated an elevated TLC with neutrophilia and decreased platelet count, while anti-*Brucella* antibodies were not detected. Ultrasonography revealed increased vascularity in the left testicle and a para-testicular collection. An incision and drainage procedure was performed, and the patient was admitted to the intensive care unit, commencing empirical intravenous therapy with meropenem (500 mg, intravenous (IV) 8 hourly). Blood and urine cultures were obtained, both revealing *K. pneumoniae* isolates resistant to multiple antibiotics, except imipenem, meropenem, tigecycline and colistin. His treatment was then adjusted by adding tigecycline 100 mg, intravenous, 12 hourly for 6 weeks. However, the patient's condition continued to deteriorate rapidly, with poor response to treatment, ultimately leading to his demise on the 35th day.

#### 4. Discussion

EO represents a prevalent clinical syndrome in urological practice, necessitating accurate diagnosis and management to prevent severe complications. This study, to the best of our knowledge, constitutes the first investigation into the clinical and laboratory characteristics as well as treatment outcomes of EO in patients at a referral hospital in southern Saudi Arabia. The most frequently observed symptoms in EO cases were scrotal pain and swelling, closely followed by testicular pain. Fever was present in 24% of the patients. These

symptoms align with previous findings in the scientific literature regarding EO cases [7, 20, 22]. Similarly, a study conducted at a tertiary hospital in Riyadh between 1983 and 2000 revealed that common symptoms in adult patients with *Brucella*-related EO included swollen and painful testicles, undulant fever, chills and arthralgia [18]. Likewise, scrotal pain, swelling, fever, erythema, malaise and arthralgia were frequently reported symptoms among patients with *Brucella*-related EO in Turkey [7, 23].

In our study, 35% of patients exhibited seropositivity for *Brucella* with titers  $\geq 1:80$ . In *Brucella*-endemic regions, including our study area, a substantial number of individuals may possess anti-*Brucella* antibody titers  $\geq 1:80$  without necessarily having an active infection [24]. In a recent investigation examined the correlation between baseline *Brucella* antibody titers, culture positivity and clinical presentation in an area endemic for brucellosis, Alsubaie *et al.* [11] reported that *Brucella* serology was not significantly correlated with clinical outcomes at the end of therapy or with culture positivity at baseline. However, culture positivity was significantly associated with high antibody titers of  $\geq 1:640$ . Thus, the diagnosis and monitoring of brucellosis patients should rely on clinical manifestations, epidemiological history, bacterial cultures and serological tests [24]. In this study, 17% of EO patients were confirmed to have active brucellosis, a percentage higher than the 9% incidence of brucellosis reported in EO patients in Egypt [25]. However, our findings align with those from Pakistan, where *Brucella*-related EO was reported in 16.7% (n = 23) of 138 EO cases [26]. Similarly, a study in China revealed that 30.7% of patients with confirmed brucellosis experienced EO complications [27]. Numerous studies have

documented that EO can be a subsequent manifestation of systemic disease following a prior *Brucella* infection [2, 3, 24, 25]. In regions with a high incidence of brucellosis, clinicians should consider *Brucella* as a potential etiological agent of EO [24]. Nonetheless, *Brucella*-related EO can be differentiated by its gradual onset, longer duration, typical undulant fever, history of contact with animals or consumption of unpasteurized dairy products, serological testing and scrotal ultrasonography [2, 17]. Thus, early identification of brucellosis and the selection of appropriate therapy can lead to a favorable recovery without complications [2].

In our present study, patients diagnosed with EO displayed significantly high total leukocyte counts (TLC) and neutrophil counts, suggesting the presence of inflammation. However, platelet counts remained nearly within the normal range. It is recognized that neutrophils and lymphocytes may play pivotal roles in inflammatory processes, with lymphocyte counts showing transient changes during inflammatory conditions [22]. A recent study revealed that individuals with EO have significantly higher neutrophil counts but lower lymphocyte counts compared to those with *Brucella*-related EO [22], suggesting the potential utility of total and differential leukocyte parameters as differentiating factors between different types of EO [18].

In our current study, urinalysis revealed abnormal findings in 20.6% of the patients. Previous reports have documented UTIs in cases of acute right EO complicated by thrombosis of the pampiniform plexus [28]. Urine cultures yielded positive results for 14% of the patients, predominantly showcasing enteric Gram-negative pathogens such as *E. coli* and *K. pneumoniae*. It's worth noting that all these positive cultures were obtained from freshly collected midstream voided-urine samples. Our findings are slightly lower than those reported in Iran, where bacterial pathogens were identified in 26% of EO patients *via* urine culture [29]. Similarly, a study conducted in the United States reported 20% positive urine cultures among men presenting with EO at emergency departments [1]. Enteric Gram-negative bacteria have been well-documented as infectious agents responsible for EO in adult patients, with *E. coli* being the most commonly implicated pathogen [1]. The hematogenous route, originating from the bladder or ascending from the urethra, vas deferens, prostate and ejaculation duct, is considered a potential path of infection in cases of infective EO or testicular abscess [30]. Therefore, routine urinalysis and culture hold significant diagnostic value in identifying infectious causes of EO [28, 31]. Noteworthy, one patient with EO was diagnosed with *Neisseria gonorrhoeae*, highlighting the importance of obtaining a sexual contact history to rule out sexually transmitted diseases (STDs) as potential contributors to EO.

Ultrasonography serves as a highly accurate imaging modality for diagnosing testicular and scrotal pathology and plays a crucial role in evaluating testicular vascularity [28]. It can be used to confirm the diagnosis of scrotal infections with testicular causes, such as malignancy, abscesses and testicular torsion, which may present with similar clinical findings [4, 19]. Furthermore, ultrasonography can reveal additional findings, including the presence of hydrocele, scrotal wall thickening, fistula formation, calcifications and abscess formation, which

may manifest as avascular hypoechoic areas in the epididymis [20]. In our present study, patients diagnosed with EO exhibited increased vascularity in both the testes and epididymis, a characteristic indicative of infection. These findings are consistent with those reported in existing scientific literature [7, 31–33]. Additionally, our study identified scrotal abscesses and hypoechoic lesions on ultrasonography in seven and three cases, respectively. Notably, one patient with a testicular abscess that did not respond to treatment ultimately underwent orchiectomy, and this approach aligns with recommendations from other studies, which have advocated orchiectomy for patients with focal hypoechoic lesions in the testis, necrotizing orchitis, suspected malignancy and larger abscesses [17, 33].

To date, there is no specific recommended regimen for the treatment of EO, leading to the utilization of the same regimen for uncomplicated brucellosis [19]. Multiple treatment regimens have been proposed for EO, with their selection based on the individual patient's baseline characteristics and clinical data [19, 31, 34]. Among the commonly prescribed antibiotic combinations for EO treatment, ceftriaxone is often combined with either a fluoroquinolone (such as ciprofloxacin, levofloxacin or ofloxacin), an aminoglycoside (such as amikacin, gentamicin or streptomycin), doxycycline, trimethoprim/sulfamethoxazole or rifampicin [34]. Various studies have used different combinations of medications for EO treatment, ranging from two to six regimens [2, 31, 35]. Fortunately, most therapy combinations administered to our EO patients proved to be effective. However, one case treated with the ceftriaxone and gentamicin regimen eventually underwent orchiectomy, resulting in a similarly low rate (3.8%) of orchiectomy reported among 53 cases of *Brucella* EO in previous studies [35]. Inadequate treatment can potentially prolong the infection and lead to testicular loss [18, 33]. Conversely, another case with a testicular abscess did not respond to empirical treatment. Ultimately, cure was achieved after an abscess incision and drainage, a preferable option for preserving the testicle compared to orchiectomy. It is essential to emphasize that appropriate source control encompasses draining abscesses and removing infected fluids, which can significantly improve patient outcomes and help in the selection of appropriate antimicrobial therapy [36]. Obtaining cultures from the abscess drainage site and urine samples from suspected UTIs is crucial for identifying possible pathogens and their resistance patterns, thus guiding the choice of antimicrobial therapy.

Our study revealed that only one case (1.6%) of relapse occurred after a 6-month treatment period, which is notably lower than the rates reported in Iran (26.3%) and Spain (25%) among EO patients [31, 34]. In the case of relapse, treatment was extended by two months, ultimately resulting in a successful cure. It has been suggested that patients experiencing treatment failure with any regimen at 45 days may achieve a cure by extending the treatment course to 2 months [35]. Moreover, several studies have recommended the exploration of alternative combination therapies to achieve the desired treatment outcome [2, 31, 34]. In our study, ciprofloxacin monotherapy demonstrated efficacy in treating two cases. Guidelines advocate for the empirical use of fluoroquinolones, including ciprofloxacin, in men over 35 years presenting with EO

due to their favorable tissue penetration into the epididymis [18]. However, it is important to note that ciprofloxacin may not be effective when the causative microorganism exhibits resistance to quinolones [5]. Prior studies have documented an increased resistance rate to ciprofloxacin among Gram-negative pathogens in our local setting [37–40]. Therefore, the selection of antibiotic therapy should be guided by local antibiogram patterns.

While most patients achieved recovery, it is essential to note that one patient succumbed to sepsis caused by multidrug resistant (MDR) *K. pneumoniae* infection. MDR Gram-negative bacteria, such as *K. pneumoniae*, have emerged as a frequent cause of sepsis, leading to extended hospitalizations and elevated rates of morbidity and mortality [13, 41, 42]. Thus, a comprehensive understanding of local microbial data, encompassing prevalent pathogens and their resistance profiles, is important for facilitating effective empirical treatment and enhancing clinical outcomes.

## 5. Conclusions

In conclusion, EO remains a significant health concern among adult males, necessitating prompt investigation and treatment. Ultrasonography is invaluable in confirming the initial clinical diagnosis and ruling out abscesses or tumors for differential diagnosis. In regions endemic to *Brucella*, clinicians should remain vigilant regarding the potential involvement of brucellosis in EO cases. Nevertheless, a combination of clinical data, patient history and serological tests typically suffices for accurate diagnosis. Most EO cases can be effectively managed and completely resolved through appropriate antibiotic therapy. Notably, combination antibiotics featuring cefuroxime and/or ciprofloxacin from various drug classes have demonstrated efficacy in the treatment of most EO cases. However, in cases of uncomplicated EO that do not respond to standard therapy, an extended treatment duration of two months or an alternative regimen may be necessary.

## AVAILABILITY OF DATA AND MATERIALS

The raw data of the study are available upon reasonable request. All the data generated or analyzed during the study are included in this manuscript.

## AUTHOR CONTRIBUTIONS

AA and MEI—designed the research study. AA, RA, SKS and SFR—collected the data. AA and RA—clinically supervised. AA, NZA, OBA and MEI—analyzed the data. AA, SKS, NZA, OBA and MEI—wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval for this study was granted by the Ethical Committee at King Abdullah Hospital, Bisha, Saudi Arabia (E-

CTS REF no.BIS-23-00008-20062023) and adhered to the ethical principles outlined in the Helsinki Declaration. Informed consent was not sought as this is a retrospective study, and data were solely extracted from the hospital database.

## ACKNOWLEDGMENT

The authors extend their appreciation to the Deanship of Scientific Research, University of Bisha, for funding this research through the promising program under grant number (UB-Promising-46-1445).

## FUNDING

This research was funded by the Deanship of Scientific Research, University of Bisha, Bisha, Saudi Arabia, grant number (UB-Promising-46-1445).

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## REFERENCES

- Bonner M, Sheele JM, Cantillo-Campos S, Elkins JM. A descriptive analysis of men diagnosed with epididymitis, orchitis, or both in the emergency department. *Cureus*. 2021; 94: e15800.
- Khodadadi J, Dodangeh M, Nasiri M. Brucellar epididymo-orchitis: Symptoms, diagnosis, treatment and follow-up of 50 patients in Iran. *IDCases*. 2023; 32: e01736.
- Celik M, Akgul F, Alkan S, Altindag D, Esmer F, Sahin A, *et al*. Testicular involvement of brucellosis: a 10-year, multicenter study. *The Journal of Infection in Developing Countries*. 2023; 17: 1285–1291.
- Street EJ, Justice ED, Kopa Z, Portman MD, Ross JD, Skerlev M, *et al*. The 2016 European guideline on the management of epididymo-orchitis. *International Journal of STD & AIDS*. 2017; 28: 744–749.
- Ryan L, Daly P, Cullen I, Doyle M. Epididymo-orchitis caused by enteric organisms in men >35 years old: beyond fluoroquinolones. *European Journal of Clinical Microbiology & Infectious Diseases*. 2018; 37: 1001–1008.
- Nicholson A, Rait G, Murray-Thomas T, Hughes G, Mercer CH, Cassell J. Management of epididymo-orchitis in primary care: results from a large UK primary care database. *British Journal of General Practice*. 2010; 60: e407–e422.
- Gozdas HT, Bal T. Brucellar epididymo-orchitis: a retrospective study of 25 cases. *The Aging Male*. 2020; 23: 29–32.
- Al-Tawfiq JA, AbuKhamis A. A 24-year study of the epidemiology of human brucellosis in a health-care system in Eastern Saudi Arabia. *Journal of Infection and Public Health*. 2009; 2: 81–85.
- Alaidarous M. Prevalence of brucellosis in Hawtat Sudair city, Riyadh province, Saudi Arabia. *Majmaah Journal of Health Sciences*. 2018; 7: 17–25.
- Al Anazi M, AlFayyad I, AlOtaibi R, Abu-Shaheen A. Epidemiology of brucellosis in Saudi Arabia. *Saudi Medical Journal*. 2019; 40: 981–988.
- Alsubaie SA, Turkistani SA, Zeaiter AA, Thabit AK. Lack of correlation of brucella antibody titers with clinical outcomes and culture positivity of brucellosis. *Tropical Diseases, Travel Medicine and Vaccines*. 2021; 7: 5.
- Edathodu J, Alamri M, Alshangiti KA, Alfagyh NS, Alnaghmush AS, Albaiz F, *et al*. Clinical manifestations and treatment outcomes of human brucellosis at a tertiary care center in Saudi Arabia. *Annals of Saudi Medicine*. 2021; 41: 109–114.
- Al-Faifi J, Ibrahim ME. Congenital brucellosis associated with subsequent *Klebsiella pneumoniae* co-infection in a premature neonate: a rare case report. *Journal of Infection and Public Health*. 2022; 15: 586–588.



- [14] Ibrahim ME, Al-Shahrani MS. The incidence and clinical manifestations of human brucellosis in a referral hospital in Southern Saudi Arabia between 2015 and 2019. *Acta Microbiologica et Immunologica Hungarica*. 2021; 68: 128–134.
- [15] Alkahtani AM, Assiry MM, Chandramoorthy HC, Al-Hakami AM, Hamid ME. Sero-prevalence and risk factors of brucellosis among suspected febrile patients attending a referral hospital in southern Saudi Arabia (2014–2018). *BMC Infectious Diseases*. 2020; 20: 26.
- [16] Kanjo MA, Ahmed HM, Alnahari EA. Unusual presentation of neurobrucellosis in Jeddah, Kingdom of Saudi Arabia. *Neurosciences*. 2021; 26: 385–388.
- [17] Hamoda TAA, Bahassan O, Almalki AM, Alkhzaim AH, Khogeer AN, Ahmed EM, *et al.* Brucellar testicular abscess: the 17th case report and review of literature. *Urology Annals*. 2023; 15: 340–348.
- [18] Memish ZA, Venkatesh S. Brucellar epididymo-orchitis in Saudi Arabia: a retrospective study of 26 cases and review of the literature. *BJU International*. 2001; 88: 72–76.
- [19] Nahas RS, Alsulami A, Lashkar MO, Thabit AK. Brucella epididymo-orchitis successfully treated with dual oral drug regimen: a case report with differential diagnoses of malignancy and tuberculosis. *Radiology Case Reports*. 2022; 17: 3485–3489.
- [20] Sieger N, Di Quilio F, Stolzenburg J. What is beyond testicular torsion and epididymitis? Rare differential diagnoses of acute scrotal pain in adults: a systematic review. *Annals of Medicine and Surgery*. 2020; 55: 265–274.
- [21] Alsubaie S, Almuneef M, Alshaalan M, Balkhy H, Albanyan E, Alola S, *et al.* Acute brucellosis in Saudi families: relationship between brucella serology and clinical symptoms. *International Journal of Infectious Diseases*. 2005; 9: 218–224.
- [22] Cift A, Yucel MO. Comparison of inflammatory markers between brucella and non-brucella epididymo-orchitis. *International Brazilian Journal of Urology*. 2018; 44: 771–778.
- [23] Çalışma BER. Brucellar Epididymo-orchitis: a retrospective study. *Trakya Üniversitesi Tıp Fakültesi Dergisi*. 2009; 26: 220–225.
- [24] Jin M, Fan Z, Gao R, Li X, Gao Z, Wang Z. Research progress on complications of brucellosis. *Frontiers in Cellular and Infection Microbiology*. 2023; 13: 1136674.
- [25] Salem S, Alarbid A, Alenezi T, Alenezzi A, Alali K, Ajrawi F, *et al.* Early predictors of brucella epididymo-orchitis. *Urology Annals*. 2023; 15: 158–161.
- [26] Korkmaz N, Ölçücü MT, Ateş F. Comparison of brucella and non-brucella epididymo-orchitis. *Journal of College of Physicians and Surgeons Pakistan*. 2020; 30: 403–406.
- [27] Ye H, Xing F, Yang J, Lo SK, Lau RW, Chen JH, *et al.* High index of suspicion for brucellosis in a highly cosmopolitan city in southern China. *BMC Infectious Diseases*. 2020; 20: 22.
- [28] Alshubaili HM, Alharbi KI, Elsirafy MN, Abuaz SM, Hasan RM. Acute right epididymo-orchitis complicated by pampiniform plexus thrombosis. *Urology Case Reports*. 2020; 31: 101171.
- [29] Abolghasemi S, Alizadeh M, Hashemi A, Tehrani S. Etiology and clinical features of epididymo-orchitis: a single-center study in Tehran, Iran. *Infectious Disorders—Drug Targets*. 2021; 21: 142–145.
- [30] Tan J, Tian M, Zhao F, Deng S, Jin P, Wang Y, *et al.* An investigation of the male genitourinary abscess originated from urinary tract in a tertiary hospital, Shanghai, China, from 2004 to 2019. *Infection and Drug Resistance*. 2021; 14: 1795–1803.
- [31] Navarro-Martínez A, Solera J, Corredoira J, Beato JL, Martínez-Alfaro EM, Atieénzar M, *et al.* Epididymo-orchitis due to *Brucella mellitensis*: a retrospective study of 59 patients. *Clinical Infectious Diseases*. 2001; 33: 2017–2022.
- [32] Huang Y, Chen B, Cao D, Chen Z, Li J, Guo J, *et al.* Surgical management of tuberculous epididymo-orchitis: a retrospective study of 81 cases with long-term follow-up. *BMC Infectious Diseases*. 2021; 21: 1068.
- [33] Zehri AA, Ismail A, Adebayo P, Ali A. Testicular torsion induced by epididymo-orchitis: a case report. *International Journal of Surgery Case Reports*. 2021; 83: 106038.
- [34] Gul HC, Akyol I, Sen B, Adayener C, Haholu A. Epididymo-orchitis due to brucella melitensis: review of 19 patients. *Urologia Internationalis*. 2009; 82: 158–161.
- [35] Roushan MR, Baiani M, Javanian M, Kasaeian AA. Brucellar epididymo-orchitis: review of 53 cases in Babol, northern Iran. *Scandinavian Journal of Infectious Diseases*. 2009; 41: 440–444.
- [36] Coccolini F, Sartelli M, Sawyer R, Rasa K, Viaggi B, Abu-Zidan F, *et al.* Source control in emergency general surgery: WSES, GAIS, SIS-E, SIS-A guidelines. *World journal of emergency surgery*. 2023; 18: 41.
- [37] Ibrahim ME. High antimicrobial resistant rates among Gram-negative pathogens in intensive care units. *Saudi Medical Journal*. 2018; 39: 1035–1043.
- [38] Ibrahim ME, Algak TB, Abbas M, Elamin BK. Emergence of *bla*<sub>TEM</sub>, *bla*<sub>CTX-M</sub>, *bla*<sub>SHV</sub>, and *bla*<sub>OXA</sub> genes in multidrug-resistant *Enterobacteriaceae* and *Acinetobacter baumannii* in Saudi Arabia. *Experimental and Therapeutic Medicine*. 2021; 22: 1450.
- [39] Alshahrani AM, Ibrahim ME, Aldossary AK, Alghamdi MA, Ahmed OB, Bin Abdulhak AA. Molecular epidemiology of carbapenem-resistant *K. pneumoniae* clinical isolates from the adult patients with comorbidities in a tertiary hospital, Southern Saudi Arabia. *Antibiotics*. 2022; 11: 1697.
- [40] Ibrahim ME. Risk factors in acquiring multidrug-resistant *Klebsiella pneumoniae* infections in a hospital setting in Saudi Arabia. *Scientific Reports*. 2023; 13: 11626.
- [41] Tufa TB, Mackenzie CR, Orth HM, Wienemann T, Nordmann T, Abdissa S, *et al.* Prevalence and characterization of antimicrobial resistance among gram-negative bacteria isolated from febrile hospitalized patients in central Ethiopia. *Antimicrobial Resistance & Infection Control*. 2022; 11: 8.
- [42] Mukherjee S, Mitra S, Dutta S, Basu S. Neonatal sepsis: the impact of carbapenem-resistant and hypervirulent *Klebsiella pneumoniae*. *Frontiers in Medicine*. 2021; 8: 634349.

**How to cite this article:** Abdullah Ayed, Raed Alwadai, Shahzada K. Sohail, Syeda F. Rizvi, Najim Z Alshahrani, Omar B. Ahmed, *et al.* Clinical characteristics, management, and treatment outcomes of epididymo-orchitis among patients in a referral hospital in Southern Saudi Arabia. *Journal of Men's Health*. 2024; 20(5): 21–29. doi: 10.22514/jomh.2024.066.