

Clinical Features and Treatment Differences Among Tuberculous, Brucellosis, and Pyogenic Spondylitis: A Cohort Study

Jiao-Jiao Shen^{1,2,*}, Rui-Xuan Yao^{1,2,*}, Ying Ye¹, Yu-Feng Gao¹, Jia-Bin Li^{1,2}, Li-Fen Hu^{1,2}

¹Department of Infectious Diseases & Anhui Center for Surveillance of Bacterial Resistance, The First Affiliated Hospital of Anhui Medical University, Hefei, 230022, People's Republic of China; ²Anhui Province Key Laboratory of Infectious Diseases & Institute of Bacterial Resistance, Anhui Medical University, Hefei, 230022, People's Republic of China

*These authors contributed equally to this work

Correspondence: Jia-Bin Li; Li-Fen Hu, Email lijabin@ahmu.edu.cn; hulifen@ahmu.edu.cn

Purpose: There was an increasing incidence of spinal infections. This study aimed to compare and contrast the clinical characteristics and treatment regimens for diverse types of spondylitis and to provide guidance for clinicians to make timely diagnosis and treatment.

Patients and Methods: One hundred and twenty-five patients with spinal infections admitted to the First Affiliated Hospital of Anhui Medical University from October 2019 to December 2024 were recruited. The patients were classified as having tuberculous spondylitis (TBS), brucellosis spondylitis (BS), or pyogenic spondylitis (PS). The patient's treatment regimen and course were dynamically followed up during hospitalization and after discharge. Comparisons of clinical characteristics and treatment among the three groups were performed by SPSS 26.0 and GraphPad Prism 10 statistical software.

Results: The proportion of male patients was greater than female patients (65.00% vs 35.00%). Fever accompanied by pain was more prevalent in the BS and PS groups than in the TBS group ($P=0.003$). Compared with the TBS and BS groups, the PS group had the shortest duration from symptom onset to hospitalization ($P<0.001$). Sepsis, invasive manipulation, elevated inflammatory markers, psoas abscesses, and the involvement of three or more vertebrae were significantly associated with the PS. In this study, the median duration of treatment was 77 weeks for TBS, 19 weeks for BS, and 13 weeks for PS. Adverse drug reactions (ADRs) should be monitored during treatment. Our results indicated that omadacycline and contezolid exhibited remarkable efficacy in the treatment of spinal infections.

Conclusion: Patients of spinal infections with diverse etiologies presented varied clinical features and risk factors, the treatment should be individualized. Due to the long course of treatment, ADRs need to be monitored during treatment, and newer drugs such as omadacycline and contezolid are efficacious and have favorable safety profiles.

Keywords: spinal infectious diseases, clinical characteristics, treatment regimens, treatment durations

Introduction

Spinal infectious diseases are caused by pathogenic microorganisms invading the spine and surrounding tissues, with incidence of 0.5 to 2.5 cases per 100,000 people.^{1–3} Population aging, high prevalence of chronic diseases as hypertension and diabetes, and more invasive medical procedures have contributed to the incidence of spine infection.^{4,5} On the basis of their pathogenetic characteristics, spinal infectious diseases can be classified into specific and nonspecific infections. Specific spinal infections are caused primarily by special pathogens, such as *Mycobacterium tuberculosis* (MTB), *Brucella* spp., and fungi (eg, *Candida* spp. and *Aspergillus* spp). Nonspecific spinal infections, also known as pyogenic spondylitis (PS), are typically caused by common bacteria, with *Staphylococcus aureus* being the most common.^{6–8} Owing to the insidious onset of symptoms and the high overall prevalence of back pain in the general

population, spinal infectious diseases are often diagnosed with a delay of 2–6 months,^{9–12} with a high rate of misdiagnosis.¹³

The primary objectives of treatment are to eradicate the infection, alleviate pain, and restore the structure and function of the spine. Conservative treatment is the first-line approach. If the pathogen is unknown, broad-spectrum antibiotics should be used for empirical treatment. Commonly used drugs for tuberculous spondylitis (TBS) with a clear pathogen are isoniazid, rifampicin, pyrazinamide, and ethambutol. The WHO recommends a 9-month course of antituberculosis treatment for bone and joint tuberculosis, whereas Chinese experts recommend a 12- to 18-month course of antituberculosis treatment for bone and joint tuberculosis.¹⁴ Different combinations of antimicrobial drugs are used to treat brucellosis spondylitis (BS), with the gold standard treatment being rifampin, doxycycline, streptomycin, tetracycline, and ofloxacin, which are administered over a treatment period of approximately six months.^{15,16} With regard to PS, the effectiveness of rifampicin combined with β -lactams, ciprofloxacin, and vancomycin for the treatment of *Staphylococcus aureus* infections has been emphasized. A study involving 359 participants demonstrated that the efficacy and safety of a 6-week antibiotic regimen for PS were comparable to those of a 12-week regimen.¹⁷ However, the duration of treatment for spinal infections varies greatly among patients on the basis of individual characteristics. There is ongoing debate about the optimal duration of treatment.

Current studies are mostly limited to case reports and specific pathogens.^{4,18,19} Delayed diagnosis and treatment, uncertain treatment duration, and drug side effects of spinal infections warrant attention.^{6,20–22} We therefore conducted a case–control study to identify unique signatures in clinical characteristics and treatment regimens for diverse types of spondylitis and to provide guidance for clinicians to make timely diagnosis and treatment.

Materials and Methods

Research Subjects and Data Collection

We collected data from patients with spinal infectious diseases admitted to the First Affiliated Hospital of Anhui Medical University from October 2019 to December 2024. The following data were obtained from the cases: age, sex, clinical manifestations, white blood cell count (WBC), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), risk factors for spinal infections, imaging findings, and treatment regimens. Patients with spinal infections were also followed up to understand their course of treatment and prognosis. This research protocol adheres to the principles outlined in the Declaration of Helsinki. This study was approved by the Biomedical Ethics Committee of Anhui Medical University (approval no. PJ20250641). The ethics committee waived the requirement for informed consent, as this was a retrospective study. We ensure the anonymity and confidentiality of the data.

Clinical Diagnosis Criteria

The diagnostic criteria for TBS included the following:^{12,23} (1) clinical manifestations such as low-grade fever, night sweats, and localized chronic pain; (2) results of imaging tests such as computed tomography (CT) or magnetic resonance imaging (MRI) that are suggestive of spinal infection; (3) a history of previous tuberculosis or close contact with a patient who has open tuberculosis; (4) a positive PPD test or T-spot test (or both positive); and (5) effective antituberculosis treatment. Criteria for the diagnosis of BS included the following:¹² (1) the presence of clinical signs such as severe pain in the spinal region with fever; (2) positive imaging findings of the spine; (3) the presence of a previous epidemiologic history or history of exposure to the patient; (4) serum *Brucella* tubular agglutination titers $\geq 1/160$ or positive *Brucella* blood cultures; and (5) a positive blood culture or a positive blood count. The diagnostic criteria for PS included the following:^{12,24,25} (1) the presence of clinical signs such as high fever and pain in the spinal region; (2) positive findings on spinal imaging; (3) laboratory indices such as elevated white blood cell count (WBC), C-reactive protein (CRP) level, and erythrocyte sedimentation rate (ESR) or positive bacterial culture; and (4) the exclusion of TBS and BS.

Clinical Cure Criteria

Clinical cure criteria of patients with spinal infections included: 1) Disappearance of clinical symptoms and signs: no fever or back pain, 2) Subdued inflammatory indicators: white blood cell count, CRP level, and the ESR returned to normal, 3) Improvement in imaging of the involved vertebrae: later follow-up imaging suggests regression or stabilization of the destruction associated with the spinal infection compared with baseline imaging.

Inclusion and Exclusion Criteria

The inclusion criteria were as follows: patients must be over the age of 16 years; the primary spinal disease must be caused by infection; and a clinically confirmed diagnosis of tuberculous spondylitis, brucellosis spondylitis, or non-specific suppurative spondylitis must be in place. The exclusion criteria were as follows: patients with spinal infections for which the pathogen is unclear, patients with spinal tumors that are complicated by infection, and patients with spinal disorders that are degenerative and inflammatory.

Statistical Methods

SPSS 26.0 statistical software and GraphPad Prism 10 software were used for statistical analysis, data processing, and chart creation. Normally distributed data are presented as the mean \pm standard deviation. Independent sample *t* tests were used for comparisons between two groups. Nonnormally distributed data are expressed as medians (interquartile ranges), and the Mann–Whitney *U*-test or Kruskal–Wallis test was used for intergroup comparisons. Categorical variables are expressed as case numbers (*n*) and percentages (%), and differences were tested using Pearson’s chi-square test and Fisher’s exact probability test. For pairwise comparisons, Bonferroni correction was applied to adjust the *P* values, with a significance level of $\alpha = 0.05$. We considered a *P* value <0.05 to indicate statistical significance.

Results

Characteristics of Study Participants

As shown in Figure 1, during the period from October 2019 to December 2024, a total of 196 patients were diagnosed with spinal infectious diseases in the Department of Infectious Diseases at the First Affiliated Hospital of Anhui Medical

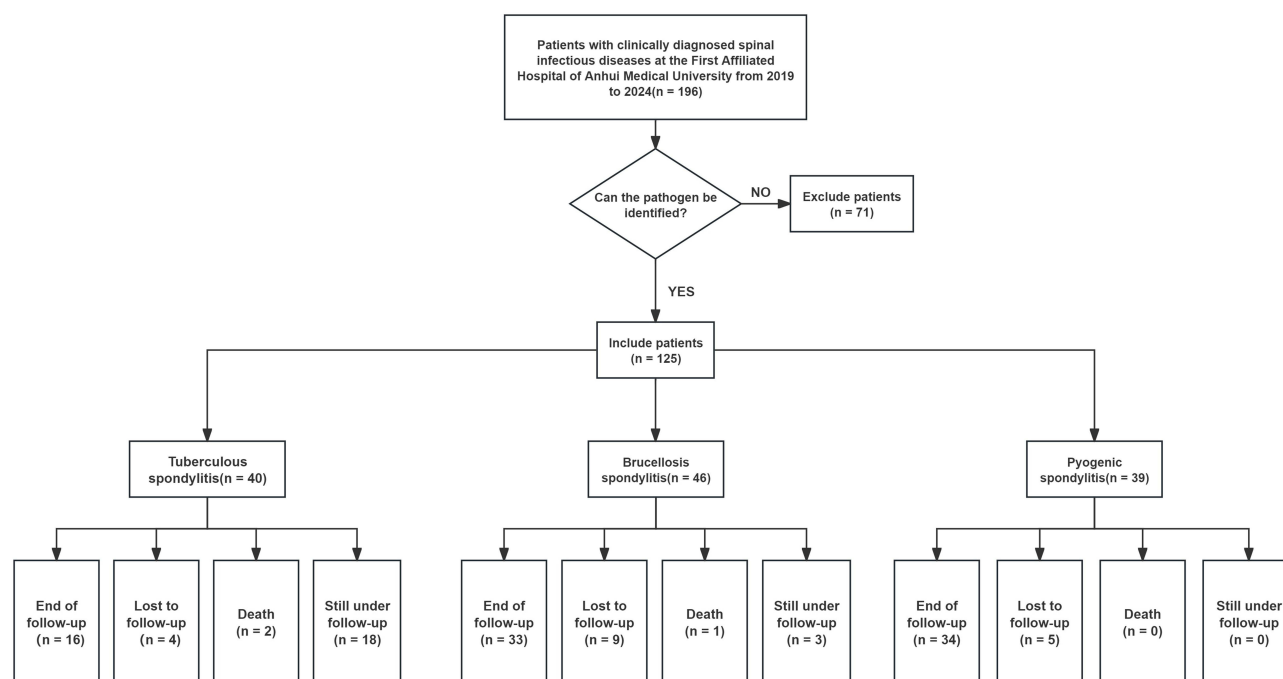


Figure 1 Flow diagram of patient recruitment and exclusion criteria.

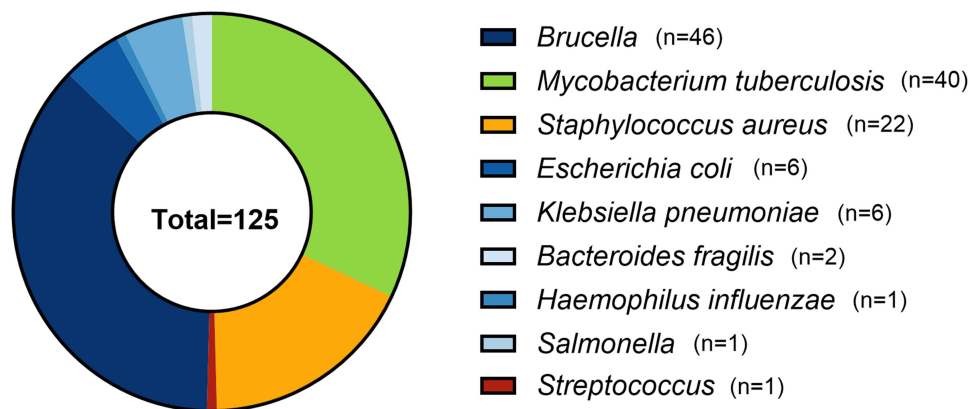


Figure 2 Pathogens of spinal infections.

University. Among them, 125 patients with a pathogen diagnosis were included in the study. *Mycobacterium tuberculosis* was identified in 40 cases (32%), *Brucella* in 46 cases (36.8%), and other gram-negative bacteria in 16 cases (12.80%), primarily *Escherichia coli* (4.8%), *Haemophilus influenzae*, and other species. Gram-positive bacteria accounted for 23 cases (18.40%), with *Staphylococcus aureus* being the predominant species (17.60%), and other pathogens, including *streptococci* (Figure 2). The patients were divided into TBS (40), BS (46), and PS (39) groups on the basis of the causative pathogens.

Among the 125 patients, the median age was 60.00 (IQR 52.00–69.00) years, and 81 patients (65.00%) were male. The median ages of the patients were 66.50 (IQR 55.25–73.50), 57.00 (IQR 51.75–63.25), and 62.00 (IQR 55.00–71.00) years, with 65%, 65.22%, and 64.10% male, in the TBS, BS, and PS groups, respectively. Patients with TBS were significantly older than patients with BS, as shown in Figure 3A. Although the proportion of male patients was greater than that of female patients in all three groups, no significant differences were observed ($P=0.994$).

Fever and pain were the most common clinical manifestations in patients with spinal infections. Among the patients included in this study, 84 (67.20%) presented with fever, and 111 (88.80%) presented with pain. Fever was observed in 21 (52.50%), 33 (71.74%), and 30 (76.92%) patients in the TBS, BS, and PS groups, respectively. Fever was significantly more common in patients with PS than in those with TBS (76.92% vs 52.50%; $P = 0.034$). Pain was present in 32 (80.00%), 43 (93.48%), and 36 (92.31%) patients with TBS, BS, and PS, respectively. We found that more than 80% of patients with spinal infections experienced pain, without significant differences in the frequency of pain between the groups ($P = 0.100$). The occurrence of fever with pain was significantly greater in both the BS (67.39% vs 35.00%; $P = 0.003$) and the PS (69.23% vs 35.00%; $P = 0.002$) groups than in the TBS group, as shown in Table 1.

The incidence of sepsis and a prior history of invasive spinal procedures was significantly higher in the PS group than TBS group and BS group ($P < 0.05$). The median time from symptom onset to hospital admission was 60.00 days (30.00–90.00), 60.00 days (30.00–90.00), and 20.00 days (10.00–30.00) in the TBS, BS, and PS groups, respectively. With respect to the duration from symptom onset to hospitalization, patients with PS had a shorter duration than those with TBS and BS, as shown in Figure 3B. Similarly, the treatment duration was shorter in patients with PS than in those with TBS and BS, as shown in Figure 3C.

Laboratory test results revealed significant differences in white blood cell count (WBC), C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) among the three groups of patients. The PS group had a higher WBC than the TBS group [9.56 (7.18, 13.22) vs 6.86 (5.53, 8.69), $P < 0.05$] and the BS group [9.56 (7.18, 13.22) vs 6.04 (5.33, 8.71)]. The levels of CRP and ESR in the PS group were significantly higher than those in the TBS group [78.82 (34.18, 132.61) vs 35.98 (13.19, 70.32), 77.00 (58.25, 95.00) vs 53.00 (28.00, 73.00)] and the BS group [78.82 (34.18, 132.61) vs 39.67 (18.80, 57.44), 77.00 (58.25, 95.00) vs 55.00 (37.25, 76.50)], as shown in Table 1 and Figure 3D–F.

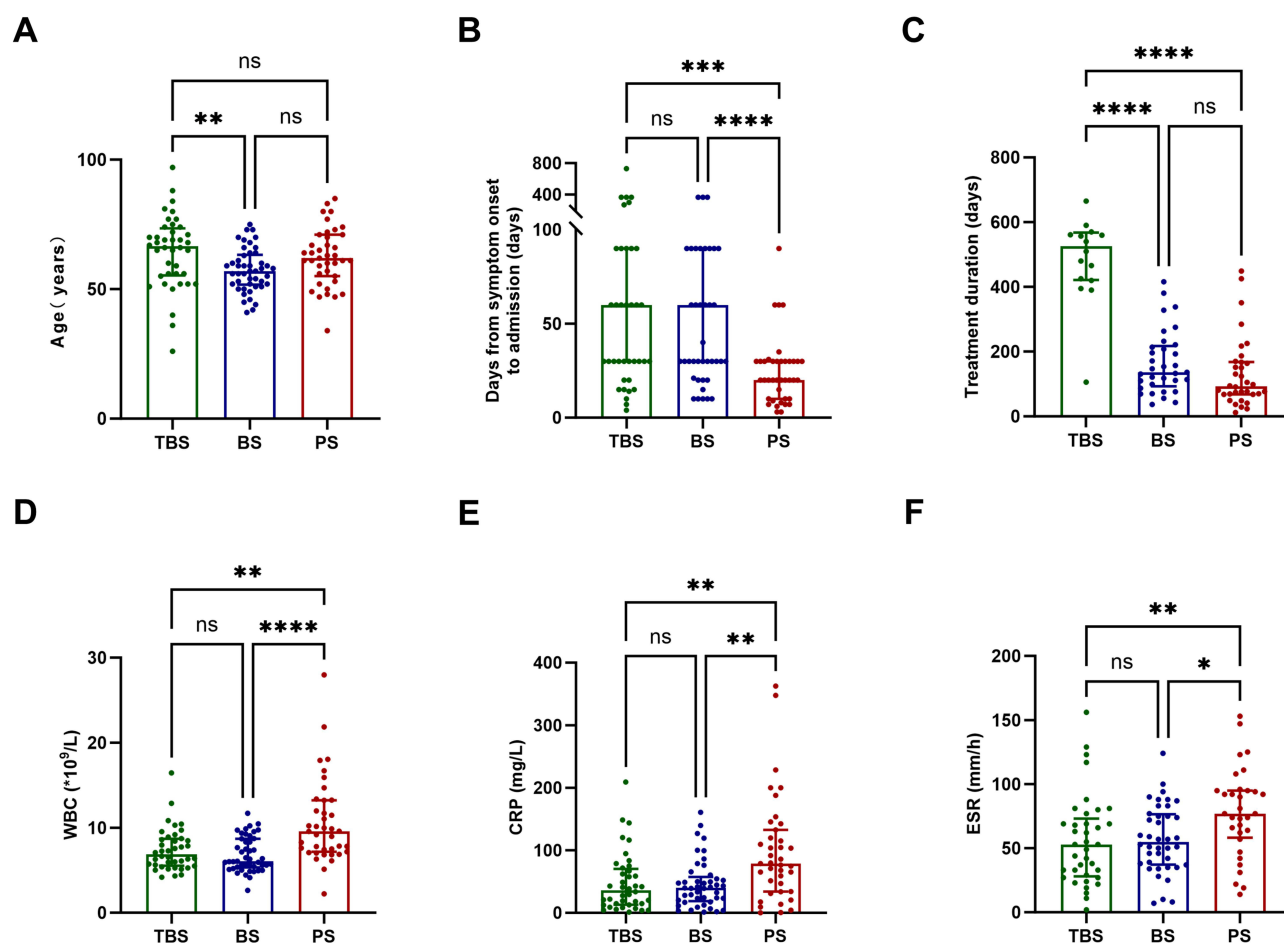


Figure 3 Comparison of clinical parameters among TBS, BS and PS groups. **(A)** Scatter plots of age levels in TBS, BS and PS groups, respectively. **(B and C)** Scatter plots of days from symptom onset to admission and treatment duration in TBS, BS and PS groups, respectively. **(D–F)** Scatter plots of plasma levels of WBC, CRP, and ESR in TBS, BS and PS groups, respectively. **p*-value ≤ 0.05 ; ***p*-value ≤ 0.01 ; ****p*-value ≤ 0.001 ; *****p*-value ≤ 0.0001 .

Abbreviations: TBS, tuberculous spondylitis; BS, brucellosis spondylitis; PS, pyogenic spondylitis; WBC, white blood cell count; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; ns: not significant.

Image Characteristics

The three groups exhibited analogous imaging findings, which included narrowing of the intervertebral space, pointed osteophytes, paraspinal abscesses, psoas abscesses, soft tissue swelling, and nerve root or spinal cord compression as shown in Tables 2 and 3. The incidence of narrowed intervertebral spaces was highest in the BS group (45.65%), followed by the TBS group (30.00%), and lowest in the PS group (20.51%). The incidence of psoas abscess in the PS group was significantly higher than that in the TBS group (28.21% vs 7.50%, $P=0.016$) and the BS group (28.21% vs 6.25%, $P=0.007$). Thoracic spine involvement was significantly more frequent in both the TBS group (35.00% vs 6.52%; $P=0.001$) and the PS group (33.33% vs 6.52%; $P=0.002$) than in the BS group. The frequency of lumbar involvement was significantly greater in the BS group than in the TBS group (91.30% vs 65.00%, $P=0.003$). Involvement of three or more vertebrae was significantly more common in the PS group than in the TBS group (48.72% vs 20.00%; $P=0.007$) and the BS group (48.72% vs 19.57%; $P=0.016$).

Treatment and Prognosis

Among the 40 patients with TBS, 35.00% (14/40) received five-drug anti-TB therapy, and 9 (22.50%) received four-drug anti-TB regimens. The mean duration of the five-drug treatment was 547.75 days, and the mean duration of the four-drug treatment was 424.80 days. Although there was a difference in the treatment duration, it was not statistically significant. Notably, in this study, an elderly male patient with spinal tuberculosis with paraspinal abscesses and bone

Table 1 Baseline Characteristics of the Study Participants

	TBS Group (n = 40)	BS Group (n=46)	PS Group (n=39)	P Value ^a
Clinical characteristics, symptoms or signs				
Ages, median (range)	66.50 (55.25, 73.50)	57.00 (51.75, 63.25)	62.00 (55.00, 71.00)	0.005
Male, n (%)	26 (65.00%)	30 (65.22%)	25 (64.10%)	0.994
Fever, n (%)	21 (52.50%)	33 (71.74%)	30 (76.92%)	0.049
Pain, n (%)	32 (80.00%)	43 (93.48%)	36 (92.31%)	0.100
Fever with pain, n (%)	14 (35.00%)	31 (67.39%)	27 (69.23%)	0.003
Laboratory parameters, median (range)				
WBC (10 ⁹ /L)	6.86 (5.53, 8.69)	6.04 (5.33, 8.71)	9.56 (7.18, 13.22)	0.001
CRP (mg/L)	35.98 (13.19, 70.32)	39.67 (18.80, 57.44)	78.82 (34.18, 132.61)	0.006
ESR (mm/h)	53.00 (28.00, 73.00)	55.00 (37.25, 76.50)	77.00 (58.25, 95.00)	<0.001
Risk factors, n (%)				
Malignancy/immunodeficiency	4 (10.00%)	3 (6.25%)	0	0.152 ^b
Long-term use of hormones	1 (2.50%)	0	1 (2.56%)	0.535 ^b
Cardio-cerebrovascular diseases	16 (40.00%)	12 (26.09%)	13 (33.33%)	0.389
Diabetes mellitus	4 (10.00%)	9 (19.57%)	10 (25.64%)	0.177
Sepsis	4 (10.00%)	2 (4.35%)	27 (69.23%)	<0.001
Spinal invasive procedures	8 (20.00%)	4 (8.70%)	12 (30.77%)	0.031
Course, median (range)				
Days from symptom onset to admission (days)	60.00 (30.00, 90.00)	60.00 (30.00, 90.00)	20.00 (10.00, 30.00)	<0.001
Treatment duration (days)	540.00 (422.50, 570.00)	136.00 (93.00, 217.50)	92.50 (68.00, 167.75)	<0.001

Notes: ^a: the difference among the 3 groups. ^b: based on 10,000 Monte Carlo simulations.

Abbreviations: WBC, white blood cell count; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

Table 2 Comparison of Imaging Findings

	TBS Group (n = 40)	BS Group (n=46)	PS Group (n=39)	P Value ^a
Imaging findings, n (%)				
Narrowing of intervertebral space	12 (30.00%)	21 (45.65%)	8 (20.51%)	0.044
Pointed osteophytes	23 (57.50%)	35 (76.09%)	28 (71.79%)	0.159
Paraspinal abscess	13 (32.50%)	10 (21.74%)	8 (20.51%)	0.389
Psoas abscess	3 (7.50%)	3 (6.25%)	11 (28.21%)	0.009
Soft tissue swelling	14 (35.00%)	24 (52.17%)	19 (48.72%)	0.521
Nerve root/spinal cord compression	4 (10.00%)	4 (8.70%)	8 (20.51%)	0.237
Extent of spinal Involvement, n (%)				
Cervical vertebrae	1 (2.50%)	2 (4.35%)	2 (5.13%)	0.866
Thoracic vertebrae	14 (35.00%)	3 (6.52%)	13 (33.33%)	0.001
Lumbar vertebrae	26 (65.00%)	42 (91.30%)	31 (79.49%)	0.011
Sacral vertebrae	3 (7.50%)	4 (8.70%)	4 (10.26%)	0.712
2 Vertebrae or less	32 (80.00%)	37 (80.43%)	20 (51.28%)	0.004
3 Vertebrae or more	8 (20.00%)	9 (19.57%)	19 (48.72%)	0.010

Notes: ^a: difference among the 3 groups.

Table 3 Intergroup Comparison of Vertebral Involvement

	TBS vs BS	TBS vs PS	BS vs PS
Thoracic vertebrae	0.001	1.0	0.002
Lumbar vertebrae	0.003	0.210	0.134
2 Vertebrae or less	0.960	0.007	0.004
3 Vertebrae or more	0.781	0.007	0.016

destruction underwent surgical treatment, and he had the longest course of continuous antituberculosis treatment, 1095 days. There were two deaths among the 40 patients: one 95-year-old male and one 65-year-old male with multiorgan failure. We observed 24 (60.00%) patients whose treatment regimens included linezolid, and 4 (16.66%, 4/24) experienced adverse drug reactions (ADRs) after 1–2 weeks of linezolid dosing. This included 2 gastrointestinal reactions (8.33%, 2/24) and 2 cases of myelosuppression (8.33%, 2/24). After switching to contezolid, three patients showed significant improvement in gastrointestinal reactions and myelosuppression compared with their previous linezolid regimen and thus were maintained on contezolid therapy. In addition, other drug-related ADRs included 2 cases of elevated blood pressure due to rifampicin, 1 case of hyperuricemia due to pyrazinamide, and 1 case of severe gastrointestinal reaction.

In the BS group, a combined antimicrobial regimen based on tetracyclines was used in all 46 patients. Four patients received dual therapy, 37 underwent triple therapy, and 5 required quadruple therapy because of inadequate fever and pain control. The treatment regimens of tetracycline plus rifampicin and second/third-generation cephalosporins were given to 50.00% of the patients. Tetracycline treatment included minocycline in 38 patients, doxycycline in 4 patients, and omadacycline in 4 patients. Omadacycline was used because of persistent high fever with unrelieved low back pain in 4 patients who initially received minocycline, and the change resulted in a significant improvement in clinical symptoms, such as pain and fever. Among the BS patients, 91.3% (42/46) received triple or more antimicrobial regimens, with a median treatment duration of 136 days (IQR 93–217.5). In this study, two patients had a course of treatment of more than 1 year, one 50-year-old woman with osteomyelitis and lesions involving adjacent ribs and soft tissues recovered with a treatment duration of 416 days, the other 51-year-old man with diabetes mellitus who had lesions involving the intervertebral discs recovered after the treatment duration of 381 days.

Treatment regimens in the PS group varied depending on the pathogens. The PS group as a whole was dominated by single- or two-agent anti-bacteria regimens (89.74%, 35/39), with a median duration of treatment of 92.50 days (IQR 68.00–167.75). For patients with gram-positive bacterial infections, the mean treatment duration was 94.55 days, while for those with gram-negative bacterial infections, it was 129.64 days. However, there was no statistically significant difference in the duration of therapy between the two groups ($p=0.462$). The main causative agent in this group was *Staphylococcus aureus* (56.41%, 22/39), and the most common treatment regimen was linezolid in combination with rifampicin for anti-infection (31.82%, 7/22). One patient was switched to omadacycline because of intolerance of gastrointestinal reactions to linezolid. Among the 6 patients with *Klebsiella pneumoniae* infection, 2 had their antibiotics adjusted to omadacycline for persistent fever, the temperature returned to normal after 3 days of omadacycline use. A typical case involved an elderly woman with a urinary tract infection from *Haemophilus influenzae* that led to bacteremia, which then spread to cause spinal infection. After 8 days of treatment with omadacycline and levofloxacin, she had significant relief from lumbar pain.

Discussion

In the present study, we characterized the clinical characteristics and treatment regimens of TBS, BS, and PS. Results showed that PS is more commonly associated with sepsis, invasive manipulation, elevated inflammatory markers, psoas abscesses, and involvement of three or more vertebral bodies compared to TBS and BS. Furthermore, treatment strategies demonstrate individualised differences across various spondylitis subtypes. As in previous studies,^{26–29} this study found a male-to-female ratio of 1.84:1, with an average age of 61.83 years. Unlike the study by Hajar et al,²⁷ the patients in the TBS group in the present study were the oldest.

Spinal infectious diseases typically present with nonspecific back and neck pain as the earliest symptom.^{30–32} In our study, pain was reported by almost all the patients. Fever occurred in more than half of the patients, with the PS group exhibiting the highest prevalence. Therefore, pain in the affected area should not be ignored, regardless of the presence or absence of fever. Notably, the incidence of symptoms of fever with pain was significantly greater in the PS and BS groups than in the TBS group in this study. The proportion of patients with combined sepsis and invasive spinal manipulation was significantly greater in the PS group than in the other two groups, and the time from symptom onset to consultation was the shortest. Therefore, in the presence of susceptibility factors, combined with low back pain and fever, physicians should promptly consider the possibility of spinal infection.

Magnetic resonance imaging (MRI) is the preferred method for detecting spinal infection, which showed that the lumbar spine region is the most affected area.^{33,34} In this research, more than 90% of the patients in the BS group had involvement of the lumbar spine, which was consistent with the results of a study in Saudi Arabia.²⁷ A recent study revealed that the presence of a lumbar major muscle abscess is an important predictor for differentiating TBS from BS.³⁵ However, in our cohort, psoas abscess occurred most commonly in the PS group. In contrast to reports by Turunc et al and Waheed et al,^{36,37} our data demonstrated significantly elevated peripheral blood WBC, CRP, and ESR levels in the PS group compared with those in the TBS and BS groups, which helped in making the pathogenetic diagnosis of spinal infection.

According to relevant studies, conservative management successfully treats the infection and alleviates pain in approximately 90% of cases.^{38–40} In the present study, a combination of drugs was the main treatment in all groups. In the TBS group, most patients received a standard quadruple anti-TB regimen as baseline therapy. Notably, more than half of the tuberculous spondylitis patients in our cohort were treated with linezolid combined with other agents. Although linezolid is essential for the treatment of multidrug-resistant tuberculosis, it is associated with myelosuppression, gastrointestinal reactions, and peripheral neuropathy, especially when it is used for long periods of time.^{41–44} In our study, linezolid caused gastrointestinal reactions and myelosuppression in two patients each. Symptoms improved after switching to contezolid. Several recent case reports and prospective studies have indicated that contezolid can be an effective alternative to linezolid without causing severe hematological toxicity or peripheral neuropathy, which is consistent with our findings.^{45–47}

In our study, more than 90% patients in the BS group received ≥ 3 combinations of drugs. While the WHO guidelines recommend doxycycline plus aminoglycosides or doxycycline plus rifampicin,⁴⁸ relevant studies have shown an infection recurrence rate of 59.3% in patients treated with the doxycycline-rifampicin regimen.⁴⁹ In a large multicenter retrospective comparative study of 293 patients with BS, five treatment regimens consisting of three triple anti-BS therapies and two double anti-BS therapies were used for at least 12 weeks, and the outcomes were compared.²⁸ Consistent with the results of the present study, there were no significant differences in outcomes among these five antibiotic groups. Nevertheless, recent studies have suggested that many clinicians favor the use of triple anti-BS therapy,⁵⁰ which was consistent with the choice of our treatment protocol.

In our PS group cohort, 69.23% (27/39) of patients received two-drug antimicrobial therapy. With respect to the predominant *S. aureus* infections, over 30% were treated with rifampicin combined with linezolid. Although rifampicin is commonly used to treat tuberculosis, its efficacy in treating orthopedic staphylococcal infections has also been confirmed.^{51–54} Notably, the rifampicin–fluoroquinolone combination constitutes an established oral regimen for staphylococcal bone infections in Europe.^{17,55} In the present study, omadacycline, a new and highly publicized agent, was used to treat both BS and PS. Omadacycline has a broad spectrum of antimicrobial activity against a wide range of clinical pathogens, including gram-positive, gram-negative, and atypical pathogens and multidrug-resistant isolates, as well as overcoming resistance to tetracycline.⁵⁶ Notably, a study has demonstrated 80.0% treatment success rates for bone/joint infections with omadacycline.⁵⁷ The combination of omadacycline with rifampicin has emerged as a promising alternative for treating patients with MRSA osteomyelitis.^{56,58} The results of the present study also confirm that oral omadacycline can be used to treat these conditions with a low incidence of adverse effects.

The optimal duration of antibiotic therapy for treating spinal infections is highly controversial.⁵⁹ Recommendations for the treatment of spinal infections endorsed by international guidelines include minimum durations of 6 weeks, 12 weeks, and 9 months for PS, BS, and TBS, respectively.^{12,60} However, real-world studies have shown that the treatment course often exceeds these guidelines. One study from southern Tunisia reported a median treatment duration for BS of 24 weeks, with a range of 3–13 months, and the duration varied considerably according to the clinical response and complications.⁶¹ In our study, the median treatment duration for BS was 19 weeks, with a range of 1.5 to 13 months. With respect to TBS, 145 patients received medication for 18 months in a study that included 863 patients, which is consistent with the results of our study.⁶² Patients in the PS group appeared to require shorter treatment durations than those in the TBS and BS groups did. The median duration of treatment in the PS group in this study was only 13 weeks, which is shorter than the 17 weeks reported in Saudi Arabia. We concluded that patients' final treatment duration needs to be individualized according to their clinical response and complications.

This study has several limitations. First, the sample size for spinal infections is relatively small. Second, because of the long overall course of spinal infections, some patients were lost to follow-up, making it difficult to systematically assess the efficacy of different treatment regimens and perform between-group difference analyses. Therefore, prospective studies with larger sample sizes should be conducted in the future to dynamically monitor the clinical outcomes of patients and further explore treatment options for patients with spinal infections.

Conclusion

Clinicians must thoroughly understand the distinct clinical presentations and epidemiological profiles of spinal infections caused by different pathogens. Our findings emphasize that treatment typically requires individualized regimens, making timely and accurate etiological diagnosis fundamental for therapeutic optimization. The selection of effective and adequate anti-infective regimens based on pathogens and patients, as well as the strengthening of follow-up management, are essential to significantly improve patient prognosis and reduce the risk of recurrence. Future studies with larger samples are needed to overcome current limitations and further validate optimal treatment strategies.

Data Sharing Statement

The data that support the findings of this study are included and will be available from the corresponding author(s) upon reasonable request.

Ethics/Ethical Approval

The study protocol adhered to the principles outlined in the Declaration of Helsinki and complied with relevant national laws and policies. Approval for this study was obtained from the Human Ethics Committee of Anhui Medical University (approval no. PJ20250641).

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests.

References

1. Baryeh K, Anazor F, Iyer S, Rajagopal T. Spondylodiscitis in adults: diagnosis and management. *Br J Hosp Med.* 2022;83(10):1–9. doi:10.12968/hmed.2021.0448
2. Isenberg J, Jubel A, Hahn U, Seifert H, Prokop A. Die mehrzeitige Spondylodese. *Der Orthopde.* 2005;34(2):159–166. doi:10.1007/s00132-004-0722-4
3. Merino P, Candel FJ, Gestoso I, Baos E, Picazo J. Microbiological diagnosis of spinal tuberculosis. *Intl Orthopaed.* 2012;36(2):233–238. doi:10.1007/s00264-011-1461-x
4. Schilling A, Seibold M, Mansmann V, Gleissner B. Successfully treated Candida krusei infection of the lumbar spine with combined caspofungin/posaconazole therapy. *Med Mycol.* 2008;46(1):79–83. doi:10.1080/13693780701552996

5. Rutges JPHJ, Kempen DH, van Dijk M, Oner FC. Outcome of conservative and surgical treatment of pyogenic spondylodiscitis: a systematic literature review. *Eur Spine J*. 2015;25(4):983–999. doi:10.1007/s00586-015-4318-y
6. Chang W-S, Ho M-W, Lin P-C, et al. Clinical characteristics, treatments, and outcomes of hematogenous pyogenic vertebral osteomyelitis, 12-year experience from a tertiary hospital in central Taiwan. *J Microbiol Immunol Infect*. 2018;51(2):235–242. doi:10.1016/j.jmii.2017.08.002
7. Colmenero JD, Jiménez-Mejías ME, Sánchez-Lora FJ, et al. Pyogenic, tuberculous, and brucellar vertebral osteomyelitis: a descriptive and comparative study of 219 cases. *Ann Rheum Dis*. 1997;56(12):709–715. doi:10.1136/ard.56.12.709
8. Moritani T, Kim J, Capizzano AA, Kirby P, Kademian J, Sato Y. Pyogenic and non-pyogenic spinal infections: emphasis on diffusion-weighted imaging for the detection of abscesses and pus collections. *Br J Radiol*. 2014;87(1041). doi:10.1259/bjr.20140011
9. Cheng H, Wu H, Tan N, et al. Diagnostic Efficacy of Metagenomic Next-Generation Sequencing in Patients with Spinal Infections: a Retrospective Study. *Infect Drug Resist*. 2023;16:7613–7620. doi:10.2147/idr.S435466
10. Zarghooni K, Röllinghoff M, Sobottke R, Eysel P. Treatment of spondylodiscitis. *Intl Orthopaed*. 2012;36(2):405–411. doi:10.1007/s00264-011-1425-1
11. Qi M, Du Y, Guan J, et al. The clinical management and efficacy of metagenomic next-generation sequencing in patients with pyogenic spinal infection: a single-center cohort study. *J Orthopaedic Surg Res*. 2024;19(1):3. doi:10.1186/s13018-024-05188-8
12. Barbari EF, Kanj SS, Kowalski TJ, et al. Infectious Diseases Society of America (IDSA) Clinical Practice Guidelines for the Diagnosis and Treatment of Native Vertebral Osteomyelitis in Adults. *Clin Infect Dis*. 2015;61(6):e26–e46. doi:10.1093/cid/civ482
13. Katsevman GA, Emery E, France JC, Sedney CL. Secondary Discitis Masquerading as Treatment Failure of Primary Discitis: case Report and Review of the Literature. *Int J Spine Surg*. 2019;13(2):120–124. doi:10.14444/6016
14. Tang L, Fu C-G, Zhou Z-Y, et al. Clinical Features and Outcomes of Spinal Tuberculosis in Central China. *Infect Drug Resist*. 2022;15:6641–6650. doi:10.2147/idr.S384442
15. Altunçekiç Yildirim A, Kurt C, Çetinkol Y. Brucellosis with rare complications and review of diagnostic tests: a case report. *J Med Case Rep*. 2022;16(1):2. doi:10.1186/s13256-022-03702-2
16. Ekici MA, Özbek Z, Kazancı B, Güçlü B. Collapsed L4 Vertebral Body Caused by Brucellosis. *J Korean Neurosurgical Soc*. 2014;55(1). doi:10.3340/jkns.2014.55.1.48
17. Bernard L, Dinh A, Ghout I, et al. Antibiotic treatment for 6 weeks versus 12 weeks in patients with pyogenic vertebral osteomyelitis: an open-label, non-inferiority, randomised, controlled trial. *Lancet*. 2015;385(9971):875–882. doi:10.1016/s0140-6736(14)61233-2
18. Cho WM, Lee JS, Chung SW, et al. Infectious Spondylitis Caused by *Streptococcus gordonii*. *Cureus*. 2023;2023:36657. doi:10.7759/cureus.36657
19. Qiangsheng F, Xiaoqin H, Tong L, Wenyun G, Yuejuan S. Brucella cultures characteristics, clinical characteristics, and infection biomarkers of human Brucellosis. *J Infect Public Health*. 2023;16(3):303–309. doi:10.1016/j.jiph.2023.01.002
20. Luzzati R, Giacomazzi D, Danzi MC, Tacconi L, Concia E, Vento S. Diagnosis, management and outcome of clinically-suspected spinal infection. *J Infect*. 2009;58(4):259–265. doi:10.1016/j.jinf.2009.02.006
21. Fleege C, Rauschmann M, Arabmotlagh M, Rickert M. Development and current use of local antibiotic carriers in spondylodiscitis. *Der Orthopäde*. 2020;49(8):714–723. doi:10.1007/s00132-020-03942-4
22. Geisler Crone C, Mose Tetens M, Bengaard Andersen A, Obel N, Lebech A-M. Clinical characteristics of pyogenic vertebral osteomyelitis, and factors associated with inadequate treatment response. *Inter J Infect Dis*. 2021;108:487–493. doi:10.1016/j.ijid.2021.05.078
23. Internal Clinical Guidelines T. *National Institute for Health and Care Excellence: Clinical Guidelines. Tuberculosis: Prevention, Diagnosis, Management and Service Organisation*. National Institute for Health and Care Excellence (UK) Copyright © 2016 National Institute for Health and Care Excellence. 2016.
24. Lee KY. Comparison of pyogenic spondylitis and tuberculous spondylitis. *Asian Spine J*. 2014;8(2):216–223. doi:10.4184/asj.2014.8.2.216
25. Tsantes AG, Papadopoulos DV, Vrioni G, et al. Spinal Infections: an Update. *Microorganisms*. 2020;8(4):476. doi:10.3390/microorganisms8040476
26. Mete B, Kurt C, Yilmaz MH, et al. Vertebral osteomyelitis: eight years' experience of 100 cases. *Rheumatol Int*. 2012;32(11):3591–3597. doi:10.1007/s00296-011-2233-z
27. AlQahtani H, Alzahrani F, Abalkhail G, Hithlayn HB, Ardah HI, Brucellar AA. Pyogenic, and Tuberculous Spondylodiscitis at Tertiary Hospitals in Saudi Arabia: a Comparative Retrospective Cohort Study. *Open Forum Infect Dis*. 2023;10(9):ofad453. doi:10.1093/ofid/ofad453
28. Ulu-Kilic A, Karakas A, Erdem H, et al. Update on treatment options for spinal brucellosis. *Clin Microbiol Infect*. 2014;20(2):O75–82. doi:10.1111/1469-0691.12351
29. Cottle L, Riordan T. Infectious spondylodiscitis. *J Infect*. 2008;56(6):401–412. doi:10.1016/j.jinf.2008.02.005
30. Jung WS, Choi SR, Kwon JW, et al. Infective Spondylitis in Adults: a Journey Through Diagnosis, Management, and Future Directions. *Antibiotics*. 2025;14(4):391. doi:10.3390/antibiotics14040391
31. Mylona E, Samarkos M, Kakalou E, Fanourgiakis P, Skoutelis A. Pyogenic vertebral osteomyelitis: a systematic review of clinical characteristics. *Semin Arthritis Rheum*. 2009;39(1):10–17. doi:10.1016/j.semarthrit.2008.03.002
32. Gonzalez GA, Porto G, Tecce E, et al. Advances in diagnosis and management of atypical spinal infections: a comprehensive review. *N Am Spine Soc J*. 2023;16:100282. doi:10.1016/j.xnsj.2023.100282
33. Li T, Liu T, Jiang Z, Cui X, Sun J. Diagnosing pyogenic, brucella and tuberculous spondylitis using histopathology and MRI: a retrospective study. *Exp Ther Med*. 2016;12(4):2069–2077. doi:10.3892/etm.2016.3602
34. Qin C, Dai LP, Zhang YL, et al. The value of MRI radiomics in distinguishing different types of spinal infections. *Comput Methods Programs Biomed*. 2025;264:108719. doi:10.1016/j.cmpb.2025.108719
35. Abudukadier M, Zhang Y, Li M, et al. A Novel Differentiation Nomogram Model for Brucellar Spondylitis and Tuberculous Spondylitis. *Infect Drug Resist*. 2024;17:5895–5907. doi:10.2147/idr.S497404
36. Waheed G, Soliman MAR, Ali AM, Aly MH. Spontaneous spondylodiscitis: review, incidence, management, and clinical outcome in 44 patients. *Neurosurg Focus*. 2019;46(1):E10. doi:10.3171/2018.10.Focus18463
37. Turunc T, Demiroglu YZ, Uncu H, Colakoglu S, Arslan H. A comparative analysis of tuberculous, brucellar and pyogenic spontaneous spondylodiscitis patients. *J Infect*. 2007;55(2):158–163. doi:10.1016/j.jinf.2007.04.002
38. Roblot F, Besnier JM, Juhel L, et al. Optimal duration of antibiotic therapy in vertebral osteomyelitis. *Semin Arthritis Rheum*. 2007;36(5):269–277. doi:10.1016/j.semarthrit.2006.09.004

39. Karadimas EJ, Bungler C, Lindblad BE, et al. Spondylodiscitis. A retrospective study of 163 patients. *Acta Orthop.* 2008;79(5):650–659. doi:10.1080/17453670810016678
40. Cheung WY, Luk KD. Pyogenic spondylitis. *Int Orthop.* 2012;36(2):397–404. doi:10.1007/s00264-011-1384-6
41. Motta I, Cozzi SN, Pontali E. QT prolongation for old and new drugs: how much should we really worry? *Int J Tuberc Lung Dis.* 2022;26(4):298–301. doi:10.5588/ijtld.22.0072
42. Veerman K, Goosen J, Spijkers K, Jager N, Heesterbeek P, Telgt D. Prolonged use of linezolid in bone and joint infections: a retrospective analysis of adverse effects. *J Antimicrob Chemother.* 2023;78(11):2660–2666. doi:10.1093/jac/dkad276
43. Hasan T, Medcalf E, Nyang'wa BT, et al. The Safety and Tolerability of Linezolid in Novel Short-Course Regimens Containing Bedaquiline, Pretomanid, and Linezolid to Treat Rifampicin-Resistant Tuberculosis: an Individual Patient Data Meta-analysis. *Clin Infect Dis.* 2024;78(3):730–741. doi:10.1093/cid/ciad653
44. Wasserman S, Brust JCM, Abdelwahab MT, et al. Linezolid toxicity in patients with drug-resistant tuberculosis: a prospective cohort study. *J Antimicrob Chemother.* 2022;77(4):1146–1154. doi:10.1093/jac/dkac019
45. Xiong YJ, Xiao Y, Xie L, et al. Contezolid for the Treatment of Drug-Resistant Tuberculosis in China: a Clinical Case Series. *Infect Drug Resist.* 2024;17:3491–3499. doi:10.2147/idr.S469509
46. Jiang G, Liu R, Xue Y, et al. Contezolid Harbored Equivalent Efficacy to Linezolid in Tuberculosis Treatment in a Prospective and Randomized Early Bactericidal Activity Study. *Infect Drug Resist.* 2025;18:261–268. doi:10.2147/idr.S499816
47. Wang J, Nie W, Ma L, et al. Clinical Utility of Contezolid-Containing Regimens in 25 Cases of Linezolid-Intolerable Tuberculosis Patients. *Infect Drug Resist.* 2023;16:6237–6245. doi:10.2147/idr.S425743
48. Joint FAO/WHO expert committee on brucellosis. *World Health Organ Tech Rep Ser.* 1986;740:1–132.
49. El Miedany YM, El Gaafary M, Baddour M, Ahmed I. Human brucellosis: do we need to revise our therapeutic policy? *J Rheumatol.* 2003;30(12):2666–2672.
50. Spernovasilis N, Karantanis A, Markaki I, et al. Brucella Spondylitis: current Knowledge and Recent Advances. *J Clin Med.* 2024;13(2):595. doi:10.3390/jcm13020595
51. El Zein S, Berbari EF, Passerini M, et al. Rifampin Based Therapy for Patients With Staphylococcus aureus Native Vertebral Osteomyelitis: a Systematic Review and Meta-analysis. *Clin Infect Dis.* 2024;78(1):40–47. doi:10.1093/cid/ciad560
52. Cho OH, Bae IG, Moon SM, et al. Therapeutic outcome of spinal implant infections caused by Staphylococcus aureus: a retrospective observational study. *Medicine.* 2018;97(40):e12629. doi:10.1097/md.00000000000012629
53. Zimmerli W, Sendi P. Role of Rifampin against Staphylococcal Biofilm Infections In Vitro, in Animal Models, and in Orthopedic-Device-Related Infections. *Antimicrob Agents Chemother.* 2019;63(2):1. doi:10.1128/aac.01746-18
54. Diekema DJ, Pfaller MA, Shortridge D, Zervos M, Jones RN. Twenty-Year Trends in Antimicrobial Susceptibilities Among Staphylococcus aureus From the SENTRY Antimicrobial Surveillance Program. *Open Forum Infect Dis Mar.* 2019;6(Suppl 1):S47–s53. doi:10.1093/ofid/ofy270
55. Spilf. Primary infectious spondylitis, and following intradiscal procedure, without prosthesis. Short text. *Med Mal Infect.* 2007;37(9):554–572
56. Huband MD, Fedler KA, Mendes RE, et al. Surveillance of omadacycline against 35,000 bacterial clinical isolates from the United States. *Diagn Microbiol Infect Dis.* 2025;111(3):116711. doi:10.1016/j.diagmicrobio.2025.116711
57. Morrisette T, Alosaimy S, Lagnf AM, et al. Real-World, Multicenter Case Series of Patients Treated with Oral Omadacycline for Resistant Gram-Negative Pathogens. *Infect Dis Ther.* 2022;11(4):1715–1723. doi:10.1007/s40121-022-00645-5
58. Karau MJ, Schmidt-Malan SM, Cunningham SA, et al. Activity of Omadacycline in Rat Methicillin-Resistant Staphylococcus aureus Osteomyelitis. *Antimicrob Agents Chemother.* 2022;66(1):e0170321. doi:10.1128/aac.01703-21
59. Saeed K, Esposito S, Ascione T, et al. Hot topics on vertebral osteomyelitis from the International Society of Antimicrobial Chemotherapy. *Int J Antimicrob Agents.* 2019;54(2):125–133. doi:10.1016/j.ijantimicag.2019.06.013
60. Rajasekaran S, Soundararajan DCR, Shetty AP, Kanna RM. Spinal Tuberculosis: current Concepts. *Global Spine J.* 2018;8(4 Suppl):96s–108s. doi:10.1177/2192568218769053
61. Koubaa M, Maaloul I, Marrakchi C, et al. Spinal brucellosis in South of Tunisia: review of 32 cases. *Spine J.* 2014;14(8):1538–1544. doi:10.1016/j.spinee.2013.09.027
62. Cao G, Rao J, Cai Y, et al. Analysis of Treatment and Prognosis of 863 Patients with Spinal Tuberculosis in Guizhou Province. *Biomed Res Int.* 2018;2018:3265735. doi:10.1155/2018/3265735

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