The Role of Serological and Tuberculosis Tests in the Diagnosis of Vertebral Osteomyelitis and the Medical Treatment of Paravertebral Involvement

Ali Kutta Çelik [1], Çiğdem Yalçın[2], Mustafa Uğuz[1], Fatih Erdem[1], Berfin Çirkin Doruk[1]

1 Department of Infectious Diseases and Clinical Microbiology, Mersin Training and Research Hospital, Mersin, Türkiye
2 Department of Algology, Mersin Training and Research Hospital, Mersin, Türkiye

Abstract

Aim: Vertebral osteomyelitis (VO) is an uncommon but clinically significant infection that should be considered in patients presenting with axial back pain. Because its symptoms are often nonspecific, diagnosis is frequently delayed, and identification of the causative microorganism is not always possible.. This study aimed to evaluate the diagnostic value of serological and tuberculosis-related tests and to assess treatment strategies in patients with paravertebral involvement.

Methods: A total of 127 adult patients diagnosed with VO between February 2017 and February 2022 who completed treatment were retrospectively evaluated. Demographic characteristics, laboratory findings, imaging results, etiological classification, treatment regimens, need for treatment modification, and outcomes were recorded. Statistical analyses were performed using appropriate parametric and nonparametric tests, and a p-value < 0.05 was considered statistically significant.

Results: A total of 127 patients were included in the study. Pyogenic bacteria were the most common etiological agents (71.6%), followed by tuberculous VO (24.4%) and brucellar VO (3.9%).. C-reactive protein (CRP) levels were significantly higher in tuberculous VO, whereas erythrocyte sedimentation rate (ESR) values were significantly higher in pyogenic VO. White blood cell (WBC) count and procalcitonin levels demonstrated limited diagnostic utility. Paravertebral involvement was significantly more frequent in tuberculous and brucellar VO than in pyogenic VO ($p < 0.001$). Purified protein derivative (PPD) and interferon-gamma release assay (IGRA) results did not reliably differentiate etiological subgroups. Monthly follow-up with contrast-enhanced magnetic resonance imaging (MRI) was useful in identifying patients who required treatment modification.

Conclusions: Definitive etiological diagnosis in vertebral osteomyelitis (VO) cannot be established solely on the basis of serological tests and tuberculosis (TB) investigations. Brucellosis serological tests may yield false-positive results not only in acute brucellosis and miliary TB but also in cases of tuberculous osteomyelitis. Therefore, this possibility must be carefully considered during treatment planning and patient follow-up.

Close clinical monitoring combined with serial magnetic resonance imaging (MRI) evaluations constitutes the cornerstone of disease management. The duration of therapy should be individualized, and both clinical and radiological responses should be assessed together. If necessary, treatment may need to be extended until complete radiological resolution is achieved.

Keywords: *Vertebral osteomyelitis; serology; medical treatment; paravertebral involvement*

1. Introduction

Vertebral osteomyelitis (VO) accounts for approximately 1–7% of all osteomyelitis cases and represents the third most common type of osteomyelitis, particularly in individuals over 50 years of age[1-3]. Its incidence has increased in recent years, likely due to an aging population, the increased use of invasive procedures, and advances in diagnostic imaging[4].

The clinical presentation of VO is often nonspecific. Although axial back pain is the most common symptom, diagnosis may be delayed for weeks or even months. Diagnostic delays of up to four months have been reported[5]. In the absence of standardized diagnostic and therapeutic ainorithms, management remains challenging. Tissue sampling is performed in relatively few centers, and many physicians avoid these interventions due to the risk of complications.

Contrast-enhanced magnetic resonance imaging (MRI) is the most used imaging modality for the diagnosis of VO. imaging modality of choice, with diagnostic accuracy exceeding 90%. Although histopathological examination and microbiological culture are considered the gold standard for identifying the etiological agent, tissue sampling is performed in relatively few centers and many physicians avoid these interventions due to the risk of complications. Etiological diagnosis, invasive sampling is not always feasible, and the

Corresponding Author: Ali Kutta Çelik, drakcelik27@yahoo.com.tr, Received: 02.02.2026, Accepted: 13.03.2026, Available Online Date: 15.03.2026.
https://doi.org/10.36516/jocass.1880005

causative organism may remain unidentified[5]. Consequently, empirical treatment decisions are frequently based on clinical findings and serological tests, including the Brucella standard tube agglutination test (SAT), the tuberculin skin test (PPD), and interferon-gamma release assays (IGRAs).

This condition, which develops mostly spontaneously and partly secondary to surgical or invasive procedures, is more common in elderly and immunosuppressed patients.[6] Due to its rarity and non-specific presentation, VO is frequently overlooked.

This study aimed to evaluate the role of serological and TB tests in the etiological classification of VO, to determine treatment durations according to the causative microorganism, and to assess the clinical significance of paravertebral involvement.

2. Materials and Methods

Study Design and Population

This retrospective study was conducted in the Infectious Diseases and Clinical Bacteriology Department. Adult patients (≥18 years) diagnosed with VO between February 2017 and February 2022 who completed treatment were included. Patients with prior spinal surgery, hematological malignancy, or incomplete treatment were excluded. A total of 127 patients met the inclusion criteria. We would like to clarify that none of the patients included in this study underwent open or percutaneous biopsy.

The study was approved by the Non-Interventional Clinical Research Ethics Committee (25 April 2022; Decision No: 2022/283) and was conducted in accordance with the Declaration of Helsinki.

Data Collection

Demographic data, comorbidities, laboratory parameters (CRP, ESR, WBC, procalcitonin, and vitamin D), pain severity (Numeric Rating Scale), vertebral level of involvement, paravertebral involvement, microbiological findings, treatment regimens, duration of therapy, and outcomes were analyzed.

Statistical Analysis

Normality was assessed using the Kolmogorov–Smirnov and Shapiro–Wilk tests. Continuous variables were expressed as mean ± standard deviation or median (interquartile range), as appropriate. Normally distributed variables were expressed as mean ± standard deviation, while non-normally distributed variables. The Mann–Whitney U test was used to compare two independent groups for non-normally distributed variables. The Kruskal–Wallis test was applied for comparisons of more than two groups, and Conover post hoc analysis was performed to identify the source of statistically significant differences. A p-value of <0.05 was considered statistically significant.

Table 1

Demographic data and laboratory findings

Average age			56.86 SD years (28-90 years)		
					p
Age			<65	83 (65.4%)	p<0,001
			≥65	44 (34.6%)	
Gender			Female	88 (69.3%)	p<0,001
			Male	39 (30.7%)	
			Treatment		
		Pyogenic	Tuberculosis	Brucellosis	P
WBC	Normal	85 (93,4%)	29 (93,5%)	5 (100,0%)	0,390
	Leucopenia	2 (2,2%)	2 (6,5%)	0 (0,0%)	
	Leukocytosis	4 (4,4%)	0 (0,0%)	0 (0,0%)	
Crp	Normal	72 (79,1%)	15 (50,0%)	3 (60,0%)	0,010
	High	19 (20,9%)	15 (50,0%)	2 (40,0%)	
Pct	Normal	91 (100,0%)	30 (96,8%)	5 (100,0%)	0,241
	High	0 (0,0%)	1 (3,2%)	0 (0,0%)	
ESR	Normal	65 (71,4%)	15 (48,4%)	1 (20,0%)	0,009
	High	26 (28,6%)	16 (51,6%)	4 (80,0%)	
Vitamin D	Normal	19 (34,5%)	5 (35,7%)	0 (0,0%)	0,430
	Low	36 (65,5%)	9 (64,3%)	2 (100,0%)	

Presence of chronic disease(n:77)	n%
Diabetes mellitus (DM)	12 (15.6%)
Hypertension (HT)	34 (44.2%)
Chronic obstructive pulmonary disease (COPD)	10 (13%)
Malignancy	4 (5.2%)
Hypothyroidism	2 (2.6%)
Hyperthyroidism	1 (1.3%)
Heart failure	8 (10.4%)
Osteoporosis	4 (5.2%)
Rheumatological disease	2 (2.6%)

Table 2
The anatomical regions involved, effective treatment times, mean treatment times, MR recovery time, and PVI distribution

		Treatment			P
		Pyogenic	Tuberculosis	Brucellosis	
Zone of involvement	Cervical (n:15)	13 (14.3%)	1 (3.2%)	1 (20.0%)	0,055
	Thoracic (n:13)	6 (6.6%)	7 (22.6%)	0 (0%)	
	Lumbar (n:99)	72 (79.1%)	23 (74.2%)	4 (80.0%)	
Paravertebral zone infection	None (n:101)	81 (89.0%)	18 (58.1%)	2 (40.0%)	<0,001
	Yes (n:26)	10 (11.0%)	13 (41.9%)	3 (60.0%)	
Effective treatment time (months)		3,0 (2,0-4,0)	12.0 (6.0-12.0)	4.0 (3.0-7.5)	<0.001
MR recovery time (mean, months)		3,0 (2,0-4,0)	5.0 (4.0-9.0)	5.0 (3.5-6.5)	<0.001
Mean treatment time		3 months	12 months	4 months	

3. Results

Of the 127 patients 69.3% were female. And the mean age was 56.86 ± 13.19 years. Demographic characteristics, sites of involvement, etiological factors, and mean treatment durations are presented in Table 1.

VO was more frequent among females and individuals younger than 65 years. No significant association was observed between vitamin D levels and either pyogenic or granulomatous VO. Among comorbid conditions, hypertension was the most common.

Pyogenic VO was diagnosed in 91 patients (71.6%), tuberculous VO in 31 patients (24.4%), and brucellar VO in 5 patients (3.9%).

The most frequently affected vertebral regions were identified, in descending order, as the lumbar (78%), cervical, and thoracic vertebral segments (Table 2)

Blood cultures were positive in 14 patients (11%). Among these, *Brucella* spp. was isolated in 2 patients, methicillin-resistant *Staphylococcus aureus* (MRSA) in 5 patients, and methicillin-sensitive coagulase-negative *Staphylococcus* (MSCNS) in 7 patients.

Identified pathogens included methicillin-resistant *Staphylococcus aureus*, methicillin-sensitive coagulase-negative *Staphylococcus*, and *Brucella* spp.

PPD and IGRA results did not reliably differentiate etiological groups (p = 0.245). Among patients with tuberculous VO, only 58.1% had positive PPD and/or IGRA results.

Even in patients with positive PPD or IGRA results, pyogenic VO treatment was administered for at least one month. Anti-tuberculosis(anti-TB) therapy was initiated in cases without regression on contrast-enhanced MRI performed after one month of treatment and in whom clinical findings did not improve. In four patients with thoracic and paravertebral involvement and strong PPD or IGRA positivity, anti-TB therapy was initiated directly.

In patients with negative PPD and IGRA tests, anti-TB therapy was also started if no clinical or radiological improvement was observed after three months of pyogenic VO treatment and *Brucella* agglutination tests remained negative.

Patients with SAT positivity at any titer had a significantly higher likelihood of *Brucella* spp. or *Mycobacterium tuberculosis* etiology (p < 0.001). Among six patients initially treated for brucellosis but later switched to anti-TB therapy due to treatment failure, four had SAT titers >1/160 and two had titers <1/160.

CRP levels were significantly higher in tuberculous VO, whereas ESR values were significantly higher in pyogenic VO. WBC count and procalcitonin levels demonstrated limited diagnostic value. No significant association was found between vitamin D levels and VO subtype.

Paravertebral involvement was detected in 26 patients (20.5 was significantly more common in tuberculous and brucellar VO than pyogenic VO (p < 0.001). Twelve patients had associated abscess formation; all responded to medical therapy alone. The lumbar spine was the most frequently affected region across all etiological groups. Mean treatment durations, MRI resolution times, and PVI distributions are shown in Table 2.

Among all patients, 112 (88.1%) were initially treated as pyogenic VO, 11 (8.7%) as brucellar VO, and 4 (3.1%) as TB VO. Following treatment modifications based on clinical examination and MRI findings, complete cure was achieved in 91 pyogenic VO patients, 31 TB VO patients, and 5 brucellar VO patients (Table 2).

All four patients who received direct anti-TB therapy had thoracic and paravertebral involvement. Two of these patients were IGRA-positive, one had a PPD induration of 15 mm, and one was PPD-anergic.

Table 3
Initial and final treatments in VOM patients

n:127	Pyogenic	Tuberculosis	Brucellosis
Initial treatment	112(%88.1)	4 (%3.1)	11(%8.7)
Final treatment	91 (%71.6)	31 (%24.4)	5 (%3.9)

Treatment Protocols

Patients with pyogenic VO received initial therapy with teicoplanin plus ciprofloxacin. Those who did not demonstrate clinical or radiological improvement after one month were switched to daptomycin plus a carbapenem.

Patients with brucellar VO were treated with streptomycin–rifampicin–doxycycline for the three weeks, followed by rifampicin–doxycycline.

Patients with tuberculous VO received isoniazid–rifampicin–ethambutol–pyrazinamide for the first two months, followed by isoniazid–rifampicin.

Treatment modifications were guided by clinical findings and serial MRI evaluations. None of the patients required surgical intervention. Treatment modification was required in 27 patients (21.3%). Of these patients, 22 (81.5%) had lumbar VO and 4 (14.8%) had thoracic VO. In all of these cases, treatment was switched to anti-tuberculosis therapy.

The mean duration of treatment was 3 months (1.5–9 months) for pyogenic VO, 12 months (6–12 months) for tuberculous VO, and 4 months (3–9 months) for brucellar VO.

Treatment modification was required in 27 patients (21.3%), most commonly involving a switch from pyogenic to anti-TB

therapy.

Complete clinical and radiological cure was achieved in all patients.

Initial treatment regimens and final treatments after therapy modifications are summarized in Table 3.

Data analysis revealed that PPD and IGRA tests were not useful in distinguishing disease type (p = 0.245). Among patients who underwent PPD testing, 8 were positive, 13 negative, and 10 anergic. Of the 13 patients tested with IGRA, 10 were positive and 3 negatives.

Among the 31 patients treated for TB VO, only 58.1% (n = 18) had positive PPD and/or IGRA results (PPD anergy or ≥15 mm induration was considered positive).

Table 4

Number and Percentages of PPD and Quantiferon gold test groups in patients who recovered with anti-tuberculosis therapy in the final treatment

	Positive	Negative	Anergic
Ppd	8	13	10
Quantiferongold test	10	3	

**LR*

Table 5

Cross-Table of PPD and Quantiferon results

			Quantiferon -	Quantiferon +	Total	P
PPD	-	N	2	3	5	
		%	66,7%	30,0%	38,5%	
	+	N	1	3	4	
		%	33,3%	30,0%	30,8%	0,245
	0 mm	N	0	4	4	
		%	0,0%	40,0%	30,8%	
Total		N	3	10	13	
		%	100,0%	100,0%	100,0%	

**LR*

4. Discussion

This study evaluated etiological distribution, diagnostic testing, and treatment strategies in a relatively large cohort of patients with VO. Pyogenic infections were the most common cause, consistent with contemporary epidemiological data, although regional differences may explain variations reported in other studies. The mean patient age was 56.8 years, consistent with the literature. Female predominance (69.3%) was observed; while some studies report higher prevalence among females[4], others report male predominance[3,7].

In the literature, the most commonly involved regions are reported as lumbar, thoracic, and cervical vertebrae, respectively[8]. In contrast, our study identified lumbar, cervical, and thoracic vertebrae as the most frequent sites of involvement. Despite evaluating etiological factors, trauma history, and intravenous drug use, no clear explanation for the relatively high cervical involvement was identified, indicating the need for larger, well-designed studies. Lumbar involvement was the most frequent overall, whereas paravertebral involvement was significantly associated with tuberculous and brucellar VO. Importantly, all paravertebral abscesses were successfully managed with medical therapy alone, suggesting that close monitoring may eliminate the need for surgical drainage in selected patients.

Historically, granulomatous infections were the predominant cause of VO; however, with improvements in animal vaccination, sanitation, and surgical techniques, pyogenic infections and TB have become more prevalent[9,10]. Our findings are consistent with the literature[11], although some studies report brucellosis as the leading cause[10], likely due to regional epidemiological differences.

Consistent with prior reports, TB VO predominantly involved the thoracolumbar region, whereas brucellar and pyogenic VO were more common in the lumbar and cervical regions[8]. Differences compared with Gökmen et al.[10] may be attributable to regional livestock exposure.

Vitamin D deficiency has been associated with increased susceptibility to infections, including TB, malignancies, multiple sclerosis, and diabetes[12,13], and may predispose to osteomyelitis[14]. However, no prior study has evaluated vitamin D levels in VO. In our cohort, no significant association between vitamin D levels and VO was identified.

VO often presents with nonspecific symptoms, leading to diagnostic delays. While diagnosis is usually prompted by imaging performed for pain, rare asymptomatic cases have been reported[15]. The mean diagnostic delay in our study was 18 weeks, consistent with reported delays ranging from 6 weeks to 7 months[16].

MRI has over 90% diagnostic accuracy in VO[17] and served as the primary diagnostic and follow-up modality in our study. Although tissue biopsy remains the diagnostic gold standard, its invasive nature limits its use, and diagnosis often relies on serological testing[18], which may be inconclusive.

CRP and ESR were more informative than WBC count or procalcitonin levels; however, none were disease specific. Serial contrast-enhanced MRI played a central role in evaluating treatment response and guiding therapy modification.

Serological and TB tests demonstrated limited discriminatory value. Negative PPD or IGRA results did not exclude tuberculous VO, and false-positive SAT results were observed in patients ultimately diagnosed with TB. Cross-reactivity and false-positive SAT results may occur in endemic regions due to exposure to other pathogens such as *Francisella*, *Yersinia*, *Legionella*, and *Mycoplasma*[19]. SAT may yield false-positive results not only in acute brucellosis and miliary TB but also in TB osteomyelitis, and this possibility should be considered during management. Only 7 of 21 patients who were switched from pyogenic to TB therapy had positive PPD or IGRA results, indicating that negative tests do not exclude TB VO. PPD anergy should not be interpreted as absence of disease.

Although current guideline recommends 6–9 months of therapy for extrapulmonary TB, the mean treatment duration for tuberculous VO in this cohort was 12 months. We therefore suggest continuing therapy until complete radiological resolution is achieved.

A major limitation of this study is the absence of histopathological confirmation, as no patient underwent biopsy. Nevertheless, the findings reflect real-world clinical practice in which invasive procedures are often avoided.

5. Conclusion

Vertebral osteomyelitis is a rare but clinically challenging disease with diagnostic difficulties due to nonspecific early

symptoms and potential morbidity in chronic stages. There is a need for standardized diagnostic and therapeutic algorithms supported by well-designed clinical studies. Our findings indicate that serological tests alone are insufficient for diagnosis and that treatment response should be assessed through close clinical follow-up and MRI. Treatment duration should be individualized and extended until complete radiological recovery. Larger studies are required to support guideline-level recommendations.

Statement of ethics

This study was conducted in accordance with 25 April 2022; Decision No: 2022/283, which was granted by the Clinical Research Ethics Committee of Mersin Training and Research Hospital. The study adhered to the Helsinki Declaration.

genAI

No artificial intelligence-based tools or generative AI technologies were used in this study. The entire content of the manuscript was originally prepared, reviewed, and approved by both authors.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of interest statement

The authors declare that they have no conflict of interest.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

References

1. Gregori F, Grasso G, Iaiani G, Marotta N, Torregrossa F, Landi A. Treatment algorithm for spontaneous spinal infections: a review of the literature. J Craniovertebr Junction Spine. 2019;10(1):3-9. Crossref
2. Eser O, Aslan A, Coşar M, Şahin Ö, Korkmaz S. Spontaneous cervical vertebral osteomyelitis: case report. Duzce Med J. 2008;2:34-36.
3. Herren C, Jung N, Pishnamaz M, Breuninger M, Siewe J, Sobottke R. Spondylodiscitis: Diagnosis and Treatment Options. Dtsch Arztebl Int. 2017;114(51-52):875-882. Crossref
4. Beronius M, Bergman B, Andersson R. Vertebral osteomyelitis in Göteborg, Sweden: a retrospective study of patients during 1990-95. Scand J Infect Dis. 2001;33(7):527-532. Crossref
5. Calmenero JD, et al. Ann Rheum Dis. 1997;56:709-715.
6. Müller EJ, Russe OJ, Muhr G. Osteomyelitis of the spine. Orthopade. 2004;33(3):305-315. Crossref
7. Yoon SH, Chung SK, Kim K-J, Kim H-J, Jin YJ, Kim HB. Pyogenic vertebral osteomyelitis: identification of microorganism and laboratory markers used to predict clinical outcome. Eur Spine J. 2010;19(4):575-582. Crossref
8. Mavrogenis AF, Papagelopoulos PJ, et al. Spondylodiscitis revisited. EFORT Open Rev. 2017;2(11):447-461. Crossref
9. Lehovsky J. Pyogenic vertebral osteomyelitis/disc infection. Baillieres Best Pract Res Clin Rheumatol. 1999;13(1):59-75. Crossref
10. Gok S, Kaptanoglu E, Celikbas A, Ergonul O, Baykam N, Eroglu M, Dokuzoguz B. Vertebral osteomyelitis: clinical features and diagnosis. Clin Microbiol Infect. 2014;20(10):1055-1060. Crossref
11. 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):20140011. Crossref
12. Walker VP, Modlin RL. The vitamin D connection to pediatric infections and immune function. Pediatr Res. 2009;65(5 Pt 2):106R-113R. Crossref
13. Abdollahi H, Salehinia F, Badeli M, Karimi E, Gandomkar H, Asadollahi A, Sedighiyan M, Abdolahi M. The Biochemical Parameters and Vitamin D Levels in ICU Patients with Covid-19: A Cross-Sectional Study. Endocr Metab Immune Disord Drug Targets. 2021;21(12):2191-2202. Crossref
14. Signori V, Romanò CL, Vecchi ED, Mattina R, Drago L. May osteoarticular infections be influenced by vitamin D status? An observational study on selected patients. BMC Musculoskelet Disord. 2015;16:183. Crossref
15. Sohatee MA, Shields DW. Painless vertebral osteomyelitis: an unusual presentation. BMJ Case Rep. 2013;2013:bcr2012008298. Crossref
16. McHenry MC, Easley KA, Locker GA. Vertebral osteomyelitis: long-term outcome for 253 patients from 7 Cleveland-area hospitals. Clin Infect Dis. 2002;34(10):1342-1350. Crossref
17. Love C, Patel M, Lonner BS, Tomas MB, Palestro CJ. Diagnosing spinal osteomyelitis: a comparison of bone and Ga-67 scintigraphy and magnetic resonance imaging. Clin Nucl Med. 2000;25(12):963-977. Crossref
18. Nickerson EK, Sinha R. Vertebral osteomyelitis in adults: an update. Br Med Bull. 2016;117(1):121-138. Crossref
19. Kilic S, Celebi B, Bayram Y, Citil B. Investigation of cross-reactions with Francisella tularensis antibodies to Brucella. Turk Hij Den Biyol Derg. 2013;70(2):65-70. Crossref
20. Guo et al. Differentiating brucella spondylitis from tuberculous spondylitis by the conventional MRI and MR T2 mapping: a prospective study. Eur J Med Res. 2021;26:125. Crossref
21. Eren S, Büyükavcı M, Ezirmik N, Ertek M. Spinal Brucellosis with Paraspinal Abscess Formation Treated with CT Guided Percutaneous Abscess Drainage. Interv Neuroradiol. 2004;10(4):329-334. Crossref
22. Enercan M, Ozturk C, Karaca S, Hamzaoglu A. Infections of the spinal column. J Turk Spinal Surg. 2011;10(3):245-257.
23. Graeber A, Cecava ND. Vertebral osteomyelitis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022.