



Original Article

## Multidrug-resistant tuberculosis of spine diagnosis and management: An institutional experience of 21 cases

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### ABSTRACT

**Background:** We aimed to establish a standardized protocol for managing multidrug-resistant (MDR) spinal tuberculosis (TB), addressing the surgical options, ranging from computed tomography-guided biopsy to intraoperative sampling.

**Methods:** This study developed a treatment/management protocol based on an analysis of clinical, radiological, and postoperative outcomes for 21 patients with spinal MDR-TB. Over 24 months, 21 patients with multidrug-resistant spinal TB underwent the following testing: erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), numerical rating scale (NRS), and the American Spinal Injury Association Scale. Radiological criteria were based upon a comparison of preoperative and 6-month to 2-year postoperative plain radiographs.

**Results:** The 21 patients underwent guided biopsies (35%) or intraoperative sampling (65%). For the surgical cases, dorsal vertebrae were most frequently involved (75%), and 90% underwent posterior surgical procedures. Postoperatively, ESR, CRP, kyphosis angle, and NRS score were significantly reduced. The 3 MDR patients who failed treatment were transitioned to the extensively drug-resistant (XDR) protocol wherein bedaquiline, linezolid, cycloserine, and clofazimine were given after drug sensitivity testing drug regimen, needed no further surgery, and none exhibited additional neurological deterioration.

**Conclusion:** Regular clinical, laboratory, radiological, and outcome analysis is vital for following MDR spinal TB patients; early detection of relatively rare treatment failures (i.e., 3/21 patients in this series) allows for prompt initiation of XDR treatment, resulting in better outcomes.

**Keywords:** Drug-resistant tuberculosis, Extensively drug resistant, Multidrug resistant, Spinal tuberculosis, Surgery

### INTRODUCTION

Spinal tuberculosis (TB) is the most common form of skeletal TB, accounting for about 50% of cases.<sup>[3]</sup> In this study, we reviewed our experience with the management of spinal multidrug-resistant (MDR) TB in 21 patients undergoing a combination of surgical approaches and medial/chemotherapeutic modalities. Early diagnosis and treatment of spinal MDR TB are key to avoiding chronic neurological disability, increased morbidity, and mortality rates. Although advances in molecular biology and molecular diagnostic techniques may be applied

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to spinal MDR TB, unfortunately, improper dosing, inadequate duration of treatment, and inappropriate selection of candidates for chemotherapy have resulted in the resurgence of TB and multidrug-resistant strains.<sup>[4,5]</sup> Here, we evaluated the clinical, radiological, laboratory, and surgical outcomes of 21 patients with MDR spinal TB better to define the best operative and chemotherapy treatment protocols.

## MATERIALS AND METHODS

This Institutional Review Board-approved study was performed over 24 months and included 21 consecutive patients with MDR TB utilizing multiple inclusion and exclusion criteria [Table 1]. The study included 16 females and 5 males, averaging 20.55 years of age. Nine patients had involvement of the lower thoracic levels, with 3 patients being in D8–D9. Eight patients underwent computed tomography-guided biopsy, while 13 patients had open surgical biopsies performed [Figure 1]. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were obtained preoperatively and followed postoperatively. Plain radiographs were taken preoperatively and followed postoperatively between 6 months and 2 years and were utilized to assess the % resolution of kyphosis [Figures 2-4 and Table 2]. MRI scans were performed only preoperatively [Figure 5]. Outcomes were analyzed utilizing the numerical rating scale (NRS) and the American Spinal Injury Association (ASIA) scale [Table 2].

## RESULTS

Patients demonstrated an 85.7% improvement in their postoperative ASIA grade. The 3 MDR cases that failed treatment required transitioning to an extensively drug-resistant (XDR) protocol wherein bedaquiline, linezolid, cycloserine, and clofazimine were started after drug-sensitivity testing; they maintained their preoperative neurological status but failed to improve. We additionally observed significant reductions in postoperative ESR, CRP, radiological kyphosis angles, and improvement in outcomes [Table 2] such as NRS and ASIA scale.

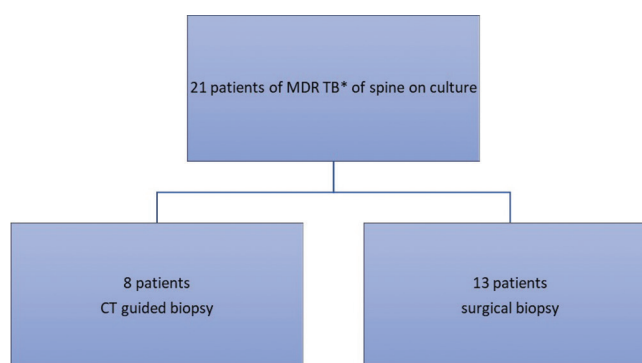
## DISCUSSION

More than 50% of drug-resistant spinal TB cases have been reported in India and China.<sup>[1]</sup> Drug-resistant spinal TB has been the subject of multiple investigations that typically include histological and/or bacteriological confirmation of TB. In Li *et al.*, 127 (51%) of 249 patients had spinal TB histologically confirmed (i.e., positive cultures); 39 (30.7%) were proven to be drug resistant (i.e., isoniazid [54.3%], rifampicin [48.6%], and streptomycin [34.3%]).<sup>[5]</sup> Mohan *et al.*

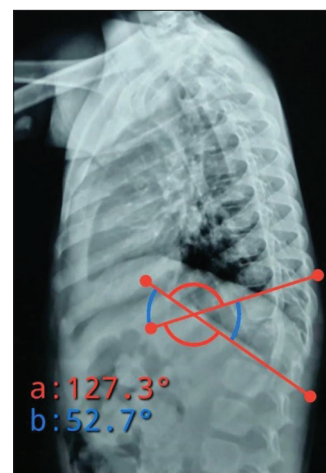
**Table 1:** Inclusion and exclusion criteria for the enrolment of the patient for the study.

Inclusion criteria	Exclusion criteria
1. Only patients with proven MDR-TB of the spine with a positive culture were enrolled in the study.	1. Patients with other infective spondylodiscitis (pyogenic, fungal, etc.), those with inadequate follow-up, and those who did not provide consent for the study were excluded.
2. Cases of MDR spinal tuberculosis, irrespective of age, sex, and other comorbidities were chosen	
3. With the availability of preop and postop follow-up up to 2 years.	

MDR: Multidrug resistance, TB: Tuberculosis



**Figure 1:** Flowchart demonstrating the selection of patients during the study.



**Figure 2:** Lateral radiograph of dorsolumbar spine showing D11 vertebral body complete collapse with kyphotic deformity at the level. b=kyphosis angle=52.7 degree

**Table 2:** Summarizing data.

Variable	Findings		
Number of patients	21		
Males	5		
Females	16		
Average follow-up duration	24 months		
Average age	20.55 years		
Range	38		
Preop/Postop ESR+CRP Values	Values ESR	Values CRP	
Mean preop ESR/CRP	82.61	70.04	
Mean postop ESR/CRP at 6 months	47.42	30.71	
Mean postop ESR CRP at 24 months	13.00	10.71	
Plain X-ray radiological assessment/mean kyphosis angles			
Preop	34.04		
6-month postop	18.14		
2-year postop	15.42		
NRS and ASIA preop/postop grades	Preop values	Postop 6 months	Postop 24 months
Preop versus postop NRS grades	8.52	3.19	1.61
Preop vs. Postop ASIA scale	A-11	A-0	A-0
	B-0	B-2	B-0
	C-4	C-4	C-2
	D-4	D-6	D-7
	E-4	E-9	E-12
(%) Tissue sampling methods			
CT-guided biopsies	8 (35%)		
Intraoperative sampling	13 (65%)		
Lower dorsal surgical location	75%		
Posterior surgery	90%		
Patients successfully treated MDR	18		
Failed cases requiring XDR	3		
Required additional surgery	0		
Exhibited increased neurological deficits	0		

NRS: Numerical rating scale, ASIA: American spinal injury association, Preop: Preoperative, Postop: Postoperative, XDR: Extensively drug-resistance, MDR: Multi-drug resistance, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein

also found drug resistance to multiple first-line TB treatments – isoniazid (92.7%), rifampicin (81.9%), ethambutol (51.3%), and pyrazinamide (46.8%).<sup>[6]</sup> In Pawar *et al.* 28 patients (11.7%) of 238 patients of spinal TB had histological confirmation and were discovered to have multidrug-resistant strains.<sup>[7]</sup>

### Levels of spinal TB

Fareeha Rauf found TB involved in descending order the thoracic (45%), followed by the lumbosacral (33%) and cervical (10%) levels. Notably, 70% of our cases involved the thoracic spine, followed by 30% in the lumbosacral spine; interestingly, 12% involved multiple levels [Table 3].

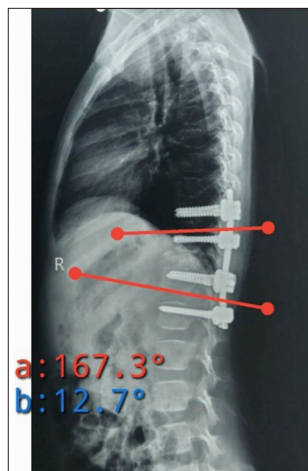
### Surgical approaches

In our study, patients 90% had posterior procedures (i.e., mostly laminectomy), 5% were posterolateral approaches

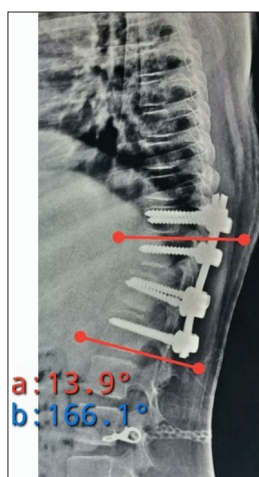
(5%), and 5% involved transthoracic procedures [Table 2]. Yang *et al.* similarly emphasized that posterior approaches resulted in better clinical outcomes when compared to anterior or combined 360° procedures.<sup>[8,9]</sup>

### Neurological recovery following spinal surgery for TB

The majority of studies demonstrated significant preoperative neurological compromise from spinal TB but significant postoperative improvement. In Charde *et al.*, most preoperative patients were in Frankel ASIA Grade E (40%), Grade C (27.5%), and Grade A (15%); 18 months postoperatively, they had improved to ASIA Grade E (62.5%), Grade D (17.5%), and Grade C (10%).<sup>[2]</sup> In Shah *et al.*, postoperatively, 23 (46%) patients improved by 1 Frankel Grade.<sup>[8]</sup> Preoperatively, our patients were in Frankel Grade A (52.3%) and in each of Grades C, D, and E (19%); at



**Figure 3:** Postoperative 6-month lateral radiograph showing partial fusion at D11-D12 level due to anterior reconstruction.  $b$ =kyphosis angle =12.7 degree. Kyphosis angle is angulation between the superior and inferior plates of the curved portion of spine. Upper red line is passing through superior end plate of superior most vertebra of most curved portion of spine. Lower red line is passing through inferior end plate of inferior most vertebra of most curved portion of spine.



**Figure 4:** Postoperative 2-year lateral radiograph showing complete fusion at D11-D12 of the graft due to anterior reconstruction.  $a$ =Cobb's angle =13.9 degree.

**Table 3:** Distribution on the basis of level.

Level	Frequency	Percentage
D1	2	9.5
D10-D11	1	4.8
D12-L3	1	4.8
D5-D6	1	4.8
D5-D7	1	4.8
D6-D9	1	4.8
D7-D8	1	4.8
D8-D10	3	14.3
D8-D9	3	14.3
D9-D11	1	4.8
L1-L3	1	4.8
L2-L3	1	4.8
L2-L3-L4	1	4.8
L3-L4	1	4.8
L3-S1	1	4.8
Total	21	100.0



**Figure 5:** T2-weighted (a) Saggittal and (b) Axial sequence of MRI showing complete collapse of D11 vertebral body with anterior epidural abscess with pre and paraspinal collection.

24 postoperative months, they too demonstrated significant neurological recovery (i.e., 57.1% ASIA Grade E, 33.3% ASIA Grade D, and 9.5% ASIA Grade C) [Table 2].

#### Use of ESR and CRP to follow the resolution of spinal TB infections

ESR and CRP preoperative and postoperative values are typically used to track the resolution of spinal TB infections. Our preoperative average ESR values of 80.60 improved to 11.95 postoperatively, while our average preoperative CRP values of 69.10 improved to an average of 11.18 postoperatively [Table 2].

#### CONCLUSION

Regular clinical, laboratory, radiological, and outcome analysis is vital for following patients with spinal TB infection. Early detection of treatment is critical to attaining the best postoperative outcomes.

**Ethical approval**

The research/study approved by the Institutional Review Board at Seth GS Medical college and KEM hospital, number EC/105/2022, dated December 17, 2022.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

**Use of artificial intelligence (AI)-assisted technology for manuscript preparation**

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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