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Epidemiological Insights from 1,652 Patients with Spinal Tuberculosis Managed at a Single Center: A Retrospective Review of 5-Year Data

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Study Design: Retrospective cohort.

Purpose: To report the demographic characteristics, clinico-radiological presentation, laboratory findings, and outcomes of "middle-path" treatment in patients with spinal tuberculosis from a single public healthcare facility in a developing country.

Overview of Literature: Tuberculosis is a global health problem that is endemic in developing countries and undergoing resurgence in developed ones. Spinal tuberculosis can cause disabling back pain, progressive deformity, and neurological involvement. However, there is a lack of large-scale epidemiological studies quantifying the size and severity of the problem of spinal tuberculosis.

Methods: Hospital records of spinal tuberculosis patients treated at a single center over a period of 5 years were retrospectively reviewed. A diagnosis of spinal tuberculosis was based on standard clinical, radiological, microbiological, and histopathological evidence. Patients were treated in accordance with the "middle-path" regimen; surgery was reserved for selective indications.

Results: A total of 1,652 patients were included. Their median age was 32.4 years, with 53% being male. Axial pain (98%) was the most common presenting symptom; 19% of patients had neurological deficit. Lumbar spine (37%) was the most common site of involvement, with a paradiscal pattern (82%) of involvement predominating. Multi-level involvement was seen in 19% of patients; skip lesions were noted in 2.8%. Transpedicular biopsy was performed in 667 patients; at least one tissue test was diagnostic of tuberculosis in 65% of patients. Forty-four patients had drug resistance to rifampicin. Surgery was required in 10.5% of patients. The "middle-path" regimen was associated with high compliance and significant improvements in pain (Visual Analog Scale score) and function (36-Item Short Form Health Survey).

Conclusions: Our findings confirm the widespread prevalence of spinal tuberculosis and describe various epidemiological characteristics of a large sample of spinal tuberculosis patients. Adoption of the "middle-path" regimen is associated with high compliance and favorable outcomes in spinal tuberculosis.

Keywords: Epidemiology; Infections; Pott's disease; Spinal tuberculosis; Tuberculosis

Introduction

With the advent of anti-tubercular chemotherapy and early radiographic diagnosis, it was believed that the eradication of tuberculosis (TB) would be possible. However, not only has TB survived, but it has thrown up new

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challenges such as drug resistance and co-infection with human immunodeficiency virus (HIV). Globally, more than 10 million people contracted TB in 2019 [1]. India has the highest share of TB cases, accounting for 26% of the global TB burden, which is 3 times the levels of the countries ranked second (Indonesia, 8.5%) and third (China, 8.4%) [1]. In 2019, a staggering 2.5 million new cases of TB were reported in India; in comparison, 8,920 TB cases were reported in the United States in the same year [2]. Given this context, any path to the global control or eradication of TB would inevitably pass through India. Likewise, the burden of extrapulmonary TB (EPTB) in India is high, accounting for approximately 16% of total new TB cases. This proportion is even higher among HIV-positive people [3]. Skeletal TB accounts for 10% of EPTB, with the spinal column alone accounting for half of skeletal TB cases [4]. While this may be only a fraction of the total TB burden, the ubiquity of TB in India makes spinal TB a diagnosis that is commonly encountered by orthopedic surgeons. Owing to its importance from a public health perspective, most of the country's resources for research, diagnosis, and treatment have conventionally been directed toward pulmonary TB. Nevertheless, spinal TB can cause significant ill health due to disabling back pain, progressive deformity, and neurological involvement [5].

The size and severity of the TB problem, along with its socioeconomic impact, suggest that the foundation for TB control has to be laid by large-scale public health programs. Achieving the control of TB requires a consolidated effort from various specialties, with each specialty battling a specific form of EPTB, within the framework of a larger war waged against TB. As spine surgeons, one of our major contributions would be to understand and report the demographic trends and epidemiological patterns of spinal TB, and to formulate and fine-tune treatment regimens that are appropriate in the context of resource-constrained healthcare settings, where spinal TB is more common. There is a dearth of large-scale epidemiological studies focusing solely on spinal TB; understanding various epidemiological features of spinal TB can help in generating awareness among physicians, quantifying the scale of the problem, guiding resource allocation, and providing information regarding the prevalence of various clinical and radiological findings. Likewise, the management of spinal TB has also evolved from radical surgery to a more conservative "middle-path" approach, with the recognition that uncomplicated spinal TB is essentially a "medical" disease [6,7]. However, there is still no global consensus over most aspects of treatment, such as the choice of anti-tubercular drugs, duration of chemotherapy, indications for surgery, and choice of surgical approach. The objectives of this study are: (1) to report on the demographic features, clinical presentation, radiographic presentation, and initial laboratory findings in a large sample of patients with spinal TB presenting to a single, tertiary-level, public healthcare facility in India, and (2) to describe various components of the "middle-path" regimen adopted at our center along with the outcomes of such a management approach.

Materials and Methods

The procedures used in this study adhere to the tenets of the Declaration of Helsinki. After approval from the Institutional Ethics Committee of All India Institute of Medical Sciences, New Delhi (IRB approval no., IEC-671/RP-38/2020), data prospectively collected from the hospital records of patients who had received treatment for spinal TB at a single, tertiary-level, public healthcare facility in India between 2014 and 2018 were retrospectively analyzed. Patients signed informed consent regarding publishing their data and photographs. These included both patients who were operatively treated and those who were managed without surgical intervention. A diagnosis of spinal TB was ascribed to a patient in accordance with a composite reference standard, which required the fulfillment of one or more of the following criteria: (1) identification of *Mycobacterium tuberculosis* in one or more microbiological tests (growth on Lowenstein–Jensen [LJ] solid culture, mycobacterial growth indicator tube [MGIT] liquid culture, acid-fast-positive staining on Ziehl–Neelsen [ZN] staining, Xpert MTB/RIF assay), (2) identification of typical histological features of TB (epithelioid granulomas, granulomatous inflammation, caseous necrosis, Langerhans giant cells) on histopathological examination (HPE), and (3) negativity in microbiological tests and HPE, but having clinical and radiological findings strongly suggestive of tubercular spondylodiscitis with a documented clinical, serological, and radiological response to empirical anti-tubercular treatment (ATT).

As part of the standard work-up in patients suspected or confirmed of having spinal TB, the following investigations were performed in addition to detailed history-

taking and physical examination: plain radiographs of the spine, chest radiograph, complete blood count, erythrocyte sedimentation rate (ESR), renal function test, liver function test (LFT), C-reactive protein (CRP), and whole-spine magnetic resonance imaging (MRI). If a large psoas abscess was present, ultrasound-guided drainage with or without pigtail insertion was performed. Patients were screened for comorbid conditions and directed to appropriate specialty clinics for simultaneous management of these conditions. In approximately 40% of patients, we performed transpedicular biopsy under CT/fluoroscopy guidance. The biopsy samples were sent for histopathological and microbiological investigations (Xpert MTB, ZN staining, LJ/MGIT culture). Treatment was allocated in accordance with the "middle-path" regimen advocated by Tuli [6]. For rifampicin-sensitive patients, the total duration of anti-tubercular chemotherapy was 12 months, which comprised an intensive phase (4HRZE) of 4 months and a continuation phase (8HR) of 8 months. In rifampicin-resistant patients, second-line chemotherapy was started after consultation with an infectious disease specialist. Strict bed rest was not advised; patients remained ambulant, with an orthosis being prescribed for 3 months. Patients were followed up at monthly intervals during the intensive phase and at every 3 months thereafter until the completion of chemotherapy; a final follow-up visit was scheduled 6 months after the completion of chemotherapy to rule out disease relapse. Healing of the disease was documented by contrast-enhanced MRI performed after 12 months of chemotherapy, and correlating it with clinical improvement and normalization of ESR and CRP. Surgery was reserved for certain indications: no clinical or radiological response to treatment in 12 weeks, new-onset neurological deficit or worsening of existing neurological deficit on treatment, severe (Kumar and Tuli stage 3 or stage 4) paraplegia at onset, mechanical instability consequent to bony pathology causing back pain, and progressive or severe spinal deformity. Patients reported their Visual Analog Scale (VAS) scores and completed the 36-Item Short Form Health Survey (SF-36) questionnaire at stipulated follow-up intervals. The final outcome of treatment for each patient was graded into four categories (excellent, good, fair, and poor) based on a set of clinical, radiological, and functional criteria, as outlined in Table 1. Similar combinations of clinical, radiological, and functional criteria were also used in previous studies to grade final outcomes [8,9].

Descriptive statistics were noted in the form of mean with standard deviation for normally distributed continuous data, median with range for continuous data not in a normal distribution, and frequency/percentage for categorical data. Changes in VAS score, SF-36 domain scores, ESR, and CRP at three different time-points (pre-chemotherapy, 3 months, and 12 months) were analyzed using

Table 1. Grading of outcome using clinical, radiological, and functional criteria

Grade	Criteria[a]		
	Clinical	Radiological	Functional
Excellent	- Compliance to treatment - No/minimal side effects to ATT - Normalization of inflammatory markers at final follow-up	- Complete radiological resolution of disease on contrast-enhanced MRI and plain radiographs at 12-month follow-up - Post-treatment kyphotic angle <30° (thoracic spine) and <20° (cervical and lumbar spine)	- Improvement or no worsening of pre-treatment neurological status - 12-month follow-up VAS <2
Good	- Compliance to treatment - Mild side effects to ATT not necessitating temporary cessation/change of drugs, but needing additional medical management - Normalization of inflammatory markers at final follow-up	- Complete radiological resolution of disease on contrast-enhanced MRI and plain radiographs at 12-month follow-up - Post-treatment kyphotic angle >30° (thoracic spine) and >20° (cervical and lumbar spine)	- Improvement or no worsening of pre-treatment neurological status - 12-month follow-up VAS <4
Fair	- Non-compliance to treatment; treatment default - Severe side effects to ATT necessitating temporary cessation/change of drugs - Raised inflammatory markers at final follow-up	- Incomplete radiological resolution of disease on contrast-enhanced MRI and plain radiographs at 12-month follow-up	- Improvement or no worsening of pre-treatment neurological status - 12-month follow-up VAS >4
Poor	- Clinical deterioration necessitating surgical intervention	- Radiological deterioration necessitating surgical intervention	- Worsening of neurological status necessitating surgical intervention

ATT, anti-tubercular treatment; MRI, magnetic resonance imaging; VAS, Visual Analog Scale.
[a]The 'grade' ascribed was in accordance with the lowest of the clinical, radiological, and functional criteria met by the patient. A similar combination of clinical, radiological, and functional criteria has been used to grade final outcomes in previous studies as well [8,9].

paired *t*-test or Wilcoxon's rank-sum test as applicable. A *p*-value <0.05 was considered to be statistically significant.

Results

Our study population comprised 1,652 patients, including 875 males (53%) and 777 females (47%). The median age was 32.4 years (range, 4–87 years), with the most commonly afflicted age group being 21–30 years (33%). Pediatric patients (age <12 years) accounted for 6.9%, whereas geriatric patients (age ≥65 years) accounted for 4.6% of the study population. One or more comorbidities were seen in 528/1,652 patients (32%), with hypertension (11.8%) and diabetes mellitus (9.2%) being the most common. Overall, 19/1,652 patients (1.1%) had HIV infection. Table 2 summarizes the baseline demographic characteristics of the study population.

Concomitant active pulmonary TB was seen in 69/1,652 patients (4.1%), whereas a previous history of pulmonary TB was encountered in 101 patients (6.1%). Six patients (0.3%) had a previous history of EPTB: four patients had TB lymphadenitis and two had intestinal TB. Disseminated TB with spinal involvement was seen in four patients. The most common site of involvement in the spinal column was the lumbar spine (611/1,652 patients [37%]) followed by the thoracic spine (439/1,652 patients [26.6%]). The involvement of junctional areas of the spinal column was observed in 404/1,652 patients (24.5%). The most common morphological pattern of involvement was paradiscal (1,354/1,652 patients [82%]). Multi-level, contiguous involvement was present in 314/1,652 patients (19%); this was determined to be present in patients who had more than one disc with its adjacent vertebrae involved if the morphology of the lesion was paradiscal. In patients with central or appendiceal morphology, the involvement of more than one contiguous vertebra was considered to be multi-level, contiguous involvement. Skip lesions/multifocal, non-contiguous involvement was seen in 46/1,652 patients (2.8%). Table 3 summarizes the baseline radiological findings in the study population.

Back pain/neck pain (98%) was overwhelmingly the most common symptom at presentation. Fewer patients presented with fever (33%), loss of appetite (22%), recent weight loss (21%), radicular pain (12%), and deformity (9%). On average, patients had been suffering from one or more symptoms for 4.5±2.9 months before presentation. Neurological involvement was seen in 314/1,652 patients (19%), as graded by the Kumar and Tuli classification [10], 127/1,652 patients (7.7%) had stage 1 neurological involvement, 99/1,652 patients (6%) had stage 2 neurological involvement, and 74/1,652 (4.4%) patients had severe (stage 3 or 4) neurological involvement. A summary of the clinical findings in the study population is presented in Table 2.

Transpedicular biopsy from the lesion was performed in 667/1,652 patients. Xpert MTB/RIF assay was positive in 367/667 patients (55%); 44 of these had rifampicin resistance. Positive ZN staining was noted in 37/667 patients (5.5%). HPE was suggestive of TB in 267/667 patients (40%). Growth on LJ culture was noted in only 19/667 patients (2.8%). Combining all of the histopathological and microbiological investigations performed on the biopsy samples yielded sensitivity of 65% for the diagnosis of spinal TB; the biopsy was non-contributory in the rest of the cases. ESR was normal (<20 mm/hr) in 365 patients (22.1%), while serum CRP was normal (<10 mg/L) in 455 patients (27.5%). A summary of the findings from various laboratory investigations in the study population is presented in Table 4.

Data regarding the final outcome of management were available for 1,612/1,652 patients (Table 5). Overall, 37 patients were lost to follow-up, while three patients expired due to factors unrelated to spinal TB or its treatment. The rate of compliance with chemotherapy was 99%; 16 patients turned into treatment-defaulters. Mild side effects of chemotherapy (nausea, mild arthralgia, gastrointestinal disturbance, generalized itching), which were successfully managed with additional medications without necessitating a change in the ATT, were seen in 212/1,612 patients (13%). Moderate-to-severe side effects necessitating temporary cessation or modification of the ATT were seen in 66/1,612 patients (4%). These included drug-induced hepatotoxicity (n=58), skin hypersensitivity reaction/dermatitis (n=4), optic neuropathy (n=3), and severe arthralgia (n=1). Based on the indications for surgical treatment outlined earlier, 173/1,612 patients (10.7%) required operative intervention. Severe neurological deficit at presentation was the most common indication for surgery; in these cases, patients were operated on without any delay. The average duration between diagnosis of spinal TB and surgical intervention in the remaining patients was 8.5 weeks. Significant improvements in mean VAS score and mean individual SF-36 domain scores were noted with the adoption of the "middle-path" regimen.

Table 2. Summary of demographic and clinical characteristics of the study population (n=1,652)

Characteristic	Value
Age group (yr)	32.4 (4–87)
<10	101 (6.1)
11–20	251 (15.2)
21–30	551 (33.3)
31–40	294 (17.8)
41–50	188 (11.4)
51–60	130 (7.9)
61–70	73 (4.4)
71–80	47 (2.8)
81–90	17 (1.0)
Sex	
Male	875 (53.0)
Female	777 (47.0)
Comorbidities/co-existing medical conditions	
Diabetes mellitus	152 (9.2)
Hypertension	195 (11.8)
Chronic liver disease	44 (2.7)
Chronic kidney disease	61 (3.7)
Coronary artery disease	49 (2.9)
Cerebrovascular disease	24 (1.5)
Rheumatoid arthritis/ankylosing spondylitis/ seronegative spondyloarthropathy	20 (1.2)
HIV co-infection	19 (1.1)
Others	45 (2.7)
Associated pulmonary TB	
Active	69 (4.1)
Past history	101 (6.1)
Associated extrapulmonary TB	
Active	4
Past history	2
Symptoms	
Pain (back/neck)	1,620 (98.1)
Pain (radicular)	196 (11.9)
Fever	551 (33.0)
Weight loss	344 (20.8)
Loss of appetite	368 (22.2)
Deformity	149 (9.0)
Mean duration of symptoms (mo)	4.5±2.9
Neurological status (Kumar-Tuli staging)	
No deficit	1,338 (81.0)
Stage-1	127 (7.7)
Stage-2	99 (6.0)
Stage-3	59 (3.6)
Stage-4	15 (0.9)
Indications for surgery (n=173)	
Severe paraplegia at presentation	74
Worsening neurological status while on ATT	26
Vertebral destruction/mechanical instability causing intractable pain	25
Failure of response to conservative treatment at 12–16 weeks	20
Progressive deformity	26
Uncertain diagnosis	2
Surgical approach	
Cervical[a]	22 (anterior)
Cervicothoracic[b]	5 (anterior)
Thoracic[c]	1 (anterior trans-thoracic) 57 (posterior)
Thoracolumbar[c]	19 (posterior)
Lumbar[d]	58 (posterior)
Lumbosacral[d]	11 (posterior)

Values are presented as median (range), number (%), or mean±standard deviation.
HIV, human immunodeficiency virus; TB, tuberculosis; ATT, anti-tubercular treatment.
[a]Smith-Robinson approach. [b]None of the cases required a manubriotomy/sternotomy. [c]Anterolateral decompression was done by a posterior midline incision by performing costotransversectomy/trans-facetal approach/trans-pedicular approach. [d]Anterolateral decompression was done by a posterior midline incision by a transforaminal approach/transverse process osteotomy.

This was accompanied by significant declines in the levels of inflammatory markers (ESR, CRP). Complete clinical and radiological resolution of the disease was observed at the end of 12 months of chemotherapy for 1,540/1,612 patients. In the remaining 72 patients, while an improvement was noted compared with the baseline findings, the ATT was continued for 18 months in view of persistent/residual disease activity on contrast-enhanced MRI and raised inflammatory markers. Graded by the clinical-radiological-functional criteria outlined earlier, 1,363/1,612 patients (84.6%) had an excellent or good outcome with the "middle-path" regimen, whereas a poor outcome was noted in 102/1,612 patients (6.3%). None of the patients had relapse of the disease at final follow-up.

Table 3. Summary of imaging characteristics of the study population

Variable	Value
Regional distribution	
Craniocervical (occiput–C2)	18 (1.1)
Cervical (C2/C3 disc–C6/C7 disc)	227 (13.7)
Cervicothoracic (C7–T1/T2 disc)	18 (1.1)
Thoracic (T2–T11)[a]	439 (26.6)
Thoracolumbar (T11/12 disc–L1)	169 (10.2)
Lumbar (L1/L2 disc–L4/L5 disc)	611 (37.0)
Lumbosacral (L5–S1)	199 (12.0)
Sacrum (below S1) and coccyx	11 (0.7)
Morphology of lesion	
Paradiscal	1,354 (82.0)
Central	250 (15.1)
Appendiceal	48 (2.9)
No. of levels involved[b]	
1	1,338 (81.0)
2	199 (12.0)
≥3	115 (7.0)
Non-contiguous, multifocal involvement/skip lesions	46 (2.8)

Values are presented as number (%).
[a]Upper thoracic (T2–T4)=54; middle thoracic (T4/5 disc–T8)=119; and lower thoracic (T8/T9 disc–T11)=266. [b]A classical paradiscal lesion involving the adjacent end-plates of two contiguous vertebrae was considered as a single level involvement.

Table 4. Summary of laboratory findings in the study population

Investigation	Positive	Negative
LJ medium culture[a]	19 (2.8)	648 (91.2)
Presence of acid-fast bacilli on Ziehl Neelsen staining[a]	37 (5.5)	630 (94.5)
Xpert TB assay[a]	367 (55.0)	300 (45.0)
Rifampicin resistance on Xpert TB assay	44 (MDR+)	323
Histopathological features suggestive of TB[a]	267 (40.0)	400 (60.0)
ESR ≤20 mm/hr[b]	365 (22.0)	1,287 (78.0)
CRP ≤5 mg/L[b]	455 (27.5)	1,197 (72.5)

Values are presented as number (%).
TB, tuberculosis; MDR, multi-drug resistant; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.
[a]Test was performed only in 667 patients who underwent transpedicular biopsy; percentages have been reported accordingly. [b]Reference range for: ESR: <10 mm/hr (males), <20 mm/hr (females); CRP ≤5 mg/L.

Discussion

Spinal TB is the most common form of osteo-articular TB, accounting for 1%–5% of all TB cases [11,12]. While TB has declined in developed countries, it remains at large in the developing world. Owing to its designation as a global public health challenge, it is important to estimate the disease burden and study the demographic trends of TB. The WHO publishes the Global Tuberculosis Report every year and similar annual reports are published by individual countries; however, these quote consolidated figures for all TB cases. There is a dearth of large-scale epidemiological studies reporting the demographic, clinical, radiological, and laboratory findings in spinal TB. Most published studies are in the form of small case series with the study population comprising fewer than 100 patients. Considering that India harbors a quarter of the global TB burden, it is imperative that it takes the lead in undertaking such studies. Here, we report the demographic profile, clinico-radiological presentation, and initial laboratory findings in 1,652 patients who underwent treatment for spinal TB at a single center in India over a period of 5 years (2014–2018). In addition, we report the outcomes of the "middle-path" regimen for spinal TB followed at our center. The pioneering work of Tuli [6] in the "post-antitubercular drugs" era has made the indications of surgery in spinal TB selective; radical debridement has become a thing of the past. While such an approach has been wholeheartedly embraced in developing countries, routine surgery is still often practiced in developed countries, even for uncomplicated spinal TB, particularly with the increasing popularity of minimally invasive approaches. Most studies reporting on the outcome of conservative management of spinal TB have been limited by a small sample size or heterogeneity of data due to the involvement of multiple centers.

The earliest studies exclusively reporting on the epidemiological characteristics of patients with spinal TB in a large (>100 patients) study population were published from France and Turkey, by Pertuiset et al. [13] and Turgut [14], respectively. A major shortcoming of these studies was that patients were treated at multiple centers, with a lack of uniformity in the data reported, the diagnostic approach adopted, or the surgical indications. In the decade that followed, two other multi-center studies—this time from developing countries in Africa—reported on the epidemiological characteristics of spinal TB patients [15,16]. The first large study from a single center was reported from China in 2012, involving a retrospective review of a total of 284 patients with spinal TB who were

Table 5. Outcome measures at different time-points in the study population who completed final FU (n=1,612)

Outcome measure	At presentation	3-mo FU	*p*-value[a]	12-mo FU	*p*-value[b]
Visual Analog Scale	8.2±2.9	4.7±1.1	0.045	1.1±0.8	0.009
SF-36					
PF	54.4±9.6	62.6±9.6	0.11	78.8±10.2	0.023
RP	38.6±7.6	54.8±8.6	0.048	70.7±11.7	0.018
BP	24.8±6.6	45.6±7.8	0.045	80.1±10.8	0.008
GH	58.6±8.0	69.6±9.6	0.19	80.2±12.2	0.012
VT	60.8±8.0	69.9±10.1	0.11	84.8±9.6	0.033
SF	48.5±7.6	54.8±7.8	0.22	75.5±9.7	0.032
RE	48.2±8.6	64.8±9.7	0.048	78.8±12.2	0.021
MH	55.8±8.7	64.4±8.8	0.09	78.8±11.4	0.029
Erythrocyte sedimentation rate (mm/hr)	54 (4–124)	42 (1–78)	0.11	12 (1–36)	0.02
C-reactive protein (mg/L)	60 (6–119)	14 (0.1–78)	0.03	5 (0.1–32)	0.012

Values are presented as mean±standard deviation or median (range). Overall outcome grading: excellent: 970 (60.2%); good: 393 (24.4%); fair: 147 (9.1%); and poor: 102 (6.3%). The SF-36 consists of eight domains: PF, RP, BP, GH, VT, SF, RE, and MH.
FU, follow-up; SF-36, 36-Item Short Form Health Survey; PF, physical functioning; RP, role-physical; BP, bodily pain; GH, general health; VT, vitality; SF, social functioning; RE, role-emotional; MH, mental health.
[a]Representing comparison of outcomes between "at presentation" and 3-month FU. [b]Representing comparison of outcomes between "at presentation" and 12-month FU.

Table 6. Comparison of demographic characteristics of various studies reporting on epidemiology of spinal tuberculosis

Authors (year)	Country	Study period	No. of hospitals	No. of patients	Mean age (yr)	Sex ratio (male:female)	Time from symptom onset to diagnosis (range)
Pertuiset et al. [11] (1999)	France	1980–1994	7	103	41	1.94:1	4 mo (1 wk–3 yr)
Turgut [12] (2000)	Turkey	1985–1996	Multiple	694	32.4	0.98:1	NR
Sakho et al. [13] (2003)	Senegal	1986–1998	3	255	34.9	1.14:1	10.7 mo (1 mo–10 yr)
Godlwana et al. [14] (2008)	South Africa	2005–2006	1	104	NR	1.36:1	NR
Wang et al. [15] (2012)	China	2004–2010	1	284	38	1.07:1	18.0 mo (3 day–360 mo)
Garza Ramos et al. [16] (2017)	USA	2002–2011	Multiple	2,789	51	1.56:1	NR
Liu et al. [17] (2019)	China	2007–2016	Multiple	1,378	43.7	1.40:1	16 mo (15 day–240 mo)
Our study	India	2014–2018	1	1,652	32.4	1.12:1	4.5 mo (15 day–11 mo)

NR, not reported.

treated at a hospital in southwest China over a period of 7 years [17]. The mean age of the study population was 38.2 years, with nearly a third of patients being infected in the fourth decade of life (31–40 years). The study population was almost equally split between males and females (male:female ratio=1.07). Back pain (92.6%) was the most common presenting symptom, while deformity (28%), fever (26%), and neurological deficit (21%) were less frequent. Thoracic spine (45%) was reported to be the most commonly affected region. Skip lesions were observed in 5.6% of patients, whereas 28% of patients had more than three contiguous vertebral bodies involved. MRI was not performed in all of the patients in this study, which may have compromised the accuracy of the radiological findings. Surprisingly, the authors reported the duration between symptom onset and diagnosis of the disease to be 18 months, with 43% of patients being diagnosed over a year after their symptom onset. In 2017, de la Garza Ramos et al. [18] reported on the epidemiology of 2,789 cases of spinal TB treated between 2002 and 2011 included in the Nationwide Inpatient Sample Database of the United States. A higher median age (51 years) and a

Table 7. Comparison of clinical and radiological findings of various studies reporting of epidemiology of spinal TB

Authors (year)	Most common presenting symptom (%)	Patients with neurological deficit at presentation (%)	Patients with HIV infection (%)	Patients with concomitant pulmonary TB (%)	Most common level of involvement	Patients who had surgical intervention (%)	Multi-level involvement (%)	Skip lesions (%)
Pertuiset et al. [11] (1999)	Back pain (97)	50	0	18	Lumbar	25	25	6
Turgut [12] (2000)	Neurological deficit (69)	69	NR	45	Thoracic	98	NR	0.3 (single patient)
Sakho et al. [13] (2003)	Back pain (91)	79	2.7	59	Thoracic	15	NR	NR
Godlwana et al. [14] (2008)	NR	56	28	100	Thoracic	NR	NR	NR
Wang et al. [15] (2012)	Back pain (92)	22	0	12.7	Thoracic=lumbar	82	27	5.6
Garza Ramos et al. [16] (2017)	NR	NR	4	NR	NR	22	NR	NR
Liu et al. [17] (2019)	Back pain (92)	50	0	26	Lumbar	72	23	NR
Our study	Back pain (98)	19	1.1	4.1[a]	Lumbar	10.5	19	2.8

TB, tuberculosis; HIV, human immunodeficiency virus; NR, not reported.
[a]Only includes patients with active concomitant pulmonary TB. Another 6.1% patients had a past history of pulmonary TB.

higher proportion of males (61%) were reported in this study. Hypertension (28%) was the most common associated comorbidity, followed by diabetes (11.6%); overall, 4% of patients were HIV-positive. Surgery was performed in 619/2,789 patients (22.2%). Neither the presenting clinical features nor the radiological findings were reported. Another retrospective study reviewed the epidemiological profile of 1,378 spinal TB cases treated at various hospitals in south-central China between 2007 and 2016 [19]. The mean age of the study population was 43.7 years, with males accounting for 58% of the cases. Almost half of the patients had neurological impairment—this high proportion was possibly due to only in-hospital admissions being included. Lumbar spine (38%), closely followed by thoracic spine (36%), was the most commonly affected site. Concomitant pulmonary TB was present in 26.6% of patients. Surgical treatment was applied in 1,000/1,378 patients (73%). Comparisons between the major findings in these studies and our study are presented in Tables 6 and 7.

To the best of our knowledge, our work is the first epidemiological study extensively reporting on the demographic, clinical, and radiological profile and noting the initial laboratory findings at presentation in a large sample of patients with spinal TB from India, the country with the highest TB burden. With all of the patients being recruited from a single center with a high volume of such cases, the diagnostic approach, management strategy, and operative indications remained standardized throughout the study period. The mean age of our study population was 32.4 years, with a third of patients being infected in the third decade of life (21–30 years). The lower mean age than in earlier studies is consistent with the much younger population of India. Geriatric patients (age ≥65 years) accounted for 4.6% of the study population; the presence of comorbid conditions, a protracted and complicated course of illness, and risks of recumbency merit special attention to the management of these patients [12]. HIV-positivity was noted in only 1.1% of patients, which may be explained by the widespread social taboos associated with this condition, leading these patients to avoid mainstream medical care. Axial pain at the site of involvement was almost universally present (98%); in comparison, constitutional symptoms such as fever (33%), weight loss (21%), and loss of appetite (22%) were present less frequently. Unlike pulmonary TB, a clinician is more likely to encounter a patient with spinal TB with only a non-

specific complaint of pain, rather than a more specific constellation of symptoms that stand out for TB. Despite the emphasis on public health awareness regarding TB, we observed that patients presented with neurological deficit (19%) and deformity (9%), and noted a mean delay of 4.5 months between symptom onset and diagnosis. A dedicated information drive to raise awareness of spinal TB may help in improving these figures. The most commonly affected region of the spinal column in our study was the lumbar spine (37%), which contrasts with previous studies reporting that the thoracic spine was the most commonly involved site. Junctional areas of the spine are biomechanically critical due to their predisposition to instability and progressive deformity. In contrast to earlier studies, we noted that the lumbosacral junction (12%) was more commonly affected than the thoracolumbar junction (10%). Despite performing whole-spine MRI in all of our patients, the proportions of patients with multi-level, contiguous involvement (19%) and skip lesions (2.8%) were similar to those noted in earlier studies. Owing to the high case burden and logistic limitations, we could not perform a transpedicular biopsy in all of the patients.

However, among the 667 patients who underwent a biopsy, an overall diagnostic yield of 65% was observed. The paucibacillary nature of spinal TB lesions may have led to the biopsy being non-contributory in over a third of patients. Operative intervention was necessary in 173/1,652 patients (10.5%), a much smaller proportion than in earlier studies. This can be ascribed to the widespread adoption of the "middle-path" regimen in India. Most of the patients in our study were treated with ambulant chemotherapy; in contrast, earlier studies by de la Garza Ramos et al. [18] and Liu et al. [19] only included inpatient hospital admissions, which were more likely to be operated upon. The "middle-path" regimen adopted at our hospital comprised ambulant chemotherapy for a duration of 12 months. This longer duration of treatment including a 4-month intensive phase was applied in consideration of the poor penetration of anti-tubercular drugs in spinal lesions and the difficulty in assessing healing response in spinal TB. However, a recent study reported no difference in healing response or relapse rate with short-course (6 months) chemotherapy [20]. We observed a high compliance rate (99%) and a low incidence of side effects of anti-tubercular drugs. Serial monitoring via LFTs and more frequent follow-ups during the intensive phase can aid the early detection of drug-induced hepatotoxicity, which was the most commonly encountered side effect necessitating a change in drug regimen. Using composite clinical, radiological, and functional criteria to define the outcome of management, 84.5% of patients had an excellent-to-good outcome with the "middle-path" regimen. In comparison, 6.3% of patients, largely comprising those who had to undergo surgery for preventing or addressing mechanical or neurological complications, had a poor outcome. Mean VAS scores and CRP levels showed significant improvement as early as 3 months after the institution of chemotherapy, whereas all individual SF-36 domain scores showed significant improvement at 12-month follow-up. For thoracic, thoracolumbar, and lumbar spine, the posterior approach allows global access, adequate ventral decompression of the spinal cord, and anterior column reconstruction by rib autograft or cage. This has largely obviated the need for the more morbid anterior transthoracic or retroperitoneal approach in our practice. Our experience with the "middle-path" regimen in a larger study population echoes the findings of earlier studies reporting success with ambulant chemotherapy and selective surgery for spinal TB, even in cases with mild (grade 1 or 2) neurological deficit, albeit with smaller sample sizes [7,8,21-23].

We recognize certain limitations in our study, with its retrospective nature being the foremost among them. The robustness of the data presented was reliant on hospital records analyzed retrospectively. In addition, all patients were recruited from a single center. The inclusion of patients from multiple centers would strengthen the observations, provided that there is uniformity in the diagnostic approach, decision-making, and treatment indications. Transpedicular biopsy was not performed in all patients, so the prevalence of drug-resistant TB in our study population could not be estimated. A robust notification and information management system is the bedrock of a successful program to control TB. While the focus of governments and public health organizations has been on consolidated the reporting and surveillance of TB cases, there is a lack of literature focusing solely on spinal TB, possibly due to the low incidence of this condition in developed countries. With real-time, paperless, electronic health record systems being embraced by most countries, it is important to undertake epidemiological studies that can serve as a template for data collection. Simultaneously, well-defined treatment protocols, based on the "middle-path" philosophy, should be in place.

Conclusions

The findings of our study confirm that spinal TB is widespread in India, with more than 300 spinal TB patients seeking treatment at our hospital annually. The disease most commonly affects young adults, with most patients presenting only pain—a rather non-specific symptom—after an average delay of 4.5 months. In the vast majority of patients, operative intervention is not needed. With increasing prevalence of drug resistance, it is advisable to seek a microbiological or histopathological confirmation of diagnosis in all cases before instituting first-line ATT; our findings suggest that biopsy may not be contributory, and one may need to rely on clinical and radiological findings while being watchful for a response to ATT. Treatment protocols based on the "middle-path" philosophy are associated with favorable clinical, radiological, and functional outcomes, largely mitigating the need for routine surgery in spinal TB. Large-scale, prospective, multi-center epidemiological studies, preferably from geographically, ethnically, and socioeconomically diverse study sites, should be undertaken to understand where we stand today in our fight against spinal TB.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

References

1. World Health Organization. Global tuberculosis report 2020. Geneva: World Health Organization; 2020.
2. Schwartz NG, Price SF, Pratt RH, Langer AJ. Tuberculosis: United States, 2019. MMWR Morb Mortal Wkly Rep 2020;69:286-9.
3. World Health Organization. Tuberculosis control in the South-East Asia region: annual TB report 2014. New Delhi: WHO Regional Office for South-East Asia; 2014.
4. Rajasekaran S, Soundararajan DC, Shetty AP, Kanna RM. Spinal tuberculosis: current concepts. Global Spine J 2018;8(4 Suppl):96S-108S.
5. Sharma SK, Ryan H, Khaparde S, et al. Index-TB guidelines: guidelines on extrapulmonary tuberculosis for India. Indian J Med Res 2017;145:448-63.
6. Tuli SM. Results of treatment of spinal tuberculosis by "middle-path" regime. J Bone Joint Surg Br 1975;57:13-23.
7. Bakhsh A. Medical management of spinal tuberculosis: an experience from Pakistan. Spine (Phila Pa 1976) 2010;35:E787-91.
8. Nene A, Bhojraj S. Results of nonsurgical treatment of thoracic spinal tuberculosis in adults. Spine J 2005;5:79-84.
9. Valsalan R, Purushothaman R, Raveendran M, Zacharia B, Surendran S. Efficacy of directly observed treatment short-course intermittent regimen in spinal tuberculosis. Indian J Orthop 2012;46:138-44.
10. Jain AK, Kumar S, Tuli SM. Tuberculosis of spine (C1 to D4). Spinal Cord 1999;37:362-9.
11. Tuli SM. General principles of osteoarticular tuberculosis. Clin Orthop Relat Res 2002;(398):11-9.
12. Fuentes Ferrer M, Gutierrez Torres L, Ayala Ramirez O, Rumayor Zarzuelo M, del Prado Gonzalez N. Tuberculosis of the spine: a systematic review of case series. Int Orthop 2012;36:221-31.
13. Pertuiset E, Beaudreuil J, Liote F, et al. Spinal tuberculosis in adults: a study of 103 cases in a developed country, 1980-1994. Medicine (Baltimore) 1999;78:309-20.
14. Turgut M. Spinal tuberculosis (Pott's disease): its clinical presentation, surgical management, and outcome: a survey study on 694 patients. Neurosurg Rev 2001;24:8-13.
15. Sakho Y, Badiane SB, N'Dao AK, N'Diaye A, Gueye M, N'Diaye IP. Pott's disease in Senegal. Eur J Orthop Surg Traumatol 2003;13:13-20.
16. Godlwana L, Gounden P, Ngubo P, Nsibande T, Nyawo K, Puckree T. Incidence and profile of spinal tuberculosis in patients at the only public hospital admitting such patients in KwaZulu-Natal. Spinal Cord 2008;46:372-4.
17. Wang H, Li C, Wang J, Zhang Z, Zhou Y. Characteristics of patients with spinal tuberculosis: seven-year experience of a teaching hospital in Southwest China. Int Orthop 2012;36:1429-34.
18. De la Garza Ramos R, Goodwin CR, Abu-Bonsrah N, et al. The epidemiology of spinal tuberculosis in the United States: an analysis of 2002-2011 data. J Neurosurg Spine 2017;26:507-12.
19. Liu Z, Wang J, Chen GZ, et al. Clinical characteristics of 1378 inpatients with spinal tuberculosis in general

hospitals in South-Central China. Biomed Res Int 2019;2019:9765253.
20. Nene AM, Patil S, Kathare AP, Nagad P, Nene A, Kapadia F. Six versus 12 months of anti tubercular therapy in patients with biopsy proven spinal tuberculosis: a single center, open labeled, prospective randomized clinical trial: a pilot study. Spine (Phila Pa 1976) 2019;44:E1-6.
21. Moon MS, Moon YW, Moon JL, Kim SS, Sun DH. Conservative treatment of tuberculosis of the lumbar and lumbosacral spine. Clin Orthop Relat Res 2002;(398):40-9.
22. Wimmer C, Ogon M, Sterzinger W, Landauer F, Stockl B. Conservative treatment of tuberculous spondylitis: a long-term follow-up study. J Spinal Disord 1997;10:417-9.
23. Kotil K, Alan MS, Bilge T. Medical management of Pott disease in the thoracic and lumbar spine: a prospective clinical study. J Neurosurg Spine 2007;6:222-8.

■ SPINE

Diagnostic yield of image-guided biopsy in patients with suspected infectious spondylodiscitis

A PROSPECTIVE STUDY FROM A TUBERCULOSIS-ENDEMIC COUNTRY

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Aims

The aims of this study were to determine the diagnostic yield of image-guided biopsy in providing a final diagnosis in patients with suspected infectious spondylodiscitis, to report the diagnostic accuracy of various microbiological tests and histological examinations in these patients, and to report the epidemiology of infectious spondylodiscitis from a country where tuberculosis (TB) is endemic, including the incidence of drug-resistant TB.

Methods

A total of 284 patients with clinically and radiologically suspected infectious spondylodiscitis were prospectively recruited into the study. Image-guided biopsy of the vertebral lesion was performed and specimens were sent for various microbiological tests and histological examinations. The final diagnosis was determined using a composite reference standard based on clinical, radiological, serological, microbiological, and histological findings. The overall diagnostic yield of the biopsy, and that for each test, was calculated in light of the final diagnosis.

Results

The final diagnosis was tuberculous spondylodiscitis in 250 patients (88%) and pyogenic spondylodiscitis in 22 (7.8%). Six (2.1%) had a noninfectious condition-mimicking infectious spondylodiscitis, and six (2.1%) had no definite diagnosis and improved without specific treatment. The diagnosis was made by image-guided biopsy in 152 patients (56%) with infectious spondylodiscitis. Biopsy was contributory in identifying 132/250 patients (53%) with tuberculous spondylodiscitis, and 20/22 patients (91%) with pyogenic spondylodiscitis. Histological examination was the most sensitive diagnostic modality, followed by Xpert MTB/RIF assay.

Conclusion

Image-guided biopsy has a reasonably high diagnostic yield in patients with suspected infectious spondylodiscitis. A combination of histological examination, Xpert MTB/RIF assay, bacterial culture, and sensitivity provides high diagnostic accuracy in a country in which TB is endemic.

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Introduction

Infectious spondylodiscitis involves infection of an intervertebral disc and the adjacent vertebrae. When neglected or inadequately treated, it can lead to disabling back pain, progressive spinal deformity, severe neurological deficits, septicaemia, and death. Its incidence varies greatly between the developed and developing countries. In developed countries, it is usually caused by pyogenic organisms and accounts for a small proportion (0.5% to 15%) of patients with osteomyelitis.[1-3] This is in stark contrast to the epidemiological picture seen in developing countries, where tuberculous spondylodiscitis is overwhelmingly more common, accounting for 50% of patients with osteoarticular tuberculosis (TB).[4]

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The timely initiation of appropriate treatment in patients with infectious spondylodiscitis can lead to favourable outcomes, avoiding surgery in most patients. However, relying on clinical and radiological findings alone to guide the treatment of this condition has several drawbacks. The clinical features in most patients are relatively non-specific and overlap with many noninfectious conditions, including degenerative spinal disorders. Radiologically, noninfectious conditions, such as spinal metastasis, vertebral haemangioma, modic type 1 endplate changes, and multiple myeloma, can mimic infectious spondylodiscitis.[5,6] Attempts have been made to identify features by which tuberculous and pyogenic infections of the spine can be distinguished on the basis of imaging alone. However, there is much overlap between the two conditions, and no pathognomic radiological signs which permit a conclusive diagnosis to be made have been identified.[7,8]

The conventional practice in resource-constrained healthcare settings in developing countries, where TB is endemic, is to start empirical anti-TB treatment in all patients in whom the diagnosis of infectious spondylodiscitis is suspected clinically and radiologically. This may lead to an underestimation of the incidence of non-TB spondylodiscitis, as rifampicin and the fluoroquinolones, which are commonly prescribed anti-TB drugs, are also effective against pyogenic organisms, such as *Staphylococcus*, *Streptococcus*, *Escherichia coli*, and *Brucella*, leading to a clinical and radiological response, even in these 'misdiagnosed' cases of pyogenic spondylodiscitis.[9-11] The difficulties of instituting empirical anti-TB treatment have become even more important with the increase in multidrug-resistant (MDR) TB and HIV co-infections, presenting with atypical clinical and radiological features. Social and economic upheavals in countries such as India and China, where these conditions are common,[12] may to lead to changes in the epidemiology of infectious spondylodiscitis. Empirical treatment based on conventionally accepted epidemiological patterns of disease without microbiological or histological confirmation of the diagnosis may therefore not be appropriate.

The microbiological or histological confirmation of the diagnosis of this condition can therefore help to avoid the unnecessary administration of prolonged empirical treatment with antibiotics, combat the emergence of drug resistance, and prevent complications arising from inadequate treatment. In this context, percutaneous vertebral biopsy has emerged as a safe and effective method of providing tissue specimens for microbiological and histological examination in patients with suspected infectious spondylodiscitis.[13–15] Microbiological culture can identify causative organisms, and antibiotic susceptibility studies can guide appropriate chemotherapy. Culture studies typically take six to eight weeks for the diagnosis of tuberculous spondylodiscitis to be confirmed. The World Health Organization (WHO) has recommended the use of the Xpert MTB/RIF assay for rapid diagnosis in these extrapulmonary cases.[16] This assay deploys a cartridge-based platform that uses microfluidic technology and automated nucleic acid analysis to purify, concentrate, and rapidly identify targeted nucleic acid sequences in the biopsy samples.[17] Considering that 95% of all rifampicin-resistant strains of TB contain well-localized mutations within the *rpoB* gene, the presence of mycobacteria and rifampicin resistance can be detected simultaneously using the Xpert MTB/RIF assay. Compared with conventional culture studies, this test provides results within two hours.[17,18] When microbiological tests fail to identify a pathogen, histological evidence of cellular and tissue-level changes can help in differentiating between tuberculous spondylodiscitis, non-tuberculous spondylodiscitis, and noninfectious conditions mimicking infectious spondylodiscitis.[19] A wide range of diagnostic accuracy of different microbiological and histological tests in infectious spondylodiscitis has been reported.[15,20] This inconsistency can be attributed to small sample sizes, retrospective study designs, a lack of a consistently applied reference standards, and variation in diagnostic yields in different series. Knowledge of the diagnostic potential and yield of percutaneous biopsy in a particular clinical setting can guide clinicians in the selection of appropriate tests and interpretation of the results.

The aims of this study were to determine the diagnostic yield of image-guided vertebral biopsy in providing a diagnosis in suspected cases of infectious spondylodiscitis; to report the diagnostic accuracy of various microbiological tests and histological examinations in these patients; and to report the epidemiology of infectious spondylodiscitis from a TB-endemic country, including the incidence of drug resistance.

Methods

This prospective study was conducted at the All India Institute of Medical Sciences, New Delhi, a tertiary-level public healthcare facility in India, where TB is endemic. The study was conducted after institutional ethical approval was obtained and informed, written consent was taken from all patients or their guardians. The study included all patients attending the orthopaedic outpatient department between April 2018 and March 2020 who were suspected of having infectious spondylodiscitis on the basis of clinical and radiological findings, and who had not received any recent antibiotic treatment. Whether a patient had suspected infectious spondylodiscitis was determined at a weekly, multidisciplinary conference attended by orthopaedic spinal surgeons, radiologists, and infectious disease specialists. Patients in whom the radiological findings strongly favoured an alternative diagnosis were excluded. We also excluded those who already had a definitive microbiological and histological diagnosis of infectious spondylodiscitis made elsewhere, those who had received anti-TB treatment in the past (treatment 'relapse' or 'defaulters'), those who were admitted or underwent surgery on an emergency basis, and those in whom an image-guided biopsy was contraindicated due, for instance, to pregnancy, bleeding/coagulation disorders, and skin infection on the back. Due to the logistical issues of requiring general anaesthesia for an image-guided biopsy in young children, we also excluded patients aged < ten years.

All patients had detailed clinical, radiological, and laboratory work-up, following which image-guided biopsy, either under CT guidance in the radiology suite, or under fluoroscopic guidance in the orthopaedic operating theatre, was performed as a day-case. The vertebral level, side of approach, and the precise target location of the biopsy needle was determined by the radiologist or spinal surgeon from MRI scans. The biopsy was performed with the patient in a prone position, under aseptic conditions

Table I. The diagnostic performance of various microbiological tests and histological examinations in 284 patients with suspected infectious spondylodiscitis.

Investigation	True positive	True negative	False positive*	False negative	Diagnostic accuracy, %†
Tuberculous infections, n					
ZN staining (AFB smear)	11	34	0	239	SEN 4.4, NPV 12.5
Xpert MTB/RIF assay	86	34	0	164	SEN 34.4 , NPV 17.2
MGIT liquid culture‡	23	27	0	210	SEN 9.9 , NPV 11.4
LJ solid culture‡	21	27	0	212	SEN 9 , NPV 11.3
Any microbiological test	97	34	0	153	SEN 38.8, NPV 18.2
HPE	119	34	0	131	SEN 47.6, NPV 20.6
Overall (microbiology plus HPE)	132	34	0	118	SEN 52.8, NPV 22.4
Pyogenic infections, n					
Gram staining	10	262	0	12	SEN 45, NPV 95.6
Bacterial C/S	18	262	0	4	SEN 82, NPV 98.5
HPE	16	262	0	6	SEN 72.7, NPV 97.7
Overall (microbiology plus HPE)	20	262	0	2	SEN 91, NPV 99.2

*The use of a 'composite reference standard', which includes a 'positive' result on any microbiological or histological test on a biopsy sample as one of the criteria for a final diagnosis of infectious spondylodiscitis, makes the concept of 'false positive' null and void. Due to the absence of any 'false positives', the specificity and positive predictive value of each of the tests is 100%, and hence have been omitted.
†Calculated against the composite reference standard.
‡Due to an inadequate sample, mycobacterial culture study was not done in 24/284 patients.
AFB, acid fast bacilli; C/S, culture and sensitivity; HPE, histopathological examination; LJ, Lowenstein-Jensen; MGIT, mycobacterial growth indicator tube; NPV, negative predictive value; PPV, positive predictive value; SEN, sensitivity; SPE, specificity; ZN, Ziehl-Neelson.

and local anaesthetic (5 ml to 10 ml of 2% lignocaine). An 11 G diamond-tip, bone-biopsy needle was used for both procedures. CT-guided biopsy was performed using a Somatom Definition Flash 256 Slice Scanner (Siemens, Germany). After an initial thin-slice planning CT scan, the affected area was targeted using a transpedicular approach. Fluoroscopy-guided biopsy was performed either using a Ziehm Vision RFD 3D (Ziehm Imaging, Germany) or BV Pulsera 12 (Philips, Netherlands) machine. The bull's eye appearance of the pedicle on the AP view was used to target the needle, as previously described.[14,21] At least three non-fragmented cores of tissue were obtained; fragmented or crushed tissue and blood clots were sifted out. The pathology of infectious spondylodiscitis and the haematogenous spread in adults implies that the infection typically seeds in the subchondral bone first and later involves the adjacent disc. This typical paradiscal morphology usually means that in the active stage of infection, it is often difficult to demarcate the endplate and disc separately as both become a mixture of liquefied pus, granulation tissue, caseous debris, and bone fragments. By directing the needle into the subchondral bone with some cephalad/caudal angulation, we ensured that the disc material was also sampled along with bone fragments, which means that ethe 'endplate disc unit' was sampled. However, in order to ensure uniformity in the amount and quality of tissue sampled, we used a minimum of three non-fragmented cores of tissue from the endplate disc unit as a criterion, as a similar quantification or standardization of disc material was difficult to apply. The specimens were sent for the following tests: gram staining, aerobic and anaerobic bacterial culture and sensitivity (C/S), KOH staining, fungal culture and sensitivity, Ziehl-Neelson staining for acid-fast bacilli, Xpert MTB/RIF assay, mycobacterial growth indicator tube liquid culture, Löwenstein-Jensen culture, and histological examination.

Further management depended on the results of the investigations. When a tissue diagnosis of spinal TB was made, the patient was started on first-line anti-TB treatment, which was continued for 12 months (four months with HRZE (isoniazid, rifampicin, pyrazinamide, ethambutol) and eight months with HR (isoniazid, rifampicin)), with serial monitoring of liver function tests and inflammatory markers (CRP and ESR). If the Xpert MTB/RIF assay or the mycobacterial culture study suggested resistance to rifampicin, a diagnosis of MDR-TB was made. These patients were started on second-line anti-TB treatment, in accordance with WHO guidelines and under the supervision of an infectious disease specialist.[22,23] When a tissue diagnosis of pyogenic spondylodiscitis was made, antibiotic treatment was determined by the antibiotic sensitivity testing, and treatment (oral/intravenous) continued for six to eight weeks. If a noninfectious condition was diagnosed on biopsy, appropriate treatment was instigated. In the event of all the tests on the biopsy specimens being negative, the radiological findings were reviewed by the multidisciplinary team and unless specific features which favoured a noninfectious condition or pyogenic spondylodiscitis were noted, a provisional diagnosis of tuberculous spondylodiscitis was made as this was overwhelmingly more common in our patients. Empirical first-line anti-TB treatment was given, and the patient was kept under close review to look for clinical improvement. If there was no improvement or serological response in 12 weeks, a repeat biopsy was undertaken. Surgery in patients with tuberculous spondylodiscitis was reserved for select indications: no clinical and/or radiological response to treatment within 12 weeks, the onset of a new neurological deficit or worsening of an existing deficit on treatment, severe (Kumar and Tuli stage 3 or stage 4)[24] paraplegia at presentation, spinal instability due to bony pathology causing back pain, and progressive or severe spinal deformity (in these cases, an open biopsy was also taken). The final diagnosis ascribed to each patient was in accordance with a composite reference standard which necessitated satisfaction of any one or more of the following criteria: i) isolation of a causative organism (bacteria, mycobacteria, or fungi) on microbiological tests; ii) the identification of typical histological

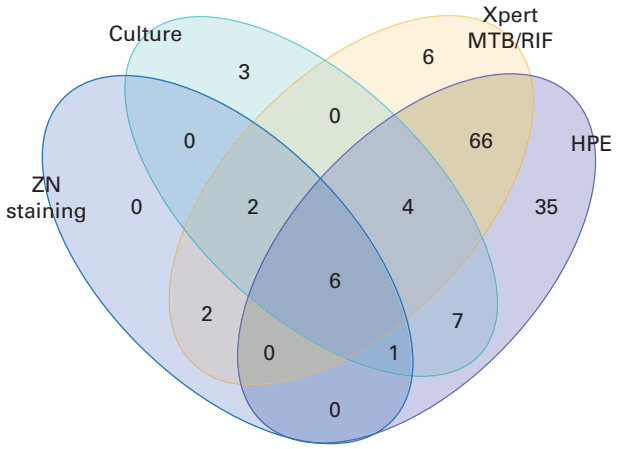

Fig. 1

Venn diagram showing the rate of positive results in various microbiological tests and histological examinations for the diagnosis of tuberculous spondylodiscitis. An overlap between the positive results of various tests is visible. The combination of Xpert MTB/RIF assay and histological examination could detect all but three of the patients who had a final diagnosis of tuberculous spondylodiscitis. HPE, histopathological examination; ZN, Ziehl-Neelson.

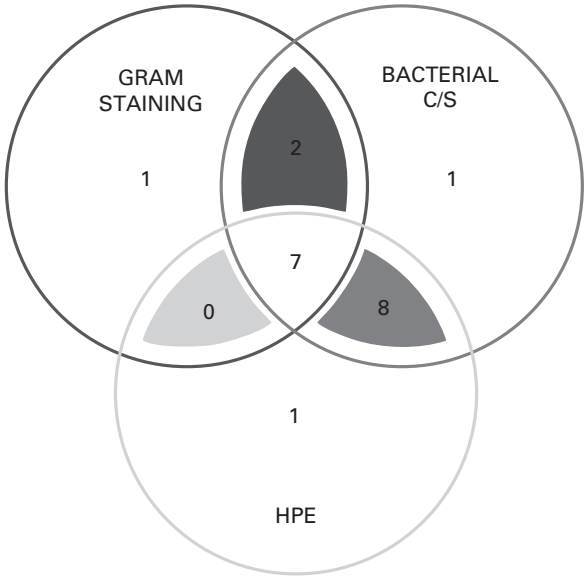

Fig. 2

Venn diagram showing the rate of positive results in various microbiological tests and histological examinations for the diagnosis of pyogenic spondylodiscitis. C/S, culture and sensitivity; HPE, histopathological examination.

tuberculous features including epithelioid granulomas, granulomatous inflammation, caseous necrosis, and Langhans giant cells, or pyogenic features including infiltration by neutrophil polymorphs; and iii) negative microbiological and histological tests, but clinical and radiological findings strongly favouring infectious spondylodiscitis with clinical, serological, and radiological response to empirical treatment (anti-TB or antibiotics).

Statistical analysis. Statistical analysis was performed using using Stata 15 software (StataCorp, USA). Descriptive statistics were recorded as mean with standard deviation for normally distributed continuous data, and median with interquartile range (IQR) for continuous data not in a normal distribution and frequency/percentage for categorical data. Sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) were calculated for each test performed on the biopsy specimens. Significance was set at $p < 0.05$.

Results

A total of 284 patients (168 male, 116 female) met the inclusion criteria and underwent an image-guided biopsy for suspected infectious spondylodiscitis during the study period. This included 97 patients who underwent CT-guided biopsy, and 187 who underwent fluoroscopy-guided biopsy. A repeat biopsy (CT-guided in all the cases) was carried out in five patients. The median age of patients was 30.9 years (24; IQR 11 to 77), with 176 patients (62%) aged < 40 years. Despite including only those in whom the clinical and radiological findings strongly suggested a diagnosis of infectious spondylodiscitis, the biopsy revealed a noninfectious condition-mimicking infection in six patients (2.1%), including multiple myeloma/solitary plasmacytoma (n = 3), osteoid osteoma (n = 2), and metastasis from a colorectal carcinoma (n = 1). The distribution of lesions according to the vertebral level was: cervical (C1 to C7) (n = 9), thoracic (T1 to T10) (n = 99), thoracolumbar (T11 to L1) (n = 47), lumbar (L2 to L5) (n = 120), and sacral (S1 to S5) (n = 12); three patients had skip lesions involving more than one region of the spine.

The study included 250 patients (88%) with tuberculous spondylodiscitis, 22 (7.8%) with pyogenic spondylodiscitis, six (2.1%) with a noninfectious, condition-mimicking infectious spondylodiscitis, and six (2.1%) with no specific diagnosis in whom clinical and radiological improvement was noted without any particular treatment. No patient had a fungal infection of the spine.

The diagnostic performance of the various microbiological tests which were performed is shown in Table I. The Xpert MTB/RIF assay was the most sensitive test for tuberculous spondylodiscitis, with 86/250 patients (34.4%) with this diagnosis having a positive result; nine patients (3.6%) were also shown to have resistance to rifampicin (MDR-TB). All other microbiological tests for detecting mycobacteria in the biopsy samples fared poorly, with a sensitivity of < 10%. Overall, at least one microbiological test was positive for 97 patients (39%) with tuberculous spondylodiscitis. In contrast, the causative organism could be successfully cultured in 18/22 patients (82%) with pyogenic spondylodiscitis. *Staphylococcus aureus* (MSSA, n = 5; MRSA, n = 4) was the most commonly cultured causative organism. The other organisms were coagulase-negative staphylococcus (CoNS; *Staphylococcus epidermidis*, n = 3), *Escherichia coli* (n = 3), *Pseudomonas sp.* (n = 1), *Enterococcus sp*. (n = 1), and *Burkholderia vietnamiensis* (n = 1).

Histological features suggestive of tuberculous infection were identified in 119/250 patients (48%) with this diagnosiss. These features included epithelioid granuloma, granulomatous inflammation without definite epithelioid granulomas, the presence of Langhans giant cells, and caseous necrosis with chronic

inflammatory infiltrate. The presence of numerous neutrophil polymorphs was taken as histological evidence of pyogenic spondylodiscitis. Based on the histological methods and criteria described by Iwata et al,[19] neutrophil polymorph infiltration was noted in 16/22 patients (73%) who had a final diagnosis of pyogenic spondylodiscitis.

Excluding the six patients with a noninfectious, condition-mimicking spondylodiscitis and six with a negative biopsy who improved without any therapy, 272 patients (95.8%) had a final diagnosis of infectious spondylodiscitis. A definite diagnosis was made on biopsy in 152/272 patients (56%) with infectious spondylodiscitis. Biopsy was contributory in identifying 132/250 patients (53%) with tuberculous spondylodiscitis (Figure 1), and 20/22 patients (91%) with pyogenic spondylodiscitis (Figure 2). Histological testing was the most sensitive diagnostic modality, followed by Xpert MTB/RIF assay, bacterial culture and sensitivity, and MGIT liquid culture.

Discussion

The early diagnosis and prompt treatment of infectious spondylodiscitis can prevent disastrous consequences in most patients. Reaching the diagnosis is hampered by the non-specific clinical symptoms and changes in inflammatory markers like ESR or CRP seen in this condition. The excellent sensitivity and specificity of MRI can provide strong suspicion and encourage the empirical treatment of suspected cases, a practice routinely followed in resource-constrained, developing countries. However, changing epidemiological patterns, the emergence of drug resistance, the high incidence of atypical imaging features seen in immunocompromised patients, and the recognition of many noninfectious conditions that radiologically mimic infectious spondylodiscitis have exposed the fallacies of empirical chemotherapy. The Infectious Diseases Society of America recommends that all patients with suspected vertebral osteomyelitis should undergo an image-guided biopsy, unless a causative organism has been identified on blood culture.[25]

The sensitivity and diagnostic yield of image-guided biopsy in patients with suspected infectious spondylodiscitis reported in the literature ranges widely from 30% to 90%.[13,15,20,21,26–28] Using a combination of clinical, radiological, microbiological, and histological criteria, Michel et al[13] determined a final diagnosis of infectious spondylodiscitis in 18 of 41 patients in whom a percutaneous CT-guided biopsy was performed. Seven patients had negative microbiological examinations, and three had negative histological examinations. Sehn et al[20] retrospectively reviewed 323 image-guided biopsy procedures performed on 297 patients, who were categorized into a high, intermediate, and low probability of having a spinal infection, as determined by the clinician's observations based on the history, examination, and imaging. The positive culture rate was 30.4% among patients with a radiologically high probability of infection, but dwindled to 16.1% and 5%, respectively, in those with an intermediate and low probability of infection. In another retrospective review of 84 CT-guided biopsies performed for vertebral osteomyelitis at a single centre in the USA, Garg et al[26] reported a 19% positive culture rate and a 41% sensitivity for histological examination. The diagnostic yield was not calculated against a treatment-based reference standard; instead, it was calculated with respect to a suspicion of osteomyelitis raised by the clinician on the radiology request form. In a retrospective review by Joo et al[29] of 100 confirmed cases of infectious spondylodiscitis (67 pyogenic and 33 tuberculous), an organism was isolated in 42 patients. The sensitivity of culture studies was 61% (20/33 patients) for tuberculous infections and 33% (22/67) for pyogenic infections. In comparison with these studies from developed countries where pyogenic spondylodiscitis (most commonly *S. aureus*) predominates, those from developing countries have focused on spinal TB. Waqas et al[15] reported a diagnostic yield of 75.8% (69/91) for CT-guided biopsy for suspected spinal TB. Granulomatous inflammation on histological examination (58/91 patients; 63.74%) was the most common diagnostic feature, while acid fast bacillus smear and culture fared poorly as diagnostic tools. More recently, Guha et al[30] reported a sensitivity of 76% and specificity of 76% for Xpert MTB/RIF assay, considering histology as the gold standard in 92 patients who underwent fluoroscopy-guided biopsy for spinal TB.

Our study was conducted in India where TB is endemic. A total of 284 patients with suspected infectious spondylodiscitis were prospectively recruited. The inclusion of patients and the indication for undergoing image-guided biopsy was standardized and authorized by a multidisciplinary team of clinicians and radiologists. We used a composite reference standard as the criterion for determining the final diagnosis. This has been used in previous studies,[19,29] and we believe that it is preferable to using only the clinician's opinion or histological report as the benchmark, as other studies have done.[26,30] Consistent with the endemic nature of TB in our country, tuberculous spondylodiscitis was much more common than other diagnoses (250/284 patients; 88%). Despite the strict inclusion criteria, six patients were found to have a histologically proven, noninfectious, condition-mimicking infectious spondylodiscitis. This highlights the shortcomings of MRI in conclusively diagnosing infective conditions of the spine. The sensitivity of biopsy for diagnosing infectious spondylodiscitis was 56%; this falls within the wide range of 30% to 90% which has been reported.[27] It was higher in our patients for the diagnosis of pyogenic (91%) compared with tuberculous spondylodiscitis (53%). A causative organism could be successfully isolated or identified in 116/272 patients (42.6%). Image-guided biopsy could help identify 32/284 patients (11%) with a diagnosis other than TB. These patients avoided receiving unnecessary prolonged anti-TB treatment, and its associated side-effects. This included 20 patients with pyogenic spondylodiscitis in whom an appropriate course of antibiotics could be swiftly initiated, and the condition resolved in six to eight weeks. There were also nine patients with resistance to rifampicin on Xpert MTB/RIF assay, in whom the timely provision of second-line anti-TB treatment was possible. The incidence of MDR-TB in our study was 3.6%. However, this is likely to be an underestimate as patients who did not take their prescribed medication or had a relapse of TB were excluded. The Xpert MTB/RIF assay was most successful in the identification of mycobacteria in the biopsy samples with a sensitivity of 34.4% for diagnosing tuberculous spondylodiscitis, compared with the composite reference standard. This is lower than the sensitivity reported by two previous

studies from India: 86% by Patel et al,[31] and 88% by Arockiaraj et al.[32] We believe that this is explained by the fact that both studies used the diagnostic accuracy of Xpert MTB/RIF assay, keeping culture as the benchmark in comparison to our use of the composite reference standard, and between 33% and 50% of the samples obtained in these studies were from open biopsy or surgery, compared with all the samples being obtained by percutaneous biopsy in our study. Other microbiological tests, notably liquid and solid culture, fared poorly in our study. Sending samples for histological examination resulted in an additional diagnostic yield of 40 tuberculous cases and one patient with pyogenic spondylodiscitis; microbiological tests were negative in these 41 cases. Histology alone was contributory to the diagnosis of infectious spondylodiscitis in half of the cases. There are several factors that may have contributed to the high numbers of false-negatives, including: technical factors, such as the location of biopsy, the type of tissue sampled, type of needle used, and the experience of the operator in performing the biopsy, the paucibacillary nature of the condition,[4] particularly in tuberculous spondylodiscitis, and the fact that infection by strains of low virulence may not generate a strong inflammatory reaction, which negatively affects the sensitivity of histological examination.[33] With the prospective design of the study, we were able to ensure reasonable uniformity in most periprocedural technical metrics and eliminate another factor, the effect of the previous administration of antibiotics, which may influence the final diagnostic yield. In keeping with the recommendations made by Michel et al,[13] we preferred sampling the subchondral bone with the disc material (endplate disc unit), rather than the paravertebral abscess which is less likely to yield a diagnostic organism. Although our patients included a heterogenous mixture of CT-guided and fluoroscopy-guided biopsies, a comparison between the two was not done. However, a previous meta-analysis concluded that there was no difference between the two in terms of diagnostic yield.[34]

The study had limitations. First, there was no attempt to correlate biopsy yield with radiological findings. Spira et al[35] have previously analyzed this aspect, and concluded that paravertebral infiltration was more often associated with positive culture than disc infiltration, epidural infiltration, or endplate erosion, although Chang et al[36] found no difference between the yield of the endplate, disc, and paravertebral soft-tissue biopsies. Second, the study was conducted at a single centre; involvement of several centres would have diluted the potential bias induced by technical factors related to the biopsy and made the results more generalizable. Third, the possibility of false-positive results arising from the growth of skin contaminants or contamination during the handling of the samples in the laboratory was ignored, as all patients with positive microbiology tests or histological examinations were treated appropriately. This may overestimate the specificity and positive predictive value of the diagnostic tests. However, considering the high incidence of infectious spondylodiscitis in our country, and the potentially catastrophic consequences of delay in initiating treatment, we opted to administer anti-TB treatment or appropriate antibiotics for the entire prescribed duration in all patients who tested positive on any of the diagnostic tests.

Nonetheless, our results confirm that image-guided biopsy has a reasonably high diagnostic yield (sensitivity = 56%) for confirming the diagnosis in clinically and radiologically-suspected cases of infectious spondylodiscitis, and should be a routine part of the diagnostic investigations. The isolation of the causative organism in more than one-third of patients, and the early identification of patients with MDR-TB, can avoid the prolonged administration of ineffective empirical antibiotics in these patients. Noninfectious condition-mimicking infectious spondylodiscitis can also be diagnosed in a timely fashion. A combination of Xpert MTB/RIF assay, bacterial culture, and sensitivity and histological examination constitutes the optimum battery of tests to generate the best possible diagnostic yield. Other microbiological tests may be added depending on the available resources. Many patients with this condition have a negative biopsy, suggesting that there is still a role for empirical chemotherapy in these patients, and their management is best planned in multidisciplinary team meetings comprising of surgeons, physicians, and radiologists. Clinicians should note the changing epidemiological patterns of disease in their healthcare setting, and look for subtle radiological clues that can differentiate between tuberculous spondylodiscitis, pyogenic spondylodiscitis, and noninfectious conditions that mimic spondylodiscitis.

Take home message

- Knowledge of the diagnostic potential of various microbiological tests and histological examination helps clinicians decide the best combination of tests to evaluate suspected infectious spondylodiscitis.
- Identification of causative pathogen and drug-resistant infections can help in avoiding prolonged administration of ineffective chemotherapy.

References

1. **Gouliouris T**, **Aliyu SH**, **Brown NM**. Spondylodiscitis: Update on diagnosis and management. *J Antimicrob Chemother*. 2010;65 Suppl 3:iii11-24.
2. **Butler JS**, **Shelly MJ**, **Timlin M**, **Powderly WG**, **O'Byrne JM**. Nontuberculous pyogenic spinal infection in adults: A 12-year experience from a tertiary referral center. *Spine (Phila Pa 1976)*. 2006;31(23):2695–2700.
3. **Cheung WY**, **Luk KDK**. Pyogenic spondylitis. *Int Orthop*. 2012;36(2):397–404.
4. **Rajasekaran S**, **Soundararajan DCR**, **Shetty AP**, **Kanna RM**. Spinal tuberculosis: Current concepts. *Global Spine J*. 2018;8(4 Suppl):96S-108S.
5. **Garg RK**, **Malhotra HS**, **Kumar N**. Spinal tuberculosis: Still a great mimic. *Neurol India*. 2019;67(6):1402–1404.
6. **Kumaran SP**, **Thippeswamy PB**, **Reddy BN**, **Neelakantan S**, **Viswamitra S**. An institutional review of tuberculosis spine mimics on MR imaging: Cases of mistaken identity. *Neurol India*. 2019;67(6):1408–1418.
7. **Jung N-Y**, **Jee W-H**, **Ha K-Y**, **Park C-K**, **Byun J-Y**. Discrimination of tuberculous spondylitis from pyogenic spondylitis on MRI. *AJR Am J Roentgenol*. 2004;182(6):1405–1410.
8. **Chang M-C**, **Wu HTH**, **Lee C-H**, **Liu C-L**, **Chen T-H**. Tuberculous spondylitis and pyogenic spondylitis: comparative magnetic resonance imaging features. *Spine*. 2006;31(7):782–788.
9. **Cottle L**, **Riordan T**. Infectious spondylodiscitis. *J Infect*. 2008;56(6):401–412.
10. **Viale P**, **Furlanut M**, **Scudeller L**, **et al**. Treatment of pyogenic (non-tuberculous) spondylodiscitis with tailored high-dose levofloxacin plus rifampicin. *Int J Antimicrob Agents*. 2009;33(4):379–382.
11. **Ioannou S**, **Karadima D**, **Pneumaticos S**, **Athanasiou H**, **Pontikis J**, **Zormpala A**. Efficacy of prolonged antimicrobial chemotherapy for brucellar spondylodiscitis. *Clin Microbiol Infect*. 2011;17(5):756–762.
12. **No authors listed**. Global tuberculosis report 2019. World Health Organization. https://apps.who.int/iris/handle/10665/329368 (date last accessed 15 November 2021).
13. **Michel SC**, **Pfirrmann CW**, **Boos N**, **Hodler J**. CT-guided core biopsy of subchondral bone and intervertebral space in suspected spondylodiskitis. *AJR Am J Roentgenol*. 2006;186(4):977–980.

14. **Dave BR**, **Nanda A**, **Anandjiwala JV**. Transpedicular percutaneous biopsy of vertebral body lesions: a series of 71 cases. *Spinal Cord*. 2009;47(5):384–389.
15. **Waqas M**, **Qadeer M**, **Faiz F**, **Alvi MA**, **Bari ME**. Computed tomography-guided biopsy for Potts disease: An institutional experience from an endemic developing country. *Asian Spine J*. 2015;9(3):394–398.
16. **No authors listed**. Automated real-time nucleic acid amplification technology for rapid and simultaneous detection of tuberculosis and rifampicin resistance: Xpert MTB/RIF assay for the diagnosis of pulmonary and extrapulmonary TB in adults and children: policy update. World Health Organization. 2013. https://apps.who.int/iris/handle/10665/112472 (date last accessed 24 November 2021).
17. **Lawn SD**, **Mwaba P**, **Bates M**, **Piatek A**, **Alexander H**, **Marais BJ**. Advances in tuberculosis diagnostics: the Xpert MTB/RIF assay and future prospects for a point-of-care test. *Lancet Infect Dis*. 2013;13(4):349–361.
18. **Denkinger CM**, **Schumacher SG**, **Boehme CC**, **Dendukuri N**, **Pai M**, **Steingart KR**. Xpert MTB/RIF assay for the diagnosis of extrapulmonary tuberculosis: a systematic review and meta-analysis. *Eur Respir J*. 2014;44(2):435–446.
19. **Iwata E**, **Scarborough M**, **Bowden G**, **McNally M**, **Tanaka Y**, **Athanasou NA**. The role of histology in the diagnosis of spondylodiscitis: correlation with clinical and microbiological findings. *Bone Joint J*. 2019;101-B(3):246–252.
20. **Sehn JK**, **Gilula LA**. Percutaneous needle biopsy in diagnosis and identification of causative organisms in cases of suspected vertebral osteomyelitis. *Eur J Radiol*. 2012;81(5):940–946.
21. **Sahoo MM**, **Mahapatra SK**, **Sethi GC**, **Sahoo A**, **Kar BK**. Role of percutaneous transpedicular biopsy in diagnosis of spinal tuberculosis and its correlation with the clinico-radiological features. *Indian J Tuberc*. 2019;66(3):388–393.
22. **Falzon D**, **Schünemann HJ**, **Harausz E**, **González-Angulo L**, **Lienhardt C**, **Jaramillo E**. World Health Organization treatment guidelines for drug-resistant tuberculosis, 2016 update. *Eur Respir J*. 2017;49(3):1602308.
23. **No authors listed**. Consolidated guidelines on drug-resistant tuberculosis treatment. World Health Oganization. 2019. https://apps.who.int/iris/handle/10665/311389 (date last accessed 24 November 2021).
24. **Jain AK**, **Kumar S**, **Tuli SM**. Tuberculosis of spine (C1 to D4). *Spinal Cord*. 1999;37(5):362–369.
25. **Berbari EF**, **Kanj SS**, **Kowalski TJ**, **et al**. Executive Summary: 2015 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):859–863:.
26. **Garg V**, **Kosmas C**, **Young PC**, **Togaru UK**, **Robbin MR**. Computed tomography–guided percutaneous biopsy for vertebral osteomyelitis: a department's experience. *Neurosurg Focus*. 2014;37(2):E10.
27. **Pupaibool J**, **Vasoo S**, **Erwin PJ**, **Murad MH**, **Berbari EF**. The utility of image-guided percutaneous needle aspiration biopsy for the diagnosis of spontaneous vertebral osteomyelitis: a systematic review and meta-analysis. *Spine J*. 2015;15(1):122–131.
28. **McNamara AL**, **Dickerson EC**, **Gomez-Hassan DM**, **Cinti SK**, **Srinivasan A**. Yield of image-guided needle biopsy for infectious discitis: a systematic review and meta-analysis. *AJNR Am J Neuroradiol*. 2017;38(10):2021–2027.
29. **Joo EJ**, **Yeom JS**, **Ha YE**, **et al**. Diagnostic yield of computed tomography-guided bone biopsy and clinical outcomes of tuberculous and pyogenic spondylitis. *Korean J Intern Med*. 2016;31(4):762–771.
30. **Guha M**, **Lal H**, **Boruah T**, **et al**. Clinico-radio-histopathological correlation by c-arm image-guided biopsy in spinal tuberculosis. *Indian J Orthop*. 2021;55(4):1028–1036.
31. **Patel J**, **Upadhyay M**, **Kundnani V**, **Merchant Z**, **Jain S**, **Kire N**. Diagnostic efficacy, sensitivity, and specificity of Xpert MTB/RIF assay for spinal tuberculosis and rifampicin resistance. *Spine*. 2020;45(3):163–169.
32. **Arockiaraj J**, **Michael JS**, **Amritanand R**, **David KS**, **Krishnan V**. The role of Xpert MTB/RIF assay in the diagnosis of tubercular spondylodiscitis. *Eur Spine J*. 2017;26(12):3162–3169.
33. **Bürger J**, **Palmowski Y**, **Strube P**, **Perka C**, **Putzier M**, **Pumberger M**. Low sensitivity of histopathological examination of peri-implant tissue samples in diagnosing postoperative spinal implant infection. *Bone Joint J*. 2020;102-B(7):899–903.
34. **Nourbakhsh A**, **Grady JJ**, **Garges KJ**. Percutaneous spine biopsy: a meta-analysis. *J Bone Joint Surg Am*. 2008;90-A(8):1722–1725.
35. **Spira D**, **Germann T**, **Lehner B**, **Hemmer S**, **Akbar M**, **Jesser J**. CT-guided biopsy in suspected spondylodiscitis–the association of paravertebral inflammation with microbial pathogen detection. *PLoS One*. 2016;11(1):e0146399.
36. **Chang CY**, **Simeone FJ**, **Nelson SB**, **Taneja AK**, **Huang AJ**. Is biopsying the paravertebral soft tissue as effective as biopsying the disk or vertebral endplate? Ten-year retrospective review of CT-guided biopsy of diskitis-osteomyelitis. *AJR Am J Roentgenol*. 2015;205(123–1291.

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