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Spinal Infections

Active tuberculosis of spine: Current updates

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ABSTRACT

Background: Spinal tuberculosis (TB) is the most common extrapulmonary form of tuberculosis. In both developing and developed countries, TB has been on the rising trend due to factors such as increasing HIV coinfection, multidrug resistance of the organism, and global migration. Spinal TB, which most often affects the lower thoracic and thoracolumbar area, accounts for 50% of all musculoskeletal tuberculosis.

Methods: Using the Cochrane Database of Systematic Reviews, EMBASE, and PubMed, a systematic computerized literature search was performed. Analyses of studies published within the past 10 years were conducted. The searches were performed using Medical Subject Headings terms, with "spinal tuberculosis," "diagnosis," "epidemiology," and "etiology","management," "surgery," and "therapy" as subheadings.

Results: Progressive collapse, kyphosis, and neurological deficiency are hallmarks of the disease because of its destructive effect on the intervertebral disc and adjacent vertebral bodies. The condition may be identified using laboratory testing and distinctive imaging features, but the gold standard for diagnosis is tissue diagnosis using cultures, histology, and polymerase chain reaction. Uncomplicated spinal TB is today a medical condition that can be adequately treated by multidrug ambulatory chemotherapy. Surgery is reserved for individuals who have instability, neurological impairment, and deformity correction. Debridement, deformity correction, and stable fusion are the cornerstones of surgical treatment.

Conclusions: Clinical results for the treatment of spinal TB are generally satisfactory when the disease is identified and treated early. However, the major health issue and the biggest obstacle in achieving the goals of the "End TB strategy" is the recent rise in the emergence of drug resistance. Hence strict vigilance and patient perseverance in the completion of the treatment is the main need of the hour.

Introduction and epidemiology

Eleven million people are infected with tuberculosis, and every year there are around 150,000 new cases of spinal tuberculosis (TB) [1]. India, China, Nigeria, Pakistan, Indonesia, and South Africa account for 64 percent of all recorded cases. In developed countries, the presence of immunodeficiency and the emergence of drug resistance poses fresh challenges. However, the natural history of the illness is still being reported in developing nations, where a substantial proportion of patients are initially diagnosed at an advanced stage [2].

The rise of MDR strains and the current global migration crisis provide additional obstacles for the world's healthcare systems. A number of factors point to a comeback of tuberculosis, including the increased prevalence of chronic debilitating medical conditions and the number of people living with HIV [3]. Human Immunodeficiency Virus (HIV) is a major risk factor for TB infection, increasing the likelihood of contracting the illness by a factor of 21 to 30 times [4].

The World Health Organization is making steady progress toward its goal of reducing the TB incidence rate by 80% and the number of TB-related fatalities by 90% by adopting the WHO End TB strategy for 2030 [5]. However, the success of curtailing the disease as seen in polio is not seen in TB. Real success towards TB eradication can be achieved only with the improvement in the socio-economic conditions. Until then TB will be a real threat for decades to come.

Pathophysiology

Mycobacterium TB complex, which causes TB, consists of over 60 different types of bacteria. Mycobacterium TB is the most common cause of disease in humans; the others are Mycobacterium bovis, Mycobac-

FDA device/drug status: Not applicable.

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terium microti, and Mycobacterium africanum. This bacillus is a slow-growing aerobic organism [6]. Lungs, mediastinal lymph nodes, mesentery, GI tract, GU tract, and genitourinary system are all possible initial infection sites. The bacilli can lay dormant for weeks at a time, and when conditions are right, they can multiply by 15 or 20 times in only hours. Hematogenous dispersion of the bacillus from a main focus is the only known mechanism for the development of a spinal infection.

Paradiscal arteries branch out on each side of the disc and reach the subchondral area of the top and lower endplates of each disc, making the intervertebral disc an avascular structure. Subchondral bone involvement on either side of the disc, known as "paradiscal," is the most often reported variety due to the vertebra's vascular supply [7]. Nonosseous abscess development, "posterior" involvement (where posterior appendicular tissues are affected), and "central" involvement (leading in loss of vertebral body) are the other kinds of involvement. Caseating necrosis of afflicted tissues forms cold abscesses as a result of granulomatous inflammation caused by tuberculosis. This inflammation is characterized by lymphocytic infiltration and epithelioid cells [8,9].

Clinical presentation

Spinal TB can appear with a wide range of symptoms. The emergence of symptoms is often gradual, and the disease itself takes its time to advance. Historically, the time it takes for symptoms to appear before a diagnosis was made was approximately 12 months; however, with the use of modern imaging technology, that time has been cut down to between 3 and 6 months. The constitutional signs of spinal TB, including fever, anorexia, weight loss, malaise, and weariness, often appear first. Patients with concomitant malnutrition had a higher prevalence of these symptoms (17%–54%). Back pain is a common symptom, with 90% to 100% of patients experiencing back pain weeks before seeking consultation. Pain might be moderate or severe, axial or radicular, and is often localized to the affected area. The disintegration of vertebrae and spinal instability, nerve root compression, and pathological fracture are closely related to the degree of pain [6,10].

TB of the spine manifesting with deformity, instability, and neurologic deficit is known as complicated TB and may necessitate surgical intervention. When TB of the spine is diagnosed early enough, before complications arise, it responds well to antitubercular treatment. A higher risk of complications and the necessity for surgery is linked to a delay in the diagnosis of spinal tuberculosis. The lack of specificity of the presenting symptoms and the normality of early plain X-rays contribute to a high rate of misdiagnosis [11,12]. Therefore, a high index of suspicion and prompt diagnosis are crucial for treating spinal TB.

Cold abscess

A "cold" abscess, devoid of acute inflammatory symptoms, is a characteristic of spinal TB that can be seen on magnetic resonance imaging (MRI) in more than 70% of patients. This manifests in the cervical spine as a retropharyngeal abscess that swells in the axilla, anterior, or posterior neck triangle. Retropharyngeal abscesses may result in pressure-related symptoms such as dysphagia, hoarseness, and respiratory stridor. The cold abscess often manifests in the thoracic area as a fusiform paravertebral swelling that might travel down the intercostal vessels and appear as a swelling in the chest wall. Through the arcuate ligament, the entrance of the aorta and esophagus in the diaphragm, a thoracic cold abscess can also track down and manifest as a lumbar abscess. Lumbar cold abscesses can manifest as a swelling in the Petit's triangle and the groin, or they might go down into the psoas muscle causing fixed flexion deformity of the hip. If the collection travels down the femoral or gluteal vessels, it might cause an abscess in the Scarpa's triangle or the gluteal region [13,14] (Fig. 1).

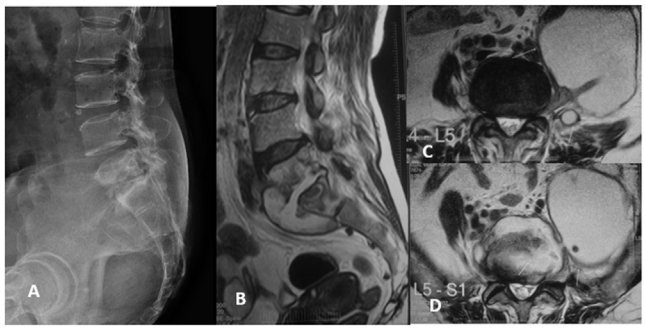

Fig. 1. (A) Radiograph of the patient with L5-S1 TB spondylodiscitis with narrowing of disc space and endplate erosion, (B) T2W MRI sagittal images showing prevertebral and epidural abscess (C, D) T2W MRI Axial images showing left psoas abscess.

Instability

One of the main reasons for patients undergoing surgical stabilization in spinal TB is the presence of "instability" pain. While there is consensus on how to evaluate for the neurological deficit, there is a clear lack of consensus on how to evaluate for instability, leading to wide variations in surgical indications throughout the world.

Rajasekaran et al. devised a score for spinal TB that applies to both acute and healing cases. The authors identified 5 significant factors related to spinal instability through a multinational expert consensus study involving 68 surgeons. These include age ≤15 years, involvement of the cervicothoracic/thoracolumbar junction, a sagittal deformity angle ratio ≥ 15°, a vertebral body loss-segmental ratio ≥ 0.5, and the presence of spine-at-risk signs. Age below 15 years was given a score of 1 because the spine of a child is very flexible and has a low Young's modulus because of the relatively higher ratio of the disc to the bone. So, children suffer a higher deformity for the same amount of vertebral body destruction. It is also been documented that children can continue to have progressive deformity due to growth modulation even after the cure of the disease. Cervicothoracic and thoracolumbar junctions are given a score of one as they form a transition between a kyphotic and lordotic area and are prone to higher collapse. However, a kyphotic deformity of more than 30 degrees and a vertebral body loss were given a score of 2 as both lead to a higher collapse and also secondary facetal subluxation or dislocation. A maximum score of 3 was given for the presence of "Spine at risk" signs as it documents an established instability with loss of both columns [15] (Table 1).

Deformity

In 95% of patients with spinal TB, the anterior spinal column is affected. A kyphotic deformity, caused by damage to the disc and surrounding vertebral bodies, can take the form of a knuckled deformity (the collapse of a single vertebra), a gibbus deformity (the collapse of 2 or 3 vertebrae), or a global kyphosis (including many adjacent vertebrae). In occipitocervical and atlantoaxial lesions, patients can present with torticollis. Adults only experience deformity progression during the diseases active stage; after the deformity has healed, there is no further advancement. The degree of vertebral body damage correlates to the severity of the eventual deformity.

In children, the deformity progresses throughout puberty and beyond, even if the underlying condition has been cured. Rajasekaran found that even in cases where the condition was treated successfully, the deformity worsened over time in 40% of the children, improved spontaneously in 43%, and remained unchanged in 17%. The "spine at risk" signs described by Rajasekaran allow for the early identification of children at a higher risk of developing deformities. These in-

Table 1
Instability score for spinal TB.

Variables	Score
Age ≤15 years	1
Cervicothoracic/thoracolumbar junction	1
Kyphotic deformity ≥30° (single vertebra) sagittal DAR ≥15° in (>1 vertebral involvement)	2
VBL-segmental ratio ≥0.5	2
Spine at risk sign	3
Total score	9

A score of 0 or 1 is considered stable, whereas a score of 2 is considered potential instability, and a score of ≥ 3 is considered definitive instability.

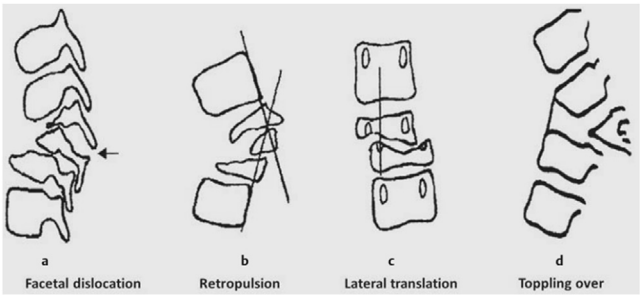

Fig. 2. The "spine at risk" signs to identify children at risk for severe deformity include: (A) separation of facet joints in lateral radiographs which indicates instability, (B) retropulsion of the posterior part of the affected vertebra, (C) lateral translation of vertebrae in the antero-posterior radiograph, and (D) toppling of one vertebra over the other vertebra. Here, a line drawn from the anterior surface of the caudal normal vertebra crosses the mid-point of the anterior surface of the cranial normal vertebra.

clude retropulsion, subluxation, lateral translation, and toppling [16,17] (Fig. 2).

The course of spinal deformity might be different at different stages of disease involvement. Type A healing can be seen in small lesions and in the lumbar area, where there is minimal collapse of the vertebral body and the posterior column stays intact. In cases of more extensive vertebral damage, type-B healing takes place. When 1 or 2 facet joints become dislocated, the result is moderate kyphosis. The distal normal vertebra stabilizes over the proximal vertebra through a "point contact." Compressive stress causes growth inhibition, leading to a deformity of 40 to 60 degrees. Type-C restabilization happens when more than 2 vertebral bodies are destroyed, and it is more prevalent in children under the age of 10. A kyphosis of more than 100 and a "buckling collapse" result from the increasing collapse of the anterior column, which causes the dislocation of many facet joints. With their anterior borders resting on 1 another, the proximal and distal vertebral bodies rotate over a 90-degree arc. Since the growth plates are no longer subject to compressive forces from gravity, the vertebrae may become horizontally aligned and grow longer. This further exacerbates kyphosis and increases pressure on the spinal cord, increasing the risk of secondary neurological impairment [18].

Neurological deficit

Patients with involvement in the thoracic and cervical spine are more likely to experience neurological complications, with a prevalence of 23% to 76% [19] In the case of the tuberculous spine, neurological deficits can appear either during the active period of the disease (early start) or long after the healing process has been completed (late onset). Mechanical pressure on the spinal cord from an abscess, granulation tissue, or sequestrum, or from instability induced by pathological subluxation or distraction, may contribute to neurologic impairments observed over the course of an active illness. Reactivation of illness or due to chronic ventral pressure on the spinal cord due to being tightly draped over the internal "gibbus." can cause neurological deficits to manifest late in life. Ossification of the ligamentum flavum proximal to the kyphosis, caused by abnormal motion in that location, is a rare cause of late-onset neurological impairment. The prognosis for neurological recovery is excellent in patients with active disease. Neurological recovery is poor when it develops in patients after the disease has resolved, with 30% to 40% of patients progressing to complete deficit [11]. Possible causes of sudden onset neurological impairment include vascular involvement as a result of either sudden vascular blockage by bone displacement or inflammatory vascular thrombosis of the spinal arteries.

Diagnosis

The most definitive diagnostic test for spinal TB is the successful culture of Mycobacterium in tissue samples taken from the diseased area. Histopathological examinations showing typical granulomas and staining of smears to identify acid-fast bacilli (AFB) are accepted as reference standards for all other diagnostic modalities, despite the fact that they have relatively low sensitivity. Indirect serological indicators of inflammation have been utilized, although immunological testing has had mixed success. Because of its efficiency and dependability, molecular diagnostics is increasingly being employed.

The early diagnosis of spinal TB cannot be accomplished using plain radiography. It is not until the latter stages of the illness that the kyphosis and instability that result from the progressive deterioration of disc space and vertebral endplates become apparent. In contrast to conventional radiographs, computed tomography (CT) can show vertebral damage rather early on, making it a valuable diagnostic tool for determining the whole degree of bone destruction, as well as the involvement of the posterior column, any junctional pathology, and regional stability [20]. In descending order of prevalence, researchers have identified 4 distinct forms of damage to bones: fragmented, osteolytic, subperiosteal, and localized sclerotic lesions [21]. Percutaneous CT-guided biopsy, obtained with the use of CT, is also quite helpful in making a diagnosis.

Because of its ability to detect even the earliest of changes, magnetic resonance imaging has become the modality of choice. TB can be distinguished from other causes of infective spondylodiscitis with the aid of gadolinium-enhanced MRI [22,23]. MRI is the gold standard for visualizing the severity of soft tissue involvement, abscess spread, and neurological compression. The common findings in the MRI are the presence of marrow edema, preservation of the disc space, the subligamentous spread of abscess, septate paravertebral abscess, epidural abscess, and endplate erosion. Skip lesions can be found with the help of whole-spine screening. In determining how well a patient is responding to treatment, MRI is also quite helpful [24].

Since 18F-fluorodeoxyglucose (18F-FDG) is known to concentrate in inflammatory cells like neutrophils and activated macrophages at the site, nuclear imaging by 18F-fluorodeoxyglucose (18F-FDG) labeled positron emission tomography (PET) scan aids in the real-time evaluation of disease activity compared with CT and MRI [25,26].

Laboratory investigation

The erythrocyte sedimentation rate (ESR) can be used as a sensitive measure of infection and to track the effectiveness of treatment, but its limited specificity is cause for caution. In TB, the ESR is often above 20 mm/h and drops when the disease is treated. C-reactive protein (CRP) is a better indicator of recent infection than ESR [27,28]. Serological testing for IgM and IgG levels, which are elevated in the acute and chronic infective stages of tuberculosis, respectively, is not suggested since it cannot distinguish between the 2 states, nor can it distinguish between spontaneous infection and BCG vaccination.

Although the Mantoux tuberculin skin test is recommended by the World Health Organization (WHO) for use in low-income nations, it has little diagnostic value in endemic regions and may potentially be false negative in immunodeficient patients. Interferon-gamma (IFN-g) release assays, which measure the quantity of IFN-gamma released in response to Mycobacterium TB antigens, and whole blood-based enzyme-linked immunosorbent assays are 2 further tests utilized in latent TB [29]. These tests are specific and can tell the difference between latent TB and active TB, but they cannot tell the difference between natural TB and BCG vaccination. Although the Mantoux tuberculin skin test is recommended by the World Health Organization (WHO) for use in low-income nations, it has little diagnostic value in endemic regions and may potentially be false negative in immunodeficient patients.

Interferon- γ (IFN- γ) release assays, which measure the quantity of IFN- γ released in response to Mycobacterium TB antigens, and whole blood-based enzyme-linked immunosorbent assays are 2 further tests utilized in latent TB [30]. Studies have shown that IGRA has a limited ability to predict the development of active TB. QuantiFERON-TB Gold In-Tube had a PPV of 3.3%, whereas T-SPOT TB was claimed to have a PPV of 4.2% [31]. Therefore, based on this evidence, currently, we treat a large number of subjects who scored IGRA positive to prevent 1 individual from developing TB disease. Therefore, there is an urgent need to develop a new generation of assays that can predict disease progression with greater accuracy and to focus diagnostic efforts on this population [32].

Besides histopathological examination, it is preferable to perform antibiotic sensitivity testing using line probe assays, polymerase chain reaction (PCR), and other molecular diagnostic tests on tissue samples obtained due to the well-documented importance of tissue diagnosis. Compared to the typical AFB culture procedures, which need a 4-week incubation period, BACTEC radiometric culture only takes 2 weeks [33]. The Gene Xpert MTB/RIF test is a rapid, completely automated diagnostic test that may provide results in less than 90 minutes. When used as an initial test replacing smear microscopy Xpert achieved a pooled sensitivity of 88% and a pooled specificity of 98%. As an add-on test following a negative smear microscopy result Xpert yielded a pooled sensitivity of 67% and a pooled specificity of 98%. In clinical subgroups, the pooled sensitivity was 98% for smear-positive, culture-positive TB and 68% for smear-negative, culture-positive TB. For rifampicin resistance detection Xpert achieved a pooled sensitivity of 94% and a pooled specificity of 98% [34,35].

For improved detection rates of Mycobacterium TB in specimens with low numbers of bacilli, particularly in smear-negative, culture-positive specimens, pediatric specimens, and extrapulmonary specimens, the World Health Organization (WHO) recommended the use of a next-generation Xpert MTB/RIF assay, named Xpert MTB/RIF Ultra, in March 2017 [36]. Caseative necrosis, epithelioid cell granuloma, and Langhans large cells are the characteristic histological hallmarks of TB, and their presence has been recorded in anywhere from 72% to 97% of cases [37,38]. Spinal TB is diagnosed using a combination of clinical symptoms and characteristic MRI abnormalities; a positive result from a culture and sensitivity test, a Gene Xpert PCR test, or histological analysis confirms the diagnosis. However, with the rapid growth of the aging population and the widespread adoption of advanced medical imaging techniques, Next-generation sequencing, and blood-based biomarker tests may prove revolutionary in the future for the detection and management of spinal TB. Table 2 summarizes the stated sensitivity and specificity of the currently available diagnostic battery of examination for either diagnosing or monitoring spinal TB.

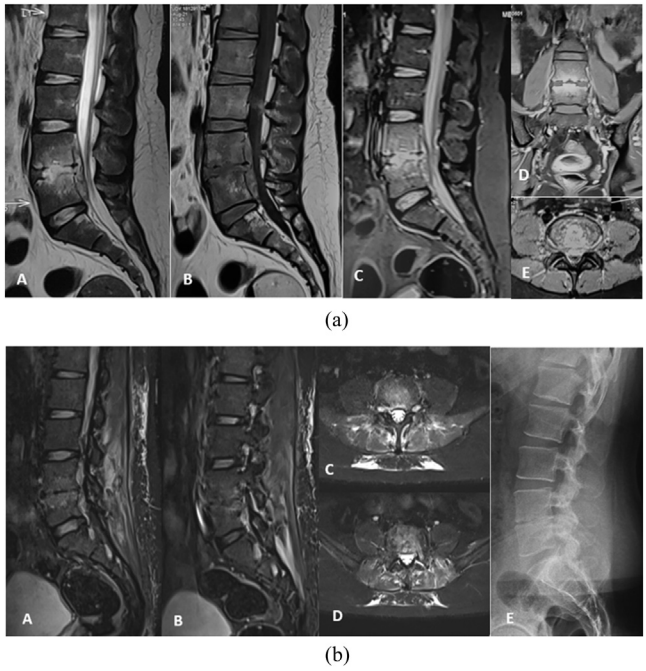

Fig. 3. (a) A case of L4–L5 TB spondylodiscitis (A) T2 weighted, (B) T1 weighted and (C, D, E) Postcontrast images with anterior epidural abscess and endplate erosion. (b) One-year follow-up following conservative management with ATT treatment. (A, B,C, D) MRI showing complete resolution of the infection, (E) Radiograph shows completely healed L4–L5 lesion.

Management of spinal TB

Chemotherapy

The antitubercular medication regimen known as ATT is the cornerstone of treatment for both complicated and uncomplicated forms of TB [39–42].

Due to the wide variety of bacilli types present in a lesion, multidrug ATT is necessary. Each of the many possible forms—intracellular, extracellular, quiescent, or quickly replicating—exhibits unique characteristics in terms of development and metabolism [43]. Additionally, the occurrences of drug resistance are decreased by multidrug ATT [44]. The World Health Organization (WHO) recommends 9 months of treatment for spinal TB, with 4 drugs given in the “initiation” phase for 2 months (isoniazid, rifampicin, pyrazinamide, ethambutol, or streptomycin), followed by isoniazid and rifampicin for 7 months in the “continuation” phase. The relative merits of the “daily dose” and “intermittent” dosing schedules remain contentious [45].

Due to their higher cost and greater risk of adverse effects, second-line ATT medications (such as kanamycin, amikacin, capreomycin, levofloxacin, etc.) should be used with caution. First-line ATT treatments include isoniazid [INH], rifampicin, ethambutol, and pyrazinamide [46]. Directly Observed Treatment, Short Course (DOTS) and self-administered therapy were found to be equivalent in a 2013 meta-analysis of clinical trials and observational studies [47]. The World Health Organization and other TB programs are still using DOTS despite concerns about the development of resistance to the drugs [48]. Uncomplicated spinal TB is a medical condition that may be adequately treated with chemotherapy alone (Fig. 3A, B). However, the best outcomes for people with complex TB can be achieved with a combi-

Table 2
Diagnostic investigation in spinal TB.

Modality	Investigation	Sensitivity	Specificity	Comments
Imaging modalities	Plain radiograph	15%	NA	Changes prominent only after 30% of the destruction
	MRI	100%	80%	Gold standard imaging technique
	CT	100%	NA	Fragmentary > osteolytic > subperiosteal > localized
	Nuclear scan; FDG-PET scan	NA	NA	Does not differentiate from malignancy and other infections; detects activity and treatment response
Blood investigations	ESR > 20 mm	60%–90%	NA	Serial values show a gradual drop after initiating treatment
	CRP	71%	NA	Reaches normal levels after 14 days of treatment
Skin test	Mantoux assay	40%–55%	75%	False positive results in BCG-vaccinated individuals
IGRA (Interferon-gamma release assay)	Quantiferon TB Gold (whole blood IGRA)	84%	95%	Less false-negative results in immunosuppressed individuals; are specific for MTB infection
	T-SPOT TB assay (PBMC-based IGRA)	86%	96%	
Microscopic diagnostics	Gram staining	25%–75%	99%	Ziehl-Neelsen technique—bright red bacilli; 104 to 105 bacilli/mL required
	Histopathology	53%–81%	NA	Epithelioid cell granulomas, Langhans giant cells, caseous necrosis
Bacterial culture	AFB Culture	47%	100%	Lowenstein Jensen media, 6–8 weeks, requires 101 to 102 bacilli/mL (live bacilli)
	BACTEC	56%	100%	4–10 days, radiometric assay
Molecular testing (NAA)	GeneXpert MTB/RI	82.9%	98%	Results <48 hours + rifampicin resistance detection
	Xpert MTB/RIF Ultra	87.8%	94.8%	Useful in HIV-associated and smear-negative TB
Line probe assay (LPA)	Genotype MTBDRplus	100%	94%	Rapid diagnosis of drug resistance TB
Serological test	Serum biomarkers	92%	72%	Fibrinogen, α2-macroglobulin, CRP, MMP-9, transthyretin, complement factor H, interferon-γ, interferon-γ inducible protein-10 and TNF-α

PBMC, purified peripheral blood mononuclear cells.

nation of medical treatment and surgery. Additional large-scale clinical studies are needed to define the end goal of therapy and the optimal length of ATT for spinal TB. Dosage adjustments for ATT in children should be made at each follow-up appointment based on the child's weight as determined by the WHO's recommended weight bands.

Drug-resistant TB

Multiple-drug-resistant TB is TB that is resistant to both isoniazid (INH) and rifampicin. Inadequate treatment is the primary cause of this resistance; however, infectious strains may play a role as well. When resistance is shown not only to INH and rifampicin but also to fluoroquinolones and at least 1 injectable second-line anti-TB treatment, this is known as extensively drug-resistant TB (XDR-TB) [49,50]. Five factors were proposed by Pawar et al. as indicators of successful outcomes in MDR-TB: (1) progressive clinical improvement after 6 months of chemotherapy; (2) radiographic improvement during treatment; (3) strain resistance to less than 3 anti-TB drugs; (4) use of fewer than 4 second-line drugs in the treatment regimen; and (5) absence of regimen changes during treatment [1]. To characterize bacteria that showed in vitro resistance to all tested first- and second-line medications, Velayati et al. coined the term "totally drug-resistant tuberculosis" (TDR-TB) in 2009. In such instances, it is recommended to consult a specialist in infectious diseases who has experience in treating resistant strains [51,52]. Against these strains, which have been detected in India, Iran, Italy, and South Africa, novel tactics and medications (including delam53,anid, bedaquiline, SQ109, and sutezolid) are being tested in clinical trials at the moment [53].

Surgical treatment

The surgical indications in spinal TB have been outlined in Table 3. The goals of surgery are (1) abscess drainage, (2) removal of the infected tissue, (3) debridement and fusion with or without stabilization thereby preventing deformity progression and encouraging early neurological recovery in patients with neurological deficit [54]. In addition to this adequate samples can be obtained for histological confirmation of the diagnosis. The success of the surgery depends on the strict chemotherapy regimen and the patients should be sensitized to it.

Table 3
Indications for surgery in spinal TB.

Indications for surgery in spinal TB
➢ *With neurological deficit:*
• Severe neurological deficit at presentation
• New onset neurological deficit while on ATT
• Worsening of the existing neurological deficit while on ATT
• No neurological improvement after 6 weeks of ATT
• Spinal tumor syndrome
➢ *Without neurological deficit:*
• Loss of one vertebra in the thoracic spine or 1.5 vertebrae in the lumbar spine
• Children with "spine-at-risk" signs
• Kyphosis of more than 30 degrees
• Posterior lesion with pedicle destruction
• Lack of clinical response with 6 weeks of ATT
• Recurrence of disease with ATT
➢ *Other indications:*
• Large paraspinal abscess
• Prevertebral abscess causing respiratory distress
• Uncertainty of diagnosis

To facilitate proper debridement of disease focus, Hodgson et al. developed the modified Hong Kong anterior surgical techniques [55]. Debridement was accomplished with extrapleural anterolateral decompression in thoracic and thoracolumbar TB without compromising the thorax or diaphragm [56,57]. In order to accomplish arthrodesis in patients with postdebridement defects, the surgical approach was later modified to include rib and/or iliac crest bone graft. However, the results were not consistently replicated in terms of deformity treatment and spinal alignment preservation.

When the graft length covered >2 disc heights (4–5 cm), >40% of patients experienced an unacceptable increase in deformity due to graft failure, slippage, fracture, and/or absorption [58]. In order to preserve bone grafts and achieve anterior fusion, spinal instrumentation has become increasingly used. Oga et al. demonstrated that, in contrast to pyogenic organisms, tubercle bacilli do not adhere to the implant or create

any biofilm, making surgical stabilization using pedicle screw safe even in the presence of active illness. When correcting kyphosis greater than 50 degrees, twin rod structures were first recommended because of their greater stability compared to anterior plates and/or rods [59,60]. Poor purchase in inflammatory osteopenic bone, inability to span multiple segments, especially across junctional pathologies, difficulty in extending the instrumentation when necessary, and difficult surgical accessibility in the lumbosacral, occipitocervical, and high thoracic regions all contribute to the difficulty of anterior instrumentation [61].

Majority of cold abscesses may be treated with antibiotics alone, and drainage is only suggested in extreme cases, such as when there is a risk of respiratory distress or dysphagia from a big cervical paravertebral abscess, or when there is a risk of pseudo-hip flexion deformity from a large psoas abscess [62].

Surgery in active disease

Surgical approaches in active disease depend on the stage of the disease, the amount of vertebral body destruction, and the presence of deformity. In cases of active disease, especially in the early stages characterized by minimal collapse and flexible deformities, posterior spinal stabilization combined with transpedicular decompression is frequently sufficient without the need for anterior reconstruction [63]. In cases requiring minimal debridement, spinal shortening can be used to accomplish direct bone-to-bone contact, thereby obviating the need for anterior reconstruction. In patients with more extensive involvement, the excision of facets and the sacrifice of an intercostal nerve provide adequate exposure for comprehensive debridement and anterior reconstruction with either a bone graft or a titanium cage [64]. Various approaches used for debridement are an anterior approach, a posterior approach, a posterior approach with global reconstruction, or a combination of these techniques.

Anterior approach

Because spinal TB mostly affects the anterior column, the anterior approach allows for easy exposure, debridement, and reconstruction [65]. Hodgson et al supported radical debridement and arthrodesis when anterior debridement alone failed to halt deformity development [56,66]. These findings, however, were not replicated in other investigations and were linked to respiratory failure, death, and graft-related complications [67].

Rajasekaran documented graft slippage, fracture, absorption, or subsidence in 59% of instances of anterior body fusion without instrumentation, and these problems were more prevalent when the graft spanned 2 or 3 vertebral bodies [58]. Anterior instrumentation in the form of plates, rods, and screws is required, particularly when considerable kyphosis correction is attempted [68]. When the posterior elements are intact, an anterior procedure is advised, but it is better avoided in panvertebral illness.

Posterior approach

As a result of the easiness, widespread use, and low learning curve, posterior operations have become the norm in modern medicine. The advantage of the posterior approach includes (1) Bilateral costotransversectomy approach allows extrapleural access to the thoracic spine thereby reducing the risk of pulmonary complications (2) The use of pedicle screws via the posterior approach provides 3-column stability to the diseased vertebra (3) It provides sufficient exposure for circumferential spinal cord decompression, and (4) There is a possibility of instrumentation extension whenever required [69]. In addition, deformity progression, and neurological consequences may be avoided in the early stages of illness, and patients can recover more quickly after transpedicular decompression and posterior instrumentation (Fig. 4).

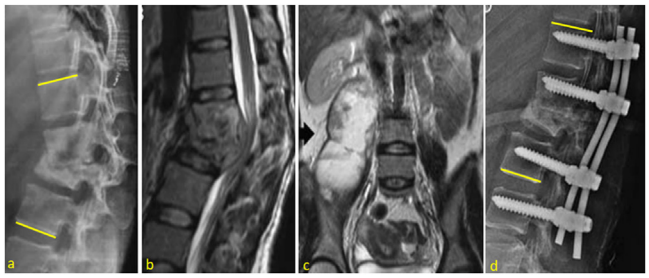

Fig. 4. (A) Lateral radiograph of thoracolumbar spine showing kyphosis of 34.2 degrees; (B) Mid Sagittal T2W MRI showing epidural abscess; (C) Coronal MRI showing paravertebral and psoas collection; (D) Lateral postoperative radiograph after posterior column shortening showing good deformity correction.

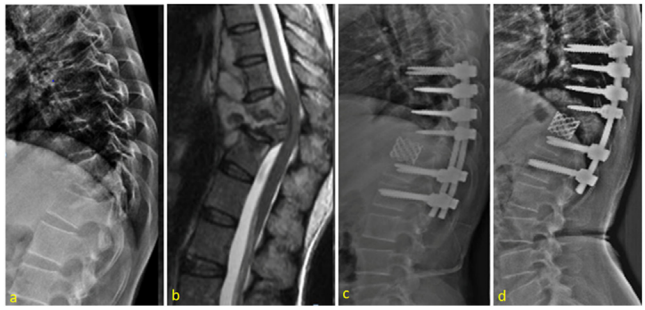

Fig. 5. (A) Lateral radiograph of lower thoracic spine showing involvement of T10–T11 vertebrae; (B) Mid Sagittal T2W MRI showing epidural abscess causing spinal cord compression; (C) Lateral postoperative radiograph showing posterior instrumentation with anterior column reconstruction; (D) 2 years follow-up lateral radiograph showing no significant loss of correction.

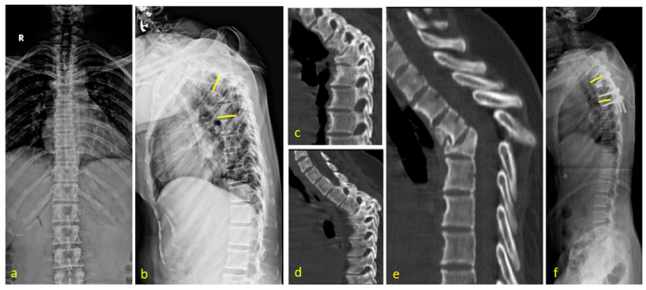

Fig. 6. (A, B) AP and Lateral radiographs showing focal kyphosis (59.4 degrees) at the upper thoracic region (Type IIA); (C–E) Sagittal Ct scan image showing only anterior column loss with intact posterior column (Type IIA). Note the presence of 2 pedicles in a single anterior fusion mass; (F) Postoperative radiograph following Disc- Bone Osteotomy with kyphosis reduced to 23.4 degrees.

Global reconstruction by posterior approach

Posterior approach alone is currently recommended for global reconstruction worldwide (Fig. 5). Several posterior and posterolateral approaches to the thoracic and lumbar spine have been identified, allowing for safe access to the anterior and lateral columns [64,70,71]. They may be extrapleural, transpedicular, transfacetal, or include a costotransversectomy [72,73].

Reconstruction without undergoing costotransversectomy may be difficult in the thoracic spine, despite the fact that transpedicular and transfacetal techniques may be performed with relative ease in the lumbar spine (Fig. 6,7). This extrapleural approach which is performed by a T-shaped incision or a posterior midline incision permits anterior struc-

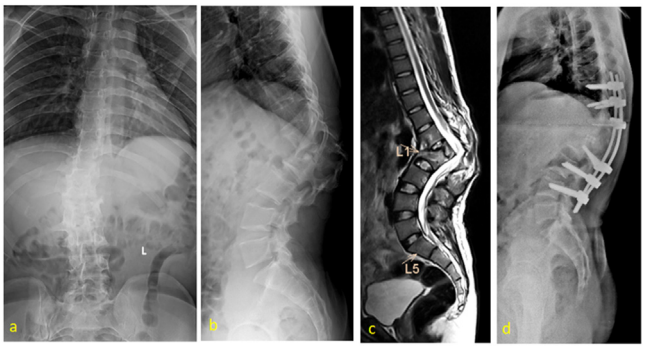

Fig. 7. (A, B) AP and Lateral radiograph showing a lateral translation and focal kyphosis at the thoracolumbar region. Anterior column destruction is accompanied with functional failure of the posterior column (Type IIIB). (C) Mid Sagittal T2W MRI showing stretching of the conus at the level of T12. (D) Postoperative radiograph after closing opening wedge osteotomy (COWO) showing kyphosis correction.

tural support and direct visualization during spinal cord decompression [73,74].

Guna et al. performed a study including 122 patients who underwent an all-posterior surgery for spinal TB. The patients were divided into 3 groups based on the anterior reconstruction performed. Forty-nine patients in Group A underwent anterior cage reconstruction, 21 patients in Group B underwent anterior autologous bone grafting, while 52 patients in Group C underwent posterior column shortening without anterior reconstruction. A comparative analysis of the 3 groups was performed concerning the kyphosis correction achieved, kyphosis at final follow-up, and degree of correction lost. Though the kyphosis correction achieved was significantly higher in the group who underwent anterior cage reconstruction, the surgical duration, blood loss, and hospital stay were significantly higher in this group. The study showed that there was no difference in the loss of correction, neurological and functional outcomes between the 3 groups, with the posterior column shortening patients having the advantages of shorter surgical duration, hospital stay, and blood loss [75].

Combined approach

In the context of osteoporotic bones, the involvement of multiple vertebral bodies, and the prevalence of severe kyphotic deformities, the incorporation of multiple techniques play an essential role [76]. In such instances, a combination of posterior instrumentation with anterior decompression and fusion may be utilized, either in a single or 2-stage procedure. The anterior debridement eliminates infected foci, allowing for direct neural decompression and the establishment of a strong anterior reconstruction [77]. Simultaneously, posterior instrumentation facilitates better deformity correction and reduces tension on anteriorly placed grafts, thereby contributing to the maintenance of sagittal deformity correction. Due to the substantial morbidities associated with combined approaches, they are typically reserved for cases of severe destructive lesions and junctional pathologies that are inherently unstable [78].

Active TB in special situations

Pediatric age group: The vertebral body in children is cartilaginous and more prone to rapid destruction. Damage to the VB cartilage from active TB leads to severe deformities in children. Vertebral development is slowed when pressure is applied to the ring apophysis but is hastened when the pressure is relieved. When the ring apophysis is loaded unevenly, it may lead to the development of new deformities or the worsening of existing ones, both of which can have serious neurological consequences [79]. Since residual deformity may worsen owing to a developing spine and physical activity, children should continue to have periodic clinical and radiological evaluations even after being declared healed. Thirty-one percent of the children had at least 2 of the 4 risk factors for spinal deformity. Progression is more common among children under the age of 7, diseases affecting more than 3 vertebral bodies, and those with involvement of thoracic or thoracolumbar junction [17,80].

According to Rajasekaran, children who exhibit 2 or more spine at-risk signs may have posterior facet dislocation, which requires surgical treatment. In addition, he classified the development of the deformity in children into 3 distinct stages: In type 1 curves, the deformity worsens as the child grows and eventually requires surgery; in type 2 curves, the deformity improves with age; and in type 3 curves, there is little to no change in the deformity during either the active or healed phases of the disease [17,81].

Elderly age group

Specific challenges that the elderly confront include diminished health, multiple chronic conditions, and drug interactions. There is a 3 fold rise in the likelihood of adverse medication responses in the senior population, a 6 fold increase in the likelihood of death, and a 20 fold increase in the likelihood of misdiagnosis [82].

Factors that enhance the likelihood of developing spinal TB include malignancy, diabetes, poor nutrition, immunosuppression, extended hospitalization, and others. Look for evidence of TB meningitis, disseminated TB, or other system involvement while evaluating an aged patient. Unfortunately, degenerative disorders are often overlooked as a cause of elderly low back pain [83,84].

HIV-infected patients

HIV individuals are 37 times more likely to get TB than the general population [85]. Spinal TB in HIV patients follows the same principles of therapy, treatment duration, and prognosis as in immunocompetent individuals [86].

Risk of medication interactions and the possibility of immunological reconstitution are of particular concern to this subgroup. Rifampicin interacts with the vast majority of antiretroviral treatment drugs, including protease inhibitors and non-nucleoside reverse transcriptase inhibitors. Antiretroviral treatment initiated in a TB patient with immune reconstitution syndrome improves the inflammatory response but paradoxically worsens TB symptoms. Antiretroviral treatment (ATT) in a patient who has never been on ATT before has the potential to reveal latent tuberculosis.

Junctional TB

The cervicothoracic, thoracolumbar, and lumbosacral junctions of the spine are particularly vulnerable to tuberculosis. These parts of the spine are called the “stress transition zone,” and a TB infection can lead to progressive deformity or neurological impairment. The importance of junctional TB was highlighted by Rajasekaran et al. following the results of the multinational expert consensus study involving 68 surgeons. Among the 3 junctional regions, the cervicothoracic (CT) and thoracolumbar (TL) junctional lesions were considered to be unstable lesions (86.57%) when compared to the lumbosacral (LS) junction (26.86%) by the expert committee [15]. The retrospective study of 77 patients with junctional TB by Yin et al highlighted that anterior debridement with strut grafting with instrumentation is sufficient in cervicothoracic and thoracolumbar TB. However additional posterior stabilization is essential in multilevel involvement. On the other hand, lumbosacral junction TB needs anterior debridement, strut grafting, and posterior internal fixation [87].

Table 4
Various criteria for assessing healing in spine TB.

Category	Criteria	Positive response
Clinical	Pain/tenderness	VAS < 3/10 till treatment completion
	Swelling/sinus	Disappearance of swelling/ sinus
	Paraspinal spasm	Disappearance of spasm
	Weight	Weight gain of 5% per month and maintained for at least 2 months (to assess progression)
Serological	ESR	Reduction of values by more than 80% of initial values or to normal taken as a positive response
	CRP	Reduction of values by more than 80% of initial values or to normal taken as a positive response
Radiological (X-RAY)	Osteopenia/appearance of sclerosis	Reduction of osteopenia to a comparable region available (e.g., normal hip) or adjacent normal bone or Appearance of sclerosis, taken as a positive response
	Sharpening of articular and cortical margins	Indicates healing
	Remineralization and reformation of bony trabeculae	Indicates healing
	Bony ankylosis /fusion	A clear sign of healing, and is seen in around 50% of patients.
MRI Scan	Resolution of bone marrow inflammatory edema	Indicates healing, however, bone marrow edema can sometimes persist for up to 14 months
	Decrease in contrast enhancement	Within a few weeks or months of treatment indicates healing
	Decrease in paravertebral, and epidural abscess and granulation tissue	Indicates healing
	Fatty change within the bone marrow is seen as a hyperintense signal on both T1 and T2 weighted images	It is a gradual process and is seen in 40% of patients at 6 months and 75% of patients at 12 months of treatment
18 F-FDG PET	Evaluates metabolic activity in the lesion	Decrease in FDG uptake can indicate a response to antitubercular therapy and is useful in the early detection of nonresponders, and multidrug resistant tuberculosis (MDR-TB),

Defining the endpoint of treatment

The lack of definitive criteria for identifying “healed status” is the main problem with spinal TB. Therefore, it is hard to know when to stop using antitubercular drugs. Due to the paucibacillary nature of the TB spine, the “gold standard” in pulmonary TB- repeated tissue biopsy and culture conversion—is not used to determine the end point of treatment for spinal TB. In addition, there is no reliable way to assess the extent of M. TB infection or predict its clinical outcomes. For this reason, the triad of clinical progress, laboratory markers, and radiographic assessment remains the gold standard for confirming healing [88] (Table 4).

Successful surgical treatment of spinal TB requires a tailored strategy for each patient. The patient’s age, the site of the bone lesion, the existence of any medical comorbidities, the degree of kyphosis, the number of afflicted spinal levels, the area of the spine implicated, and the surgeon’s expertise and preferences are all important considerations. Lower cervical TB treatment continues to focus on anterior debridement and fusion, despite the growing popularity of all-posterior global reconstruction in the thoracic and lumbar spine. Cases involving the thoracolumbar area, revision operations, and patients with significant vertebral defects affecting 2 or 3 vertebrae benefit greatly from combined treatments [89,90]. A successful cure for the disease involves a comprehensive approach

Conclusion

The objectives of treatment for spinal TB are eradication of the disease, prevention and/or correction of spinal deformity, and restoration of neurological function. Spinal TB surgery goals include decompression and debridement, stability maintenance and strengthening, and preventing the progression of deformity or correcting it in patients with healed disease. It is very vital to comply with the multidrug treatment that is mandated by the WHO in order to achieve a positive result and maintain a relapse rate of less than 2%.

In the last 30 years, an important innovation in the medical field is that uncomplicated TB is a medical disease that is amenable to antitubercular chemotherapy. We have understood the fact that childhood TB and adult TB are 2 different entities, and deformity progresses in childhood TB up to skeletal maturity inspite of infection cure. The future lies not in surgical innovation alone but actually in the control of the disease. However, the worsening fact is the increasing trend of multidrug resistance and coinfection with HIV. So, the focus of future research should be on drug-host interaction (bacteriology of TB, drug sensitivity, and how to augment host immunity) and host-directed therapy in the management of spinal TB.

Declarations of Competing Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.xnsj.2023.100267.

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