



Diagnostic and therapeutic outcomes in spinal tuberculosis: a retrospective study integrating GeneXpert MTB/RIF, histopathology, and clinical management strategies

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Abstract

Purpose Spinal tuberculosis (STB) remains prevalent in developing nations and significantly contributes to morbidity, often resulting in kyphotic deformity and neurological deficits. In this study, we correlate the diagnostic, therapeutic and prognostic factors according to the current standard of management of STB.

Methods This retrospective study evaluated diagnostic and prognostic factors in 77 patients with STB treated surgically (37.7%) or non-surgically (62.3%) between 2018 and 2023. Diagnostic tools included GeneXpert MTB/RIF (GXMTB/RIF)- a rapid molecular test for detecting *Mycobacterium tuberculosis* and rifampicin resistance- and histopathological confirmation via biopsy. Clinical outcomes were assessed using Visual Analogue Scale, Oswestry Disability Index, inflammatory markers (ESR, CRP), kyphotic deformity correction, and neurological improvement.

Results GeneXpert MTB/RIF detected *Mycobacterium tuberculosis* in 94.8% of cases, with 5.2% showing rifampicin resistance. Histopathology revealed granulomatous infiltration in 96.1% of biopsies, underscoring the importance of combining diagnostic methods. Both groups showed significant improvement over 12 months, with surgical patients exhibiting higher baseline kyphosis angles (47.41° vs. 19.27°, $p < 0.001$) and greater post-treatment correction (14.14° vs. 2.71°, $p = 0.04$). Neurological status, evaluated via ASIA Impairment Scale improved post-treatment, with 93.5% achieving normal neurology. Deformity presence strongly correlated with surgical intervention (51.9% vs. 8%, $p < 0.001$).

Conclusion The study highlights the efficacy of anti-tubercular therapy (ATT) and the role of surgery in severe deformity or neurological compromise. Notably, rare discrepancies between GXMTB/RIF and histopathology (5.2% GXMTB/RIF - negative but histopathology- positive) emphasize the need for clinical judgment alongside laboratory findings. Surgical intervention is pivotal for deformity correction and neurological recovery, while ATT remains the cornerstone.

Keywords Spinal tuberculosis · GeneXpert · Antitubercular therapy · Spinal surgery · Histopathology · Clinical outcome · Surgical outcome · Rifampicin sensitivity · Resource-poor setting

Introduction

Spinal tuberculosis (STB) remains a significant global health issue, particularly in regions with high tuberculosis (TB) prevalence [1]. Together, China and India made up 67.55% of the cases, with osteoarticular tuberculosis predominantly affecting those younger than 30 years (58.94%). Spinal involvement is the most prevalent form (57.62%),

and concurrent pulmonary tuberculosis is seen in 16.55% of patients [2].

STB continues to present diagnostic challenges. Despite advancements in diagnostic modalities, certain cases of STB remain diagnostically challenging for spine surgeons owing to the high false negativity of our available tools and variable presentation of the patients. Gold standard test for confirmation of STB is isolation of the bacteria in culture,

which usually takes six to eight weeks, hence limiting its usefulness. GeneXpert MTB/RIF (GXMTB/RIF) is a rapid automated molecular test that can be used to enable early diagnosis of STB and simultaneous assessment of rifampicin resistance. GXMTB/RIF shows a high diagnostic accuracy for STB, with a pooled sensitivity of 92% and moderate specificity of 71% when compared to culture, surpassing acid fast bacilli (AFB) smear and polymerase chain reaction (PCR) in sensitivity [3].

Imaging is essential for diagnosing and managing STB, starting with plain radiographs in resource-limited settings and increasingly depending on MRI due to its superior sensitivity and specificity, capacity to identify early disease, assess neurological involvement, and locate non-contagious or skip lesions [4].

It is still arduous to distinguish STB from non-tubercular pathology, emphasizing the necessity of tissue diagnosis via histopathological examination. In this situation, percutaneous transpedicular needle biopsy is one of the vital, minimally invasive procedure that aids in precise diagnosis and directs suitable management [5].

Majority of patients of STB responds very well to medical treatment. The treatment response is apparent in form of pain relief, improvement in neurological status, and even correction of spinal deformity. The literature describes a variety of treatment regimens for STB, resulting in heterogeneity in clinical practice and outcomes. This situation is

further complicated by the increasing encounter of drug-resistant strains [6, 7].

STB continues to pose significant diagnostic and therapeutic challenges in resource-limited settings, frequently resulting in kyphotic deformity and neurological impairment. The aim of this study was to evaluate the diagnostic value of GXMTB/RIF and histopathology, as well as clinical and radiological outcomes in patients with STB treated surgically (S) versus non-surgically (NS), particularly concerning neurological recovery, correction of deformity, and functional improvement in resource poor setting.

Methods

A retrospective analysis of a single center (Hospital for Advanced Medicine and Surgery) case series was performed, and a total of 77 patients who were diagnosed with STB, managed S or NS between 2018 and 2023, were analysed. Approval was obtained from the Institutional Review Committee (Ref: HAMS/IRC No. 13-2025) and all procedures adhered to the principles of the Declaration of Helsinki.

This retrospective observational study included consecutive patients diagnosed with STB during the study period. The institutional medical records archive, managed by the hospital's medical records department, was used to obtain patient data. The inclusion criteria comprised patients diagnosed with STB, confirmed through a combination of clinical features, imaging findings (x-ray, MRI and/or CT), and microbiological or histopathological confirmation. The study excluded patients who had incomplete records or an alternative final diagnosis (Fig. 1).

Trained research personnel carried out data extraction independently, using a standardized proforma to guarantee consistency and reliability. The variables extracted included demographic information, presenting symptoms, neurological status, anatomical location of spinal involvement, diagnostic methods used, treatment modalities, and clinical outcomes.

The primary outcome measures consisted of neurological improvement (evaluated with the AIS), correction of kyphotic deformity (through radiographic angle measurement), pain reduction utilizing visual analogue scale (VAS), and functional improvement assessed with the Oswestry disability index (ODI). Secondary outcomes included the diagnostic accuracy of GXMTB/RIF versus histopathology, alterations in inflammatory markers (ESR, CRP), identification of rifampicin resistance, and the relationship between deformity or neurological deficit and the necessity for surgical intervention.

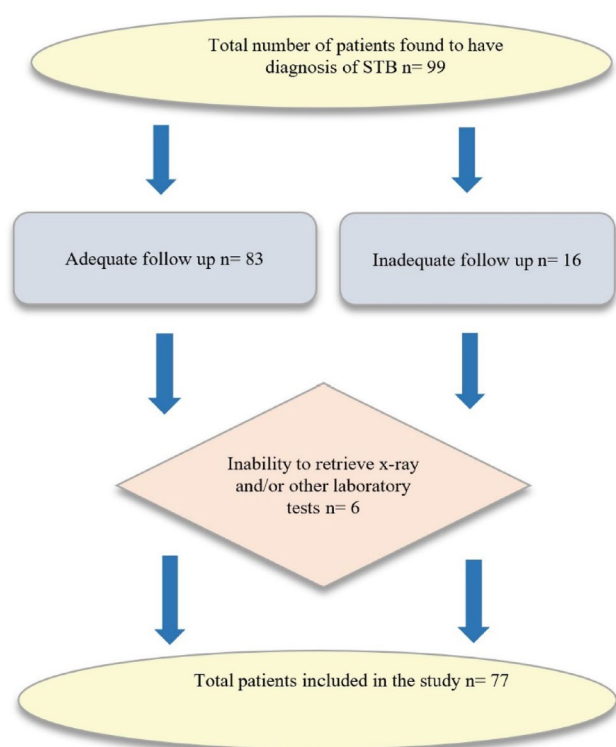


Fig. 1 Flowchart depicting the inclusion of the patients in our study

Baseline demographic characteristics (age and gender), clinical parameters - chief complaints, neurological status (AIS grading), pain intensity from VAS score, ESR and CRP of patients; radiological parameters- region and number of vertebral body involvement (contiguous or non-contiguous), degree of kyphotic deformity; and treatment type (S and NS), were evaluated. Samples that were collected from the afflicted site via percutaneous biopsy or via surgery in those with need of immediate surgery were recorded. Tissue samples or aspirate that were sent to the laboratory for histopathology as well as GXMTB/RIF were retrieved.

All patients received standard anti-tubercular therapy (ATT) regimens, i.e., four drugs (isoniazid, rifampicin, pyrazinamide, and ethambutol) for 3 months and two drugs (isoniazid and rifampicin) for the following 9 months [8]. The S group consisted of patients treated surgically followed by ATT regimen. The NS group consisted of patients treated with ATT regimen and orthosis (Halo brace, Philadelphia Collar, Soft cervical collar, Thoraco-lumbo-sacral

orthosis, Lumbar corset). Drainage of abscess or transpedicular biopsy were not considered in S groups, rather they were included in NS group.

In the surgical group, patients were reviewed 2 weeks post-operatively for suture removal and subsequently at 6 weeks, and at 3, 6, 9, and 12 months during chemotherapy. Clinical healing was assessed via pain reduction, improved general health, and sinus/abscess resolution; hematological healing via ESR and CRP normalization; and radiological healing through signs such as vertebral remineralization and fusion on plain radiographs (Figs. 2 and 3). Neurological recovery was also recorded. Patients who completed treatment were followed biannually for two years post-therapy to ensure sustained clinical and radiological remission.

Statistical method

The mean values of each clinical metric variable in the S and NS group were calculated. Chi-square test and t-test were used to analyze the effect of metric and categorical variables distributions in S and NS groups. $P < 0.05$ was considered statistically significant. All comparisons between groups are exploratory and unadjusted. We report p-values and 95% confidence intervals but acknowledge the absence of adjustment for multiple comparisons, which may increase the risk of Type I error.

Neurological status was set as dependent variable while the VAS score, contiguity of the disease and kyphotic deformity were set as independent variables. Statistical analysis was performed using IBM SPSS v21.0 software from Armonk, NY: IBM Corp.

Results

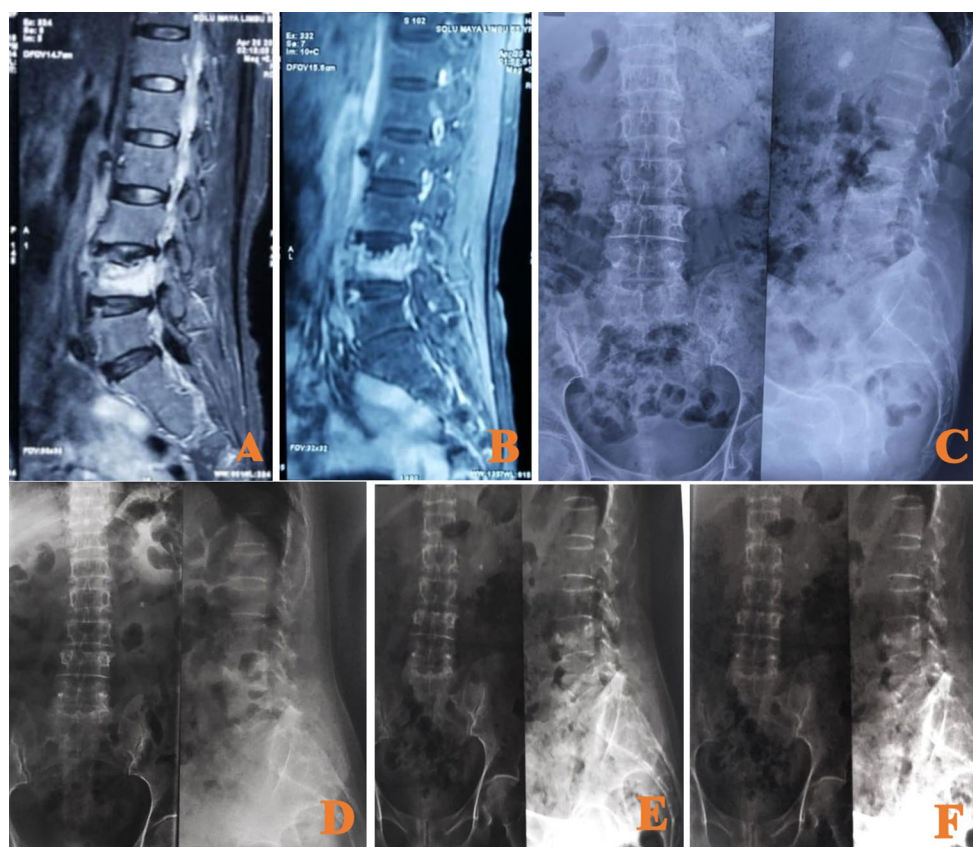
A total of 77 patients diagnosed with STB were enrolled in the study. There were six cases of pulmonary TB along with the STB. The mean age of the participants was 49.05 ± 18.57 years (17–86 years). There were 35 (45.5%) male and 42 (54.5%) female participants. Deformity at the time of presentation was noted on 52 (67.5%) patients. Contiguous form of STB were present in 63 (81.8%) patients. The most commonly affected site was lumbar 27 (35.1%) followed by dorsal 25 (32.5%). Two vertebral level involvement was noted among the majority of the patients 34 (44.2%). Surgery was needed in 29 (37.7%) patients with posterior approach being utilized in 15 (19.5%) patients (Table 1).

Neurological status was recorded via Asia Impairment Scale (AIS). Prior to the treatment, 67 (87%) of participants had normal neurological status, which improved to 72 (93.5%) following completion of therapy, reflecting favorable neurological outcomes (Table 2).



Fig. 2 Sagittal T2-weighted MRI (A) and sagittal STIR image (B) showing epidural pus collection at L4/L5/S1 compressing the thecal sac; intraoperative image (C) demonstrating pus drainage (blue arrow); follow-up AP and lateral radiographs at immediate postoperative period (D), 6 weeks (E), 3 months (F), 6 months (G) and 12 months (H) showing titanium interbody bullet and mesh cages and posterior instrumentation in situ

Fig. 3 Sagittal T2-weighted MRI (A), sagittal STIR image (B) and AP, lateral radiograph at initial presentation (C) showing tubercular spondylitis of L4 vertebra; follow-up AP and lateral radiographs at 3 months (D), 6 months (E) and 12 months (F) showing resolving lesion of L4 tubercular spondylitis with subsequent follow up



The mean duration of symptoms prior to diagnosis was 94.74 ± 100.9 days (3–720 days), while the mean follow-up period was 248.40 ± 168.73 days (30 to 1000 days).

Among the cases of STB, *Mycobacterium tuberculosis* (MTB) was detected in sample fluid (GXMTB/RIF positive) in 73 (94.8%), while 4 (5.2%) were devoid of MTB in the sample fluid (GXMTB/RIF negative). Among the total participants positive of GeneXpert MTB/RIF, 69 (89.6%) were sensitive for rifampicin while 4 (5.2%) were resistant (Table 3). There was the statistically significant relationship between GXMTB/RIF positivity and rifampicin sensitivity results (Table 4). A small subset of patients 4 (5.2%) demonstrated negative GeneXpert MTB/RIF results but had positive histopathological findings and were consequently treated empirically based on histopathological confirmation.

Among the total participants who underwent biopsy, 74 (96.1%) patients had necrotic granulomatous infiltration, consistent with TB while 3 (3.9%) patients had necrotic bony tissue without visible granulomatous infiltration or other histopathological features of tuberculosis. These patients with only GXMTB/RIF positivity without positive histopathological finding were also considered positive for TB and were subsequently given the standard TB treatment (Table 5). There were no statistically significant relationship between histopathological results and rifampicin sensitivity results (Table 6).

Among the patients who have had a chief complaint of back pain with radicular pain and fever, 7.8% underwent surgery while 3.9% underwent a NS treatment, however this relationship was not significant ($p=0.47$) (Table 7).

Among the participants who have had the deformity either clinical or radiological at the time of presentation, 27 (51.9%) underwent S treatment while 25 (48.1%) underwent a NS treatment ($p<0.001$) (Table 8).

The mean VAS score, ODI score, CRP and ESR of the patients group at pre-operative, post-operative after 6 weeks, 3 months, 6 months, 9 months and 12 months revealed decrement in pain, disability, ESR/CRP over time (Table 9). The mean pre-treatment kyphosis angle was 29.87 ± 30.53 (20 to 100 degrees) and the mean post-treatment kyphosis angle was 7.01 ± 24.27 (5 to 50 degrees). Difference between S treatment and NS group in accordance to mean preoperative kyphosis angle were statistically significant ($p<0.001$). Difference between S treatment and NS group according to mean post-treatment kyphotic angle were also statistically significant ($p=0.04$) (Table 9).

Table 1 Baseline demographic characteristics of the study population

Variables	Number (N)	Percentage (%)
Gender		
Female	42	54.5
Male	35	45.5
Deformity		
Present	52	67.5
Absent	25	32.5
Contiguity of STB		
Contiguous	63	81.8
Non-contiguous	14	18.2
Regions involved		
Dorsal	25	32.5
Lumbar	27	35.1
Cervical- dorsal	2	2.6
Dorso-lumbar	14	18.2
Lumbo-sacral	4	5.2
Cervical	3	3.9
Cervico-dorsal-lumbar-sacral	1	1.3
Sacral	1	1.3
Number of vertebrae involved		
1	12	15.6
2	34	44.2
3	15	19.5
4	5	6.5
5	4	5.2
6	5	6.5
8	2	2.6
Treatment method utilized		
Surgical	29	37.7
Anterior approach	2	2.6
Posterior approach	15	19.5
Combined approach	12	15.6
Non-surgical	48	62.3

Table 2 Comparison of pre- and post-treatment neurological status (AIS grading) in surgical and non-surgical groups

Neurological status (AIS grade)	Pre-treatment neurological status Number (%)	Post-treatment neurological status Number (%)
A	1 (1.3)	—
B	3 (3.9)	—
C	4 (5.2)	3 (3.9)
D	2 (2.6)	2 (2.6)
E	67 (87)	72 (93.5)
Total	77 (100)	77 (100)

Table 3 GXMTB/RIF results of the participants in accordance to rifampicin sensitivity

Rifampicin	Number	Percent
NA*	4	5.2
Sensitive	69	89.6
Resistant	4	5.2
Total	77	100.0

*NA = GXMTB/RIF-negative cases

Table 4 Comparison of GXMTB/RIF results and rifampicin sensitivity

GXMTB/RIF Positivity	Rifampicin Sensitivity			Total N (%)	p-value**
	NA*	Sensitive N (%)	Resistance N (%)		
Present	0	69 (94.5%)	4 (5.5%)	73 (100%)	<0.001
Absent	4 (100%)	0	0	4 (100%)	

*NA = GXMTB/RIF-negative cases, **chi-square test

Table 5 Comparison of positive GXMTB/RIF test and histopathological results

GXMTB/RIF positivity	Histopathology result		Total	p-value*
	Necrotic tissue	Granuloma- tous tissue		
Present	3 (4.1%)	70 (95.9%)	73 (100%)	0.68
Absent	0	4 (100%)	4 (100%)	

*chi-square test

Table 6 Comparison of histopathological results and rifampicin sensitivity

Histopa- thology result	Rifampicin sensitivity			Total	p-value**
	NA*	Sensitive	Resistance		
Necrotic tissue	0	3 (100%)	0	3 (100%)	0.83
Granulo- matous tissue	4 (5.4%)	66 (89.2%)	4 (5.4%)	74 (100%)	

*NA = GXMTB/RIF-negative cases, **chi-square test

Table 7 Comparison of presenting symptoms in surgical versus non-surgical groups

Presenting symptoms	Surgical group	Non- surgical group	p-value*
	N (%)	N (%)	
Back pain	11 (14.3)	19 (24.8)	0.47
Back pain and fever	3 (3.9)	5 (6.5)	
Back pain, radicular pain and fever	6 (7.8)	3 (3.9)	
Back pain and radicular pain	7 (9.1)	17 (22.1)	
Back pain and cough	2 (2.6)	3 (3.9)	
Back pain, radicular pain, fever and cough	0 (0)	1 (1.3)	
Total	29 (37.7)	48 (62.3)	

*chi-square test

Table 8 Treatment modalities in patients presenting with spinal deformity: surgical versus non-surgical group

Deformity	Surgical		Non-surgical		p-value*
	N	%	N	%	
Yes	27	51.9	25	48.1	<0.001
No	2	8	23	92	

*chi-square test

Table 9 Longitudinal assessment of VAS, ODI, CRP, and ESR and kyphosis angle in study participants across follow-up visits

Variables	Surgical	Non-surgical	<i>p</i> -value*	95% CI
VAS Score				
Pre-treatment	9.55±0.78	9.19±0.89	0.07	−0.76–0.35
6 weeks	5.17±1.14	4.60±1.13	0.03	−1.09 – (−0.39)
3 months	3.07±1.09	2.96±1.06	0.66	−0.62–0.39
6 months	2.07±0.98	1.93±1.06	0.58	−0.63–0.36
9 months	1.57±0.92	1.35±0.90	0.30	−0.66–0.21
12 months	0.89±0.74	0.78±0.92	0.59	−0.52–0.29
ODI Score				
Pre-treatment	37.31±5.54	28.54±8.61	<0.01	−12.33 – (−5.20)
6 week	28±7.19	18.71±7.74	<0.01	−12.83 – (−5.76)
3 month	16.48±6.16	12.67±5.93	0.009	−6.63 – (−0.99)
6 month	9.03±5.19	6.96±3.76	0.04	−4.11 – (−0.03)
9 month	4.34±3.12	3.04±2.18	0.03	−2.51 – (−0.09)
12 month	2.07±1.96	1.29±1.57	0.06	−1.59 – (0.03)
CRP level (mg/L)				
Pre-treatment	61.87±31.11	58.25±26.15	0.58	−16.79–9.54
6 week	32.75±18.38	30.49±14.85	0.55	−9.88–5.36
3 month	15.69±8.84	14.85±8.39	0.67	−4.85–3.18
6 month	7.69±4.55	7.41±4.43	0.79	−2.37–1.83
9 month	3.13±2.32	3.53±2.96	0.53	−0.88–1.69
12 month	1.74±1.83	1.69±1.19	0.88	−0.73–0.64
ESR level (mm/hour)				
Pre-treatment	77.72±27.90	67.42±24.97	0.09	−22.54–1.92
6 week	36.10±12.22	32.17±11.94	0.16	−9.58–1.71
3 month	20.86±7.39	19.69±8.55	0.54	−4.98–2.65
6 month	15.34±5.57	14.50±6.06	0.54	−3.60–1.91
9 month	11.59±4.21	10.84±4.36	0.46	−2.76–1.27
12 month	9.28±3.36	9.12±3.37	0.84	−1.74–1.42
Kyphosis angle				
Pretreatment kyphosis	47.41±29.72	19.27±26.01	<0.001	−41.00 – (−15.28)
Posttreatment kyphosis	14.14±24.53	2.71±23.31	0.04	−22.57 – (−0.29)

*t-test

Discussion

In 2023, it is estimated that 10.8 million people worldwide developed tuberculosis, resulting in an incidence rate of 134 cases per 100,000 individuals. The WHO South-East Asia Region reported the highest burden (45%), followed by Africa (24%) and the Western Pacific (17%). The Eastern Mediterranean had lower proportions (8.6%), as did the Americas (3.2%) and Europe (2.1%). It is significant that 6.1% of all reported TB incidents involved people with HIV [9]. STB represents the most prevalent musculoskeletal manifestation, impacting approximately 1 to 2% of all tuberculosis cases [10].

The clinical manifestations of STB most frequently included neurological deficits and back pain, with the former often indicating a late-stage presentation. Constitutional symptoms were common, especially in low-resource settings, where diagnostic delays and limited surgical options exacerbate disease severity [11]. In our study, the

most prevalent symptoms were back pain, followed by back pain combined with radicular pain. Studies has reported cases more prevalent in male as well as no differences on the basis of gender with younger and adolescent population being affected more [2, 11]. Our study has demonstrated that females are predominant across various age groups, with the average age being in the fourth decade. STB mainly targets the thoracolumbar region, usually affecting the vertebral bodies and intervertebral spaces, while isolated involvement of the posterior elements is uncommon [12]. In our study, the lumbar spine was the most frequently affected region, followed by the thoracic and thoracolumbar segments.

The GXMTB/RIF assay, a WHO-endorsed, fully automated molecular test, rapidly detects MTB and rifampicin resistance via *rpoB* gene mutations within two hours [13, 14]. It has demonstrated high diagnostic accuracy in extra-pulmonary TB, with sensitivity and specificity reaching up to 100% in osteoarticular samples, though performance varies by specimen type [15]. In our study, four GXMTB/

RIF-negative cases were confirmed as TB through histopathology, while three GXMTB/RIF-positive cases lacked histopathological evidence, highlighting the complementary roles of both modalities [13, 15].

The optimal duration and regimen for anti-tubercular therapy (ATT) in STB still remains the subject of ongoing debate. The World Health Organization (WHO) classifies STB under Category I, recommending an intensive phase of 2 months with four first line drugs- isoniazid, rifampicin, pyrazinamide, and streptomycin, followed by a 4-month continuation phase with isoniazid and rifampicin, though it advises extending treatment to at least 9 months for osteo-articular TB due to the difficulty in monitoring therapeutic response and the risk of long-term disability [16]. The American Thoracic Society suggests 6 months of treatment in adults and 12 months in children, while the British Thoracic Society supports a 6 month four-drug regimen regardless of age [16]. Despite these guidelines, many clinicians favor extended regimens of 12–24 months, particularly in cases with extensive disease or delayed radiological improvement. Notably, a pilot study by Nene et al. demonstrated comparable long-term outcomes in patients treated with either 6 or 12 months of ATT, suggesting that shorter regimens may be effective in selected cases [7]. In our study, All patients received standard ATT comprising four drugs for 3 months (isoniazid, rifampicin, pyrazinamide, and ethambutol), followed by two drugs (isoniazid and rifampicin) for the subsequent 9 months as per the WHO regimen.

In our cohort, surgical intervention was undertaken primarily in patients with diagnostic uncertainty requiring tissue sampling, worsening neurological deficits despite ATT, or structural instability and deformity. These decisions reflect our institutional protocols and patient presentations. In select pediatric cases, early surgery was considered to mitigate future deformity, aligning with established concerns about growth-related progression [8, 17].

At our center, anterior, posterior, and combined surgical approaches were employed based on patient-specific factors such as the anatomical location and extent of disease. These techniques, including osteotomies and vertebral column resections where appropriate, were used for spinal decompression, stabilization, and deformity correction, as previously described in the literature. [18]. Over time, we observed a shift toward a posterior-only approach, which in our experience was associated with favorable outcomes and fewer complications, particularly outside the cervical region. This evolving trend in our surgical practice is consistent with findings reported in recent studies [18–20].

STB remains the most common cause of kyphotic deformity worldwide, affecting the anterior column in 90% of cases, with posterior involvement in only 5–10% [21, 22]. Risk factors for sequelae, especially in children, include

thoracic spine involvement, young age, paravertebral abscesses, positive bacteriology, and multilevel disease [23]. Rajasekaran identified key predictors of severe deformity progression: age < 10 years, pre-treatment kyphosis > 30°, junctional lesions, and ‘spine at risk’ signs [21, 24]. Our study similarly demonstrated significantly higher preoperative kyphosis angles in the surgical group ($p < 0.001$) and greater correction postoperatively ($p = 0.04$), likely due to selection for surgery based on severe initial deformity. The final kyphosis estimation formula proposed by Rajasekaran may aid in early risk stratification [25].

Our study takes into account a single center experience with the current standard of care of STB. In addition to presenting epidemiological data from a low-resource setting and comparing clinical outcomes between S and NS groups, our study highlights the diagnostic concordance and discrepancies between GXMTB/RIF and histopathological examination in STB.

Our study are not devoid of its limitations. First, it is a retrospective, single-center analysis conducted in a resource-limited setting, which may limit the generalizability of our findings. The sample size is relatively small, reflecting the patient population served by our institution in a developing country. Second, although our intention was to assess clinical and radiological outcomes over a 2-year period, the actual mean follow-up duration was shorter. Long-term outcomes such as the progression of kyphotic deformity, which may manifest or worsen decades after treatment, could not be adequately evaluated. Third, while previous trials have explored shorter treatment durations (e.g., 6 months) for spinal TB, we adhered to the 12-month anti-tubercular therapy regimen in alignment with current WHO recommendations for extrapulmonary TB management, particularly in complex cases such as spinal involvement. Finally, our comparative analysis of S and NS groups is exploratory and unadjusted. Due to baseline clinical differences between the groups (e.g., neurological deficits, severity of deformity), we were unable to perform multivariable or propensity-adjusted analyses. This raises the potential for selection bias and limits causal inference. Additionally, multiple statistical comparisons were made without correction, increasing the risk of Type I error.

Conclusion

A 12-month anti-tubercular therapy regimen was effective in managing spinal tuberculosis in our study population. Discrepancies observed between GeneXpert MTB/RIF and histopathology highlight the importance of integrating multiple diagnostic tools to enhance diagnostic accuracy. In rare situations where both tests yield negative results, clinical

judgment becomes essential, and further steps such as culture or repeat biopsy may be necessary. These findings support the value of a comprehensive diagnostic strategy that aligns laboratory evidence with clinical context. Treatment decisions should be tailored to individual patients, based on diagnostic results, clinical presentation, and available resources, rather than a uniform protocol.

Patient consent Not required as per the Institutional Review Committee policy for the retrospective study at the institution.

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Author contributions Prashant Adhikari: Conceptualization, Methodology, Writing- Original draft preparation; Isha Amatya: Software, Data curation, Methodology; Pradeep Regmi: Reviewing and Editing; Jeevan Kumar Sharma: Writing- Original draft preparation, Methodology, Reviewing and Editing; Raju Pangen: Reviewing and Editing; Nishma Pokharel: Reviewing and Editing; Smriti Bhatta: Reviewing and Editing; Deepak Shrestha: Reviewing and Editing; Bhaskar Raj Pant: Reviewing and Editing; Sandeep Bhandari: Reviewing and Editing; Arun Dhakal: Reviewing and Editing; Eldin Karaikovic: Supervision, Reviewing and Editing; Emre Acaroglu: Supervision, Reviewing and Editing.

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Data availability No datasets were generated or analysed during the current study.

Declarations

Competing interests The authors declare no competing interests.

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