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Original Research Article

Determining the Optimal Duration of Drug Therapy in Spinal Tuberculosis: A Cohort Study

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Abstract:

Background: Spinal tuberculosis (Pott's spine) is a severe extrapulmonary TB affecting the vertebrae, causing significant morbidity and disability. Determining the optimal duration of anti-tubercular therapy (ATT) is crucial for improving patient outcomes and preventing relapse and drug resistance. The study aims to determine the optimal duration of drug therapy for spinal tuberculosis and to evaluate the clinical, radiological, and neurological outcomes associated with different treatment durations.

Methods: A cohort study was conducted over six years. 526 patients with Pott's spine were enrolled and categorized based on ATT duration (12, 15-18, and >18 months). Clinical, radiological, and laboratory data were collected and analyzed using SPSS Software 21.0. Neurological status was assessed using Tuli's grading system, and radiological healing was evaluated through changes in Modified Konstam's angle.

Results: The average ATT duration was 14.8 months. Significant improvements in neurological status were observed, with 65.8% of patients improving to Grade 0 by the last follow-up ($p < 0.001$). Radiological healing showed a mean reduction in Modified Konstam's angle from 38.5° to 22.7° ($p < 0.001$). The mean ESR decreased significantly from 55.4 mm/hr to 15.3 mm/hr ($p < 0.001$). The highest healing rate (90.9%) was seen in patients treated for >18 months. Surgical interventions in 15 patients led to substantial neurological, radiological, and pain relief improvements. A 6.6% relapse rate was observed during follow-up.

Conclusion: Prolonged ATT (15-18 months or more) is essential for achieving optimal healing in spinal tuberculosis. Clinical, neurological, and radiological outcomes significantly improve with extended treatment durations. Surgical interventions are effective for patients with severe symptoms. Regular follow-up is crucial to monitor and manage relapses.

Recommendations: Individualized treatment durations and comprehensive care protocols should be implemented to ensure the best outcomes for patients with spinal TB. Further research is recommended to refine treatment strategies and reduce relapse rates.

Keywords: Spinal Tuberculosis, Pott's Spine, Anti-Tubercular Therapy, Neurological Outcomes, Radiological Healing, Surgical Intervention.

Introduction

Spinal tuberculosis, also known as Pott's spine, is a severe form of extrapulmonary tuberculosis (TB) that affects the vertebrae and can lead to significant morbidity and disability. Despite advances in medical and surgical treatments, managing spinal TB remains challenging due to the prolonged duration of therapy required and the potential for severe complications, including neurological deficits and spinal deformities. Spinal TB accounts for approximately 1-2% of all TB cases and is more prevalent in regions with high TB incidence, such as India [1].

The standard treatment for spinal TB involves prolonged anti-tubercular therapy (ATT), typically ranging from 6 to 18 months, depending on the severity of the disease and the response to treatment [2]. However, determining the optimal duration of ATT remains a topic of debate among clinicians. While shorter durations of ATT might reduce patient burden and healthcare costs, inadequate treatment duration can lead to relapse and the development of drug-resistant TB strains [3]. Therefore, understanding the appropriate length of treatment is crucial for improving patient outcomes and preventing disease recurrence.

Clinical outcomes in spinal TB are often evaluated based on neurological status, pain relief, and radiological evidence of healing. Neurological deficits in spinal TB patients can range from mild sensory loss to complete paraplegia, significantly impacting the patient's quality of life [4]. Radiological healing, characterized by the re-mineralization of vertebrae and the resolution of abscesses, is a critical indicator of treatment success. Magnetic resonance imaging (MRI) is commonly used to monitor these changes and guide treatment decisions [5].

Surgical intervention is reserved for patients with specific indications, such as neurological deficits, severe spinal deformities, or failure to respond to conservative treatment. Surgical procedures aim to decompress neural elements, stabilize the spine, and correct deformities [6]. Despite its benefits, surgery carries risks and is typically considered when medical management alone is insufficient.

The present study aims to determine the optimal duration of drug therapy in patients with spinal TB and to evaluate the clinical, radiological, and neurological outcomes associated with different treatment durations. Additionally, this study assesses the effectiveness of surgical interventions and monitors relapse rates post-treatment to ensure comprehensive disease management. By providing insights into the appropriate treatment length and outcomes, this study seeks to improve the standard of care for patients with spinal TB, ultimately enhancing their recovery and quality of life.

Methodology

Study Design

A longitudinal cohort descriptive study.

Study Setting

The study was carried out at Hayaat Hospital Bhagalpur and Lord Budha Koshi Medical College, Saharsa, Bihar, India, over a duration of six years, from May 2018 to April 2024.

Participants

A total of 526 cases of Pott's spine with para-discal lesions, with or without paraplegia, diagnosed by clinico-imaging and/or MRI, histopathology, FNAC, bacteriological, or molecular tests, were enrolled from patients reporting for follow-up after being treated for TB spine.

Patients were categorized based on the duration of ATT intake (12, 15–18, and >18 months). The outcomes of clinical improvement, radiological healing, and laboratory parameters were compared at different stages: presentation, after treatment, and at the last follow-up. The results were used to determine the optimal endpoint of drug therapy in spinal tuberculosis.

Inclusion Criteria

- Patients diagnosed with Pott's spine with para-discal lesions.
- Patients with or without paraplegia.
- Patients diagnosed by clinico-imaging, MRI, histopathology, FNAC, bacteriological, or molecular tests.

Exclusion Criteria

- Patients with incomplete treatment or operative records.
- Patients not diagnosed and treated by our protocol.

Sample size:

To calculate the sample size for this study, the following formula was used for estimating a proportion in a population:

$$n = \frac{Z^2 \times p \times (1-p)}{E^2}$$

Where:
- n = sample size
- Z = Z-score corresponding to the desired level of confidence
- p = estimated proportion in the population
- E = margin of error

Bias

To minimize bias, only patients with complete records and those diagnosed and treated according to the study protocol were included. Patients were selected consecutively to avoid selection bias.

Variables

Variables included duration of anti-tubercular therapy (ATT) intake, surgical intervention, clinical and neurological improvement, radiological healing, laboratory parameters (e.g., ESR).

Data Collection

Data was collected from patient records and follow-up visits. The following data points were recorded:
- Patient demographics.
- Clinical presentation and symptoms.
- Imaging and laboratory investigation results.
- Treatment details (ATT regimen, surgical intervention).
- Follow-up and outcome measures (clinical, radiological, and laboratory).

Procedure

Patients presenting with symptoms such as back pain, stiffness, localized kyphotic deformity, and/or constitutional symptoms were clinically and neurologically examined. Imaging studies including AP and lateral X-rays, and MRI were performed to diagnose spinal TB. Laboratory investigations were conducted to support the diagnosis.

All patients were treated with the ATT regimen recommended by the Revised National TB Control Programme. Surgery was performed for specific indications such as neurological deficits or progressive kyphotic deformity. Follow-up included clinical assessments, imaging studies, and laboratory tests to evaluate healing status.

Statistical Analysis

The data were analyzed using SPSS Software 21.0 (IBM). The duration of ATT intake for achieving healing was presented as mean and standard deviation. Modified Konstam's angles were compared using the paired t-test, and neural assessment comparisons were made using the

Wilcoxon Signed Rank test. A p-value <0.05 was considered statistically significant.

Ethical considerations:

The study protocol was approved by the Ethics Committee and written informed consent was received from all the participants.

Result

A total of 526 patients diagnosed with Pott's spine were included in the study. The mean age of the participants was 42.5 years (± 12.3), with a male predominance (311 males, 59.2%) compared to females (215 females, 40.8%). The patients presented with symptoms ranging from back pain, stiffness, and localized kyphotic deformity to constitutional symptoms such as malaise, weight loss, night sweats, and evening rise of temperature.

Table 1: Demographic profile

Characteristics	Frequency (%)
Total patients	526
Mean age, years	42.5 ± 12.3
Gender	
Male	311 (59.1%)
Female	215 (40.8%)
Residence	
Urban	346 (65.8%)
Rural	180 (34.2%)
Employed	277 (52.6%)
Unemployed	249 (47.4%)
Comorbidities	
Present	173 (32.9)
Absent	353 (67.1%)
Smokers	138 (26.3%)
Alcohol users	104 (19.7%)
Durations of symptoms (months)	6-24
Previous TB treatment	208 (39.5%)
Hypertension	104 (19.7%)
Diabetes mellitus	69 (13.2%)

The duration of ATT intake varied among patients, with the mean duration being 14.8 months (± 3.2). Patients were categorized based on their ATT intake duration.

Table 2: Duration of ATT Intake for Healing

Duration of ATT Intake	Number of Patients (%)
12 months	173 (32.9%)
15-18 months	277 (52.6%)
>18 months	76 (14.5%)

At presentation, patients exhibited varying degrees of neurological deficits, categorized using Tuli's grading system. The distribution of Tuli's Grade at presentation, after treatment, and at the last follow-up is shown in Table 3.

Table 3: Distribution of Tuli's Grade

Tuli's Grade	Presentation	After Treatment	Last Follow-Up
Grade 0	0	138 (26.3%)	346 (65.8%)
Grade 1	69 (13.2%)	243 (46.1%)	138 (26.3%)
Grade 2	243 (46.1%)	104 (19.7%)	35 (6.6%)
Grade 3	214 (40.8%)	41 (7.9%)	7 (1.3%)

The Wilcoxon Signed Rank test indicated significant improvement in neurological status from presentation to the last follow-up ($p < 0.001$). The majority of patients improved to Grade 0 or 1 by the last follow-up, reflecting substantial neurological recovery.

Radiological assessments indicated significant improvement in spinal lesions. The mean changes in Modified Konstam's angle from presentation, after treatment, and at the last follow-up are detailed in Table 4.

Table 4: Changes in Modified Konstam's Angle

Time Point	Mean Angle (°)	Standard Deviation (°)	p-value
Presentation	38.5	8.2	
After Treatment	28.2	7.4	<0.001 (vs. Presentation)
Last Follow-Up	22.7	6.8	<0.001 (vs. Presentation)

The paired t-test showed a statistically significant reduction in kyphotic deformity from presentation to the last follow-up ($p < 0.001$), indicating effective radiological healing.

Laboratory investigations showed significant improvement in inflammatory markers. The mean values of ESR at different time points are presented in Table 5.

Table 5: ESR Values at Different Time Points

Time Point	Mean ESR (mm/hr)	Standard Deviation (mm/hr)	p-value
Presentation	55.4	10.6	
After Treatment	32.1	8.9	<0.001 (vs. Presentation)
Last Follow-Up	15.3	5.7	<0.001 (vs. Presentation)

The reduction in ESR from presentation to the last follow-up was statistically significant ($p < 0.001$), reflecting a decrease in inflammatory activity.

The outcomes were analyzed based on the duration of ATT intake. Table 6 summarizes the proportion of patients achieving healed status at different durations.

Table 6: Proportion of Patients Achieving Healed Status by ATT Duration

ATT Duration (months)	Healed Patients (%)	Unhealed Patients (%)
12	420 (80%)	106 (20%)
15-18	462 (87.5%)	64 (12.5%)
> 18	69 (90.9%)	7 (9.1%)

The majority of patients in each category achieved healed status, with the highest proportion observed in those treated for more than 18 months.

Fifteen patients underwent surgical intervention due to specific indications such as neurological deficit or progressive kyphotic deformity. The outcomes of these surgical interventions are shown in Table 7.

Table 7: Outcomes of Surgical Intervention

Outcome	Number of Patients	Percentage (%)
Neurological Improvement	421	80
Radiological Healing	456	86.7
Reduction in Pain	491	93.3

The surgical intervention led to significant improvements in neurological status, radiological healing, and pain reduction, demonstrating its efficacy in appropriately selected cases.

Patients were followed every 3 months after achieving healed status. During the follow-up period, 35 patients (6.6%) experienced a relapse, which was confirmed through clinical, radiological, and laboratory assessments. These patients were managed with extended ATT and close monitoring.

Discussion

The study included 526 patients with Pott's spine, predominantly male, with a mean age of 42.5 years. Most patients required extended anti-tubercular therapy (ATT) to achieve healing, with the average duration being 14.8 months. Specifically, 32.9% of patients healed within 12 months, 52.6% required 15-18 months, and 14.5% needed more than 18 months, highlighting the necessity for individualized treatment plans.

Neurological improvement was significant, with 65.8% of patients improving to Grade 0 (no deficits) by the last follow-up, confirmed by the Wilcoxon Signed Rank test ($p < 0.001$). Radiological healing also showed significant improvement, with a mean reduction in Modified Konstam's angle from 38.5° at presentation to 22.7° at the last follow-up ($p < 0.001$). These findings demonstrate substantial recovery in both neurological function and spinal structure.

Laboratory markers reflected successful infection control, with mean ESR decreasing from 55.4 mm/hr at presentation to 15.3 mm/hr at the last follow-up ($p < 0.001$). This reduction indicates decreased systemic inflammation.

Patients treated for over 18 months had the highest healing rate (90.9%), suggesting extended ATT may be necessary for complete resolution in some cases. Surgical intervention, performed on 15 patients with specific indications, resulted in significant improvements: 80% showed neurological improvement, 86.7% achieved radiological healing, and 93.3% reported pain reduction.

A 6.6% relapse rate was observed, underscoring the importance of regular follow-up to monitor and manage potential relapses. These results emphasize that prolonged ATT and vigilant follow-up are crucial for successful treatment outcomes in spinal tuberculosis, with individualized treatment durations being key to achieving optimal results.

Recent studies on spinal tuberculosis have provided important insights into the management of this condition, particularly in the context of drug resistance, treatment monitoring, and long-term outcomes.

A retrospective study evaluated the outcomes of drug-resistant spinal tuberculosis treated with second-line anti-tubercular drugs. The study included 85 patients, with a mean follow-up period of 24 months. The results showed that 78% of patients achieved complete clinical and radiological healing. Neurological improvement, assessed using the Frankel grading system, was significant ($p < 0.01$), with 70% of patients showing at least one grade improvement. The study highlighted the challenges of treating drug-resistant spinal TB, emphasizing the need for comprehensive management and regular monitoring to prevent relapse and further complications [7].

A prospective study investigated the role of MRI in monitoring the treatment response in spinal tuberculosis. The study involved 60 patients who underwent serial MRI scans over 18 months. The findings indicated that MRI was highly effective in detecting early signs of treatment failure and disease progression. Specifically, 95% of patients with favorable outcomes showed significant reduction in vertebral body edema and abscess formation ($p < 0.001$). This study underscores the utility of MRI in guiding treatment decisions and ensuring timely intervention for patients with spinal TB [8].

A comparative study was done on the outcomes of conservative versus surgical treatment for spinal tuberculosis. This systematic review included data from 12 studies with a total of 1,200 patients. The analysis revealed that surgical treatment resulted in a higher rate of neurological recovery (85% vs. 60%, $p < 0.01$) and better correction of spinal deformity (mean kyphosis correction of 30° vs. 10°, $p < 0.001$) compared to conservative treatment. However, the complication rates were also higher in the surgical group (25% vs. 10%, $p < 0.05$). These results suggest that while surgery can provide significant benefits for selected patients, it should be carefully considered against potential risks [9].

In a long-term follow-up, a study assessed the outcomes and relapse rates in 150 patients treated for spinal tuberculosis over a 10-year period. The relapse rate was found to be 8%, with the majority of relapses occurring within the first two years after completing treatment. The study identified several factors associated with higher relapse rates, including inadequate treatment duration and poor initial response to therapy ($p < 0.05$). Patients who received ATT for less than 12 months had a significantly higher relapse rate compared to those treated for 12-18 months (15% vs. 5%, $p < 0.01$) [10].

A multicenter study evaluated the clinical and radiological outcomes of 120 patients with multidrug-resistant spinal tuberculosis. The results showed that 82% of patients achieved clinical improvement, and 75% showed radiological healing after 24 months of treatment. The study found that early surgical intervention combined with second-line ATT significantly improved outcomes ($p < 0.01$). Patients who underwent surgery had a higher rate of neurological improvement (90% vs. 70%, $p < 0.05$) and lower complication rates compared to those who received medical treatment alone [11].

Conclusion

The comprehensive analysis indicates that the optimal duration of ATT for spinal tuberculosis varies among patients, with significant healing observed within 15-18 months. Both clinical and neurological improvements were evident, supported by substantial radiological healing and normalization of laboratory parameters. Surgical intervention proved effective for patients with specific indications, leading to improved outcomes. Regular follow-up is essential to monitor for potential relapse, ensuring long-term success in the management of spinal tuberculosis.

Limitations: The limitations of this study include a small sample population who were included in this study. Furthermore, the lack of comparison group also poses a limitation for this study's findings.

Recommendation: Individualized treatment durations and comprehensive care protocols should be implemented to ensure the best outcomes for patients with spinal TB. Further research is recommended to refine treatment strategies and reduce relapse rates.

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List of abbreviations:

ATT: Anti-Tubercular Therapy

TB: Tuberculosis
MRI: Magnetic Resonance Imaging
FNAC: Fine-Needle Aspiration Cytology
ESR: Erythrocyte Sedimentation Rate
HRZE: Isoniazid, Rifampicin, Pyrazinamide, and Ethambutol (Anti-tubercular drugs regimen)
CE-MRI: Contrast-Enhanced Magnetic Resonance Imaging
PET-CT: Positron Emission Tomography-Computed Tomography
HIV: Human Immunodeficiency Virus
SD: Standard Deviation
OPD: Outpatient Department
TB spine: Tuberculosis of the spine (Pott's spine)

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