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ABSTRACT

Objective: To identify factors indicating disease severity in patients with thoracolumbar tuberculosis requiring surgical intervention.

Design: Medical charts of patients who underwent surgery for thoracic and lumbar spinal tuberculosis from 1990-2005 were reviewed. Patients with different levels of disease were compared in terms of neurological deficits, duration of symptoms, previous antituberculous therapy, nutritional status and associated co-morbidities.

Results: Ninety-three patients aged 7-77 years (mean age 40 years) were included. Thoracic spine was involved in 80% of operated patients, and lumbar spine in 20%. Severe neurological impairment (Frankel A to C) was present in 68% of patients with thoracic disease, as compared to 5% with lumbar disease ($p < 0.05$). Postoperatively, complete neurological recovery occurred in 65% with thoracic versus 100% with lumbar disease ($p < 0.05$). Based on the disease location and pertinent elements in clinical history, physical signs, radiographic and biochemical features, a scoring system was developed.

Conclusion: In endemic areas with limited resources, strategies for cost-effective care are needed. By objectively outlining the treatment approach, the judicious use of surgery offers hope for enormous cost savings in countries endemic for tuberculosis, averting complications from disease progression.

Keywords: Thoracolumbar tuberculosis, spondylodiscitis, scoring system, disease severity, surgery

Running title: *Thoracolumbar tuberculous spondylodiscitis*

Introduction

Tuberculosis (TB) has been predicted to be the largest single infectious cause of death between 1990 and 2020¹. In 2004 there were nine million new TB cases globally and

approximately two million deaths attributable to TB. Pakistan belongs to the Asian region endemic for TB²⁰ and has an annual incidence of 181 per 100,000, prevalence of 329 cases per 100,000 population, and ranks seventh among the 22 high-burden TB countries worldwide². Although the primary focus of

disease is pulmonary, extra-pulmonary disease is quite frequent, with the spine being the commonest site for skeletal TB involvement. Thus, nearly one-third of all compressive lesions of the spine in developing countries are caused by TB^{1, 3-6}. Spinal TB generally starts in the vertebral bodies and the intervertebral discs and is thus called "spondylodiscitis". It is not only important due to the high prevalence but also because up to 30% of cases develop serious neurological sequelae from compression of the spinal cord, such as paresis and paraplegia. The latter, on a national basis, lead to major social and economic implications, particularly for overcrowded poor endemic countries where health and other social services are inadequately funded and delivered. Moreover, there is a lack of objective guidelines upon which cost-effective preventive and therapeutic treatment decisions on individual patients could be based, in such countries.

There is reason to believe that tuberculosis of the thoracic spine may differ from disease of the lumbar spine in the natural history due to anatomical and biomechanical differences. It has been observed that thoracic spine TB often entails paraparesis or paraplegia, which is less commonly seen in lumbar spine TB. We hypothesize that the need for surgical intervention for spinal stabilization and neurological decompression arises more often in thoracic spine TB as compared to lumbar spine TB. Therefore, a retrospective study was undertaken to identify factors indicating disease severity in patients with thoracolumbar tuberculosis requiring surgical intervention. Based on this data we developed a novel scoring system to guide whether the treatment of thoracolumbar tuberculosis should initially be medical or surgical.

Methods

Medical records of patients who underwent surgery for thoracic and lumbar spinal tuberculosis by Orthopaedic and Neurosurgery Sections from January 1990 to June 2005 were reviewed. Patients with cervicothoracic and lumbosacral junction tuberculosis were excluded. Also excluded were patients with healed spinal tuberculosis who were operated upon for spinal instability. Demographic factors, history and physical examination findings and results of laboratory and radiological investigations were recorded. Neurological status was classified according to Frankel grades⁷. Three varieties of TB of the spine were distinguished: i) TB of the spine without neurological impairment (Frankel grade E) ii) TB of the spine with useful motor function (Frankel grade D) and iii) TB of the spine with severe neurological deficit (Frankel grades A, B and C). Patients were divided into three groups – thoracic (T1-T10), thoracolumbar (T11-L2) and lumbar (L3-L5) tuberculous spondylodiscitis. These groups were compared in terms of proportions of patients undergoing surgery, the neurological deficits involved, duration of symptoms, previous antituberculous therapy (ATT), nutritional status (absolute lymphocyte count), associated co-morbid particularly diabetes mellitus, hepatitis B and C, HIV, blood markers (complete blood count, C-reactive protein CRP, ESR) and radiological findings. The diagnosis was established on the basis of at least one of the following criteria: histological evidence of caseating granuloma, microscopic demonstration of acid-fast bacilli in the lesion, growth of mycobacterium on culture of tissue specimen, therapeutic response to drug therapy in patients with clinical, or radiological and operative evidence of spinal TB.

Several methods were used for assessment of the chronologic changes of deformity of the spine on lateral radiographs. The first method was the deformity angle that is formed by the upper and lower borders of the diseased

vertebrae, which assesses the deformity irrespective of the influence of adjacent normal discs and vertebrae⁸. The second method was the kyphosis angle, which was measured by a technique similar to that described earlier^{9,10}. Two lines are drawn, one through the superior surface of the first normal vertebra cephalad to the lesion and one through the inferior surface of the first normal vertebra caudad to the lesion¹¹. As sagittal plane deformities appear to be most closely correlated to prognosis, we used the Sagittal Index (SI) to help assess the segmental kyphotic deformity at the level of the tuberculous infection¹¹. In addition to spine radiographs, spine Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) images were also reviewed. To evaluate the self-reported functional outcome of the surgery, results were categorized into three grades according to the following criteria: a) Excellent, no back pain and no limitation of activities; b) good, back pain improved with little medication and minimal restriction of activities; and c) poor, no improvement or worse with severe restriction of activities. A satisfactory outcome included an excellent or good result.

Statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS 10.0 for Windows, Chicago, Illinois). Based on this data we developed a scoring system to objectively guide the initial treatment of patients with thoracolumbar tuberculosis.

Results

A total of 93 patients were included in the study. Of these, 55 (60%) were female and 38 (40%) male with an age range from 7 to 77 years (mean age 40 years). Mean follow-up was 22 months. In patients who required surgical intervention, there was a higher proportion with thoracic tuberculous

spondylodiscitis (20%) as opposed to 80% with lumbar involvement ($p < 0.05$). 45 of 74 (61%) patients with thoracic and 9 of 19 (47%) patients with lumbar tuberculosis had received pre-operative drug therapy, for a mean of 9 and 7 weeks respectively. Preoperative Frankel grades differed significantly for patients with thoracic and lumbar tuberculosis. Thus, sixty-eight percent of patients with thoracic tuberculosis had severe neurological impairment (Frankel A to C), as compared to five percent with lumbar involvement ($p < 0.05$). Long term follow-up was available for 63 patients (Figure 1). Postoperatively, complete neurological recovery occurred in 65% of patients with thoracic versus 100% with lumbar tuberculosis ($p < 0.05$). For the remaining variables, including radiological findings, patients with thoracic and lumbar disease did not differ significantly (Table 1).

Although there are a number of scoring systems addressing the diagnostic, neurologic deficit levels and quality of life aspects in patients with pulmonary and central nervous system tuberculosis, to date to our knowledge there is no scoring system to guide the treatment of spinal tuberculosis. Therefore we would like to propose our own scoring system to objectively outline the treatment approach (Table 2). This scoring system is based on the disease location and neurological deficits, and additionally integrates factors which have been reported in literature to influence the final outcome. The scoring system is divided into two broad categories; the first includes parameters from history and the second includes factors from examination and investigations. The history category includes duration of back pain, ambulation status, urinary and bowel continence, prior use and duration of medical treatment for TB, presence or absence of systemic immunosuppressive disease and the use of immunosuppressive drugs. The examination category includes neurological function

(Frankel grade), radiographic findings including sagittal index on X-ray and presence/absence of canal compression and focal myelopathy on MRI and immunological status as assessed using absolute lymphocyte count and serum albumin level. The final score is calculated using the following formula: $A+(B \times L)$, 'L' being the location coefficient; for thoracic disease it is 2, thoracolumbar junction 1.5 and lumbar disease 1. If the final score is ≤ 5 , antituberculous drug therapy and observation is recommended. If the score is 6-7, antituberculous drug therapy and close observation with probable surgery is recommended, while if it is ≥ 8 , the management of choice is antituberculous drug therapy with surgery.

Discussion

Our data shows substantial differences between thoracic and lumbar spondylodiscitis in terms of clinical presentation and outcome. It is likely that these are due to anatomic and biomechanical differences between the two regions. The underlying disease process initially entails destruction of two adjacent vertebral bodies and the intervening intervertebral disc, with or without a paravertebral abscess¹² (figure 2). With encroachment of the neural canal due to retropulsed sequestered bone, granulation tissue or intra-canal abscess, neurological deficits may evolve. Moreover, due to vertebral collapse, a kyphotic deformity develops, resulting in an internal gibbus which may cause anterior compression on the neural elements. However, the end result of these events substantially varies with the location of the disease, i.e. thoracic or lumbar spine, which may be explained by differences in sagittal alignment, canal dimensions and vascularity.

Sagittal alignment

In the thoracic spine there is a normal kyphosis ranging from 30° to 50° (mean 37°) with the weight bearing axis anterior to the thoracic spine and thoracolumbar junction. Thus, when the anterior and middle columns in vertebrae and discs are destroyed by TB, physiological loading results in a progressive kyphus deformity producing the characteristic external gibbus deformity¹³ and paraplegia of late onset due to the internal gibbus^{14, 15}. On the other hand, the sagittal alignment of the lumbar spine is in lordosis of about 50° with the weight bearing axis posterior to the bodies of the lumbar spine. This retards the tendency of anteriorly located disease to cause a kyphosis, minimizing spinal deformity and consequent neurologic compression¹¹ from tuberculous disease.

Dimensions of the spinal canal and its contents

The thoracic spine has a small canal-to-cord ratio as compared to a wider canal-to-cauda-equina ratio in the lumbar spine which is lordotic. In case of the lumbar spine, which has a capacious spinal canal, tuberculous involvement producing upto 60% to 80% canal compromise may not result in neurologic injury⁹. However, in the thoracic spinal canal, even minor encroachment may produce significant spinal cord compression necessitating surgical decompression¹⁶. Moreover, paraplegia can be produced at lesser compromise of the spinal canal when vascular catastrophe or mechanical instability are also present¹⁷.

Vascularity

In the lumbar spine, vascularity of the neural elements is less precarious than in the "watershed" region of the thoracic spine. The neural elements of the lumbar spine below the L1-L2 disc are usually floating spinal nerve rootlets (cauda equina). These roots are less likely to be injured in that they have more

room in the canal and are not tethered to the same degree as the spinal cord. Additionally, the motor nerve root is composed of lower motor neuron axons, which are more resilient to ischemia than the spinal cord¹⁸. Moreover, there is extensive collateral circulation distally from the nerve roots and proximally from the spinal cord, making this region less prone to vascular compromise and more likely to recover with a good prognosis.

Proposed scoring system

We describe a new scoring system that is based on patient characteristics and investigations that can be used to decide whether an individual patient should receive drug therapy alone or drug therapy and close observation with or without surgery. There is greater propensity of early paraplegia in thoracic spine TB because of the combined effect of physiologic kyphosis, decreased canal-to-cord ratio and poor blood supply to the cord which makes it more vulnerable as compared to the lumbar spine, which is protected by physiological lordosis, wide canal-to-cauda equina ratio and a more robust blood supply to the relatively resistant cauda equina¹⁹. This explains our findings that among patients requiring surgical intervention, there were a higher proportion of patients with thoracic involvement as opposed to those with lumbar involvement. The latter, because of the relatively benign involvement as delineated above, have a higher probability of being managed conservatively with drug therapy. This is also reflected in the postoperative outcomes of surgical treatment of spinal tuberculosis where patients with lumbar involvement achieved better functional improvement than those with thoracic tuberculosis. Hence the vertebral level of tuberculous involvement and its attending neurological deficits appear to be the major factors influencing the mode of treatment and prognosis.

Our new scoring system for the management of thoracolumbar tuberculous spondylodiscitis is pertinent for countries such as Pakistan, a global priority country for the control of TB. It objectively outlines the treatment approach and is expected to reduce costs of such treatment by preventing unnecessary surgery. In the absence of such objective treatment guidelines, it is a common observation that for surgeons the threshold for surgical intervention is low compared to physicians who may rely on drug therapy alone until serious neurological deficit and deformity develops.

The limitations of this study include its retrospective methodology (chart review), the inclusion of multiple implants and surgeons; and the long time period studied, during which techniques, retractors, implants and indications for surgery have been evolving. Importantly, the higher proportion of patients with thoracic disease undergoing surgery may well be due to a higher prevalence of this disease in the thoracic region; this could not be controlled in this retrospective study. Therefore, to validate this scoring system, a prospective study is planned whereby representative proportions of patients with disease of the thoracic and lumbar regions would be sampled and their outcome in terms of success of anti-tuberculous therapy versus conversion to surgery would be ascertained, providing the predictive value of the scoring system.

Conclusion

In conclusion, the new scoring system that we have developed, once validated, is expected to assist in clinical decision making regarding the need to embark upon surgical intervention in patients with tuberculous thoracolumbar spondylodiscitis. This judicious use of surgery

offers hope for enormous cost savings in countries endemic for tuberculosis.

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Table 1: Characteristics of the study population

| | Disease location | | | P-value |
|-----------------------------------------------|------------------|-------------------|-----------------|---------|
| | Thoracic | Thoracolumbar | Lumbar | |
| Number of patients | 43 | 31 | 19 | |
| Age (mean \pm SD) | 40 \pm 20 | 34 \pm 17 | 45 \pm 16 | NS * |
| Male : Female ratio | 1:2 | 1:1 | 1:1.7 | NS # |
| Median duration of symptoms | 4 months | 12 months | 10 months | NS * |
| Previous anti-tuberculous therapy | 52% | 71% | 47% | NS # |
| Neurological deficit: Frankel A-C | 67% | 65% | 5% | <0.01 # |
| Frankel D-E | 33% | 35% | 95% | |
| Absolute lymphocyte count (/mm ³) | 1,900 \pm 700 | 2,100 \pm 1,200 | 1,500 \pm 330 | NS * |

NS - Differences not significant

* One-way ANOVA

Chi squared test

Table 2: Proposed Scoring System

| Section A: History | | Section B: Examination and Investigation | |
|---------------------------------------------------------------------------------|---|------------------------------------------|---|
| 1. Duration of back pain | | 7. Neurological function# | |
| ≤ 3 months | 0 | Frankel E | 0 |
| >3 months | 1 | Frankel D | 1 |
| 2. Ambulation | | Frankel A,B,C | |
| Independent | 0 | | |
| Assisted | 1 | 8. Radiographic findings | |
| Chair / bed bound | 2 | X-ray: Sagittal index ≤ 15° § | 0 |
| 3. Urinary and bowel sphincter control | | Sagittal index > 15° | |
| Continent | 0 | | |
| Incontinent | 2 | MRI: Canal compression Absent | 0 |
| 4. Duration of medical treatment for TB | | Present | |
| No prior treatment | 0 | | |
| ≤ 3 months | 1 | Focal myelopathy Absent | 0 |
| >3 months | 2 | Present | 1 |
| 5. Systemic immunosuppressive disease* | | 9. Immunological status | |
| Absent | 0 | Abs. lymphocyte count ≥1500 | 0 |
| Present | 1 | <1500 | 1 |
| 6. Immunosuppressive drugs* | | Serum Albumin ≥2.5 g/dl | |
| Not being used | 0 | <2.5 g/dl | 1 |
| Being used | 1 | | |
| <i>Cumulative score for section A</i> — | | <i>Cumulative score for section B</i> — | |
| Section C: Location coefficient (L) | | | |
| For thoracic disease (T1-T10) | | 2 | |
| For thoraco-lumbar junction (T11-L2) | | 1.5 | |
| For lumbar disease (L3-S1) | | 1 | |
| <i>Final score = A + (B × L) = _____</i> | | | |
| <i>Recommendation:</i> | | | |
| Score ≤ 5 : Antituberculous therapy | | | |
| Score 6-7 : Antituberculous therapy and close observation with probable surgery | | | |
| Score ≥ 8 : Antituberculous therapy and surgery ¥ | | | |

Explanation:

*e.g., diabetes mellitus, hepatitis, steroids, immunomodulators

Frankel classification of neurologic deficit:

- Frankel A Absent motor and sensory function
- Frankel B Sensation present, motor function absent
- Frankel C Sensation present, motor function active but not useful (grades 2/5 to 3/5)
- Frankel D Sensation present, motor function active and useful (grade 4/5)
- Frankel E Normal motor and sensory function

§ Sagittal index: Angle (°) between endplates of vertebra above and below the diseased vertebra/e

¥ Neurological recovery after surgery is doubtful if duration of paraplegia exceeds 6 months

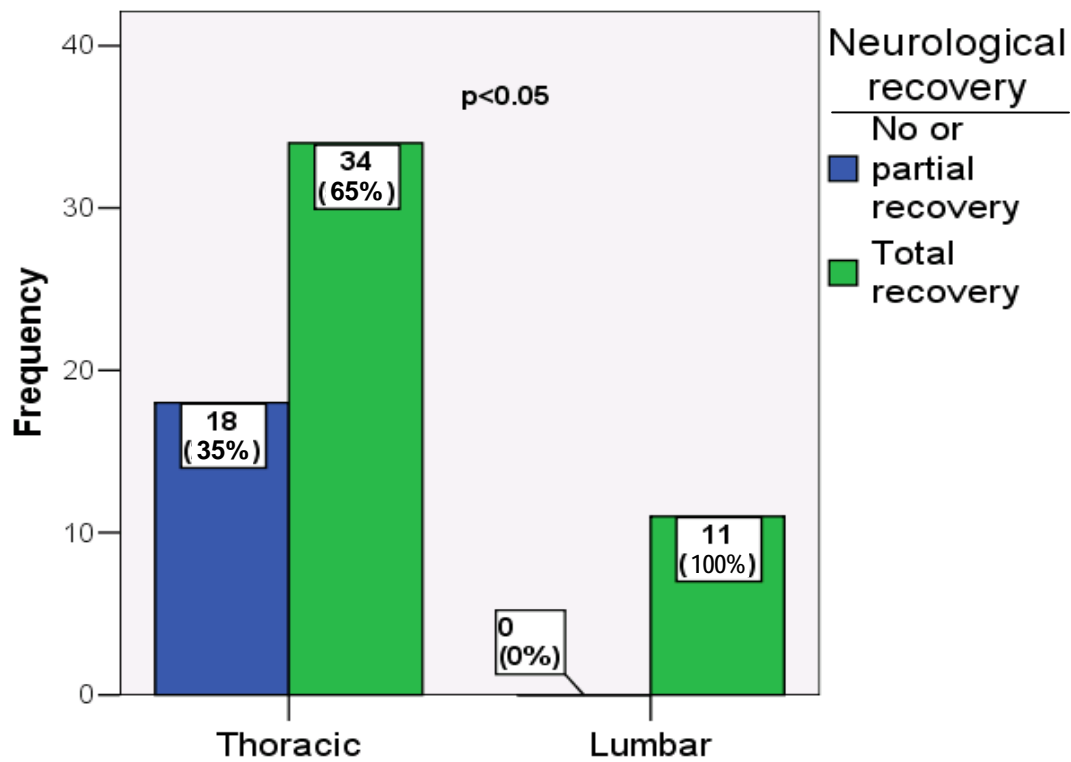


Figure 1: Postoperative recovery in patients (n=63) with thoracic versus lumbar tuberculous spondylodiscitis

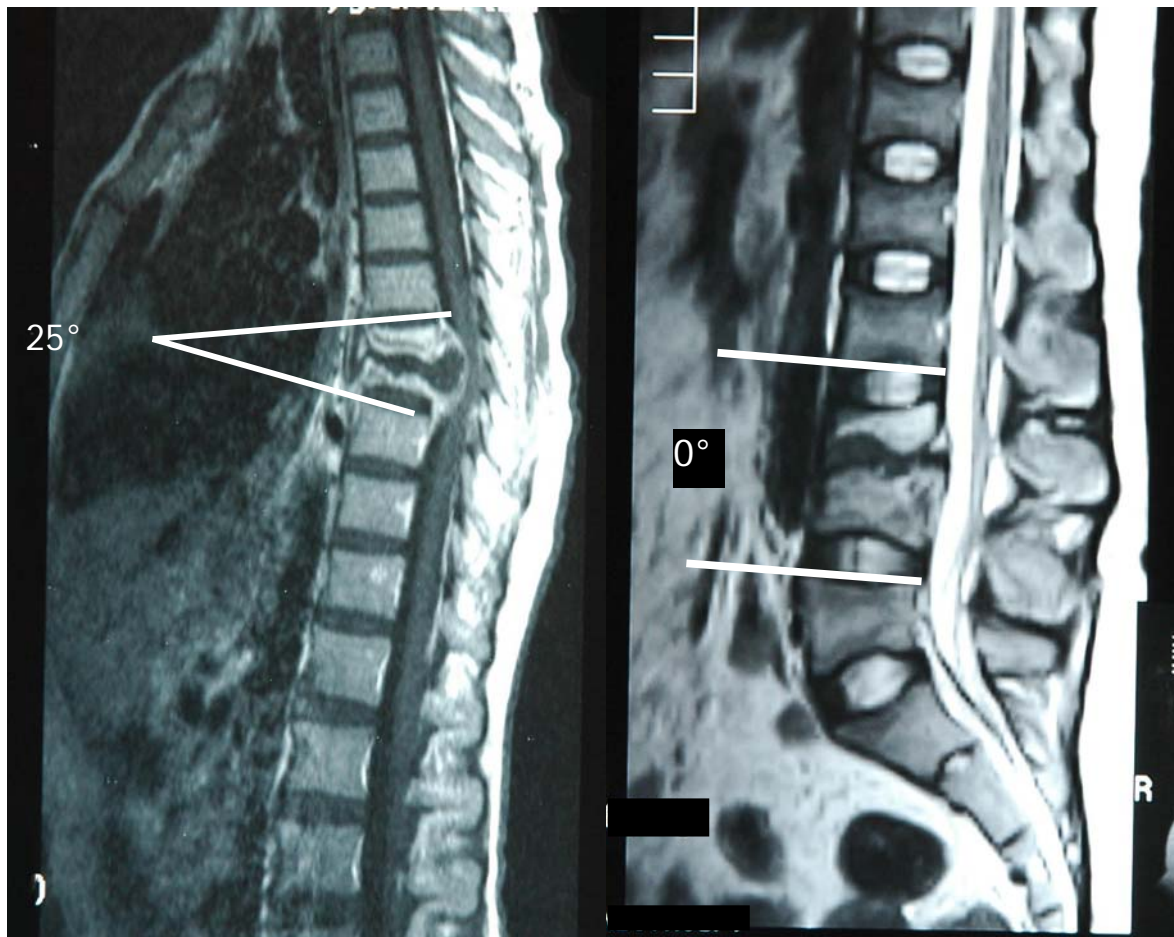


Figure 2: A,B- Sagittal MRI showing (A) tuberculous destruction of two thoracic vertebrae with 25° kyphosis leading to internal gibbus and cord compression. (B) Similar tuberculous destruction of two lumbar vertebral bodies resulting in reversal of the normal 30° lordosis to 0°, and yet relatively preserved cauda equina space