REVIEW

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Prevalence and prognosis from the disability related to spinal tuberculosis: a systematic review

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ABSTRACT

Objective: To review the disabilities caused by Spinal TB in relation to the prevalence and prognosis of the disabilities caused by the disease.

Method: We conducted systematic search of the literatures based on PRISMA (*Preferred Reporting Items for Systematic Reviews and Meta-Analyses)* and PICO criteria. Our inclusion criteria were: 1) Patients with spinal TB; 2) full original articles; 3) articles written in English; 4) the period of publication of articles from 2012 to 2022. Evaluation of each article was done by checklist *Strengthening the Reporting of Observational Studies in Epidemiology* (STROBE).

Results: From all articles in the publication year of 2012 to 2022, we reviewed five retrospective cohort studies, all studies coming from Asian countries. The five articles observed the prevalence of disabilities caused by spinal TB reflected through some important outcome variables pre-treatment, where they continued to compare with the post-treatment outcome variables. All of the studies reviewed had agreed that immediate or delayed treatment would give significant benefits to the patients of spinal TB, even better with combined treatments of conventional pre-operative anti-TB drugs and surgical intervention. It was found that poor prognosis associated with preoperative neurological status of the patients.

Conclusion: Conventional anti-TB drugs and surgical intervention can be of great help and benefit for patients with spinal TB, reducing their disabilities severity and improving their prognosis.

Keywords: Spinal tuberculosis, disability, prevalence, prognosis.
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INTRODUCTION

Tuberculosis (TB) is still a global health problem. Based on WHO report, TB affects around 10 million people in the world in 2019, with an incidence rate of 5.8 million men, 3.2 million women and 1 million children. Each year, TB can kill up to more than 1 million people.[1] Spinal involvement in patients with TB is very rare (less than 1%), but along with the increase in the number of people affected by TB disease, the incidence of spinal TB is also increasing.[2] The spine itself is still the most common place affected by skeletal TB, one of extrapulmonary TB. Although it can affect any parts of the spine, spinal TB is most commonly found in the thoracolumbar joints, and then in the lumbar spine and cervical spine. Spinal TB is more common in children and young adults.[3]

Disability is one of the complications that occurs in TB patients, including spinal TB.[4] But the prevalence and prognosis of spinal TB-related disability in the world is still not widely documented. According to the WHO international classification of functions, disability, and health (ICF), disability is defined as "a difficulty in functioning at the body, person, or societal levels, in one or more life domains, as experienced by an individual with a health condition in interaction with contextual factors".[5]

Patients with spine TB may or may not experience complications. Complications in spinal TB patients can cause disability. In complicated Spinal TB, deformity, instability, and neurological deficits may occur. The presence of anterior column involvement results in spinal kyphosis deformity.[3] A literature review by Jain et al suggested that any kyphotic deformity of 60° or more can cause paralysis and increase the risk of neurologic sequelae.[6] In children with spinal TB, their immaturity and flexibility of the spine leads to a more rapid and severe development of the deformity.[7] Even after the disease has been cured in the child, the development of the deformity can still occur due to the growth nature of the spine.[3]

Treatment for spine TB consists of conservative therapy (anti-TB medications) and operative therapy. There are various studies showed effectiveness of each type of therapy (anti-TB medications[8] and early surgery[9]) in terms of improving the prognosis of TB spine. In addition, combined therapy of preoperative anti-TB drugs and surgery have promising more satisfying outcomes than conservative drugs alone.[9-13] Despite the importance of collecting data on the prevalence and prognosis of TB spine-related treatment and disability, studies discussing this topic are still very rare. Therefore, this systematic review aims to document the prevalence

and prognosis of TB spine-related disabilities in the world. We hope that the data presented in this article can be used by health care providers and policy makers in an effort to reduce disability rates.

METHOD

Literature search was done systematically based on PRISMA (*Preferred Reporting Items for Systematic Reviews and Meta-Analyses)* to improve completeness and transparency of the review. We used PICO criteria, Patient (P): patients with spinal TB, Intervention (I): patients with spinal TB who received conventional and surgical treatment, Control (C): patients with spinal TB before treatment. Outcome (O): evaluation of prevalence and prognosis of the disability experienced by patients with spinal TB. The search limitation was limited to articles within publication time from 2012 to 2022, which focused on the topic of prevalence and prognosis from the disability related to spinal TB.

The inclusion criteria for the article search included: 1) Patients with spinal TB; 2) full original articles; 3) articles written in English; 4) the period of publication of articles from 2012 to 2022. The exclusion criteria were review articles and those that have no clear methods and intervention of the patients. Quality assessment by risk of bias of each article was evaluated by using the checklist from Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) (**Table 2**). The green circle explains that the criteria are met, the yellow circle represents that the criteria were not discussed in full and in detail thus half-met, and the red circle means that the point was not explained. The more one article has green circles, the better the quality. Poor quality is defined by many red circles in the STROBE checklist.

Literature Search and Selection

We used PubMed and Google Scholar as databases in this systematic review. The literature search strategy in this systematic review includes identifying keywords that are relevant to the topic and then identifying possible synonyms related to the keywords. Search was then carried out using the Boolean operator method to get specific and related topics. The keywords and Boolean operators used in this study are ("Spinal tuberculosis" OR "Spinal TB") AND ("disability") AND ("prevalence") AND ("prognosis"). Furthermore, restrictions based on inclusion criteria were done.

After searching with keywords and time range, we conducted the initial selection process by identifying the suitability of the title, abstract and keywords with the studied topic. Any articles that cannot be accessed and do not meet the inclusion criteria were immediately excluded. The articles that have fulfilled the inclusion criteria were then evaluated by using the PICO approach, in which unsuitable articles were immediately excluded. We conducted reviews of each article by scanning through the methods, results, discussions, conclusions and other essential components of the article (funding, author contribution, conflict of interest and ethical requirement). Subsequently, we proceeded to meticulous review of all sections of the article to serve as the basis in this systematic review.

Data Collection

All selected articles were then extracted manually for key points of the article. The data collected included the name of the main author, country of origin, year of publication, study design, the total number of participants involved in the study, mean age of the participants involved, types of intervention and outcome variables of each study. In each article, a critical review was also carried out to assess the quality of the article. Types of data used in this systematic study were quantitative data obtained by identifying the prevalence and prognosis of the disability related to spinal TB.

RESULTS

All articles selected in this systematic review were published in the last ten years of year 2012 until 2022. Of all the literatures searched, we found five articles that satisfied the eligibility criteria where all five articles were retrospective cohorts. All studies were from Asian countries, with four studies originated from China (upper middle income country) and one study from India (lower-middle income country). All studies involved at least 50 patients,[9-13] with only one study from China included more than 1000 patients.[12]

All five studies evaluated the prevalence of disabilities related to spinal TB and showed prognosis after treatments. Most spinal TB involved two or more vertebrae, which mostly affected the thoracic and lumbar segment,[12] followed by other segments such as cervical and sacral segment.[10] The spinal TB often leads to poor outcome if not treated such as irreversible neurological injury or even mortality. Instruments used in the five studies to evaluate neurological function were the Frankel scoring system, ASIA scale score and Lower Extremity Motor Score (LEMS). Frankel scoring system consists of grade A-D where each indicates loss of any motor or sensory function, with grade A being the most severe (complete motor and sensory loss) and grade E being the least with no neurological symptoms were found. The rest are grade B (complete motor loss, but incomplete sensory loss), grade C (incomplete motor loss without practical use) and grade D (incomplete motor loss, but still able to ambulate with or without walking aids). The next most common used instrument is ASIA scale score, which is similar to Frankel that involves grade A-E. While LEMS grades motor function on a scale of 0 to 5 for each one of five lower extremity muscle groups. More outcome variables were identified such as lumbosacral angle, Visual Analogue Score (VAS), Erythrocyte Sedimentation Rate (ESR) and C-reactive protein (CRP).[9-11]

There are two types of treatments for spine TB; conservative and surgical therapy. Conservative treatment uses standardized anti-TB drugs, which consists of isoniazid, rifampicin, ethambutol and pyrazinamide, with streptomycin could be considered as an addition to the regimen of intensive phase.[13] In most cases of the five studies reviewed, patients had taken combined therapy of preoperative anti-TB drugs followed by surgery, as this seemed to be promising more satisfying outcome than conservative drugs alone.[9-13]

The disabilities experienced by the patients as reported before treatment were compared to their post treatment outcomes, which all five studies agreed to show significant improvement. All outcome variables seemed to show

improvement, especially neurological function even better with preoperative anti-TB drugs prior to surgery.[9-13] A 10-years cohort has shown that spinal TB treatment could cure more than 80% of the patients, indicating the urgency of surgical action for this matter.[12] Even it was proved that delayed decompression and fixation of spinal TB did not change the effectiveness of the therapy, where neurological improvement and overall outcome could still be achieved. It was the preoperative neurological status that determined the postoperative neurological outcome.[9]

Risk of Bias

Quality evaluations of the five articles were based on the STROBE checklist. It has been shown that over all, the five articles have fulfilled most of the criteria in the checklist, thus considered as good quality papers.

DISCUSSION

Deformities

TB spine and spinal deformity are two things that go hand in hand. The type and shape of the spinal deformity depends on the area of the vertebra that is affected. The development of deformity in TB spine occurs in 2 separate phases, namely the first phase (the active phase) and the second phase (the phase after the lesion has healed). Progression of neurologic deficits and paraplegia that occurs after the second phase has a worse prognosis than in the first phase.[14]

Kyphotic deformity as the most common deformity is a deformity that occurs due to lesions of the thoracic vertebrae. This disorder is often found, especially in developing countries. The number of vertebrae involved can determine the severity of kyphosis. An increase in kyphotic deformity of 10° or more can be seen in up to 20% of cases, even after treatment.[15]

Neurological Deficit

Based on the studies summarized in this article, the incidence of neurological dysfunction in spinal TB was reported in half of the study subjects Cao, Rathod. Neurological disorders can occur due to compression of nearby nerve structures.

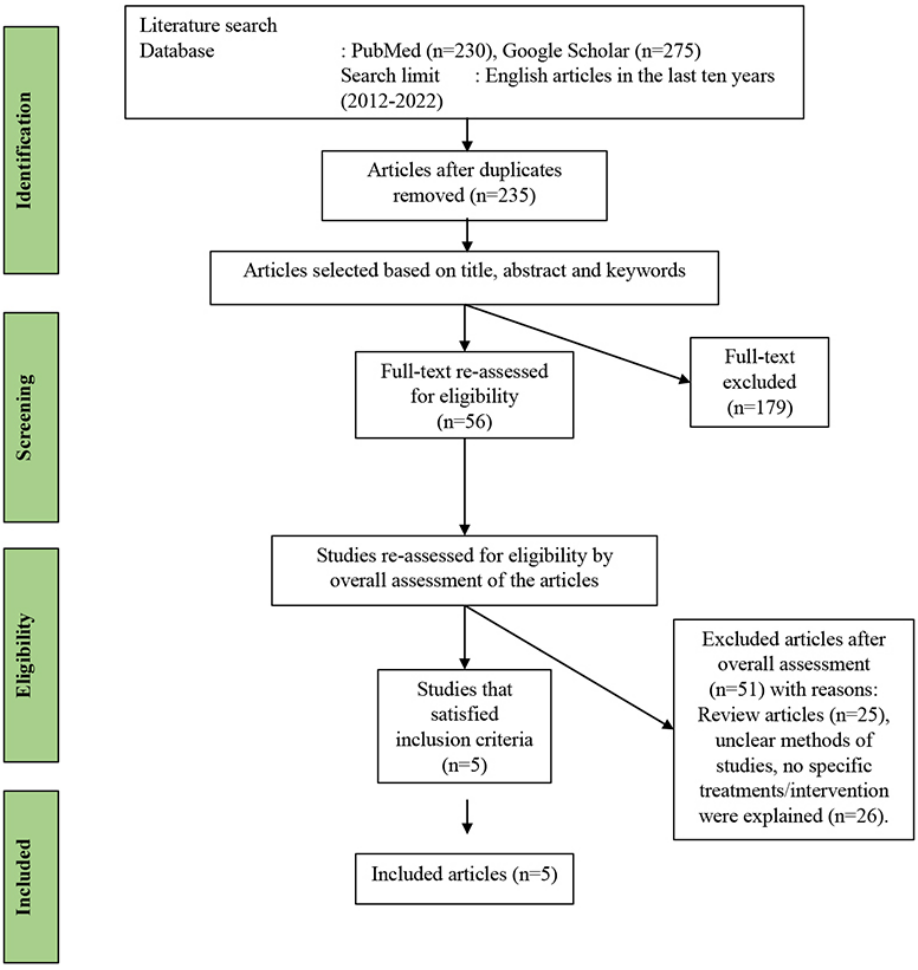

Figure 1. Selection flow chart based on PRISMA

Table 2. Literature assessment with STROBE Checklist

Author	STROBE Checklist																				
	Title and abstract	Background	Objectives	Study design	Setting	Participants (Methods)	Variables	Data sources/ measurement	Bias	Study size	Quantitative variables	Statistical methods	Participants(Result)	Descriptive data	Outcome data	Main results	Other analyses	Key results	Limitations	Interpretation	Generalisability	Funding
Jiang et al	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Cao et al	◐	●	●	◐	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Guang Jia et al	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Rathod et al	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Liu et al	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●

● : Fulfilled criteria
◐ : Half-met criteria
● : Unfulfilled criteria

Several things that can underlie compression of this nerve structure include progressive bone destruction leading to spinal collapse and kyphosis, cold abscess formation (due to extension of infection to adjacent ligaments and soft tissues), narrowing of the spinal canal by abscess, granulation tissue or dural invasion.

directly.[14] A literature review by Jain et al suggested that any kyphotic deformity of 60° or more can cause paralysis and increase the risk of neurologic sequelae.[6]

Two studies in this systematic review reported that most spinal TB involves 2 or more vertebrae, with the thoracic and lumbar segments being the main areas affected[12] followed by the cervical and sacral segments.[10] If not treated promptly, neurologic involvement may develop into paraplegia or tetraplegia based on the area of spinal cord involvement. In spinal TB involving the cervical segment, tetraplegia may occur which begins with symptoms of cord and root compression such as pain, weakness, and numbness in all four. Meanwhile, involvement of the thoracic or lumbar areas will show symptom progression in the lower extremities only. This can lead to paraplegia. The patients with cauda equina compression in lumbar and sacral spinal TB will experience symptoms such as weakness, numbness, and pain. In this condition there is also a decrease in reflexes between the affected muscle groups.[8]

Prognosis after Treatment

Treatment for spine TB consists of conservative therapy (anti-TB medications) and surgery. Patients who were subjects in all five studies reviewed in this review used combination drug and surgical therapy because they were thought to have a more promising outcome. The use of drugs in TB spine is supported by data from a literature review that summarizes various studies. Those studies show that the majority (82-95%) of spine TB patients respond very well to medical treatment. Treatment response is seen in the form of pain relief, correction of spinal deformities, and reduction of neurological deficits.[8]

Guang Jia et al through their study of 234 patients who received preoperative anti-TB therapy stated that active and effective preoperative anti-TB treatment is essential. For active-phase spinal TB patients who do not require urgent surgery with progressive neurologic deficits, adequate anti-TB treatment should still be given before surgery, to improve the safety and prognosis of surgery.[9]

There are also several outcome variables measured in related studies, including lumbosacral angle, Visual Analogue Score (VAS), Erythrocyte Sedimentation Rate (ESR) and C-reactive protein (CRP). In this review, it was shown that the five studies showed statistically significant improvement of these outcome variables after therapy.[9-13]

It is known that spinal TB patients with ESR >40 mm/hour are not recommended for surgical treatment, while ESR >80 mm/hour are prohibited for surgery. However, it may delay the treatment of neurological deficits in some patients, and even lead to more serious consequences, including paraplegia. Various researches showed statistically significant improvement before and after. treatment in regards to ESR.[9-11] Regarding these results, it was reported that early surgery is the best option for postoperative neurologic recovery. And to be able to pass the safe surgery, prevent the recurrence and spread of TB postoperatively, all patients must receive standard anti-TB treatment at least 4 weeks before surgery. Standard treatment has been shown to improve anemia and hypoproteinemia (Hb>100 g/dl; serum albumin >30 g/l), and control ESR <40 mm/hour.[9]

CONCLUSION

Spinal TB disabilities included spinal deformities, neurological deficits, persistent neuropathy pain, systemic toxicity symptoms and in some cases, abscess. Conventional and surgical interventions are essential for better prognosis of the patient as in reducing morbidity and mortality.

AUTHOR CONTRIBUTION

All authors contributed in the writing of this article.

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CONFLICT OF INTEREST

No conflict interest was involved, all authors understood and agreed to the publication of the final manuscript.

REFERENCES

1. WHO. Global tuberculosis report 2020. Geneva; 2020
2. Garg RK, Somvanshi DS. Spinal tuberculosis: a review. J Spinal Cord Med. 2011;34(5):440-54.
3. Rajasekaran S, Soundararajan DCR, Shetty AP, Kanna RM. Spinal Tuberculosis: Current Concepts. Global Spine J. 2018 Dec;8(4 Suppl):96S-108S.
4. Alene KA, Wangdi K, Colquhoun S, Chani K, Islam T, Rahevar K, Morishita F, Byrne A, Clark J, Viney K. Tuberculosis related disability: a systematic review and meta-analysis. BMC Med. 2021 Sep 9;19(1):203
5. Leonardi M, Bickenbach J, Ustun TB, Kostanjsek N, Chatterji S. The definition of disability: what is in a name? Lancet. 2006;368:1219–21.
6. Jain AK. Treatment of tuberculosis of the spine with neurologic complications. *Clin Orthop Relat Res*. 2002;(398):75–84.
7. Shetty A, Kanna RM, Rajasekaran S. TB spine—Current aspects on clinical presentation, diagnosis, and management options. *Semin Spine Surg*. 2016;28:150
8. Garg RK, Somvanshi DS. Spinal tuberculosis: a review. J Spinal Cord Med. 2011;34(5):440-54.
9. Jia C, Gao J, Liu F, et al. Efficacy, safety and prognosis of treating neurological deficits caused by spinal tuberculosis within 4 weeks' standard anti-tuberculosis treatment: A single medical center's experience. *Exp Ther Med*. 2019:519-526. doi:10.3892/etm.2019.8253.
10. Cao G, Rao J, Cai Y, et al. Analysis of Treatment and Prognosis of 863 Patients with Spinal Tuberculosis in Guizhou Province. *Biomed Res Int*. 2018;2018. doi:10.1155/2018/3265735.
11. Jiang T, Zhao J, He M, Wang K, Fowdur M, Wu Y. Outcomes and treatment of lumbosacral spinal tuberculosis: A retrospective study of 53 patients. *PLoS One*. 2015;10(6):1-15. doi:10.1371/journal.pone.0130185.
12. Liu Z, Wang J, Chen GZ, et al. Clinical Characteristics of 1378 Inpatients with Spinal Tuberculosis in General Hospitals in South-Central China. *Biomed Res Int*. 2019;2019. doi:10.1155/2019/9765253.
13. Rathod TN, Sathe AH, Marathe NA. It's Never Too Late: Neurological Outcome of Delayed Decompression in Tuberculosis of Spine. *Glob Spine J*. 2021;11(5):716-721. doi:10.1177/2192568220922209.
14. Rasouli MR, Mirkoohi M, Vaccaro AR, Yarandi KK, Rahimi-Movaghar V. Spinal tuberculosis: diagnosis and management. Asian Spine J. 2012 Dec;6(4):294-308. doi: 10.4184/asj.2012.6.4.294. Epub 2012 Dec 14.
15. Jain AK, Kumar J. Tuberculosis of spine: neurological deficit. Eur Spine J. 2013 Jun;22 Suppl 4(Suppl 4):624-33.

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Table 1. Descriptive summary of the reviewed articles

First author (publication year)	Country	Study design	Sample size (N)	Mean age (years)	Types of treatment	Outcome variables	Results summary
Jiang et al (2015)[11]	China	Retrospective cohort	53	37.5	- Conservative treatment: anti-TB drugs, - Surgical treatment: anterior debridement, interbody fusion with and without instrumentation, one-stage anterior debridement combined with posterior instrumentation.	Neurologic status (Frankel scoring system), lumbosacral angle, ESR, CRP	Of 53 patients involved, baseline data showed patients with conservative treatment to have wider mean of lumbosacral angles ($23.00^{o} \pm 2.90^{o}$) than surgically treated patients ($22.36^{o} \pm 3.92^{o}$). Based on Frankel grading of neurologic status, 19 patients were in Frankel grade B, 21 patients in Frankel grade C, 9 patients in Frankel grade D and only 4 patients in Frankel grade E. Baseline ESR and CRP were also quite high in the conservatively managed patients with average of 27.91 ± 17.54 mm/h and 12.09 ± 4.06 mg/dL consecutively. As in the surgically treated patients, the average preoperative ESR and CRP were 32.45 ± 17.78 mm/h and 18.61 ± 9.70 mg/dL consecutively. At the final follow-up showed that both types of treatment resulted in significant improvement ($p<0.05$) of the mean lumbosacral angles with $24.10^{o} \pm 2.96°$ in patients with conservative treatment and 28.13° ± 1.93° in surgically treated patients. No worsen neurological deficit were found after the treatments. There were also significant decrease of ESR and CRP after the treatments ($p<0.05$). All patients were reported to have achieved bone fusion.
Cao et al (2018)[10]	China	Retrospective cohort	783	- Conservative treatment: 47.3 - Surgical treatment: 44.6	- Conservative treatment: anti-TB drugs, - Surgical treatment: Preoperative and postoperative anti-TB drugs + lesion removal, bone graft fusion and internal fixation	Cobb angle correction, neurological status (Frankel scoring system), interbody fusion with bone graft, tuberculosis outcome, ESR, CRP, VAS.	Among 783 patients, 393 were with neurological dysfunction, 69 patients were found to have degenerative neurological dysfunction. Based on Frankel classification, 17 patients were classified as Frankel grade A, 52 as Frankel grade B, 138 as Frankel grade C, 186 as Frankel grade D and 390 as Frankel grade E. Baseline Cobb angle of the vertebrae was 17.68 ± 4.38^{0}, average baseline VAS was 6.90 ± 2.00, ESR 44.65 ± 16.30 mm/h and CRP 53.34 ± 38.21 mg/L. There were 252 patients complicated with paravertebral abscess, 41 patients with intraspinal abscess and 261 with both paravertebral and intraspinal abscess, 44 patients were with psoas abscess. Of 145 patients with conservative treatment only, 107 were clinically cured, 29 achieved relief of clinical symptoms, with 5 had no response to the treatment. There were 31 patients with neurological symptoms who had improved Frankel grade at the final follow-up from grade D to grade E. It was found that 7 patients had multidrug-resistant M. tuberculosis, which resulted in poor efficacy. Of 638 patients underwent surgery, 501 were clinically cured and 114 achieved relief of clinical symptoms, with 15 had no response to the treatment. VAS score was reported to be significantly improved ($p<0.05$), the Cobb angle significantly decreased to 3.99 ± 2.34^{0} postoperatively, as well as improved neurological symptoms ($p<0.05$).

Guang Jia et al (2019)[9]	China	Retrospective cohort	238	48.5	Preoperative anti-TB drugs (<4 weeks vs ≥4 weeks) + surgical treatment	Neurological injury (ASIA scale score), Preoperative Cobb angle, VAS, ESR, CRP	Of the 238 patients, preoperative Cobb angles were 33.6±5^0. There were significantly higher preoperative ESR and CRP in the <4 weeks of anti-TB treatment prior to surgery group. No difference of VAS and ASIA scale score were found between the two groups. ESR was found to be consistently higher in <4 weeks of anti-TB group at 1 week to 1 month after surgery. ASIA scale scores in both groups increased significantly 1 to 6 months after surgery, with higher score in the <4 weeks of anti-TB group.
Rathod et al (2021)[13]	India	Retrospective cohort	50	34.7	Surgical treatment (posterior decompression and instrumented fusion + anti-TB drugs.	Neurological function (Lower Extremity Motor Score/ LEMS)	All 50 patients of thoracolumbar TB of spine were divided into two groups based on their LEMS score at the end of 1-year follow-up (satisfactory of LEMS>10 vs no satisfactory of LEMS≤10). All patients' LEMS scores improved significantly ($p<0.001$) at the end of 1 year (40.80±10.46) compared to their LEMS scores on admission (27.72±12.88). A significant difference ($p<0.001$) of preoperative mean LEMS score was found between the two groups (satisfactory outcome group of 34.62 and no satisfactory outcome group of 20.25). However, no difference was found for median time interval between the appearance of neurological deficit and decompression surgery in both groups ($p=0.110$).
Liu et al (2019)[12]	China	Retrospective cohort	1378	43.7	- Anti-TB drugs, - Surgery treatment	Neurological injury (ASIA scale score), onset of back and radicular pain, systemic toxicity symptoms, abscess	In 10 years of cohort, there were pretty common incidence of back pain (92.5%), radicular pain (40.1%) and symptoms of systemic toxicity (32.1%). Almost half of the sample population had neurological impairment (49.9%) in which 1.5% of them were in ASIA grade A and 2.8% were in grade B. Abscesses were found in 65.5% of patients. About 1000 patients (72.6%) were treated with surgery and 378 (27.4%) were only with anti-TB drugs. Cure was achieved in 88.2% of patients, while 3.5% had relapses. There were 366 patients (26.6%) who were diagnosed with concomitant pulmonary TB.