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ORIGINAL ARTICLE

Diagnostic accuracy of whole spine magnetic resonance imaging in spinal tuberculosis validated through tissue studies

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Abstract

Introduction Conventional diagnosis of spinal tuberculosis (TB) is based on a combination of clinical features, laboratory tests and imaging studies, since none of these individual diagnostic features are confirmatory. Despite the high sensitivity of MRI findings in evaluating spinal infections, its efficacy in diagnosing spinal TB is less emphasized and remains unvalidated through tissue studies.

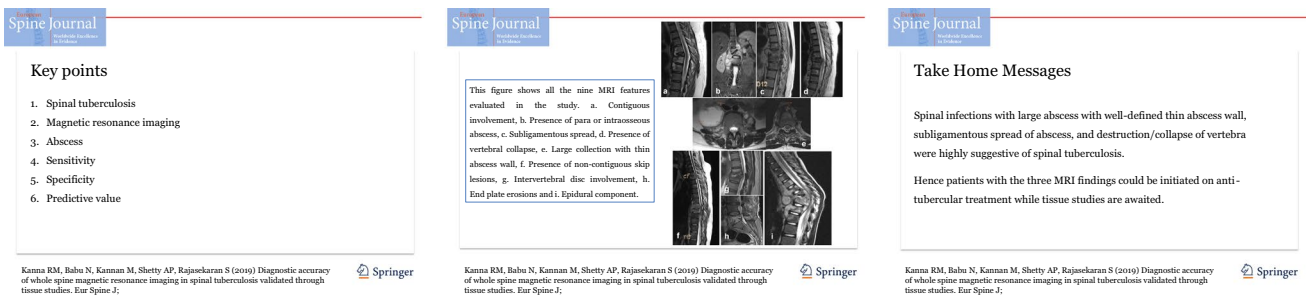
Methodology We reviewed consecutive patients evaluated for spondylodiscitis with documented clinical findings, MRI spine, and tissue analysis for histopathology, TB culture and genetic TB PCR. MRI features documented include location, contiguous/non-contiguous skip lesions, para/intraosseous abscess, subligamentous spread, vertebral collapse, abscess size/wall, disc involvement, end plate erosion and epidural abscess. Based on the results, patients were divided into two groups—CONFIRMED TB with positive culture/histopathology and NON-TB. The efficacy of MRI findings in accurately diagnosing spinal TB was compared between the two groups.

Results Among 150 patients, 79 patients were TB positive, and 71 were TB negative. Three MRI parameters showed significant differences ($p < 0.001$), namely subligamentous spread (67/79, 84.8%), vertebral collapse > 50% (55/79, 69.6%) and large abscess collection with thin abscess wall (72/79, 91.1%) being strongly predictive of TB. Combination of MRI findings had a higher predictive value. 97.5% of TB positive patients had at least one of these three MRI features, 89.8% patients had any two and 58.2% had all three.

Conclusion Our study validated different MRI findings with tissue studies and showed spinal infections with large abscess with thin wall, subligamentous spread of abscess and vertebral collapse were highly suggestive of spinal tuberculosis.

Graphical abstract

These slides can be retrieved under Electronic Supplementary Material.



Keywords Spinal tuberculosis · Magnetic resonance imaging · Abscess · Sensitivity · Predictive value

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Extended author information available on the last page of the article

Introduction

The diagnosis of spinal tuberculosis has remained an enigma. It has conventionally been based on a combination of clinical features, laboratory tests and imaging studies, since none of these individual diagnostic features are confirmatory. Early clinical symptoms including axial pain and malaise are non-specific, while constitutional symptoms are typically uncommon in spinal tuberculosis making diagnosis difficult based on early clinical findings [1]. Late clinical features such as neurological deficit, kyphotic deformity and cold abscess formation are more confirmatory in diagnosis but associated with significant morbidity when diagnosed at this stage [2]. Radiographic features including para-discal erosions and vertebral destruction have a lag of at least 3–4 weeks after the onset of clinical symptoms and hence not beneficial in the early stages [3, 4]. While tissue studies such as Ziehl Nielson staining, tubercular culture and histopathology can be confirmatory, they have poor positivity rates since spinal tuberculosis has less bacterial load (pauci-bacillary infection, $< 10^5$ bacteria per ml) [5].

MRI is commonly performed to evaluate patients with suspected spinal infections. It has several advantages of being highly sensitive and non-invasive, can be performed early in suspected cases, can be repeated at different time intervals and can also evaluate the whole spinal column and spinal cord [6]. Though MRI has the potential to provide early and accurate diagnosis of spinal tuberculosis, its importance is less emphasized and many of its diagnostic findings have not been validated by confirmatory tissue studies.

A key limitation of MRI is that certain MRI findings of spinal tuberculosis can be confused with pyogenic infections and other non-infective disorders including Modic changes, osteoporotic fractures, metastasis and marrow infiltrative disorders [7–9]. Jung et al. compared 20 patients each with spinal tuberculosis and pyogenic infections and noted that the presence of well-defined paraspinal abnormal signal, a thin and smooth abscess wall, paraspinal or intraosseous abscess, subligamentous spread, involvement of multiple vertebral bodies and thoracic spine involvement is more predictive of spinal tuberculosis [10]. However, a major lacuna in such studies is that they have included cases of spinal tuberculosis based on clinical suspicion of tuberculosis which could lead to false positive findings. Ideally typical MRI findings observed in patients with tissue positive tuberculosis infection would have more validity and hence would help the clinician in initiating early and appropriate anti-tubercular therapy in patients with positive MRI features. Hence there is a need for a large-scale study to demonstrate the validity and efficacy of specific MRI findings in the diagnosis of spinal tuberculosis, confirmed through tissue studies.

Materials and methods

The study was approved by the Institutional Review Board. We performed a review of case records and image archives of consecutive patients evaluated and treated for spondylodiscitis between 2013 and 2015. All patients had detailed documentation of their symptoms, clinical findings and had undergone MRI of the whole spine. All patients had undergone biopsy of the afflicted segment, either transpedicular or as part of the surgical debridement. The tissue specimen was analysed for histopathological examination, culture for aerobic organism, tuberculous culture in Middlebrook culture media and genetic PCR studies for mycobacterium tuberculosis. Blood inflammatory parameters including erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and blood cell counts were performed. Patients who presented with post-procedural (post-operative/iatrogenic discitis) were excluded from the study. Further, children less than 12 years were not included in the study since their radiological and clinical presentation will be different from adults.

MRI was performed using 1.5 Tesla scanner (Magnetom Symphony 1.5T; Siemens medical solutions, Germany) with eight channels and equipped with a dedicated spine coil. Pulse sequences included T1W and T2W sagittal sections, T2 STIR sagittal and coronal, T2W SE axials and T2W SE whole spine screening. Section thickness was 4 mm with a 1-mm intersection gap. Whole spine sagittal T2 screening was done in all patients irrespective of primary location of vertebral involvement. For the T2 whole spine sequence, a cranial sequence of 45 cm FoV including the vertex to the mid-thoracic spine and a caudal sequence of 45 cm FoV including the mid-thoracic to pelvic region were performed and merged using the software *syngo* (Siemens medical solutions, Germany). The scan parameters were as follows: TR: 2800–3500, TE: 85–110, slice thickness 4 mm; number of slices: 11 in each station.

MRI features considered in our study included location of vertebral infection, contiguous involvement, para or intraosseous abscess, subligamentous spread, vertebral destruction/collapse, large abscess collection with thin abscess wall, non-contiguous skip lesions, intervertebral disc involvement, end plate erosion and epidural abscess/granulation tissue (Fig. 1). The descriptive standards for each of the MRI findings are stated in Table 1. MRI features were documented by two independent observers (musculo-skeletal radiologist and spine surgeon with more than 7 years of experience), checked for good inter-observer reliability (kappa > 0.82) and any disparate findings were confirmed by consensus.

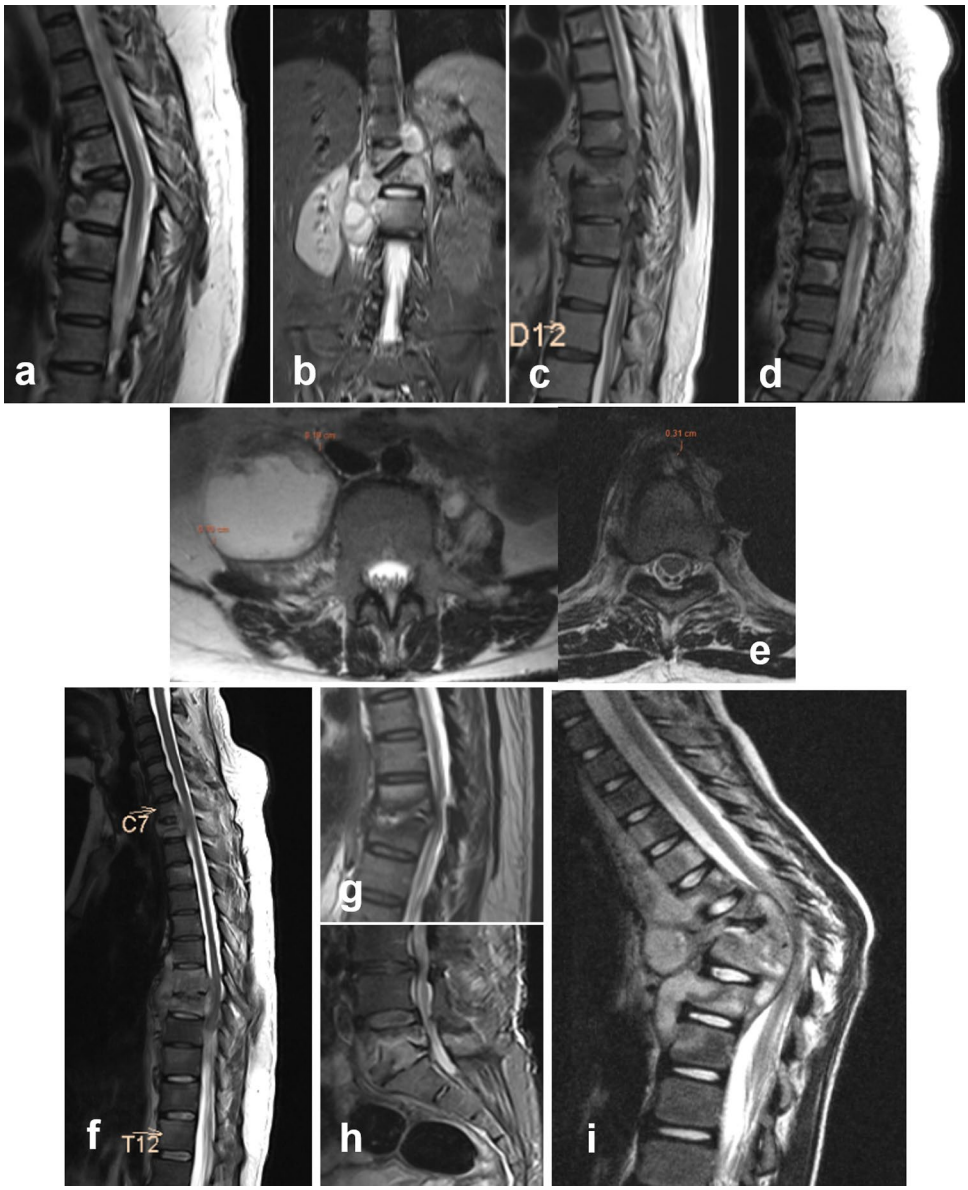

Fig. 1 Figure shows all the nine MRI features evaluated in the study. **a** Contiguous involvement, **b** presence of para or intraosseous abscess, **c** subligamentous spread, **d** presence of vertebral collapse, **e** large collection with thin abscess wall, **f** presence of non-contiguous skip lesions, **g** intervertebral disc involvement, **h** end plate erosions and **i** epidural component

Table 1 Description of individual MRI features

S. no.	Radiological parameter	MRI features in identification
1.	Contiguous involvement	Involvement of more than two adjacent vertebrae
2.	Presence of para or intraosseous abscess	Presence of collections within the vertebra or in adjacent paravertebral soft tissues
3.	Subligamentous spread	Presence of anterior subligamentous bone signal alterations and abscess which extends more than two vertebral levels
4.	Presence of vertebral collapse	Vertebral body destruction with reduction in body height of more than half
5.	Large collection with thin abscess wall	Abscess extending more than more vertebra, with a wall thickness < 2 mm (> 2 mm was considered thick walled)
6.	Presence of non-contiguous skip lesions	Involvement of different non-contiguous vertebral levels in different regions of spine
7.	Intervertebral disc involvement	Disc showed altered morphology with iso-intensity to fluid signal, i.e. hypointense on T1 W and hyperintense on T2 W images
8.	End plate erosion	Irregularity of margins of vertebral body endplate as observed in T2 W/STIR images
9.	Epidural component	Epidural encroachment or indentation by pus or granulation tissue

Based on the results, patients were divided into two groups—**confirmed TB** with positive culture and or positive HPE, and **non-TB**, when both culture and HPE were negative. Positive histopathology for tubercular infection was determined based on the presence of three hallmark signs of tuberculosis (epitheloid granuloma, Langerhans giant cells with or without caseation) (Fig. 2). The efficacy of MRI findings in accurately diagnosing spinal tuberculosis was studied by comparing the two groups.

Statistical methods

For continuous variables, mean ± SD (Min–Max) was assessed and for categorical measurements, significance was assessed using Chi-square test. Significant level of correlation was set at p value < 0.05. Distribution of scores between the groups was assessed using independent Chi-square test. Binary logistic regression analysis was done for associating factors with outcome. Odds ratio was used to calculate possibility of patient having spinal tuberculosis when significant MRI features are present.

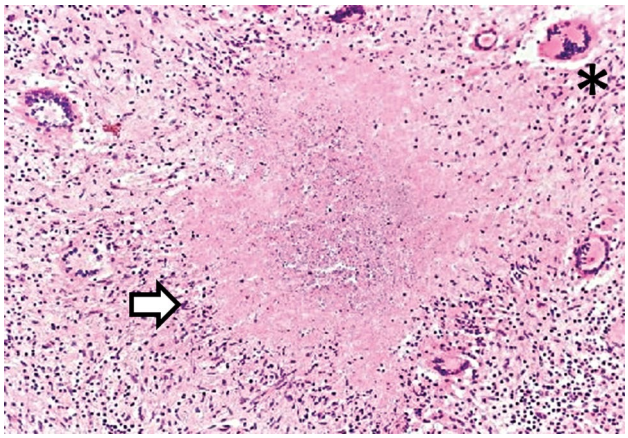

Fig. 2 Typical histopathological picture of a patient with tubercular spondylodiscitis. The arrow identifies the central caseating tubercle lined by the epitheloid cells and Langhans giant cell (marked with *)

Results

In the defined study period, 150 patients with spondylodiscitis were available for the study. 79 patients had tubercular culture positive or histopathological evidence of spinal tuberculosis (**TB positive Group),** and 71 patients had both tubercular culture and histopathological examination negative (**TB negative Group**). In the TB positive group, both histopathology and culture were together positive in 24 cases, while in 55 cases, histopathology alone was positive. The mean age of the patients in the TB positive and TB negative groups was 51.5 years and 50.9 years, respectively ($p > 0.05$). The mean ESR and CRP levels were also comparable without significant differences ($p > 0.05$) between the two groups (Table 2).

MRI features

The sensitivity, specificity, positive predictive value and prevalence of each MRI parameter between the two groups (TB positive and TB negative) were studied. The Pearson's Chi-square test showed significant differences for the following three MRI findings: (1) subligamentous spread, (2) vertebral collapse > 50% and (3) large abscess collection with thin abscess wall. No significant statistical correlation was observed for the presence of skip lesions (non-contiguous lesions as observed in whole spine MRI), multiple vertebral involvement, end plate erosions, intervertebral disc involvement, psoas abscess and epidural abscess, between the two groups.

Subligamentous spread was seen in 67/79 (84.8%) patients in TB positive group and 29/71(40.8%) patients in TB negative group with a sensitivity of 84.81% and specificity of 59.15% and positive predictive value of 69.79% and p value < 0.001 (Table 3).

Large abscesses with thin wall (thickness < 2 mm) was present in 72/79 (91.1%) patients in TB positive group and 35/71 (49.3%) patients in TB negative group with a sensitivity of 91.1% and specificity of 50.7% and positive

Table 2 Mean age and serum inflammatory markers in the two groups

Variable	Tubercular status	*N*	Mean	Standard deviation	Standard error mean	*p* value
ESR	Positive	79	66.7	37.4	4.2	0.765
	Negative	71	64.8	40.2	4.7	
CRP	Positive	79	45.9	46.7	5.2	0.821
	Negative	71	44.4	41.6	4.9	
Mean Age	Positive	79	51.5	17.3	1.9	0.847
	Negative	71	50.9	19.1	2.2	

ESR erythrocyte sedimentation rate, *CRP* C-reactive protein

Table 3 Sensitivity, specificity, positive predictive value and prevalence of each MRI parameter between the two groups (TB positive and TB negative)

No	Radiological parameter	Group A	Group B	Sens %	Spec %	PPV %	*p*
1	Contiguous involvement	28/79 (35.4%)	17/71 (23.9%)	35.44	76.06	62.22	0.125
2	Presence of paravertebral or psoas abscess	24/79 (30.4%)	20/71 (28.2%)	30.4	71.8	54.54	0.767
3	**Subligamentous spread**	67/79 (84.8%)	29/71 (40.8%)	84.81	59.15	69.79	***< 0.001***
4	**Presence of vertebral collapse**	55/79 (69.6%)	13/71 (18.3%)	69.62	81.69	80.88	***< 0.001***
5	**Large collection with thin abscess wall**	72/79 (91.1%)	35/71 (49.3%)	91.14	50.70	67.29	***< 0.001***
6	Presence of non-contiguous skip lesions	8/79 (10.1%)	3/71 (4.2%)	10.1	95.8	72.72	0.166
7	Intervertebral disc involvement	77/79 (97.5%)	67/71 (94.4%)	97.5	5.6	53.47	0.333
8	End plate erosion	78/79 (98.7%)	70/71 (98.6%)	98.7	1.4	52.70	0.939
9	Epidural component	52/79 (65.8%)	38/71 (53.5%)	65.8	46.5	57.77	0.125

Radiological parameters shown in bold had a strong statistical significance

p value was considered significant, if < 0.05

Sens sensitivity, *Spec* specificity, *PPV* positive predictive value

predictive value of 69.29% and *p* value < 0.001 in diagnosing spinal tuberculosis.

Vertebral body destruction with reduction in body height of more than half was observed in 55/79 (69.6%) patients in TB positive group and 13/71 (18.3%) patients in TB negative group. Thus, in diagnosing spinal tuberculosis, it had a sensitivity of 69.6% and specificity of 81.7% and positive predictive value of 80.9% and *p* value < 0.001 which is highly significant (Figure 3).

Fig. 3 MRI in a patient with tubercular spondylodiscitis. **a** The sagittal whole spine T2 weighted MR image shows multiple vertebral contiguous involvement. **b** Focussed sagittal T2 image shows vertebral collapse, anterior subligamentous spread of abscess **c**, **d** coronal T2 and axial T2 images show large paravertebral collections, epidural abscess and thin abscess wall. The histopathology and culture were confirmatory of spinal tuberculosis

Combination of specific MRI findings

Further, we analysed the utility of the presence of combination of the three significant MRI findings, namely subligamentous spread, large abscess with thin wall and vertebral destruction, and noted that the predictive value of MRI in diagnosing a tubercular infection with the combination of MRI findings was much higher (Table 4). Among 79 TB positive—Group A cases, 64(81%) were having both *subligamentous spread and large abscesses with thin wall*, and only 5% did not have either of the findings. Similarly, in Group A, 60.8% were having both *subligamentous spread and vertebral destruction* > 50% *positive* and only 6.3% of TB positive patients had neither of the findings. For the third combination of *large abscess with thin abscess wall and vertebral destruction* > 50%, among 79 TB cases positive, 96% patients had these two findings in combination or singularly.

We also observed that 97.5% of TB positive patients were having at least one of these three features on MRI, 89.8% patients had any two features and 58.2% had all three MRI findings, thus indicating a high predictive value in diagnosing spinal tuberculosis with these MRI findings. Between the three diagnostic MRI findings, large abscess with thin wall characteristic was the most significant individual feature with an odds ratio of 10, and a 95% confidence interval of 4.3–26.2, but when present in combination (thin abscess wall, vertebral destruction and subligamentous spread), the odds ratio improved significantly to 16.3 with 95% confidence interval of 5.3–50.1 showing higher possibility of patient having spinal tuberculosis when these three features are present together in the MRI.

Discussion

MRI scanning has revolutionized the diagnosis of spinal infections. It has immense strengths by being non-invasive and providing a rapid diagnosis [6, 11, 12]. The higher sensitivity of MRI enables detection of pathological changes in spine, even in the early stages of spinal infections. However, several MRI findings in spinal infections have been found to be overlapping with other spinal disorders [8, 9], thus mitigating its diagnostic value, especially in spinal TB. While most previous studies have used a presumptive diagnosis of tuberculosis, our study is the first and unique study to include tissue confirmed patients to validate the MRI findings. Based on tissue confirmation in our study, we have noted three specific MRI findings, namely *subligamentous spread, large abscess with a thin wall and vertebral destruction* > 50% to be highly sensitive and specific findings in the diagnosis of spinal tuberculosis.

Subligamentous spread of the tubercular abscess beneath the anterior longitudinal ligaments seems to be a unique feature of spinal TB, with a strong diagnostic accuracy. It was seen in 85% of patients with spinal TB in our study with a sensitivity of 84.8, and specificity of 59.2%. In a study by Jain et al. subligamentous spread of abscess was seen in 45/49 (92%) cases [6]. Chang et al. in their study reported subligamentous spread in 24/33 (73%) which is comparable with our results [13]. Exuberant cold abscess formation and the presence of proteolytic enzymes result in gradual elevation of the longitudinal ligaments from the vertebral bodies with subsequent spread of the abscess.

Apart from the spread of the abscess, the size of the abscess and the thickness of abscess wall showed significant difference among both groups. Larger-sized abscesses with thinner walls were seen in tubercular group, while smaller abscesses with thick irregular wall were more commonly seen in pyogenic infections. Jung et al. in their study found a combination of a well-defined paraspinal abnormal signal and thin, smooth abscess wall in 90% of instances in spinal TB [10]. Similarly, in our study, we found thin and smooth walled abscess in 91.1% cases in TB positive group. Since the tubercular abscess does not elicit a strong inflammation, the abscess wall is usually thin when compared to a pyogenic infection.

Vertebral body collapse > 50% is an important diagnostic feature of spinal tuberculosis. Chang et al. observed that a vertebral body height reduction of 50% or more was seen in 82% cases of tuberculous spondylitis in comparison with 30% cases in pyogenic spondylitis [13]. Jain et al. reported loss of vertebral body height in 94/161(58.38%) cases. But the study included 49 patients of spinal tuberculosis diagnosed either by clinic-radiological details and or tissue

Table 4 Sensitivity, specificity, positive predictive value and prevalence of *combination* of predictive MRI features—subligamentous spread, collapse of vertebra and abscess wall characteristics

MRI characteristics	Positive	Negative	Sensitivity	Specificity	PPV	*p* value
Subligamentous spread and large thin walled abscess	64/79 (81%)	4/79 (5%)	85.33	54.55	76.19	< 0.001
Subligamentous spread and collapse of vertebra	48/79 (60.8%)	5/79 (6.3%)	64.86	86.49	90.57	< 0.001
Large thin walled abscess and collapse of vertebra	51/79 (64.6%)	3/79 (3.8%)	67.11	80.00	86.44	< 0.001
Subligamentous spread, collapse of vertebra and large thin walled abscess	46/79 (58.2%)	2/79 (2.5%)	59.74	91.67	92.00	< 0.001

studies [6]. As described earlier, the uniqueness of the present study is the inclusion of tissue confirmed cases of spinal tuberculosis, a large patient sample and a control group to validate the observed MRI findings. Vertebral body destruction characterized by reduction in vertebral body height by >50% was observed in 55/79 (69.6%) patients in TB positive group while only in 13/71(18.3%) patients in TB negative group. Thus, in diagnosing spinal tuberculosis, it had a sensitivity of 67.1% and specificity of 78.9%. Since spinal tuberculosis has an insidious onset and smoldering progression, there is relatively a greater vertebral destruction at the time of clinical presentation. On the other hand, due to their virulence and rapidity of destruction, pyogenic infections of spine generally have less severe vertebral destruction.

More than the individual findings, combination of these MRI features (*subligamentous spread, large abscess with a thin wall and vertebral destruction* >50%*)* had more significance and diagnostic efficacy in our study. It was interesting to note that 97.5% of TB positive patients had any one of these three features on MRI, while 89.8% patients had any two features and 58.2% had all three MRI findings. While the usefulness of individual MRI findings in the diagnosis of spinal tuberculosis has been described before, the efficacy of a combination of these MRI features has not been studied before. Among individual features, we found that thin abscess wall as a single feature had an odds ratio of 10.6 to have tubercular spondylitis and when present in combination (abscess wall + vertebral destruction + subligamentous spread), the odds ratio increased significantly to 16.3 showing higher possibility of a patient having spinal tuberculosis when these three features are present together in MRI spine.

Interestingly, in our study, we noted that certain MRI features like the presence of skip lesions, multiple vertebral involvement, end plate erosions and intervertebral disc involvement, epidural involvement and psoas abscess were not significantly effective in making a diagnosis of spinal tuberculosis. Though studies have reported that preservation of intervertebral disc in spite of extensive bone destruction is a characteristic feature of spinal tuberculosis [6, 14, 15], involvement of disc was observed in high incidence in both tubercular positive and negative groups (97.5% patients in TB positive group and in 94.4% patients in TB negative group) in our study. We presume that the specific inclusion criteria of having tissue positive cases as confirmed cases in our study could be the reason that only three of the multiple MRI findings showed significant differences between the two groups.

The use of above-mentioned MRI parameters can lead to a reasonably reliable diagnosis of spinal tuberculosis, thus indicating that whole spine MRI scanning should be considered as the primary investigation in a suspected case of spinal tuberculosis for confirmation of diagnosis and initiation of early anti-tubercular treatment. While CT-guided needle biopsy/aspiration or surgical biopsy should be done and samples of bone tissue or abscess evaluated for tissue tests including culture, antibiotic sensitivity and histopathology, the presence of the three MRI findings would help the surgeon in initiating appropriate therapy till tissue results are awaited.

The study had a few limitations. We have considered tissue studies as gold standard investigations to assess the utility of MRI findings, but there could be false negative results in a few patients since vertebral infections are pauci-bacillary. Hence such patients could actually have tubercular infection but grouped under non-TB group. However, this is a potential lacuna of all studies that employ tissue tests for infection as the gold standard investigation. Though TB PCR test has high sensitivity and specificity, we did not include it as a confirmatory test for TB since it can detect even dead bacilli leading to false positive results. The study also did not consider the time interval between the onset of symptoms/disease and the presentation for MR imaging, as the MRI findings in early and late infections could vary. Finally, while the use of contrast enhanced MRI studies for spinal infections has also been described for demonstrating heterogeneous vertebral body enhancement, we have not employed contrast enhancement since all the findings mentioned were detectable sufficiently by routine plain MRI scan.

Conclusion

Whole spine MRI is a non-invasive, easily available investigation which could help in early diagnosis of spinal tuberculosis. While the ability to ascertain significance to various MRI findings was doubtful due to its overlap with other spinal disorders, our study has shown that a large abscess with well-defined thin and smooth abscess wall, subligamentous spread to three or more vertebral levels and destruction/collapse of vertebra were highly suggestive of spinal tuberculosis. These findings have been validated with the use of gold standard tissue tests. Hence, patients with the three MRI findings can be initiated on appropriate anti-tubercular treatment, while tissue studies are awaited.

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Compliance with ethical standards

Conflict of interest There are no conflicts of interest.

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