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Evaluation of the role of computed tomography guided biopsy in effective diagnosis and management of patients with Koch's spine in India

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ABSTRACT

Background: In the Indian population, tuberculosis and malignancy are the most common spinal pathologies. Radiological findings are often non-specific, thus non-diagnostic and fail to provide a prognostic perspective if the disease is established. Therefore, bacterial and/or histological evidence must be obtained to distinguish one infection from another or neoplasm. In this study, we evaluated the role of Computed Tomography-guided biopsy in Koch's spine by assessing diagnostic yield, the incidence of patients with drug-resistant tuberculosis, and drug sensitivity.
Methods: Patients with suspected Koch's spine attending outpatient department of tertiary health care centre in India were selected for the study. Data were collected using proforma containing demographic, clinical, radiological and other laboratory variables. In addition, biopsy samples were sent for microbiological and histopathological analysis. Patients were followed up at an interval of 3 months to one year.
Results: Most patients had Lumbar vertebra involvement followed by dorsal and least with cervical spine.41.25% of cases were drug resistant. In resistant cases, Isoniazid resistance is more seen, followed by Rifampicin. The clinical assessment revealed a significant difference in fever, back pain, Weight WBC count, Erythrocyte Sedimentation Rate and C Reactive Protein post-biopsy and treatment.
Conclusions: Patients with Koch's spine should have tissue sampling for diagnosis and drug sensitivity; otherwise, they will not receive adequate treatment, leading to delayed recovery, disease worsening and resistance. Computed tomography guided biopsy thus helps early diagnosis and guides to proper anti-tuberculous treatment. In addition, it helps to decrease the burden of morbidity associated with Koch's spine.

Keywords: Koch's spine, CT-guided biopsy, Drug resistance, Drug sensitivity

INTRODUCTION

In the Indian population, tuberculosis and malignancy are the most common spinal pathologies. Spinal tuberculosis is one of the significant manifestation of extrapulmonary tuberculosis. The clinical features of spinal tuberculosis include constitutional symptoms, spinal symptoms, and neurological symptoms. A high index of suspicion and appropriate imaging and diagnostic tests are necessary for accurate diagnosis and prompt treatment. Imaging studies such as X-rays, CT scans, and MRI can help to detect the characteristic changes in the spine. No other imaging modality shows changes at earlier stages of the disease, but MRI shows early signal changes. MRI is recommended

when suspect spondylitis as early detection can avoid severe spinal cord compression and neurological complications. MRI helps in detecting exact anatomical locations in a different plane and detects early bone destruction and disc changes. It also helps in identifying skip lesions.[1] However, there are no definitive signs in MRI to define spinal tuberculosis, and a biopsy is still necessary.[2] Gene Xpert MTB/RIF assays allow rapid detection of the mycobacterium genome along with Rifampicin resistance using rpoB gene mutation testing.[3] The gold standard technique is to isolate organisms in culture, and drug sensitivity testing becomes paramount in resistance cases. Early diagnosis and appropriate treatment can prevent long-term complications and improve patients' quality of life. While the clinical-radiological diagnosis was considered sufficient to start anti-tubercular treatment in the earlier days with modern-era evidence-based medicine, it is essential to establish the diagnosis by biopsy.[4-6] Compared to open biopsy, closed one has the advantages of being less morbidity, easy and quick execution, absence of significant procedure-related complications and cost-effective.[7-11] However, due to the lack of image-guided biopsy centres in rural areas, most patients were diagnosed and treated on clinical grounds. In such cases, patients would not receive adequate therapy, which leads to many complications. It was decided to conduct a study to find the yield in detecting Koch's spine by CT-guided biopsy and determine the current scenario of drug-resistant spinal tuberculosis in India, as tertiary care hospitals currently offer computed tomography-guided biopsy.

METHODS

This prospective study was conducted from September 2020 to August 2021 in the department of orthopaedics Topiwala National Medical College and B. Y. L Nair Hospital Mumbai, India. The study was conducted after receiving approval from the institutional ethics committee. We studied 91 patients with suspected Koch's spine diagnosed via clinical and radiological methods attending orthopaedic outpatient department and undergoing CT-guided biopsy for the same. Patients with less than grade 3 power were excluded from the study. A radiologist reviewed the CT films to determine whether CT-guided biopsy is feasible or not. 13G Cook's bone biopsy needle is used for the biopsy procedure. The procedure was done in the prone position by the Transpedicular approach. After preliminary axial CT screening, the most appropriate slice will be selected for needle insertion. At least two samples were collected and sent for AFB smear, Genexpert, Histopathology study and culture and sensitivity. The presence of acid-fast bacilli in the Ziehl-Neelsen stain, caseating granuloma in histopathology, and growth in the Lowenstein Jensen medium and Gene Xpert will be used to define the evidence of tuberculosis. Data of selected patients were collected using a proforma, which contains variables like age, sex, duration of illness, symptoms like fever, back pain by VAS (visual analogue scale), weight loss, neuro deficit; laboratory data including WBC count, ESR, CRP; Radiological features including the level of vertebra involved, the pattern of destruction, presence of paravertebral, epidural and disc space abscess which supports the clinical diagnosis. Data were collected before biopsy and post-biopsy at 3, 6 and 12 months. Data were analysed using SPSS ver.17 (SPSS Inc.) Post biopsy patient was started on the appropriate drug depending upon biopsy reports, but the final regimen was decided after TB culture, drug and sensitivity report.

RESULTS

In our study, around 31.0% of the cases belong to the age group up to 20 years, and 36.6% belong to the group 21-30 years.

Table 1: Distribution of sex.

Sex	N	%
Male	40	56.3
Female	31	43.7

Table 2: Level of lesion.

CT Findings	N	%
Level of Lesion		
Lumbar Vertebra	53	58.2
Dorsal Vertebra	34	37.36
Cervical Vertebra	4	4.3

Almost 32.4% of cases with an age of more than 30 years were also noted. The average age was 31.10 years, with a standard deviation of 14.96. The minimum and maximum age was 8 and 69 years, respectively. Distribution of age is shown in (Figure 1) and distribution of sex shown in (Table 1).

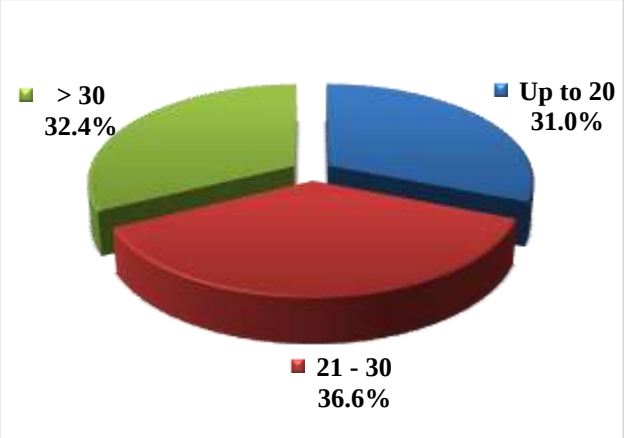

Figure 1: Distribution of age.

Among 91 cases taken for the study, around 56.3% were male, and 43.7% were female**.** In our study, around 56.3% of patients had a duration of illness below five months. The average duration of illness was 5. The minimum and maximum duration of illness was one and 15 months,

respectively. In this study, 49.45% of patients had compression fractures, 29.67% presented with disc space narrowing, lytic lesions were seen in 13.10%, and 7.6% were seen with kyphosis. The level of lesion is described in (Table 2). The findings of the tissue study are shown in (Table 3).

Table 3: Findings of tissue study.

Tissue Diagnosis	N	%
Presence of AFB	63	88.70
GeneXpert		
MTB seen Rifampicin Sensitive	47	51.64
MTB seen Rifampicin Resistant	33	36.62
MTB not seen	11	12.08
Drug sensitivity		
Sensitive to first line drugs	47	58.75
MDR TB	28	35
XDR TB	5	6.25
Histopathology		
Tuberculous granuloma	70	76.92
Undifferentiated squamous cell	5	5.40
Non-specific tissue	16	17.58

Table 4: Details of individual drug resistance.

Drug	N	%
Isoniazid	30	32.96
Rifampicin	28	30.76
Pyrazinamide	9	9.89
Ethambultol	13	14.28
Streptomycin	5	5.49
Amikacin	1	1.09
Levofloxacin	5	5.49

The (Figure 2) shows granuloma in histopathology study. In drug resistance, TB isoniazid resistance was more seen (32.96%), followed by Rifampicin (30.76%). Among injectable streptomycin, 5.49% and Amikacin, 1.09% showed the resistant strain. The (Table 4) shows details of individual drug resistance. Statistical analysis showed that there is a significant difference in pain at 3, 6, and 12 months ($p<0.01$). Study reveals that the cases with severe pain are significantly reduced at three months (0.0%) and six months (0.0%) compared to the cases with pain at pre-biopsy (8.79%). The (Table 5) shows the distribution of VAS scores for pain. While comparing mean weight, there was a significant improvement over the period of the study. Following are the mean weight in our study at three months (49.13±11.21), at six months (51.64±11.50) and at 12 months (52.53±10.9) compared to the weight at pre-biopsy (48.17±11.85). The difference in weight during the study is shown in (Figure 3). Similarly, WBC count and fever also showed significant differences during the study period. A significant fall in ESR and CRP was also observed, which is depicted in (Figure 4, Table 6). Both ESR and CRP fell in values which were statistically significant. Follow-up radiological images also showed healing by the end of 12 months.

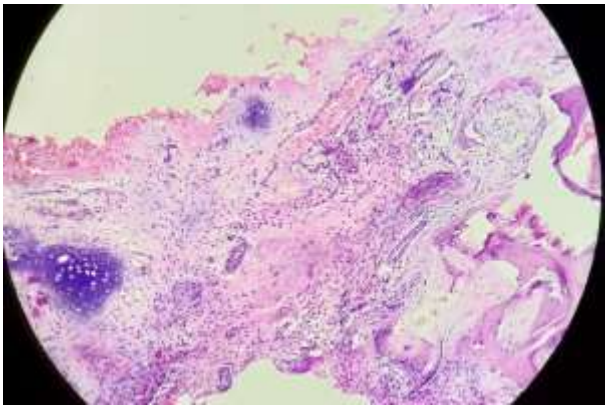

Figure 2: Histopathology study shows granuloma.

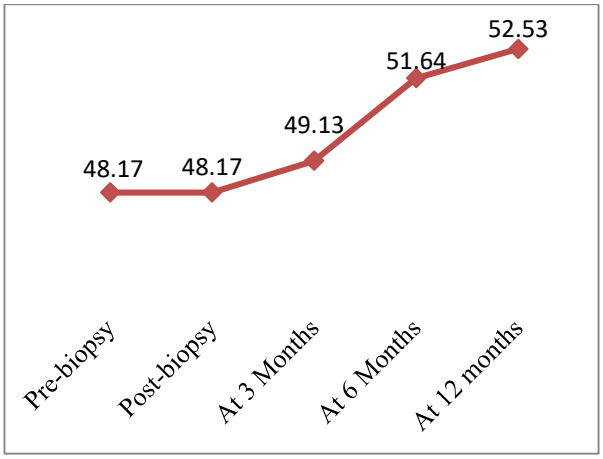

Figure 3: Mean weight during the study.

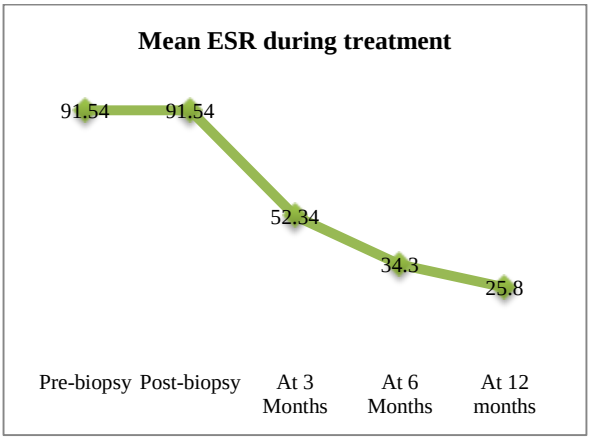

Figure 4: Difference in ESR during the study.

DISCUSSION

Among 91 cases in this study, 56.3% were male, and 43.7% were female. The minimum and maximum age was 8 and 69 years, respectively. In a study conducted by Fareeha Rauf et al out of 2000 cases of the tuberculous spine, 1080 (54%) were male, and 920 (46%) were female.[12] Their age ranged from 8-60 years. About 90% of patients were below the age of 40 years.

Table 5: Distribution of VAS score for pain.

Pain (VAS)	Nil, N (%)	Mild, N (%)	Moderate, N (%)	Severe, N (%)
Pre-biopsy	0 (0.0)	34 (37.36)	49 (53.84)	8 (8.79)
Post-biopsy	0 (0.0)	34 (37.36)	49 (53.84)	8 (8.79)
At 3 Months	7 (7.69)	37 (40.65)	26 (28.57)	0 (0.0)
At 6 Months	55 (60.43)	25 (27.47)	11 (12.08)	0 (0.0)
At 12 Months	65 (71.42)	25 (27.47)	1 (1.09)	0 (0.0)

Peak age among the males and females was 20-29 years and 14-35 years, respectively. Moghtaderi et al reviewed 43 patients with spinal TB the mean age of patients was 45.4±21 years (range, 10-75 years), and 70% of the patients were between 35 and 55 years.[13] In the study conducted by Rauf et al the most common site of involvement was the dorsal spine (45%), followed by the lumbosacral spine (33%), cervical spine (10%) and at multiple levels (12%).[12]

Table 6: Difference in CRP during study.

CRP	Mean	SD	P value
Pre-biopsy	22.13	10.76	-
Post-biopsy	22.13	10.76	1
At 3 months	4.543	2.78	<0.01
At 6 months	2.443	1.03	<0.01
At 12 months	2.33	0.94	<0.01

Vertebral end plate destruction and reduced disc space were the commonest sequelae in all the biopsied cases, while in our study most common site was the lumbar spine. In our study, there were no cases with skipped lesions. 49.45% of patients had a compression fracture, 29.67% presented with disc space narrowing, and lytic lesions were seen in 13.10% and 7.6% with kyphosis.

In an Indian study, a fine needle aspiration biopsy done under CT guidance successfully diagnosed spinal tuberculosis in 34 out of 38 patients.[14] Smear positivity for acid-fast bacilli was seen in up to 52% of cases, and culture positivity in about 83%.[15] In our study, 88.7% of cases are smear positive, and 76.92% showed typical tuberculoid sgranuloma in histopathological examination. 63 out of 91 cases showed smear positivity for AFB 3137 patients with spinal TB and 272 patients with MDR spinal TB were analysed in one another study showed that MDR spinal TB remains a public health concern and commonly affects patients 15-30 years of age (34.19%).

The most common site involved is the thoracolumbar spine (35.66%). Li et al reported 249 histologically proven spinal tuberculosis patients, of which 127 (51%) produced a positive culture.[16] 39 (30.7%) of the 127 bacterial culture-positive patients were found to have drug resistance. 12 out of 35 patients were found to have MDR-TB. Sixteen patients were found to have mono-drug resistance, while the remaining seven patients were found to have resistance to additional anti-tubercular drugs. The rates of resistance to isoniazid were 54.3%, rifampicin (48.6%) and streptomycin (34.3%) amongst the drug-resistant cases. Pawar et al evaluated 238 histologically proven spinal tuberculosis cases and found 28 patients (11.7%) to have multidrug-resistant strains.[17]

The authors have not reported on mono-drug resistance and resistance to other anti-tubercular drugs. Mohan et al in their 686 culture-positive spinal tuberculosis patients, found 111 patients (16.2%) have drug-resistant strains.[18] 87 of 111 patients were multidrug-resistant; three patients were diagnosed with XDR strains, while the remaining 21 patients had mono-drug-resistant strains. Prevalence of resistance to isoniazid was 15. 0% (93/686), to rifampicin turned into 13.5% (93/686) and 11.2% (77/686) for streptomycin. Lan et al evaluated 152 Koch's spine patients and reported bacteriological culture positivity in 76 patients.[19] 23 of 76 patients (30.3%) were found to have drug-resistant tuberculosis. Thus, the prevalence of drug-resistant spinal tuberculosis in the native population varies from 11.7% to 30.7% of culture-positive patients.

A recent retrospective study among the Indian population conducted by Garg et al concluded that among 667 patients, 65% of them were diagnosed with Koch's spine based on at least one tissue test. Forty-four patients had drug resistance to rifampicin. In our study, 58.75% of cases are sensitive to first-line drugs, and MDR and XDR cases are 35% and 6.25%respectively.[20] Among drugs, isoniazid is the most common, with 32.96% (30 cases), followed by rifampicin 30.76% (28) cases. 35% of cases were MDR TB, and 6.52% were XDR TB. In a similar study, after 4-6 weeks of chemotherapy, tuberculosis symptoms and vertebral pain improved in almost all patients, and the ESR and C-reactive protein (CRP) also decreased.[21]

ESR and CRP are reliable parameters evaluating the response to treatment and prognosis of spinal tuberculosis.[22,23] In our study, ESR and CRP were significantly reduced. Weight is also significantly improved at three months (49.13±11.21) and six months (51.64±11.50) compared to the weight at pre-treatment (48.17±11.85). Our study reveals that the number of cases with fever is reduced post-biopsy and post-treatment (12.7%) and further reduced at three months (0.0%) and six months (0.0%) compared to the cases with fever at pre-treatment (60.6%). There is no significant change in pulse rate and BP before and after the procedure. No post-procedure complication was detected.

Limitations

Our study had 91 patients which could have been higher for better comparison. Time period in our study is 12 months but long term follow up required in Koch's spine patients to determine the final clinical outcome.

CONCLUSION

Spine tuberculosis is a challenging disease. Most of the patients may present with back pain. The advanced disease might present with neuro deficit and deformity. CT-guided biopsy for diagnosis of the Koch's spine is a technically demanding procedure, and it requires coordination from a pathologist, microbiologist and radiologist for diagnosis. CT-guided biopsy has greater acceptance due to the absence of many surgical complications due to open biopsy, short hospital duration, and fewer biopsy-related complications. Out of 91 patients, 70 were found to have TB. 41.25 % of patients in our study were drug-resistant TB, of which 35% is MDR TB, and 6.25% is XDR TB. This accounts for nearly half of the patients in the study; without proper tissue sampling, diagnosis and drug sensitivity tests, these patients would have been treated with first-line drugs only. This leads to delay in recovery, worsening of disease and emergence of a new resistance. Thus, early diagnosis and treatment with proper ATT is the main success formula in addressing this issue. Tissue sampling helps in the confirmation of diagnosis as well as helps to identify the drug sensitivity, and it determines the line of management.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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