Study of clinical outcome and prevalence of multi-drug resistance in spinal tuberculosis and detection with gene-expert test, antibiotic susceptibility pattern

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Abstract
We have conducted a study of 40 cases on Clinical outcome and Prevalence of Multi-Drug Resistant in Spinal Tuberculosis and detection with Gene-Expert Test, Antibiotic susceptibility pattern in our Anil Neerukonda Hospital, NRI Institute of Medical Sciences, Visakhapatnam, with patients presenting directly or being referred from other primary and secondary care centers.

Patients presenting to our institute with clinico-Radiological Scenario of Spinal Tuberculosis were evaluated thoroughly using Biochemical, Radiological and Histo-pathological studies. The Study was done, with the duration of 30 months for Evaluation and Management of Resistant T.B spine, from April 2016 to September 2018.

Patients were categorised primarily according to the need for further invasive investigation (biopsy). Those patients without Neurological Deficit or with no indication for Surgery will undergo for Biopsy of the lesion on out-patient basis and were followed-up regularly on Out-Patient basis itself for further Management as planned. Remaining patients with Neurological Deficit or with Indication of Surgery were admitted and were subjected to Biopsy pre-operatively or the Biopsy material was collected Intra-Operatively and sent for Investigations.

For the study a valid written informed consent was obtained from each patient after proper explanation of the study and the management protocol that was to be followed.

Keywords: prevalence, spinal tuberculosis, susceptibility pattern, gene-expert

Introduction

Inclusion criteria: Patients with clinico-radiological scenario of spinal tuberculosis.
Exclusion criteria: Those who are not willing for enrolment, Being lost to follow up, Biopsy was diagnosed to other pathology such as malignancy, etc.

Management protocol
All the selected patients were evaluated in the following protocol,
1. Basic demographic information
2. Chief presenting complaints
   ▪ Back pain
   ▪ Difficulty or inability to walk
   ▪ Neurological symptom like weakness, tingling numbness, bowel & bladder involvement
   ▪ Deformity
3. Level of spine involved (x-ray or MRI if available)
4. Parameter evaluated pre-operatively were
   ▪ Back pain by using VAS (Visual Analogue Score)
   ▪ Neurological status using ASIA SCALE
   ▪ Oswestry Disability Index (ODI) score for back pain
   ▪ Blood parameter (HB/TLC/ESR/Total bilirubin/SGOT/SGPT)

Anti-tuberculosis treatment was empirically started in all the patients on initial suspected clinico-radiological diagnosis of spinal tuberculosis. Once the result of gene expert test was available when Mycobacterium tuberculosis
In our study Fluoroscopic guided Trans-Pedicular Biopsy was done under local anaesthesia. In those who definitely required surgical management sample was collected intra-operatively. Once sample was collected, it was sent for gene expert test and histo-pathological examination. Gene-Xpert test carried out collected samples at our institute Central laboratory. Sample is processed by mixing with the expert sample reagent (NAOH + Isopropyl alcohol) in 1:2 ratios (sample: Reagent). Then mixture is vortexed and waits for 10 min, again mixture vortexed wait for 5 min for mixture sediment. Then 2 ml of mixture is collected with partial pipette add to the expert cartridge. The barcode scanning done and cartridge load into the machine. After establishment of definite indication for surgery, the patients were operated accordingly combined with postoperative course of anti-tuberculous drug therapy.

All cases were followed up at 3 month, 6 month, 9 month and 24 month or longer on following basis.

1. Any 1st line drug to which isolate had proved to be sensitive
2. An injectable drug for minimum period of six months
3. A quinolone
4. Addition of appropriate any second line drug such as Ethionamide and Cycloserine, to achieve combination of four to five effective drug regimen
5. Other drug such as Amoxicillin / clavulanate and Clofazimine
6. And chemotherapy was ensued for 18-24 month or longer

1) Visual Analogue Scale
VAS is a uni-dimensional measure of pain intensity. For example, the amount of pain that a patient feels ranges across a continuum from none to an extreme amount of pain.

**Scale:** The VAS for pain quantification is a continuous scale comprised of a horizontal or vertical line, usually 10 centimetres in length, anchored by two verbal descriptions, one for each symptom extreme. For pain intensity, the scale is most commonly anchored by no pain (score 0) and „pain as bad as it could be” or worst imaginable pain (score 10). To avoid clustering of score around preferred numeric value, number or verbal descriptor at intermediate point is not recommended.

**Method of administration:** The pain VAS is self-completed by the respondent. The respondent is asked to place a line perpendicular to the VAS line at the point that represents his/her pain intensity.

**Scoring:** Using a ruler, the score is determined by measuring the distance on the 10 cm line between the „no pain” anchor and the patient mark, providing a range of score from 0-10.

2) Oswestry disability questionnaire for low back pain (ODI)

This questionnaire for ODI score has been designed to give us information as how your back is affecting your ability to manage in everyday life. The test is considered the „gold standard” of low back functional outcome tools. Patients are supposed to by check ONE box in each section for statement which best applies to them.

**Scoring instructions:** For each section the total possible score is 5: if the first statement is marked the section score = 0; if the last statement is marked score = 5. If all 10 sections are completed the score is calculated as follows: Example: 16 (total score) 50 (total possible score) x 100 = 32%. If one section is missed or not applicable the score is calculated: 16 (total scored), 45 (total possible score) x 100 = 35.5%

Minimum detectable change (90% confidence): 10% points (change of less than this may be attributable to error in the measurement)

**Interpretation of score**

| Score | Description |
|-------|-------------|
| 0% to 20%: minimal disability | The patient can cope with most living activities. Usually no treatment is indicated apart from advice on lifting sitting and exercise. |
| 21% - 40%: moderate disability | The patient experiences more pain and difficulty with sitting, lifting and standing. Travel and social life are more difficult and they may be disabled from work. Personal care, sexual activity and sleeping are not grossly affected and the patient can usually be managed by conservative means. |
| 41% - 60%: severe disability | Pain remains the main problem in this group but activities of daily living are affected. These patients require a detailed investigation. |
| 61% - 80%: crippled | Back pain impinges on all aspects of the patient's life. Positive intervention is required |
| 81% - 100%: | These patients are either bed-bound or exaggerating their symptoms. |

1) **ASIA (American spinal injury association) impairment:**

As per international standard for neurological classification of spinal cord injury

| ASIA grade | Clinical status |
|------------|----------------|
| A Complete: No motor or sensory function is preserved in the sacral segments S4-S5. |
| B Incomplete: Sensory but not motor function is preserved below the neurological level and includes the sacral segments S4-S5 |
| C Incomplete: Motor function is preserved below the neurological level, and more than half of key muscles below the neurological level have a muscle grade less than 3. |
2) Bridwell criteria for spinal fusion.
At post-operatively at the time of follow up X-ray evaluation for bony fusion done by using Bridwell criteria [64] Posterior fusion grades

| Grade | Description                                                                 |
|-------|-----------------------------------------------------------------------------|
| I     | Solid trabeculated transverse process and facet fusion bilaterally (Definitive fusion) |
| II    | Thick fusion mass on one side, difficult to visualise on the other side (Probab fusion) |
| III   | Suspected lucency or defect in fusion graft (probable no fusion) Grade IV  Definite resorption of graft with fatigue of instrument (Definitive nofusion) |

Observation & Result
In our study total 40 patients were included. One patient died at home and the cause could be ascertained. 39 cases were further followed for analysis. Various parameters of cases were analysed as follow

1. Age distribution: Frequency of distribution of patients according to age group is shown in table 1 and graph 1.

| Age group (years) | N  | %     |
|------------------|----|-------|
| 21-30            | 10 | 25.0% |
| 31-40            | 12 | 30.0% |
| 41-50            | 11 | 27.5% |
| 51-60            | 4  | 10.0% |
| 61-70            | 3  | 7.5%  |
| Total            | 40 | 100.0%|

Mean age - 39.95 +/- 12.78 (21-70) years

In this study, age group of patients ranged from 21 years to 70 years. Maximum patients (30%) belonged to age group of 31-40 years. Mean age of the patients was 39.95 ± 12.78.

2. Gender distribution: Frequency distribution of patients according to gender is shown in table 2 and graph 2

| Sex    | N  | %     |
|--------|----|-------|
| Female | 15 | 37.5% |
| Male   | 25 | 62.5% |
| Total  | 40 | 100.0%|

In the study, 62.5% (25) of cases were male, 37.5% (15) were female. Ratio of male: female 1.6:1.8

3. Clinical symptomatology: Distribution of patients according to the chief presenting complaints

| Chief complaints | N  | %     |
|------------------|----|-------|
| Back Pain        | 40 | 100.0%|
| Constitutional Symptoms | 28 | 70.0% |
| Neurodeficit     | 23 | 57.5% |
| Deformity        | 8  | 20.0% |

Back pain was universally common complaint seen at presentation in all (N = 40, 100%) cases, followed by constitutional symptoms of TB in 28 Cases and neurodeficit in 23 cases

4. Distribution of cases according to region of vertebral column involved.

| Affected Region | N | %   |
|-----------------|---|-----|
| Cervical        | 1 | 2.5%|
| Thoracic        | 23| 57.5%|
| Thoracolumbar   | 7 | 17.5%|
| Lumbosacral     | 9 | 22.5%|
| Total           | 40| 100.0%|

Thoracic region was most commonly involved (57.5%) followed by lumbosacral (22.5%), thoracolumbar junction was involved in 17.5% of cases.

5. Distribution of cases according to number of vertebral levels involved.

| No. of Vertebrae | No. of cases | %   |
|------------------|--------------|-----|
| One              | 3            | 7.5%|
| Two              | 25           | 62.5%|
| Three            | 7            | 17.5%|
| Four             | 2            | 5.0% |
| Five             | 1            | 2.5% |
| Six              | 2            | 5.0% |
| Total            | 40           | 100.0%|

In maximum number of cases only two vertebrae were affected (25 cases), followed by three vertebrae were affected in 9 cases and maximum 6 vertebrae involvement in 2 cases.

6. Tissue sample collection

| Biopsy Method                      | N  | %     | MTB Detected | MTB Detected |
|------------------------------------|----|-------|--------------|--------------|
| Tissue collection Through fluoroscopic biopsy | 21 | 52.5% | 12          | 57.14%       |
| Tissue sample by CT guided biopsy  | 2  | 5.0%  | 0            | 0.00%        |
| Tissue sample Collection intraoperatively | 17 | 42.5% | 11          | 64.71%       |
| Total                              | 40 | 100.0%| 23          | 57.50%       |

In most of the cases, tissue samples were collected through fluoroscopy guided transpedicular biopsy (21 cases), followed by collection of tissue samples intra-operatively 17 cases and in 2 cases samples were collected through CT guided biopsy by the radiologist.

Table 2: table showing distribution of cases by management

| Management methods | N  | %   |
|--------------------|----|-----|
| ALD*+PS**+C****+A* | 19 | 47.5%|
| Ant Cervical Plate | 1  | 2.5% |
| Conservative       | 20 | 50.0%|
| Total              | 40 | 100.0%|

(*= Antero-Lateral Decompression, **=Pedicular Screws fixation, ****= cylindrical Cage insertion, *= autograft)

Amongst all 40 cases half of the cases were managed conservatively and half of the cases were treated surgically (Anterolateral Decompression with pedicular screw fixation with cylindrical cage insertion along with autograft). Out of 20 cases 1 case of cervical spinal tuberculosis was managed by anterior cervical plating + corpectomy + bone grafting.
3. Distribution of cases according to the result of Gene expert test.

| Gene Xpert          | N | %   |
|---------------------|---|-----|
| Detected (Positive) | 23| 57.5%|
| Not Detected (Negative) | 17| 42.5%|
| Total               | 40| 100.0%|

Out of 40 patients of suspected spinal tuberculosis, mycobacterium tuberculosis was detected in 23 patients by gene expert test.

### Table 3.1: Rifampicin sensitivity/Resistance in MTB detected sample

| Rifampicin Resistance (Gene Xpert) | N | %   |
|-----------------------------------|---|-----|
| Resistance                        | 3 | 13.0%|
| Sensitive                         | 20| 87.0%|
| Total                             | 23| 100.0%|

Out of 23 Gene-expert positive cases, 20 cases showed mycobacterium tuberculosis sensitivity to rifampicin and 3 cases were resistant to rifampicin. In our study out of 40 cases, rifampicin resistance were noted in three cases, out of these only one case had culture positive result. We had performed Drug Susceptibility Test in same case. MTB grown in that case were resistant to Streptomycin, Ethambutol, Isoniazid, Rifampicin and Ofloxacin, were sensitive to Amikacin, kanamycin and Capreomycin. Individualised chemotherapy. Formulated as per protocol. Six antitubercular drug including injectable given for 6 months (Inj Kanamycin, Tb pyrazinamide, Tb Para-aminosalicylic acid (PAS), Tb Ethionamide, Tb Cycloserine and Tb Levofloxacin) and Five antitubercular drugs ( Tb Para-aminosalicylic acid [PAS],Tb pyrazinamide, Tb Ethionamide, Tb Cycloserine and Tb Levofloxacin) for 12 months, still on antitubercular treatment. Clinical outcome of these case were excellent till last follow up visit. However, clinical outcome of rest of this two case (rifampicin resistance with culture negative) were also good till last follow up visit.

### Table 3.2: Summary of Gene-expert test results (Cont.)

| Parameters     | %   |
|----------------|-----|
| Sensitivity    | 100.0%|
| Specificity    | 58.6%|
| PPV            | 47.8%|
| NPV            | 100.0%|
| Accuracy       | 70.0%|

Sensitivity and negative predictive value of gene expert test in comparison with the gold standard culture test are 100%. But specificity and positive predictive value are 58.6% and 47.8% respectively. Accuracy of gene expert in our test found to be 70%.

4. Distribution of cases according to histopathological findings

### Table 3.3:Histopathological findings

| Histopathological findings | N | %   |
|----------------------------|---|-----|
| Suggestive of tuberculosis pathology | 18| 45%|
| Non tuberculosis changes   | 22| 55%|
| Total                      | 40| 100.0%|

Out of 40 cases, 18 cases showed histopathological examination of specimen slides suggestive of chronic granulomatus changes in favour of tuberculous pathology and in rest of the 22 cases histopathological examination of specimen slides were in favour of Non-tuberculous pathology.

### Table 4.1: histopathological findings sensitivity, specificity and other parameters

| Parameters     | %   |
|----------------|-----|
| Sensitivity    | 70.0%|
| Specificity    | 63.3%|
| PPV            | 39.0%|
| NPV            | 86.0%|
| Accuracy       | 65.0%|

The accuracy of histopathological examination in our study was found to be 65%.

### Table 5: Distribution of patients as per radiological findings.

| Pre-op X-ray Finding          | N | %   |
|-------------------------------|---|-----|
| Paravertebral Soft Tissue Shadow | 3 | 7.5%|
| Destruction                   | 31| 77.5%|
| Intact                        | 6 | 15.0%|
| Total                         | 40| 100.0%|

Out of 40 cases, maximum number of cases had Destruction 77.5% (31 cases), paravertebral soft tissue shadow in 3 cases and rest of 6 cases had intact vertebral bodies. Cases with destruction of vertebral bodies with classical involvement easily suspected having spinal TB on radiograph and rest of the 9 cases were difficult to diagnose on plain x-ray.

6. Comparison of back pain between base-line VAS (Visual analogue score) score vs. 3 month follow up visit VAS score

| VAS Score (Baseline) | N | %   |
|----------------------|---|-----|
| 5                    | 3 | 7.5%|
| 6                    | 14| 35.0%|
| 7                    | 19| 47.5%|
| 8                    | 4 | 10.0%|
| Total                | 40| 100.0%|

Mean VAS - 6.6 +/- 0.77

Out of 40 cases, Maximum number of cases VAS score were in the range of 6-7 (82.5%), 4 cases VAS score has 8 and 3 cases VAS score has 5.

7. Distribution of cases by baseline ASIA scoring and its improvement over the further periodic follow up

| ASIA | N  | %   |
|------|----|-----|
| A    | 5  | 12.8%|
| B    | 8  | 20.5%|
| C    | 5  | 12.8%|
| D    | 4  | 10.2%|
| E    | 17 | 43.5%|
| Total| 39 | 100.0%|

Out of 40 cases, maximum numbers of cases were in the grade E 17 cases (42.5%), followed by grade B 9 cases (22.5%), followed by 5 cases each in Grade A and Grade C, rest of the 4 cases were in Grade D.
Table 7.1: Table illustrating progression of ASIA grading over periodic

| ASIA | A | B | C | D | E | Total |
|------|---|---|---|---|---|-------|
| Asia | A | B | C | D | E | N    |
| Baseline | 5 | 12.8% | 8 | 20.5% | 5 | 12.8% | 4 | 10.2% | 17 | 43.5% | 39 | 100.0% |
| 3 Month | 3 | 7.7% | 7 | 17.9% | 7 | 17.9% | 3 | 7.7% | 19 | 48.7% | 39 | 100.0% |
| 6 Month | 0 | 0.0% | 2 | 5.1% | 8 | 20.5% | 7 | 17.9% | 22 | 56.4% | 39 | 100.0% |
| 9 Month | 0 | 0.0% | 0 | 0.0% | 1 | 4.5% | 5 | 22.7% | 16 | 72.7% | 22 | 100.0% |
| 12 Month | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 1 | 7.1% | 13 | 92.9% | 14 | 100.0% |
| 15 Month | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 7 | 100.0% | 7 | 100.0% |
| 18 Month | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | 5 | 100.0% | 5 | 100.0% |

At 6 months follow-up, out of 39 cases, 22 were in grade E, 7 cases in grade D, 8 cases in grade C and only one case in grade B. Significant improvement was noted in neurological status of the cases over the time.

8. Comparison of baseline Oswestry disability index (ODI) with subsequent follow-up visit ODI score

| ODI (%) | N | % |
|---------|---|---|
| 40-50   | 7 | 17.5% |
| 51-60   | 10 | 25.0% |
| 61-70   | 5 | 12.5% |
| 71-80   | 8 | 20.0% |
| 81-90   | 5 | 12.5% |
| 91-100  | 5 | 12.5% |
| Total   | 40 | 100.0% |

9. Comparison of baseline erythrocyte sedimentation rate (ESR), with subsequent follow up visit ESR

| ESR <= 20 | 4 | 10.0% |
| 21-40     | 10 | 25.0% |
| 41-60     | 15 | 37.5% |
| 61-80     | 10 | 25.0% |
| 81-100    | 1 | 2.5% |
| Total     | 40 | 100.0% |

Maximum numbers of cases were in the range of 20-60 mm at the end of 1 hour. 87.5% (35 cases). There was significant improvement in Erythrocyte Sedimentation Rate (ESR) over the subsequent follow up visit up to 6 months. The mean Baseline ESR rate was improved from 49.59±18.64 to 21.72±10.66 mm at the end of 1 hr in 1st 6 months for all 39 cases.

Clinical cases

A case Managed conservatively: Plain radiograph of thoracic spine ap/lat view, Recent MRI showing improvement. (Conservatively managed) sagittal (a) and axial (b) cut of MRI showing altered signal intensityD8-D11 vertebrae (Fig.1)

A Case Managed Surgically: X-ray and MRI affected level D8-D9 (Fig 2)
Discussion

Tuberculosis of spine is an ancient disease. Its outcome has improved significantly due to availability of potent antitubercular drug, early detection with various molecular amplification based method, availability of various imaging technique and surgical technique. Early detection of multidrug resistant spinal tuberculosis, with proper chemotherapy only or if required surgical intervention with chemotherapy play vital role for the management of drug resistant spinal tuberculosis.

This study was conducted to study the prevalence of multidrug resistant spinal tuberculosis. For early detection of drug resistant spinal tuberculosis Gene xpert test was used. It is also planned to do further drug susceptibility test on samples tested Rifampicin resistance by Gene-xpert test. It was also followed-up to know the clinical outcome. Total number was 40 patients, who were enrolled in this study, patients follow up, was also done. The average follow up period of patients in months (maximum follow up of 18 months with and minimum 6 months). In this study it was noted that patients were detected having spinal tuberculosis in the range of 21-70 years.. Thus supporting the fact that spinal tuberculosis mostly affects the population in the productive age group.

This was comparable to a study Ayush Sharma et al., Magnetic Resonance Imaging and Gene-Xpert: A Rapid and Accurate Diagnostic Tool for the Management of Tuberculosis of the Spine of 145 patients, average age of the patients was 45.8±19.1 years [9]. However, Tuli SM, Tuberculosis of the skeletal system: bones, joints, spine and bursal sheaths reported spinal tuberculosis mostly affected patients in the 1st three decades [8].Kumar M, et al, Sensitivity of PCR IS6110 in relation to culture and staining in Pott's disease of 65 cases, reported mean age was 40.7 years [10].

This will be comparable to study conducted Ayush Sharma et al., Magnetic Resonance Imaging and Gene-Xpert: A Rapid and Accurate Diagnostic Tool for the Management of Tuberculosis of the Spine of 145 patients [9] reported male: female ratio of 1:0.96. However, Tuli SM, Tuberculosis of the skeletal system: bones, joints, spine and bursal sheaths reported spinal tuberculosis noted there was no sex difference in prevalence of spinal tuberculosis [10]. Kumar M, et al., Sensitivity of PCR IS6110 in relation to culture and staining in Pott's disease of 65 cases, reported male to female ratio of 1.3:1 [10]. In this study thoracic region of vertebral column was most commonly involved (57.5%), followed by Lumbosacral (22.5%) and thoracolumbar junction (17.5%). This was comparable to study by Sadik I Shaikh et al., 2013(53) in which also thoracic vertebrae were involved in 60% of study population followed by lumbar spine [11]. The study by Qing-Yi et al [12] in 54 patients of spinal tuberculosis in which thoracic region was most commonly involved, in about 52% (28 out of 54 patients). The Tuli SM, Tuberculosis of the skeletal system: spine [8] reported dorsal spine most commonly affected 42%, followed by lumbar spine 27% and dorsolumbar in 12% patients. In this study, 62.5% patients had involvement of 2 levels, 17.5% patients had involvement of 3 levels, 7.5% patients had involvement of one level and 5 patients had involvement of 4 levels. This was comparable to study by Litao Li et al [13] where they found 46% (16 out of 35 cases) involvement of 2 levels their study, and the maximum number of levels involved was 13 in one patient.

The study is related to, back pain which would be the most common symptoms seen in all (100%) cases, followed by a constitutional symptom in 28 cases (70%), followed by neurodeficit 57.5% and deformity in 20% patients. These results were comparable with study conducted by Kumar M, et al. Sensitivity of PCR IS6110 in relation to culture and staining in Pott's disease of 65 cases, reported back pain was most common complaints in all 65 patients in different grades [13]. Similar incidence of neurodeficit (51.4%) and of deformity of 23% was reported by Litao Li et al. [12].

Most of the cases of spinal tuberculosis diagnosed on the basis of x-ray findings and the sensitivity of plain radiograph ranges from 91-99% [14]. It has been reported by Peter/ Polley et al that incidence of Non-contiguous spinal tuberculosis is increasing. They reported 16 patients having radiographic changes suggestive of Non-contiguous spinal tuberculosis out of 98 patients (16%). In our study skip lesions were reported in 6 patients out of 40 patients (15%).

We need to perform fluoroscopic guided transpedicular biopsy number of patients under local anaesthesia, CT guided biopsy in number of patients and in some patients samples were collected intraoperatively. Out of these patients, Mycobacterium tuberculosis was detected by gene xpert test in patient’s sample (57.14%), this was similar to study conducted by Shrestha D, Shrestha R, Dhoju DF, Fluoroscopy Guided Percutaneous Transpedicular Biopsy for Thoracic and Lumbar Vertebral Body Lesion: Technique and Safety in 23 Consecutive Cases. However they reported accuracy rate 92% (12 patients detected by histopathology out of 23 patients) and procedure performed under general anaesthesia [15].

CT scan, fluoroscopy or MRI will be used for image guidance. CT scan provides better image quality and small lesion can be reached more accurately. However, increased radiation
exposure to the patients and physician, cost, availability and difficulty on adjusting into CT gantry machines during biopsy are some of the issues related with CT guidance. Fluoroscopy is easily available in our centres, provides real time image while passing the guide wire and biopsy trocar. When this procedure is performed in operation theatre either in general anaesthesia or local anaesthesia, any unexpected complications such as bleeding, pneumothorax or vascular injury can be immediately addressed which could be difficult in CT scan room in radiology department [16].

Pain will be assessed using Visual Analogue Scale (VAS) with mean baseline score of 6.6±0.77, and see for significant improvement in the VAS score for the back pain over the duration. The improvement in the VAS score will show a consistent pattern, with improvement being significant at each follow up visit up to 12 months. The mean VAS score at final follow, at the end of 18 month was 1.2±0.84, and periodic interval at 15 month, 12 months, 9 month & 6 month follow up. The maximum improvement in VAS scores were in 1st 6 month (50%). Qing-Yi He et al [10] reported similar improvement in VAS score in there study of treatment effect and postoperative complication in 54 patient of thoracic and lumbar spinal tuberculosis. In their study VAS score of 7.8±1.7 improved to 3.2±2.1 at the last follow up. At the onset of study as per Oswestry Disability Index (ODI) score, 42.5% cases presented with severe disability, 32.5% cases were crippled and 25% cases were bed ridden. At 6 month follow up of all 39 patient 20% cases showed minimal disability, 30.8% showed moderate disability, 20% cases showed severe disability, 18% cases still crippled and 2.5% bed ridden.

There was significant improvement in the Oswestry Disability Index score for disability arising as a consequence of the backpain. The improvement in disability score was consistently significant at each follow up visit up to 12 month, suggestive of progressive decrease in the disability due to the back pain.

The mean ODI score at the baseline 65.79±16.07 improved to 38.16±21.82 at 6 month follow up of all 39 patients. The result are comparable to a study by Jia Huang et al [71] in which they evaluated the clinical outcomes of surgical treatment of non-contagious spinal tuberculosis in 23 cases. In their study, mean ODI was improved from 52.57 before surgery to 25.36 at the last visit

The American Spinal Injury Association (ASIA) score was used to evaluate neurological deficit. Baseline ASIA score were Grade A5 cases, Grade B 8 cases, Grade C 5 cases, Grade D 4 cases and Grade E 17 cases. At 6 month ASIA score of 39 cases, Grade B 2 cases, Grade c 8 cases, Grade D 7 cases and Grade E 22 cases. 22 patients followed up for 9 month showed one case with Grade C, 5 cases with Grade D and rest of 16 Cases with Grade E. Further follow up of 14 patients up to 12 month showed one case with one case with Grade D and rest of 13 cases belongs to Grade E. This was comparable to study conducted Ayush Sharma et al, Magnetic Resonance Imaging and Gene Xpert: A Rapid and Accurate Diagnostic Tool for the Management of Tuberculosis of the Spine of 145 patients [9]. This study result was also comparable to study conducted by Litaoh Li et al. [13] on retrospective analysis of management of drug resistant spinal tuberculosis in 35 patients reported improvement in ASIA scores from 17 cases with Grade E at the initial presentation to 29 Cases with Grade E at the final follow up visit.

Our study for Assement of Erythrocyte Sedimentation Rate has to be seen and compared with other study conducted by Huang J et al [14]. The clinical outcome of surgical treatment of noncontagious spinal tuberculosis: A Retrospective study in 23 cases ESR return from 55.86 mm/h, 19.86 mg/ml respectively, preoperatively to normal with 12–16 weeks. Our study of 20 patients managed conservatively without neuro-deficit, and other 20 patients in which surgery was indicated, were operated through posterior approach, Posterolateral in lumbar spine / anterolateral decompression in thoracic spine with Pedicular screw instrumentation with cylindrical cage insertion with auto graft (19 patients) and one cervical spine patients operated through anterior approach, decompression (Corpectomy) with bone-grafting fusion with cervical plating done.

The average time were for bony fusion in our study found to be 10 to 11 month, this was in contrast to study By Mohammad Reza Hayeri, et al [16] average time for bony fusion 6 to 9 months.

Histologic studies confirm the diagnosis of spinal tuberculosis in approximately 60% of patients [74]. In our study histopathological examination of samples showed result in favour of spinal tuberculosis in 65% patient (accuracy=65%). These were comparable with study conducted by Tuli SM Ravindra Kumar Garg; Dilip Singh Somvansi Spinal tuberculosis reported positive histological finding in favour of spinal tuberculosis in 60% cases [18]. With the advent of PCR method to test for TB, various studies have reported that the sensitivity of non-automated PCR test ranges from 61-83% [1-3]. The PCR method has the advantages of needing much smaller quantities of mycobacterium tuberculosis and gives rapid diagnosis by amplification of nucleic acid of the pathogen. Its detection limit of 130 colony-forming units (CFU) per millilitres, compared with 10,000 CFU/ml in cultures, increase the probability of diagnosing extra-pulmonary tuberculosis even with samples containing only a few bacteria. In our study sensitivity and specificity of gene expert reported 100% and 58.8% respectively.

We were used study Gene-Xpert test for early detection of drug resistant spinal tuberculosis; out of 40 patients 23 patients (57.5%) had detected Mycobacterium Tuberculosis growth by Gene-Xpert test. Out of 23 patients, 3 patients had Mycobacterium strain showed resistance to Rifampicin. Out of 3 patients 2 patients had culture negative and one patients had culture positive result with DST for 1st and 2nd line Anti Tubercular drugs showed resistance to all 1st line antitubercular drugs (isoniazid, rifampicin, Ethambutol, pyrazinamide and streptomycin) and Ofloxacim and Ciprofloxacin from second line anti-tubercular drugs, and sensitive to remaining 2nd line anti-tubercular drugs. This patient clinical outcome was excelent till the last follow-up visits. The two patients had culture negative result also clinical outcome were good at the last follow-up visits.

The prevalence rate of multidrug resistance spinal tuberculosis in our study was 2.5% (1 out of 40 patients). This was comparable with rate of multidrug spinal tuberculosis in new cases 2.3% by World Health Organization [19]. Furthermore, rate of rifampicin resistance was 7.5% in our study (3/40). This was similar to a study by Ayush Sharma et al. [9], they noted rate of rifampicin resistance was 4.8% (7/145).

Definitive Multidrug resistance spinal tuberculosis reported in one patients i.e. 2.5% and rest of 2 patients with rifampicin resistance had culture negative report considered as probable Multidrug resistance spinal tuberculosis 5% (2 out of 40 patients ), because of low sensitivity of culture test, culture
In our study, two patients detected with Rifampicin Resistance and culture negative report had histology suggestive of Granulomatous lesion. Considered as probable Multi-Drug Resistance spinal TB. In our study two patients had Rifampicin-Resistance with culture negative report have been missed without Gene-Xpert test. This was comparable study conducted by M. Held, Gene-Xpert polymerase chain reaction for spinal tuberculosis, in there study they reported out of 69 patients 4 patients had rifampicin resistance with gene expert test, out of 4 patients one patient had culture negative [6].

Our study is based on other studies, about Sensitivity of PCR, relation to culture and staining sensitivity and specificity of gene expert test. Kumar M, et al. Sensitivity of PCR IS6110 in relation to culture and staining in Pott's disease of 65 cases, the sensitivity and specificity of gene expert test 94% and 64% respectively. However, by Ayush Sharma et al. [66] reported sensitivity of gene expert test was 93.4% and by M. Held [6], the sensitivity and specificity of Gene Xpert test was 95.6% and 96.2% respectively.

One of the disadvantages of Gene-Xpert (PCR) test is that, in contrast to TB culture, gene expert testing will give a positive result even if the pathogen are not viable [21]. In these patients active spinal tuberculosis has to be confirmed clinically and by means of various imaging modalities. Another concern about gene expert method is that it tests drug resistance only for rifampicin; there for a mono resistance to Isoniazid can only be detected with other tests. According to current treatment guidelines Isoniazid mono-resistance does not alter conventional TB regime for patients without Isoniazid mono-resistance [22]. Other PCR tests like line probe assay detect resistance simultaneously for Isoniazid and rifampicin, but sensitivity and specificity for extra-pulmonary tuberculosis detection of Gene-Xpert test is more as compared with line probe assay. Line probe assay technically more difficult, long duration (takes 5 day) carried only on smear positive samples and extra-pulmonary samples Pauci Bacillary, and they are mostly smear negative [1].

Conclusion
The spinal tuberculosis encountered 15% of amongst all extra-pulmonary cases, mostly affecting productive age groups, leads to increase Morbidity and Mortality in community and increasing socioeconomic burden in community. Prevalence of Pott’s disease is continuously increasing in developing countries. A delay in both the diagnosis and initiation of treatment as well as the failure to recognise cases of drug resistance lead to adverse effect on prognosis of spinal tuberculosis. Drug resistance has been recorded in history as old as the development of antibiotics. The bacteria undergo mutation when exposed to newer antibiotics and it occurs more if the drugs are exposed in subclinical doses. Drug resistance is a mammade problem and arises as a consequence of in appropriate treatment. Early detection of MDR spinal Tuberculosis would be helpful to avoid consequences of inappropriate chemotherapy and result in favourable outcomes.

1. The prevalence of MDR-TB, our study which will be comparable to the 2.3% reported by WHO in India. But, a firm conclusion can be made depending on our sample size (20 cases).
2. Our study based on high sensitivity of Gene Expert test in detection of mycobacterium Tuberculosis with immediate results.
3. The clinical result in the one MDR spinal tuberculosis patient, will be with support and fact that, early detection of MDR spinal tuberculosis and appropriate chemotherapy according to DST will led to favourable outcomes.
4. Finally we recommend its use in following situations because of its high sensitivity and rapid results:
   - Therapeutically refractory cases.
   - Cases, where the imaging is atypical that of potts spine.
   - Patients undergoing surgery, as not separate procedure if required for obtaining the tissue sample intraoperatively.
   - Inspite of this, we cannot make a statement with regard to Gene-Expert Test, being used as routine diagnostic tool.
5. Gene-Expert test can be included in routine diagnostic profile of spinal tuberculosis or in all extra-pulmonary tuberculosis cases, for precise diagnosis, appropriate treatment and control of MDR spinal TB. More such studies are needed on large sample size of cases.

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