Original Article

Postoperative Neurological Outcome in Spinal Tuberculosis Patients Presenting with Severe Neurological Deficits

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ABSTRACT

Objective: To determine the postoperative neurological outcome in spinal tuberculosis patients presenting with severe neurological deficits.

Materials and Methods: 57 patients of 22 to 65 years of spinal tuberculosis were included in this study from January 2018 to March 2023. Data was collected from the hospital records of the patients who were admitted and operated on for tuberculosis of the spine. All regions of the spine were taken for study. ASIA scoring was done and patients were labeled from ASIA scores A to E. All patients were operated and postoperative ASIA scoring was also done on follow-up visits. An Independent sample t-test was used to assess the difference in the mean of these variables.

Results: The mean age was 44.45 ± 8.54 years. Males were 39 and females 18. Preoperatively 27 patients had ASIA B, 28 patients had ASIA C and 02 patients had ASIA D score. All these patients improved postoperatively. The mean preoperative ASIA Score was 2.03 ± 2.4 and the mean postoperative ASIA score was 4.1 ± 1.3 with p-value of 0.02. Patients having old age, who present late and with poor grades in neurology had worse outcomes postoperatively.

Conclusion: Patients with spinal tuberculosis presenting even with severe neurological deficits had significant improvement in neurology postoperatively.

Keywords: Spinal tuberculosis (TB), American Spinal Injury Impairment Score (ASIA), Mycobacterium Tuberculosis, Potts disease, Trans-pedicular decompression and fusion, Laminectomy, Magnetic resonance imaging (MRI).

DOI: 10.36552/pjns.v27i3.916
INTRODUCTION

There is a very high incidence of tuberculosis of the spine or Potts disease in this area of the world (30-40%).¹ This ratio is very high compared to developed countries. Spinal tuberculosis is caused by the microorganism Mycobacterium Tuberculosis. 60 species of this bacterium have been identified but only a few are being associated with the disease.² This is an aerobic microorganism that primarily affects the lungs and causes pulmonary tuberculosis. It then spreads secondarily from the lungs to the other parts of the body via a hematogenous route. Spinal tuberculosis may be caused by the spread of microorganisms from the genitourinary tracts.³ Spinal TB is primarily an anterior pathology of the spine. It affects the metaphysis of vertebral bodies. If one vertebra is affected the disc will remain normal but if two vertebrae are affected, the intervening disc which is a vascular and cannot receive the proper nutrition ultimately collapses. This leads to caseous necrosis, pus formation, and destruction of the vertebral bodies. This usually affects the thoracolumbar region but it can affect any part of the spine from the cranio-vertebral junction down to the lumbosacral region.⁴⁵ The infection spreads from the vertebral bodies to the adjoining tissues and leads to paravertebral collections and abscess formation. Psosas abscess formation is very common. These abscesses and necrotic material damage the anterior and posterior longitudinal ligaments and form epidural collections. These cold abscesses and epidural collections cause the compression of the spinal cord and nerve roots which leads to neurological deficits.⁶

Clinically there should be a high index of suspicion in patients having constitutional symptoms, weight loss, low-grade fever, and presenting with back pain. Clinical manifestations depend on the location of the disease and the stage of pathology. In uncomplicated cases, a patient presents with back pain which is due to inflammation of the disease process or the destruction of the bone and instability.⁷⁸ Pain at rest is pathognomonic of infection but sometimes the radicular pain is the presenting symptom in patients of spinal tuberculosis. In complicated cases, the patients will present with spinal deformity, instability, or with neurological deficits. Spinal deformity is due to the destruction of vertebral bodies anteriorly leading to kyphosis.⁹ This occurs mostly in thoracic and thoracolumbar regions and there will be gibbus formation at the back. Neurological deficits are due to compression of the nervous tissue or due to spinal instability which causes the mechanical traction of the spinal cord and leads to neurological deficits. The diagnosis is made based on the chest x-ray, sputum cultures, and Mantoux tuberculin skin test. The gold standard in the diagnosis of spinal tuberculosis is the MRI of the spine with intravenous contrast. This demonstrates the disc space infection, osteomyelitis, its extension into the paravertebral tissues, and destruction of longitudinal ligaments. The spinal cord status and nerve root compression are very clearly demonstrated on MRI.¹⁰¹¹ Sometimes the diagnosis is not clear, so tissue diagnosis with needle biopsy under CT guidance is required to obtain tissue diagnosis. This aspiration also helps in drainage of pus which also improves the pain of the patient.¹²

The goals of the treatment of the patient with spinal TB are as follows. The first goal is to treat the infection of the patient. The second goal is to prevent the development of drug resistance during treatment.¹³ The third goal is to prevent the disability caused by spinal deformity and neurological deficits. The fourth goal is to prevent the relapse of disease. Initially, the patient is given
the medical management by antituberculosis medications. These are isoniazid, rifampicin, pyrazinamide, ethambutol. These are given according to body weight. Patients who fail medical management or those who develop neurological deficits, spinal deformities, or severe pain due to spinal instability need surgical treatment. The treatment protocol varies depending on the location of the disease, an extension of the disease process, and the goals of surgery. The primary goals of surgery are drainage of the pus, debris, and necrotic material, decompression of the neural elements, and spinal stabilization and fusion. These goals can be achieved by the anterior approach, anterolateral approach, posterolateral approach, or the posterior approach to the spine. In the anterior surgical approach, transthoracic thoracotomy is done which is followed by debridement of debris and necrotic material and fusion with a mesh cage. In the posterior or posterolateral approach, laminectomy or transpedicular decompression is done which is followed by transpedicular screw fixation and fusion with bone graft. In both cases, the ultimate goals of surgery including debridement, decompression of neural tissue, and fusion must be achieved.

The post-operative outcome of the patient with spinal TB depends on various factors. It depends on the age of the patient, stage of the disease, socioeconomics of the patient, proper compliance with the treatment, and neurological deficits. Patients usually present with severe neurological deficits. Patients presenting at a younger age had a good neurological outcome as compared to patients with old age because of the micro-vascular changes in the spinal cord blood supply. Patients presenting with spasticity had a good neurological outcome as compared to patients having flaccidity. Patients presenting late with neurological deficits had a bad prognosis as compared to patients presenting early. As the duration increases, there is myelomalacia of the spinal cord, and intramedullary signal changes. These changes if prolonged may lead to permanent changes in the spinal cord and adversely affect the neurological outcome.

In this study, those patients with spinal tuberculosis will be evaluated who present with severe neurological deficits leading to surgical treatment. So what will be the outcome for these patients? This is the question of this study. The rationale for selecting this question is that spinal TB is a very common disease that is daily encountered in outdoor clinics and these patients frequently require both medical and surgical treatments. No local study is available on the surgical outcome of these patients who present with severe neurological deficits.

MATERIALS AND METHODS

Study Design and Setting
This retrospective study was conducted in the Neurosurgery department of Bakhtawar Amin Hospital Multan from January 2018 to March 2023.

Inclusion Criteria
57 patients of 22 to 65 years with spinal tuberculosis were included in this study.

Exclusion Criteria
Patients having other spine pathologies like spondylolisthesis, spine or pelvic tumors, pyogenic infections of the spine, spine deformity like scoliosis, and patients who are medically unfit for surgery were excluded from the study.

Sampling Technique and Sample Size
57 patients were included by simple random sampling technique in our study. The sample size was calculated using the software G-Power version 3.1.9.4. Considering the values of effect size as 0.3, alpha as 0.05, and power of the test as 80% a sample size of 98 was calculated. However,
we took a sample size of 57 patients.

**Data Collection**

Data was collected from hospital records, patient files, and patient databases. The follow-up records were collected and operation theater register was checked and data was collected from all these sources. 57 patients were included in our study who was admitted to our hospital with spinal tuberculosis during the time period all patient had neurological deficits. These were examined by a consultant neurosurgeon having more than 5 years of experience. The ASIA score was used to evaluate the state of neurological deficits\(^2\) (Table 1). Patients having ASIA A, B, and C were taken as having severe neurological deficits, and ASIA D and E were taken as good grades. Data was collected on the age, gender of patients, and clinical features. Clinical features include pain, fever, deformity, spasticity, and sphincter involvement. The patients were categorized by level of lesion whether cervical, thoracic, or lumbosacral regions.

**Table 1:** ASIA Score\(^2\).

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
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<tbody>
<tr>
<td>A</td>
<td>Complete No motor, no sensory, and no sacral sparing.</td>
</tr>
<tr>
<td>B</td>
<td>Incomplete No motor but sensory only intact. 50% of muscles having power grade</td>
</tr>
<tr>
<td>C</td>
<td>Incomplete LESS than grade 3 (cannot raise arm or leg off the bed). 50% of muscles having power grade</td>
</tr>
<tr>
<td>D</td>
<td>Incomplete MORE than grade 3 (can raise arm or leg off the bed).</td>
</tr>
<tr>
<td>E</td>
<td>Normal Motor and sensory functions are normal.</td>
</tr>
</tbody>
</table>

**Clinical and Radiological Management**

All patients started anti-tuberculosis treatment under the kind supervision of a consultant physician. Drugs were isoniazid at a dose of 10 mg/kg body weight (10-15 mg/kg) for 18 months, rifampicin 15 mg/kg body weight (10-20 mg/kg) for 18 months, pyrazinamide 35 mg/kg body weight (30-40 mg/kg) for 3 months and ethambutol at 20 mg/ kg body weight (15-25 mg/kg) for 3 months.

Every patient was clinically evaluated by a consultant neurosurgeon. X-ray radiography was being done on all patients. In the radiology department during the x-ray, all patients were told to stand straight and fully relaxed. Both anteroposterior and lateral X-rays were done. The Cobbs angle was calculated on a lateral x-ray of the spine to determine the kyphotic deformity of the spine. Magnetic resonance imaging is done of all patients with intravenous contrast to determine the caseous necrotic material, pus formation, spinal cord and nerve root status, disc status, and paravertebral collections.

**Surgical Management**

All patients have undergone surgery. The surgical approach varies depending on the level of the lesion, extension of the pus and necrotic material, and goals to achieve. The ultimate goals of surgery were debridement of dead tissue, decompression of the spinal cord, and kyphotic deformity correction. As far as the anterior approach is concerned in which corpectomy and mesh cage fusion were done, this was done in the cervical region via transverse cervical approach, in the thoracic and thoracolumbar region by transthoracic thoracotomy approach, and in the lumbar region by retroperitoneal approach. In this approach, the complete vertebral body, debris, granulation tissue, and pus were drained. This leads to anterior decompression and fusion with a mesh cage impregnated with bone. A posterior surgical approach was done in which decompression with laminectomy and instrumental fusion was done with transpedicular screws (Figure 2). At cranio-vertebral junction TB, occipitocervical fusion was done. In tuberculosis of the lumbosacral junction the lumbo-pelvic fixation was done (Figure 1). In the thoracic
region, a posterolateral approach was done in which costotransversectomy and transpedicular decompression was done. This leads to vertebral column resection and cage fusion (Figure 3). Patients were discharged in about 5-7 days. They were sent to rehabilitation treatment.

**Outcome Assessment**
Patients were assessed pre-operatively for ASIA score. They were categorized into ASIA A to E depending on their neurological status. Their mean and SD were calculated. Sphincter involvement and spasticity were also checked preoperatively. These patients were checked again on follow-up on 3-6 months and later on 9-12 months. ASIA scoring was done again depending on the neurological improvement. These were compared to pre-operative scores. X-ray was done on all patients to determine the implant status and fusion rate.

**Statistical Analysis**
SPSS (Statistical Pack of Social Sciences 26.0) was used to do statistical analysis. Categorical variables were evaluated by percentages. Numeric variables were assessed by mean and Standard deviation. An Independent sample t-test was used to assess the difference in the mean of the quantitative variables. A 5% level of significance was taken and p-value < 0.05 was taken as significant.

**RESULTS**

**Gender & Age Information**
Total 57 patients enrolled. The mean age of the patients was 44.45 ± 8.54 years. There were 39 males (68.4%) and 18 females (31.5%). ASIA scoring was done.

**Clinical Information**
44% of patients had ASIA A, ASIA B, and ASIA C was recorded in 49% of preoperative patients and ASIA D and E were there in 7% of patients. Sphincter involvement of the bladder region including urinary retention or incontinence was in 74% of patients. Back pain either due to pus formation or due to deformity was present in 84% of patients. (6% of patients were having spasticity of limbs on presentation. Sensory impairment either in the form of loss of touch, temperature, or two-point tactile discrimination was observed in 95% of patients. Spinal deformity in the form of kyphosis was recorded in 55% of patients presenting with spinal tuberculosis (Table 2).

**Table 2: Demographic analysis.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Results</th>
</tr>
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<tbody>
<tr>
<td>Age</td>
<td>44.45 ± 8.54</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>- Males</td>
<td>39 = 68.4%</td>
</tr>
<tr>
<td>- Females</td>
<td>18 = 31.5%</td>
</tr>
<tr>
<td>ASIA A</td>
<td>44%</td>
</tr>
<tr>
<td>ASIA B &amp; C</td>
<td>49%</td>
</tr>
<tr>
<td>ASIA D &amp; E</td>
<td>7%</td>
</tr>
<tr>
<td>Sphincter involvement</td>
<td>74%</td>
</tr>
<tr>
<td>Pain</td>
<td>84%</td>
</tr>
<tr>
<td>Spasticity</td>
<td>96%</td>
</tr>
<tr>
<td>Sensory impairment</td>
<td>95%</td>
</tr>
<tr>
<td>Spinal deformity (Kyphosis)</td>
<td>55%</td>
</tr>
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</table>

**Surgical Procedure**
Anterior surgical approach including corpectomy and fusion was done in 8 cervical, 8 thoracic, and 3 lumbar region TB cases. A posterior surgical approach which includes laminectomy, decompression, and transpedicular fusion was done in 6 cervical regions, 18 thoracic regions, and 10 lumbar region TB cases. The posterolateral approach of costotransversectomy was done in 4 thoracic TB cases (Table 3).

**Neurological Improvement**
In the cervical region, 14 patients were operated. 8 patients had ASIA B and 6 patients had ASIA C scores preoperatively. Patients with ASIA B
improved to ASIA D on follow-up and patients with ASIA C improved to ASIA D in 5 patients and ASIA E in 1 patient. Patients of thoracic TB had ASIA B in 19 patients and ASIA C in 11 patients. Patients of ASIA B improved to ASIA D on follow-up. Patients of ASIA C improved to ASIA D in 08 patients and ASIA E in 3 patients (Figure 2). Patients having lumbar spine TB had ASIA C in 11 patients who improved to ASIA D postoperatively on follow-up (Figure 3). Neurological improvement occurred in all patients (Table 4). Analytical analysis was done of ASIA score both preoperatively and postoperatively. The mean and SD of the ASIA score preoperatively was 2.03 ± 2.4 and postoperatively 4.1 ± 1.3 with p value of 0.02. This shows significant improvement in neurology postoperatively (Table 5).

Table 3: Surgical procedures (Regions and type of procedure)

<table>
<thead>
<tr>
<th>Surgical Procedure</th>
<th>Cervical</th>
<th>Thoracic</th>
<th>Lumbar</th>
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<tbody>
<tr>
<td>Anterior approach corpectomy and fusion</td>
<td>8 (14.0%)</td>
<td>8 (14.0%)</td>
<td>3 (5.2%)</td>
</tr>
<tr>
<td>Laminectomy, decompression, and fusion</td>
<td>6 (10.5%)</td>
<td>18 (31.5%)</td>
<td>10 (17.5%)</td>
</tr>
<tr>
<td>Posterolateral transpedicular decompression and fusion</td>
<td>-</td>
<td>4 (7.0%)</td>
<td>-</td>
</tr>
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</table>

Figure 1: A = Preoperative picture of the tuberculosis of the spine at the lumbosacral junction. B = Postoperative picture of the lumbopelvic fixation via iliac screws (Pictures of radiographs and MRI are added with permission of the patients).

Figure 2: Preoperative picture of the tuberculosis of the spine with pus formation B = Postoperative picture of decompression and transpedicular screws fixation (Pictures of radiographs and MRI are added with permission of the patients).

Figure 3: A = Preoperative picture of the tuberculosis of the thoracic spine with spinal cord compression. B = Postoperative picture of transpedicular decompression, transpedicular screws fixation, and anterior mesh cage (Pictures of radiographs and MRI are added with permission of the patients).
Factors Determining Neurological Improvement

As far as factors affecting neurological improvement were concerned, age was checked for patients with neurological improvement. Patients were taken of more than 45 years of age and they were compared to young patients. There was a significant delayed improvement in old-age patients with a p-value = 0.03. Patients were taken having more than 1 month of neurological deficits. These were 26 patients. Out of them, 5 improved in 3-6 months follow-up and 21 improved in 9-15 months follow-up with a p-value = 0.46. Bladder involvement was observed in 39 patients. 13 patients improved in 3-6 months and 26 patients were observed in 9-26 months with a p-value of 0.02. This showed that there is no significant improvement in patients with a duration of neurological involvement more than 1 month. Spinal cord intramedullary changes were observed in 17 patients preoperatively. 5 patients improved in 3-6 months and 12 patients improved in 9-15 months with a p-value of 0.04. This showed that spinal cord changes had a significant effect on the improvement of neurological status postoperatively. 27 patients had ASIA B preoperatively and 6 patients improved in 3-6 months and 19 improved in 9-15 months with a p-value of 0.12. This showed no significant relation of improvement in patients of ASIA B. 28 patients were presented with ASIA C. Out of these 6 improved in 3-6 months and the rest 19 in 9-12 months with p value 0.01. This showed significant improvement in ASIA C patients (Table 6).

DISCUSSION

Spinal Tuberculosis is a very common pathology we encounter in our daily clinical practice in developing countries. The spine is always affected secondarily because primary tuberculosis occurs elsewhere in another part of the body. This occurs in the lungs or in the genitourinary tract which then affects the spine. Mycobacterium tuberculosis is the causative organism. This aerobic bacillus destroys the metaphyseal region of the vertebrae which leads to sequestrum formation, caseous necrosis, and abscess.
formation. This leads to compression of the spinal cord and neural elements. The necrosis also causes endarteritis, infective thrombosis, and myelitis. Treatment initially is via anti-tuberculosis medications which continue for a period of 16 to 18 months. The majority of patients get better with these medications. The patients, who develop intractable pain either due to pus formation or spinal deformity, develop progressive neurological deficits or spinal instability and need surgical intervention. Pathology varies depending on the location of the disease in the spine. In the cervical region, it may affect the cranio-vertebral junction and vertebra bodies anteriorly and may cause retropharyngeal abscess formation. In the thoracic region, it causes the abscess formation and causes the compression of the spinal cord. In the lumbosacral region, it causes psoas abscess formation.

Surgical technique varies depending on the location of the lesion. In the cervical region, mostly anterior trans-cervical approach was used with decompression of the vertebral bodies and discs. This was followed by cage fusion. In 8 patients anterior trans-cervical approach was done and in 6 patients posterior approach was done. The anterior cervical approach was good in providing adequate decompression and anterior stabilization. But the posterior cervical approach was good in maintaining the cervical lordosis by using lateral mass screws and posterior laminectomy. In the thoracic spine, transthoracic approach was done in our 8 cases(Figure 2). For this thoracic surgeon help was taken for doing thoracotomy. At 1 to 2 level decompression, removal of dead tissues, and stabilization with titanium mesh cage was done. In the rest of the 18 cases, posterior decompression, transpedicular decompression of the anterior debris, and pedicle screw fixation and fusion were done (Figure 3). In this, there was an improvement in neurological status postoperatively in both surgical approaches. However, the improvement in neurological status was early in patients having an anterior approach on follow-up as compared to a posterior approach because TB spine is primarily an anterior disease and during anterior decompression, there is adequate removal of dead tissue. Our study collaborated with the international literature. Jain et al, studied transpedicular decompression in patients having Potts disease. They used Frankel grading to assess the preoperative and post-operative neurological improvement of patients and they found improvement in Frankel Grade post-operatively after transpedicular decompression. Alruwaili et al, studied TB spine surgery in the dorsal spine by transthoracic approach and found improvement in neurology postoperatively. In the lumbar region, 3 patients required a retroperitoneal approach with decompression and fusion with cage and bone graft but in 10 patients’ posterior decompression, debridement, and fusion with trans-pedicile screw fixation were done (Table 3).

As far as neurological improvement postoperatively was concerned, the majority of patients presented in our clinics were ASIA B, C, or D. These were having spasticity in limbs. Almost all patients improved postoperatively and there was significant improvement with p value of 0.02. The majority of patients with ASIA B recovered to ASIA C or D postoperatively. Other patients with ASIA C recovered to ASIA D or E in a 9-12-month period. One study was done by Choi et al, which showed neurological recovery in 63-65% of patients. Other studies done by Dunn et al, showed similar results with all patients improved including 4 patients of ASIA A. 17 patients started walking postoperatively as compared to 5 patients who were non-ambulatory preoperatively. Zaho et al, studied surgical results in patients in patients of TB spine with severe lower limb weakness, these also showed 75-85% recovery in them. In this research, 40% of patients recovered in the initial
3-6 months, and 97% of patients recovered in 15 months of follow-up (Table 4).

The factors affecting neurological improvement were also taken into consideration. These were the age of patients, bladder involvement, spasticity, and duration of neurological involvement. First of all, patients were considered according to the age of the patient. Various studies have been done on this topic. One is by Okazaki et al, in the treatment of patients with Potts paraplegia, another by Medin et al, on the vasogenic edema on the chronic spinal cord compression. The younger patients improve early as compared to old age patients. Ridlen et al, showed that old age patients had atherosclerosis of arteries so they lose their compensatory dilation of the arterioles as a result of decompression. In young patients, this phenomenon occurred resulting in early neurological improvement. This also correlated with our research in which young age patients improve early.

Patients having the status of neurological deficits at the time of presentation have a significant role in the outcome after treatment. Khorasanizadeh et al, found that patients having severe deficits improve later as compared to moderate deficits. Debnath et al, studied the status of neurological deficits in patients with TB spine. They found no such difference in patients presented with ASIA A B or C preoperatively. They found 87% recovery in patients of ASIA A or B and 93% recovery in patients of ASIA C. This study showed that 27 patients had ASIA B preoperatively 6 patients improved in 3-6 months and 19 improved in 9-15 months with p value 0.12. This showed no significant relation of improvement in patients of ASIA B. Like this 28 patients were presented with ASIA C. Out of these 6 improved in 3-6 months and the rest 19 in 9-12 months with p value 0.01. This showed significant improvement in ASIA C patients. So the patients who were presented with a good neurological grade of ASIA C preoperatively had a better neurological outcome as compared to patients with a bad neurological grade of ASIA B.

As far as the duration of neurological symptoms was concerned preoperatively, various studies have been done. Gautam et al, studied paraplegic patients for more than 6 months. These all improved gradually. Vaishnav et al, studied patient TB spine patients in West India and they found a relation between spinal cord compression and duration in TB spine patients. They found that early presentation leads to early recovery. In this study, patients were taken who present for more than 1 month after the development of neurological deficits. These were 26 patients out of them 5 improved in 3-6 months and the rest improved in 9-15 months. There was no significant difference in the outcome of a patient who presented late with neurological deficits as compared to those who presented early.

Spinal cord intramedullary changes in presentation affect the outcome of symptoms. Banaszek et al, dis studied patients with intramedullary signal changes and the outcome of surgery. They found that patients who had intramedullary signal changes had a significantly delayed outcome after surgery. In this study, 17 patients had intramedullary signal changes, out of these 5 improved in 3-6 months and 12 improved in 9-12 months with a p-value of 0.04 which showed significant improvement in patients who did not have intramedullary signal changes as compared to those who had intramedullary signal changes (Table 6).

Sphincter involvement especially bladder involvement affected the outcome of surgery. Zaouii et al, found that sphincter fibers are located in the medial location of the cross-section of the spinal cord. When extradural compression occurs, these fibers are affected at the end. If they are affected, it means there is severe and prolonged compression. In this study, 39 patients had bladder involvement. Out of these 13 improved in 3-6 months and the rest 26 improved.
in 9-15 months with a p-value of 0.02 which shows a significant effect of bladder involvement on the outcome of surgery.

LIMITATIONS
One limitation of this study was that it was a retrospective study in which data was collected from the hospital records of the patients. The next study should be prospective to determine a better understanding of the results after surgery. The second limitation was that we took only the ASIA score in this study. Other disability scores like the Oswestry disability index and, the Frankel grading system.

CONCLUSION
This study concluded that patients presenting with worse neurological deficits had significant improvement in neurology postoperatively. Patients presenting with neurological deficits with better grades had good outcomes as compared to patients presenting with poor neurological grades.

REFERENCES


Additional Information

Disclosures: Authors report no conflict of interest.

Ethical Review Board Approval: The research was a retrospective study.

Human Subjects: Consent was obtained by all patients/participants in this study.

Conflicts of Interest:

In compliance with the ICMJE uniform disclosure form, all authors declare the following:

Financial Relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.

Other Relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

Data Availability Statement: The data supporting the results of this study can be provided at the request of the corresponding author.

Funding: This study received no specific donation from any funding association in the public, commercial, or not-for-profit sectors.
## AUTHOR CONTRIBUTIONS

<table>
<thead>
<tr>
<th>Author's Full Name</th>
<th>Intellectual/Contribution to Paper in Terms of:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waqas Noor Chughtai</td>
<td>1. Study design and methodology.</td>
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<td>Muhammad Adeel Razzaque</td>
<td>2. Data collection and calculations</td>
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<tr>
<td>Muhammad Shafiq</td>
<td>3. Paper writing, referencing, data calculations and analysis of data</td>
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<tr>
<td>Nauman Ahmed</td>
<td>4. Analysis of data and interpretation of results etc.</td>
</tr>
<tr>
<td>Muhammad Zahid Siddiq</td>
<td>5. Literature review and manuscript writing</td>
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<tr>
<td>Tahira Fatima</td>
<td>6. Analysis of data</td>
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