



Infective Spondylodiscitis – An Indian Perspective

KEYWORDS

spondylodiscitis, pyogenic, tuberculosis, osteomyelitis.

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ABSTRACT **Introduction:** Spondylodiscitis is a morbid illness resulting in neurological deficits in one third of individuals affected. Few studies have been done from India looking at the differences in the pathogen, course and outcome of this disease. This study aims at providing an Indian perspective to the epidemiology of this disease. **Methods:** A retrospective observational study was undertaken looking at data over the last 12 years (2003-2015) among all patients admitted as inpatients into the General Medicine ward in a tertiary level care hospital in South India, with a discharge diagnosis of infective spondylodiscitis from any cause. 61 patients were identified and followed up using electronic records of patient's visits to the outpatient after discharge. The details of their clinical features and imaging findings were also retrieved from the online database of this hospital and analysed using SPSS 16 software. **Results:** Of 61 patients with infective spondylodiscitis, 35 were of tuberculous origin, 23 were of pyogenic origin and 2 were fungal. In one patient no microbe was identified. The time to presentation was significantly different in the two groups with tuberculosis having an average of 6 months vs. only 1 month in the pyogenic group. Back pain was the predominant symptom. MRI had an almost similar appearance in both pyogenic and tuberculous infection offering few distinguishing features between the two. Percutaneous biopsy was done in large number of patients and proved a useful tool to diagnosis. **Conclusions:** Spondylodiscitis in the India shows a different microbiological profile with tuberculosis being the commonest etiology followed by Staphylococcal infections. The time to presentation is longer than seen in western data. MRI of the spine offers little differentiation between tuberculous and pyogenic infection in comparison to western data. The majority of patients underwent medical treatment with surgery being used in only a small number of individuals. While the mortality is less than in literature, the morbidity of neurological deficit is similar.

Introduction

Infective spondylodiscitis is an infection of the vertebral body, its posterior arch and the intervening disc. Accounting for 2-7% of all musculoskeletal infections, this is a potentially fatal disease with hospital mortality rates of 2% to 17%. It usually has an insidious onset and slow progression, presenting initially with non-specific symptoms that make an early diagnosis difficult. The average interval between the presenting symptom and diagnosis ranges between two to six months. Furthermore, due to low back pain being a common complaint in the general population, diagnosis is further delayed. This results in longer hospital stays, poorer outcomes and higher disability rates. Current studies report an average hospital stay of 30 to 57 days.

Spondylodiscitis may pathologically be divided into two broad categories – acute pyogenic and chronic. *Staphylococcus aureus* is the commonest causative organism of the former and *Mycobacterium tuberculosis* of the latter group. While the vertebral body and/or the intervertebral disc are involved in 95% of cases, involvement of the posterior elements of the spine is seen in only 5%. The disease predominantly affects people in the fifth decade and males appear to be affected twice as often as females.

Though a large body of published literature on the clinico-epidemiological profile of infective spondylodiscitis from western nations exists, similar data from the Indian

sub-continent is lacking. Indigenous studies on spondylodiscitis are important due to the stark differences in infectious disease epidemiology between the two regions. In this context, our study highlights unique aspects of the clinico-epidemiological and microbiological profile of infective spondylodiscitis in the Indian sub-continent and captures recent trends in its investigation and management.

Methodology

Setting:

This is a cohort study based on a retrospective review of data, conducted at a 2200-bed tertiary care referral centre in Tamil Nadu. The study was approved by the institutional review board and the human research ethics committee. Data was collected through a review of medical records of all patients more than 18 years of age admitted with a diagnosis of infective spondylodiscitis from 2003 to 2015 (12 years).

Case definition:

The diagnosis of infective spondylodiscitis was based on a combination of clinical features, microbiological and radiological evidence of the same. Patients with an alternate diagnosis such as spondylosis or spondylolysis were excluded.

Variables and outcome:

Clinical data included demography, primary admission diagnosis and history of diabetes mellitus, hyperten-

sion, smoking, significant alcohol consumption or immunosuppressive or other drug therapy. A past history of cardiovascular, renal, respiratory, hepatic dysfunction or underlying neoplastic process was noted. Microbiological and serological data was collected from culture, serology and polymerase chain reaction (PCR) test reports. Radiological data was collected from relevant, x-ray, computed tomography (CT), ultrasound and magnetic resonance (MR) images.

Outcomes:

The primary outcome was in-hospital all cause mortality. Secondary outcome measures included duration of hospital stay and the degree of recovery at discharge. The degree of recovery at discharge was classified as total neurological recovery, partial neurological recovery or cure. Total recovery was defined as complete neurological recovery to pre-morbid baseline levels of functional activity. Partial recovery was defined as only part improvement; either incomplete recovery in a single domain or no recovery in other domains. No recovery was a record of absent recovery from all initial deficits.

Statistical methods:

Data were analysed using STATA version 10.0 (Stata-Corp, College Station, Texas, USA). All statistical tests were two tailed. A p-value <0.05 was considered as statistically significant. Continuous variables which were normally distributed were summarized using mean and standard deviations (SD). Non-normally distributed continuous variables were summarized using median with interquartile ranges. Patients were divided into the three groups; pyogenic, tuberculous and fungal spondylodiscitis for analysis. Continuous variables were compared between the two study groups (pyogenic and tuberculous spondylodiscitis) using either independent two sample t-test or Mann-Whitney U test, as appropriate. Dichotomous variables were compared between the two groups using chi-square or Fisher's exact test, as appropriate. Since fungal infections were few they were not included in the calculation of the tests of significance.

Results

Demography:

A total of 12,062 admissions were screened. Of the 79 patients recruited, 61 patients were included (47 males and 52 females) and 18 excluded. The flow diagram of recruitment and reasons for exclusion are given in Figure 1. The mean (SD) age of the study population was 45(±15.7) years. Details of patient characteristics at admission are given in Table 1.

The state wise distribution of the study population is shown in Figure 2. Of all the patients visiting the study hospital a majority are domiciliary to the states of Tamil Nadu, West Bengal and Jharkhand. These states contributed 62,795, 14,525 and 6454 annual inpatients respectively in 2015. In this study a majority of patients were referred from the states of West Bengal (19/61) and Andhra Pradesh (11/61).

Of the 61 patients, 23(37.8%) had pyogenic spondylodiscitis, 35(57.3%) had tuberculous spondylodiscitis and 2(3.27%) had fungal spondylodiscitis. Overall, the most common associated co-morbidity was diabetes mellitus 38.3% (23/61) followed by HIV, chronic kidney disease and spine surgery [6.7 % (4/61) in each case respectively]. Other co-morbidities such as intravenous drug

abuse and corticosteroid use, although present, were rare 1.7% (1/61) and 3.3% (2/61) respectively. Co-morbid conditions such as haematological malignancy, solid organ transplant, stem cell transplant, abdominal surgeries, epidural procedures, genito-urinary disease and chronic liver disease, described in other published studies were not noted in this study population.

Clinical characteristics:

The clinical characteristics of the patients are described in figures 2 and 2a. The average duration of symptoms prior to presentation was 6.8 months. The time to presentation was markedly different between the tuberculous and pyogenic groups (6 months vs. 1 month). The predominant presenting symptom was pain, [96.7% (59/60)] of the study population followed by fever [58.3% (35/60) of the study population. At the first visit, 23% (14/60) had a motor deficit, 11.5% (7/60) had a sensory deficit and 8.2% (5/60) had an associated autonomic deficit.

Imaging features:

Imaging findings are represented in Figures 4 and 4a. All participants had features of osteomyelitis. 93.3% (56/60) had involvement of the vertebral body and 91.7% (55/60) had features of discitis. Canal compression was a less frequent finding, present in only 33.3% (20/60). 95% (57/60) had evidence of paravertebral involvement.

There were no statistically significant differences between the tuberculous and pyogenic groups with regard to their imaging findings. The site of involvement is represented in Figure 5. The average number of vertebrae affected was 3. In pyogenic spondylodiscitis, the most common site affected was the lumbar vertebrae. This site was involved in 78.3% (18/23) of individuals with pyogenic involvement. In tuberculous spondylodiscitis, the thoracic site was more commonly involved than the lumbar being involved in 60% (21/35) individuals.

Microbiological characteristics:

Laboratory investigations are represented in Figure-6. A percutaneous biopsy has yield of 57.8% (26/45). Blood cultures were diagnostic in 25% (15/25). Open biopsy was done in 13.1% (8/60) patients requiring a diagnostic or therapeutic surgical intervention and was diagnostic in all individuals for whom it was done.

Following the inception of TB-PCR in the host institution in 2011, 8/24 cases were TB-PCR positive. Figure-7 is a graphical representation of the micro-organisms isolated during diagnostic testing. Tuberculosis was the most common micro-organism isolated [57.4% (35/61)]. Pyogenic infections accounted for 37.7% (25/61) and fungal infections for 3.2% (2/61) of all cases respectively. Staphylococcus aureus was the most frequent causative organism in the pyogenic spondylodiscitis group and accounted for approximately half of all non-tuberculous cases [39.1% (9/24)].

Management strategies and outcomes:

Management strategies and outcomes are depicted in figure-8. Medical management was carried out in 100% (60/60) patients. Surgical intervention was required for treatment in one fifth of all patients. Only 51.7% (31/60) patients were confirmed to be cured over the follow up. 46.7% (28/60) patients were lost to follow up. The

mean follow up was 6 months. 41.7% (25/60) people reported complete neurological recovery. Partial recovery and absent recovery were seen in 10% (6/60) and 5% (3/60) respectively. There was only one mortality was recorded in this study from a patient with drug resistant tuberculosis. There were no relapses recorded in the study data. However, it must be noted that both mortality and relapse rate may not be reflective of the actual outcome since 28 (46.7%) of patients were lost to follow up.

Discussion

Infective spondylodiscitis is a relatively rare disease, associated with a significant burden of disability due to clinical diagnosis at a late stage. There exists a paucity of Indian data on this subject. Our study attempts to provide an Indian perspective on the disease, ranging from etiological agents to clinical and imaging characteristics. This study also attempts to identify clinico-epidemiological features that may be unique in Indian subjects.

Clinical features

A male predominance was noted (77%). This observation was similar to other studies, which report disease incidence in males ranging from 51% to 81%. The average age of the study population was 45 years. The study population appeared to largely be between 20-50 years with the minority below 20 years. Other studies describe a bimodal age distribution in infective spondylodiscitis, with one peak at < 20 years of age and the second at the age of 50-70 years. All age groups may however be affected. Multiple studies have been done till date to look at the association of infective spondylodiscitis with other diseases. The most common co-morbidities seen in our study include diabetes mellitus, HIV and preceding spine surgery. Diabetes mellitus, in multiple series has been found to be the most common co-morbidity, reported in 18-66% of all patients. Other co-morbidities such as epidural procedures, lumbar punctures, haematological abnormalities, stem cell transplant, chronic liver disease and infections from other sites such as the respiratory site, genito-urinary source or oral cavity were not seen in our study.

The average time to presentation in this study was 6.8 months. Other studies have described time to presentation between 14-90 days. This may be due to the large number of tuberculous spondylodiscitis cases which have a significantly longer time to presentation than the pyogenic group. It may also reflect a referral bias considering this study was done in a tertiary care setting. People may have sought simpler treatment options or primary care prior to presenting to our center.

Back pain was the most common presenting complaint seen in 96.7% of patients, followed by fever. This is keeping with other studies which show back pain to be the clinical hallmark of this disease, being present in 100% of people. Fever was seen only in 35% of this study population. The most common neurological deficits involved the motor domain seen in 14% of people. Butler et al reported an incidence of 29% individuals with neurological deficits, the majority of whom had an incomplete deficit with only mild weakness.

Laboratory evaluation

In other studies ESR was found to have a good

sensitivity for infective spondylodiscitis, being elevated in almost 90% of cases, although it lacked specificity. In this study it was elevated in 41% of people. Both ESR and CRP are better used to follow up the patients rather than help with the diagnosis of disease owing to poor sensitivity. The leucocyte count was elevated in 52% of people with pyogenic infection. This is in keeping with other studies where the leucocyte count contributes poorly to diagnosis as it often does not increase in infective spondylodiscitis

Blood cultures though done in 48.3% of people were diagnostic in only 24.6% of people. This differs markedly from the results of other studies which show blood culture positivity in up 40-60% of cases. Although blood cultures are positive in only a small section of the study population, they still provide a safe and cost-effective method to diagnose infections in those in whom they are positive. The yield of the test was markedly different in the pyogenic and tuberculous subsets of the population. In the pyogenic subset it serves as useful test being positive in 80% of the population in whom it is done.

Diagnostic procedures

Percutaneous biopsy had a yield of 57.8% in diagnosing individuals with infective spondylodiscitis. The pathogen detection rate in other studies has varied widely from 43-78% , , of cases. A total of 8 patients underwent open biopsies in this study. Open biopsies yielded diagnosis in 100% of cases in this series. Although effective, they are invasive and often the last resort when other methods fail. Procedure related complication rates were noted to be < 5% with the most common procedure related adverse affect being local pain.

Imaging

The lumbar region was the most common site of infection – affected in almost 63.3% of the study population. This was followed by the thoracic region (55%), sacral region (13.3%) and the cervical region (8.3%). This finding is in keeping with that reported from other studies where the lumbar region is the most commonly affected, contributing to about 50% of the sites involved followed by the thoracic region . Sacral involvement however has rarely been reported in other case series.

Magnetic resonance imaging has been known to help provide few distinguishing features between pyogenic and tuberculous infections. In tuberculous infections the site affected is predominantly thoracic as compared to lumbar region in pyogenic infections. In addition tuberculosis is more likely to involve the vertebral body than the disc region; it is more often associated with paravertebral collections as compared to pyogenic infections. Pyogenic infections are thought to involve less than 2 vertebral bodies while tuberculous infection is thought to involve multiple vertebral. In this case series, we found that there were no significant differences between the two. Pyogenic infections caused almost as many paravertebral infections and affected almost as many vertebrae as tuberculous infections.

Treatment and outcomes

The average duration of antibiotic therapy in pyogenic infection was 12 months while that in tuberculous spondylodiscitis was 18 months. Surgical treatment was used in only 11% of individuals. Surgery has been used less over the years with a medical management preferred especially in neurologically normal individuals. This may also be due to the fact that the study population was drawn from a medical cohort rather than from a group of patients referred directly to the surgical specialties. Spondylodiscitis, in published literature has always been associated with a low mortality rate of <5%. In this

study, the in-hospital mortality was 2.9%. 17.3% of all study patients were noted to have had residual neurological complications. In other case series this was present in approximately 33% of individuals. As with other studies, the major problem with reporting relapse was the large numbers who are lost to follow up.

Conclusion

Infective spondylodiscitis is a rare musculoskeletal infection associated with high rates of morbidity due to late diagnosis. It has a prolonged course and requires long term antibiotic therapy. This is the first case series from India studying a significantly large cohort of patients. There are a number of differences in clinico-epidemiological profile with tuberculosis being the predominant microbe isolated and imaging findings offering poor distinguishing characteristics between the two infections. While case related mortality was low the major problem appears to be the morbidity conferred by residual neurological deficits in 17% of the study population. A limitation of this study is the absence of long term follow up data of patients due to high loss to follow up rates.

Figures with the study

Figure 1: Consort Diagram

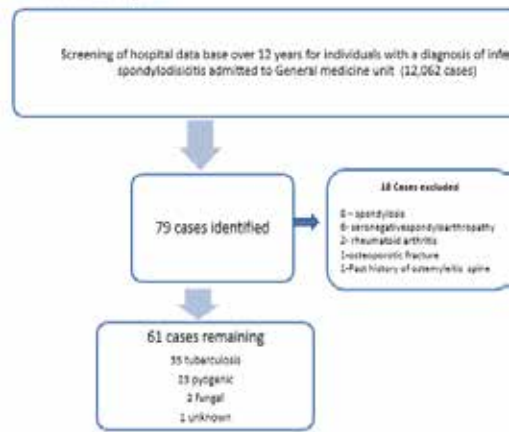


Figure 2: Baseline characteristics of the population

Figures with the study

Figure 1: Consort Diagram

Clinical Characteristics	Total (n= 60) n(%)	Pyogenic (n= 23) n(%)	Tuberculosis (n=35) n(%)	Fungal (n=2) n(%)	P value
Age (in years)	45.6± 15.7	52.7±13.5	40.5 ± 15.8	53.5 ±2.1	
Less than 20 years	3(5)	1(4.3)	2(5.7)	-	0.025
20-50 years	31(51.6)	8(34.8)	23(65.7)	-	
More than 50 years	26(42.6)	14(60.9)	10(28.6)	2(100)	
Sex					
Male	46(76.7)	19(82.6)	25(71.4)	2(100)	0.631
Female	14(23.3)	4(17.4)	10(28.6)	-	
Time to presentation	3.0(1.0,8.0)	1.0(0.75,3.0)	6.0(3.0,12.0)	4.5(3.0,6.0)	<0.001
Fever					
Present	35(58.3)	17(73.9)	17(48.6)	1(50)	0.080
Absent	25(41.7)	6(26.1)	18(51.4)	1(50)	
Pain					
present	58(96.7)	22 (95.7)	34 (97.1)	2 (100)	1.000
absent	2 (3.3)	1 (4.3)	1 (2.9)	-	
Neurological deficit					
Motor	14(23.3)	5(21.7)	9(25.7)	-	1.000
Sensory	7(11.9)	3(13.0)	4(11.8)	-	1.000
Autonomic	5(8.3)	3(13.0)	2(5.7)	-	0.476
Spinal tenderness	19(33.9)	6(27.3)	12(37.5)	1(50)	0.611
Deformities present	10(16.7)	1(4.3)	9(25.7)	-	0.113
Co-morbidities					
HIV	4(6.7)	1(4.5)	3(8.6)	-	1.000
Diabetes	23(38.3)	14(60.9)	9(25.7)	-	0.011
Corticosteroid use	2(3.3)	1(4.3)	-	1(50)	-
Chronic Kidney disease	4(6.7)	1(4.3)	2(5.7)	1(50)	0.148
IV drug abuse	1(1.7)	-	-	1(50)	0.033
Spine Surgery	4(6.7)	2(8.7)	-	2(100)	0.001
Respiratory tract infection	1(1.7)	-	-	1(50)	0.033

Figure 2a: Graphical representation of the clinical features of the study population

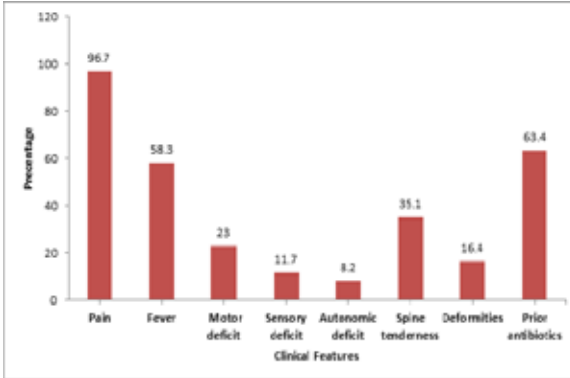


Figure 3: State wise distribution of the study population

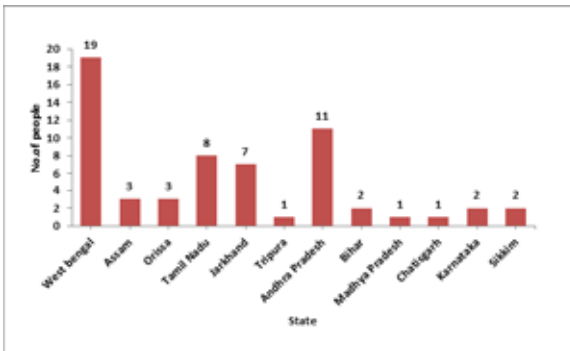


Figure 4: Imaging Findings

Imaging finding	Total (n= 60) n(%)	Pyogenic (n= 23) n(%)	Tuberculosis (n=35) n(%)	Fungal (n=2) n(%)	P value
Osteomyelitis	60(100)	23(100)	35(100)	2(100)	-
Average number of vertebrae affected	3.0(2.0,4.0)	2.0(2.0,4.0)	3.0(2.0,4.0)	4.5(4.0,5.0)	0.135
Most common site affected	Lumbar	Lumbar	Thoracic	Thoracic and lumbar	
Cervical	5(8.3)	1(4.3)	4(11.4)	-	0.698
Thoracic	32(53.3)	10(43.5)	21(60)	1(50)	0.422
Lumbar	38(63.3)	18(78.3)	19(55.9)	1(50)	0.153
Sacral	8(13.3)	4(17.4)	3(8.6)	1(50)	0.155
Vertebral body involvement	56(93.3)	22(95.7)	33(97.1)	1(50)	0.100
Discitis	55(91.7)	20(90.9)	33(97.1)	2(100)	0.600
Canal compression	20(33.3)	9(40.9)	10(30.3)	1(50)	0.544
Paravertebral abscess	57(95.0)	20(87.0)	35(100)	2(100)	0.150
Epidural abscess	46(76.7)	20(90.9)	25(73.5)	1(50)	0.125
Psoas abscess	24(40.0)	11(47.8)	13(37.1)	-	0.503
Meningitis	5(8.3)	2(8.7)	3(8.6)	-	1.000

Figure 4b: Graphical representation of Imaging Findings of the study population

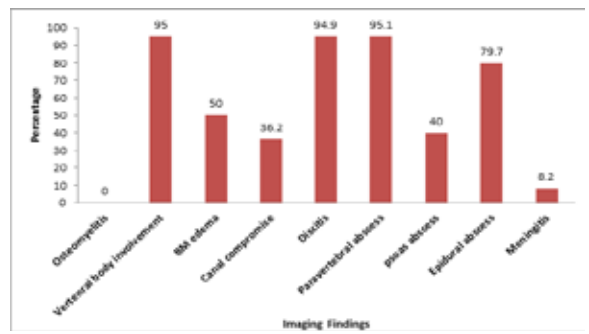


Figure 5: Distribution of patients according to site of the spine affected

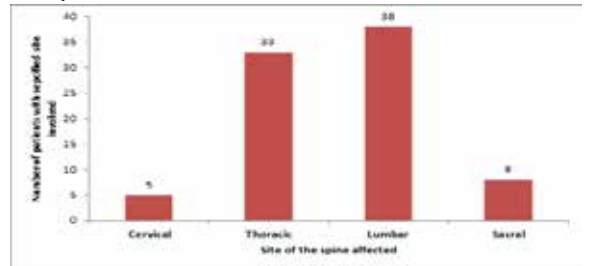


Figure 6: Investigations aiding a diagnosis

Investigation	Total (n= 60) n(%)	Pyogenic (n= 23) n(%)	Tuberculosis (n=35) n(%)	Fungal (n=2) n(%)	P value
ESR					
ESR done	50	16	32	2	0.673
Elevated ESR (>60mm)	25(41.7)	10(62.5)	14(43.8)	1(50)	
CRP					
CRP done	34	12	20	2	0.398
Elevated CRP	31(51.7)	12(100)	17(85.0)	2(100)	
Total count					
the total count was done	59	23	34	2	0.082
less than 4000	4(6.8)	1(4.3)	3(8.8)	-	
3600-11,000	36(61.0)	10(43.5)	24(70.6)	2(100)	
>11,000	19(32.2)	12(52.2)	7(20.6)	-	
Blood culture					
Blood culture done	29(48.3)	17(73.9)	10(28.6)	2(100)	<0.001
Blood culture diagnostic	15(25) 51.7%	13(59.1) 76.4%	1(3.2) 11.1%	1(50) 50%	
Yield of the test					
Percutaneous biopsy					
Percutaneous biopsy done	45(75%)	17(73.9)	28(80.0)	-	0.083
Percutaneous biopsy diagnostic	26(43.3%) 57.8%	9(39.1) 52.9%	17(48.6) 60.7%	-	
Yield of the test					0.199

Open biopsy					
Open biopsy done	8(13.1)	2(8.7)	4(11.4)	2(100)	
Open biopsy diagnostic	8(13.3)	2(8.7)	4(11.4)	2(100)	0.022
Yield of the test	100%	100%	100%	100%	0.022
TB PCR					
TB PCR not done					
TB PCR diagnostic	37(61.7)	15(65.2)	19(54.3)	2(100)	
TB PCR Non-diagnostic	8(13.3)	1(17.4)	7(20.0)	-	0.421
Yield of the test	34.7%	12.5%	43.8%	-	

Figure 7: Microbe isolated in the study population

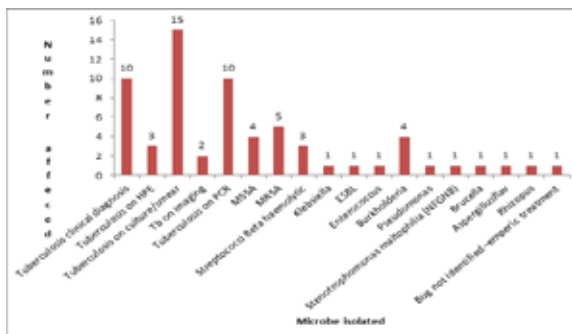


Figure 8: Management and Outcomes

Variable	Total n= 60	Pyogenic n= 23 n(%)	Tuberculosis n=35 n(%)	Fungal n=2 n(%)	P value
Mortality	1 (1.7)	-	2.9% (1)	-	1.000
Medical management done	60(100)	23(100)	35(100)	2(100)	-
Surgical intervention required	11(18.3)	5(21.7)	5(14.3)	1(50)	0.416
Duration of IV antibiotics in months	0(0,0.75)	0.5(0.5,1.5)	0(0,0)	0.75(0.5,1.0)	<0.001
Duration of oral antibiotics in months	9.3(3,12)	2.5(1.5,5.5)	12(12,18)	12.7(1,24.5)	<0.001
Cured	31(51.7)	12(52.2)	18(51.4)	1(50)	1.000
Missing data	28(46.7%)				
Mean follow up	6(1,18)	5(0,15)	6(2,18)	18.5(1,36)	0.442
Clinical recovery					
Total neurological	25(41.7)	11(47.8)	13(37.1)	1(50)	0.891
Partial neurological	6(10)	3(13.0)	3(8.6)	-	0.982
No recovery	3(5)	1(4.3)	2(5.7)	-	1.000
Missing data	27 (45)				
Imaging follow up					
MRI normal	2(3.3)	1(4.3)	1(2.9)	-	0.015
MRI Improved	14(23.3)	2(8.7)	11(31.4)	1(50)	0.064
MRI same	2(3.3)	-	2(5.7)	-	0.050
MRI worse	2(3.3)	-	2(5.7)	-	0.050
MRI not done/missing	40 (66.7%)				

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