THE SURGICAL RECONSTRUCTION OF THE ANTERIOR COLUMN IN THE MANAGEMENT OF THE TUBERCULOSIS OF THE SPINE (CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL EXPERIENCE: 2012 – 2015)

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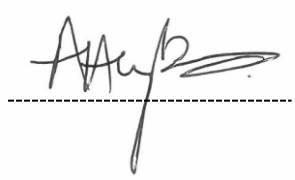
DECLARATION

I, Akinwande Akinjolire declare that this research report is my own work. It is being submitted for the degree of Master of Medicine in the branch of Orthopaedic Surgery at the University of Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.



31st day of May, 2017

DEDICATION

This report is dedicated to the memory of my parents:

Mrs. Rachael Adetinuwe Akinjolire (1943-1997)

and

Mr. Joseph Akintolire Akinjolire (1935-2010)

PRESENTATIONS ARISING FROM THIS STUDY

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Abstract number: 1804

Abstract Title: "Does anterior column reconstruction works in the surgical management of tuberculosis of the spine?"

Presenting author: Akinwande Akinjolire

ABSTRACT

Background: The anterolateral approach to the spine for the surgical management of the Tuberculosis of the spine has been described. The surgical technique has evolved since the gold standard published by Hodgson *et al.* in 1956. The use of a Titanium Mesh Cage and the anterior instrumentation to construct the anterior column after adequate debridement defined the evolution. The aim of the study is to review the results of the patients that underwent this procedure between January 2012 and December 2015.

Methods: The study was a retrospective study where 60 patients treated with this technique from 2012 – 2015 were reviewed. Sixty-one percent (61%) of the tested patients were HIV positive and 70.4% of the patients were female in the age group of 31-45 years. The surgical procedure was standardised for all the patients irrespective of their HIV status. The clinical and radiological outcomes measured consisted of the patients' disability using the Oswestry Disability Index (ODI), the Frankel Neurological grading to measure neurological deficits and the Cobb angle to measure Kyphosis. The diagnosis of Tuberculosis of the Spine was confirmed in all the patients.

Results: At a mean follow up period of 21.25 months, the ODI improved from a mean of 95.42% ± 6.57% before surgery to a mean of 8.00% ± 12.15% at the last follow up. There were 58 patients who were unable to walk independently before the surgery (Frankel A or B) but at the last follow up, 52 of the patients had achieved independent ambulation (Frankel D or E). The mean kyphosis was 33.90 ± 12.44 degrees before surgery, and in the immediate post-operative period, the mean kyphosis was 23.69 ± 10.31 degrees, and a mean of 26.27 ± 10.91 degrees was measured at the last follow up. There was a 30.12% correction achieved in the immediate post-operative period and an overall correction of 22.51% at the last follow up reflecting a loss of 7.61% in the kyphosis correction in the period between the immediate post-operative period and the last follow up. Complications were documented in six patients including two deaths unrelated to the procedure.

Discussion: The ODI score showed an improvement as the mean value decreased by 87.42%. This is statistically and clinically significant (p=0.001). According to the work of Solberg *et al.* (2013) in degenerative spine, the threshold for a success is a mean change of 20% in the

ODI scoring after lumbar disc surgery. Using this value as a proxy, an improvement of 87.42% is an excellent outcome.

Before surgery, fifty-eight patients (96.7%) were non-ambulatory using the Frankel Neurological score. At the last follow up, 53 patients (91.4%) achieved a Frankel score of D or E and independent ambulation. This outcome compares favourably with ones published in the literature.
The overall post-operative kyphosis correction achieved was 26.27 degrees (which translated to 22.51% correction) at the last follow up. This reflects a kyphosis correction loss of 7.61% that was not associated with any neurological deterioration and is therefore of no clinical significance. There were six cases of complications including two deaths unrelated to the procedure but the general debilitation of military Tuberculosis and Nosocomial infection.

Conclusion: The anterior column reconstruction using the Titanium Mesh Cage and Anterior Instrumentation is safe and effective for the surgical management of the Tuberculosis of the Spine. There were good clinical outcomes as measured by the ODI score and the Frankel Neurological Grading system, and even though there was a loss of Kyphosis correction at the last follow up, this was not associated with a negative neurological outcome.

Despite its limitation as a retrospective study, this study demonstrates that the procedure is safe and effective when used as an adjunct to the medical treatment of the Tuberculosis of the Spine.

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NOMENCLATURE

ACR	Anterior Column Reconstruction
ADL	Activities of Daily Living
AFB	Acid Fast Bacilli
AIDS	Acquired Immunodeficiency Syndrome
AP	Anteroposterior
BC	Before Christ
BCG	Bacilli Calmette Guerin
CHBAH	Chris Hani Baragwananth Academic Hospital
CM	Centimeter
CRP	C-Reactive Protein
CT Scan	Computerised Tumography Scan
ESR	Erythrocyte Sendimentation Rate
HIV	Human Immunodeficiency Virus
L	Lumbar Spinal Level
M. Tuberculosis	Mycobacterium Tuberculosis
MDR	Multiple Drugs Resistance
MRI	Magnetic Resonance Imaging
ODI	Oswestry Disability Index
PACS	Picture Archiving and Communication Systems
PCR	Polymerase Chain Reaction
RVD	Retroviral Disease
STIR	Short Tau Inversion Recovery
T	Thoracic Spinal Level
TLSO	ThoracoLumboSacral Orthosis
WHO	World Health Organisation

CHAPTER ONE – INTRODUCTION AND LITERATURE REVIEW

1.1. Historical aspect of tuberculosis

The Tuberculous infection of the musculoskeletal system was reported in the pre-historic man and specific Mycobacterial infection of the spine was noted in man before 1000 BC according to the Western European literature (1). Ancient Indian literature also described a disease called "Yakshama" and this was documented by the Rig Veda and Atharva Veda in 3500-1800 BC (2). Tuberculosis of the Spine can therefore be acknowledged as one of the oldest diseases known to mankind as it was also found in the Egyptian mummies as far back as 3400 BC. However, it was not until 1799 that Tuberculosis of the Spine was described by Percival Pott as "that kind of palsy of the lower limbs which is frequently found to accompany a curvature of the spine" (3).

Other important milestones in the diagnosis and management of the disease include (3):

- the identification of Mycobacterium as the pathogenic organism in 1870
- the use of Bacilli Calmette Guerin (BCG) vaccination in 1945, and
- radiographic capabilities and the advent of anti-tuberculous drugs between 1948-1951.

All these events enabled clinicians to understand and manage the disease better (4).
In recent years, the advent of the Magnetic Resonance Imaging (MRI Scan) and Computerised Tomography Scan (CT Scan) have enhanced our capability to detect the disease entity before it progresses to the destructive phase and also improved the ability to make a diagnosis of the disease in difficult body areas such as the Craniovertebral and the Sacrococcygeal regions (5).

The World Health Organisation (WHO) stated that tuberculous infection will continue as long as there are people living with malnutrition, poor sanitation, alcohol and substance abuse, immunodeficiency, diabetes and the elderly (6). In the same vein, immunocompromised people that become infected with tuberculosis will continue to present with florid clinical features of the disease (7).

1.2. Pathogenesis and Pathology

The tuberculosis infection of the lungs shares the same predisposing factors as the extra-pulmonary form of the disease including the Tuberculosis of the Spine. These predisposing factors include poverty, overcrowding, malnutrition, illiteracy, alcoholism, drug and substance abuse, diabetes mellitus, immunosuppression and Human immunodeficiency virus (HIV) infection (8). An Iranian study also identified additional predisposing factors that include older age, male gender, chronic peritoneal dialysis, imprisonment and a history of previous tuberculous infection for developing Tuberculosis of the Spine (9). A genetic predisposition to the disease was found in the Chinese population. This was defined by a *FokI* polymorphism in the Vitamin-D receptor gene (10).

The routes of the Mycobacterial infection to the Spine have been described. The commonest route is the haematogenous spread of *Mycobacterium Tuberculosis* (*M. tuberculosis*) from a primary source. The primary source is often from infected lungs or from an infected genitourinary system (4). This spread could be via the arterial or venous route. The arterial plexus formed by the confluence of the anterior and posterior spinal arteries in the subchondral region of each vertebra facilitates the infection of the paradiskal regions. The paravertebral Batson's venous plexus comprises a valve-less system that facilitates blood flow in either direction depending on the intra-abdominal and intrathoracic pressure from strenuous activities such as coughing (4).

Other routes of spread can include intra-osseous venous spread that may result in central vertebral body lesions and the vertebral venous system has also been implicated in the non-contiguous vertebral lesions affecting multiple vertebrae simultaneously (11).

The effect of this spread localises the lesions in the vertebral body as paradiskal, anterior and central lesion types. The disk involvement in the disease process depends on the age of the patient. In the young adult, the disk is vascularised and it is the primary site of involvement. In the older patient, the disk is less involved because of the age-related desiccation. Also, the central lesions do not involve the disk. Although there is a variation in the degree of the vertebral body collapse as the disease destroys the bone, a complete collapse of the vertebral body produces the "vertebral planar" which is seen only in central vertebral body Tuberculosis of the spine in its atypical form and is uncommon (11).

The bifurcation of the segmental arteries to supply two adjacent vertebrae makes it possible that more than one vertebra may be involved. The spread of the disease process under the anterior or posterior longitudinal ligament may result in a multiple contiguous vertebrae involvement. This subligamentous spread is promoted by the lack of proteolytic enzymes associated with the Mycobacterial infection as compared to pyogenic infection (11).

The characteristic destruction of the intervertebral disk space and the adjacent vertebra bodies leads to the collapse of the spinal elements and anterior wedging resulting in the typical deformity referred to as "gibbus". The lower thoracic and upper lumbar spine are mostly affected, and more than one vertebra is typically affected. The disease typically affects the vertebral body more than the posterior elements. This disruption of the vertebral column alignment leads to the spinal deformities manifested by the patients (12).

Apart from the deformity described above, paraplegia is another complication of Tuberculosis of the Spine. Hodgson in 1967 classified the paraplegia into two groups in his classic paper referred to as Pott's paraplegia ((13). This classification is based on the activity of the disease process. The early-onset paraplegia occurs during the active disease stage and the late-onset of paraplegia occurs in the healed stage. The early-onset paraplegia is known to have a better prognosis and is usually seen in young adults. The mechanism of early- and late-onset paraplegia is shown in Table 1.1.

The destruction of the anterior column by the disease process results in the subluxation and later dislocation of the spine as the disease progresses. This leads to spinal instability, consequent deformity, pain and the associated neurology. Spinal instability can also result from the spread of the disease to the posterior elements with the consequent disruption, and even dislocation, of the spine.

Table 1.1: Mechanism of paraplegia/tetraplegia in spinal tuberculosis (13)**.**

Causes of neurological involvement	
Early-onset paraplegia	**Description**
Mechanical Pressure	Tuberculous debris, sequestrum of bone or disk, abscess, subluxation and dislocations, concertina collapse and internal gibbus
Tuberculous granuloma	Tuberculoma in extradural, intradural or intramedullary regions
Tuberculous myelitis	Uncommon. May involved spinal cord parenchyma
Spinal artery thrombosis	Infective thrombosis of anterior spinal artery
Tuberculous arachnoiditis	Meningeal inflammation and fibrosis
Late-onset paraplegia	**Description**
Transection of spinal cord by bony bridge	Transverse ridge of bone produced by severe kyphosis
Fibrosis of the dura (Pachymeningitis)	Formation of tough, fibrous membrane encircling the cord

1.3. Diagnosis of Tuberculosis of the Spine

The patient usually complains of back pain, difficulty with walking and may have an associated deformity called "gibbus". The patient typically presents late because of the insidious nature of the disease and poor access to effective medical care may also result in a delayed diagnosis. Dunn in 2011 published the various tests and radiological investigations necessary to make a diagnosis of tuberculosis of the Spine and these are discussed below (14).

1.3.1. Tuberculin skin test

This is administered as an intra-dermal injection of the Tuberculin which then elicits an inflammatory response. The various types of the test include the Mantoux, Heaf and the Tine tests. The degree of the inflammatory response is directly proportional to the degree of patient's exposure to the Mycobacterium.

Although the test is simple and easily available, it is fraught with false positive and false negative outcomes. The false positives are usually due to previous BCG vaccination or exposure to the environmental Mycobacterium. The false negatives may result from immunosuppressive conditions such as HIV/Acquired Immunodeficiency syndrome (AIDS) infection, Cytotoxic medications, malnutrition etc.

1.3.2. Sputum

The identification of the acid-fast Bacilli in the sputum of a patient with Pulmonary Tuberculosis confirms the diagnosis. Usually, three or more serial tests are done to improve the yield. Yield also varies with the method of sputa collections: Expectorated sputum (55%), induced sputum (38%) and Bronchial lavage (26%).

1.3.3. Blood

The Erythrocyte Sedimentation Rate (ESR) and the C-Reactive Protein (CRP) are usually elevated. There is usually anaemia of chronic illness and the albumin may be decreased because of associated malnutrition. The white cell count is usually normal.

1.3.4. Culture

Special culture medium is required because of the fastidious nature of *M. Tuberculosis*; therefore, Lowenstein-Jensen or Broth culture media are used. The required average period of culture is 6-8 weeks but this period may be shortened to less than two weeks if microscopy indicates a positive result.

1.3.5. Histology

The histological picture is that of necrotising caseous necrosis with associated giant cells referred to as the "Langerhans Cells". Occasionally, there may be positive Acid-Fast Bacilli (AFB) on special staining using Ziell Nielson stain.

1.3.6. Polymerase Chain Reaction (PCR)

This test is based on Nucleic Acid amplification by PCR and the result is available within 24 hours. The test can be used to detect Multidrug Resistant Tuberculosis. As of now, the test is not routinely done as it is expensive and not generally available. The tissue used is the diseased bone.

The World Health Organisation (WHO) in its publication on implementing Tuberculosis Diagnostics Policy Framework published in 2015, developed different algorithms with the intention of strengthening Laboratories' capability to make an early diagnosis, detect "Drug Resistant" Tuberculosis and diagnose extra-pulmonary Tuberculosis. The publication promoted the use of GeneXpert (PCR) as a molecular basis of testing and diagnosing Tuberculosis (15, 16).

1.4. Radiological investigations

1.4.1. Plain X-rays

Thoracolumbar and Chest X-Rays are usually done. The typical features of Tuberculosis of the Spine are the destruction of two adjacent vertebral bodies and the opposing end plates, destruction of the intervening intervertebral disk and paravertebral or psoas abscess. This destruction and the consequent collapse results in kyphosis of the affected spine region called gibbus (17).

Atypical Tuberculosis of the Spine presents in various forms which include spondylitis without diskitis, central single vertebral body lesion, non-contiguous (Skip) vertebral elements and isolated involvement of the posterior vertebral elements and isolated intraspinal lesions (17). The chest X-Rays may also reveal the presence of active or latent pulmonary Tuberculosis.

1.4.2. Magnetic Resonance Imaging (MRI)

This is indicated in the presence of neurological deficits, to further delineate the extent of the soft tissue involvement and to look for atypical manifestations of the Tuberculosis of the Spine as described above. The entire spine is scanned by the MRI.

The MRI findings include the vertebral changes of intraosseous abscess, paravertebral abscesses, diskitis, scoliosis and kyphosis, skip lesions, spinal canal encroachment, and nerve root distortion (18).

These findings are easily delineated on routine sagittal, axial and coronal images using the T1- and T2- weighted sequences together with the short tau inversion recovery (STIR)

sequence and followed by the contrast-enhanced sequence with the administration of the intravenous gadolinium contrast agent (18).

1.5. Treatment of Tuberculosis of the Spine

1.5.1. Medical treatment

Historically, Tuberculosis of the Spine was managed by rest and offloading of the diseased vertebrae with the use of immobilising bandage to promote natural healing (19).

Tuberculosis of the Spine is a medical disease and the anti-Tuberculosis drug treatments are the mainstay of the treatment that leads to patients' recovery. Several studies (5, 14, 20-22) have proved the efficacy of drug treatment in the absence of Neurologic deficits, spinal instability and deformity irrespective of the presence of a paravertebral abscess. However, there is a controversy around the number of drug combinations required and length of time needed for treatment (23).

Adequate anti-Tuberculosis drug treatment prevents the severe and catastrophic complications associated with the disease and a combination of Rifampicin, Isoniazid, Ethambutol and Pyrazinamide for two months, followed by a combination of Rifampicin and Isoniazid for a further period of 6, 9,12 or 18 months has been described in the literature (24).

WHO proposed a total of six months of treatment comprising two months of Rifampicin, Isoniazid, Pyrazinamide and Ethambutol followed by four months of Isoniazid and Rifampicin. Even though WHO does not give detailed attention to the Tuberculosis of the Spine, the recommendations of the American Thoracic Society are nine months of treatment using the same four drugs for two months followed by seven months of the Rifampicin and Isoniazid in the continuation phase. The Canadian Thoracic Society recommends a total time of treatment as long as 9-12 months. The South African National Treatment Guideline recommends nine months for the treatment of extra-pulmonary tuberculosis(25). Medical treatment alone improves the neurological deficits and surgery may not be the most appropriate first choice of treatment in many cases (20).

1.5.2. Surgical treatment

The role of surgery in the management of spinal tuberculosis has been a subject of controversy. This difference in position dated back to the era of Hodgson and Stock (1960) when they advocated surgical treatment, and that of Konstam and colleagues (1962) who advocated conservative management (26, 27). The general position of the experts is that not all cases should be treated non-operatively since approximately 40% of affected patients with paraplegia had shown recovery with anti-Tuberculosis drug treatments, bed rest and with or without the use of traction.

The Medical Research Council Working Party demonstrated that in selected cases, there are no added benefits of surgery (resection of the spinal focus and bone grafting) when combined with drug treatments compared to drug therapy alone in randomised controlled trials on tuberculosis of the spine (28, 29).

These controversies and differences in opinions on the indications for surgery in the treatment of the Tuberculosis of the Spine made Tuli (1975) propose a "middle path regimen" for the treatment of spinal tuberculosis (30). In his proposal, Tuli explained that surgery is only indicated for a specific situation and also reiterated that combination drug treatment forms the basis of non-operative management.

In certain situations, surgery has been shown to be beneficial. The indications for surgery include: pan-vertebral lesions, refractory disease, severe kyphosis, a diagnostic biopsy, an evolving neurological deficit and clinical deterioration or lack of clinical improvement (30, 31). The potential benefits of surgery include: less deformity, decompression of the neural tissue, pain relief, a higher rate of arthrodesis, less relapse, earlier return to activities of daily living and less osteolysis. Furthermore, late-onset paraplegia may also be prevented (32).

There are two types of surgery that can be performed. The first type is debridement of the infected material only without stabilisation of the spine in the form of reconstruction. The second type of surgery involves the use of a bone graft or artificial materials such as steel, carbon fibre or titanium to achieve stabilisation; however, this form of stabilisation is a lot more complex but more beneficial to the patients.

1.5.3. Treatment of spinal Tuberculosis in HIV co-infection

Patients who have HIV and Tuberculosis co-infection can be treated successfully irrespective of their HIV status and the treatment of Tuberculosis of the Spine can be combined with antiretroviral medications (22). However, it is important to be mindful of some significant differences when treating these patients compared to their HIV-negative counterparts. These differences include potential drug interactions, especially between Rifampicin and antiretroviral drugs, paradoxical reactions that may be construed as worsening clinical condition and the potential for the developing resistance to Rifampicin (22).

Major orthopaedic surgery in HIV-positive patients has potential for increased risk for sepsis. However, Govender *et al*. (2001) carried out a prospective study and reported no difference between HIV-positive and HIV-negative patients who had anterior spinal decompression for Tuberculosis of the Spine in terms of immediate post-operative complications (22). This was because their patients were optimised medically and nutritionally before the elective surgery, thus promoting wound healing and prolonging their life expectancy.

1.6. Surgical Techniques

Several techniques have been described for the surgical treatment of Tuberculosis of the Spine. Some techniques are based on an anterolateral approach, others are based on a posterior approach while some are a combination of the anterolateral and posterior approaches (33). This study will focus on the Gold standard procedure as described by Hodgson *et al*. in 1956, which is the anterolateral approach (27).

Ma *et al.* in 2012 acknowledged the lack of consensus in the literature for the option of instrumentation modality (anterior or posterior instrumentation) in the surgical management of the Tuberculosis of the spine. They advised that the position and the extent of the infected foci should guide appropriate surgical technique. A combination of anterior radical debridement and anterior column reconstruction with posterior instrumentation is indicated in patients with severe spine destruction by the disease that makes anterior surgery impossible. This approach is also used in patients with severe lower lumbar kyphosis who require deformity correction and restoration, and in those wherein the anterior surgery has failed (34).

In the setting of limited resources such as the availability of theatre time, the anterolateral surgery with the resultant anterior column reconstruction has been shown to be feasible and safe. This is because it provides a direct exposure to the lesions localised in the anterior of posterior instrumentation vertebral body from the second thoracic vertebra the fifth lumbar vertebra (35).

1.6.1. Anterior spine column surgery: The rationale

The pathology of tuberculosis of spine is typically anterior in its location. Therefore, the surgical treatment that utilises the anterolateral approach in combination with anti-tuberculous drugs treatment is acceptable. The anterolateral approach offers direct access to the diseased tissue enabling surgical debridement and rapid removal of all diseased vertebrae, and this often results in large intervertebral defects that necessitates the use of instrumentation and graft to achieve surgical stabilisation (36).

The gold standard approach for the surgical treatment of Tuberculosis of the Spine comprises anterior radical debridement, followed by anterior column reconstruction using a strut graft from the patient's own bone (the iliac crest). This procedure was popularised by the works of Hodgson *et al.* in 1956 (27).

In the aforementioned landmark study, the authors had acknowledged earlier work done by Muller in 1906 on the anterior approach to the spine (37). They also noted that while Hibbs in 1911 (38) and Albee in 1911(39) had described the importance of posterior fusion, Henderson in 1917 (40) indicated that "the posterior approach does nothing to the focus of the lesion and in a way, not radical enough to remove the lesion".

Hodgson *et al.* (1956) then proposed that "the complete removal of the diseased vertebrae, together with their associated pus, granulation tissue, caseous material, thereby decompressing the abscess as an important first step in the surgical management of the Tuberculosis of the Spine" (34). This was proposed to be similar to the decompression of an acute osteomyelitis to prevent its progression to the chronic stage and promote healing. They believed that unless the spine is approached anteriorly, the extent of disease remained unknown. The objective is to leave a clean, raw, bleeding surface after the completion of the anterior debridement.

The surgical technique entails evacuation of the diseased focus as far posteriorly as the spinal cord leaving behind a clean, bleeding cavity, and the insertion of a strut graft (Iliac crest autograft) to keep the spine sprung apart to partially correct the kyphosis by direct pressure on the spine posteriorly. The patients then continue with the anti-tuberculosis drug treatment that was started preoperatively (27, 41). In their preliminary report, fourteen of the first seventeen patients achieved complete spinal fusion and the remaining three cases showed encouraging results.

A subsequent detailed study published in 1960 by the same authors described their experience with this operative technique in four hundred and twelve patients diagnosed with Tuberculosis of the Spine (27). In this study, a detailed review of the operative technique, their findings and complications were documented. They indicated that in their experience, the anterior approach revealed that the disease is much more extensive than was suspected clinically and radiologically, and that they achieved a 93% fusion rate. The study concluded that the technique has a low mortality rate (2.9%) and a high healing rate, and that the technique represented a significant development in the treatment of Tuberculosis of the Spine. The authors also believe that the best place to fuse the vertebrae is anteriorly as this location provides a large surface area, protecting the graft in compression. This proposal also dove-tailed into natural ways of healing the Tuberculosis of the Spine. This is because the spine heals by fusion of the vertebral bodies as proposed by Percival Pott's criterion for healing (41).

There are several advantages to using the anterolateral approach and these include the ability to achieve an effective reconstruction of the weight-bearing anterior column, strong torsional forces (in the thoracic region because of the additional support of the ribs) and axial stability, short segment fixation, avoidance of the posterior paraspinal muscle damage and improved healing. It also negates the requirement for a second procedure especially in our environment where theatre time availability is a premium. In comparison to the combined approach, there is less blood loss, shorter hospital stay and less post-operative complications (35). However, the procedure is not without its challenges. These challenges relate to the approach itself and to the associated loss of correction. The challenges associated with the approach include morbidity related to lung adhesions to parietal pleural in the thoracic region, the need to do diaphragm resection, hence exposing the two cavities in the thoracolumbar region, and for the

retroperitoneal approach there is a risk of injury to the ureter, ascending lumbar veins and the genitofemoral nerve for the lumbar region. For many who are not familiar with the anterolateral approach, an access surgeon is usually required. The second challenge relates to the loss of the kyphosis correction due to the quality of the autograft, especially when the rib is utilised. Many authors have observed mechanical complications such as bone graft dislodgement, fracture, resorption or subsidence (from pistoning into the end plates). Coupled with a lack of instrumentation, the recurrence of the kyphosis ensues with increased risk of neurological re-injury. An additional challenge is the availability of the required iliac crest graft in adequate volume, particularly when more than two segments are involved. There are also issues with donor site morbidity such as chronic pain and infection risk associated with the iliac crest graft harvesting (42).

To overcome the shortcomings associated with the autograft use and its lack of stability, several modifications have been made to the technique.

In 1999, Govender *et al.* published their study on the use of allografts to support the anterior column after debridement in the treatment of Tuberculosis of the spine. They used fresh humeral allografts to reconstruct and stabilise the anterior spinal column in forty-seven children operated on for tuberculosis of the spine. The authors acknowledged the inadequacy of rib autografts to support the anterior column in children especially when two or more vertebrae are removed. Other problems that were identified included: slippage, resorption or fracture of the graft in patients with severe deformity, and rib autograft plastic deformation and small graft footprints because of the small contact surface area with adjacent normal vertebral bodies. There was no anterior instrumentation utilised in their series (43).

Although the use of structural allografts such as a femoral ring solved these problems, it is not without its own challenges. Cortical allografts promote an inflammatory response that may lead to bone resorption and delays revascularisation. This problem can be avoided with the use of fresh frozen cortical allografts. However, the use of fresh frozen allografts is also fraught with the risk of transmission of infection and occasionally fracture (43).

Another challenge is the concern about the use of the allograft to reconstruct the anterior column in patients undergoing anterior decompression that are HIV-positive; however, Govender *et al*. in 2001 published their study on 39 HIV-infected adults with spinal

tuberculosis who underwent anterior decompression for neurological deficit (22). Fresh frozen allografts were used to achieve anterior column reconstruction and the patients had completed 18 months of anti-tuberculosis treatment. Of importance is that none of the patients used anti-retroviral treatment, the patients achieved neurological recovery and allograft incorporation at a mean period of 38 months and six patients died within two years of the surgery (22). They could achieve such a remarkable result by adequately optimising their patients nutritionally and medically in the preoperative period and ensured compliance with their anti-tuberculous treatments. Thus, the study proves that the technique is safe in the surgical management of patients with spine tuberculosis who are HIV-positive.

In 2011, Dunn *et al.* published their review of twenty-nine adult thoracic tuberculosis patients who underwent anterior-only transthoracic surgery. They used anterior only debridement, allograft strut reconstruction and instrumentation for spinal tuberculosis. Of significance to note is that 21 of the 29 patients were tested for HIV infection and 8 were positive representing 38%. In this study, the graft of choice was the humeral allograft from the bone bank and in one case, a metal cage was utilised to do the anterior column reconstruction because the patient presented with vertebral planar and a malignancy was suspected but final histology revealed that it was Tuberculosis of the Spine. The other six patients had fibular allografts. In this study, no case of implant failure, loosening or dislodgment was experienced. Of importance is to note that the study did not report any complication associated with the one case in which a metal cage was used to reconstruct the anterior column. The study also documented 38% HIV positive rate out of the 21 patients that were tested but none of the complications reported were associated with the HIV positive status of the patients. They reported a high success rate with return to ambulation and few complications. Even though there was early loss of sagittal correction, this was judged to be non-significant as to affect the neurological outcome. The authors also advised that it is important to maintain intra-operative vigilance to the end plate integrity in order to prevent graft subsidence (35).

Christoloudou *et al.* (2006) published their study that retrospectively reviewed twelve patients that had undergone surgical treatment of tuberculous spondylitis with anterior stabilisation and Titanium Cage reconstruction. The patients had Spine Tuberculosis involving the Thoracic and Lumbar regions. None of the patients in the study were identified as HIV positive. They all had radical debridement, anterior decompression, interbody fusion

using the anterior interbody Titanium cage and autologous bone grafts. The anterior instrumentation was done with Moss-Miami uniaxial screw and rod system (DePuy Spine, Leeds, UK) to augment the anterior stabilisation. All the patients had concomitant anti-tuberculous drug treatments. In their experience, the use of a cage and bone grafts as opposed to structural allografts promoted a more secure, accurate and dependable deformity correction. This is because the cage provides a more rigid fixation and reduced the risk of subsidence or displacement. It also enabled regional stability at the surgical site thereby encouraging earlier and safer mobilisation. The improved stability was also noted to promote the eradication of infection, incorporation of graft and achievement of solid fusion. Mycobacterium has low adherence to titanium and has a mechanical property that is very similar to the bone. The study reported no loss of kyphosis correction and it concluded that radical debridement with anterior instrumentation and bone grafting offers a satisfactory result in selected patients with Tuberculous Spondylitis when surgery is indicated (21).

Wang *et al.* (2011) published their experience in the use of anterior radical debridement and reconstruction using a Titanium mesh cage for the surgical treatment of thoracic and thoracolumbar spinal tuberculosis with a minimum of a 5-year follow up. All sixty-nine patients had undergone the anterior-only approach with the use of either thoracotomy or thoraco-lumbar approaches, radical debridement and anterior column reconstruction using a Titanium Mesh Cage to maintain structural integrity. Anterior instrumentation was utilised to maintain the structural integrity and stability of the spinal column. The type of instrumentation used depends on the spinal level involved in the disease process.

For the spinal level above T10, a single-rod titanium-alloy fixation (Ventrofix, AO, Synthes, Switzerland) was used. This is because of the increased stability afforded by the thoracic cage and the associated horizontal orientation of the thoracic facet joints. This was done in 39 patients involved in the study.

For the spinal level below the T10, this area is biomechanically unstable and formed a transitional zone of the spine as it changes from the rigid thoracic region to the mobile lumbar region. Therefore, a double-rod construct was utilised to improve the spinal stability at the Thoracolumbar region. There were 17 patients in this group where Ventrofix (AO, Synthes, Switzerland) was utilised and another 13 patients had ISOLA (Depuy-Acromed, USA).

There was no indication in the study about the HIV status of the patients. The choice of bone graft depended on the surgical approach. For the thoracotomy, the resected rib combined with allograft bone was used to fill the cage and only allograft was used to fill the cage in the case of the thoracolumbar group. All the patients had resolution of their infections, achieved solid fusion without fixation failure and experienced improvement in their neurological deficits and pain control. The results were deemed to be good to excellent clinically. The loss of kyphotic angle correction over time was not clinically significant. The study concluded that the surgical technique is an acceptable and safe treatment option (36).

Patankar (2016) published the outcome of his treatment on patients with Tuberculosis of the Spine documenting his experience of 30 cases treated over two years. The HIV status of the patients was not indicated in the study. He divided the study population into three groups. Group one had four patients that were treated with Anti-Tuberculosis chemotherapy, analgesia and bed rest, and Group two had five patients that were treated with Ultrasound guided abscess drainage plus medications. Group three had twenty-one patients that were treated surgically with a single-stage anterolateral approach using thoracotomy for the thoracic region and a retroperitoneal approach for lumbar region disease to achieve anterior spinal decompression and anterior column reconstruction with a titanium mesh cage and anterior instrumentation. The details of the anterior instrumentation utilised in the study were not discussed or revealed. All the nine patients in groups one and two were completely healed. Nineteen of these twenty-one patients in group three had significant improvement in neurological status and returned to normal activities. Of the remaining two patients, one died and the neurological status of the other patient did not improve until one month after surgery and was lost to follow up. The study advised that the anterolateral approach should be the initial approach of choice for Tuberculosis of the Spine after adequate debridement, and that the posterior approach is best suited for kyphosis correction and should be reserved for cases which go on to develop progressive kyphosis. The study did not report on any loss of kyphosis correction in the operated group (44).

1.7. Problem statement and aim

There are challenges associated with the use of bone autograft for anterior spinal column reconstruction in the surgical management of Tuberculosis of the Spine, as identified above. Thus, the surgical technique has evolved to address these challenges. One variation of the surgical technique incorporates the use of a Titanium Mesh Cage and anterior instrumentation as described in the literature.

The use of this technique in the surgical management of Tuberculosis of the Spine has been practiced for over a decade at Chris Hani Baragwanath Academic Hospital (CHBAH). During this period, a significant number of patients have undergone the procedure with good to excellent results. Therefore, the aim of this study is to review the results of this procedure that was performed on patients at CHBAH. The procedure incorporated the use of a Titanium Mesh Cage for the anterior column reconstruction, and in some patients, rods and screws were also utilised to reconstruct the anterior column after adequate anterior debridement of the diseased spinal segment. Both the clinical and radiological outcomes, as measured by the Oswestry Disability Index, the Frankel Neurological Scale, and Kyphosis correction, are evaluated.

All the adult patients above the age of 18 years with the diagnosis of Tuberculosis of the spine who underwent the described surgical procedure were included in the study.

The objectives of the study include:

1. To determine the deformity correction using the Cobb angle
2. To assess the neurological recovery using the Frankel Scale
3. To assess the disability recovery using the Oswestry Disability Index questionnaire

CHAPTER TWO: MATERIALS AND METHODS

2.1. Approval process and patient selection

The project site was the Chris Hani Baragwanath Academic Hospital (CHBAH), in Soweto-Johannesburg. CHBAH is one of four Teaching Hospitals of the University of the Witwatersrand, Faculty of Health Sciences. Approval from the Clinical Medical Superintendent of the CHBAH and the University of the Witwatersrand's Human Research Ethics Committee (medical) was obtained (Appendix A and B).

This was a retrospective study comprising of 60 consecutive adult patients who presented at the CHBAH orthopaedic spine unit with Tuberculosis of the thoracolumbar spine. They underwent debridement, anterior spinal reconstruction using the Mesh Cage and Bone Graft as well as adjuvant anterior stabilisation or instrumentation (known henceforth as "the surgical procedure").

The study period spanned between January 2012 and December 2015. All adult patients with the diagnosis of Tuberculosis of the spine that had the surgical procedure as described above were included.

Most of the patients presented with back pain, a deformity and/or difficulty to walk. There were constitutional symptoms of weight loss, loss of appetite and easy fatigability. Two patients had active miliary Tuberculosis.

The patients were recruited from a prospectively maintained Orthopaedic Surgery Spinal Unit database in search for demography (age and gender), the date of surgery and last follow up, clinical features (i.e. Gibbus), neurological deficits (Frankel Scoring), HIV status, Blood results (ESR and CRP), Oswestry Disability Index (ODI: pre-op and last follow up), histology and microbiology results. A total of 85 patients underwent this procedure during the study period but only 60 patients had sufficient information available to be included in the study.

Plain X-Rays of the Thoracolumbar spine and the chest were obtained upon presentation and the radiographic findings of the spine were reviewed on three consecutive occasions; pre-operatively, immediately post-operatively and at the last follow up. The X-Rays identified

any pulmonary involvement, the diagnosis and magnitude assessment of spine TB. Magnetic Resonance Imaging was used to identify the causes of neurological deficit and establish the diagnosis of atypical Tuberculosis of the spine. CT scans of the thoracolumbar spine were utilised in some patients for the diagnosis of Tuberculosis of the Spine and to provide an evidence of fusion.

The patients' neurological deficits were captured at two different time points using the Frankel Grading system (which is further described in Chapter 2.5.2). The Oswestry Disability Index was collected preoperatively and at the last follow up. Any complications that occurred were also documented.

The diagnosis was confirmed on histology and microbiology with the presence of Necrotizing Granulomatous inflammation and the identification of positive Acid-fast Bacilli (AFB), respectively. In some patients, positive Mycobacterial Tuberculosis culture results were identified. Polymerase Chain Reaction (PCR) tests were used to confirm a diagnosis when results of the other tests were inconclusive. In this study, all the patients were confirmed to have Tuberculosis of the Spine.

2.2. Sampling and sample size

A sample size of 23, as demonstrated in a similar study (35), enables an effect size of 0.8 with a confidence interval of 95% and a significance level of 0.05 to be sufficient to determine whether there is a difference between the pre- and post-operative findings in patients. An effect size of 0.8 was used in this study as this value was used by Beurskens *et al.* (1996) (45).

2.3. Data analysis

Data was analysed using the IBM® SPSS® Statistics 23.0 software. The Shapiro-Wilk test was used to test for normality of the data. As the data was shown to follow a normal distribution (see figure 3.1), parametric tests were used for further data analyses.

The Student's t-test was used to determine whether there was a significant difference between the means of the same population as in the case of the mean ODI for the pre-operative and the post-operative method. The association between the clinical outcome measures and

demographics, as well as follow up and HIV status, was determined using the Pearson correlation coefficient for continuous variables and the one-way ANOVA for categorical variables (dependent).

The Pearson Correlation Coefficient is an inferential statistical tool used to determine the correlation between two continuous variables assuming the data follows a normal distribution. As the data obtained in this study is continuous, and was shown to follow a normal distribution, the Pearson correlation coefficient was used to determine the association between the three clinical outcome measures pre- and post-operatively.

The ANOVA is a statistical tool used to determine the association between a continuous variable and categorical variable (gender and HIV status) assuming the data follows a normal distribution. In this study, the one-way ANOVA was used to determine the association between the clinical outcome measures and the demographics of the study population.

2.4. Surgical procedure

After informed consent had been granted, all the patients were subjected to transpleural or retroperitoneal approaches, under general anaesthesia, in a right lateral decubitus position.

2.4.1. The surgical approaches

The surgical approach used was dictated by the level of the lesion. In the upper thoracic region, a high trans-thoracic approach was utilised. For lesions above Thoracic spinal level 7, a periscapular incision was made and the second or third rib was removed. The scapula was mobilised by isolating and dividing the rhomboids and the trapezius muscles off the lower edge of the scapula.

The anterolateral approach to the thoracic spine provides access to Thoracic spinal levels 2 to 12 and a left side approach is preferred because the presence of the liver on the right side limits exposure. Also unexpected injury to the aorta which lies on the left side is easier to manage compared to the thinner-walled inferior vena cava on the right.

A single-lumen endotracheal intubation was inserted and a left sided Thoracotomy was performed in most of the cases. The skin incision was based on the identified rib level which

was two levels above the diseased vertebral level. The rib was dissected subperiosteally by cutting the subcutaneous tissue and the muscles overlying it. The rib was removed by cutting it at the costochondral junction and disarticulating it from the transverse process. Due care was taken to prevent injury to the intercostal nerves. The parietal pleural was incised in line with the skin incision and the lungs and other mediastinal structures were retracted using the malleable retractor. The parietal pleural overlying the vertebral bodies was dissected to expose and identify the segmental vessels which are ligated and cauterised. The periosteum was lifted off the vertebral bodies to expose the vertebral bodies and pedicles.

In the thoracolumbar junction, the presence of the diaphragm which originates from the upper lumbar (L) vertebrae and the twelfth rib presents a technical problem for exposure. The incision was therefore centred on the 10^{th} rib to facilitate exposure between T10 and L2. The incision made was curvilinear and can be extended in either a caudal or cephalad direction. The diaphragm was identified and divided at its periphery to avoid postoperative paralysis due to the damage to the phrenic nerve. The diaphragm was incised 2.5cm from its insertion and tagged with sutures to facilitate closure later.

In the lumbar region, an anterior retroperitoneal approach was utilised. This approach facilitates exposure of the L1-L5 region of the spine. The patient was positioned right side down. The incision was made on the left side to avoid the liver and inferior vena cava, as explained above. The skin incision was placed parallel to the 12^{th} rib, in the abdominal region depending on the level of exposure required. The subcutaneous tissue, external oblique, internal oblique, *transversus abdominus* and the transversalis fascia were all incised in line with the skin incision and care was taken to prevent entering the peritoneal cavity. The peritoneum was reflected anteriorly using blunt dissection to expose the psoas muscle. The structures anterior to the psoas muscles (the sympathetic chain, and the genito-femoral nerve) were identified and protected. The targeted vertebral body was exposed by elevating the psoas muscle from the vertebral bodies. The lumbar segmented vessels were also identified and ligated. The pedicles of the vertebral bodies were identified and the neural foramen was located.

2.4.1.1. Corpectomy and debridement of the diseased vertebrae

After visualisation and confirmation of the correct level using a localising hypodermic needle as opposed to the gold standard of radical debridement, a thorough (adequate) debridement of diseased vertebrae, together with granulation tissues and abscesses, up to the posterior longitudinal ligament was carried out. The intervertebral disks cephalic and caudal to the resected vertebrae were removed and care was taken not to violate the integrity of the bony end plates, in preparation for cage implantation.

Specimens were taken for histology, microscopy, culture (including Tuberculosis culture), sensitivity and parasitic and fungal analysis.

The anterior spinal column was reconstructed using a Titanium Mesh Cage (Medtronic or DePuy Synthes) in all the patients. The gap left in the spine after debridement was measured with the aid of a laminar spreader and an appropriately-sized Titanium Mesh Cage. The Titanium Mesh cage from the DePuy Synthes is called SynMesh, which is an oblong implant that is designed to treat defects in the thoracic and lumbar spine. It has dimensions ranging from 17x22mm, 22x28mm and 26x33mm and heights of 6-88mm. The construct from DePuy Synthes uses Rods and screws together with the Titanium Mesh Cage to reconstruct the anterior spinal column. Even though it comes with the end rings, the rings were not utilised in the construct. The anterior instrumentation utilised was the SynMesh Cage and Titanium Rods from the Expedium^{TM} 5.5 Spine system. This instrumentation was utilised in six patients.

The Titanium Mesh Cage from Medtronic is called ‘Pyramesh Titanium Mesh’ which is cylindrical and ovoid surgical mesh that is available in a variety of diameters, lengths and styles. It can be trimmed to specific heights. The construct from Medtronic utilises plates and screws, together with the Titanium Mesh Cage to reconstruct the anterior spinal column. The anterior instrumentation utilised the Medtronic VANTAGE^{TM} Anterior Fixation System. This instrumentation was utilised in the 54 patients.

The resected rib was morcellised, and in some instances mixed with bone graft substitutes to fill up the cage. When a retroperitoneal approach was used, due to the absence of the rib, the cage was filled with bone graft substitutes. The graft was impacted into the cage and was inserted in the gap.

The Anterior instrumentation, as described above, was utilised to support and maintain the structural integrity of the graft and increase its stability. This construct was used in all the cases irrespective of the spinal level.

An Intercostal Chest Drain was inserted to decompress the pleural cavity and the surgical wounds were closed in layers in the cases in which a thoracotomy was done. The patients were admitted into the High Care Unit for immediate post-operative monitoring for 24-48 hours. Once in the ward, the rehabilitation phase of their treatment commenced and they were given customised thermoplastic ThoracoLumboSacral Orthosis (TLSO) to aid mobilisation.

As CHBAH serves as a referral centre for a large part of the region, most of the patients had already been on empirical anti-Tuberculous treatment for a variable period of time before presentation. The patients that were not on drug treatment were commenced on empirical treatment if the clinical and radiological features were suggestive of Tuberculosis of the Spine. Depending on the biopsy report, the treatment was continued if Tuberculosis of the Spine was confirmed or stopped if there was no Tuberculosis. In this study, it was confirmed that all the patients had Tuberculosis of the Spine.

The South African National Treatment Guidelines recommends 9 months of treatment for Musculoskeletal Tuberculosis comprising 2 months of the intensive phase and 7 months of the maintenance phase. However, in most cases, the treatment period can be extended to 12 months if the patients are still symptomatic. Invariably, all the patients in the study were on anti-Tuberculous combination drug treatment for 12 months. If the patients had already started treatment prior to surgery, they continued with the treatment. The drug treatment regimen included the use of Rifafour which is a combination of the four drugs Rifampicin, Isoniazid, Pyrazinamide and Ethambutol. Rifafour was combined with Pyridoxine and administered for 2 months during the intensive phase. Thereafter, a maintenance phase consisting of Rifampicin and Isoniazid was administered for 7-10 months depending on when the patients achieved healing from the disease.

The patients were followed up for 2-3 weeks in the post-operative period for wound care, to monitor compliance with drug treatment and for rehabilitation purposes. Thereafter, they were seen in the clinic at 3 months, 6 months and yearly until discharge, for clinical (Frankel

Neurological scoring, as well as disability from low back pain assessment) and radiological evaluation. Drug therapy was completed when the patient has achieved a good clinical response over the treatment period, which is shown by radiological evidence of healing and by a normalised ESR.

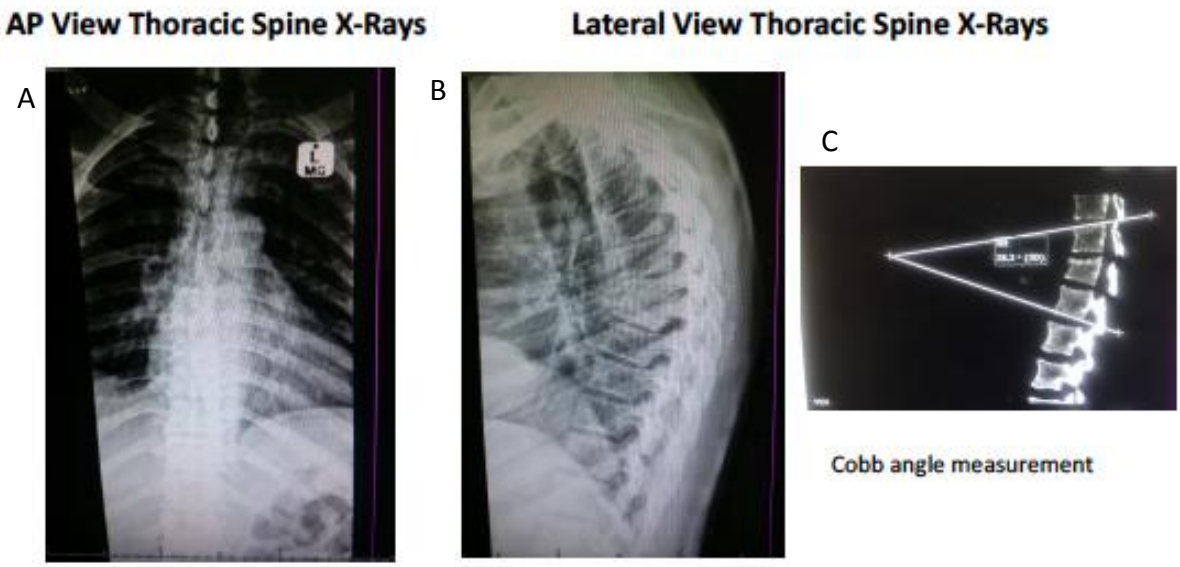

Figure 2.1: (A) Anteroposterior (AP) view and (B) Lateral view of the T7/T8 Tuberculosis of the Spine showing evidence of Bony destruction, loss of definition of intervertebral space involving the T7 and T8 Vertebral bodies (features suggestive of the Tuberculosis of the Spine). (C) Cobbs angle measurement method.

Figure 2.2 below displays the T1- and T2-weighted image of the same patient.

A) T1 weighted image **B) T2 weighted image**

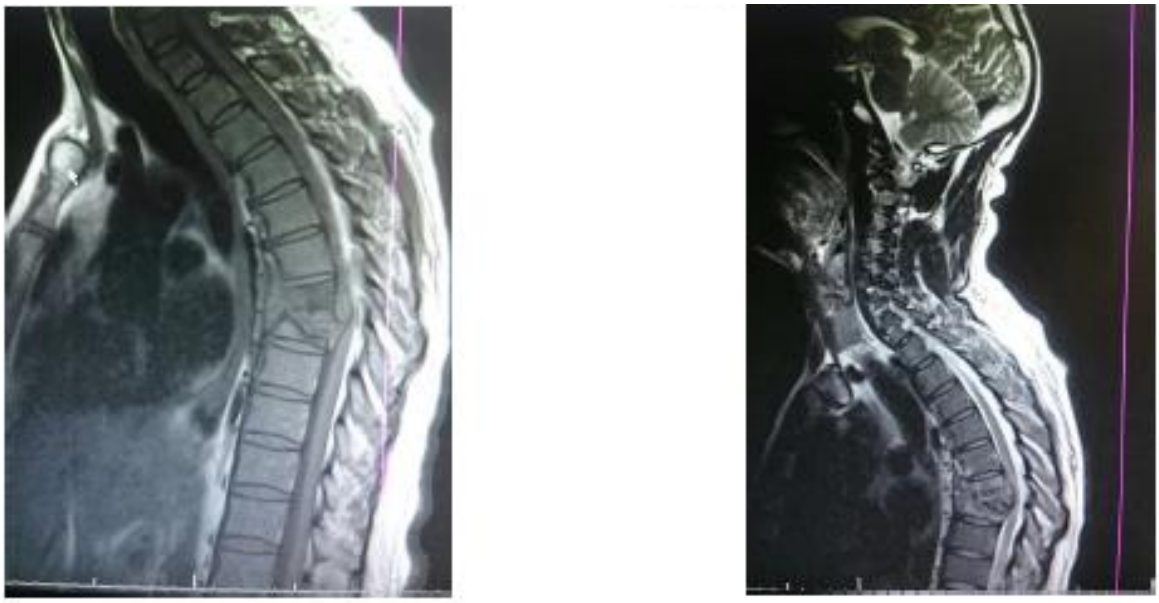

Figure 2.2: (A) T1- and (B) T2-weighted MRI images of the same patient demonstrating the destruction of the T7 and T8 vertebral bodies with extradural collection and spinal cord signal change.

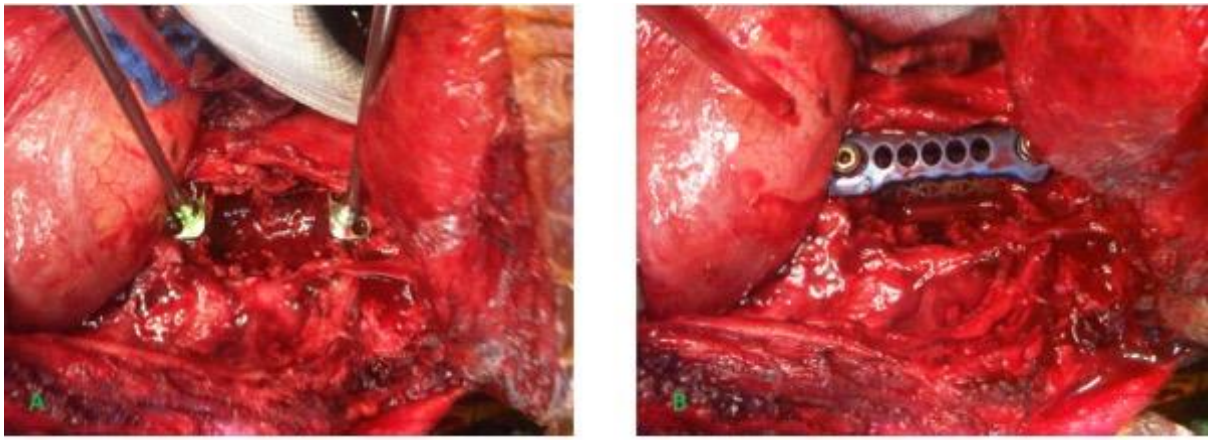

Figure 2.3: (A) and (B) shows the intra-operative images of the gap left in the spine after debridement and anterior spinal column reconstruction using Titanium Cage Mesh packed with morcellised bone (rib) from the patient and interbody fusion (plates and screws).

Figure 2.4 below displays the post op X-Rays of the Johnson & Johnson instrumentation: The Mesh cage, Rods and the screws.

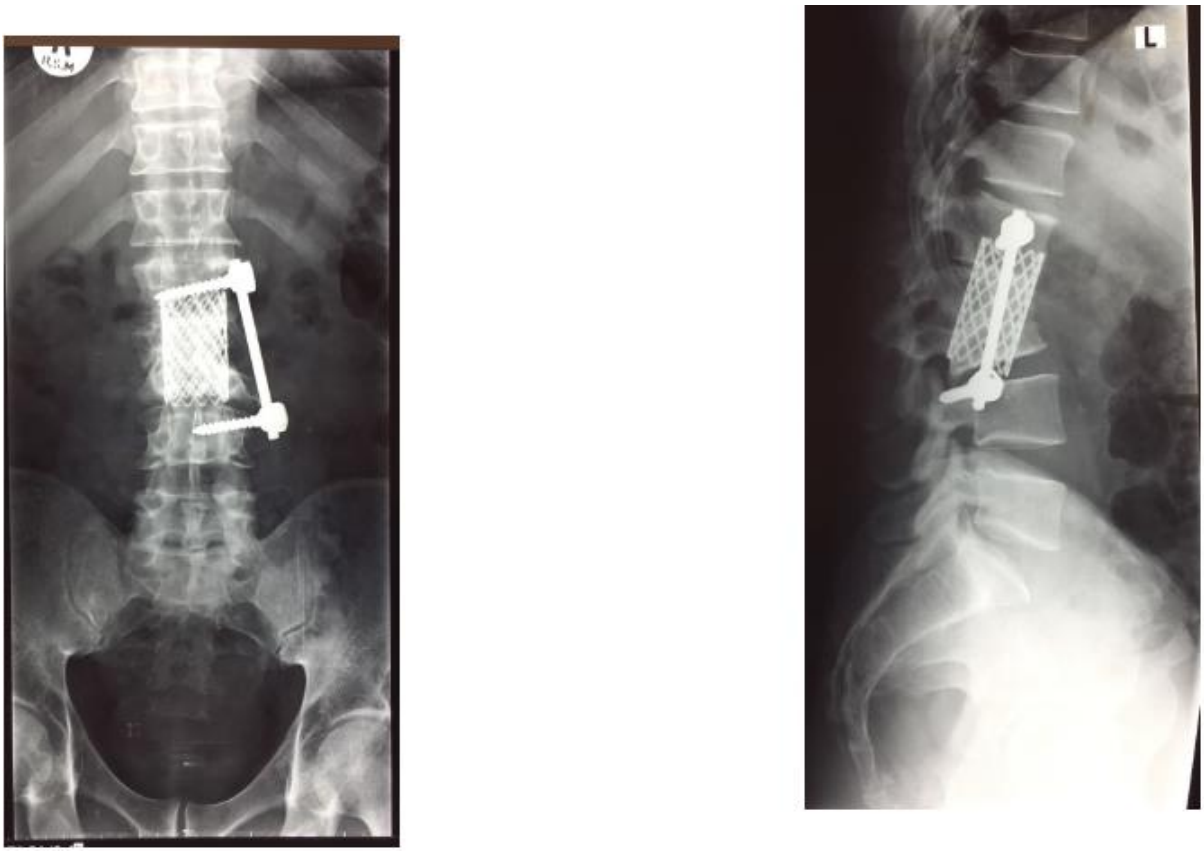

Figure 2.4: The Post Op X-Rays of the J&J construct.

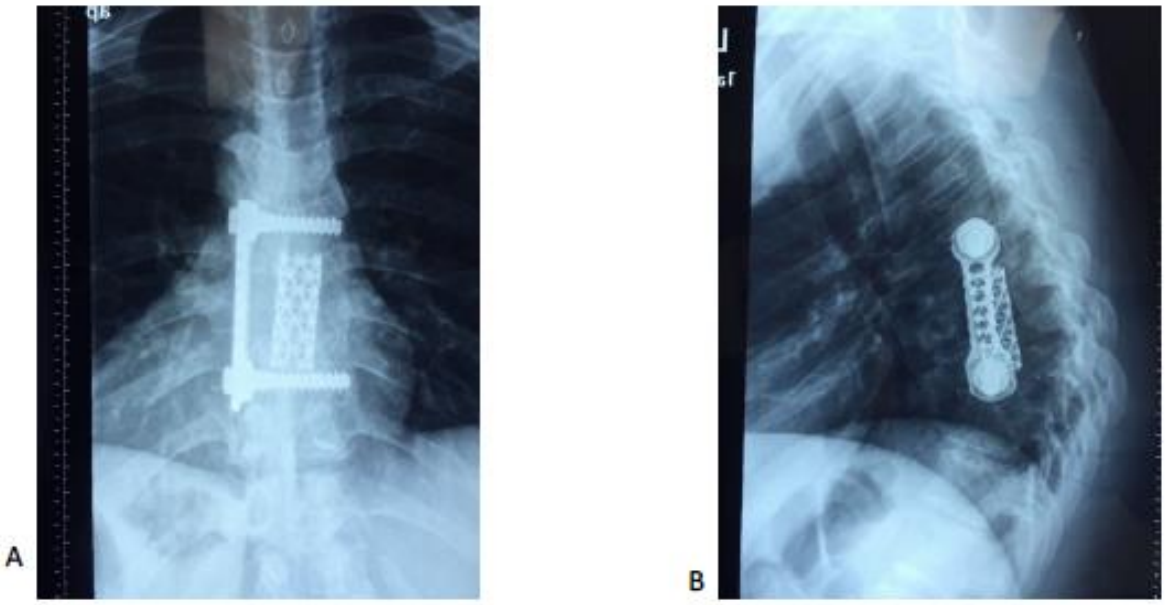

Figure 2.5: (A) and (B): Post-operative Plain X-Rays showing the construct in a patient with residual kyphosis with Medtronic implants.

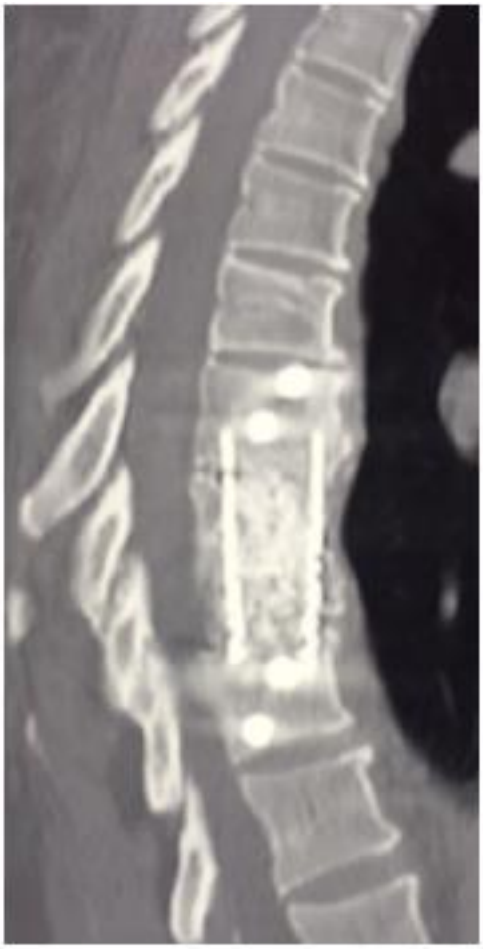

Figure 2.6: CT Scan (Sagittal view) confirming fusion and Titanium Mesh cage incorporation, in a clinical situation where bony fusion of the spine is in doubt.

2.5. Clinical and radiological Outcome Measures

The Oswestry Disability Index (ODI), the Frankel Neurological Grading System and Kyphotic Angles (which were determined using Cobb Angle measurements) were used to measure disability and pain, neurological function and deformity (Kyphosis) in the pre-operative and post-operative periods for all the patients, respectively.

2.5.1. Oswestry Disability Index

The Oswestry Disability Index (ODI) is the most commonly utilised outcome-measure questionnaire used to measure lower back pain in the clinical setting (45). As a self-

administered tool, it is divided into sections that measures the limitation of the patient's activities of daily living (ADL) due to back pain (46). This tool was used to measure disability and pain in all the patients included in this study. The ODI questionnaire is considered the gold standard of the lower back functional outcome tools (47).

Table 2.1: Interpretation of ODI Scores (47)

Score	**Interpretation**
0% to 20%: minimal disability	The patient has the ability to do most he activities of daily living.
21% to 40%: moderate disability	The patient reports more pain and difficulty with activities such as sitting, lifting and standing. Travel and participating in social activities are more difficult and they may not be able to work. However, personal care, sexual activity and sleeping are not affected.
41% to 60%: severe disability	Pains remain the major problem but activities of daily living are not affected.
61% to 80%	Back pain impairs all facets of the patient's life.
81% to 100%	The patients are either bed-ridden or exaggerating their symptoms

2.5.2. Frankel Neurological Grading Scale

The Frankel Neurological Grading scale was published in 1969 by Frankel *et al*. as shown in Table 2.2 (48). The scale was used to grade neurological deficits from A to E in all the patients included in this study pre-operatively, and at the last outpatient follow up.

Table 2.2: Scale by Frankel *et al*. (1969)

Frankel	**Neurological Deficit**
A	Full sensitive and motor palsy below the injury level
B	Full motor palsy, but some residual sensitivity present
C	Presence of sensitivity with residual motor function, not useful for the patient
D	Presence of sensitivity and motor function, but below normal levels
E	No neurological change

2.5.3. Deformity/Kyphosis as measured by the Cobb Angle

The Cobb angle is a measure of spinal deformity and was first published by Cobb in 1948 (49). This method is the most common method used to determine the degree of spinal deformity on plain X-Rays (49). In this study, spinal deformity was determined using radiographic measurements of the kyphotic deformity. A method similar to the one described by Konstam and Blesovsky in 1962 was used (50).

In the Konstam and Blesovsky method, two lines are drawn. The first line through the superior surface of the first normal vertebra proximal to the lesion and the second line through the inferior surface of the first normal vertebra distal to the lesion. Next, a line perpendicular to each of the lines is connected at the point of intersection and the angle subtended by the perpendicular lines defines the degree of kyphosis. The plain X-rays were reviewed at three stages: the pre-operative, immediate post-operative and at the last clinic follow up stages.

CHAPTER THREE - RESULTS

3.1. Test for normality of data

The Shapiro - Wilk test for normality showed a normal distribution of the data set ($p = 0.15$) as shown in Figure 3.1. Therefore, parametric tests were used to determine the association between the dependent and the independent variables.

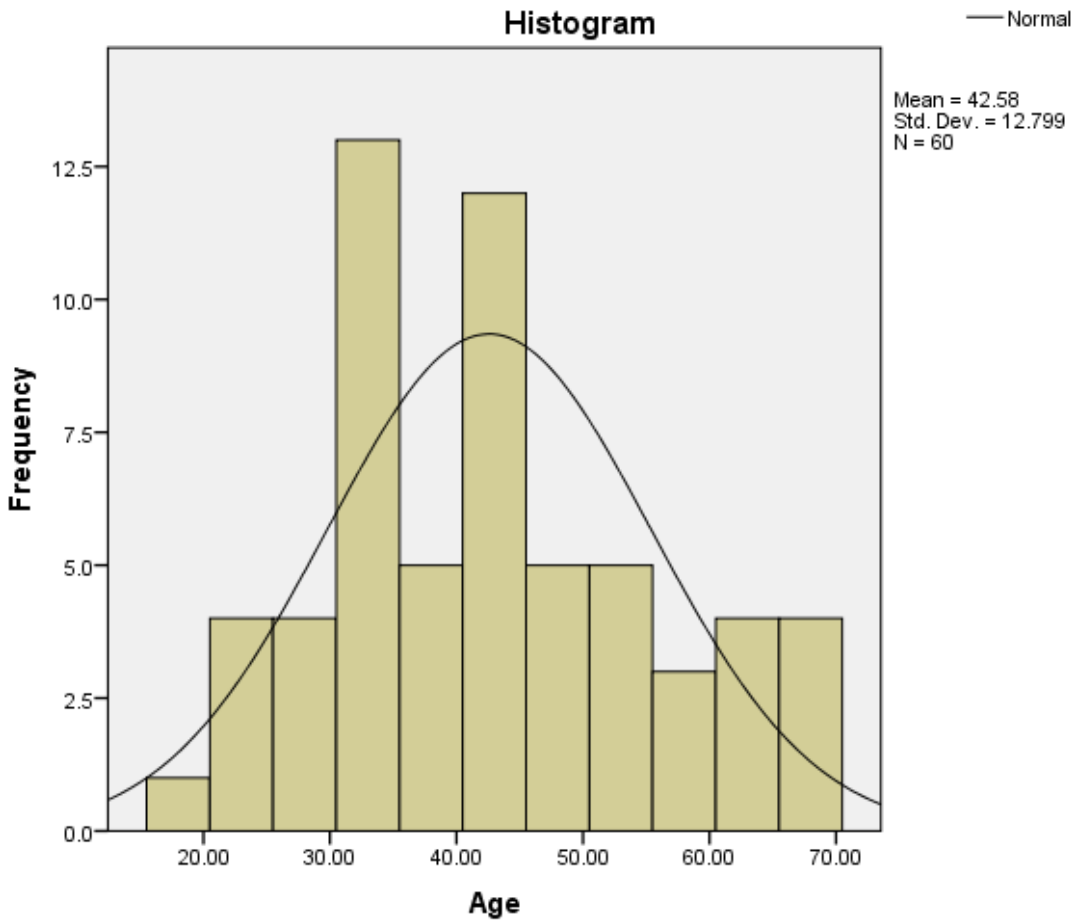

Figure 3.1: Normal distribution of the data set.

3.2. Demographic characteristics of the patients

A total of 60 patients diagnosed with Tuberculosis of the spine underwent anterior column reconstruction as described in Chapter 2 (surgical technique) between 2012 and 2015 at the Orthopaedic Spinal Unit of Chris Hani Baragwanath Academic Hospital in Soweto, Johannesburg. Of the 60 patients, 27 (45.8%) of the 44 tested patients were HIV positive and the HIV status of 16 (26.7%) patients was unknown. The mean age of the patients was 42.58 ± 12.80 years, 49.2% were between the ages of 31 – 45 years. The gender distribution of the patients showed that 68.9% of the patients were females. The mean follow-up period was 21.25 ± 8.35 months (range = 5 – 35 months). At the last follow up, two patients had died and one was not contactable. Table 3.1 shows the demographic distribution of the patients included in this study.

Table 3.1: Demographics of Tuberculosis of the spine who patients that underwent anterior column reconstruction between 2012 and 2015.

	HIV + (n=27)	**HIV – (n=17)**	**HIV unknown (n=16)**	**Total (N=60)**
Age, Mean ± SD years	40.15 ± 10.66	44.24 ± 15.42	45.13 ± 13.34	42.59 ± 12.91
Age range, years	24 - 66	18 - 70	21 – 67	18 – 70
Age category, n (%)				
≤ 30	4 (14.8)	3 (17.6)	3 (18.8)	10 (16.4)
31-45	16 (59.3)	7 (41.2)	6 (37.5)	30 (49.2)
46-64	6 (22.2)	5 (29.4)	6 (37.5)	17 (27.9)
≥65	1 (3.7)	2 (11.8)	1 (6.3)	4 (6.6)
Gender, n (%)				
Male	8 (29.6)	7 (41.2)	4 (25)	19 (31.1)
Female	19 (70.4)	10 (58.8)	12 (75)	42 (68.9)

3.3. Diagnostic tests

The diagnosis was confirmed by histology in fifty-seven patients. In three patients, the histology was inconclusive but Polymerase Chain Reaction (PCR) was used to confirm the diagnosis. Only five patients had positive staining of the Acid Fast Bacilli (AFB). The thoracic region (79.7%) was the most commonly affected area of anterior column reconstruction (ACR) as shown in Figure 3.2 below.

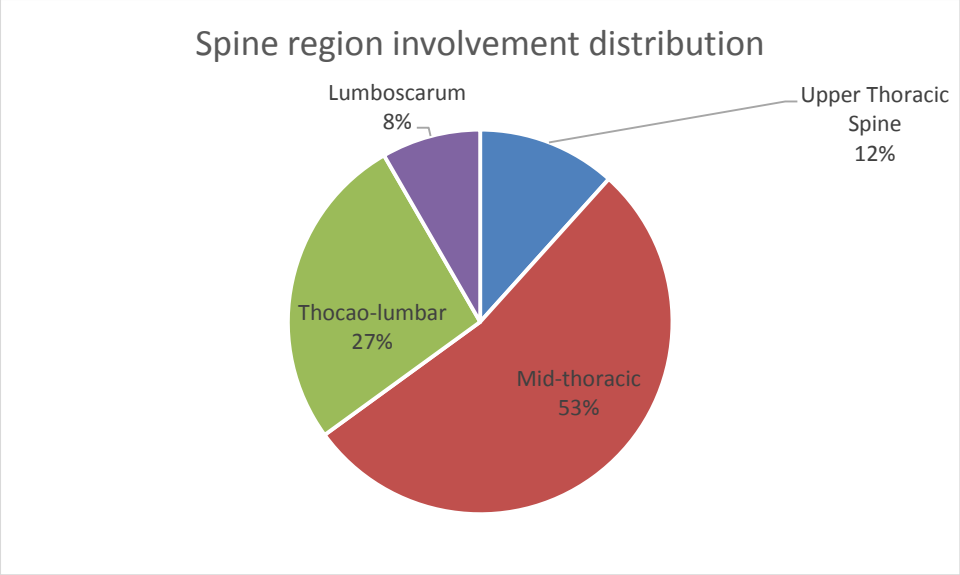

Figure 3.2: Percentage distribution of surgical area of reconstruction in the thoracolumbar region.

Figure 3.2 demonstrates that the mid-thoracic region (53%) was the most commonly reconstructed area, followed by the thoracolumbar region (27%).

3.4. Clinical and radiological outcome measures

3.4.1. Oswestry disability index (ODI)

The ODI score was used to measure the degree of disability due to back pain. The ODI score pre-operatively was 95.42% ± 6.57%, and post operatively the ODI score was 8.00% ± 12.15% and had decreased (improved) by 87.42% ± 12.85% on average among the patients. The results of the paired sample T-test showed a significant difference in the ODI score pre- and post-operatively (t=51.36, df = 56, p=0.001).

Table 3.2: Oswestry Disability Index scores pre-and post-operatively

	ODI T0	**ODI T2**	**p-value**
ODI	95.42% ± 6.57%	8.00% ± 12.15%	0.001
Mean difference		87.42% ± 12.85%	

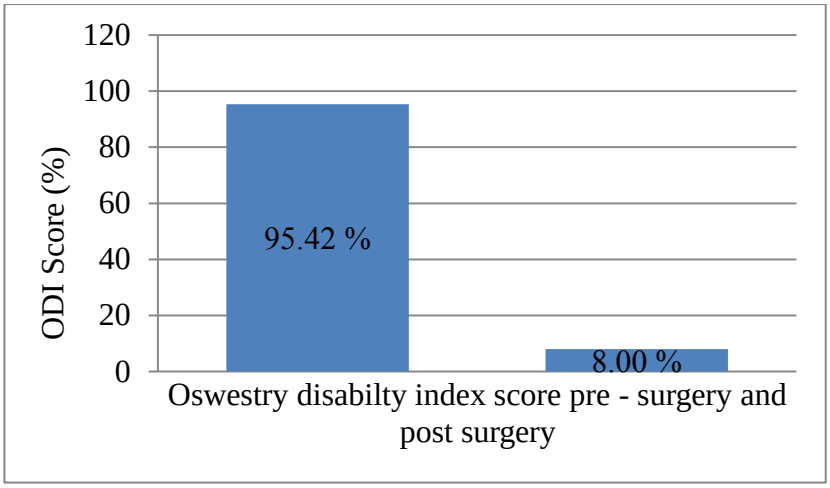

Figure 3.3: Graphical illustration of the ODI scores preoperatively (ODI T0) and at the last follow up (ODI T1) among the patients.

3.4.2. Frankel neurological classification

Pre-operatively, 58 (96.7%) patients were classified as either A, B or C on the Frankel neurological classification scale. At the last follow up, 52 (91.2%) patients were classified as either D or E on the Frankel neurological classification scale as shown in Table 3.3. There were 28 patients who were graded as Frankel A pre-operatively which at the last follow up, 16 were graded Frankel E and 6 were Frankel D. The four patients that were Frankel C pre-operatively were graded Frankel E at the last follow up. The graphical illustration of the Frankel neurological classification pre-operatively and at the last follow up is shown in Figure 3.4.

Table 3.3: Frankel neurological classification pre-and at the last follow up

Neurology at Pre-op (NT 0)	A	1		2	6	16
	B			2	6	18
	C					4
	D					1
	E					1
		A	B	C	D	E
Frankel Scale	Neurology at the last follow up (NT2)					

NT 0 is the Neurological scoring before surgery and NT2 is the score at the last follow up.

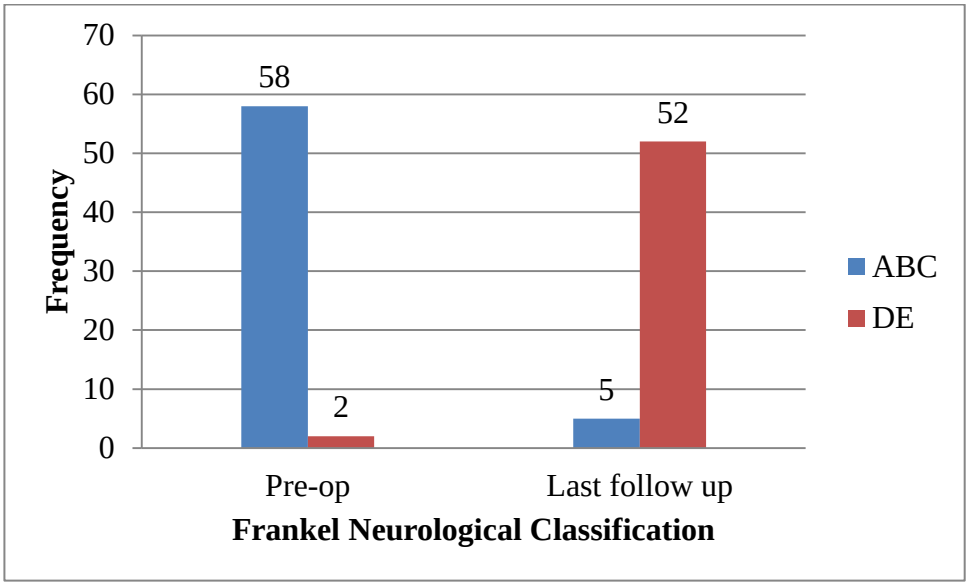

Figure 3.4: A graphical illustration of the pre-op and the last follow up Frankel neurological classification.

3.4.3. Kyphotic angle

The mean pre-operative kyphotic angle (K0) was 33.90 ± 12.44 degrees. The mean kyphotic angle in the immediate post-operative period (K1) was 23.69 ± 10.31 degrees and the mean kyphotic angle at the last follow up (K2) was 26.27 ± 10.91 degrees. These results indicated a 30.12% correction of the kyphosis in the immediate post-operative period and an overall correction of 22.51% over the preoperative kyphosis at the last follow up as shown in Table 3.4. This reflects a loss of 7.61% in the kyphosis correction for the period between the immediate post-operative and the last follow up.

Table 3.4: Mean kyphotic angle measurements pre and post operatively

	Mean (degrees)	**% change in kyphotic angle**	**p-value**
K0	33.90 ± 12.44		
K1	23.69 ± 10.31		0.001
K2	26.27 ± 10.91		
K1-K0	-12.81 ± 10.11	30.12% correction	
K2-K0	- 8.11 ± 9.46	22.51% correction	

K0 represents the mean Kyphotic angle measurements at Presentation; K1 represents the mean kyphotic angle measurements in the immediate post-operative period while K2 represents the mean measurements at the last follow-up.

CHAPTER FOUR: DISCUSSION

According to the 2016 WHO Global Tuberculosis report, Tuberculosis is a recognised major cause of global health problems affecting millions of people every year. Together with HIV infection, it remains a leading cause of death throughout the world. In 2015, there were 1.4 million deaths and an estimated 10.4 million new cases (51).

The incidence of the Tuberculosis in South Africa is reported to be 1200 in 100,000 people (52). There is a 1:300 risk that a patient with pulmonary tuberculosis will develop skeletal involvement (53). Moon in 1997 reported that patients who are HIV negative have between 3-5% skeletal involvement while up to 60% of the HIV positive patients diagnosed with pulmonary Tuberculosis will have skeletal involvement (12, 54).

The burden of HIV co-infection is clearly demonstrated in this study as 61% (27 out of 44) of tested patients were HIV positive with 70.4% of them being female. The mean age of the HIV positive patients is 40.15 years, and 70.4% are females with an age range of 31-45 years. This age group are the economically active people who are unable to contribute to the economic development of the country due to the disability caused by the disease. Thus the effect of the disease burden is further amplified not only by the cost of treatment but also by the fact that these patients also claim from the Social Security Disability Grants during their treatment period and are economically unproductive.

For most of the patients in this study, the diagnosis of Tuberculosis of the Spine was established by histology (95%), and PCR was used to confirm the diagnosis in three cases where the histological diagnosis was inconclusive. Furthermore, only five patients had positive staining for AFB. This could be explained by the fact that the majority of patients were already on anti-Tuberculosis drug treatment before their referral to CHBAH. According to the study published by Kanda *et al*. (2015), it was established that it takes about two months of continuous anti-Tuberculosis drug treatment for patients with open pulmonary Tuberculosis to become culture negative and therefore non-infectious (55). Thus if this finding is used as a proxy to the patients included in the current study, this may explain the high incidence of negative culture outcomes in the study.

The use of PCR to confirm the diagnosis in the doubtful cases supports the movement by WHO to make PCR a standard method used in the diagnosis of Tuberculosis. However, PCR

is still relatively expensive and is not available at the local clinics where the diagnosis of Tuberculosis is usually initially made.

Only one patient in the study was diagnosed with Multi-Drug Resistant (MDR) Tuberculosis. This was a female patient who was referred by the Infectious Disease Hospital with a diagnosis of Tuberculosis of the spine and Frankel B neurology. Similarly, as in the case of patients who are HIV positive, the standardised procedure was successfully performed, and the patient went back to the referring hospital to continue her medical treatment. She subsequently went on to make a full clinical and radiological recovery.

The indication for surgery in the study group was neurological deficits (59 of the 60 patients were non ambulatory at presentation). All the patients had low back pain that affected their activities of daily living and had difficulty with walking. They were disabled and not economically active.

The surgical procedure was standardised for all patients, including those with HIV co-infection and MDR Tuberculosis. Even though radical debridement was not performed, as this is an infective process, the results obtained from the study showed that there was no difference in the outcomes when compared to the gold standard. The goal of the procedure was to adequately decompress neurological elements and debride necrotising granulation, leaving viable contralateral cortical bone of the involved vertebral bodies that has a possible added advantage of promoting stability.

The patients were all operated on by the same set of surgeons, thus providing a uniform approach regarding operative techniques and post-operative management. A cohort of 60 patients with an effect size of 0.8, a 95% confidence interval and a significance level of 0.05 is sufficient to show a significant difference in the pre-operative and post-operative status of the patients. The patients were followed up for a mean period of 21.25 ± 8.35 months (range: 5 – 35 months).

In this study, patients were bed-ridden before they underwent surgery (mean ODI score: 95.42% ± 6.57%) and were able to undertake most of their activities of daily living following surgery (mean ODI score at the last follow up: 8.00% ± 12.15%). This demonstrates a mean improvement of 87.42% ± 12.85% in the ODI scoring, and is statistically and clinically

significant (p=0.001). According to the work of Solberg *et al*. (2013) in degenerative spine, the cut off values for success is a mean change of 20% in the ODI scoring after lumbar disc surgery (56). Using this as a proxy, an improvement of a mean score of 87.42% is an excellent outcome post-surgery.

Before surgical intervention, 58 patients (96.7%) were classified as non-ambulatory according to their Frankel Neurological score. At the last follow up, 53 patients (91.4%) had achieved a neurological score of either D or E, and independent ambulation. This result is comparable to the findings reported by Reimer *et al*. (2011) and Govender *et al*. (1999) (35, 43). In the study by Govender *et al.* (1999), 77% of the patients had made useful neurological recovery without the use of ambulatory support (Frankel D or E) at one year follow up, while in the Reimer *et al.* (2011) study, 70% made useful neurological recovery by achieving independent ambulation without any support at the last follow up. Christodoulou *et al*. (2006) did not discuss the neurological outcomes in their study (21). Furthermore, Hodgson *et al*. (1957 and 1960) did not discuss details of the neurological recovery in their studies. They however, noted that the longer the paraplegia before surgery, the longer it takes for the patients to recover from their neurological deficits (27, 41). Wang *et al.* (2011) noted neurological improvement in their study but did not give further detail in terms of the degree of recovery (36).

The post-operative Kyphosis deformity correction achieved in this study series compares favourably with that reported in the literature by Reimer *et al*. (2011) (35) and other similar studies. Although the initial correction of the deformity achieved at surgery had a mean value of 23.69 degrees compared to a mean of 33.90 degrees at presentation, the Kyphosis at the last follow up had a mean value of 26.27 degrees. There was a 30.12% correction achieved in the immediate post-operative period and an overall correction of 22.51% at the last follow up reflecting a loss of 7.61% in the kyphosis correction during the period between the immediate post-operative and the last follow up. This finding is similar to what has been reported in the literature. Reimer *et al*. (2011) reported a loss of correction with a mean of 10 degrees, Christodoulou *et al*. (2006) reported a loss of correction between 3-5 degrees and Wang *et al*. (2011) reported a loss of correction with a mean of 4.2 degrees at the last follow up, respectively (21, 34, 35). Even though, there was a loss of correction at the last follow up, it has no clinical significance as there was no associated negative neurological outcome. This value is comparable to the one reported by Verlaan *et al.* in 2004, who demonstrated the

failure to maintain the operatively achieved spine alignment in the post-operative period with an approximate loss of 10 degrees (57). The loss of correction could be due to the associated bony oedema of the adjacent vertebrae from the disease process, and from compression due to the inherent biomechanics of the spine which may lead to collapse because of the rigidity of the anterior instrumentation used. Also, no cage rings were utilised in the reconstruction of the anterior column and this could have reduced the risk of cage subsidence. However, when compared to the neurological grading of the patients, there was no relationship at immediate and last follow up. This is because the stability of the reconstruction provides an enabling environment for the neural elements to recover.

Complications were reported in six patients. One patient experienced cage dislodgement within the first week following surgery (Medtronic Construct). The cage migrated posteriorly into the spinal canal, resulting in neurological deterioration (from Frankel D to Frankel B). The patient underwent urgent revision surgery and went on to achieve full neurological recovery. Two patients had sepsis (both of them were HIV positive). The first patient had a superficial surgical site infection that was treated with antibiotics, local wound care and healing was achieved. The second patient presented one year after the surgery with a deep surgical site infection and a draining sinus. X-Rays confirmed fusion and incorporation of the cage in this patient. However, the patient declined further surgery. Thus, this study reveals that the concerns regarding the use of implants in the presence of sepsis is unfounded as evidenced by complete resolution of sepsis in all the patients except for one. It has been documented that Mycobacterium does not form biofilms and that Titanium does not promote adherence of the biofilms (58).

Two deaths were reported in this study giving it a mortality rate of 3.3%. One death was due to nosocomial infection and surgical wound dehiscence. The patient had an HIV co-infection and had been in the hospital for more than two months with a lung infection. The other death was due to general debilitation due to miliary Tuberculosis. Based on the study published by Govender *et al*. in 2001, it was decided that patients would not have an operation done until they were medically and nutritionally optimised (22). The mortality rate was 2.9% in the study where the gold standard procedure was used (27), 15.4% in the study by Govender *et al.* (22) and 6.9% in the study by Reimer *et al*. (34). Thus, this study's mortality rate of 3.3% compares well to those reported by other authors.

There was one case of intercostal neuropathic pain. This may have been due to the surgical approach used with the resultant intercostal damage and/or neuroma. The patient was managed with routine pain medication and was subsequently referred to the local pain clinic for further management.. Other studies (21, 35, 36) report minimal and comparable complication rates similar to the one reported in this study. Hence, attention to detail is recommended when using this approach.

The main limitation of this study is its retrospective nature. As a result, it was difficult to follow up all the patients. Johannesburg is a cosmopolitan city and the patients are people with ambition and dream, and they are economic migrants. Thus when they become sick, they may go back to their hometowns, to start life afresh upon achieving healing. This usually makes long term follow up difficult. As CHBAH does not have the Picture Archiving and Communication System (PACS), this also adds to the difficulty of tracing the full clinical, laboratory and radiological records of patients. Furthermore, a control group was unavailable as this is usually difficult to establish in spine research. However, since all patients had been operated by the same team of surgeons, a uniform approach regarding operative techniques and post-operative management was maintained.

4.1. Conclusion and recommendations

Based on this review, anterior column reconstruction using Titanium Mesh Cage and anterior instrumentation is safe and effective for the surgical management of Tuberculosis of the Spine. There were good outcomes in terms of the ability of the patients to return to their activities of daily living due to pain relief as measured by the ODI score, neurological recovery as determined by the Frankel Neurological Grading system and kyphosis correction as measured by the Cobb angle. Even though there was some loss of kyphosis correction in patients at the last follow up, this was not associated with neurological deterioration.

Despite some of the limitations identified in this study, it has been shown that this procedure is safe and effective as an adjunct to medical treatment in patients with the tuberculosis of the spine.

REFERENCES

1. Lichtor J, Lichtor A. Paleopathological evidence suggesting pre-Columbian Tuberculosis of the Spine. J Bone Joint Surg Am. 1957;39(A(6)):1938-9.
2. Duraiswami PK, Ortho M, Tuli SM. 5000 years of Orthopaedics in India. Clinical Orthop Relat Res. 1971(75):269-80.
3. Bick KM. Classics of Orthopaedics. Philadelphia: JB Lippincott Co; 1976.
4. Tuli SM. Tuberculosis of the Skeletal System. 4th ed. New Dehli: Jaypee Brothers Medical Publishers; 2010.
5. Barns PF, Barrows SA. Tuberculosis in the 1990s. Am Intern Med 1993(119):400-10.
6. Patel S, Collins DA, Bourke BE. Dont forget Tuberculosis. Ann Rheum Dis. 1995;54(3):174-
7. Scott JE, Taor WS. The changing pattern of bone and joint tuberculosis. J Bone Joint Surg (Br). 1982;64:250.
8. McLain RF, Isada C. Spinal tuberculosis deserves a place on the radar screen. Cleve Clin J Med. 2004;71(7):543-9.
9. Alavi SM, Sharifi M. Tuberculous spondylitis: risk factors and clinical/paraclinical aspects in the south west of Iran. J Infect Public Health. 2010;3(4):196-200.
10. Zhang HQ, Deng A, Guo CF, Wang YX, Chen LQ, Wang YF. Association between FokI polymorphism in Vitamin-D receptor gene and susceptibility to spinal tuberculosis in Chinese population. Arch Med Res. 2010;41(1):46-9.
11. Boachie-Adjei O, Squillante RG. Tuberculosis of the Spine. Orthop Clin North Am. 1996;27(1):95-103.
12. Moon M-S. Tuberculosis of the Spine. Controversies and a new challenge. The spine journal : official journal of the North American Spine Society. 1997;22(15):1791-7.
13. Hodgson AR, Yau A. Pott's paraplegia: A classification based upon the living pathology. Paraplegia. 1967;5(1):1-16.
14. Dunn R. The medical management of spinal tuberculosis. SA Orthopaedic Jounal. 2010;Autumn:37-41.
15. Tuberculosis Diagnostics Policy Framework 2015. <http://apps.who.int/iris/bitstream/10665/162712/1/9789241508612_eng.pdf?ua=1&ua=1> [Accessed 30.05.2017]
16. Organization WH. Global Tuberculosis Report 2015. <http://apps.who.int/iris/bitstream/10665/191102/1/9789241565059_eng.pdf> [Accessed 27.06.2016]
17. Momjian R, George M. Atypical imaging features of tuberculous spondylitis: case report with literature review. J Radiol Case Rep. 2014;8(11):1-14.
18. Ansari S, Amanullah MF, Ahmad K, Rauniyar MY, Unalan H, Oz B. Pott's spine: Diagnostic imaging modalities and technology advancements. NAmJ Med Sci. 2013;5(7):404-11.

19. Ito H, Suchiya J, Asami G. a new radical operation for Pott's disease: report of ten cases. J bone Joint Surg Am. 1934;16:499-515.
20. Bakhsh A. Medical management of spinal tuberculosis: an experience from Pakistan. The spine journal : official journal of the North American Spine Society. 1976;35:E787-91.
21. Christodoulou AG, Givissis P, Karataglis D, Symeonidis PD, Pournaras J. Treatment of tuberculous spondylitis with anterior stabilization and titanium cage. Clin Orthop Relat Res. 2006;444(60-5):60-5.
22. Govender S, Parbhoo AH, Kumar KPS, Annamalai K. Anterior spinal decompression in HIV positive patient with TB Spine.pdf. J Bone Joint Surg (Br). 2001;83-B:864-7.
23. Kotil K, Alan MS, Bilge T. Medical management of Pott disease in the thoracic and lumbar spine: a prospective clinical study. J Neurosurg Spine. 2007;6(3):222-8.
24. Jain AK. Tuberculosis of the Spine: a fresh look at an old disease. J Bone Joint Surg (Br). 2010;92:905-13.
25. National Department of Health P. National treatment guideline for TB 2014.pdf. In: Health NDo, editor. Pretoria2014.
26. Konstam PG, Konstam ST. Spinal tuberculosis in Southern Nigeria with special reference to ambulant treatment of thoracolumbar disease. J Bone Joint Surg Br. 1958;40(B)(1):26-32.
27. Hodgson AR, Stock FE, Fang HS, Ong GB. Anterior spinal fusion. The operative approach and pathological findings in 412 patients with Pott's disease of the spine. Br J Surg. 1960;48(September):172-8.
28. MRC UK. Twelfth report of trhe Medical Research Council Working Party on Tuberculosis of the spine. Controlled trial of short-course regimens of chemotherapy in the ambulatory treatment of Spinal Tuberculosis: results at three years of a study in Korea. J Bone Joint Surg (Br). 1993;75(2):240-8.
29. MRC UK. Fourteenth report of the Medical Research Council Working Party on Tuberculosis of the Spine. Five-year assessment of controlled trials of short-course chemotherapy regimens of 6, 9, or 18 months' duration for spinal tuberculosis in patients ambulatory from the start or undergoing radical surgery. International orthopaedics. 1999;23(2):73-81.
30. Pattison PRM. Pott's paraplegia: an account of the treatment of 89 consecutive patients. Paraplegia. 1986;24(2):77-91.
31. Leong JC. Tuberculosis of the spine. J Bone Joint Surg (Br). 1993;75(2):73-5.
32. Hsu LC, Cheng CL, Leong JC. Pott's paraplegia of late onset: the cause of compression and results after anterior decompression. J Bone Joint Surg Br 1988;70(4):534-8.
33. Okada Y, Miyamoto H, Uno K, Sumi M. Clinical and radiological outcome of surgery for pyogenic and tubeculous spondylitis: comparisons of surgical techniques and disease types. J Neurosurg Spine. 2009;11:620-7.

34. Ma YZ, Cui X, Li HW, Chen X, Cai XJ, Bai YB. Outcomes of anterior and posterior instrumentation under different surgical procedures for treating thoracic and lumbar spinal tuberculosis in adults. International orthopaedics. 2012;36(2):299-305.
35. Reimer B, Dunn R. Anterior-only transthoracic surgery for adult spinal tuberculosis. SA Orthopaedic Jounal. 2011;10(3):43-7.
36. Wang B, Guohua L, Liu W, Cheng I. Anterior radical debridement and reconstruction using Titanium mesh cage for the surgical treatment of Thoracic and Thoracolumbar Spinal Tuberculosis: Minimum five-year follow up. Turkish neurosurgery. 2011;21(4):575-81.
37. Muller W. Dtsch Z Chir. 1906(85):128.
38. Hibbs RA. An operation for Pott's disease of the spine. J Am Med Assoc. 1911(59):433-6.
39. Albee FH. Transplanatation of a portion of the tibia into the spine for Pott's disease. A preliminary report. J Am Med Assoc. 1911(57):887-6.
40. Henderson MD. Surg, Gynec Obstet. 1917(24):600.
41. Hodgson AR, Stock FE. Anterior spinal fusion a preliminary communication on the radical treatment of Pott's disease and Pott's paraplegia. Br J Surg. 1956;44(185):266-75.
42. Rajasekaran S, Soundarapandian S. Progression of kyphosis in tuberculosis of the spine treated by anterior arthrodesis. J Bone Joint Surg Am. 1989;71(9):1314-23.
43. Govender S, Parbhoo AH. Support of the anterior column with allografts in tuberculosis of the spine. J Bone Joint Surg (Br). 1999;81(B):106-9.
44. Patankar AP. Tuberculosis of spine: An experience of 30 cases over two years. Asian J Neurosurg. 2016;11(3):226-31.
45. Beurskens AJHM, de Vet HCW, Koke AJA. Responsiveness of the functional status in low back pain: a comparision of different instruments. Pain. 1996;65:71-6.
46. Mehra A, Baker D, Disney S, Pynsent PB. Oswestry Disability Index scoring made easy. Ann R Coll Surg Engl. 2008;90(6):497-9.
47. Fairbank JC, Pynsent PB. The Oswestry Disability Index. The spine journal : official journal of the North American Spine Society. 2000;15(25(22)):2940-52.
48. Frankel HL, Hancock DO, Hyslop G, Melzak J, Michaelis LS, Ungar GH, et al. The value of postural reduction in the initial management of closed injuries of the spine with paraplegia and tetraplegia. I. Paraplegia. 1969;7(3):179-92.
49. Cobb JR. Outline for the study of scoliosis. Am Acad Orthop Surg Inst Course Lect. 1948;5:261-74.
50. Konstam PG, Blesovsky A. The ambulant treatment of Spinal Tuberculosis. Brit J Surg,. 1962(50):26-38.
51. <WHO Global Tuberculosis Report 2016.pdf>.
52. Donald PR. The epidemiology of tuberculosis in South AFrica. Norvatis Foundation Symposium Genetics and tuberculosis. Chichester: John Wiley; 1998.

53. Strebel PM, Seager JR. Epidemiology of tuberculosis in South Africa In: H.M. C, Benatar SR, editors. A century of tuberculosis: South African perspectives. Cape Town: Oxford University Press; 1991. p. 58-90.
54. Moon M-S. Tuberculosis of spine—Contemporary thoughts on current issues and perspective views. Current Orthopaedics. 2007;21(5):364-79.
55. Kanda R, Nagao T, Tho NV, Ogawa E, Murakami Y, Osawa M, et al. Factors Affecting Time to Sputum Culture Conversion in Adults with Pulmonary Tuberculosis: A Historical Cohort Study without Censored Cases. PLoS One. 2015;10(11):e0142607.
56. Solberg T, Johnsen LG, Nygaard OP, Grotle M. Can we define success criteria for lumbar disc surgery? : estimates for a substantial amount of improvement in core outcome measures. Acta Orthop. 2013;84(2):196-201.
57. Verlaan JJ, Diekerhof CH, Buskens E, al e. Surgical treatment of traumatic fractures of the thoracic and lumbar spines: A systematic review of literatureon techniques, complications and outcomes. The spine journal : official journal of the North American Spine Society. 2004(29):803-14.
58. Chang CC, Merritt K. Infection at the site of implanted materials with and without preadhered bacterial. J Orthop Res. 1994;12:526-31.

APPENDIX A: INSTITUTIONAL APPROVAL

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

MEDICAL ADVISORY COMMITTEE
CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

PERMISSION TO CONDUCT RESEARCH

Date: 31 Aug 2016

TITLE OF PROJECT: The surgical reconstruction of the anterior column in the management of spinal tuberculosis (Chris Hani Baragwanath Academic Hospital experience 2012-2015)

UNIVERSITY: Witwatersrand

Principal Investigator: A Akinjolire

Department: Orthopaedic Surgery

Supervisor (If relevant): UN F Ukunda

Permission Head Department (where research conducted): Yes

Date of start of proposed study: Aug 2016
Date of completion of data collection: Dec 2018

The Medical Advisory Committee recommends that the said research be conducted at Chris Hani Baragwanath Hospital. The CEO /management of Chris Hani Baragwanath Hospital is accordingly informed and the study is subject to:-

- Permission having been granted by the Human Research Ethics Committee of the University of the Witwatersrand.
- the Hospital will not incur extra costs as a result of the research being conducted on its patients within the hospital
- the MAC will be informed of any serious adverse events as soon as they occur
- permission is granted for the duration of the Ethics Committee approval.

.....
Recommended
(On behalf of the MAC)
Date: 31 August 2016

.....
Approved/Not Approved
Hospital Management
Date: 06/09/16

APPENDIX B: ETHICAL APPROVAL

R14/49 Akinwande Akinjolire

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M150722

NAME: (Principal Investigator)	Akinwande Akinjolire
DEPARTMENT:	Orthopaedic Surgery Chris Hani Baragwanath Academic Hospital
PROJECT TITLE:	The Surgical Reconstruction of the Anterior Column in the Management of Spinal Tuberculosis (Chris Hani Baragwanath Academic Hospital Experience: 2012-2015)
DATE CONSIDERED:	31/07/2016
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr Fred Ukunda
APPROVED BY:	Professor P Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL:	19/09/2016

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Administrators in Room 301, 302,304,Third floor, Faculty of Hea th Sc ences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193 University of the Witwatersrand.

I/We fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report** The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in July and will therefore be due in the month July each year.

Principal Investigator Signature Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

APPENDIX C: OSWESTRY DISABILITY INDEX

Section 1 – Pain Intensity

- ❑ I have no pain at the moment.
- ❑ The pain is very mild at the moment.
- ❑ The pain is moderate at the moment.
- ❑ The pain is fairly severe at the moment.
- ❑ The pain is very severe at the moment.
- ❑ The pain is the worst imaginable at the moment.

Section 2 – Personal Care (washing, dressing, etc.)

- ❑ I can look after myself normally but it is very painful.
- ❑ I can look after myself normally but it is very painful.
- ❑ It is painful to look after myself and I am slow and careful.
- ❑ I need some help but manage most of my personal care.
- ❑ I need help every day in most aspects of my personal care.
- ❑ I need help every day in most aspects of self-care.
- ❑ I do not get dressed, wash with difficulty, and stay in bed.

Section 3 - Lifting

- ❑ I can lift heavy weights without extra pain.
- ❑ I can lift heavy weights but it gives extra pain.
- ❑ Pain prevents me from lifting heavy weights off the floor, but I can manage if they are conveniently positioned (i.e. on a table).
- ❑ Pain prevents me from lifting heavy weights, but I can manage light to medium weights if they are conveniently positioned.
- ❑ I can lift only very light weights.
- ❑ I cannot lift or carry anything at all.

Section 4 – Walking

- ❑ Pain does not prevent me walking any distance.
- ❑ Pain prevents me walking more than 1mile.
- ❑ Pain prevents me walking more than ¼ of a mile.
- ❑ Pain prevents me walking more than 100 yards.
- ❑ I can only walk using a stick or crutches.
- ❑ I am in bed most of the time and have to crawl to the toilet.

Section 5 – Sitting

- ❑ I can sit in any chair as long as I like.
- ❑ I can sit in my favorite chair as long as I like.
- ❑ Pain prevents me from sitting for more than 1 hour.
- ❑ Pain prevents me from sitting for more than ½ hour.
- ❑ Pain prevents me from sitting for more than 10 minutes.
- ❑ Pain prevents me from sitting at all.

Section 6 – Standing

- ❑ I can stand as long as I want without extra pain.
- ❑ I can stand as long as I want but it gives me extra pain.
- ❑ Pain prevents me from standing more than 1 hour.

- ❑ Pain prevents me from standing for more than ½ an hour.
- ❑ Pain prevents me from standing for more than 10 minutes.
- ❑ Pain prevents me from standing at all.

Section 7 – Sleeping

- ❑ My sleep is never disturbed by pain.
- ❑ My sleep is occasionally disturbed by pain.
- ❑ Because of pain, I have less than 6 hours sleep.
- ❑ Because of pain, I have less than 4 hours sleep.
- ❑ Because of pain, I have less than 2 hours sleep.
- ❑ Pain prevents me from sleeping at all.

Section 8 – Sex life (if applicable)

- ❑ My sex life is normal and causes no extra pain.
- ❑ My sex life is normal but causes some extra pain.
- ❑ My sex life is nearly normal but is very painful.
- ❑ My sex life is severely restricted by pain.
- ❑ My sex life is nearly absent because of pain.
- ❑ Pain prevents any sex life at all.

Section 9 – Social Life

- ❑ My social life is normal and cause me no extra pain.
- ❑ My social life is normal but increases the degree of pain.
- ❑ Pain has no significant effect on my social life apart from limiting my more energetic interests, i.e. sports.
- ❑ Pain has restricted my social life and I do not go out as often.
- ❑ Pain has restricted social life to my home.
- ❑ I have no social life because of pain.

Section 10 – Traveling

- ❑ I can travel anywhere without pain.
- ❑ I can travel anywhere but it gives extra pain.
- ❑ Pain is bad but I manage journeys of over two hours.
- ❑ Pain restricts me to short necessary journeys under 30 minutes.
- ❑ Pain prevents me from traveling except to receive treatment.

Section 11 - Previous Treatment

Over the past three months have you received treatment, tablets or medicines of any kind for your back or leg pain? Please check the appropriate box.

- ❑ No
- ❑ Yes (if yes, please state the type of treatment you have received)

APPENDIX D: DATA COLLECTION SHEET

DATA COLLECTION SHEET		
Patient Research ID		
Age		
Gender		
Spine Level disease		
Region		
Spine Level Fusion		
Date of Surgery		
Date of Last assessment		
Duration post-surgery (months)		
Kyphotic angle (T0)		
Kyphotic Angle (T1)		
Kyphotic Angle (T2)		
Percentage correction at T2		
Neurology T0 (Before surgery)		
Neurology T2 (After surgery)		
ODI at T1		
ODI at T0		
RVD status		
ESR		
CRP		
Histology		
Special staining		
PCR		
Tissue Culture		
Albumin		
Complication		