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Tuberculosis spine 'radiological spine at risk signs' in the adult population

Kanyemba, Stanley Ndakoro

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Tuberculosis Spine 'Radiological Spine at Risk Signs' In the Adult Population

Stanley Ndakoro Kanyemba
MB ChB (UKZN)
Student number: 560901
Department of Orthopaedics
School of Clinical Medicine

Supervisors:

Dr. Fred Ukunda
MD (Lubumbashi), MMed (Orth), FCS (Orth) SA
Consultant Department Orthopaedics Chris Hani Baragwaneth Hospital

Professor Mkhululi Lukhele
MBChB, MMed (Orth), FCS (Orth) SA
Professor and Head of Orthopaedics, University Of Witwatersrand

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Faculty of Health Sciences
University of the Witwatersrand, Johannesburg.

24 November 2016

Declaration

I **Stanley Ndakoro Kanyemba** hereby declare that this is entirely my own work and that I submit this report for the degree of Master in Medicine (Orthopaedics) at the University of the Witwatersrand, Johannesburg.

Furthermore I declare that this work has never been submitted for any exam at this or any other University. I agree that the Library may lend or copy this report on request.

The University of the Witwatersrand granted ethics clearance, through its ethics committee. (See Appendix I page 39).

_____

Signature

24th November 2016

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My sincere gratitude goes to the faculty of the Department of Orthopaedics Surgery at my University of Witwatersrand in general under the leadership of Professor. M.T Ramokgopa for allowing me this opportunity. I particularly thank my supervisors, Dr. Fred Ukunda and Professor Mkhululi Lukhele whose encouragement, guidance and support from the initial to the final stage enabled me to develop an understanding of this research topic.

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I offer my regards my fellow registrars, junior colleagues and secretarial staff who supported me in any respect during the completion of the project.

Lastly, Charlotte Maxeke Johannesburg Academic Hospital for allowing me to conduct the research at their institution.

Stanley Ndakoro Kanyemba

Abstract

Introduction:

Spine Tuberculosis is a common location of bone tuberculosis infection, often resulting in a kyphotic deformity with significant structural and neurological functional fall-out and mortality. [1, 3-6] Prevention of this kyphotic deformity is key in management of spinal Tb.

Radiological studies done by Rajasekaran et al. is the only extensively published literature describing this kyphotic deformity with a predictable pattern of 4 radiographical features referred to as the 'Spine at Risk Signs'.[3-6, 8, 10] In describing these 4 Radiological signs, Rajasekaran et al. state that any 2 or more out of 4 imply a significant risk to the spine, thus providing a useful classification, treatment and prognostication tool.

Importantly however, these 4 features where described only in the paediatric population and we 'borrow' this description to describe all TB-spine Xrays. Therefore, with this study we set-out to see if the same observations could be made in the adult population.

Method:

Cross sectional retrospective review based on patient records and radiographs kept by the Spine-Orthopaedics Unit at Charlotte Maxeke Johannesburg Academic Hospital.

Data collected:

Data was collected from a sample of 61 adults (adults as defined for the purposes of this study to be ≥16 years of age) patients with TB spine.

Demographic data (Gender, Age)

Radiological (X-rays were read by five examiners: the researcher, two specialists and two junior residents)

- Level of Disease Involvement
- Presence / absence of each of the four Spine At Risk Signs (SARS) as described by Rajasekaran:

Diagram of the tuberculosis radiological signs for the 'spine at risk' according to Rajasekaran[3, 11]

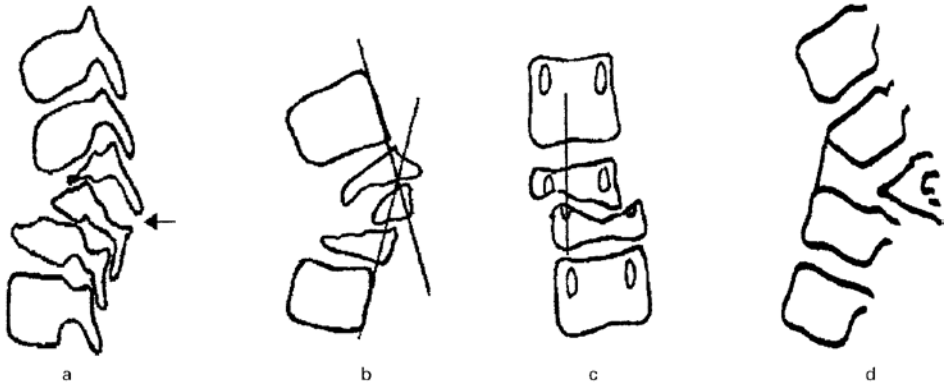
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Fig. 1

a) – *Separation of the facet joint*. The facet joint dislocates at the level of the apex of the curve, causing instability and loss of alignment.

b) – *Posterior retropulsion.* This is identified by drawing two lines along the posterior surface of the first upper and lower normal vertebrae. The diseased segments are found to be posterior to the intersection of the lines.
c) – *Lateral translation*. This is confirmed when a vertical line drawn through the middle of the pedicle of the first lower normal vertebra does not touch the pedicle of the first upper normal vertebra.

d) – *Toppling sign*. In the initial stages of collapse, a line drawn along the anterior surface of the first lower normal vertebra intersects the inferior surface of the first upper normal vertebra. 'Tilt' or 'toppling' occurs when the line intersects higher than the middle of the anterior surface of the first normal upper vertebra

- Total SARS score
  - Scoring system is developed from each of the Rajasekaran signs, each sign representing a value of 1
  - There for 4 signs, the maximum value is 4 meaning all signs are present and minimal score = 0, meaning no signs are present.

Data file was assembled in consultation with a statistician.

Results:

Five researchers looked at Anteroposterior and lateral X-rays of the Thoracic, Thoracolumbar and lumbar spine affected by Tb to establish the presence of the four Tb Spine at Risk signs as described by Rajasekaran. A Sample size of 61 patients deemed statistically significant and representative of the prevalence of Tb spine in the population older than 15 years, ages ranging from 16 to 72 years.

In keeping with major prevalence data, the mean age of our study group was 42 years with the highest incidence in the age group 36 to 49 years old, with a female preponderance of spine Tb at 54.1 %. The other 2 age groups are 17-35 at 32.8% and 50+ age group at 29, 5%.

The lumbar spine 54.1% was the most affected, followed by the thoracic 29.5 % and thoracolumbar spine 16.4 %, we excluded the cervical spine for the purposes of this study.

Tabulation of Spine at Risk observations,

% who identified the SARS out of 61	**SARS a) Separation**	**SARS b) Retropulsion**	**SARS c) Translation**	**SARS d) Toppling**
Observer 1	57.4	52.5	21.3	31.2
Observer 2	18.0	9.8	13.1	4.9
Observer 3	24.6	4.9	4.9	6.6
Observer 4	32.8	34.4	27.9	49.2
Observer 5	3.3	21.3	16.4	18.0

Table. 1 Spine at Risk Observations

The above observations show tabulated observations per percentage, with no agreement of what was seen by the different observers.

The significance of this observations points to the poor reliability of this classification system to everyday use. Furthermore, using Cochran's Q statistics there is significant interobserver variability showing inconsistency in the same observation about the presence of 'Spine At Risk Signs'.

Additionally, looking at Spine at risk Classification.

% who identified the patient as being at risk	Spines at risk
Observer 1	49.2
Observer 2	0.0
Observer 3	8.2
Observer 4	44.3
Observer 5	21.3

Table. 2 Spine at Risk Classification

The classification **Fig. 1**, such as the patients scored out of 4 show a similar trend as the Observation. There is also no agreement between the observers as to what was seen to be at Risk.

Conclusion:

Scoring and classification systems are an important tool in clinical practice, therefore our need to use them. The ‘Rajasekaran Spine At risk signs’ are such a valuable tool, but was only describe to be used in the population group 15 years and younger. Therefore, our need to extend its use in all adults affected by TB spine.

However, in our study we see significant interobserver variability with the same X-rays presented to different observers. It is important to have agreement between observers before we can say that a given tool is acceptable for wide clinic use. Additionally, we could not accept the application of the scoring system within the ‘Spine at Risk Signs’.

There is an overall paucity of literature on this subject; perhaps, a follow up study should be undertaken with prior training of observers, observers going through a few X-Rays together followed by clear instructions to review the X-Rays.

Table of contents

Title……1
Declaration…….2
Acknowledgements……3
Abstract…… 4
Table of contents……8
List of tables and figures……10
List of abbreviations and definition of terms…….11

Chapter 1 - Introduction and Literature review

Tuberculosis……..12
Epidemiology……12
Spine Anatomy and Biomechanics…..……..12
Spine at Risk……..13

Chapter 2 - Research Question

Background ……..15
Aim……15
Objectives ……..……15
Significance ……..15

Chapter 3 – Study design and methodology

Participants/Setting …….16
Inclusion criteria …….16
Exclusion criteria ……16
Methodology ……...16
Data Files ……17
Data Preparation /Cleaning …….17
Sample Size …….17
Data Analyses ……..17

Chapter 4 – Results

Description of the demographics and Clinical characteristics of the study group……..18
Level of spine affected……19
Presence/Absence of each of the SARS …….20
Spine at Risk Classification ……23
SARS Score ……25

Chapter 5 – Discussion ……29

Chapter 6 – Conclusions and recommendations …….31

References ……32

Appendix ……..34

Ethics approval …….34
Spine at Risk Signs explained ……..35
Scoring Sheet ……36

List of Tables and Figures

Table 1: Presence/Absence of each of the SARS
Table 2: Agreement SARS
Table 3: Agreement and Bias
Table 4: Spine at Risk Classification
Table 5: Agreement on Spine at Risk Classification
Table 6: Agreement and Bias between each pairs of Raters
Table 7: SARS Score
Table 8: Agreement between each pair of raters

Chart1: Age Distribution
Chart2: Age Grouping
Chart3: Level of Spine affected
Chart5: The percentage of patients with each of the four SARS
Chart6: SARS scores
Chart7: SARS and Age distribution

Figure 1: Diagram of the tuberculosis radiological signs for the 'spine at risk' according to Rajasekaran 26

List of abbreviations

WHO -	World Health Organization
TB/Tb-	Tuberculosis
SARS-	Spine at Risk Signs
HIV-	Human Immunodeficiency Virus
C1…-	Cervical
T-	Thoracic
L-	Lumbar
X-Ray-	Roentgenogram
Std Dev-	Standard Deviation
Pctl-	Percentile
ICC-	Intraclass Correlation Coefficient
vs-	Versus
y-	Year
EBM-	Evidence Based Medicine

Chapter 1 - Introduction and Literature review

Tuberculosis

Robert Koch, 24 March 1882 described an acid-fast, rod shaped, non-spore forming, and thin aerobic bacterium measuring 0.5 µm by 3 µm, for which he got the Nobel Prize in physiology/medicine 1905. This organism is the causative agent for Tuberculosis infection and is therefore often referred to as Koch's bacillus.[1]

In the disease patterns, Extra-Pulmonary Tuberculosis forms 5 to 10%, of all Tuberculosis infections and 50 % of this extra-pulmonary TB affects the spine.

Epidemiology

The World Health Organization (WHO) states that Tuberculosis (TB) is still the commonest cause of infectious disease related mortality worldwide. With an estimated 2 billion people worldwide having latent Tuberculosis. Which means that a third of the World's population is affected. In 2009 an estimated mortality rate of 1.7 million people worldwide was directly due to Tuberculosis.[2]

The figures further show that Sub-Saharan Africa is the hardest hit by the tuberculosis pandemic in general, with South Africa having the 3rd highest prevalence figures worldwide. In 2012 South Africa had an estimated Incidence of 718 per 100 000 population, with a uniquely dual pandemic alongside the Human Immunodeficiency Syndrome (HIV). The mortality rates recorded by WHO 2004 of 56 per 100 000 population amongst the HIV negative patients and 78 per 100 000 population in the HIV positive patients.[2]

The literature suggests, up to 80% of patients with spinal involvement will present with some detectable kyphosis at presentation, which can be cosmetically and functionally disabling, and lead to a possible contribution to neurological fall-out and mortality.[3-6]

Spine Anatomy and Biomechanics

Spinal tuberculosis typically affects and destroys the anterior structures of the spine in majority of patients.[3] The implications of this can be understood by a look at the spinal anatomical biomechanics. This can be explained by 2 interconnected 'anato-biomechanical' concepts.

The functional unit of the spine consist of 2 adjacent vertebrae with their intervening intervertebral disc. This functional unit is the structural unit affected by Tb, compromising the stability of the entire spine. [5, 12, 14]

Tuberculosis affects this balance through the destruction of the passive musculoskeletal subsystem consisting of vertebrae, facet articulations, intervertebral discs, spinal ligament and joint capsule forming the constituents of a structural spinal segment that are directly affected in spinal tuberculosis.

The anterior column destruction; results in a tensile stress on the posterior structures severely increasing, causing dislocation of the facets joints that lead to spine instability.[3]

Spine at Risk Signs

In his longitudinal observational study over a period of 15 years, S. Rajasekaran[3, 11] described the widely accepted tuberculosis 'spine at risk signs'.[8, 10] In that study, 61 children were involved ages ranging from 6 to 15 years old. Their antero-posterior and lateral x-rays were assessed at months 1,3,6,9, 12 and 18 months subsequently every year thereafter for 15 years.
Included in the study were patients with active TB from the 1st thoracic vertebra (T1) to the 1st sacral vertebrae (S1). Vertebral levels were further defined as **Thoracic** if from the 1st thoracic vertebra (T1) till the 10th thoracic vertebra (T10); **Thoraco-lumbar** from 11th thoracic vertebra (T11) till the 2nd lumbar vertebra (L2). Lastly **lumbar**, from 3rd lumbar (L3) vertebrae till the 1st sacral vertebra (S1). This group was part of a larger prospective multicentre control trial of 304 patients with TB spine, investigating the efficacy of short course ambulatory chemotherapy as compared with short-course chemotherapy combined with anterior spinal radical debridement and bone grafting surgical procedure. [3, 5,8,10]

Development of the deformity and subsequent kyphosis though influenced by the amount of destruction, the level of the lesion and the age of the patient showed two distinct phases. These phases where described as active phase and the healed phase. Characteristically these two phases showed a significant difference in the progression of deformity, with the active phase showing an almost logarithmic increase in deformity, plateau at around 18 months. The healed phase starts at around 18 months and last around 180 months. By comparative observation the healed phase in the adult is static with no further change in deformity versus a child in which it is a dynamic phase marked by slight improvement in deformity. [3,11,15,16]Therefore, as stated before deformity prevention is a major priority in the treatment of spinal tuberculosis.

S. Rajasekaran, described four radiological signs that would predict the severity of deformity. He termed these signs the 'Spine at risk signs' (SARS) of tuberculosis spine. The signs follow a predictable pattern based on spinal biomechanics, and may implicate a progression in deformity.

Figure 1: Diagram of the tuberculosis radiological signs for the 'spine at risk' according to Rajasekaran[3, 11]

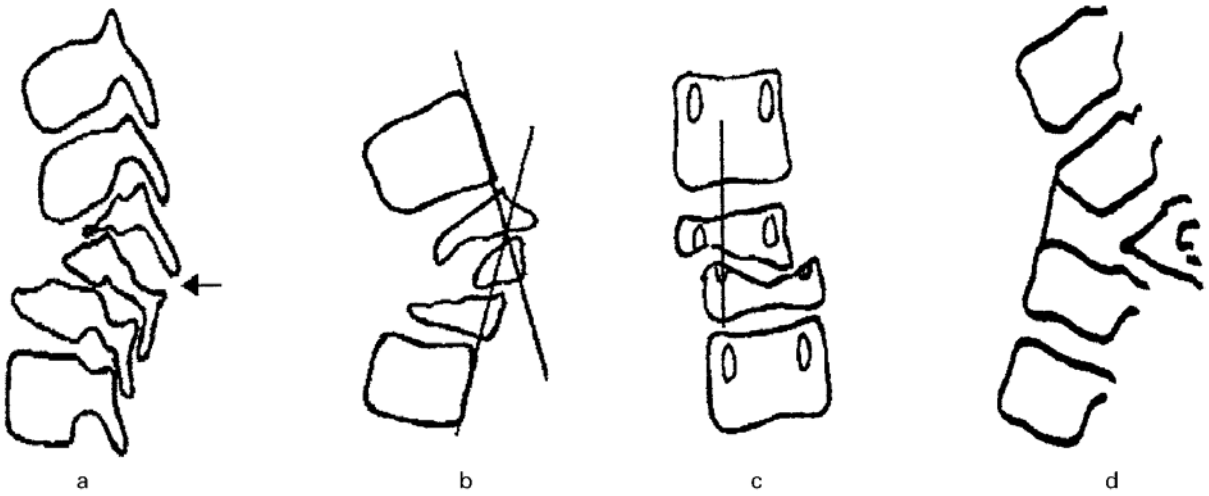


Figure 1a – *Separation of the facet joint.* The facet joint dislocates at the level of the apex of the curve, causing instability and loss of alignment. In severe cases the separation can occur at two levels.

Figure 1b – *Posterior retropulsion.* This is identified by drawing two lines along the posterior surface of the first upper and lower normal vertebrae. The diseased segments are found to be posterior to the intersection of the lines.

Figure 1c – *Lateral translation*. This is confirmed when a vertical line drawn through the middle of the pedicle of the first lower normal vertebra does not touch the pedicle of the first upper normal vertebra.

Figure 1d – *Toppling sign*. In the initial stages of collapse, a line drawn along the anterior surface of the first lower normal vertebra intersects the inferior surface of the first upper normal vertebra. 'Tilt' or 'toppling' occurs when the line intersects higher than the middle of the anterior surface of the first normal upper vertebra.

Thus, spine at risk signs Figure 1:

i) Facet Joint Dislocation
ii) Posterior retropulsion of diseased fragments
iii) Lateral Translation
iv) Toppling of the superior vertebra

Each of these points is allocated a score of 1 point to create a spinal instability score, thus scoring out of 4. A score of ≥ 2, was seen as a 'Spine at risk', thus probably requiring surgical stabilization in spite of medical management.[3, 11] These, signs are significant as they predict the risk of deformity progression and final outcome of spinal tuberculosis, thus the appropriate preventative intervention can be preemptively applied. Correction of deformity once established is hazardous, difficult and flawed with high rate of complications.[3, 11]

These S. Rajasekaran system only applied to the population under 16 years old, therefore it did not apply to the older (adult) population.

Chapter 2: Research Question

What is the Prevalence of TB 'Spine at Risk signs' in the adult population?

Background:

Charlotte Maxeke Johannesburg Academic Hospital carries a heavy responsibility as a level 1 Orthopaedic Spinal care centre and one of the two main teaching hospitals of the University of Witwatersrand catering for the public health of not only the entire Johannesburg but also for the whole South Gauteng, neighbouring provinces and countries.

Because of such a large drainage area cases of spinal tuberculosis are common. Medical management of such is mainstay and the indications for surgery are controversial.

Aim

The aim of the study is to determine if the radiological TB spine 'spine at risk signs' as described by S. Rajasekaran; in children are present in the Adult population affected by Tuberculosis of the Spine.

Objectives

Primary:

To determine tuberculosis spine at risk signs in the adult population by observing radiographs

Secondary:

- Determine the inter-rater agreement for the five radiological outcomes.

- Using the majority decision for the four SARS, and the total SARS score derived from this, describe the prevalence of each signs in the study group, as well as the proportion of spines at risk (total score >= 2).

- To validate the scoring system as applied by Rajasekaran to the adult (as disease reported in older than 15 years old) population by assessing inter-rata agreement

Significance

There is currently no literature published looking at the signs in the adult population.

Chapter 3: Study design and methodology

Study Design

Participants/Settings

Review the radiographs of patients treated for thoracolumbar spine tuberculosis at the Wits orthopaedic spine unit.

Inclusion and Exclusions Criteria

Inclusion

Patients affected by Tuberculosis of the spine aged ≥ 16 years. Basic records must be available i.e.:

- Demographic records (Age, Gender)
- X-Rays of affected area (Antero-posterior and Lateral)

Exclusion

Patients affected by Cranio-cervical, cervical and sacral tuberculosis below the second sacral spinal vertebra are not of interest. Patient with incomplete basic records or poor quality radiographs will not be included.

Methodology

This will be a cross sectional retrospective review based mainly on basic records and their accompanying radiographs from records kept of patients presenting at Wits University Academic Circuit. The quality and adequacy of radiographs are not the main concern as long as they cover the affected areas of interest from the 1st thoracic vertebra to the 1st sacral vertebra.

The following data were collected:

Demographic

- Gender
- Age

Clinical history

- Level of disease involvement

Radiological (X-rays were read by five examiners: the researcher, two specialists and two junior residents)

- Presence / absence of each of the four Spine at Risk Signs (SARS)
- Total SARS score (1 point per sign; thus, min=0, max=4).

Approval and Consent to use the X-rays and records were obtained from Superintendent of the hospital**.** Additional consent was also obtained from Wits Ethics (Medical) Committee**.**

Data files

SK data v3.xls excel spread sheet was created and used for data analysis

Data preparation / cleaning

Data file was assembled in consultation with a statistician.

The spine at risk status was calculated.

The majority decision rule was used to determine the final value for each of the four SARS. From this, the final SARS score and the spine at risk status were calculated.

Sample size

An estimation of sample size is based on the key research question to be answered, which in this case is the observation of 'spine at risk signs' in the adult population. Statistics will help assess inter-observer reliability for the four SARS. For all kappa-like agreement coefficients, the required number of subjects (n) depends on the relative error (r), the number of subjects in the entire population (N) and the difference p_a-p_e between the overall agreement probability p_a and the chance agreement probability p_e as follows:

$$n = \frac{n^*}{1 + \frac{n^*}{N}}, where\ n^* = \frac{1}{r^2(p_a - p_e)^2}$$

Assuming that N is very large, and that the chance-agreement probability is 0, the overall agreement probability is at least 0.6 (0.7), and a relative error of 20%, the required n is 69 (51). The actual sample size of 61 falls within this range, so is deemed to be reasonable for the purposes of this study.

Data Analysis

A Statistician has been consulted for absolute numbers needed to draw statistical significant observations.

Data will be imported from MS Excel spreadsheet for Data analysis to be carried out using SAS (Statistical Analysis System) [26].

The 5% significance level was used throughout, unless specified otherwise.

In other words, p-values <0.05 indicate significant results.

Chapter 4: Results

A) Description of the demographic and clinical characteristics of the study group

The demographic and clinical characteristics of the study group are tabulated in the spreadsheet.

4.1 Age

The mean age of the patients was 42.0 years (sd=13.4y; median=40y, interquartile range 34-52y; range 17-72y). The distribution of ages is shown below:

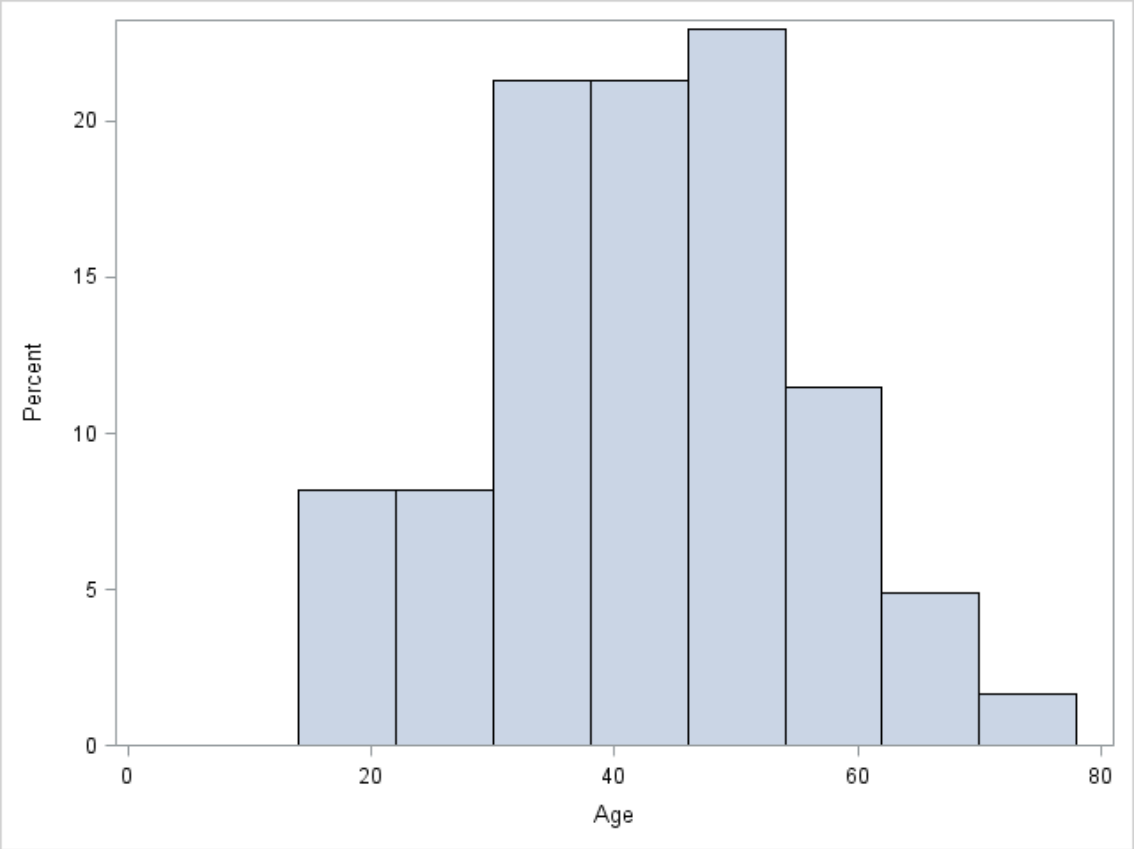


Chart 1: Age distribution

For further analysis, age was categorised as 17-35 / 36-49 / 50y+.

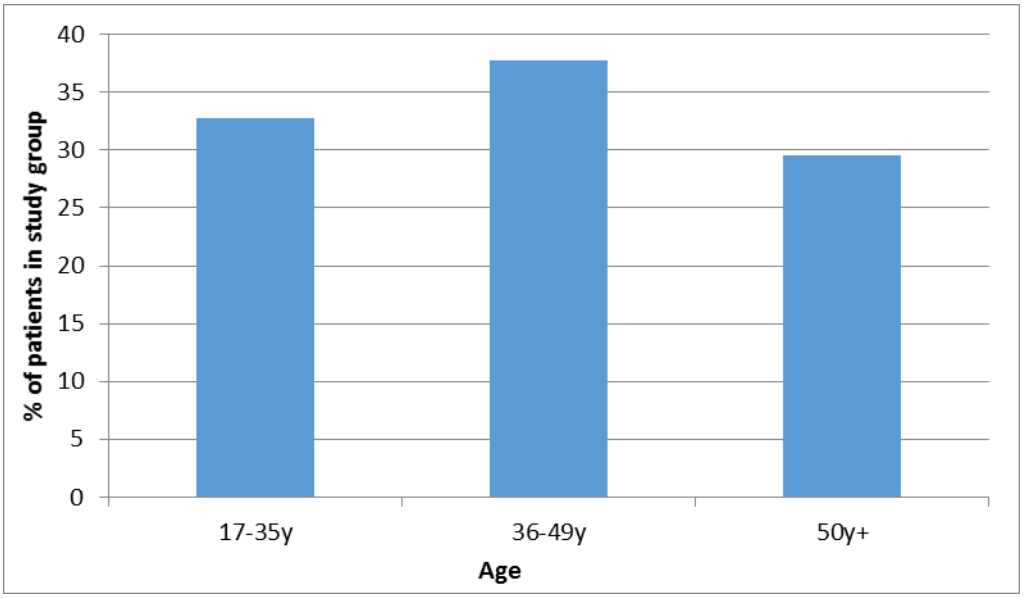


Chart 2: Age Grouping

B) 4.2 Sex

The female population of 54.1% and 45.9% of the patients were male.

C) 4.3 Level of spine affected

The lumbar spine was most frequently affected (54.1% of cases).

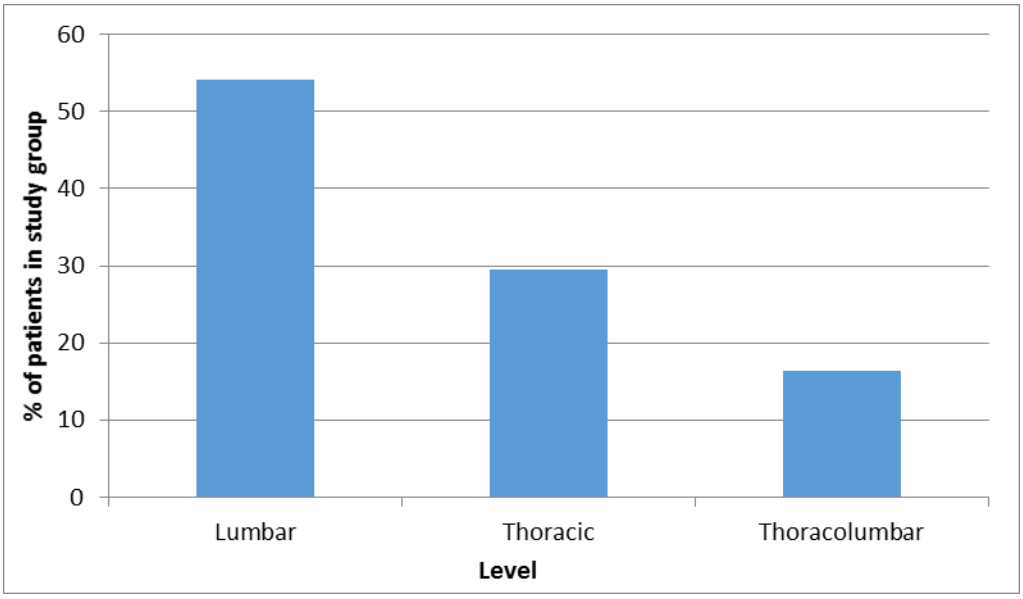


Chart 3: Level of Spine affected

D) 4.4 Presence/absence of each of the SARS

The percentage of cases with each SARS identified by each of the observers is shown below:

Table 1: **Presence/absence of each of the SARS**

% who identified the SARS	**SARS a) Separation**	**SARS b) Retropulsion**	**SARS c) Translation**	**SARS d) Toppling**
Observer 1	57.4	52.5	21.3	31.2
Observer 2	18.0	9.8	13.1	4.9
Observer 3	24.6	4.9	4.9	6.6
Observer 4	32.8	34.4	27.9	49.2
Observer 5	3.3	21.3	16.4	18.0

Table 1. Shows an enormous variation between the Observers. This will statistically result in a poor inter-observer agreement.

Agreement

In our study, we have binary outcome (i.e. score 1 = particular SARS present, 0 = none Observed) and five observers, so we use Fleiss' kappa for multiple observers and a binary outcome. [27]

$$\hat{\mathrm{K}}_f = 1 - \frac{\sum_{i=1}^{k} y_i(n_i - y_i)}{kn(n-1)\hat{\pi}(1-\hat{\pi})}$$

Where

k = number of subjects (=61)

y_i = number of positive observations for subject i

n_i =number of observers for subject I (=5)

$\hat{\pi} = \sum_{i=1}^{k} \frac{y_i}{nk}$

The results are shown below:

Table 2: Agreement SARS

	SARS a) Separation	SARS b) Retropulsion	SARS c) Translation	SARS d) Toppling
Raw agreement (%)	31.1	27.9	50.8	34.4
Chance-corrected kappa	0.18	0.04	0.20	0.05
Level of agreement	slight	slight	slight	slight
Inter-rater bias (p-value for Cochran's Q)	<0.0001	0.0026	<0.0001	<0.0001

The raw agreement (i.e. all five scored 0 or all five scored 1) between all five observers was very low.

The kappa chance-corrected measure of agreement was very low, in all four cases corresponding to 'slight' agreement. [28]

Interobserver bias

Next, we test for interobserver bias among the five observers, using Cochran's Q statistic. This was significant in all four cases, indicating significant bias between the observers in determining the presence / absence of each of the SARS.

To investigate these findings, we now look at the agreement and bias between each pair of observers, to see if we can find reasons for the low kappa and significant bias between the five observers. For each pair of observers, we report the chance-corrected kappa and the test for interobserver bias (McNemar's test for two observers; significant p-values marked in red).

The results are summarised in the table below:

Table 3: Agreement and Bias

Obsevers	kappa	Level of agreement	p-value for McNemar's test	kappa	Level of agreement	p-value for McNemar's test	kappa	Level of agreement	p-value for McNemar's test	kappa	Level of agreement	p-value for McNemar's test
	SARS I			SARS II			SARS III			SARS IV		
1 vs 2	0.04	slight	<0.0001	0.00	slight	<0.0001	0.15	slight	0.20	0.00	slight	0.0006
1 vs 3	0.27	fair	<0.0001	0.03	slight	<0.0001	0.32	fair	0.0016	0.07	slight	0.0006
1 vs 4	0.34	fair	0.0011	0.19	slight	0.028	**0.47**	**moderate**	0.25	0.37	fair	0.012
1 vs 5	0.05	slight	<0.0001	0.01	slight	0.0006	0.20	slight	0.43	0.05	slight	0.09
2 vs 3	0.22	fair	0.32	0.17	slight	0.25	0.31	fair	0.06	0.00	slight	0.71
2 vs 4	0.20	slight	0.039	0.00	slight	0.0018	0.00	slight	0.05	0.00	slight	<0.0001
2 vs 5	0.10	slight	0.007	0.21	fair	0.05	0.09	slight	0.59	0.00	slight	0.032
3 vs 4	**0.56**	**moderate**	0.13	0.18	slight	<0.0001	0.23	fair	0.0002	0.14	slight	<0.0001
3 vs 5	0.19	slight	0.0003	0.05	slight	0.0075	0.25	fair	0.019	0.33	fair	0.019
4 vs 5	0.13	slight	<0.0001	0.04	slight	0.10	0.11	slight	0.11	0.04	slight	0.0004

We see that:

- The agreement between all pairs of observers was very low, but particularly low for 1 vs 2, 1 vs 5, 2 vs 4, and 4 vs 5.
- The only pair of observers for whom there was consistently (across all four SARS) no interobserver bias, was Observers 2 and 3. But their inter-observer agreement was also very low.

There is no basis for using the majority decision rule to determine the data to be used in later analyses, nor is there any basis for choosing the ratings of one (or two) observers over that of the other observers.

E) Spine at risk classification

The approach was the same as for the four SARS indicators. The percentage of spines at risk identified by each of the observers is shown below:

Table 4: Spine at Risk Classification

% who identified the patient as being at risk	Spines at risk
Observer 1	49.2
Observer 2	0.0
Observer 3	8.2
Observer 4	44.3
Observer 5	21.3

Already, we can see that there is enormous variation between the observers, and that inter-observer agreement is going to be very poor.

Agreement

The results are shown below:

Table 5: Agreement on Spine at Risk Classification

	Spines at risk
Raw agreement (%)	34.4
Chance-corrected kappa	0.10
Level of agreement	slight
Inter-observer bias (p-value for Cochran's Q)	<0.0001

The raw agreement between all five observers was low. The kappa chance-corrected measure of agreement was very low, corresponding to 'slight' agreement.

Interobserver bias

Cochran's Q statistic was significant, indicating significant bias between the observers in determining whether or not the spine was at risk or not.

In order to investigate these findings, we now look at the agreement and bias between each pair of observers, to see if we can find reasons for the low kappa and significant bias between the five observers. The results are summarised in the table below:

Table 6: Agreement on Bias between each pairs of Observers

Observers	kappa	Level of agreement	p-value for McNemar's test
	Pt at risk		
1 vs 2	0.00	nil	<0.0001
1 vs 3	0.10	slight	<0.0001
1 vs 4	0.44	**moderate**	0.47
1 vs 5	0.11	slight	0.0011
2 vs 3	0.00	nil	0.025
2 vs 4	0.00	nil	<0.0001
2 vs 5	0.00	nil	0.0003
3 vs 4	0.20	slight	<0.0001
3 vs 5	0.37	fair	0.011
4 vs 5	0.09	slight	0.0060

We see that:

- The agreement between all pairs of observers was very low, with the exception of Observers 1 vs. 4.
- The only pair of observers for whom there was no interobserver bias, was Observers 1 and 4. But their inter-observer agreement was also quite low.

F) SARS score

The univariate statistics for the SARS score for each of the five observers is given below:

Table 7: SARS Scores

Observer	N	Mean	Std Dev	Median	25th Pctl	75th Pctl	Minimum	Maximum
Observer 1	61	1.62	1.45	1	0	3	0	4
Observer 2	61	0.46	0.50	0	0	1	0	1
Observer 3	61	0.41	0.78	0	0	1	0	3
Observer 4	61	1.44	1.34	1	0	2	0	4
Observer 5	61	0.59	0.97	0	0	1	0	3

Agreement:

We have continuous outcome and five observers, so we use the Intraclass Correlation Coefficient (ICC). [29] The ICC represents the proportion of variability in the data which is attributable to variation between subjects (patients). The ICC=0.27, indicating poor agreement between the five observers.

In order to investigate this finding, we now look at the agreement between each pair of observers, to see if we can find reasons for the low agreement between the three observers.

Table 8: Agreement between each pair of observers

Observers	ICC
1 vs 2	0.06
1 vs 3	0.31
1 vs 4	**0.55**
1 vs 5	0.20
2 vs 3	0.21
2 vs 4	0.00
2 vs 5	0.29
3 vs 4	0.44
3 vs 5	0.39
4 vs 5	0.09

The results show that the agreement between all pairs of observers is low, but that for 1 vs. 4 and 3 vs. 4 the ICC was slightly better than for the rest.

The majority decision data (as outlined in the Data Preparation section) were used for the rest of the analyses.

Given the very poor interobserver reliability, the majority decision data cannot be said to be a reflection of the true status of the patients.

Description of the SARS characteristics of the study group

The SARS characteristics of the study group are tabulated in the spreadsheet.

The percentage of patients with each of the four SARS is shown below:

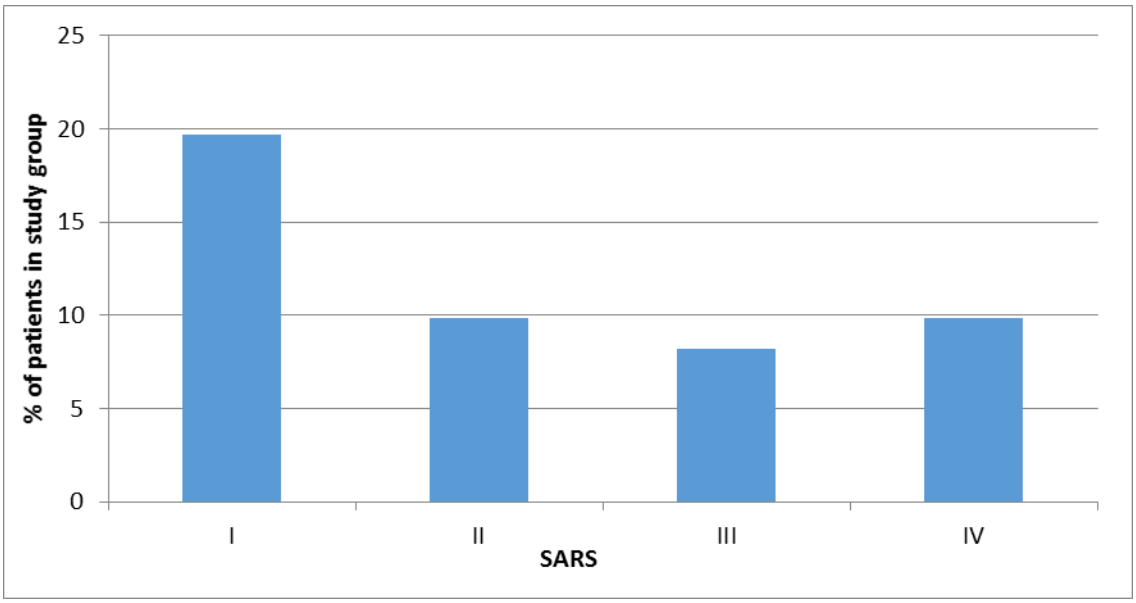


Chart 5: The percentage of patients with each of the four SARS

From this we can tell that facet dislocation is the commonest spine at risk sign seen in the adult population. This point to the initial instability as the anterior vertebral elements are destroyed.

The SARS scores are shown below. 70.5% of the patients had a SARS score of zero.

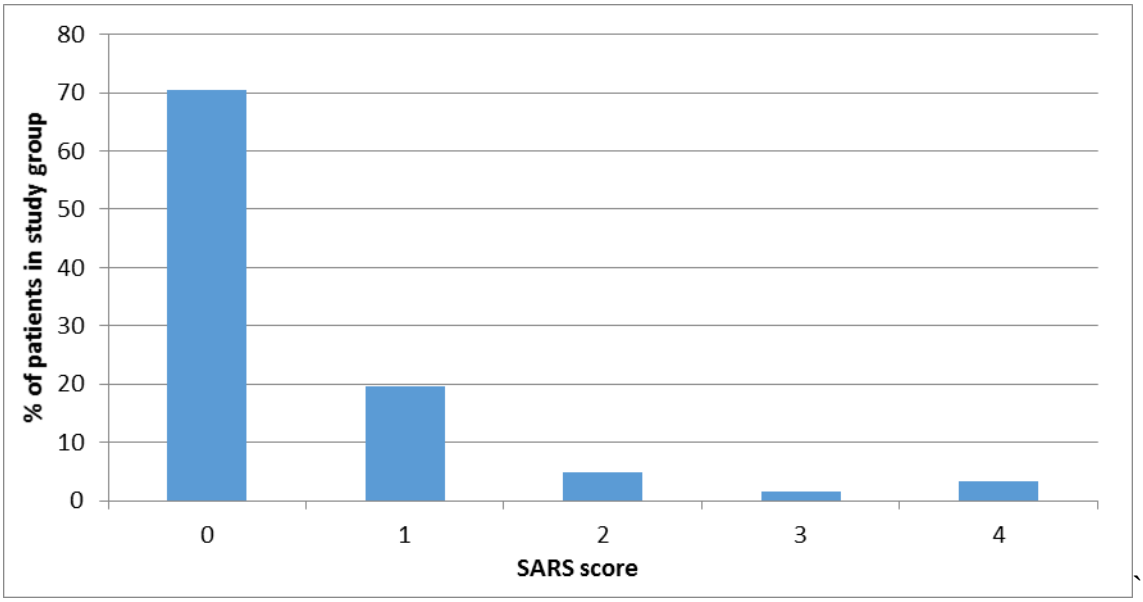


Chart 6: SARS scores

Chart 6, shows us that less than 9.8 % overall of our study population had a score of 2 or more. This is good news for the effect Tuberculosis spine has on the adult. However, we know that there was poor interobserver agreement. Therefore, we don't we don't know how much significance should be given to this finding. We can probably further correlate this finding with the number of patients that go for spine surgery and assess if there is any correlation.

Chapter 5: Discussion

Principles of Evidence Based Medicine (EBM) dictate that in our practice of medicine we adhere to standards of clinical practice that lead to measurable diagnostic and treatment guidelines. These guidelines should allow us to characterize a problem, suggest a potential prognosis, and offer guidance in determining optimal treatment method for a particular condition.[23, 24]

Clinical classification systems represent such an attempt at providing such guidelines. In our daily clinical practice within the University of Witwatersrand Orthopaedic Surgery Academic Circuit we use the 'Rajasekaran Spine at Risk Signs', as such a radiological clinical guideline, in assessing our patients affected by Tuberculosis of the spine.

The original classification was only validated in the Paediatric population, however in our current practice we use it for all patient affected by Tuberculosis of the Spine. Our study interest therefor, was to see if this can be validly and reliability used and extend to the adult population.

To be able to do this we set out to assess validity and reliability of this system in the adult population. This is an important assessment because a successful classification system must be both reliable and valid. The validity of a classification system reflects the accuracy with which the classification system describes the true pathologic process. A valid classification system correctly categorizes the attribute of interest and accurately describes the actual process that is occurring.[24, 25]

Validity measurements are difficult, because they measure or quantify observations and therefore would require the measure of interest to be measured to a gold-standard. Meaning, for each radiograph observed there should be post-mortem or at least a 3-dimention Computer Tomographic scan to confirm what is seen on the radiograph. This type of research is difficult or close to impossible. Therefore, because of the difficulty of measuring validity, it is critical for a classification system to have at least a high degree of reliability.[24, 25]

The precision of a classification system is reflected by reliability. In general, and perhaps more statistically it refers to interobserver reliability, the agreement between different observers.

Looking at our findings as illustrated in table 1. We see and enormous variation between the observers and the inter-observer agreement is very low as illustrated in Table2. Additionally, using Table 3. Makes it difficult to accept a wide use of the Spine at Risk Classification system in adults.

Just the enormous variation implies that for any given patient the likelihood of picking up the 4 varied signs does not fall within the minimum requirements of reliability. Thus, we cannot even accept the Classification system as an acceptable radiological tool.

Only Observers 2 and 3 showed some consistency (across all four SARS) of no interobserver bias, but even their interobserver agreement was very low in the adult population.

This high variability and low agreement extend throughout all variables tested i.e. [(b). Spine at Risk classification, and c). SARS Score.

Given these very poor interobserver reliability, majority decision data cannot be said to reflect the true status of the patients.

There is however some interesting clinical associations that where noted, that are in keeping with literature published on Tuberculosis affecting the spine.

The age Grouping between 36-49 years was having the highest TB spine numbers with mean age being 42 years old, this group represents our economically productive age group. Additionally, we see that female patient are the most commonly affected at 54.1 %, this may represent the continued vulnerability of this gender group. Anatomically the Lumbar spine shows the highest number lesions from our Observations.

70.5 % of the patient had SARS score of Zero with an overall only 9.8 % of patients having Spine at Risk signs.

Chapter 6: Conclusion and Recommendation

Conclusion

Radiological classifications systems are a significant attempt to find tools that are representative in the Practice of Evidence Based Medicine. These tools or systems help us to identify and describe diseases, suggest and follow specific treatments and to prognosticate outcomes and risk. Furthermore, these systems help us to find a common basis for communication to each other and in our research.

In Tb spine, the 'Rajasekaran Spine at Risk signs' and scoring system is an already established tool for the population aged 15 years and less, and is seen to represent the effects of the disease process in the paediatric population.

However, we find that this system is extended to the adult population (17 years and older) due to its convenience. The challenge herewith is that the effects of the disease process are different in the adult population due to skeletal maturity.

The aim of our study was to find this 4 Radiological 'Spine at Risk Signs' on X-Rays of 61 adult patients affected by Tb spine. We used 5 researchers with various levels of orthopaedic surgical training (Registrar to Consultant level). Their observations were recorded and statistics applied to look at the significance of these observations.

Statistically, we observed a significant variability in the observations of the same X-rays between different researchers. To justify or extend the use of the classification system it is important to see agreement between different observers. As observed by Rajasekaran this X-Ray observations are well illustrated and should be easily applied. Therefor it's important that there should be a high degree of interobserver reliability. Overall therefore, we cannot conclusively answer the research question on the prevalence on the prevalence of TB 'Spine at Risk signs' in the adult population as the statistics of the observation do not support such an answer.

The SARS should not be used in the adult population until further studies to question the large inter-observer variation has been done. Perhaps, a follow up study should be undertaken with prior training of observers, observers going through a few X-Rays together followed by clear instructions to review the X-Rays.

Recommendation

Maybe in a follow-up study the data can be re-checked and instructions given to observers can be reviewed. Additionally, the observers can go through some of the patients together to determine the cause of the poor agreement.

We could even consider training the observers and have them rate the patients again.

Perhaps X-rays as a tool are not conclusive in the adult population therefore perhaps Computerized Tomographic scans can be the basis of this type of classification in adult. However, part of our initial idea was that we would strengthen Rajasekaran's observations with a relatively low cost investigation tool like X-rays and extend it to the adult population. This because our health-care system is referral based and with a widely available routine tool like X-rays our health-care professionals at various level of experience and exposure could detect this signs early and refer appropriately to Tertiary Healthcare centers.

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Appendix I

M130741M130741

R14/49 Dr Stanley Ndakoro Kanyemba

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M130741

NAME: (Principal Investigator) Dr Stanley Ndakoro Kanyemba

DEPARTMENT: Orthopaedic Surgery
University of Witwatersrand

PROJECT TITLE: Turberculosis Spine 'Radiological Spine at Risk Signs' in the Adult Population

DATE CONSIDERED: 26/07/2013

DECISION: Approved unconditionally

CONDITIONS:

SUPERVISOR: Prof Mkhululi Lukhele

APPROVED BY:

Professor PE Cleaton-Jones, Chairperson, HREC (Medical)

DATE OF APPROVAL: 28/03/2013

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 Secretary in Room 10004, 10th floor, Senate House, University.

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.**

Principal Investigator Signature

M130741Date 23/10/2014

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix II

Illustration of Spine at Risk Signs- Observation Form:

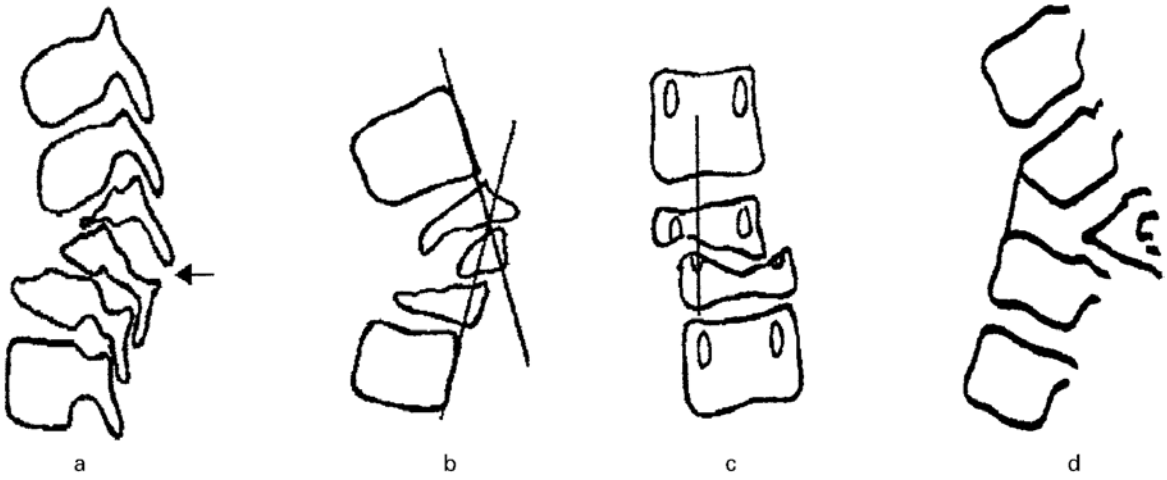


Figure 1a – *Separation of the facet joint.* The facet joint dislocates at the level of the apex of the curve, causing instability and loss of alignment. In severe cases the separation can occur at two levels.

MARK IF PRESENT: ☐

Figure 1b – *Posterior retropulsion.* This is identified by drawing two lines along the posterior surface of the first upper and lower normal vertebrae. The diseased segments are found to be posterior to the intersection of the lines.

MARK IF PRESENT: ☐

Figure 1c – *Lateral translation*. This is confirmed when a vertical line drawn through the middle of the pedicle of the first lower normal vertebra does not touch the pedicle of the first upper normal vertebra.

MARK IF PRESENT: ☐

Figure 1d – *Toppling sign*. In the initial stages of collapse, a line drawn along the anterior surface of the first lower normal vertebra intersects the inferior surface of the first upper normal vertebra. 'Tilt' or 'toppling' occurs when the line intersects higher than the middle of the anterior surface of the first normal upper vertebra.

MARK IF PRESENT: ☐

SCORE ☐

Appendix III

Scoring Sheet **Sheet Number**

Tick Box if sign observed

Patient	**Frankel Status**	**I Facet Separation**	**II Posterior Retropulsion**	**III Translation**	**IV Toppling**	**Score**
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