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Risk Factors Influencing the Degree of Tuberculous Spondylitis Based on MRI Modality

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ABSTRACT

The high prevalence and mortality of tuberculosis (TB) is serious threats to the world. Tuberculous spondylitis accounts for 50% of all bone and joint TB cases. The accuracy of diagnosis to detect disease severity using Magnetic Resonance Imaging (MRI) modalities is important when considering potential risk factors. This study aimed to analyze the association of risk factors, including age, sex, spinal lesion location, and abscess location, with the severity of tuberculous spondylitis based on MRI modality using the Gulhane Askari Tip Akademisi (GATA) classification. This study had a cross-sectional design. The study sample consisted of 50 patients who met the inclusion criteria and underwent MRI. The statistical analysis performed in this study was multivariate analysis using multiple linear regression. The results showed that 84% (n = 42) of tuberculous spondylitis affected patients aged 18-65 years, and 70% (n = 35) of cases were found in female patients. In addition, 42% (n = 21) of cases were classified as tuberculous spondylitis grade III according to the GATA classification and were the most common cases in this study. Statistical tests showed no association between age, the location of spinal lesions, and the degree of tuberculous spondylitis. However, there was an association between sex, spinal abscess location, and degree of tuberculous spondylitis. There was no significant association between age and spinal lesion location or degree of tuberculous spondylitis. However, there was a significant association between sex, spinal abscess location, and the degree of tuberculous spondylitis.

Keywords: risk factors, tuberculous, spondylitis, MRI, and Indonesia.

Highlights: Sex and spinal abscess location was found as the risk factors that affect the severity of tuberculous spondylitis based on MRI modality using the GATA classification.

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INTRODUCTION

Tuberculosis (TB) is commonly known as a deadly infectious disease that occurs worldwide.[1,2] The prevalence of TB reached 5.8 million in 2019, with India, Indonesia, and the Philippines being the most affected countries in the world. In 2013 – 2014, there were 1.6 million TB cases in Indonesia[3], and the global mortality rate of this disease has increased from 1.4 million in 2019 to 1.5 million in 2020.[1] TB exposure is a serious threat, especially when it affects other organ systems such as the musculoskeletal system.[4,5] Tuberculous spondylitis accounts for 50% of bone and joint TB cases in the musculoskeletal system.[5–8] Moreover, late diagnosis of musculoskeletal TB, especially tuberculous spondylitis, might lead to paralysis of the extremities.[9] Therefore, early diagnosis and monitoring are crucial to reduce disease severity. Moreover, the accuracy of diagnosis using Magnetic Resonance Imaging (MRI) is important when considering potential risk factors.

A study from China found that men and aged 18-45 years were at higher risk of developing this disease.[6] In contrast, other studies reported that female patients were more likely to experience tuberculous spondylitis.[10] Tuberculous spondylitis is more frequently reported in children than in adults.[11,12] A previous study reported that the thoracic segment (48.03%) was the most common location of the spinal lesions.[13] However, another study found that the lumbar segment (38.2%) was the most common location.[14] Moreover, it has been reported that the cervical and upper thoracic segments (10%) are the rarest sites for spinal abscess formation.[15] Other studies also mention that the lumbosacral segment has the fewest abscesses.[16]

Imaging modalities are the most accurate diagnostic tools for tuberculous spondylitis, considering that *Mycobacterium tuberculosis* culture is difficult and takes approximately 4-6 weeks to obtain the results.[5] A previous study compared several diagnostic modalities, which involved 40 patients: 29 patients were assessed with a CT Scan, 11 were assessed with an MRI, and 10 were assessed with a CT Scan and MRI, which included the type and level of spinal and soft tissue involvement. This study found that MRI was superior in terms of accuracy, especially for soft tissue assessment due to tuberculous spondylitis.[17] CT-Scan is more useful in assessing bone damage, such as lytic lesions and disc collapse, but has disadvantages in soft tissue assessment.[9,17]

Tuberculous spondylitis has four degrees of disease severity according to the *Gülhane Askeri Tıp Akademisi* (GATA) classification: IA, IB, II, and III. This GATA classification is based on a retrospective study of 78 tuberculous spondylitis cases followed up for the past two years. This study conducted radiological assessment using CT and MRI modalities, and the assessment was based on seven criteria. This study found that 11 patients were categorized as grade I, 48 as grade II, and 17 as grade III.[18]

Based on this description, the classification of the tuberculous spondylitis degree was assessed based on the accuracy of the MRI modality and by examining the risk factors from previous studies, such as the association of age, sex, location of the abscess, and spinal lesions with the incidence of tuberculous spondylitis, which is still under debate. Therefore, this study aimed to analyze the association of risk factors (age, sex, spinal lesion location, and abscess location) with the severity of tuberculous spondylitis based on MRI modality using the GATA classification. The severity of tuberculous spondylitis can be minimized via a comprehensive assessment of existing risk factors.

MATERIALS AND METHODS

This was an analytical, observational study with a cross-sectional design. The data

collected in this study were secondary data in the form of electronic medical records and imaging results in the form of MRI images. Data collection was conducted from June to August 2022. Fifty patients with tuberculous spondylitis who met the inclusion and exclusion criteria were included in this study at Dr. Kariadi Hospital, Semarang. The inclusion criteria in this study were patients clinically diagnosed with tuberculous spondylitis or by radiological examination obtained from medical record data in the form of MRI examination photos of the spine. Exclusion criteria in this study were Patients with spinal fractures other than those caused by tuberculous spondylitis, patients with a history of spinal tumors, and patients with a history of spinal surgery were excluded. Sample selection was performed using a purposive sampling method based on medical records, with inclusion and exclusion criteria as a reference.

The data obtained were analyzed using IBM SPSS™ 25 statistical program. Data analysis was performed using univariate, bivariate, and multivariate analyses using post-hoc follow-up tests. The characteristics of the respondents were analyzed using univariate analysis (including age, sex, location of lesions, and spinal abscesses), which are then presented in a table containing frequencies and percentages. Bivariate hypothesis testing was performed using Mann-Whitney and Kruskal-Wallis tests. Differences were considered statistically significant when the p-value was less than 0.05. A multiple linear regression test was used for multivariate analysis.

RESULTS AND DISCUSSION

The respondents' characteristics are listed in Table 1. Table 1 shows that 15 (30%) males and 35 (70%) females were included in this study. The age variable data showed that the age range of 18-65 years had the highest frequency (n= 42, 84%). The most common locations for spinal lesions were the thoracic segment in 24 patients (48%), followed by the lumbar segment in 17 patients (34%). The most frequent location of spinal abscesses was the thoracic segment in 19 patients (38%), followed by the lumbar segment in 13 patients (26%). The percentage of tuberculous spondylitis degrees found in this study was 18% for grade IA, 28% for grade IB, 12% for grade II, and 42% for grade III—which hold the highest percentage.

Table 1. Respondent's Characteristics Data.

Variable	Frequency	%
Age (year)		
0-17	2	4.0
18-65	42	84.0
> 65	6	12.0
Sex		
Male	15	30.0
Female	35	70.0
Spinal lesion location		
Cervical	4	8.0
Thoracic	24	48.0
Lumbar	17	34.0
Sacral	0	0.0
Multiple	5	10.0
Spinal abscess location		
None	8	16.0
Cervical	2	4.0
Thoracic	19	38.0
Lumbar	13	26.0
Sacral	0	0.0
Multiple	8	16.0
Tuberculous spondylitis degree		
IA	9	18.0
IB	14	28.0
II	6	12.0
III	21	42.0

Age data (Table 2) were categorized into three categories according to the WHO; 0-17 years (children), 18-65 years (adults), and > 65 years (elderly). Age data were analyzed using an alternative test: the Kruskal-Wallis test. The results of the bivariate statistical test showed a p-value > 0.05, which showed no significant association between the subject's age and the degree of tuberculosis spondylitis as a disease severity indicator.

Table 2. Association Between Age and the Degree of Tuberculous Spondylitis Statistical Test Result.

Variable	Tuberculous spondylitis degree				*p*
	IA	IB	II	III	
Age (year)					
0-17 (children)	1 (50.0)	0 (0.0)	0 (0.0)	1 (50.0)	0.834
18-65 (adult)	6 (14.3)	14 (33.3)	6 (14.3)	16 (38.1)	
>65 (elderly)	2 (33.3)	0 (0.0)	0 (0.0)	4 (66.7)	

There were two categories of sex variables, male and female. Table 3 shows the association between sex and the degree of tuberculous spondylitis with a p-value of 0.007 ($p<0.005$), which indicated that there was a significant association between sex and the degree of tuberculous spondylitis.

Table 3. Association Between Sex with The Degree of Tuberculous Spondylitis Statistical Test Result.

Variable	Tuberculous spondylitis degree				*p*
	IA	IB	II	III	
Sex					
Male	2 (13.3)	0 (0.0)	2 (13.3)	11 (73.3)	0.007
Female	7 (20.0)	14 (40.0)	4 (11.4)	10 (28.6)	

Table 4 shows that the location of spinal lesions in tuberculous spondylitis patients was categorized into five groups. The Kruskal-Wallis statistical alternative test was used to find an association between the location of spinal lesions and the severity of tuberculous spondylitis. The location of spinal lesions associated with the severity of tuberculous spondylitis showed a $p>0.05$, meaning there was no significant association between the location of spinal lesions and the severity of tuberculous spondylitis.

Table 4. Association of Bone Lesion Location with Tuberculous Spondylitis Degree Statistical Test Result.

Variable	Tuberculous spondylitis degree				*p*
	IA	IB	II	III	
Lesion location					
Cervical	0 (0.0)	2 (50.0)	0 (0.0)	2 (50.0)	0.199
Thoracic	5 (20.8)	6 (25.0)	1 (4.2)	12 (50.0)	
Lumbar	4 (23.5)	5 (29.4)	5 (29.4)	3 (17.6)	
Sacral	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Multiple	0 (0.0)	1 (20.0)	0 (0.0)	4 (80.0)	

The final factor associated with the degree of tuberculous spondylitis was the location of spinal abscess. Spinal abscess locations were categorized into five groups and analyzed using the Kruskal–Wallis alternative statistical test. Table 5 shows a p-value < 0.05, indicating a significant association between the location of the spinal abscess and the severity of tuberculous spondylitis. Moreover, a follow-up Post Hoc test using the Mann-Whitney test was performed to discover more about the association between each data point in the spinal abscess location variable.

Table 5. Association of Abscess Location with Tuberculous Spondylitis Degree Statistical Test Results.

Variable	Tuberculous spondylitis degree				*p*
	IA	IB	II	III	
Abscess location					
None	8 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	<0.001
Cervical	0 (0.0)	2 (100.0)	0 (0.0)	0 (0.0)	

Thoracic	1 (5.3)	5 (26.3)	1 (5.3)	12 (63.2)
Lumbar	0 (0.0)	5 (38.5)	5 (38.5)	3 (23.1)
Sacral	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Multiple	0 (0.0)	2 (25.0)	0 (0.0)	6 (75.0)

The results of the Post Hoc follow-up test in Table 6 show the asterisks, indicating a significant difference between the group without abscesses and the other groups — cervical, thoracic, lumbar, and multiple abscesses–in the spinal abscess location variable. Therefore, it can be assumed that spinal abscess location affects the severity of tuberculous spondylitis.

Table 6. The Results of the Follow-Up Post Hoc Test with the Mann-Whitney Test.

Abscess location		*p*	Note
I	**II**		
None	Cervical	0.003*	Significant
	Thoracic	<0.001*	Significant
	Lumbar	<0.001*	Significant
	Multiple	<0.001*	Significant
Cervical	Thoracic	0.103	Not significant
	Lumbar	0.142	Not significant
	Multiple	0.066	Not significant
Thoracic	Lumbar	0.154	Not significant
	Multiple	0.564	Not significant
Lumbar	Multiple	0.088	Not significant

Multivariate analysis (Table 7) was performed on sex, spinal lesion location, and spinal abscess location variables because multivariate analysis requires a p-value of < 0.25. Multiple linear regression analysis showed that sex and spinal abscess location had p-values <0.05. Moreover, the female sex and thoracic segments were found to be the predominant locations of spinal abscesses. Overall, among the three risk factors for tuberculous spondylitis, sex variables and location of spinal abscesses were risk factors that predominantly influenced the degree of tuberculous spondylitis. In addition, the location of the spinal abscess was the most influential risk factor for tuberculous spondylitis severity, as evidenced by a p-value of <0.001.

Table 7. Multivariate Analysis Results.

Variable	Beta	*p*	Note
Sex	-0.306	0.011	Significant
Spinal lesion location	-0.138	0.267	Not significant
Spinal abscess location	0.503	<0.001	Significant

In this study, sex and spinal abscess location variables were significantly associated with the severity of tuberculous spondylitis according to the GATA classification and assessed using MRI. This study found that there were 15 male patients with tuberculous spondylitis, which was lower than that of female patients, accounting for 35 cases. This result was in line with a previous study that found more tuberculous spondylitis cases in female patients (1378 cases) than in males (972 cases).[10] In addition, the thoracic spine was the most common spinal abscess location variable, with a total of 19 cases (38%). According to a previous study, approximately 40–50% of abscesses were found in the thoracic segment.[19] Patients with tuberculous spondylitis aged 18-65 years (84%), which were included in the adult age category, tended to be more common than those in other age categories, with a mean age of the patients was 40.48 years. This finding was in line with that of a study by Sianaturi et al. which found that adults with tuberculous spondylitis had a mean age of 39.5 years.[20]

Other characteristics, such as the location of the spinal lesion, had the thoracic spine being the most common location, accounting

for 24 cases (48%). Several previous studies also mentioned that the thoracic segment had the highest resistance and was the most common location of tuberculous spondylitis lesions.[9,13] Moreover, the most common degree of tuberculous spondylitis was grade III, which accounted for 21 cases (42%), followed by grade IB in 14 cases (28%), grade IA in nine cases (18%), and grade II in six cases (12%).

In addition, untreated tuberculous spondylitis is a serious threat because it may lead to spinal deformities, resulting in paralysis of the extremities.[9] Progressive destructive events in the spine that can cause spinal cord compression require cautious attention in both men and women.[11] A previous study reported that tuberculous spondylitis was mostly found in women.[10]

A fundamental theory regarding the influence of estrogenic hormones on bone metabolism supports this finding. A drastic decrease in estrogen levels, particularly in postmenopausal women, increases bone resorption, resulting in an imbalance between bone resorption and formation.[21] An imbalance between bone resorption and formation in patients with tuberculous spondylitis exacerbates the progression of spinal destruction and increases the severity of tuberculous spondylitis.

Cold abscess formation is a common sign in patients with tuberculous spondylitis.[22] Abscess formation involves TB bacteria and is a complex process.[23] Abscess can occur in any spinal segment, with the thoracic segment being the most common location.[19] The degree of severity of abscess formation is due to pressure and the spread of cold abscesses to the surrounding environment.[11]

In this study, a significant association was found between the location of the spinal abscess and the severity of tuberculous spondylitis. Severe tuberculous spondylitis, characterized by the formation of widespread abscesses and an increase in size, is the criterion for performing spinal surgery. However, an abscess located in the thoracolumbar segment can cause severe conditions if a psoas abscess is present. This abscess can cause complications such as paralysis of the extremities.[9]

Tuberculous spondylitis is a disease that becomes a common cause of neurological deficits in the spine following injury or fracture.[24] Severe tuberculous spondylitis cases are often found due to delays in diagnosis because most patients seek treatment after experiencing severe pain.[5] This disease can affect all age ranges owing to its morbidity, which can be preceded by a highly contagious TB infection.[13,14] In Western countries, tuberculous spondylitis mostly affects people of older age due to reactivation.[5] In contrast, tuberculous spondylitis affects many young adults and children in TB endemic areas.[8]

Tuberculous spondylitis can affect people of all ages, with varying degrees of severity.[25] The current study found no significant association between age and tuberculous spondylitis severity. The reasons for the influence of age on the severity of tuberculous spondylitis are not well understood. Various theories have been proposed, such as tuberculous spondylitis in children, which tends to be much more severe owing to the immature condition of the spine. In addition, children's bone condition is more vascular, which induces the disease to spread and progress even faster and sometimes involves severe spinal collapse.[19]

Any spinal segment can be the site of a tuberculous spondylitis lesion.[13,14] Spinal damage due to tuberculous spondylitis infection results from the hematogenous spread, and early diagnosis is often difficult because of the indolent nature of the infection.[17] The best choice for the early detection of tuberculous spondylitis to determine the location of damage and spinal abscess formation can be performed by radiological examination using MRI.[19] MRI can determine the specific location of lesions and abscesses in the spine. The most

commonly reported lesion locations are the thoracic region, followed by the lumbar and cervical regions.[19]

This study reported no significant association between the location of spinal lesions and the severity of tuberculous spondylitis. In this study, the thoracic segment was the most common location of the lesion. However, the theory states that the spinal segments with the greatest risk of being the site of a lesion are those that bear heavy loads and have great mobility, especially the lower thoracic segment. This is because the lower thoracic segment is the area with the maximum movement and the focus area of body pressure.[11] If the damage to this segment becomes more extensive, the biggest complication in the form of paraplegia can occur and increase the severity of tuberculous spondylitis.[9]

STRENGTH AND LIMITATION

The strength of this study is that it focused on risk factors for age, sex, location of lesions, and location of abscesses, which are related to the severity of tuberculous spondylitis assessed based on MRI modality. The limitations of this research are the other factors that can affect the degree of tuberculous spondylitis, such as the pattern of physical activity, length of time the subject has suffered from tuberculous spondylitis, history of pulmonary TB, and abscess size, which may affect the severity of the tuberculous spondylitis degree. Some subjects were confirmed to have tuberculous spondylitis based on clinical findings and not on the results of the histopathological examination.

CONCLUSIONS

Sex and spinal abscess location are the risk factors that affect the severity of tuberculous spondylitis. Meanwhile, age and spinal lesion location have no significant risk to contribute in severity of tuberculous spondylitis disease based on GATA classification.

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ETHICAL CLEARANCE

The research protocol was approved by the Ethics Committee of the Faculty of Medicine, Universitas Diponegoro (reference number: 127/EC/KEPK/FK-UNDIP/V/2022).

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CONFLICT OF INTEREST

The authors declare that this manuscript was approved by all authors, and that no competing interests exist.

AUTHOR CONTRIBUTION

Conception, design, and/or analysis and interpretation of data: MS. Drafting the article, discussion, and critical revision for important intellectual content: MS and HS. Review, supervision, and final approval: AP and CHNP.

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