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Predictive Factors for Clinical Outcome in Spinal Tuberculosis Patients

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ABSTRACT

Tuberculous spondylitis (TB spondylitis) is the most common and serious form of extrapulmonary TB disease that attacks the musculoskeletal system. This study will identify and analyze predictive factors related to clinical outcome in TB spondylitis patients which include age, comorbid disease, time from symptom onset to diagnosis, back pain, leg weakness, numbness in legs, incontinence, level of lesions on MRI, leukocyte, ESR, and CRP values, as well as PCR and BTA results. This study will be an analytical study with a retrospective cohort approach, at the Haji Adam Malik General Hospital, Medan from January 2015 to December 2020. The inclusion criteria were all patients diagnosed with TB spondylitis and treated with anti-Tuberculosis (OAT) drugs. patients that died from other causes while on treatment and loss to follow-up were excluded. The sample size in this study was 171 patients and using the multivariate logistic regression analysis to identify predictive factors of poor outcome in TB spondylitis patients. On 184 study subjects consisting of 89 men (48.4%) and 95 women (51.6%). Good clinical outcome was obtained in 151 patients (82.1%), while 33 patients (17.9%) had poor clinical outcome. There is a significant relationship between numbness in the limbs (n = 29; 2 good outcomes (6.9%); 27 poor outcomes (93.1%); p = < 0.001), and the ESR value (mean 18.5 mm/hour; range 7-46), had a significant relationship with the clinical outcome of TB spondylitis patients and were identified as predictive factors for poor clinical outcome. The multivariate logistic regression analysis only numbness in the legs had a significant relationship with the patient's clinical outcome. ESR is a basic laboratory value and is used in general clinical practice to evaluate an inflammatory condition, eg infection [8]. In this study, higher ESR values were found in patients with poor outcomes than in patients with good outcomes. Multivariate logistic regression analysis identified leg numbness and ESR scores as predictive factors for poor clinical outcome in TB spondylitis patients, with the greatest strength of association being ESR scores.

1. INTRODUCTION

Tuberculous spondylitis (TB spondylitis) is the most common and serious form of extrapulmonary TB disease that attacks the musculoskeletal system. Clinical manifestations of this condition include pain, vertebral destruction, and neurological deficits [1]. TB spondylitis generally occurs in the thoracic and lumbar vertebrae, which in turn will result in spinal destruction that can cause neurological compression [2]. In 2015, there were 10.4 million new TB cases worldwide. The World Health Organization (WHO) estimates that there are more than 10 million new TB cases every year [3]. Indonesia is one of the 30 countries with the highest TB burden in the world and ranks third in the world regarding the incidence of TB. The incidence of TB in Indonesia in 2018 was 316 per 100,000 population or it is estimated that around 845,000 Indonesians suffered from TB in 2018 [4]. Laboratory examinations, x-rays, and magnetic resonance imaging (MRI) will reveal pathological features of the spine and assist in making the diagnosis [5- 7].

Management of TB spondylitis can be classified based on the presence or absence of neurological complications. Anti-TB drugs (OAT) are the main treatment for this condition. However, operative management shows a better outcome in patients with neurologic complications [8]. The best clinical outcome will be achieved when rapid identification and treatment of patients at risk for neurologic deficits is carried out. The limited number of spine specialists in Indonesia, limited access, and the lack of availability of facilities and infrastructure at surgical facilities will have a major impact on clinical outcomes in TB spondylitis patients. This study will identify and analyze predictive factors related to clinical outcome in TB spondylitis patients which include age, comorbid disease, time from symptom onset to diagnosis, back pain, leg weakness, numbness in legs, incontinence, level of lesions on MRI, leukocyte, ESR, and CRP values, as well as PCR and BTA results.

2. METHODS

This study will be an analytical study with a retrospective cohort approach, which aims to identify and analyze the development of strategies to improve clinical outcomes of TB spondylitis patients. The target population of this study were TB spondylitis patients with or without neurological deficits at the Haji Adam Malik General Hospital, Medan from January 2015 to December 2020. Inclusion criteria were all patients diagnosed with TB spondylitis based on clinical, radiological, laboratory, and pathological findings and it has been adequately managed with anti-Tuberculosis (OAT) drugs based on the Guidelines for Diagnosis and Management of Tuberculosis in Indonesia and the Ministry of Health of the Republic of Indonesia number 364/MENKES/SK/V/2009 concerning Guidelines for the Management of Tuberculosis (TB). The exclusion criteria were Loss to follow-up patients. The patient died from other causes while on treatment.

The research was carried out in the medical records section of the Haji Adam Malik Central General Hospital, Medan after obtaining approval from the Research Ethics Commission of the Faculty of Medicine, University of North Sumatra. The sample size in this study was calculated based on the one-time categorical predictive multivariate analysis formula and obtained a sample size of 171 patients. The sampling method is carried out by non-probability sampling, namely the purposive sampling technique. To identify predictive factors of poor outcome in TB spondylitis patients, multivariate logistic regression analysis was used on variables that were significant in bivariate analysis.

3. RESULTS

Demographic data from 213 patients with a diagnosis of TB spondylitis at the Haji Adam Malik Central General Hospital, Medan for the period January 2015 – December 2020, 29 patients did not meet the inclusion criteria set, so the analysis was carried out on 184 study subjects consisting of 89 men (48.4%) and 95 women (51.6%). Good clinical outcome was obtained in 151 patients (82.1%), while 33 patients (17.9%) had poor

clinical outcome. The mean age of the patients was 27.63 years (range 2-74 years). Statistically there was no significant difference in mean age between the good and bad clinical outcome groups (p = 0.099; unpaired t-test).

The investigators also described the association of comorbid disease with the outcome of TB spondylitis patients. The comorbidities studied included a history of TB (n = 40; 33 good outcomes (82.5%); 7 poor outcomes (17.5%)), HIV (n = 19; 17 good outcomes (89.5%); 2 poor outcomes (10.5%))), diabetes mellitus (n = 17; 12 good outcomes (70.6%); 5 poor outcomes (29.4%)), heart disease (n = 8; 6 good outcomes (75%); 2 poor outcomes (25%)), malignancy (n = 1; 1 good outcome (100%)), and chronic kidney disease (n = 11; 11 good outcome (100%)). Data analysis using the chi-square test found that there was no significant relationship between the clinical outcomes of TB spondylitis patients and their comorbid illnesses (Table 1).

Table 1. Demographic Data on TB Spondylitis Patients

Variable	Total (n = 184)	Good clinical outcome (n = 151)	Bad clinical outcome (n = 33)	P value
Mean age (SD)	27.63	26.7 (16.4)	31.9 (15.7)	0.099[a]
gender (%)				0.711[b]
male	89 (48.4)	74 (83.1)	15 (16.9)	
female	95 (51.6)	77 (81.0)	18 (19.0)	
Time from symptoms until diagnose (SD)	45.34	45.68 (5.37)	43.81 (16.29)	0.152[c]
Comorbid (%)				
TB	40 (21.7)	33 (82.5)	7 (17.5)	0.935[b]
HIV	19 (10.3)	17 (89.5)	2 (10.5)	0.534[d]
Diabetes Mellitus	17 (9.2)	12 (70.6)	5 (29.4)	0.195[d]
Heart disease	8 (4.3)	6 (75)	2 (25)	0.636[d]
Malignant	1 (0.5)	1 (100)	0 (0)	1.000[d]
CKD	11 (5.9)	11 (100)	0 (0)	0.218[d]

For clinical manifestations, the statistical test using the chi-square method showed a significant relationship between limb weakness (n = 111; 78 good outcomes (70.3%); 33 poor outcomes (29.7%); p = < 0.001), numbness in the limbs (n = 29; 2 good outcomes (6.9%); 27 poor outcomes (93.1%); p = < 0.001), and incontinence (n = 20; 4 good outcomes (20%); 16 poor outcomes (80%); p = < 0.001) (Table 2).

Table 2. Clinical Manifestations in TB Spondylitis Patients

Variable	Total (n = 184)	Good clinical outcome (n = 151)	Bad clinical outcome (n = 33)	P value
Clinical manifestations (%)	117 (63.6)	103 (88)	14 (12)	0.005[b]
Back pain	111 (60.3)	78 (70.3)	33 (29.7)	< 0.001[b]
Limb weakness	29 (15.8)	2 (6.9)	27 (93.1)	< 0.001[b]
Limb numbness	20 (10.9)	4 (20)	16 (80)	< 0.001[d]
Incontinence				

On additional investigation, the leukocyte value (mean 10804.7/mm3; range 4300-24060) and CRP (mean 22.2 mg/L; range 0.7-441) did not have a significant difference between good and bad clinical outcome groups, while the ESR value (mean 18.5 mm/hour; range 7-46) showed a statistically significant difference. On radiological examination using MRI, the researcher found that cervical spondylitis lesions (n = 3; 1 good

outcome (33.3%); 2 poor outcome (66.7%)) did not have a significant relationship with the patient's clinical outcome. However, a significant relationship was found between patient outcomes and lesions at the thoracic (n = 77; 56 good (72.7%); 21 poor (27.3%)) and lumbar (n = 61; 56 good (91.8%) outcomes; 5 poor outcome (8.2%)).

Polymerase Chain Reaction (PCR) examination (n = 90; 65 good outcomes (72.2%); 25 poor outcomes (27.8%)) had a significant relationship with the clinical outcome of TB spondylitis patients, but not with Acid-fast Bacteria (AFB) examination. (n = 81; 68 good outcomes (83.9%); 13 poor outcomes (16.1%)) (Table 3).

Table 3. Additional test in TB Spondylitis Patients

Variable	Total (n = 184)	Good clinical outcome (n = 151)	Bad clinical outcome (n = 33)	P value
Mean Leukocyte (SD)	10804.7	10722.4 (4827.3)	11181.2 (3623.6)	0.174[c]
Mean CRP (SD)	22.2	22.9 (36.5)	19.3 (12.1)	0.711[c]
Mean LED (SD)	18.5	15.3 (6.3)	33.1 (7.8)	< 0.001[c]
Level of Lesion on MRI (%)	3 (1.6)	1 (33.3)	2 (66.7)	0.083[d]
cervical	77 (41.8)	56 (72.7)	21 (27.3)	0.005[b]
Thoracal	61 (33.1)	56 (91.8)	5 (8.2)	0.015[b]
Lumbar				
PCR (%)	90	65 (72.2)	25 (27.8)	0.001[b]
BTA (%)	81	68 (83.9)	13 (16.1)	0.554[b]

The results of the multivariate logistic regression analysis to determine the predictive factors for clinical outcome in TB spondylitis patients are presented in Table 4. Numbness in the legs (OR 42.07; IK 95% 3.65 s/d 484.42; p = 0.003) and ESR values (OR 1.18; IK 95% 1.05 s/d 1.34; p = 0.007) were identified as predictive factors for poor clinical outcome. The strength of the relationship can be seen from the value of the odds ratio (OR). The greatest and smallest relationship strengths were the ESR values and the numbness of the limbs.

Table 4. Logistics Regression Multivariate Analysis Results

Factor	Multivariate Analysis	
	OR (IK 95%)	Nilai p
Back pain	0.19 (0.03 s/d 1.36)	0.097
Weakness of the limbs	25.45 (0)	0.997
Numbness of the limbs	42.07 (3.65 s/d 484.42)	0.003
incontinence	17.49 (0.44 s/d 694.24)	0.128
ESR	1.18 (1.05 s/d 1.34)	0.007
Thoracal lesions	2.22 (0.13 s/d 36.87)	0.579
Lumbar lesions	0.85 (0.06 s/d 12.26)	0.904

4. DISCUSSION

This study investigates factors that can predict clinical outcome in patients with tuberculous spondylitis. Numbness in the limbs was one of the predictive factors identified, along with the ESR value. Bivariate analysis showed that leg weakness (p < 0.001), leg numbness (p < 0.001), and incontinence (p < 0.001) were significant predictive factors, although in the multivariate logistic regression analysis only numbness in the legs had a significant relationship. with the patient's clinical outcome. Researchers also have not been able to

find studies that describe these clinical symptoms as factors that influence outcomes in TB spondylitis patients. ESR is a basic laboratory value and is used in general clinical practice to evaluate an inflammatory condition, eg infection [9]. In this study, higher ESR values were found in patients with poor outcomes than in patients with good outcomes. The study by described ESR values at baseline, two months after treatment, six months after treatment, and at the end of treatment [10]. It was found that there was a significant difference in ESR values six months after treatment (41.7 mm/hr vs 26.2 mm/hr; $p = 0.002$) and at the end of treatment (31.9 mm/hr vs 13.4 mm/hr; $p < 0.001$).

TB spondylitis is most often found in the thoracic region [11]. This is in line with the findings in this study, which found significant results in tuberculous spondylitis lesions in the thoracic ($p = 0.005$) and lumbar ($p = 0.015$) regions on bivariate analysis. PCR is one of the main diagnostic modalities in TB spondylitis patients. This study found that positive PCR results differed ($p = 0.001$) significantly between patients with good and poor outcomes. The study by did not show similar results, where it was found that the results of a positive smear test were significantly different in patients with poor clinical outcome (43.6% vs 17.2%; $p = 0.005$) [10].

Several previous studies have identified poor prognostic factors in TB spondylitis patients. Studies by [11] show that the combination of radical surgery with OAT is a good prognostic factor [12], [13]. In contrast to the study by in a Cochrane review concluded that there was no significant difference between the clinical outcomes of TB spondylitis patients treated with OAT and the combination of OAT with surgery [14]. Showed that an increased time from symptoms to diagnosis could be associated with a poorer prognosis [15].

This study has several limitations. First, the investigators were not able to measure the leukocyte, CRP, and ESR values at two months after therapy, six months after therapy, and at the end of therapy. Second, the investigators included not only patients with TB spondylitis confirmed by histological and microbiological examination, but also patients with suspected TB spondylitis based on clinical manifestations and radiological findings.

5. CONCLUSION

Back pain, leg weakness, numbness in the legs, incontinence, ESR, thoracic and lumbar lesions, and positive PCR results in TB spondylitis patients with good clinical outcomes were significantly different when compared to patients with poor clinical outcomes. Multivariate logistic regression analysis identified leg numbness and ESR scores as predictive factors for poor clinical outcome in TB spondylitis patients, with the greatest strength of association being ESR scores.

6. REFERENCE

[1] Kementrian Kesehatan Republik Indonesia. Situasi TBC di Indonesia - TBC Indonesia [Internet]. TBC Indonesia. 2021 [cited 1 May 2021]. Available from: https://tbindonesia.or.id/pustaka-tbc/informasi/tentang-tbc/situasi-tbc-di-indonesia-2/

[2] Rasouli, M. R., Mirkoohi, M., Vaccaro, A. R., Yarandi, K. K., & Rahimi-Movaghar, V. (2012). Spinal tuberculosis: diagnosis and management. Asian spine journal, 6(4), 294–308. https://doi.org/10.4184/asj.2012.6.4.294World Health Organization. Global tuberculosis report. Genève: Word Health Organization; 2016.

[3] Al-Mulhim, F. A., Ibrahim, E. M., el-Hassan, A. Y., & Moharram, H. M. (1995). Magnetic resonance imaging of tuberculous spondylitis. Spine, 20(21), 2287–2292. https://doi.org/10.1097/00007632-

199511000-00005

[4] Jain, A. K., Sreenivasan, R., Saini, N. S., Kumar, S., Jain, S., & Dhammi, I. K. (2012). Magnetic resonance evaluation of tubercular lesion in spine. International orthopaedics, 36(2), 261–269. https://doi.org/10.1007/s00264-011-1380-x

[5] Dunn, Robert & Zondagh, Ian & Candy, Sally. (2011). Spinal Tuberculosis: Magnetic Resonance Imaging and Neurological Impairment. Spine. 36. 469-73. 10.1097/BRS.0b013e3181d265c0.

[6] Tan, S. C., Harwant, S., Selvakumar, K., & Kareem, B. A. (2001). Predictive factors in the evolution of neural deficit in tuberculosis of the spine. The Medical journal of Malaysia, 56 Suppl C, 46–51.

[7] Hayes, A. J., Choksey, M., Barnes, N., & Sparrow, O. C. (1996). Spinal tuberculosis in developed countries: difficulties in diagnosis. Journal of the Royal College of Surgeons of Edinburgh, 41(3), 192–196.

[8] Brigden M. L. (1999). Clinical utility of the erythrocyte sedimentation rate. American family physician, 60(5), 1443–1450.

[9] Kim, J. H., Ahn, J. Y., Jeong, S. J., Ku, N. S., Choi, J. Y., Kim, Y. K., Yeom, J. S., & Song, Y. G. (2019). Prognostic factors for unfavourable outcomes of patients with spinal tuberculosis in a country with an intermediate tuberculosis burden: a multicentre cohort study. The bone & joint journal, 101-B(12), 1542–1549. https://doi.org/10.1302/0301-620X.101B12.BJJ-2019-0558.R1

[10] Turgut M. (2001). Spinal tuberculosis (Pott's disease): its clinical presentation, surgical management, and outcome. A survey study on 694 patients. Neurosurgical review, 24(1), 8–13. https://doi.org/10.1007/pl00011973

[11] Park, D. W., Sohn, J. W., Kim, E. H., Cho, D. I., Lee, J. H., Kim, K. T., Ha, K. Y., Jeon, C. H., Shim, D. M., Lee, J. S., Lee, J. B., Chun, B. C., & Kim, M. J. (2007). Outcome and management of spinal tuberculosis according to the severity of disease: a retrospective study of 137 adult patients at Korean teaching hospitals. Spine, 32(4), E130–E135. https://doi.org/10.1097/01.brs.0000255216.54085.21

[12] Su, S. H., Tsai, W. C., Lin, C. Y., Lin, W. R., Chen, T. C., Lu, P. L., Huang, P. M., Tsai, J. R., Wang, Y. L., Feng, M. C., Wang, T. P., & Chen, Y. H. (2010). Clinical features and outcomes of spinal tuberculosis in southern Taiwan. Journal of microbiology, immunology, and infection = Wei mian yu gan ran za zhi, 43(4), 291–300. https://doi.org/10.1016/S1684-1182(10)60046-1

[13] Jutte, P. C., & Van Loenhout-Rooyackers, J. H. (2006). Routine surgery in addition to chemotherapy for treating spinal tuberculosis. The Cochrane database of systematic reviews, (1), CD004532. https://doi.org/10.1002/14651858.CD004532.pub2

[14] Garg, R. K., Raut, T., Malhotra, H. S., Parihar, A., Goel, M., Jain, A., Verma, R., & Singh, M. K. (2013). Evaluation of prognostic factors in medically treated patients of spinal tuberculosis. Rheumatology international, 33(12), 3009–3015. https://doi.org/10.1007/s00296-013-2841-x