

## Correlation between Gibbus and Neurological Status in Patients with Tuberculous Spondylitis and Its Impact after Operative Intervention

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### Abstract

**Background:** Tuberculous (TB) spondylitis is a chronic infectious disease associated with *Mycobacterium tuberculosis* that affects the spine. This disease is a challenging disease to treat due to its serious complications and high morbidity rate. Neurological deficits and spinal deformities that can occur along with gibbus are some of the most common complications. Early diagnosis and treatment are essential to cure this disease, with the administration of anti-TB drugs and operative intervention. This study aimed to analyze the correlation between gibbus and neurological status as well as the impact of operative intervention on the degree of gibbus and neurological status.

**Methods:** This was an observational-analytic study with a cross-sectional design on 32 medical records of TB spondylitis patients who underwent operative intervention from January 2018 to December 2021 at Dr. Hasan Sadikin General Hospital, Indonesia. Gibbus determined by x-ray analysis and neurological status determined by the American Spinal Injury Association (ASIA) impairment scale (AIS) were examined before and after the intervention. The sample was chosen based on consecutive sampling. All data collected was tested using Spearman's correlative analysis, paired t-test, and Wilcoxon sign-rank test with a p-value < 0.05 considered statistically significant.

**Results:** There was a significant correlation between gibbus and neurological status-AIS ( $r = -0.708$ ;  $p < 0.05$ ); and a significant positive impact of operative intervention on the degree of gibbus ( $p < 0.05$ ) and neurological status-AIS ( $p < 0.05$ ).

**Conclusions:** There is a correlation between gibbus and neurological status-AIS. In addition, operative intervention also has a significant positive impact on the degree of gibbus and AIS, resulting in good clinical and radiological outcomes.

**Keywords:** American Spinal Injury Association (ASIA) impairment scale, gibbus, neurological status, TB spondylitis

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### Introduction

Tuberculosis (TB) is a communicable (infectious) disease associated with *Mycobacterium tuberculosis* which causes devastating morbidity and mortality worldwide. Until the pandemic coronavirus (COVID-19), TB was the leading cause of death, ranking above HIV/AIDS.<sup>1</sup> In recent decades,

there have been increasing case reports of TB that resulted in a higher incidence of extrapulmonary TB. According to the World Health Organization (WHO), the incidence of extrapulmonary TB in 2019 was about 16% of the 7.1 million TB cases;<sup>2</sup> around 10% of which is tuberculosis of bones and joints (skeletal TB).<sup>3</sup> Spine (spondylitis) has been the most frequent site of bony dissemination, which

accounts for around 50% of all bone and joint TB cases.<sup>3</sup>

TB spondylitis is among the most challenging diseases to treat due to its serious complications and high morbidity rate. Two main complications are neurological deficit and spine deformity. Neurological deficits can occur due to the narrowing of the spinal canal and vertebral collapse which may lead to compression of the spinal cord and nerves. In developing countries, neurological deficits are still found in 20–41% of cases, especially when the thoracic vertebrae are involved. Meanwhile, in developed countries neurological involvement occurs in 10–20% of cases.<sup>4</sup> In 80% of cases, TB spondylitis is also accompanied by spinal deformity, known as gibbus, which is a type of structural kyphosis in which one or multiple vertebrae become wedged.<sup>5</sup>

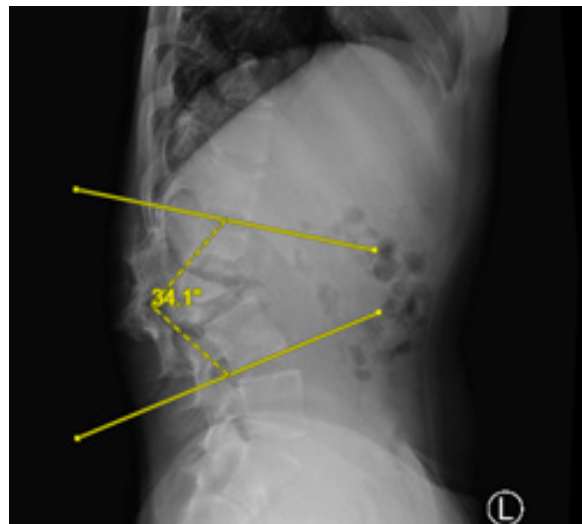
Early diagnosis and treatment are essential to prevent such devastating complications. The most important treatment of TB spondylitis is administration of anti-TB drugs, and some may require operative intervention. Debridement and reconstruction of the spine's normal sagittal plane alignment are involved in the operative intervention. This intervention is indicated if the lesion is resistant to antibiotic treatment, if there is a significant progressive kyphosis, or if a neurological deficit occurs.<sup>6</sup> This study aimed to analyze the correlation between gibbus and neurological status in TB spondylitis patients as well as the impact of the operative intervention on the degree of gibbus and neurological status.

## Methods

This was an observational-analytic study with a cross-sectional approach using secondary data acquired from the medical records of patients diagnosed with TB spondylitis who underwent operative intervention from January 2018 to December 2021 at Dr. Hasan Sadikin General Hospital, Bandung. Prior to data collection, ethical clearance was obtained from the Ethics Committee of the Faculty of Medicine, Universitas Padjadjaran (no. 583/UN6.KEP/EC/2022).

This study used a quantitative design. There were 32 patients who met the inclusion criteria. The sample were chosen based on consecutive sampling with the following inclusion criteria: (1) patients diagnosed with TB spondylitis who received anti-TB therapy and operative intervention; (2) patients with completed medical records. Meanwhile, patients with a history of stroke or other neurologic disease with sequelae were excluded from the study.

The major variables in this study were degree of gibbus and neurological status of American Spinal Injury Association (ASIA) impairment scale (AIS) assessed before and after operative interventions. Gibbus morphology was analyzed using preoperative and postoperative lateral plain radiographs. Furthermore, the degree of gibbus itself was measured and calculated with a local kyphotic angle (LKA). The angle was formed by the intersection of two lines: 1) a line parallel to the superior end plate of the first normal



**Figure 1 Measurement of the Local Kyphotic Angle (LKA)**

**Table 1 American Spinal Injury Association (ASIA) Impairment Scale<sup>9</sup>**

ASIA Impairment Scale (AIS)		Clinical Description
AIS A	Complete	No motor or sensory function is preserved in the sacral segments S4-S5.
AIS B	Incomplete	Sensory function is preserved but not motor function is preserved below the neurological level and includes the sacral segments S4-S5.
AIS C	Incomplete	Motor function is preserved below the neurological level, and more than half of key muscles below the neurological level have a muscle grade of less than 3.
AIS D	Incomplete	Motor function is preserved below the neurological level, and at least half of key muscles below the neurological level have a muscle grade of 3 or more.
AIS E	Normal	Motor and sensory functions are normal.

vertebrae cephalad to the lesion, and 2) a line parallel to the inferior end plate of the first normal vertebrae caudal to the lesion.<sup>7</sup> Degree of gibbus was further classified into 3 groups: mild (<30°), moderate (30–60°), and severe (>60°).<sup>8</sup>

The ASIA Impairment Scale (AIS) is one of many classifications used to assess neurological deficit in TB spondylitis patients. In the AIS classification, the severity of neurological deficit was influenced by the level of the affected vertebrae as well as the severity of spinal cord compression at the involved level. The AIS classification system classified the impairments into five scale scores ranging from A (complete), B-D (incomplete), and E (normal) (Table 1).

All collected data were analyzed using statistical analysis software (Microsoft® Excel 2013 and IBM® SPSS/Statistical Product and Service Solution version 26). To determine the correlation between two variables, the data were tested using Kolmogorov-Smirnov and Spearman’s correlative analysis. If the p-value <0.05, it was considered as a statistically significant relationship. Then, to assess the impact of operative intervention, data of the degree of gibbus and neurological status in different periods (before and after intervention) were compared by the paired t-test and Wilcoxon signed-rank test, p-value <0.05 was considered statistically significant.

## Results

In this study, 78 cases of skeletal TB were collected, and 54 of them were TB spondylitis. Among these 54 subjects, 32 cases of TB

spondylitis were eligible for analysis, which consisted of 14 male and 18 female patients. The characteristics of the subjects were depicted in Table 2.

The results revealed that most TB spondylitis patients were adult with a mean age of 33.06±12.98 years, with a slight female predominance (56.3% vs. 43.7%). Patients’ level of education was mostly high school (56.2%) and mostly unemployed/retired (56.3%). The average duration of illness was 10.38±7.92 months. All patients were given anti-tuberculosis drugs WHO category I (2HRZE/4HR/6HE). Preoperatively, the degree of gibbus was mild in half of the subjects, and all subjects experienced change to a milder degree. Neurological status of preoperative spondylitis TB patients was higher on ASIA Impairment Scale D/AIS D (65.6%), and none of the patients had AIS E; while after surgery patient’s neurological status tended to lead to AIS E (81.3%) and AIS D (15.6%), and no patients fell into AIS A and B.

There was a significant correlation between degree of gibbus and neurological status of AIS before operative intervention, with p=0.000 (p<0.05) and r=-0.708 (strong negative correlation), suggesting that increasing the degree of gibbus would worsen the AIS scale.

There was a significant difference between the degree of gibbus before and after operative intervention with p=0.000 (p<0.05) (Table 4).

There was a significant difference between AIS scale before and after operative intervention, all leading to improvement p=0.000 (p<0.05). Hence, it could be concluded that surgical intervention had a positive impact on gibbus and neurological status of AIS.

**Table 2 Subject Characteristics**

Characteristics	n	%
Age (year)		
Mean $\pm$ SD	33.06 $\pm$ 12.98	
Range (min-max)	11-62	
Gender		
Male	14	43.7
Female	18	56.3
Education Level		
No formal education	0	0
Primary school	7	21.9
Secondary school	4	12.5
High school	18	56.2
Bachelor degree/diploma	3	9.4
Profession		
Unemployed/retired	18	56.3
Government employee	0	0
Private employee	11	34.4
Freelance	2	6.2
Others	1	3.1
Disease duration (in month)		
Mean $\pm$ SD	10.38 $\pm$ 7.92	
Range (min-max)	1-36	
Anti-TB drug regimen		
I (2HRZE/4HR/6HE)	32	100

**Table 3 Gibbus and Neurological Status-AIS Before and After Operative Interventions**

	Pre-operation	Post-operation
Gibbus		
Mean $\pm$ SD	28.41 $\pm$ 11.16	11.02 $\pm$ 5.20
Range (min-max)	7.4-52.7	2-26
Mild (<30°)	16	32
Moderate (30-60°)	16	0
Severe (>60°)	0	0
AIS		
A	2	0
B	2	0
C	7	1
D	21	5
E	0	26

Note: AIS= American Spinal Injury Association (ASIA) impairment scale, A=complete, B=incomplete, C=incomplete, D=incomplete, E=normal

**Table 4 Impact of Operative Intervention on Gibbus**

Variable	Mean $\pm$ SD	p-value
Gibbus Pre-op (in degree)	28.41 $\pm$ 11.16	0.000 (<0.05)
Gibbus Post-op (in degree)	11.02 $\pm$ 5.20	

Note: Gibbus was defined as a localized structural kyphosis resulting in sharp angulation. This study analyzed the gibbus' degree using a lateral spine radiograph and measured the local kyphotic angle (LKA) in two periods (pre-op and post-op). Mean obtained as a result of averaging the gibbus' degree in that period

## Discussion

The TB spondylitis cases in this setting were 69.2% of total cases of bone and joint TB. In accordance, spine (spondylitis) has been the most frequent site of bony dissemination, which accounts for around 50% of all bone and joint TB cases.<sup>3</sup>

This study showed that most TB spondylitis patients were middle-aged adults. A previous study reported that TB spondylitis patients were mostly of working age, with a mean age of 37.52 years.<sup>10</sup> The cause of such finding remains elusive, but a prior study stated that TB spondylitis is highest in young adults in the endemic and developing countries, whereas in developed countries, it occurs more frequently in older age. The reason why it happened might be because TB primarily affects people who live in densely populated areas with poor hygiene, sanitation, and nutrition which conditions are more common in developing countries.<sup>11</sup>

The disease occurred a little more frequently in females than in males. The result was identical to a previous study that showed the ratio of TB spondylitis in both genders was 0.78:1 (male:female).<sup>10</sup> An explanation for this finding remains unclear, but it implies that endocrine factors might be involved. According to various cohort studies that looked at the impact of gender on the occurrence of EPTB, women were more likely than men to present their active TB as EPTB (extrapulmonary TB). The declining levels of sex hormones in perimenopause women can contribute to changes in how the immune system functions, for instance, namely the inability to confine bacilli in the lung parenchyma.<sup>12</sup> Hence, it may be the reason that women are more susceptible to EPTB such as TB spondylitis.

Patients' level of education in this study were mostly high school and followed by primary/elementary school. This finding is concurrent with a previous study that stated TB spondylitis patients had relatively low education levels, 30.8% of patients were in elementary school level.<sup>13</sup> An explanation for this finding may lie in the fact that people with higher education level are more likely to have better knowledge about health. Low levels of education (primary and less) lead to a lack of awareness of environmental hygiene and sanitation, as seen by the majority of TB patients still dumping their sputum carelessly. Low educational level may also be associated with trouble finding a job and getting inadequate income that leads to poverty and slum living, therefore susceptible to TB infection.<sup>13,14</sup>

However, the findings of this study revealed that the majority of patients had a high school educational level with primary school stood in second highest. It indicated that there may be additional factors involved that are not directly related to education.

The majority of TB spondylitis patients in this study were also unemployed/retired. This finding was consistent with a prior study which stated that a large majority of TB spondylitis patients (45%) were unemployed.<sup>15</sup> The cause of such findings may be linked to the fact that unemployment and low income are the main determining factors of poverty that can facilitate the transmission of Mycobacterium tuberculosis. It influences TB transmission mostly through 1) living conditions, such as people living in a slum and overcrowded areas with poorly ventilated homes; 2) inability to afford health services that lead to diagnostic delay; 3) higher susceptibility due to malnutrition and/or HIV infection.<sup>16</sup>

The duration of illness of patients in this study was averagely long. This result was in line with a previous study which stated that the progression of TB spondylitis was slow and insidious, the duration of illness varied from several months to years, with an average 4–11 months. This is usually because patients seek treatment after experiencing severe pain, deformity, or neurological deficiency.<sup>17</sup>

All patients in this study were given anti-tuberculosis drugs WHO category I (2HRZE/4HR/6HE), as per national guidelines. According to the National Guideline of Medical Service (*Pedoman Nasional Pelayanan Kedokteran/PNPK*) for tuberculosis 2019, Category I treatment for extrapulmonary TB comprised of 2 months intensive phase therapy with the first-line anti-TB drugs (isoniazid (H), rifampin (R), pyrazinamide (Z), and ethambutol (E)), followed by a continuation phase with INH and RIF lasting 4 months. However, the 9–12 months regimen (standard 6 months regimen plus extended continuation phase for 3–6 months) is considered for TB bones and joints, such as spine (spondylitis) TB.<sup>18</sup>

The majority of patients' gibbus before surgery were at mild degree (50%), followed by moderate (50%), and none of the patients had severe degree of gibbus. The ASIA impairment scale (AIS) of preoperative TB spondylitis patients was dominated by AIS D (65.6%) followed by AIS C (21.9%), and none of the patients had AIS E. Correlation analysis revealed a significant correlation between degree of gibbus and neurological status of



AIS before operative intervention, with  $p < 0.05$  and  $r = -0.708$  (strong negative correlation). This means that increasing the degree of gibbus would worsen the AIS scale. According to a prior study, disease reactivation and spinal cord compression by internal gibbus were thought to be the causes of neurological deficit in TB spondylitis.<sup>19</sup> This occurs as a result of vertebral collapse and gradual bone destruction that eventually narrows the spinal canal and compresses the spinal cord and neural tissue, resulting in neurological deficits such as paraplegia. The finding was consistent with previous research which stated that there was a correlation between the degree of gibbus and neurological (sensory) deficits.<sup>5</sup>

After surgery, the subjects' overall gibbus recorded at the final follow-up visit was at a mild degree, none of the patients had a moderate and severe degree of gibbus. Based on the paired t-test of the degree of gibbus, there was a significant difference between degree of gibbus before and after operative intervention with  $p < 0.05$ . According to this study, surgical intervention appears to be beneficial in correcting kyphotic deformity. Through debridement and stabilization, this intervention can provide immediate decompression of neural tissue and higher percentage of solid spinal fusion that result in less degree of kyphosis or normal spine curvature. The result was concurrent with a previous study which stated that from 32 patients who underwent operative intervention, their outcomes ranged from good to excellent. Kyphosis (gibbus) improves from 58 degrees before surgery to 11 degrees afterward. Of the 19 patients, 17 had neurological deficits before surgery. This result showed improvement of more than one ASIA grade.<sup>20</sup>

In addition to gibbus' study, we also analyzed the impact of the operative intervention on the ASIA impairment scale (AIS). Neurological status of postoperative TB spondylitis patients tends to lead to AIS E (81.3%) and AIS D (15.6%), and no patients fell into AIS A and B. Based on the Wilcoxon signed rank test, there was a significant difference between AIS scale before and after operative intervention, all leading to improvement  $p < 0.05$  (Table 5). Hence, it could be concluded that surgical intervention had a positive impact on AIS neurological status. In surgical intervention, any abscesses, granulation tissue, sequestra, caseous necrosis, necrotic endplates and discs were debrided thoroughly, that results in relief of neural tissue compression and improved

neurological status seen in ASIA impairment scale.<sup>21</sup> The result was in line with a study in China which stated that there was a significant improvement of the gibbus and AIS before and after operative correction with 2 patients from B to AIS D, 5 patients with AIS C to AIS D and 24 patients experiencing improvement from AIS C to AIS E.<sup>22</sup> The results of previous study also found that there was a significant decrease in the degree of gibbus in patients with TB spondylitis after surgery ( $p = 0.004$ ) and as many as 27 patients (90%) experienced improvement of neurological status based on the calculation of the ASIA impairment scale.<sup>23</sup>

In this study, the authors suggested that operative intervention is highly recommended for TB spondylitis patients with gibbus and neurological deficits. Several experts have demonstrated that operative intervention can provide spinal nerve decompression, correct spinal kyphosis, restored spinal stability, and enhanced quality of life.

A large number of incomplete medical records and the lack of plain radiograph data for the gibbus measurement were the study constraints. Therefore, the examination data in the future should be thoroughly contained in the medical record since complete and well-organized medical records would increase the study's quality and accuracy.

In conclusion, there is a significant correlation between gibbus and neurological status-ASIA impairment scale (AIS) before the operative intervention, thus increasing the degree of gibbus would worsen the AIS scale. The operative intervention also has a significant positive impact on the degree of gibbus and AIS, which means that surgical intervention of TB spondylitis is safe and effective, resulting in good clinical and radiological outcomes.

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