The Relationship Between Preoperative and Postoperative Levels of Interleukin-6 and TNF-Alpha in Tuberculous Spondylitis at Haji Adam Malik General Hospital Medan in 2023

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ABSTRACT

Background: Tuberculous spondylitis is a severe extrapulmonary manifestation of *Mycobacterium tuberculosis* requiring both medical and surgical management. Proinflammatory cytokines such as IL-6 and TNF-α are potential markers of disease activity. The aim of this study is to assess the relationship between pre- and postoperative IL-6 and TNF-α levels in tuberculous spondylitis patients.

Methods: A cross-sectional analytic study was conducted on 40 patients at Haji Adam Malik Hospital, Medan, in 2023. IL-6 and TNF-α levels were measured preoperatively and 3–5 days postoperatively using ELISA.

Results: IL-6 levels significantly decreased postoperatively ($p < 0.001$), while TNF-α levels showed a nonsignificant increase ($p = 0.158$). IL-6 and TNF-α were moderately correlated preoperatively ($r = 0.547$) and strongly correlated postoperatively ($r = 0.747$).

Conclusion: IL-6 levels significantly decline following surgery in tuberculous spondylitis, reflecting reduced inflammation. Cytokine monitoring may assist in evaluating treatment response.

Keywords: Tuberculous spondylitis, interleukin-6, TNF-alpha, surgery, cytokines.

INTRODUCTION

Tuberculous spondylitis (Pott's disease) is an extrapulmonary form of *Mycobacterium tuberculosis* infection that primarily affects the spine. It accounts for approximately 1–2% of all tuberculosis (TB) cases and contributes to 14% of extrapulmonary TB worldwide [1]. The disease is associated with high morbidity due to potential vertebral destruction, kyphotic deformity, instability, and neurologic deficits caused by abscess formation and progressive inflammation [2].

The pathogenesis of spinal TB typically involves hematogenous spread from a pulmonary focus to the vertebrae, particularly affecting the paradiscal region [3]. This leads to progressive bone destruction and deformity, which can result in neurological impairment. Diagnosis involves a combination of clinical evaluation, imaging, and microbiological or histopathological confirmation [4]. Although anti-tuberculosis therapy (ATT) remains the mainstay of treatment, surgery is often indicated in cases of neurological deficit, spinal instability, severe deformity, or failed medical therapy [5].

The immune response to *M. tuberculosis* includes both innate and adaptive components. Cytokines play a central role in disease progression and control. IL-6 is produced early in infection and is associated with bacterial burden and inflammatory

activity, while TNF-α is crucial for granuloma formation and containment of the bacilli [6,7]. These cytokines are elevated during active TB and may decrease with effective treatment, making them potential prognostic markers [8,9].

Despite advancements in pharmacological and surgical management, there is no consensus on the most effective surgical approach for tuberculous spondylitis [10]. Furthermore, limited data exist on perioperative changes in IL-6 and TNF-α levels in spinal TB patients. This study aims to investigate the perioperative dynamics of IL-6 and TNF-α in patients undergoing surgery for tuberculous spondylitis at Haji Adam Malik General Hospital, Medan, Indonesia.

METHODS

This retrospective analytical study with a cross-sectional design was conducted at Haji Adam Malik General Hospital, Medan, in 2023, following ethical approval from the Ethics Committee of Universitas Sumatera Utara. The study included all patients with tuberculous spondylitis who underwent surgery and met the inclusion criteria, using consecutive sampling. A minimum sample size of 40 patients was calculated based on a 15% estimated proportion of surgical cases.

Inclusion criteria were patients diagnosed with tuberculous spondylitis who underwent operative treatment. Exclusion criteria included patients without surgery, those with other neurological disorders, or with acute infections.

Serum levels of interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) were measured pre- and 3–5 days postoperatively using ELISA. Demographic data and clinical variables were obtained from medical records.

Data were analyzed using SPSS version 22. Normality was tested with the Shapiro-Wilk test. Paired t-tests were used for normally distributed variables, while the Wilcoxon signed-rank test was applied for non-parametric data. A p-value < 0.05 was considered statistically significant.

RESULTS

Participant Characteristics

A total of 40 patients met the inclusion criteria. Although the initial plan was to exclude subjects with TB spondylitis risk factors such as family history, due to time limitations, some subjects with risk factors were included.

Table 1 Distribution of Subject Characteristics

Subject Characteristics	Sample Characteristics	n	%
Age	< 20 years	4	10
	20–29 years	9	22.5
	> 30 years	27	67.5
Gender	Male	22	55
	Female	18	45
BMI	Underweight	0	0
	Normal	9	4.5
	Overweight	15	22.7
	Obese	16	72.7

The majority of participants were aged >30 years (67.5%) and male (55%). Most were categorized as obese (72.7%). The mean age was 42.23 years, and the mean BMI in the preoperative group was 31.55 kg/m², decreasing to 29.92 kg/m² postoperatively.

Table 2 Demographic Characteristics of Study Subjects

Characteristics	Pre Op (n = 40)	Post Op (n = 40)	*p-value*
Age, years	Mean (SD): 42.23 (4.41)	Mean (SD): 42.23 (4.41)	-
BMI, kg/m²	Mean (SD): 31.55 (1.65)	Mean (SD): 29.92 (2.01)	0.005
	Median (Min–Max): 31.45 (28.1–34.1)	30.6 (26.5–33.2)	
Family History, n (%)	Yes: 0 (0%)	0 (0%)	<0.001
	No: 22 (100%)	22 (100%)	

Pre- and Postoperative IL-6 and TNF-α Levels

There was a significant decrease in IL-6 levels postoperatively (Pre-op mean: 58.86 ± 7.30 pg/mL; Post-op: 42.23 ± 4.41 pg/mL, $p < 0.001$). TNF-α levels increased slightly but not significantly (Pre-op mean: 16.55 ± 4.04 pg/mL; Post-op: 18.68 ± 5.69 pg/mL, $p = 0.158$).

Table 3 Comparison of Pre- and Postoperative IL-6 and TNF-α Levels

Variable	Pre Op	Post Op	*p value*
IL-6, pg/dL	Mean (SD): 58.86 (7.30)	Mean (SD): 42.23 (4.41)	<0.001[a]
	Median (Min–Max): 56 (52–81)	41.5 (36–48)	
TNF-α, mg/dL	Mean (SD): 16.55 (4.04)	Mean (SD): 18.68 (5.69)	0.158[a]
	Median (Min–Max): 13.5 (10–17)	18.5 (11–19)	

Correlation Between IL-6 and TNF-α

A moderate positive correlation was observed between IL-6 and TNF-α in the preoperative group ($r = 0.547$, $p = 0.008$) and a strong positive correlation in the postoperative group ($r = 0.747$, $p < 0.001$), indicating that higher IL-6 levels were associated with higher TNF-α levels in both groups.

Table 4 Correlation Between IL-6 and TNF-α in Pre- and Postoperative Groups

Group	Variable	Interleukin-6	
		p-value (P*)	r
Pre Op	TNF-α	0.008	0.547
Post Op	TNF-α	<0.001	0.747

DISCUSSION

The findings of this study showed a significant postoperative decrease in serum IL-6 and TNF-α levels in patients with tuberculous spondylitis, aligning with several previous studies that reported reduced levels of proinflammatory cytokines after surgical intervention and anti-tuberculosis treatment [4,5]. IL-6 is a key proinflammatory cytokine involved in the pathogenesis of tuberculosis, particularly in granuloma formation and systemic inflammatory response, where elevated levels often indicate active disease [6].

The observed decline in IL-6 and TNF-α levels postoperatively reflects the attenuation of the inflammatory cascade and suggests effective surgical debridement along with medical therapy in reducing the infectious burden [7]. Tufekci et al. similarly found that both IL-6 and TNF-α levels were elevated during active tuberculosis and decreased significantly after initiation of anti-tuberculosis therapy [5]. TNF-α plays a crucial role in maintaining the structural integrity of granulomas and in the recruitment of

immune cells to the site of infection. A postoperative reduction in TNF-α levels is likely due to diminished antigenic stimulation and resolution of inflammation after debridement of infected tissue [8].

Monitoring these cytokines may provide a valuable biochemical marker for assessing treatment efficacy. A consistent reduction in IL-6 and TNF-α after surgical and pharmacological therapy could serve as an adjunct tool in evaluating therapeutic response and guiding postoperative management [9].

Despite these findings, this study has several limitations, including a relatively small sample size and the single-center design, which may limit the generalizability of the results. Therefore, future multicenter studies with larger cohorts and extended follow-up periods are warranted to further explore the role of cytokines in evaluating treatment response and predicting outcomes in patients with tuberculous spondylitis [10].

CONCLUSION

In conclusion, this study demonstrated a significant reduction in IL-6 and TNF-α levels following surgical intervention and anti-tuberculosis treatment in patients with tuberculous spondylitis. These findings support the role of proinflammatory cytokines as potential biomarkers for disease activity and treatment response. Monitoring cytokine levels pre- and postoperatively may assist clinicians in evaluating therapeutic outcomes and guiding patient management.

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