

Correlation Between Degrees of Kyphotic, Procalcitonin, LED, NLR, and PLR with Neurological Deficits and Pain in TB Spondylitis Patients at Adam Malik National Hospital

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ABSTRACT

Background: Infection by Mycobacterium tuberculosis (TB) affecting the vertebrae is commonly known medically as tuberculous spondylitis. As part of the spectrum of extrapulmonary TB pathology, the impact of such an infection can significantly disrupt an individual's quality of life. Kyphotic deformity, theoretically capable of inducing neurological deficits and chronic pain, is an aspect of this condition that is anticipated to be predictable based on basic diagnostic examinations. This study aims to evaluate the relationship between the degree of kyphosis and laboratory findings such as procalcitonin, erythrocyte sedimentation rate (ESR), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR) concerning the level of neurological deficit and pain.

Method: This analytical-observational study adopts a cross-sectional design involving a group of patients experiencing TB spondylitis at the Haji Adam Malik General Hospital (HAM GH), Medan, Indonesia. The researchers will evaluate the correlational aspects between independent variables (degree of kyphosis, procalcitonin, ESR, NLR, and PLR) concerning the level of neurological deficit and pain, respectively measured using the American Spinal Injury Association (ASIA) method and visual analog scale (VAS).

Results: Among the 39 patients included, with an average age of 37.44 ± 16.09 years, a significant correlation ($P < 0.05$) was found between the five independent variables and the patients' neurological deficit, with respective correlation coefficients of 0.877; -0.523; -0.568; 0.564; and 0.374. However, only the degree of kyphosis, procalcitonin, and ESR showed a significant correlation with pain, with correlation coefficients of 0.530; 0.543; and 0.690, respectively, which was not observed in the NLR/PLR analysis ($P > 0.05$).

Conclusion: The degree of kyphosis, procalcitonin, and ESR are correlated with both neurological deficits and pain scales, whereas NLR/PLR is only associated with the degree of neurological deficit in patients.

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1. INTRODUCTION

Tuberculosis (TB) is an ancient infectious disease caused by the acid-resistant bacterium *Mycobacterium Tuberculosis* that has been discovered since 9000 BC. Tuberculosis most commonly affects the lungs transmitted via *droplets*; but it can also attack other organs or also called extrapulmonary TB [1]. Percival Pott in 1779 described tuberculosis spondylitis and its clinical presentation in paraplegia patients with chyphotic deformity in the European population.[2] The identification of *Mycobacterium* as a causative organism in 1870, the discovery of *Bacilli Calmette Guerin* (BCG) vaccination in 1945, the radiography examination facility and the invention of anti-tuberculosis drugs (1948 – 1951) are important events related to the understanding and management of tuberculosis spondylitis [3].

In 2021, the incidence of TB cases according to WHO is estimated to reach 10.6 million new cases, an increase of 4.5% from 2020. While the European region only accounts for 2.2%, the Southeast Asia region alone accounted for 45% of the total TB burden globally in 2021. Indonesia is the second highest contributor to the world's TB cases, which is 9.2%. TB-related deaths also remain one of the top 10 causes of death in the world, although it has decreased by 5.9% from 2015 to 2021, but the Southeast Asian country still experienced an increase in the death rate by 8.7% compared to 2015^[4].

Extrapulmonary TB has a low incidence of about 3% and bone TB contributes about 10% of all extrapulmonary TB. Spinal TB or Spondylitis TB or *Pott's Disease* is the most common area of bone TB, accounting for approximately 50% of all cases of bone TB and the thoracolumbar junction area is the most commonly affected area in the vertebral column followed by lumbar and cervical vertebrae^[5]. TB causes granulomatous inflammation characterized by lymphocytic infiltration and epithelioid cells that can combine to form classic cells, Langhans-type giant cells, which form *cold abscesses*. Progressive destruction of the vertebral corpus forms a *kyphotic* or *gibbus deformity*. Mycobacterium tuberculosis infection in the vertebrae is always a secondary process and is caused by the dissemination of bacillus hematogenous from its primary foci.^[1]

The clinical manifestations of TB spondylitis vary widely. Typically, TB spondylitis has a hidden onset varying from 2 weeks to several years with slow progression of the disease. Manifestations depend on the severity and duration of the disease, the affected location, and complications such as abscesses, sinuses, deformities, and neurological deficits. In complicated TB spondylitis, patients usually present with deformities, vertebral instability, and neurological deficits. Back pain is the most common symptom that appears. In the active phase, back pain is caused by inflammation of the bones and is rarely radicular in nature. Pain at rest at the affected level is pathognomonic of TB spondylitis and its intensity is proportional to the amount of bone destruction^[6]. The three main symptoms of TB spondylitis include neurological deficits, both motor and sensory, where 94.9% of TB spondylitis patients in the study at Hasan Sadikin Hospital Bandung experienced neurological deficits, then 61.5% had *kyphotic* or *gibbus deformities*, and 53.8% experienced back pain^[7].

Neurological deficits by extradural compression of the spinal cord and radicals occur as a result of many processes, namely: 1) narrowing of the spinal canal by paravertebral abscesses, 2) subluxation of pathological facet joints, 3) granulated tissues, 4) vasculitis, arterial or venospinal thrombosis, 5) vertebral collapse, 6) epidural abscess or 7) direct invasion of the duramater. In addition, invasion of the spinal cord can also occur intradurally through meningitis and tuberculosis as *space occupying lesions*^[8]. Neurological deficits in spinal TB have been classified by the Frankel and ASIA scales. However, the classification does not include all types of neurological deficits in spinal TB such as initial deficits where there is only increased spasticity and tendon reflexes without sensory or motor deficits, paraplegia with involvement of *bladder* and *bowel function*, and paraplegia with flexor spasms^[9].

Deformities in TB spondylitis occur due to progressive destruction of the anterior vertebral column. When 1 affected vertebrae is called a *knuckle*, 2 affected vertebrae are called *gibbus*, and >3 affected vertebrae are called *rounded kyphosis*^[1]. Inadequate treatment can lead to progressive *kyphotic deformity*. Despite being given modern anti-TB drugs with or without surgery, the degree of *kyphotic deformity* can also persist when the disease has healed. Nearly 3% of all *Pott's Disease* patients have severe *kyphotic deformities*. And almost all of these patients experience cardiopulmonary dysfunction, severe pain due to *costo-pelvic impingement* or neurological deficits in the form of paraplegia. Patients with severe deformity after lesion healing may experience slow-onset paraplegia after 5 – 20 years after the initial lesion. Most deformities in adult patients are the result of reduced *disc-space height* and destruction of the vertebral corpus. Paraplegia is best prevented by preventing the development of severe *kyphosis*^[10]. Previous studies have shown that *kyphosis* >30° is an independent risk factor for neurological deficits in TB spondylitis^[11].

Variety Marker The laboratory is used to monitor the response of TB spondylitis therapy. Blood sedimentation rate (LED) is *Marker* sensitive but less specific. *C-Reactive protein (CRP)* is a *Marker* which is more specific to acute infections. Procalcitonin (PCT) is also used as a *Marker* inflammation to distinguish bacterial and non-bacterial infections. PCT can be used to determine the effectiveness of antibacterial therapy. PCT can be *Marker* Reliable for the prediction of post-operative infection complications in medulla injuries but there have not been many studies on the clinical role of PCT in spinal infections including spinal TB^[12,13]. There are studies that state that a decrease in CRP and PCT indicates a significant reduction in bacteria *Mtb* in pulmonary TB infection^[14].

In addition, *neutrophil-lymphocyte ratio (NLR)* is a simple indicator that has become a marker of renewed inflammation to distinguish tuberculosis spondylitis from pyogenic infection of the vertebrae^[15]. *Platelet-lymphocyte ratio (PLR)* was also found to have good diagnostic value for TB spondylitis. NLR and PLR can be useful *markers* in the diagnosis of TB spondylitis^[16].

Until now, there have not been many studies that aim to determine the correlation between the degree of *kyphotic* and inflammatory markers such as Procalcitonin (PCT), LED, NLR, and PLR with the clinical picture of TB spondylitis patients such as neurological deficits and pain. *Kyphotic degrees* are a factor known

to affect the clinical presentation and prognosis of patients. Laboratory examinations of infection marker levels such as PCT, LED, NLR, and PLR are routine examinations carried out in the enforcement of diagnosis and assessment of therapeutic responses. This study aims to determine the correlation between the degree of chyphotic, procalcitonin (PCT), LED, NLR, and PLR with neurological deficits and pain in TB spondylitis patients at Haji Adam Malik Hospital Medan.

2. RESEARCH METHODS

Research Design

This study is an observational analytical research with a *cross-sectional* design. This study aims to assess the correlation between the degree of chyphotic, procalcitonin, LED, NLR, and PLR with neurological deficits and pain in TB spondylitis patients at Haji Adam Malik Hospital Medan.

Place and Time of Research

The research was carried out at the Adam Malik Hajj Central General Hospital in Medan after passing the Ethical Clearance and the number of samples was met.

Research Variables

Independent Variables : Chiphotic degree

Procalcitonin

LED

NLR

PLR

Bound Variables : Neurological deficit

Pain

Population and Research Sample

TB spondylitis patients who are treated at Haji Adam Malik Hospital. An affordable population that meets inclusion criteria and exclusion criteria.

Inclusion Criteria

Ages 18-64

Patients with a diagnosis of TB spondylitis

Exclusion Criteria

The patient or family refused to participate in the study.

Patients who have other infections that can affect lymphocyte values.

Have a history of other spinal structural abnormalities prior to TB spondylitis.

Have a history of spinal surgery before or after TB spondylitis.

Have a history of spinal trauma before or after TB spondylitis.

Have sensory or motor disorders prior to TB spondylitis.

The patient was under the influence of pain medication when the examination was carried out.

Patients with a history of incomplete medical records.

Large Sample

The sample size can be calculated using the numerical comparative analytical research formula of two unpaired groups: ¹

$$n = \left[\frac{Z\alpha + Z\beta}{0,5 \ln \left[\frac{1+r}{1-r} \right]} \right]^2 + 3$$

Description :

n : Number of samples to be examined

α : Type I error (0.05)

Z α : Z value in degree of meaning (1.96)

β : Type II error (0.05)

Z β : Z-value on power test strength (1.64)

r : Approximate correlation coefficient (0.375)

$$n = \left[\frac{Z\alpha + Z\beta}{0,5 \ln \left[\frac{1+r}{1-r} \right]} \right]^2 + 3$$

$$n = \left[\frac{1,96+1,64}{0,5 \ln \left[\frac{1+0,375}{1-0,375} \right]} \right]^2 + 3$$

$$n = 23,2 + 3$$

$$n = 27$$

So, the minimum sample required is 27 samples.

Research Procedure

After obtaining approval from the Ethics Committee of the Faculty of Medicine, University of North Sumatra, research sampling was carried out using *the consecutive sampling* method carried out at Haji Adam Malik Hospital Medan.

The objectives, advantages, disadvantages and procedures of the research are explained to the research subject's family and *sign an informed consent* if they are willing to participate in the research.

All prospective research subjects were recorded as identity (age and gender) anamnesis either autoanamnesis or alloanamnesis and physical examination was carried out on the research subjects.

Patients who have met the inclusion and exclusion criteria will then be included in the study subjects.

The data from the laboratory examination will be recorded from the medical records of the research subjects, namely the latest procalcitonin, LED, NLR, and PLR values.

The data from the radiological examination will be obtained from patients who will be evaluated to assess the degree of chyphotics.

Neurological deficit and patient pain data will be obtained through a series of physical examinations and pain assessments.

All data obtained were statistically analyzed.

Data Analysis

Data analysis was carried out using SPSS version 26. Clinical and demographic data of subjects that include age and gender will be displayed in the form of a table. Descriptive data on patients will be displayed in the form of mean and standard deviation when the data is distributed normally or median, minimum value, and maximum value when the data is not normally distributed. correlation between kyphotic, procalcitonin, LED, NLR, and PLR degrees with neurological deficits and pain using the Pearson test if the data are normally distributed or the Spearman test if the data are not normally distributed.

3. RESEARCH RESULTS

Research Characteristics

Based on this study, a sample of 39 samples was obtained that met the inclusion and exclusion criteria. The majority of data was excluded due to incomplete medical records. All samples were analyzed for age and gender characteristics.

Table 1 Characteristic Analysis

| Characteristics | Data |
|--------------------|-------------|
| Age (years) | |
| Mean+SD | 37,44+16,09 |
| Median | 35 |
| Min-Max | 18-64 |
| Gender | |
| Male | 13 (33,3%) |
| Women | 26 (66,7%) |

Based on Table 1, it is known that the average \pm The SD of TB spondylitis patients in this study was 37.44 ± 16.09 . It is also known that the gender distribution in this study was 13 men (33.3%) and 26 women (66.7%).

Results of the Correlation Analysis of Chifotic Degree with Neurological Deficits

Correlation analysis between chyphotic degrees and neurological deficits was performed using the Spearman correlation test for ordinal and ordinal data.

Table 2 Correlation of Chiphotic Degrees with Neurological Deficits

| Chifotic Degree | Neurological Deficit (ASIA) | | | | | | | | | | | | r | P |
|--------------------|-----------------------------|------|---|-----|---|------|----|------|----|------|-------|-----|--------|---------|
| | A | | B | | C | | D | | E | | Total | | | |
| | n | % | n | % | n | % | n | % | n | % | n | % | | |
| Lightweight | 0 | 0 | 0 | 0 | 0 | 0 | 5 | 12,8 | 11 | 28,2 | 16 | 41 | -0,877 | P<0.001 |
| Medium | 1 | 2,6 | 2 | 5,1 | 8 | 20,5 | 5 | 12,8 | 0 | 0 | 16 | 41 | | |
| Weight | 5 | 12,8 | 1 | 2,6 | 1 | 2,6 | 0 | 0 | 0 | 0 | 7 | 18 | | |
| Total | 6 | 15,4 | 3 | 7,7 | 9 | 23,1 | 10 | 25,6 | 11 | 28,2 | 39 | 100 | | |

Based on Table 2, it is known that there is a significant negative correlation ($p < 0.001$) between the kyphotic degree and neurological deficits. The degree of correlation obtained was a strong correlation ($r = -0.877$).

Results of the Correlation Analysis of Procalcitonin with Neurological Deficits

A correlation analysis between procalcitonin and neurological deficits was performed using the Spearman correlation test.

Table 3 Correlation of Procalcitonin with Neurological Deficits

| Procalcitonin Ratio | Neurological Deficit (ASIA) | | | | | r | P |
|---------------------|-----------------------------|------|------|------|------|--------|-------|
| | A | B | C | D | E | | |
| | 0,46 | 0,35 | 0,38 | 0,29 | 0,29 | -0,523 | 0,001 |

Based on Table 3, it is known that there is a significant negative correlation ($p = 0.001$) between procalcitonin and neurological deficits. The degree of correlation obtained was moderate correlation ($r = -0.523$).

Results of the Analysis of the Correlation of LEDs with Neurological Deficits

Correlation analysis between LEDs and neurological deficits was performed using the Spearman correlation test.

Table 4. Correlation of LEDs with Neurological Deficits

| LED Average | Neurological Deficit (ASIA) | | | | | r | P |
|-------------|-----------------------------|-------|-------|-------|-------|--------|---------|
| | A | B | C | D | E | | |
| | 100,17 | 83,33 | 40,56 | 17,90 | 29,00 | -0,568 | P<0.001 |

Based on Table 4, it is known that there is a significant negative correlation ($p < 0.001$) between LEDs and neurological deficits. The degree of correlation obtained was moderate correlation ($r = -0.568$).

Results of NLR Correlation Analysis with Neurological Deficits

A correlation analysis between NLR and neurological deficits was performed using the Spearman correlation test.

Table 5 Correlation of NLR with Neurological Deficits

| NLR Average | Neurological Deficit (ASIA) | | | | | r | P |
|-------------|-----------------------------|------|------|------|------|-------|---------|
| | A | B | C | D | E | | |
| | 2,61 | 2,09 | 3,92 | 8,39 | 6,12 | 0,564 | P<0.001 |

Based on Table 5, it is known that there is a significant positive correlation ($p < 0.001$) between NLR and neurological deficits. The degree of correlation obtained was moderate correlation ($r = 0.564$).

Results of the Correlation Analysis of PLR with Neurological Deficits

Correlation analysis between PLR and neurological deficits was performed using the Spearman correlation test.

Table 6 Correlation of PLR with Neurological Deficits

| PLR Average | Neurological Deficit (ASIA) | | | | | r | P |
|-------------|-----------------------------|-------|-------|-------|-------|-------|-------|
| | A | B | C | D | E | | |
| | 20,16 | 14,83 | 22,26 | 37,18 | 60,02 | 0,374 | 0,019 |

Based on Table 4.6, it is known that there is a significant positive correlation ($p=0.019$) between PLR and neurological deficits. The degree of correlation obtained was low correlation ($r = 0.374$).

Results of the Correlation Analysis of Chiphotic Degree with Pain

Correlation analysis between the degree of chyfotic and pain was carried out using the Spearman correlation test for ordinal and ordinal data.

Table 7 Correlation of Chiphotic Degrees with Pain

| Chifotic Degree | Pain Average (VAS) | r | P |
|-----------------|--------------------|-------|-------|
| Lightweight | 2,44 | 0,530 | 0,001 |
| Medium | 2,94 | | |
| Weight | 5,57 | | |

Based on Table 7, it is known that there is a significant positive correlation ($p=0.001$) between the degree of chyfotic and pain. The degree of correlation obtained was moderate correlation ($r = 0.530$).

Results of the Analysis of the Correlation of Procalcitonin with Pain

A correlation analysis between procalcitonin and pain was performed using the Spearman correlation test.

Table 8 Correlation of Procalcitonin with Pain

| Procalcitonin Ratio | Pain Average (VAS) | r | P |
|---------------------|--------------------|-------|-----------|
| 0,35 | 3,21 | 0,543 | $P<0.001$ |

Based on Table 8, it is known that there is a significant positive correlation ($p<0.001$) between procalcitonin and pain. The degree of correlation obtained was moderate correlation ($r = 0.534$).

Results of the Analysis of the Correlation of LEDs with Pain

Correlation analysis between LEDs and pain was performed using the Spearman correlation test.

Table 9 Correlation of LEDs with Pain

| LED Average | Pain Average (VAS) | r | P |
|-------------|--------------------|-------|-----------|
| 43,95 | 3,21 | 0,690 | $P<0.001$ |

Based on Table 9, it is known that there is a significant positive correlation ($p<0.001$) between LEDs and pain. The degree of correlation obtained was a strong correlation ($r = 0.690$).

Results of NLR Correlation Analysis with Neurological Deficits

A correlation analysis between NLR and pain was performed using the Spearman correlation test.

Table 10 Correlation of NLR with Pain

| NLR Average | Pain Average (VAS) | P |
|-------------|--------------------|-------|
| 5,35 | 3,21 | 0,062 |

Based on Table 10, it is known that there is no significant correlation ($p=0.062$) between NLR and pain.

Results of the Analysis of the Correlation of PLR with Pain

A correlation analysis between PLR and pain was performed using the Spearman correlation test.

Table 11 Correlation of PLR with Pain

| PLR Average | Pain Average (VAS) | P |
|-------------|--------------------|-------|
| 35,84 | 3,21 | 0,382 |

Based on Table 11, it is known that there is no significant correlation ($p=0.382$) between PLR and pain.

4. DISCUSSION

The main purpose of this study was to evaluate the relationship of several variables obtained from supporting examinations such as kyphotic degree (radiological imaging) and laboratory examinations (procalcitonin, LED, NLR, and PLR), to the level of neurological deficit and pain in patients with tuberculous spondylitis (TB; *Pott's disease*). For this reason, the researchers included 39 adult individuals (aged >18 years, 66.7% female) with an average age of 37.44 ± 16.09 years. The researcher used an ASIA assessment consisting of 4 degrees of neurological deficits, namely (A: Complete, B-D: Incomplete; B: only sensory function is still intact, C: motor function is still partially maintained (>50% of key muscle groups have a level of muscle strength <3), and D: motor function is still largely maintained (<50% of key muscle groups have a level of muscle strength), while ASIA E can be defined as normal motor and sensory function). On the other hand, researchers used the VAS rating scale (1-10) to quantitatively elaborate the intensity of patients' pain.^{50,51}

The results of the first correlation analysis test between kyphotic degrees (mild, moderate, severe) based on the results of the vertebral radiological examination showed a significant difference between the test groups ($P<0.001$). This is illustrated based on observations of descriptive data which shows that the ASIA A patient group has the largest percentage of individuals with severe kyphotic degrees (12.8%) compared to other ASIA groups. The findings were significantly reduced as ASIA status improved, resulting in 50% of individuals with mild kyphotic degrees in ASIA D and 100% in ASIA E individuals (no neurological deficits). The researcher also analyzed the Spearman correlation test with the results of the r test with a value of -0.877 ; indicates a strong negative correlation between ASIA and kyphotic degrees, with higher kyphotic degrees found can be expected to experience an increase in neurological deficits based on ASIA's assessment.

Mittal *et al.*, in their study of a group of TB spondylitis, have also confirmed that the chiphotic degree of patients with neurological deficits (ASIA A-D) is significantly higher ($P<0.05$) compared to ASIA E ($26.92^\circ \pm 12.67$ vs. $21.72^\circ \pm 11.89$). Furthermore, Mittal *et al.*, also explained the finding of an *odd ratio* (OR) value of 2.68 in the findings of kyphosis $>30^\circ$ (moderate-severe kyphotic degree in this study) to experience neurological deficits (ASIA A-D).⁵² Furthermore, Hadian *et al.*, have explained that the higher the degree of gibus or chiphotic a patient due to TB spondylitis, the higher the likelihood of experiencing sensory neurological deficits ($r = 0.375$; $P<0.05$), but not with motor neurological deficits ($r = 0.125$; $P>0.05$).⁵³ Another study by Sae-Jung *et al.*, also confirmed that the group of patients with a significant Cobb angular value ($>30^\circ$) had a higher risk of developing neurological deficits (OR; 3.35; $P<0.05$), so that previous findings have consistently described the relationship between the two.⁵⁴ The Gospel of Jesus Christ

Furthermore, the researchers also evaluated two inflammatory markers that are quite common to be evaluated clinically, namely procalcitonin and LED. This study successfully observed a significant correlation between procalcitonin/LED and the degree of neurological deficit. Consecutively, a moderately significant negative correlation was found in procalcitonin analysis ($r = -0.523$; $P<0.05$) and LED ($r = -0.568$; $P<0.05$). Until now, researchers have not been able to find studies that specifically evaluate the correlation between the value of procalcitonin in TB spondylitis patients and the degree of neurological deficit experienced. In this regard, in 2015, Yoon *et al.*, tried to compare the procalcitonin values of TB and non-TB spondylitis with the results of finding relatively lower procalcitonin values (0.11 vs. 0.59; $P>0.05$); Although these values lead more to the possibility of infection based on the stratification of the findings and interpretation of procalcitonin. Therefore, the relevance of procalcitonin measurements in predicting neurological deficits has not been proven in the literature, although this study has described a moderately significant negative correlation.^{55,56}

Furthermore, Sae-Jung *et al.*, stated that they did not find an association between increased LEDs and neurological deficits (OR; 1.62; $P = 0.27$).⁵⁴ The findings were supported by Sudprasert *et al.*, who stated that there was no difference between ASIA A-D regarding ESR values ($P = 0.71$).⁵⁷ Boussaid *et al.*, also mentioned that LEDs had little effect on general clinical outcomes because there was no significant difference in the group with good and bad outcomes in their LED values.⁵⁸ Thus, the role of LEDs in predicting neurological deficits in a patient with TB spondylitis should be further evaluated given the differences between the findings of this study and previous reports.

Furthermore, the study also evaluated the correlation between NLR/PLR and neurological deficits, finding a moderate-low positive correlation that was both statistically significant ($P<0.05$; $r = 0.564$ and $r =$

0.374). Thus, it can be estimated that the higher the measured NLR/PLR value, the higher the neurological function that the patient has (the closer the ASIA E degree compared to A). It is important to understand that this study is also one of the first studies to evaluate the correlation of these variables, so validating the data against other literature is relatively difficult to do. Basically, the role of NLR has been described in the research of Liu *et al.*, which stated that NLR findings were significantly lower in the spondylitis group compared to the pyogenic spondylitis. This is theoretically acceptable given that neutrophil numbers will experience a more significant increase in other bacterial infections (and not so much in the case of TB spondylitis).⁵⁹ Although validation of other literature has not been possible, this study has succeeded in providing statistical data indicating a decrease in NLR values in TB spondylitis patients with more severe degrees of neurological deficits.

Other findings by Zanon *et al.*, support the findings of this study. The study mentioned the potential for a decrease in the ratio of lymphocytes such as NLR and PLR in TB spondylitis along with increasing severity. Basically, the decrease in NLR/PLR can be caused by two different things, namely a relative increase in neutrophils or platelets, which is accompanied or not accompanied by an increase in lymphocyte count.⁶⁰ Thus, this study has provided a brief overview of how the degree of neurological deficit is thought to be related to both processes in patients with TB spondylitis. Given that this study is also one of the earliest reports on the evaluation of NLR/PLR on one of the main outcomes of this study, it is hoped that a more comprehensive investigation can be carried out in the future.

Analysis between kyphotic degree and pain in this study showed a statistically significant moderate positive correlation ($r = 0.530$; $P < 0.05$), supported by a higher average pain in the severe kyphotic (5.57) group compared to moderate (2.94) and mild (2.44). Thus, this study basically observes the possibility that the heavier the kyphotic degree of a TB spondylitis sufferer, the higher the pain complaints felt. Although not performed on a group of TB spondylitis patients, the study of Nadri *et al.*, which evaluated the correlation between the kyphotic angle and lower back pain showed a significant correlation between the two, the higher the degree of kyphotic pain, the higher the lower back pain felt ($r = 0.686$; $P < 0.05$). An increase in the degree of kyphotic has been associated with a decrease in the overall quality of human life, especially with the addition of various other complaints such as impaired pulmonary function to other posture-related syndromes. Furthermore, theoretically a person with a higher kyphotic angle certainly has a greater risk of radical compression so that greater induction of chronic pain becomes possible in that population.⁶¹ On the other hand, studies by Mirbagheri *et al.*, found only a significant correlation between changes in the structure of lordosis type vertebrae to induce significant pain (with no further elaboration of the kyphotic degree), while this was not found in kyphotic type patients.⁶²

Increased kyphotic angle has also been associated with decreased physical function, impaired respiratory function, increased neck pain, headaches, and other posture-related conditions such as subacromial pain syndrome. The ratio of the relationship between kyphosis and the development of subacromial pain syndrome is complex. It has been proposed that with the increase of kyphosis, the scapula becomes more attracted and undergoes downward rotation, resulting in potential pressure under the acromion and subacromial tissues including the subacromial bursa and *rotator cuff*.⁶³ Thus, theoretically the correlation between changes in vertebral structure and pain has an acceptable structural link (and has been proven in this study), although to date other literature explicitly states a link between the two has not been found.

Regarding the correlation between procalcitonin and pain, it was found that the degree of moderate positive correlation was significant, so statistically higher pain would be found in individuals with high procalcitonin ($r = 0.543$; $p < 0.05$). On the other hand, there was a significant positive correlation regarding the relationship between LEDs and pain ($r = 0.690$; $P < 0.05$). These two things are thought to be related to the basic pathophysiology of inflammation (the levels of which are represented by procalcitonin and LED), so that the more severe the degree of infection that occurs, the higher the inflammatory response that occurs and pain symptoms will arise as one of the clinical manifestations. Although there have been no studies to date that specifically explain the correlation between these variables, especially in the tuberculous spondylitis population, theories that unify the inflammatory response to increased central pain sensitization are certainly acceptable. Biochemical mediators of inflammation such as cytokines, neuropeptides, *growth factors*, and neurotransmitters (related to procalcitonin and LED levels) induce central pain receptors so that an individual is likely to have higher levels of pain in populations with higher levels of inflammation.^{64,65}

Furthermore, the researchers' observations on the correlation between NLR/PLR and the patient's pain scale did not show any real significance, with a $P > 0.05$ value found in both correlations. The findings are relatively related to the report described by Turgut *et al.*, *et al.*, which stated that there was a higher need for analgesics in the group with lower NLR, indicating an indirect correlation between NLR and the degree of postoperative pain that patients felt (although these results were only found in the administration of tenoxicam; and not in tramadol and paracetamol).⁶⁶ Shu *et al.*, *on the other hand*, stated that the group with chronic postoperative pain had a higher postoperative NLR value (7.70) compared to the control group (6.61); supported by a $P < 0.05$ value.⁶⁷ Another report by Osunronbi *et al.*, stated that there was no association between pre-operative NLR and postoperative lumbar fusion pain even 12 months after ($P > 0.05$; with an OR value of

1.62).⁶⁸ Thus, the correlation between NLR and pain levels varied relatively between reports, although the study itself stated that both were not related in the context of patients with tubercle spondylitis.

Adiguzel *et al.*, have also previously stated that NLR and PLR have no predictive utility to the scale of pain that patients feel. Based on his study report conducted on a group of patients undergoing laparoscopic cholecystectomy, there was no difference in NLR and PLR values in the large and low-dose tramadol user population groups ($P = 0.79$ and $P = 0.49$, respectively).⁶⁹ In contrast, another study by Liang *et al.*, suggested that patients with ankylosing spondylitis with higher disease activity values (which are directly related to inflammatory processes and indirectly related to perceived pain) would have higher PLR ($P < 0.05$).⁷⁰ Nevertheless, the benefit of PLR measurements in inflammatory conditions to predict pain in patients, especially in specific conditions such as tuberculous spondylitis, remains one of the medical questions to date, although this study has specifically stated that the two are not correlated with each other and that other factors or variables may be more considerable in predicting the patient's pain scale.

In this regard, the main limitation of this study lies in the lack of previous studies that have evaluated the correlation between several factors evaluated on neurological deficits and the scale of perceived pain, although theoretically these factors have a molecular to functional correlation with each other. Comparing the findings of this study with previous reports will be more difficult given that the "novelty" nature of the investigation that researchers conducted can also play an important role in providing a new perspective on several potential predictive factors related to patients' quality of life.

5. CONCLUSION

There was a significant correlation ($P < 0.05$) in the relationship between kyphotic, procalcitonin, LED, NLR, and PLR degrees to neurological deficits described on the ASIA scale with consecutive r-values of -0.877; -0,523; -0,568; 0,564; and 0.374.

There was a significant correlation ($P < 0.05$) in the relationship between kyphotic, procalcitonin, and LED degrees on pain described on the VAS scale with a consecutively r-value of 0.530; 0,543; and 0.690, consecutively. However, this was not found in NLR and PLR outputs with a $P > 0.05$ tilap.

Based on the 39 patients included in the final analysis, 41% of each study population had mild and moderate kyphotic degrees, while only 18% had severe kyphotic degrees.

The average procalcitonin value in the ASIA A, B, C, D, and E groups was 0.46; 0,35; 0,38; 0,29; and 0.29.

The average LED value in the ASIAN GROUPS A, B, C, D, and E is 100.17; 83,33; 40,56; 17,90; and 29.00.

The average NLR value in the ASIAN GROUPS A, B, C, D, and E was 2.61; 2,09; 3,92; 8,39; and 6.12.

The average PLR score in the ASIAN GROUPS A, B, C, D, and E was 20.16; 14,83; 22,26; 37,18; and 60.02.

Based on the 39 patients included in this study, as many as 15.4% had ASIA A neurological deficits, 7.7% for B, 23.1% for C, 25.6% for D, and 28.2% for E.

The average pain in TB spondylitis patients was 3.21 based on VAS measurements.

6. SUGGESTIONS

The researchers suggested conducting studies with a larger population, followed by a more in-depth evaluation of the period of measurement of neurological deficits or perceived pain. It is hoped that these results can provide additional insight into the predictive ability of several factors evaluated in this study to predict the possible degree of neurological deficit or the patient's pain scale.

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