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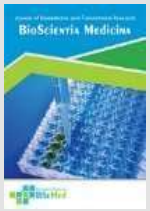

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Diagnostic Roles of Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio for Vertebral Fracture due to Tuberculosis and Malignancy

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A B S T R A C T

Background: Vertebral fracture is a serious complication that can occur due to various medical conditions, including bone tuberculosis and malignancy (eg, cancer metastasis to the vertebrae). This condition invariably causes an increase in the inflammatory process in the body, which can be identified through the Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR). This study aims to investigate the differences in NLR and PLR values in patients with vertebral fractures due to TB or malignancy. **Methods:** A retrospective observational study was conducted on vertebral fracture patients who underwent surgery in the Orthopedic Surgery Department of Dr. Kariadi Hospital Semarang between January 1st, 2022, and December 31st, 2023. Data on demographics and laboratory test results were extracted from medical records. Statistical analysis was performed using univariate analysis and presented as percentage and frequency. T-test or Mann-Whitney test was used to determine the difference based on their normality distribution. The diagnostic value of NLR and PLR was also analyzed using the receiver operating characteristic (ROC) curve and Youden index. **Results:** The study included 54 vertebral fracture patients. The mean age of patients was 41.77 ± 16.00 years, and the majority were female patients (68.5%). The Neutrophil to Lymphocyte Ratio (NLR) value was significantly higher in vertebral fracture due to malignancy patients than TB (5.5 (IQR 3.92 – 13.39) vs 4.53 (IQR 2.91 – 6.96), p=0.020). In contrast, the Platelet to Lymphocyte Ratio (PLR) value was not significantly different (p>0.05). The area under the curve for the NLR (0.69, 95% confidence interval [CI], 0.54 – 0.839) was greater than that of PLR (0.408, 95% CI, 0.246 – 0.571). **Conclusion:** NLR showed significantly different results in determining the cause of vertebral fractures, either tuberculosis or malignancy. NLR can be used as an important diagnostic marker to help differentiate between vertebral fractures caused by malignancy and those caused by infection.

1. Introduction

Vertebral fractures, a prevalent cause of morbidity and mortality globally, represent a significant public health challenge. These fractures, characterized by the collapse or compression of one or more vertebrae, can lead to debilitating pain, spinal deformity, and diminished quality of life. The etiology of vertebral fractures is diverse, encompassing a spectrum of conditions ranging from osteoporosis and trauma to infectious and neoplastic processes. Among the non-traumatic causes, tuberculosis (TB) and malignancy stand out as prominent contributors to vertebral fracture incidence. TB, an ancient infectious disease caused by Mycobacterium tuberculosis, continues to afflict millions worldwide. While pulmonary TB remains the most common presentation, extrapulmonary manifestations, including skeletal involvement, pose a significant clinical burden. Spinal

TB, also known as Pott's disease, accounts for a substantial proportion of skeletal TB cases and frequently culminates in vertebral fractures. The insidious nature of spinal TB often leads to delayed diagnosis and treatment, contributing to the development of severe complications, including neurological deficits and spinal instability. Malignancy, another major contributor to vertebral fractures, encompasses a diverse group of diseases characterized by uncontrolled cell growth and invasion. Metastatic spread of cancer to the spine is a frequent occurrence, with primary tumors originating from various sites, including the lung, breast, and prostate. Vertebral metastases can weaken the structural integrity of the spine, predisposing to pathological fractures, which are fractures that occur in bones already weakened by an underlying disease process. These fractures can cause significant pain, impair mobility, and compromise neurological function, profoundly impacting patients' quality of life.[1-4]

The diagnosis and management of vertebral fractures due to TB and malignancy present unique challenges. Differentiating between these two etiologies can be complex, as they often share similar clinical and radiological features. Accurate and timely diagnosis is crucial, as the treatment approaches for TB and malignancy differ significantly. TB requires prolonged anti-tuberculosis therapy, while malignancy may necessitate a combination of chemotherapy, radiotherapy, surgery, or palliative care. In the quest for reliable diagnostic markers to differentiate vertebral fractures caused by TB and malignancy, inflammatory markers have emerged as promising candidates. The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are two such markers that have gained increasing attention in recent years. NLR and PLR, calculated from readily available complete blood count parameters, reflect the systemic inflammatory response and have been associated with various disease processes, including infections, inflammatory diseases, and cancer. NLR, the ratio of neutrophils to lymphocytes, is considered a marker of both innate and adaptive immunity. Neutrophils, the most abundant type of white blood cells, play a crucial role in the early immune response against pathogens, while lymphocytes are essential for the targeted elimination of infected or cancerous cells. An elevated NLR has been linked to increased inflammation, disease activity, and poor prognosis in various conditions.[5-7]

PLR, the ratio of platelets to lymphocytes, also reflects the interplay between inflammation and immune response. Platelets, small cell fragments involved in blood clotting, have been increasingly recognized for their role in inflammation and tumor progression. Lymphocytes, as key players in the adaptive immune system, are responsible for recognizing and eliminating cancerous cells. An elevated PLR has been associated with increased inflammation, disease activity, and poor prognosis in several studies. The potential utility of NLR and PLR in differentiating vertebral fractures caused by TB and malignancy stems from the distinct inflammatory profiles associated with each condition. TB, a chronic infectious disease, triggers a complex immune response involving both neutrophils and lymphocytes, leading to granuloma formation and tissue destruction. Malignancy, on the other hand, is characterized by an intricate interplay between tumor cells and the host immune system, involving various inflammatory mediators and immune cells. Several studies have investigated the role of NLR and PLR in various musculoskeletal conditions, including spinal infections, inflammatory arthritis, and bone tumors. These studies have provided evidence suggesting that NLR and PLR may serve as valuable diagnostic and prognostic markers in these conditions. However, the specific role of NLR and PLR in differentiating vertebral fractures caused by TB and malignancy remains relatively unexplored.[8-10] This research aims to investigate the diagnostic accuracy of NLR and PLR in differentiating vertebral fractures caused by TB and malignancy.

2. Methods

This research was conducted as a retrospective observational study. Retrospective studies leverage existing medical records and databases, providing access to a wealth of information on patient demographics, clinical characteristics, laboratory results, and outcomes. The study will be conducted at Dr. Kariadi Hospital Semarang, a major tertiary referral hospital in Central Java, Indonesia. The study population will comprise all patients who underwent surgery for vertebral fractures at the Orthopedic Surgery Department of Dr. Kariadi Hospital Semarang between January 1st, 2022, and December 31st, 2023. The diagnosis of vertebral fracture will be confirmed by radiographic imaging and histopathological examination. Radiographic imaging, including X-ray, CT scan, or MRI, will be used to visualize the vertebral column and identify the presence and extent of fractures. Histopathological examination, considered the gold standard for diagnosis, will be used to confirm the cause of the fracture, whether it is due to TB, malignancy, or other etiologies.

To ensure the validity and reliability of the study findings, specific inclusion and exclusion criteria will be applied to the study population. Inclusion Criteria; Age 18 years or older: This criterion ensures that the study population comprises adults, as the diagnostic accuracy of NLR and PLR may differ in pediatric populations; Underwent surgery for vertebral fracture between January 1st, 2022, and December 31st, 2023: This criterion defines the study period and ensures that all patients have undergone surgical intervention for their vertebral fractures; Histopathologically confirmed diagnosis of vertebral fracture due to TB or malignancy: This criterion ensures that the study population includes only patients with confirmed TB or malignancy as the cause of their vertebral fractures. Exclusion Criteria; Incomplete medical records: This criterion excludes patients with missing or incomplete data, which could affect the accuracy of the analysis; Vertebral fracture due to causes other than TB or malignancy: This criterion excludes patients with vertebral fractures caused by osteoporosis, trauma, or other conditions, as the focus of this study is on differentiating between TB and malignancy; History of hematological disorders or immunosuppressive therapy: This criterion excludes patients with conditions that could affect NLR and PLR values, such as leukemia, lymphoma, or HIV infection, as well as those receiving medications that suppress the immune system.

Data will be collected from the patients' medical records, including the following; Demographics: Age, sex, education, marital status, occupation, comorbidity, smoking status. These variables provide a comprehensive profile of the study population and allow for the assessment of potential confounding factors; Laboratory test results: NLR, PLR. These inflammatory markers will be calculated using the absolute neutrophil count, lymphocyte count, and platelet count obtained from the complete blood count (CBC) performed preoperatively; Histopathological diagnosis: TB or malignancy.

Data will be analyzed using SPSS version 26 (IBM Corp., Armonk, NY, USA), a widely used statistical software package. Continuous variables will be presented as mean ± standard deviation or median (interquartile range), depending on the normality of the data distribution. Categorical variables will be presented as frequency and percentage. The Shapiro-Wilk test will be used to assess the normality of data distribution. This test determines whether a dataset follows a normal distribution, which is an assumption for many statistical tests. For non-normally distributed data, the Mann-Whitney U test will be used. The diagnostic value of NLR and PLR in differentiating vertebral fractures due to TB and malignancy will be assessed using receiver operating characteristic (ROC) curve analysis. The area under the ROC curve (AUC) will be calculated to determine the discriminatory power of each marker. The Youden index will be used to determine the optimal cut-off value for NLR and PLR. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) will also be calculated. A p-value of less than 0.05 will be considered statistically significant. This

threshold indicates that there is less than a 5% probability that the observed results are due to chance.

3. Results

Table 1 presents the demographic and clinical characteristics of the 54 patients included in the study, divided into two groups: those with vertebral fractures due to tuberculosis (TB) (n=33) and those with vertebral fractures due to malignancy (n=21). The average age of patients in both groups was similar (41.77 ± 16.00 years). However, the age distribution differed significantly. A majority of the TB patients (66.7%) were under 40 years old, while most malignancy patients (85.7%) were over 40. This suggests that vertebral fractures due to TB may be more prevalent in younger individuals compared to those caused by malignancy. A larger proportion of the TB group were female (75.8%) compared to the malignancy group (57.1%). This aligns with existing knowledge that TB can disproportionately affect females in certain populations. Both groups showed a similar distribution across education levels and occupations, with most individuals having completed junior high school and being employed in either the private or government sector. This suggests that socioeconomic factors may not play a major role in differentiating between vertebral fractures caused by TB and malignancy. The majority of patients in both groups were married (84.8% in the TB group and 71.4% in the malignancy group). This information may be relevant for understanding social support systems and potential caregiving needs. The prevalence of comorbidities like hypertension and diabetes mellitus was slightly higher in the malignancy group compared to the TB group. This observation could be related to the generally older age of the malignancy patients, as these conditions are more common with increasing age. The proportion of smokers was comparable between the two groups (21.2% in the TB group and 38.1% in the malignancy group). While smoking is a known risk factor for both TB and certain malignancies, the similar distribution in this study suggests that it may not be a strong differentiating factor between the two causes of vertebral fracture.

Table 1. Study population.

Characteristic	Tuberculosis (n=33)	Malignancy (n=21)
Age (years)	41.77 ± 16.00	41.77 ± 16.00
Age group		
≤ 40 years	22 (66.7%)	3 (14.3%)
> 40 years	11 (33.3%)	18 (85.7%)
Gender		
Male	8 (24.2%)	9 (42.9%)
Female	25 (75.8%)	12 (57.1%)
Education level		
Elementary school	10 (30.3%)	5 (23.8%)
Junior high school	15 (45.5%)	8 (38.1%)
Senior high school	8 (24.2%)	8 (38.1%)
Marital status		
Married	28 (84.8%)	15 (71.4%)
Single	5 (15.2%)	6 (28.6%)
Occupation		
Housewife	12 (36.4%)	4 (19.0%)
Private employee	10 (30.3%)	7 (33.3%)
Government employee	5 (15.2%)	6 (28.6%)
Others	6 (18.2%)	4 (19.0%)
Comorbidity		
Hypertension	5 (15.2%)	7 (33.3%)
Diabetes mellitus	3 (9.1%)	5 (23.8%)
Others	2 (6.1%)	3 (14.3%)
Smoking status		
Smoker	7 (21.2%)	8 (38.1%)
Non-smoker	26 (78.8%)	13 (61.9%)

Table 2 presents a comparison of the inflammatory markers NLR (Neutrophil-to-Lymphocyte Ratio) and PLR (Platelet-to-Lymphocyte Ratio) between the Tuberculosis (TB) and Malignancy groups; NLR: The median NLR was 4.53 (IQR: 2.91 – 6.96) in the TB group and 5.5 (IQR: 3.92 – 13.39) in the Malignancy group. This indicates that, on average, patients with vertebral fractures due to malignancy had higher NLR values compared to those with TB. The p-value of 0.020 is statistically significant (less than 0.05). This means that the difference in NLR values between the two groups is likely not due to chance and suggests that NLR could be a potential marker for differentiating between TB and malignancy in patients with vertebral fractures; PLR: The median PLR was 23400 (IQR: 16433.74 – 35304.55) in the TB group and 19533.33 (IQR: 13058 – 31089) in the Malignancy group. Although the median PLR appears slightly higher in the TB group, the difference is not substantial. The p-value of 0.26 is not statistically significant. This indicates that the difference in PLR values between the two groups could be due to chance and suggests that PLR may not be a reliable marker for differentiating between TB and malignancy in this context.

Table 2. Comparison of NLR and PLR between TB and malignancy groups.

Variable	Tuberculosis	Malignancy	p-value
NLR (Median (IQR))	4.53 (2.91 – 6.96)	5.5 (3.92 – 13.39)	0.020
PLR (Median (IQR))	23400 (16433.74 – 35304.55)	19533.33 (13058 – 31.089)	0.26

Figure 1 shows the receiver operating characteristic (ROC) curves for NLR (Neutrophil-to-Lymphocyte Ratio) and PLR (Platelet-to-Lymphocyte Ratio) in differentiating between vertebral fractures due to tuberculosis (TB) and malignancy. ROC curves are a graphical representation of the diagnostic ability of a binary classifier system as its discrimination threshold is varied; the X-axis: Represents "1 - Specificity". Specificity is the ability of a test to correctly identify those without the disease. So, 1-specificity represents the false positive rate; Y-axis: Represents "Sensitivity". Sensitivity is the ability of a test to correctly identify those with the disease (true positive rate); Reference Line: The diagonal green line represents a classifier with no discriminative ability (essentially a random guess). A good diagnostic test aims to have its curve as far away from this line as possible, towards the top-left corner; Curve Position: The curve for NLR (red) is situated higher and to the left compared to the curve for PLR (blue). This indicates that NLR has a better discriminatory ability than PLR in differentiating between TB and malignancy as the cause of vertebral fracture.

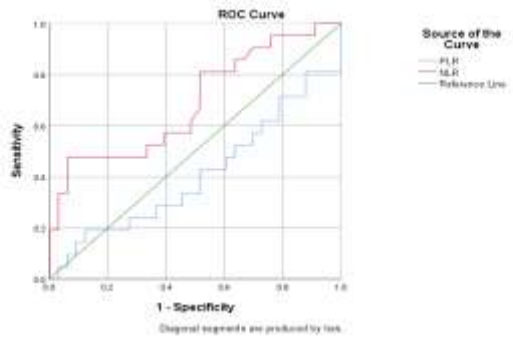

Figure 1. Comparison ROC curve between NLR and PLR.

Table 3 provides a detailed analysis of the diagnostic accuracy of NLR and PLR in differentiating between vertebral fractures due to tuberculosis (TB) and malignancy; AUC (Area Under the ROC Curve): The AUC for NLR (0.690) is higher than that for PLR (0.408). This indicates that NLR has a greater ability to discriminate between TB and malignancy as the cause of vertebral fractures. An AUC of 0.690 suggests a moderate accuracy for NLR, while an AUC of 0.408 for PLR indicates poor accuracy, even approaching random chance; Cut-off Value: The table presents the optimal cut-off values for NLR (>4.9350) and PLR (>20903.845) determined by the analysis. These values represent the thresholds at which the respective markers best differentiate between the two groups; Sensitivity and Specificity: NLR demonstrates a sensitivity of 57% and a specificity of 54%. This means that NLR correctly identifies 57% of patients with TB as having TB (true positive rate) and correctly identifies 54% of patients with malignancy as having malignancy (true negative rate). PLR shows a lower sensitivity of 42.86% and a specificity of 42.42%. This indicates that PLR is less effective in correctly identifying patients with either TB or malignancy; Youden Index: The Youden index is a summary measure of the receiver operating characteristic (ROC) curve that combines sensitivity and specificity. The Youden index for NLR (0.11) is positive, while it is negative for PLR (-0.1472). A positive Youden index further supports the better discriminatory power of NLR compared to PLR.

Table 3. Diagnostic accuracy of NLR and PLR.

Parameter	NLR	PLR
AUC	0.690 (0.54 – 0.839)	0.408 (0.246 – 0.571)
Cut-off value	>4,9350	>20903,845
Sensitivity	57%	42.86%
Specificity	54%	42.42%
Youden index	0,11	-0,1472

4. Discussion

This study's findings highlight the potential utility of NLR as a diagnostic marker in differentiating between vertebral fractures caused by TB and malignancy. Our results demonstrate that NLR is significantly higher in patients with vertebral fractures due to malignancy compared to those with TB. This observation is consistent with previous studies that have shown elevated NLR in various cancers, further supporting the notion that NLR reflects the systemic inflammatory response associated with malignancy. The higher NLR in malignancy may be attributed to several factors. Firstly, neutrophils, the most abundant type of white blood cells, play a crucial role in the early immune response against pathogens and are also involved in the inflammatory response to tumors. In malignancy, tumor cells can release various factors that stimulate neutrophil production and activation, leading to an increase in neutrophil counts. Secondly, lymphocytes, which are essential for the targeted elimination of infected or cancerous cells, may be suppressed in the tumor microenvironment, leading to a decrease in lymphocyte counts. The combination of increased neutrophil production and decreased lymphocyte activity contributes to the elevated NLR observed in malignancy. In contrast to NLR, PLR did not differ significantly between the TB and malignancy groups in our study. This finding is somewhat unexpected, as PLR has also been reported to be elevated in both infections and malignancies. The lack of difference in PLR may be due to the complex interplay of factors that influence platelet and lymphocyte counts in these conditions. The observation that NLR is significantly higher in patients with vertebral fractures due to malignancy compared to those with TB holds critical implications for

diagnostic approaches in clinical settings. This distinction is not merely a numerical observation but reflects the underlying pathophysiological processes associated with each condition. Tuberculosis (TB), a chronic infectious disease caused by Mycobacterium tuberculosis, triggers a complex immune response involving both neutrophils and lymphocytes, leading to granuloma formation and tissue destruction. The inflammatory response in TB is characterized by the activation of macrophages and the release of pro-inflammatory cytokines, which can lead to an increase in neutrophil counts. However, the lymphocyte response in TB is also robust, as lymphocytes are essential for the control of Mycobacterium tuberculosis infection. The balance between neutrophil and lymphocyte activity in TB may explain why NLR is not as elevated in TB compared to malignancy. Neutrophils are essential components of the innate immune system and play a critical role in the early stages of TB infection. They are recruited to the site of infection, where they phagocytose and kill mycobacteria. However, neutrophils also contribute to tissue damage and inflammation in TB. Lymphocytes, particularly T cells, are crucial for the adaptive immune response against TB. They recognize and eliminate infected cells, and they also contribute to the formation of granulomas, which contain the infection. The immune response in TB involves a delicate balance between neutrophils and lymphocytes. An excessive neutrophil response can lead to tissue damage and inflammation, while an inadequate lymphocyte response can result in uncontrolled bacterial growth and dissemination. Malignancy, on the other hand, is characterized by an intricate interplay between tumor cells and the host immune system, involving various inflammatory mediators and immune cells. Tumor cells can release a variety of factors that promote inflammation, including cytokines, chemokines, and growth factors. These factors can stimulate neutrophil production and activation, leading to an increase in NLR. Additionally, tumor cells can suppress lymphocyte activity, further contributing to the elevated NLR observed in malignancy. Tumor cells can release various factors that promote inflammation, including cytokines, chemokines, and growth factors. This inflammatory microenvironment can contribute to tumor growth, angiogenesis, and metastasis. Tumor-derived factors can recruit neutrophils to the tumor microenvironment and activate them. Activated neutrophils can release various factors that promote tumor growth and progression. Tumor cells can suppress lymphocyte activity through various mechanisms, including the release of immunosuppressive cytokines and the expression of inhibitory molecules. This suppression of the adaptive immune response can allow tumor cells to evade immune surveillance and destruction. The NLR, therefore, serves as a marker that reflects the dynamics of the immune system in the context of both TB and malignancy. In TB, the immune response is characterized by a balance between neutrophil and lymphocyte activity, while in malignancy, the immune response is skewed towards neutrophil activation and lymphocyte suppression. This difference in immune system dynamics is reflected in the NLR, making it a potentially useful tool for differentiating between these two conditions. The NLR is a readily available and cost-effective biomarker that can be easily calculated from routine blood tests. It has been shown to be elevated in various inflammatory conditions, including infections, autoimmune diseases, and cancer. In TB, the NLR reflects the balance between the innate and adaptive immune responses. While neutrophils are important for the early control of infection, lymphocytes are crucial for the long-term containment of the disease. In malignancy, the NLR reflects the tumor-induced inflammatory response and the suppression of the adaptive immune system. The elevated NLR in malignancy is associated with poor prognosis and increased risk of metastasis. The findings of this study suggest that NLR can be used as an adjunctive diagnostic marker to help differentiate between vertebral fractures caused by TB and malignancy. In clinical practice, NLR can be easily calculated from routine blood tests, making it a readily

accessible and cost-effective diagnostic tool. When interpreted in conjunction with other clinical and radiological findings, NLR can aid clinicians in making a more accurate diagnosis and initiating appropriate treatment strategies promptly. Differentiating between vertebral fractures caused by TB and malignancy can be challenging, as both conditions can present with similar clinical and radiological features. NLR can provide valuable information to aid in the differential diagnosis of vertebral fractures. An elevated NLR in the context of vertebral fracture should raise suspicion for malignancy. The use of NLR as a diagnostic marker can contribute to personalized medicine by facilitating more accurate diagnosis and individualized treatment strategies.[11-14]

The distinct inflammatory profiles associated with TB and malignancy provide a rationale for the potential utility of NLR and PLR as diagnostic markers. TB, a chronic infectious disease, triggers a complex immune response involving both neutrophils and lymphocytes, leading to granuloma formation and tissue destruction. The inflammatory response in TB is characterized by the activation of macrophages and the release of pro-inflammatory cytokines, which can lead to an increase in neutrophil counts. However, the lymphocyte response in TB is also robust, as lymphocytes are essential for the control of Mycobacterium tuberculosis infection. The balance between neutrophil and lymphocyte activity in TB may explain why NLR is not as elevated in TB compared to malignancy. Malignancy, on the other hand, is characterized by an intricate interplay between tumor cells and the host immune system, involving various inflammatory mediators and immune cells. Tumor cells can release a variety of factors that promote inflammation, including cytokines, chemokines, and growth factors. These factors can stimulate neutrophil production and activation, leading to an increase in NLR. Additionally, tumor cells can suppress lymphocyte activity, further contributing to the elevated NLR observed in malignancy. Inflammation is a complex biological process that plays a crucial role in both TB and malignancy. While inflammation is essential for the body's defense against infection and injury, it can also contribute to tissue damage and disease progression. In TB, the inflammatory response is triggered by the presence of Mycobacterium tuberculosis bacteria. The bacteria invade macrophages, which are immune cells that engulf and destroy pathogens. However, Mycobacterium tuberculosis is able to survive and replicate within macrophages, leading to a chronic inflammatory response. The inflammatory response in TB leads to the formation of granulomas, which are organized collections of immune cells that attempt to contain the infection. Granulomas can prevent the spread of bacteria, but they can also cause tissue damage and fibrosis. Macrophages infected with Mycobacterium tuberculosis release pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-alpha) and interferon-gamma (IFN-gamma). These cytokines recruit other immune cells to the site of infection and contribute to the inflammatory response. The inflammatory response in TB can cause tissue damage and necrosis, particularly in the lungs. This can lead to the formation of cavities and the spread of bacteria to other parts of the body. Inflammation also plays a critical role in the development and progression of cancer. Tumor cells can release various factors that promote inflammation, and the inflammatory microenvironment can contribute to tumor growth, angiogenesis, and metastasis. Chronic inflammation can promote the development of cancer by causing DNA damage and stimulating cell proliferation. The inflammatory microenvironment can provide growth factors and other signals that promote tumor growth and survival. Inflammation can suppress the adaptive immune response, allowing tumor cells to evade immune surveillance and destruction. NLR and PLR are readily available and cost-effective markers of inflammation that can be easily calculated from routine blood tests. These markers reflect the balance between different components of the immune system and can provide valuable information about the underlying inflammatory process. NLR is the ratio of neutrophils to lymphocytes. Neutrophils are the most

abundant type of white blood cell and play a critical role in the innate immune response. Lymphocytes are involved in the adaptive immune response and are responsible for recognizing and eliminating specific pathogens and tumor cells. PLR is the ratio of platelets to lymphocytes. Platelets are small cell fragments that are involved in blood clotting. They also release various factors that contribute to inflammation and tumor growth. The inflammatory response is a dynamic process that involves the interplay of various immune cells, including neutrophils, lymphocytes, and platelets. These cells communicate with each other through a complex network of cytokines and chemokines, which are signaling molecules that regulate the immune response. Neutrophils are the first responders to infection and injury. They are recruited to the site of inflammation by chemokines, where they phagocytose and kill pathogens. Neutrophils also release various factors that contribute to the inflammatory response, including reactive oxygen species (ROS) and proteases. Lymphocytes are responsible for the adaptive immune response, which is a specific and targeted response to pathogens and tumor cells. T lymphocytes recognize and eliminate infected cells, while B lymphocytes produce antibodies that neutralize pathogens. Platelets are small cell fragments that are involved in blood clotting. They also release various factors that contribute to inflammation and tumor growth, including growth factors and chemokines. NLR and PLR reflect the balance between different components of the immune system. An elevated NLR or PLR indicates an imbalance in the immune response, which can be associated with various inflammatory conditions, including TB and malignancy. In TB, the NLR reflects the balance between the innate and adaptive immune responses. While neutrophils are important for the early control of infection, lymphocytes are crucial for the long-term containment of the disease. In malignancy, the NLR reflects the tumor-induced inflammatory response and the suppression of the adaptive immune system. The elevated NLR in malignancy is associated with poor prognosis and increased risk of metastasis. The role of PLR in TB and malignancy is less well understood. However, elevated PLR has been associated with increased inflammation and poor prognosis in both conditions. The distinct inflammatory profiles associated with TB and malignancy suggest that NLR and PLR may be useful diagnostic markers for differentiating between these two conditions. However, it is important to note that these markers are not specific for either TB or malignancy and can be elevated in other inflammatory conditions. Differentiating between TB and malignancy can be challenging, particularly in cases where the clinical and radiological features are similar. NLR and PLR can provide additional information to aid in the differential diagnosis of TB and malignancy. It is essential to interpret NLR and PLR in the context of other clinical and radiological findings.[15-17]

The ROC curve analysis confirmed the superiority of NLR over PLR in differentiating TB and malignancy in our study. The AUC for NLR was 0.69, indicating a moderate discriminatory power, while the AUC for PLR was only 0.408, suggesting poor diagnostic accuracy. These findings suggest that NLR may be a more reliable marker than PLR in differentiating between these two conditions. It is important to acknowledge that NLR is not a perfect diagnostic test and should be interpreted in conjunction with other clinical and radiological findings. The moderate diagnostic accuracy of NLR suggests that it can be used as an adjunctive diagnostic marker to help differentiate between vertebral fractures caused by TB and malignancy. However, it should not be used as the sole basis for diagnosis. Diagnostic accuracy refers to the ability of a test to correctly identify individuals with and without a disease. It is a critical aspect of clinical decision-making, as accurate diagnosis is essential for appropriate treatment and management of diseases. Two key measures of diagnostic accuracy are sensitivity and specificity. Sensitivity is the ability of a test to correctly identify individuals with the disease. It is the proportion of true positives among all individuals with the disease. Specificity is the ability

of a test to correctly identify individuals without the disease. It is the proportion of true negatives among all individuals without the disease. ROC curve analysis is a graphical method for evaluating the diagnostic accuracy of a test. The ROC curve plots sensitivity against 1-specificity for different cutoff values of the test. The area under the ROC curve (AUC) is a measure of the overall diagnostic accuracy of the test. The AUC ranges from 0.5 to 1.0. An AUC of 0.5 indicates that the test has no discriminatory power, while an AUC of 1.0 indicates that the test has perfect discriminatory power. An AUC of 0.69 for NLR indicates moderate diagnostic accuracy, while an AUC of 0.408 for PLR suggests poor diagnostic accuracy. The moderate diagnostic accuracy of NLR suggests that it can be used as an adjunctive diagnostic marker to help differentiate between vertebral fractures caused by TB and malignancy. This means that NLR should be used in conjunction with other clinical and radiological findings to make a diagnosis. Clinical findings, such as patient history, physical examination, and symptoms, can provide valuable information for diagnosis. Radiological findings, such as X-rays, CT scans, and MRIs, can help visualize the vertebral fracture and identify any associated abnormalities. It is important to acknowledge that NLR is not a perfect diagnostic test. It can be elevated in other inflammatory conditions, such as bacterial or viral infections, autoimmune diseases, and chronic inflammatory diseases. Therefore, it is essential to interpret NLR in the context of other clinical and radiological findings. A high NLR may be a false positive in individuals with other inflammatory conditions. A normal NLR may be a false negative in individuals with TB or malignancy who have a less pronounced inflammatory response. Clinical judgment plays a crucial role in interpreting NLR and making a diagnosis. Clinicians should consider the patient's overall clinical picture, including their medical history, symptoms, and other diagnostic test results, when interpreting NLR. Each patient is unique, and clinicians should tailor their diagnostic approach based on the individual's specific circumstances. In complex cases, multidisciplinary collaboration between clinicians, radiologists, and pathologists may be necessary to reach an accurate diagnosis. In addition to AUC, Youden's index is another valuable metric for evaluating the diagnostic accuracy of a test. Youden's index is calculated as the maximum possible value of (sensitivity + specificity - 1) for all possible cutoff values of the test. It ranges from 0 to 1, with higher values indicating better discriminatory power. In our study, the Youden index for NLR was 0.11, further supporting its moderate discriminatory power. On the other hand, the Youden index for PLR was negative (-0.1472), indicating its poor diagnostic accuracy. When interpreting diagnostic accuracy measures, it is essential to consider the confidence intervals (CIs) around these estimates. CIs provide a range of values within which the true value of the measure is likely to lie. Wider CIs indicate greater uncertainty around the estimate. In our study, the AUC for NLR had a 95% CI of 0.54 to 0.839, while the AUC for PLR had a 95% CI of 0.246 to 0.571. These CIs highlight the inherent uncertainty associated with estimating diagnostic accuracy, particularly with a relatively small sample size.[18-20]

Our findings indicate that NLR is significantly higher in patients with vertebral fractures due to malignancy compared to those with TB. Future studies with larger sample sizes and prospective designs are needed to confirm these findings. The higher NLR in malignancy may be attributed to several factors. Firstly, neutrophils, the most abundant type of white blood cells, play a crucial role in the early immune response against pathogens and are also involved in the inflammatory response to tumors. In malignancy, tumor cells can release various factors that stimulate neutrophil production and activation, leading to an increase in neutrophil counts. Secondly, lymphocytes, which are essential for the targeted elimination of infected or cancerous cells, may be suppressed in the tumor microenvironment, leading to a decrease in lymphocyte counts. The combination of increased neutrophil production and decreased lymphocyte activity contributes to the elevated NLR

observed in malignancy. In contrast to NLR, PLR did not differ significantly between the TB and malignancy groups in our study. This finding is somewhat unexpected, as PLR has also been reported to be elevated in both infections and malignancies. The lack of difference in PLR may be due to the complex interplay of factors that influence platelet and lymphocyte counts in these conditions. Our study has several limitations. First, the sample size was relatively small. Second, the study was conducted at a single center, which may limit the generalizability of the findings. Third, the study was retrospective in nature, which may introduce bias. Despite these limitations, our findings suggest that NLR may be a useful diagnostic marker for differentiating between vertebral fractures caused by TB and malignancy.

5. Conclusion

Our study highlights the potential utility of NLR as a diagnostic marker in differentiating between vertebral fractures caused by TB and malignancy. NLR is a readily available and cost-effective biomarker that can be easily calculated from routine blood tests. When interpreted in conjunction with other clinical and radiological findings, NLR can aid clinicians in making a more accurate diagnosis and initiating appropriate treatment strategies promptly.

6. References

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