Original article

Clinical significances of neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio and lymphocyte-to-monocyte ratio in infectious spondylodiscitis

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Abstract

Background: The changes in the rate of leukocytes are simple, rapid and hopeful inflammation parameters in many diseases. Despite the close relationship between spondylodiscitis and inflammation, the roles of leukocyte subtypes in spondylodiscitis have not been previously investigated.

Objective: To evaluate the value of neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio and lymphocyte-to-monocyte ratio in predicting abscess and etiology in spondylodiscitis.

Materials and methods: A total of 121 medical records of patients were analyzed retrospectively. The data were obtained from hospital records. The neutrophil-to-lymphocyte, platelet-to-lymphocyte and lymphocyte-to-monocyte ratios were calculated using neutrophil, lymphocyte, monocyte and platelet levels in complete blood count measurements. Patients' clinical data, and their neutrophil-to-lymphocyte, platelet-to-lymphocyte and lymphocyte-to-monocyte ratio values, were analyzed statistically.

Results: A total of 121 medical records were evaluated; the male-to-female ratio was 1:1.2 and mean age was 56.1±16.6 years at the time of diagnosis. The lymphocyte-to-monocyte ratio was lower in patients with abscesses than patients with no abscesses (p=0.040). The 'area under the curve' value for lymphocyte-to-monocyte ratio was 0.626, with a cut-off point of ≤3.7 in predicting abscess in patients with spondylodiscitis. The mean neutrophil-to-lymphocyte ratio was higher and lymphocyte-to-monocyte ratio was lower in pyogenic spondylodiscitis compared to granulomatous spondylodiscitis (p=0.001 and p=0.038). The 'area under the curve' values for the neutrophil-to-lymphocyte ratio and the lymphocyte-to-monocyte ratio were 0.717 and 0.680, respectively, with cut-off points of ≥4.9 and <2.7, respectively, in discriminating pyogenic spondylodiscitis from granulomatous spondylodiscitis.

Conclusions: The neutrophil-to-lymphocyte ratio and lymphocyte-to-monocyte ratio are simple, broadly available and cost-effective parameters, and may be useful in the differential diagnosis of infectious spondylodiscitis. [*Ethiop. J. Health Dev.* 2020; 34(2):144-121]

Key words: Lymphocyte, monocyte, neutrophil, platelet, spondylodiscitis

Introduction

Spinal infections describe infections of the vertebral body, intervertebral discs, and/or paraspinal tissue (1). Vertebral body infection (vertebral osteomyelitis) can affect both vertebrae and intervertebral discs and is termed spondylodiscitis. Although isolated discitis is usually seen in childhood, vertebral osteomyelitis and discitis are thought to be different processes of the same disease (2,3). The global incidence of spondylodiscitis is reported as 2.4 cases per 100,000 per year, and spondylodiscitis accounts for only 2-7% of all osteomyelitis cases (1-4). However, incidence of spondylodiscitis has been raised in recent reports according to aging of the population, increased number of intravenous drug addiction, immunosuppression by malignancy or acquired immunodeficiency syndrome (AIDS), frequency of interventional procedures and also associated with the widespread use of magnetic resonance imaging (MRI) depending on the sensitivity of clinicians (2,3). Therefore, these infections have become an important clinical problem for public health that requires a serious medical and surgical approach.

Etiologically, spinal infections are classified as pyogenic (caused by bacteria), granulomatous (caused by *Mycobacterium tuberculosis*, *Brucella* spp. or fungi) and parasitic spondylodiscitis (1). *Brucella* and tuberculosis, which cause granulomatous spondylodiscitis, is an important public health problem, especially in developing countries. Spinal infection may develop by haematogenous spread from another infection site, direct external inoculation, or contiguous spread from adjacent infected tissues (5). Inflammation may remain localized in these infections or the progression of infection may cause abscess formation (1-3,5). Estimating the etiological agent and appropriate treatment of spondylodiscitis are important because treatment delay may cause complications, including abscess formation, and because delay is associated with unresponsiveness to treatment and increased mortality (1). Spinal infection can be diagnosed by physical examination, laboratory and imaging findings. Pathogenic microorganisms can be isolated by microbiological culture, but there is a delay in diagnosis because biopsy (or tissue sampling) is difficult, time-consuming and involves invasive techniques (1-4). In addition, culture studies do not always give positive results (1). MRI is the most reliable method of diagnosing spondylodiscitis and in evaluating spinal and/or paraspinal abscess formation (3). Nevertheless, there are disadvantages to MRI: it is expensive, time-consuming, and not a readily accessible technique at all health centers.

Chronic inflammation plays a major role in the pathogenesis of spondylodiscitis and its complications (5,6). Leukocyte counts, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are routinely available laboratory biomarkers of inflammation. The circulating neutrophil, monocyte, lymphocyte and platelet distributions vary in inflammatory process (6,7). Recent studies highlight that changes in the rate of

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leukocytes are simple and rapid inflammation parameters in many diseases (6-8). Despite the close relationship between spondylodiscitis and inflammation, the roles of leukocyte subtypes in spondylodiscitis have not been previously investigated. To the best of our knowledge, this is the first study to evaluate the circulating neutrophil, lymphocyte, monocyte and platelet distribution in spondylodiscitis. In our study, we demonstrate the value of neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR) and platelet-to-lymphocyte ratio (PLR) in predicting abscess and etiology in spondylodiscitis.

Materials and methods

Patients: A total of 121 patients diagnosed with spinal infection were analyzed retrospectively from January 2010 to February 2019 in a tertiary referral care center, Izmir Katip Celebi University Ataturk Training and Research Hospital, Turkey. The study protocol was approved by our local ethics committee (March 27, 2019, Approval Number: 162). Patients were excluded from the study in the presence of any of the following conditions: age less than 16 years, non-infectious spondylodiscitis, other foci of infection, pregnancy, and previous antibiotic use within the past two months. Demographic factors, comorbidities (including diabetes mellitus, hypertension, chronic kidney disease, chronic cardiac disease, malignancy and use of corticosteroids), site of infection, clinical findings, length of hospital stay, presence of abscess, neurological deficit (sensory or motor deficit), laboratory parameters, type and duration of treatment and recurrence rates were recorded. The etiologic agents (pyogenic or granulomatous spondylodiscitis) and presence of abscess were used as response variables.

Assessment of laboratory findings: Spinal infection was diagnosed by clinical, laboratory and radiological findings. Infection markers – such as white blood cell (WBC) counts, CRP, ESR and procalcitonin (PCT) – were analyzed as laboratory tests. These biomarkers were evaluated at the time of hospital admission. The NLR, LMR and PLR values were obtained using neutrophil, monocyte, lymphocyte and platelet levels from complete blood count measurements. Blood, sputum and urine cultures were taken from patients, if necessary. Microbiological cultures were performed on obtained tissue samples if the patients had undergone biopsy, drainage or surgery.

Assessment of clinical findings: We analyzed two different conditions separately: 1. patients were divided into two groups according to the presence of abscess (abscess [+] and abscess [-]) and the clinical and laboratory findings of two groups were compared; 2: patients were divided into two groups on the basis of pyogenic spondylodiscitis and granulomatous spondylodiscitis, and the clinical and laboratory findings of these two groups were compared. Vertebral bodies, paravertebral and epidural areas, nerve roots, spinal canal and abscess formation were evaluated in MRI. The diagnosis of abscess formation was based on the findings of MRI. MRI data were available for all patients. The diagnosis of pyogenic or granulomatous spondylodiscitis was determined according to the etiological agent obtained from clinical samples. Isolation of *Mycobacterium tuberculosis* or *Brucella* spp. from clinical specimens was defined as granulomatous spondylodiscitis. Bacterial isolation from clinical specimens was defined as pyogenic spondylodiscitis. If the causative microorganism could not be isolated in culture, the clinical response to empirical antibiotherapy was accepted as pyogenic spondylodiscitis.

Treatment and follow-up of patients: All patients were evaluated by multidisciplinary teams, including infectious disease specialists, surgeons and radiologists, in terms of treatment and follow-up. A conservative approach was the first choice of treatment. Biopsy was performed on the differential diagnosis of suspicious lesions. Initial empirical antimicrobial treatment was revised according to the culture results and antibiotic susceptibility testing. Antimicrobial treatment was administered for at least six weeks. The duration of treatment was individualized based on the clinical, laboratory and radiological response for each patient. Surgical intervention was performed in the presence of medical treatment failure, epidural abscess, neurological deficit or spinal instability/deformity. After the end of treatment, receiving a second course of antimicrobial therapy due to resumption of symptoms (fever, back pain, tenderness by palpation of the spinal process), elevation of infection markers such as WBC, CRP, ESR and PCT, and reappearance of new lesions on MRI, were defined as recurrence. The disappearance of all signs and symptoms, except for permanent neurological *sequelae* in the subsequent six months since the end of antibiotics, was defined as recovery.

Statistical analysis: All statistical analyses were performed with SPSS software version 24. Descriptive analyses were presented using means and standard deviations for normally distributed variables. Student's t-test was performed to compare the groups. The chi-square test was applied for the test of association levels of two categorical variables. The sensitivity, specificity values and receiver operating characteristic curve (ROC) analysis methods were examined using MedCalc version 14 (MedCalc Software). A p-value of less than 0.05 was considered statistically significant.

Results

Study population: A total of 121 patients were evaluated; the male:female ratio was 1:1.2 (66 men, 55 women) and mean age was 56.1±16.6 years (range 16-86 years) at the time of diagnosis. Forty-five patients (37.2%) had least one comorbid disease. The most common comorbidity was diabetes mellitus (22.3%), followed by hypertension (19%), chronic kidney disease (14%), coronary artery disease (7.4%) and malignancy (3.3%). Although comorbidities did not differ between patients with or without abscesses, the prevalence of diabetes mellitus, hypertension and chronic kidney disease was higher in pyogenic spondylodiscitis than granulomatous spondylodiscitis ($p=0.028$, $p=0.001$ and $p<0.001$, respectively) (Table 1)

Table 1: **Comparison of the abscess [+] and abscess [-] patients; and comparison of the pyogenic spondylodiscitis and granulomatous spondylodiscitis in terms of clinical and laboratory findings**

Parameters	**All patients (n=121, 100%) (mean±SD)**	**Spondylodiscitis with abscess (n=65, 53.7%) (mean±SD)**	**Spondylodiscitis without abscess (n=56, 46.3%) (mean±SD)**	**p***	**Pyogenic spondylodiscitis (n=49, 40.5%) (mean±SD)**	**Granulomatous spondylodiscitis (n=72, 59.5%) (mean±SD)**	**p***
Age (mean±SD)	56.1±16.6	54.4±17.1	58.1±15.8	*0.224*	59.9±12.8	53.5±18.3	***0.034***
Male (n, %)	66 (54.6%)	36 (55.4%)	30 (53.6%)	*0.857*	24 (49%)	42 (58.3%)	*0.355*
Comorbidities				**p****			**p****
Diabetes mellitus	27 (22.3%)	15 (23.1%)	12 (21.4%)	*>0.999*	16 (32.7%)	11 (15.3%)	***0.028***
Hypertension	23 (19%)	16 (24.6%)	7 (12.5%)	*0.107*	17 (34.7%)	6 (8.3%)	***0.001***
Chronic kidney disease	17 (14%)	11 (16.9%)	6 (10.7%)	*0.434*	16 (32.7%)	1 (1.4%)	***<0.001***
Coronary artery disease	9 (7.4%)	5 (7.7%)	4 (7.1%)	*>0.999*	6 (12.2%)	3 (4.2%)	*0.156*
Malignancy	4 (3.3%)	4 (6.2%)	0	-	3 (6.1%)	1 (1.4%)	*0.302*
Laboratory results				**p***			**p***
Hemoglobin (g/dL)	12±1.9	11.9±2	12.2±1.9	*0.429*	11.4±2	12.4±1.8	***0.007***
WBC (K/uL)	8765.9±3587.5	8952.7±3758.4	8552.7±3402.9	*0.545*	10463.7±4466.7	7634±2261.9	***<0.001***
Neutrophil (K/uL)	6112.6±3446.6	6279.5±3532.9	5921.8±3366.9	*0.573*	7761.8±4280.2	5013.1±2172.1	***<0.001***
Lymphocyte (K/uL)	1896.4±741.1	1856.3±843.8	1942.9±604.7	*0.524*	1797.8±846.8	1963.5±657.4	*0.252*
Monocyte (K/uL)	607.7±329.2	660.1±404.8	546.9±196.7	***0.049***	722.9±453.5	529.3±169.5	***0.006***
Platelet (K/uL)	309289.3±124723.7	317046.1±124343.3	300285.7±125679.9	*0.463*	322428.6±142694.2	300347.2±111022.5	*0.341*
MPV (fl)	9.2±1.2	9.2±1.2	9.1±1.2	*0.521*	9.5±1.1	8.9±1.2	***0.016***
AST (U/L)	24.9±17.9	24.9±15.9	25±20.1	*0.986*	21±12.6	27.6±20.4	***0.047***
ALT (U/L)	29.2±30.5	32.9±36.2	24.9±21.6	*0.137*	21.2±19.9	34.7±35.1	***0.017***
BUN (mg/dl)	19.6±13.2	20.1±15.3	19.1±10.3	*0.687*	24.2±17.6	16.6±7.6	***0.006***
Serum creatinine (mg/dl)	1.2±1.5	1.2±1.5	1.3±1.6	*0.791*	1.8±2.2	0.8±0.6	***0.004***
ESR (mm/h)	58.8±30.8	62.3±29.4	54.7±32.2	*0.185*	65.6±32.7	54.3±28.9	*0.052*
CRP (mg/dl)	6.6±7.7	8.4±9.1	4.5±5.3	***0.006***	8.8±9.7	5.2±5.7	***0.023***
PCT (ng/ml)	0.2±0.4	0.2±0.2	0.3±0.5	*0.523*	0.3±0.6	0.2±0.2	*0.610*
NLR	4.3±4.7	4.7±5.4	3.7±3.8	*0.256*	6.2±6.1	2.9±2.7	***0.001***
PLR	190.8±109.2	204.6±110.9	174.9±106	*0.136*	209.8±103.9	177.9±111.5	*0.115*
LMR	3.6±2	3.3±2	4±2	***0.040***	3.2±2.4	4±1.6	***0.038***

SD: standard deviation, WBC: white blood cell, MPV: mean platelet volume, AST: aspartate aminotransferase, ALT: alanine aminotransferase, BUN: blood urea nitrogen, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, PCT: procalcitonin, NLR: neutrophil-to-lymphocyte ratio, PLR: platelet-to-lymphocyte ratio, LMR: lymphocyte-to-monocyte ratio * Student's t-test was used for the analysis; ** Chi-square test was used for the analysis

The most common symptom was back pain (98.3%). Other symptoms were fever (24.8%), neurological deficit (20.7%) and tenderness on spinous process (7.4%). Anatomic site of infection was as follows: cervical (7.4%), thoracal (14%), lumbar (48.8%), thoracolumbar (14.9%), lumbosacral (14%) and cervicolumbar (0.8%).

Sixty-five (53.7%) patients had abscesses and 56 (46.3%) patients had no abscesses, according to MRI findings. Forty-nine (40.5%) patients had pyogenic spondylodiscitis and 72 (59.5%) patients had granulomatous spondylodiscitis. Of the patients with pyogenic spondylodiscitis, 44 cases had spontaneous spondylodiscitis and five had post-operative spondylodiscitis. Of the patients with granulomatous spondylodiscitis, 59 had brucellar spondylodiscitis and 13 had tuberculous spondylodiscitis.

Laboratory findings: Twenty-three patients (19%) had leukocytosis (>11,000 cells/mm³). The increased ESR value (>30 mm/h) was found in 91 (75.2%) patients. There were 98 (81%) patients with CRP> 1 mg/dl.

Compared to patients with no abscesses, the mean monocyte and CRP levels were higher, and LMR was lower, in patients with abscesses (p=0.049, p=0.006 and p=0.040, respectively). Other laboratory values did not differ between patients with and without abscesses in spondylodiscitis (Table 1).

The mean WBC, neutrophil, monocyte, MPV, aspartate aminotransferase (AST), alanine aminotransferase (ALT), blood urea nitrogen (BUN), serum creatinine, CRP and NLR levels were higher in pyogenic spondylodiscitis than granulomatous spondylodiscitis (p<0.001, p<0.001, p=0.006, p=0.016, p=0.047, p=0.017, p=0.006, p=0.004, p=0.023 and p=0.001, respectively). In addition, mean hemoglobin and LMR levels were lower in pyogenic spondylodiscitis compared to granulomatous spondylodiscitis (p=0.007 and p=0.038, respectively) (Table 1).

Blood culture was obtained from 113 patients and blood culture positivity was detected in 25 patients. Tissue culture positivity was detected in 18 of 113 patients. Both blood and tissue cultures were positive in one patient. The etiologic agent was detected in 42 patients. The isolated microorganisms were as follows: *Brucella* spp. (19), *Staphylococcus aureus* (12), *Mycobacterium tuberculosis* (7), *Escherichia coli*(2), *Pseudomonas aeruginosa* (1), coagulase-negative staphylococci (1) and *Achromobacter* spp. (1). Eleven isolates of *Staphylococcus aureus* were susceptible to methicillin, while methicillin resistance was detected in one strain. Tissue culture positivity was higher in patients with abscesses than patients who had no abscesses (p=0.011) (Table 1).

Diagnostic values of NLR, PLR and LMR: The mean NLR and PLR levels were higher in patients with abscesses than in patients with no abscesses, but the difference was not statistically significant (p=0.256 and p=0.136, respectively). The mean LMR was lower in patients with abscesses compared to the patients with no abscesses (3.3±2 and 4±2, respectively; p=0.040). The area under the curve (AUC) value for LMR was 0.626 (95% CI: 0.525-0.726) with the cut-off point of ≤3.7 in predicting abscesses in patients with spondylodiscitis. Applying ROC curve at the cut-off point of 3.7, LMR yielded 70.3% sensitivity and 57.1% specificity (Table 2 and Figure 1).

Table 2: **Diagnostic value of NLR, PLR and LMR in predicting abscess or etiology in spondylodiscitis**

Variables	AUC	p-value	Cut-off*	Sensitivity (%)	Specificity (%)	+LR	-LR	+PV (%)	-PV (%)
Presence of abscess formation									
NLR	0.562	0.236	>3.4	46.9	73.2	1.7	0.7	66.7	54.7
PLR	0.602	0.048	>186.5	47.7	73.2	1.8	0.7	67.4	54.7
LMR	0.626	0.014	≤3.7	70.3	57.1	1.6	0.5	65.2	62.7
Pyogenic spondylodiscitis									
NLR	0.717	<0.001	≥4.9	91.6	48.9	1.8	0.2	72.2	80
PLR	0.605	0.052	≥197.7	79.2	53.1	1.7	0.4	71.2	63.4
LMR	0.680	<0.001	<2.7	81.9	54.2	1.8	0.3	72.8	66.7

NLR: neutrophil-to-lymphocyte ratio, PLR: platelet-to-lymphocyte ratio, LMR: lymphocyte-to-monocyte ratio, AUC: area under the ROC curve, LR: likelihood ratio, PV: predictive value
*Youden index was used in determining cut-off value

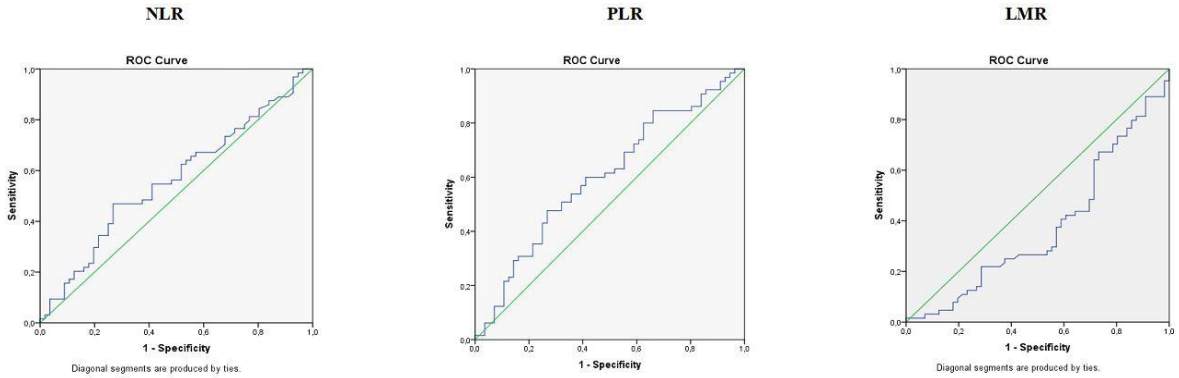

Figure 1: **Receiver operating characteristic (ROC) curve analysis for various cut-off levels of NLR, PLR and LMR in predicting abscess in spondylodiscitis**

The mean NLR level was higher in patients with pyogenic spondylodiscitis compared to patients with granulomatous spondylodiscitis (6.2±6.1 and 2.9±2.7, respectively; p=0.001). In contrast, LMR was lower in pyogenic spondylodiscitis than granulomatous spondylodiscitis (3.2±2.4 and 4±1.6, respectively; p=0.038). The mean PLR level did not differ between pyogenic and granulomatous spondylodiscitis (209.8±103.9 and 177.9±111.5, respectively; p=0.115). The AUC value was 0.717 for NLR and 0.680 for LMR. Both NLR and LMR showed high sensitivities (91.6% and 81.9%) in discriminating pyogenic spondylodiscitis from granulomatous spondylodiscitis (Table 2 and Figure 2).

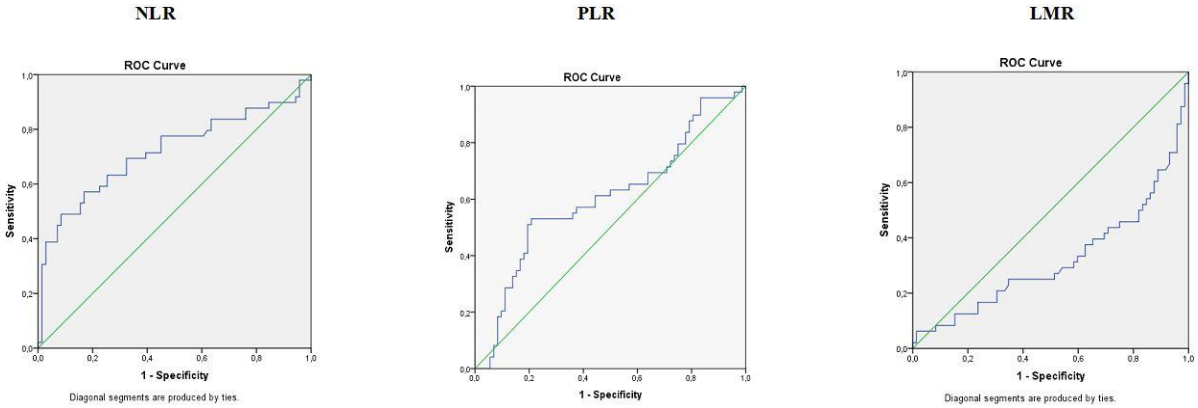

Figure 2: **Receiver operating characteristic (ROC) curve analysis for various cut-off levels of NLR, PLR and LMR in discriminating pyogenic and granulomatous spondylodiscitis**

Treatment and follow-up of patients: Conservative antibiotic therapy was applied in 90 (74.4%) patients. In addition, surgical treatment was performed on 31 (25.6%) patients. Recurrence was detected in 12 of 98 patients for whom data were available. Eight of these patients had medical treatment while four of them had undergone surgery. The recurrence rates were similar between the treatment modalities of patients (medical and surgical) (p=0.223). There was no significant difference in NLR, PLR and LMR values between the patients with and without recurrence (p=0.891, p=0.426 and p=0.277, respectively).

Discussion

Inflammation is the non-specific response of the organism to exogenous or endogenous stimuli (9). The classical initiators of inflammation are tissue injury and infection. However, it can be triggered by various physiological and pathological processes and the response to all these stimuli is similar (10). In the first instance, an acute inflammatory response is initiated by receptors of the innate immune system in response to a stimulus (9,10). Inflammatory mediators are released by the macrophages and mast cells during this initial recognition phase (9-11). As a result, vascular endothelial damage occurs, and plasma proteins and platelets reach the extravascular space (10). Platelets are activated by contact with collagen and produce inflammatory mediators (9). Leukocytes and plasma proteins are directed to the target tissue through the influence of these mediators (11). If the acute inflammatory response is effective, the repair phase begins. Through the anti-inflammatory mediators, macrophage and monocyte activations are promoted and tissue remodeling begins (12). If the acute inflammatory response is insufficient, the neutrophils are replaced by macrophages and lymphocytes, and chronic inflammation occurs (13). Therefore, we believe that the cell lines that control the immune system in chronic inflammation are best reflected by monocyte and lymphocyte levels. In our study, the fact that LMR was found useful in the differential diagnosis of infectious spondylodiscitis also supports our argument.

Recently, there has been an intense interest in the role of inflammation markers in various diseases such as

cancer, metabolic diseases, ischemic heart diseases, infectious diseases and other medical conditions (14). Current studies demonstrate that NLR, LMR and PLR may be useful in many diseases because of their ability to predict systemic inflammation (7,8,14-16). These studies are based on changes in neutrophil, lymphocyte, monocyte and platelet counts, depending on the physiological responses to stimuli (15,16). In our literature review, we observed that conflicting results have been obtained about the relationship between these biomarkers and infectious diseases (17-26). Naess and colleagues showed that NLR and MLR were higher in bacterial infection compared to viral infection (17), and that NLR and MLR were significantly higher in bacterial infection compared to non-infectious conditions (12.23±0.98 and 5.02±0.67; p<0.001 for NLR; and 2.41±0.75 and 5.02±0.67; p=0.010 for MLR) in patients hospitalized for fever (17). In addition, they indicated that patients with septicemia had significantly higher NLR compared to patients with other bacterial infections with fever for less than one week (23.17±4.40 and 10.79±2.42; p=0.006). In another study (18), 172 HBV-infected patients and 40 healthy controls were examined; PLR levels were lower in HBV-related cirrhotic patients (56±21; p<0.001). In addition, higher NLR levels were found to be useful in predicting disease progression in chronic HBV infection. HBV-related decompensated cirrhosis patients had a significantly higher mean NLR (4.0±1.1; p<0.001). In the logistic regression prediction model, a predictive probability cut-off of 0.392 had the highest sensitivity and specificity (sensitivity, 91.2%; specificity, 84.0%) in distinguishing between both HBV-related compensated cirrhosis and HBV-active carrier patients. A NLR cut-off value of 2.94 had the highest sensitivity and specificity (sensitivity, 81.8%; specificity, 88.2%) in distinguishing between HBV-related decompensated cirrhosis and HBV-related compensated cirrhosis patients. Meng *et al.* demonstrated that lower PLR levels were closely related to the virological response and disease severity in patients with chronic hepatitis C virus (HCV) infection (19). In this study, 120 HCV-infected patients and 40 healthy controls were analyzed. The HCV-related cirrhosis group and HCV-related hepatocellular carcinoma group were found to have lower PLRs (61±31 and 51±23) than the healthy controls (115±23). The PLR of the HCV cleared group (154±85) was significantly higher than that of the HCV untreated group and HCV uncleared group (90±28 and 88±40, respectively). ROC curve analysis for the PLR showed an AUC of 0.772 (95% CI; 0.674–0.869, p<0.001); for NLR, the AUC was 0.612 (95% CI; 0.495–0.730, p=0.063). Furthermore, an increasing PLR in chronic hepatitis C patients indicated a good virological response, and a stable PLR or a downward trend in PLR could predict no rapid virological response being achieved by week 4, and even no sustained virological response by week 72.

To our knowledge, this is the first study to evaluate the distribution of circulating neutrophil, lymphocyte, monocyte and platelet parameters in spondylodiscitis. In our study, LMR was found useful in predicting abscess in spondylodiscitis. The mean LMR was found to be lower in patients with abscesses compared to the patients with no abscesses (3.3±2 and 4±2, respectively; p=0.040). In addition, both NLR and LMR were found to be significant in discriminating pyogenic spondylodiscitis from granulomatous spondylodiscitis. The mean NLR level was higher in patients with pyogenic spondylodiscitis compared to patients with granulomatous spondylodiscitis (6.2±6.1 and 2.9±2.7, respectively; p=0.001). In contrast, LMR was lower in pyogenic spondylodiscitis than granulomatous spondylodiscitis (3.2±2.4 and 4±1.6, respectively; p=0.038). These parameters may be good as a diagnostic tool in spondylodiscitis.

In addition, platelet volume is defined as a marker of platelet activation and function, and is measured as MPV in the complete blood count (27). It is claimed that MPV increases in relation to thrombocytopenia in the acute phase of infection and decreases in the chronic phase associated with thrombocytosis (28). Therefore, MPV is also shown as an inflammatory marker and there are several studies showing the clinical benefit of MPV in various diseases such as malignancy, sepsis, thrombosis and even respiratory distress syndrome (28-30). Some studies have examined the changes of MPV levels in infectious diseases (20-26). MPV levels were also found to have both increased and decreased in patients with *Brucella*, chronic hepatitis B and HIV (20-25). In a study conducted by Hu *et al.* (20), a total of 120 patients, including 17 with acute hepatitis B, 62 with chronic hepatitis B, and 41 with chronic severe hepatitis B, as well as 58 healthy controls, were evaluated. They demonstrated that MPV was significantly increased in chronic severe hepatitis B (12.3±0.8 fl) and chronic hepatitis B patients (11.7±1.2 fl), compared with healthy controls (10.5±0.9 fl) and acute hepatitis B patients (10.8±1.5 fl) (p<0.001). In another study conducted by Aydin *et al*. (24), the patients with brucellar epididymo-orchitis were significantly more likely to have a lower MPV than those with non-brucellar epididymo-orchitis. Using a MPV cut-off level of less than 9.25 fl to differentiate brucellar from non-brucellar epididymo-orchitis gives a sensitivity of 78.6%, a specificity of 78.4%, a positive predictive value of 36.7%, and a negative predictive value of 95.8%. Although MPV was not significant in predicting abscess in our study, it was found to be significantly lower in granulomatous spondylodiscitis (8.9±1.2 fl) compared to pyogenic spondylodiscitis (9.5±1.1 fl) (p=0.016). MPV may be found lower in granulomatous spondylodiscitis in our study due to the more insidious progression and chronic course of granulomatous infections.

Limitations of this study

Our study has some limitations. A small number of patients was evaluated in the study. Because of the retrospective nature of our study, the biomarkers could not be assessed in terms of the predictability of acute spondylodiscitis in patients with back pain. Additionally, these biomarkers were evaluated only at the time of hospital admission; therefore, the follow-up and treatment response could not be analyzed.

Spondylodiscitis as a public health problem

Spondylodiscitis is a potentially devastating and rapidly progressing disease that may result in serious complications, such as vertebral collapse, abscess,

permanent neurologic deficits, or even death. Therefore, these infections have become an important clinical problem for public health that requires a serious medical and surgical approach. The prevalence and incidence of the disease has increased globally in the past 10 to 15 years. The increasing age burden has been proposed as one of the main reasons for the rising incidence of spondylodiscitis. Therefore, it can be predicted that the incidence of spondylodiscitis will increase due to the aging of the world's population in the coming years. In addition, *Brucella* and tuberculosis, which cause granulomatous spondylodiscitis, which is an important public health problem in many regions, especially in developing countries, is an important cause of morbidity and mortality. Spondylodiscitis is an important disease and health problem because of its potential morbidity and mortality; therefore, early diagnosis and effective antibiotherapy are crucial. It has been reported that spondylodiscitis has to be seen as a life-threatening condition and treated as an emergency. With the help of these simple laboratory tests, which are significant in demonstrating the etiology and the presence of abscess in spondylodiscitis in our study, the treatment process will be accelerated and morbidity and mortality rates can be reduced.

Conclusions

On the basis of our study, LMR was found to be useful in predicting abscess formation in patients with spondylodiscitis. In addition, both NLR and LMR can discriminate pyogenic and granulomatous etiology in patients with spondylodiscitis. These inflammatory biomarkers are simple, broadly available, cost-effective and promising parameters in spondylodiscitis. There is a need for further well-designed and prospective studies to examine the role of these biomarkers in spondylodiscitis.

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