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*Original Article*

# The diagnostic value of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in tuberculous spondylitis

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**Abstract:** The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are useful markers in various inflammatory diseases, but their diagnostic capability intuberculous (TB) spondylitishas not been evaluated. Our aim was to investigate the diagnostic capability of NLR and PLR on the diagnosis of TB spondylitis. Patients surgically treated for TB spondylitisin the First Affiliated Hospital of Guangxi Medical University from 2012 to 2015 were retrospectively investigated in this study. Correlations between NLR, PLR and laboratory indices in TB spondylitis patients were evaluated by the Spearman's correlation analysis. The sensitivity and specificity of NLR and PLR were assessed by the receiver operating characteristic (ROC) curves. Seventy-four TB spondylitis patients and 54 healthy individuals were analyzed retrospectively. The NLR and PLR between TB spondylitis patients and healthy controls were significant different. The relationship between NLR, C-reaction protein (CRP), and erythrocyte sedimentation rate (ESR) in TB spondylitis patients were significant correlation, similarly, the correlation between PLR and CRP and ESR in TB spondylitis patients were significantly correlated. The ROC curves analysis of NLR and PLR in TB spondylitis patients showed statistically significance. In conclusion, NLR and PLR might be valuable markers in diagnosing TB spondylitis.

**Keywords:** Neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, diagnosis, tuberculosis spondylitis

## Introduction

Inhalation of *Mycobacterium tuberculosis*bacilli can lead to the occurrence of pulmonary tuberculosis (PTB) infection. In terms of the annual death toll, tuberculosis (TB) may no longer be the most deadly human diseases, but it remains a serious disease threat to human health around the world, causing 1.3 million deaths globally in 2012 alone [1]. China has a high rate of TB infection [2], and thus the diagnosis and treatment of TB represents a serious health concern in this region. Of all the extra-pulmonary TB patients, skeletal involvement occurs in approximately 10% of cases [3]. TB spondylitis is a chronic progressive development disease and is rarely associated with symptoms like cough, dyspnea, or fever [4]. There are no clear guidelines for diagnosis and treatment of TB spondylitis patients [5]. In order to preventcomplications such as permanent neurological disability and the occurrence of spinal deformity in patients with TB spondylitis,early identification and timely treatment is necessary [6, 7].

It is well known that elevated neutrophils and lymphocytes are closely related to inflammatory state. Platelets have also been shown to be associated with inflammation [8, 9]. Recent studies have indicated that neutrophil to lymphocyte ratio (NLR) and/or platelets to lymphocyte ratio (PLR) could be used as biomarkersin many diseases [10-13]. Indicators such as CRP, ESR and/or platelet count have been used to assess the status of PTB and TB spondylitis inpatients [6, 14-16]. In some recent studies, NLR and PLR have been evaluated in diseases such as PTB and ankylosing spondylitis (AS) [13, 17]. However, hematological characteristics including PLR and NLR in TB spondylitis patients remains unknown. The aim of this study was thus to assess the variety of NLR and PLR in patients with TB spondylitis.

**Table 1.** Characteristics of patients withTB spondylitis

| Characteristics | Mean ± SD, median range or number (%) (n:74) |
|---|---|
| Gender | |
| Male | 46 (62.16) |
| Female | 28 (37.74) |
| Mean age (years) | 40.18 ± 16.06 |
| Age distribution , years | |
| <11 | 2 (2.7%) |
| 11-30 | 22 (29.73%) |
| 31-50 | 29 (39.19%) |
| >50 | 21 (28.38%) |
| Duration of symptoms (months) | 6 (15 days - 360 months) |
| Location | |
| Lumbar | 41 (55.41%) |
| Thoracic | 33 (44.59%) |
| Clinical symptoms and signs, *n* | |
| Back pain | 68 (91.89%) |
| Tenderness | 51 (68.92%) |
| Percussion pain | 43 (58.11%) |
| Anemia | 42 (56.76%) |
| Kyphosis | 25 (33.78%) |
| Fever | 22 (29.73%) |
| Weight loss | 20 (27.03%) |
| Previous TB infection | 9 (12.16%) |

## Materials and methods

All patient information was extracted from the medical records of the First Affiliated Hospital of Guangxi Medical University from 2012 to 2015. During this period, 74 patients were surgically treated for TB spondylitis. The diagnosis of TB spondylitis is achieved through a comprehensive evaluation of the patients' clinical features and radiological, intraoperative, and histological examinations. Fifty-four normal controls from Health Examination Centers were also included. Patients and healthy controls who met any of the following criteria were excluded: (1) current use of antibiotics or other drugs that affect white blood cell (WBC) or platelet count; (2) autoimmune disorders or other infectious diseases; (3) serious liver or renal disease; (4) hematologic diseases; (5) neoplasms; and/or (6) thyroid disease. Patients with active pulmonary tuberculosis in addition to TB spondylitis, as well as patients with incomplete data and laboratory test results in their medical records, were also excluded.

Clinical and laboratory characteristics were extracted before treatment. Demographic characteristics of TB spondylitis patients such as age and gender, were also gathered. Blood samples were collected from all TB spondylitis patients and healthy controls before treatment. The results of total WBC count, neutrophils, lymphocytes, platelets, CRP, and ESR were extracted from participants' medical records.

### *Statistical analysis*

The Kolmogorov-Smirnov normality test was performed for continuous variables. The normal distribution variables were expressed as mean ± standard deviation. Two independent sample t-test $X^2$ test were utilized to compare data between TB spondylitis patients and controls. The spearman correlation tests were done between two continuous variables. The performance of NLR and PLR was detected by ROC curves. MedCalc statistic software (version 11.3.8.0, Mariakerke, Belgium) was used to compare the area under the curves (AUCs). SPSS17.0 (SPSS Inc, Chicago, IL, USA) statistical software was used to analyze the data. $P<0.05$ was considered significant.

This study was approved by the local ethics committee, and informed consent was obtained from all participants.

## Results

### *Characteristics of TB spondylitis patients*

The characteristics of TB spondylitis patients are presented in **Table 1**. Seventy-four Patients (mean age: 40.18 ± 16.06 years) with TB spondylitis were included in the study. The percentage of males and females were 62.2% and 37.8%, respectively. The 31-50 age group (39.2%) accounted for the largest proportion of all TB spondylitis patients. The mean duration of symptoms was 6 month (range, 15 days - 360 months). The proportion of lumbar and thoracic tuberculosis was 55.4% and 44.6%, respectively. Sixty-eight (91.9%) patients had back pain, 51 (68.9%) had tenderness, 43 (58.1%) had percussion pain, 42 (56.8%) had

**Table 2.** Laboratory results of TB spondylitis patients and controls

| | Patients | Controls | *P*-value |
|---|---|---|---|
| Gender (male/female) | 46/28 | 33/21 | 0.524 |
| Age (year) | 40.18 ± 16.06 | 39.06 ± 7.71 | 0.636 |
| WBC count ($\times 10^9$/L) | 7.07 ± 1.82 | 6.81 ± 1.60 | 0.371 |
| Neutrophil count ($\times 10^9$/L) | 4.58 ± 1.57 | 3.68 ± 1.24 | 0.001 |
| Lymphocyte count ($\times 10^9$/L) | 1.54 ± 0.51 | 2.46 ± 0.63 | <0.001 |
| Platelet count ($\times 10^9$/L) | 311.99 ± 86.97 | 236.66 ± 37.97 | <0.001 |
| PDW (%) | 16.16 ± 0.64 | 16.26 ± 0.56 | 0.362 |
| MPV (fL) | 7.82 ± 0.89 | 8.36 ± 0.81 | 0.001 |
| RDW (%) | 14.89 ± 2.75 | 13.9±1.62 | 0.02 |
| NLR | 3.24 ± 1.38 | 1.58 ± 0.59 | <0.001 |
| PLR | 223.15 ± 89.59 | 102.4 ± 31.64 | <0.001 |
| CRP (mg/L) | 40.21 ± 46.42 | 0.81 ± 0.31 | <0.001 |
| ESR (mm/h) | 39.51 ± 22.12 | 7.22 ± 4.92 | <0.001 |
| HGB (g/L) | 120.43 ± 15.83 | 144.04 ± 12.30 | <0.001 |

Note: Continuous variables are expressed by the mean ± one standard deviation; NLR, neutrophil/lymphocyte ratio; PLR, platelet/lymphocyte ratio; CRP, C-reactive protein; ESR, erythrocyte sedimentationrate; HGB, haemoglobin.

anemia, 25 (33.8%) had kyphosis, 22 (29.7%) had fever, and 20 (27.0%) had weight loss.

*Laboratory results of TB spondylitis patients and healthy individuals*

As shown in **Table 2**, the age and gender of TB spondylitis patients were matched to the age and gender of healthy controls. Neutrophil and platelet levels in patients with TB spondylitis were increased significantly, yet lymphocyte levels were decreased significantly. The NLR, PLR, CRP and ESR in patients with TB spondylitis were all significantly higher than in the controls. As shown in **Figure 1**, the results of Spearman's analysis showed the correlation coefficients between NLR and CRP and ESR were0.412 ($P$<0.001) and 0.362 ($P$ = 0.002) respectively; the correlation coefficients between PLR and CRP and ESR were 0.331 ($P$ = 0.004) and 0.301 ($P$ = 0.007), respectively. NLR and PLR were significantly correlated ($r$ = 0.623, $P$<0.001). The correlation coefficient between ESR and platelets was 0.267 ($p$ = 0.022). There is a negative correlation between PLR and HGB ($r$ = -0.268, $P$ = 0.021). However, no statistically significant relationship was found between NLR and HGB (data not shown). As shown in **Table 3**, no statistically difference in neutrophils, lymphocytes, platelets, NLR and PLR was found between anemia (haemoglobin level: female<120; male<130) and non-anemia TB spondylitis patients. No statistically difference in neutrophils, lymphocytes, platelets, NLR and PLR was found between male and female patients (data not shown). No statistically significant relationship was discovered between NLR, PLR, CRP, and ESR in healthy controls (data not shown).

*Characteristics of ROC curves of NLR and PLR in TB spondylitis*

As shown in **Figure 2**, the cut-off values of NLR andPLR in TB spondylitis patients were 2.1 and 131, respectively. The area under the curve (AUC) values of NLR and PLR were 0.878 and 0.922, respectively. An 81.1% sensitivity and 83.3% specificity for NLR were identified, and an 89.2% sensitivity and 85.2% specificity for PLR were observed. However, there were no statistically significant differences between the AUCs of NLR and PLR ($P$>0.05).

## Discussion

Tuberculous spondylitis is characterized by chronic progressive development. When compared to PTB, the diagnosis of TB spondylitis is more challenging because of its delayed presentation [16]. Early diagnosis and treatment can control the development of the disease, avoid the occurrence of deformity and paralysis, and reduce financial burden.

Inflammation is involved in the pathogenesis of tuberculosis. Abakay et al. considered inflammatory reaction to be the main pathophysiology of PTB. In addition, they found that NLR and PLR might be new markers of inflammation in active PTB [17]. Muzaffar et al. described the hematological changes in TB spondylitis patients. They found thatanaemia and thrombocytosis accounted for the majority of cases [18]. Danielet al. demonstrated that patients with TB spondylitis had elevated ESR and thrombocytosis when compared to other spinal pathologies [16]. In our study, increased NLR, PLR, CRP and ESR were statistically significant in TB spondylitis patients.

ESR and CRP are makers commonly used in clinical diagnosis of many diseases. It is known

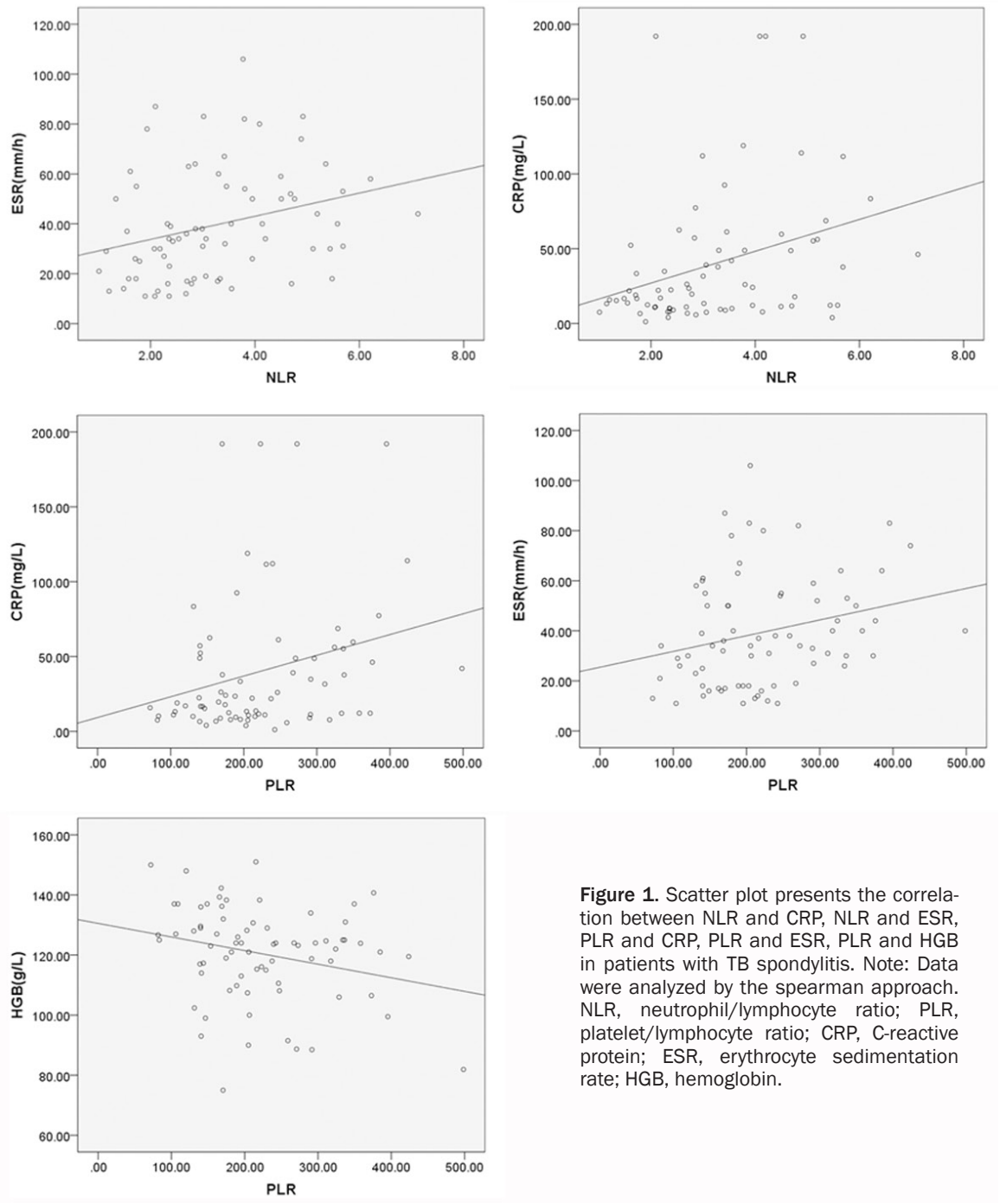


**Figure 1.** Scatter plot presents the correlation between NLR and CRP, NLR and ESR, PLR and CRP, PLR and ESR, PLR and HGB in patients with TB spondylitis. Note: Data were analyzed by the spearman approach. NLR, neutrophil/lymphocyte ratio; PLR, platelet/lymphocyte ratio; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; HGB, hemoglobin.

that ESR and CRP are elevated in pulmonary tuberculosis [19]. Recently, Daniel K *et al*. demonstrated elevated average ESR in patients with TBspondylitis [16]. Guo *et al*. found that changes of ESR and CRP had statistically significance for the determination of optimal operation times, as well as for the prognosis of TB spondylitis patients [20]. In our study, average ESR and CRP values were increased beyond the normal range. Once again, these results showed that ESR and CRP might be useful to the auxiliary diagnosis of TB spondylitis.

Systemic inflammatory response induced by infection and inflammation may result in thrombocytosis. Some inflammatory mediators stimulate the proliferation of megakaryocytics and thus lead to increased platelets [21]. In PTB, an

**Table 3.** The features of parameters between anaemia and no-anaemia patients

| | Anaemic patients (n = 42) | Non-anaemic patients (n = 32) | *P*-value |
|---|---|---|---|
| Neutrophil count ($\times 10^9$/L) | 4.56 ± 1.69 | 4.59 ± 1.43 | 0.923 |
| Lymphocyte count ($\times 10^9$/L) | 1.52 ± 0.58 | 1.57 ± 0.46 | 0.678 |
| Platelet count ($\times 10^9$/L) | 325.24 ± 87.30 | 294.60 ± 84.74 | 0.134 |
| NLR | 3.28 ± 1.35 | 3.18 ± 1.44 | 0.765 |
| PLR | 237.90 ± 95.06 | 203.80 ± 79.16 | 0.105 |

Note: Continuous variables are expressed by the mean ± one standard deviation; NLR, neutrophil/lymphocyte ratio; PLR, platelet/lymphocyte ratio; CRP, C-reactive protein; ESR, erythrocyte sedimentationrate.

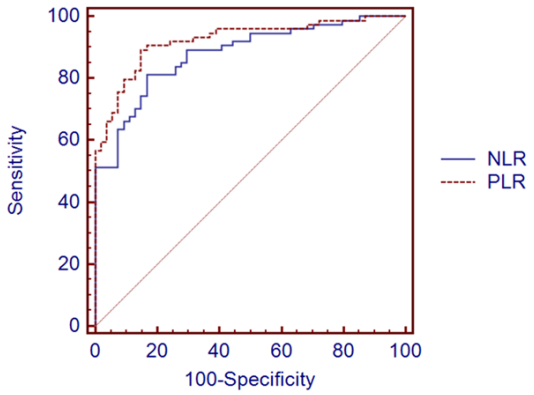


**Figure 2.** Comparison of ROC analysis of NLR and PLR in prediction of TB spondylitis. Note: Data were analyzed using the MedCalc statistic software.

acute inflammatory cascade caused by the release of interleukin-6 (IL-6) is associated with megakaryocytopoiesis, which might result in reactive thrombocythemia [9]. Daniel *et al.* observeda significantly increasednumber ofplatelets, finding that the correlation coefficient was 0.31 ($P<0.01$) between platelets and ESR in TB spondylitis patients. In addition, they found that platelets might be a diagnostic marker had a index of suspicion for the pathology of TB spondylitis [16]. Our study found that the platelet levels in TB spondylitis patients were higher than in the controls ($P<0.001$), the correlation coefficient between ESR and platelets was 0.267 ($P = 0.022$) in TB spondylitis patients.

Absoluteneutrophil, and lymphocyte, and platelet counts are parameters of complete blood count (CBC). Neutrophils are associated with the destruction of tissue in the inflammatory state. Jala *et al.* showed that a large number of inflammatory mediators released by neutrophils might contribute to tissue injury [22]. Low lymphocyte counts are indicative of physiological stress and poor health in general [23]. Recently, the use of NLR and PLR as parameters of inflammation has been evaluated in many diseases [24-26]. Horne et al. showed that NLR may be more effective than leukocyte levels in the prediction of inflammation [27]. Mercan et al. investigated the utility of NLR in autoimmune diseases. They found NLR was higher in rheumatoid arthritis (RA) patients than in controls, and NLR in patients with RA was positively correlated with ESR and CRP. In addition, they considered that NLR might be used as amaker in the evaluation of RA disease activity [28]. Iliaz et al. found that NLR in tuberculosis patients was significantly higher than in sarcoidosis patients. They considered that NLR could be useful in the differential diagnosis of sarcoidosis and tuberculosis [29]. Abakay et al. described the significantly increased NLR and PLR in patients with PTB; NLR in PTB patients showed a significant correlation with CRP and ESR. Moreover, by comparing the laboratory results of PTB patients from different periods, they determined that NLR may potentially be useful as a marker of inflammation and disease severity in PTB [17]. As far as this study's authors are aware, this is the first paper describing NLR and PLR in patients with TB spondylitis. These hematologic features demonstrate that NLR and PLR may be predictors of TB spondylitis.

Our study had some limitations. This is a retrospective study and the sample size is relatively small. Nevertheless, the clinical observation shows that the NLR and PLR may be predictors of TB spondylitis.

In conclusion, NLR and PLR were significantly increased in patients with TB spondylitis. NLR and PLR were positively correlated with traditional indices such as CRP and ESR, and the high sensitivity and specificity of NLR and PLR suggests that these values may be useful makers in the diagnosis of TB spondylitis.

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## Disclosure of conflict of interest

None.

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## References

[1] Eurosurveillance editorial t. WHO publishes Global tuberculosis report 2013. Euro Surveill 2013; 18.

[2] Wang L, Zhang H, Ruan Y, Chin D P, Xia Y, Cheng S, Chen M, Zhao Y, Jiang S, Du X, He G, Li J, Wang S, Chen W, Xu C, Huang F, Liu X, Wang Y. Tuberculosis prevalence in China, 1990-2010; a longitudinal analysis of national survey data. Lancet 2014; 383: 2057-2064.

[3] Weng CY, Chi CY, Shih PJ, Ho CM, Lin PC, Chou CH, Wang JH, Ho MW. Spinal tuberculosis in non-HIV-infected patients: 10 year experience of a medical center in central Taiwan. J Microbiol Immunol Infect 2010; 43: 464-469.

[4] Wang H, Li C, Wang J, Zhang Z, Zhou Y. Characteristics of patients with spinal tuberculosis: seven-year experience of a teaching hospital in Southwest China. Int Orthop 2012; 36: 1429-1434.

[5] Garg RK, Somvanshi DS. Spinal tuberculosis: a review. J Spinal Cord Med 2011; 34: 440-454.

[6] Jain AK. Tuberculosis of the spine: a fresh look at an old disease. J Bone Joint Surg Br 2010; 92: 905-913.

[7] Jain AK, Dhammi IK. Tuberculosis of the spine: a review. Clin Orthop Relat Res 2007; 460: 39-49.

[8] Mirsaeidi M, Peyrani P, Aliberti S, Filardo G, Bordon J, Blasi F, Ramirez JA. Thrombocytopenia and thrombocytosis at time of hospitalization predict mortality in patients with community-acquired pneumonia. Chest 2010; 137: 416-420.

[9] Unsal E, Aksaray S, Koksal D, Sipit T. Potential role of interleukin 6 in reactive thrombocytosis and acute phase response in pulmonary tuberculosis. Postgrad Med J 2005; 81: 604-607.

[10] Ahsen A, Ulu M S, Yuksel S, Demir K, Uysal M, Erdogan M, Acarturk G. As a new inflammatory marker for familial Mediterranean fever: neutrophil-to-lymphocyte ratio. Inflammation 2013; 36: 1357-1362.

[11] Li L, Xia Y, Chen C, Cheng P, Peng C. Neutrophil-lymphocyte ratio in systemic lupus erythematosus disease: a retrospective study. Int J Clin Exp Med 2015; 8: 11026-11031.

[12] Koseoglu S, Ozcan K M, Ikinciogullari A, Cetin M A, Yildirim E, Dere H. Relationship Between Neutrophil to Lymphocyte Ratio, Platelet to Lymphocyte Ratio and Obstructive Sleep Apnea Syndrome. Adv Clin Exp Med 2015; 24: 623-627.

[13] Boyraz I, Koc B, Boyaci A, Tutoglu A, Sarman H, Ozkan H. Ratio of neutrophil/lymphocyte and platelet/lymphocyte in patient with ankylosing spondylitis that are treating with anti-TNF. Int J Clin Exp Med 2014; 7: 2912-2915.

[14] Tozkoparan E, Deniz O, Ucar E, Bilgic H, Ekiz K. Changes in platelet count and indices in pulmonary tuberculosis. Clin Chem Lab Med 2007; 45: 1009-1013.

[15] Sahin F, Yazar E, Yildiz P. Prominent features of platelet count, plateletcrit, mean platelet volume and platelet distribution width in pulmonary tuberculosis. Multidiscip Respir Med 2012; 7: 38.

[16] Daniel K, Dunn R. Comparison of platelet count in tuberculosis spine to other spine pathology. Eur Spine J 2013; 22: 2810-2814.

[17] Abakay O, Abakay A, Sen HS, Tanrikulu AC. The relationship between inflammatory marker levels and pulmonary tuberculosis severity. Inflammation 2015; 38: 691-696.

[18] Muzaffar TM, Shaifuzain AR, Imran Y, Haslina MN. Hematological changes in tuberculous spondylitis patients at the Hospital Universiti Sains Malaysia. Southeast Asian J Trop Med Public Health 2008; 39: 686-689.

[19] Yu CC, Liu YC, Chu CM, Chuang DY, Wu WC, Wu HP. Factors associated with in vitro interferon-gamma production in tuberculosis. J Formos Med Assoc 2011; 110: 239-246.

[20] Guo LX, Ma YZ, Li HW, Xue HB, Peng W, Luo XB. [Variety of ESR and C-reactive protein levels during perioperative period in spinal tuberculosis]. Zhongguo Gu Shang 2010; 23: 200-202.

[21] Toptas M, Akkoc I, Savas Y, Uzman S, Toptas Y, Can MM. Novel hematologic inflammatory parameters to predict acute mesenteric ischemia. Blood Coagul Fibrinolysis 2016; 27: 127-130.

[22] Jala VR, Haribabu B. Leukotrienes and atherosclerosis: new roles for old mediators. Trends Immunol 2004; 25: 315-322.

[23] Gibson PH, Cuthbertson BH, Croal BL, Rae D, El-Shafei H, Gibson G, Jeffrey RR, Buchan KG, Hillis GS. Usefulness of neutrophil/lymphocyte ratio as predictor of new-onset atrial fibrillation after coronary artery bypass grafting. Am J Cardiol 2010; 105: 186-191.

[24] Aktar F, Tekin R, Bektas MS, Gunes A, Kosker M, Ertugrul S, Yilmaz K, Karaman K, Balik H, Yolbas I. Diagnostic role of inflammatory markers in pediatric Brucella arthritis. Ital J Pediatr 2016; 42: 3.

[25] Alan S, Tuna S, Turkoglu EB. The relation of neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and mean platelet volume with the presence and severity of Behcet's syndrome. Kaohsiung J Med Sci 2015; 31: 626-631.

[26] Akbas EM, Demirtas L, Ozcicek A, Timuroglu A, Bakirci EM, Hamur H, Ozcicek F, Turkmen K. Association of epicardial adipose tissue, neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio with diabetic nephropathy. Int J Clin Exp Med 2014; 7: 1794-1801.

[27] Horne BD, Anderson JL, John JM, Weaver A, Bair TL, Jensen KR, Renlund DG, Muhlestein JB, Intermountain Heart Collaborative Study G. Which white blood cell subtypes predict increased cardiovascular risk? J Am Coll Cardiol 2005; 45: 1638-1643.

[28] Mercan R, Bitik B, Tufan A, Bozbulut U B, Atas N, Ozturk M A, Haznedaroglu S, Goker B. The Association Between Neutrophil/Lymphocyte Ratio and Disease Activity in Rheumatoid Arthritis and Ankylosing Spondylitis. J Clin Lab Anal 2015.

[29] Iliaz S, Iliaz R, Ortakoylu G, Bahadir A, Bagci BA, Caglar E. Value of neutrophil/lymphocyte ratio in the differential diagnosis of sarcoidosis and tuberculosis. Ann Thorac Med 2014; 9: 232-235.