MedCrave
Step into the World of Research

International Clinical Pathology Journal

Research Article

Open Access

CrossMark

The utility and validity of immunological, inflammatory, and nutritional-based scores and indices in active Pulmonary Tuberculosis

Abstract

Purpose: The host immune/inflammatory cells play an important role in Mycobacterium tuberculosis (TB) evolution. We aimed to validate the utility of immunological, inflammatory, and nutritional-based indices in active pulmonary TB (APTB).

Patients and methods: fifty PTB patients with fifty healthy subjects were included. Sputum examined for acid-fast bacilli and peripheral blood samples collected to assess inflammatory indices as [neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), lymphocyte-monocyte ratio (LMR), neutrophil-platelet score (NPS), body mass index (BMI), ESR, C-reactive protein (CRP) and/or albumin-based as advanced lung cancer inflammation index (ALI), prognostic nutritional index (PNI).

Results: Patients had a significantly lower BMI, Hb, lymphocyte, MPV, WBC/MPV, MLR, LMR, albumin, PNI, ALI, (P =0.00001) and significantly higher neutrophil, monocyte, RDW, NLR, PLR, ESR, CRP (P =0.00001). The increase in mycobacterial load significantly associated with decreased BMI, albumin, PNI, ALI and increased ESR, neutrophil count, CRP, CRP/albumin ratio, GPS, mGPS, and PLR.

ROC curve analysis revealed that ESR, RDW, BMI, MLR, ALI, Hb, MPV, monocyte, NLR, PLR, albumin, and lymphocyte, had great decision power that could differentiate APTB patients from controls. The best cutoff value MPV (8.08 fL), albumin (3.99 g/dl), BMI (23.67 kg/m^2), Hb (12.3 g/dl), and lymphocyte (2600×109/l) RDW (14.8%), monocyte (550×109/l), and ALI (53%) (P =0.0001). Regression analysis approved that MPV, albumin level; BMI, Hb, lymphocyte, and ALI had the highest odds ratio as the prognostic value of APTB

Conclusion: the immunological, inflammatory, and nutritional-based scores are valuable prognostic tools that reflect the degree of host inflammatory activity that promotes disease progression.

Keywords: albumin, CRP/albumin ratio, modified glasgow prognostic score, neutrophil to lymphocyte ratio, monocyte to lymphocyte ratio, prognostic index

Volume 6 Issue 6 - 2018

Hanan Mahmoud Fayed,[1] Abdallah Elaiw Mohammed,[1] Mohamed Shahat Badawy,[2] Ayman Sabry Yassin[3]

[1]Clinical and Chemical Pathology Dept, South Valley University, Egypt
[2]Chest disease Dept, South Valley University, Egypt
[3]Microbiology and Immunology Dept., Al-Azhar University, Egypt

Correspondence: Hanan Mahmoud Fayed, Qena university hospital-mabber el-shabab street, Downtown Qena- Egypt, Tel +20963226432, Email hanenfayed@yahoo.com

Received: September 10, 2018 | **Published:** December 12, 2018

Introduction

Tuberculosis (TB) is a common infectious disease caused by Mycobacterium tuberculosis (Mtb); an acid-fast facultative intracellular obligate aerobe bacterium that favors being localized in macrophages. Mtb infection has diverse manifestations that reflect the balance between the bacillus and the host defense mechanisms,[1] where extensive tissue damage may occur through the direct action of Mtb bacilli and/or inflammatory cell invasion.[2] During APTB infection, Mtb activates macrophages and induces the production of pro-inflammatory cytokines, some of which initiate, amplify, and support the inflammatory process, others slow it down as part of the recovery of the inflammatory state,[3] hence enabling the development of a cellular immune response,[4] with excessive production of cytokines which mediate systemic inflammation perceived in TB patients.[5]

Granulomatous caseous inflammation is the classic pathological finding in PTB composed of clusters of infected macrophages surrounded by lymphocytes and fibroblasts that are recruited to the site of infection with the aim to enclose the infection,[6] at which the matrix metalloproteinases secreted by monocytes-derived cells, neutrophils, and stromal cells are involved in both cell recruitment and lung interstitial matrix destruction that might cause cavitation associated with disease severity.[7]

Acute-phase proteins perform as mediators and/or inhibitors of inflammation, immune response regulators modulation, cleaning products of inflammation, and repairing damaged tissue.[8] The albumin level decreases in response to acute phase infections; therefore, albumin is a potent prognostic marker in infection-related disease outcomes.[9] Low albumin level is also linked to malnutrition, malabsorption and systemic inflammation.[10] Therefore, the CRP to albumin ratio was proven as an inflammation-based prognostic score and was used as a prognostic marker for disease activity.[9]

Mtb infection may alter hematopoiesis or directly infect bone marrow mesenchymal stem cells.[11] And the physiological immune responses of circulating leukocytes to different stressful events are characterized by an increased neutrophil count and decreased lymphocyte count. Therefore, the neutrophil/lymphocyte ratio (NLR) efficiently reflects the alteration of the immune response toward a pro-inflammatory pattern.[12] While the monocyte to lymphocyte ratio (MLR) reflect the relative frequency of monocytes, as target cells for Mtb growth and lymphocytes, as effector cells for Mtb clearance. An

altered MLR was found to precede an active disease.[13] Alternatively, the MLR and primary hematopoietic activity may be a secondary effect and the MLR may be a sign of where along the scale of TB from latent to active disease.[14]

Current strategies for diagnosing active TB are based on clinical, microbiological and radiological examinations.[15] Although Mtb culture has the highest sensitivity for defining APTB infection, it requires ~ 2 to 6 weeks for interpretation. While sputum smear microscopy is rapid, simple, and inexpensive tool for diagnosing PTB has low and variable sensitivity.[16] Different bio-markers using inflammatory factors such as serum CRP and albumin as a marker of systemic inflammation (e.g. modified Glasgow Prognostic Score (mGPS)) has been studied in a variety of cancer types.[17] Yet it has not been evaluated in PTB patients.

The aim of the work

The objective of this study was to evaluate the diagnostic and prognostic utility and validity of a panel of inflammation-based scores and indices in patients with APTB and to clarify its association with sputum mycobacterial loads.

Material and methods

This was a cross-sectional case-control study included fifty naïve APTB cases attending Qena Chest Hospital (according to the principles expressed in the Declaration of Helsinki), with fifty healthy subjects as control group (with normal X-ray findings or no history of TB, negative Tuberculin test, no other underlying disease, and not taking any medication interfering with the tested parameters) were involved after study approval by the institutional ethical committee and obtaining of an informed consent from all subjects included in the study.

Inclusion criteria

All naïve APTB patients were diagnosed on the basis of the presence of recent clinical symptoms of TB and a positive sputum smear test for AFB, from September 2016 to December 2017 were enrolled in this study.

Exclusion criteria

Pregnancy, age before 20 or old age more than 70 years old, patients with: extra PTB, use of immunosuppressive drugs, kidney and liver diseases, diabetes mellitus, cardiovascular disease, patients with other co-morbid diseases that affect WBC counts, ESR, CRP and albumin e.g. chronic inflammatory diseases, autoimmune diseases, malignancy, hematologic disorders, or having an impaired immune system.

Sample collection

Five ml of venous blood was collected under aseptic precautions used for EDTA-tube, plain tube & ESR tube.

The healthy controls were subjected to laboratory procedure for CBC, ESR CRP, and albumin. And all patients will be subjected to:-

A. Full history taking, including the complaint, onset, course, and duration of the disease, habitual risk factors as smoking and other forms of tobacco use, alcohol consumption, socio-demographics, family history of TB and diabetes mellitus, educational and occupational status, and history of contact with active TB patient.

B. Physical examination, including body mass index (BMI) calculation, clinical general, and chest examination.

C. Sputum direct Ziehl-Neelsen (ZN) stained smear examination. The positive sputum smear was quantified by the number of resistant, acid-alcohol-fast bacilli (AFB) in the sample. The results of the AFB smears were interpreted according to WHO using Laboratory Services in TB Control Grading System, where AFB < 1+ was defined as 1-9 AFB/100 field, 1+ as 10-99 AFB/100 fields, 2 + as 1-10 AFB/field and 3+ as > 10 AFB/field.[18]

D. Complete blood count (CBC) was performed using a Cell Dyne 1700 (Sequoia-Turner Corporation, California, USA), including: hemoglobin (Hb), hematocrit (Hct), RBC indices [mean corpuscular volume (MCV), mean corpuscular Hb (MCH), mean corpuscular Hb concentration (MCHC), red cell distribution width (RDW)], (using the WHO recommendation to define anemia when Hb concentration <13.5 g/dl for men and <12.5 g/dl for women),[19] and parameters related to systemic inflammation [absolute neutrophil, monocyte, and lymphocyte, platelets counts, and mean platelet volume (MPV)]; retrieved separately for calculations of inflammatory indices platelet to lymphocyte ratio (PLR), NLR, MLR, neutrophil-platelet score (NPS).

E. Inflammatory scores and indices as BMI, prognostic index (PI), prognostic nutritional index (PNI), CRP/albumin ratio, Glasgow Prognostic Score (GPS), modified Glasgow Prognostic Score (mGPS), and advanced lung cancer, inflammation index (ALI). These scores composed of a variable with similar hazard ratios that was previously validated,[17,20] box 1.

F. Measurement of ESR (Westergren method) and CRP, serum albumin using Cobas c311 (Roche Diagnostics, GmbH, Mannheim, Germany). Normal values for albumin (3.5–5.0g/dl) and CRP (<10 mg/l).

Box 1 list of immunological, inflammatory and nutritional-based prognostic indices for APTP

Neutrophil lymphocyte ratio (NLR)= ANC÷ALC	
• Neutrophil count: lymphocyte count<3:1	0
• Neutrophil count: lymphocyte count≥3:1	1
Derived Neutrophil lymphocyte ratio (dNLR)=dNLR=ANC÷(WBC-ANC)	
Platelet lymphocyte ratio (PLR) = platelets count ÷ALC	
• Platelet count: lymphocyte count <120:1	0
• Platelet count: lymphocyte count ≥120:1	1
Mean platelet volume/platelet count (MPV/PC) ratio	
Lymphocyte monocyte ratio (LMR)= ALC÷AMC	
Monocyte lymphocyte ratio (MLR)= AMC÷ALC	
Combined NLR-PLR:	
• NLR<3 and PLR<120	0
• NLR<3 and PLR>120	1
• NLR>3 and PLR<120	1
• NLR>3 and PLR>120	2
Neutrophil platelets score	
• Neutrophil count ≤7.5 × 10^9/L and platelets≤400 × 10^9/L	0
• Neutrophils >7.5×10^9/L or platelets>400×10^9/L	1
• Neutrophils >7.5×10^9/L and platelets>400×10^9/L.	2

Table Continued....

Combination of Platelet count and Neutrophil to Lymphocyte Ratio (COP-NLR) • Platelet count (<300 x10³/ml) and NLR (<3) • Platelet count (>300 x10³/ml) or NLR (>3) • Platelet count (>300 x10³/ml) and NLR (>3)	0 1 2
Glasgow Prognostic Score (GPS) • CRP≤10 mg/L and albumin≥35g/L • CRP≤10 mg/L and albumin<35g/L • CRP>10 mg/L and albumin≥35g/L • CRP>10 mg/L and albumin 35g/L	0 1 1 2
modified Glasgow Prognostic Score (mGPS) • CRP≤10 mg/L and albumin≥35 g/L • CRP≤10 mg/L and albumin<35 g/L • CRP>10 mg/L and albumin≥35 g/L • CRP>10 mg/L and albumin<35 g/L	0 0 1 2
CRP/albumin ratio	
Advanced lung cancer inflammation index (ALI) = BMI x serum albumin÷NLR	
Prognostic index (PI): • CRP (≤10 mg/l) and white cell count (≤11,000/µl) • CRP (≤10 mg/l) and white cell count (>11,000/µl) • CRP (>10 mg/l) and white cell count (≤11,000/µl) • CRP (>10 mg/l) and white cell count (>11,000/µl)	0 1 1 2
Prognostic nutritional index (PNI)- • 10 × Albumin (g/dl) + 0.005 × total lymphocyte count (/µl)≥45 • 10 × Albumin (g/dl)+0.005 × total lymphocyte count (/µl)<45	0 1

ALC, absolute lymphocyte count; AMC, absolute monocyte count; ANC, absolute neutrophil count; BMI, body mass index.

Statistical analysis

Data analyzed using the IBM statistical package for the social science (SPSS Inc., Chicago, IL, USA) Windows version 22. The data normality tested using the Shapiro-Wilk test. The data described in terms of median and range, mean±standard deviation (M±SD), or number (percentage) when applicable. Comparison of numerical variables using student t test and one way analysis of variance (ANOVA) or Mann-Whitney U test and the Kruskal-Wallis test. Chi-square ($\chi 2$) tests used for categorical variables. Spearman's rank test used to assess the correlations between variables. All statistical tests were two-tailed, and a P value below 0.05 considered significant. To estimate the discrimination power for the inflammatory indices used in terms of sensitivity and specificity, the receiver operator curve (ROC) constructed and the area under the curve (AUC) calculated to determine the optimal cutoff values for the inflammatory variables and used to assess the predictive ability for different inflammatory indices. The sensitivity and specificity are measures of validity and inform the test accuracy and the positive and negative predictive values are measures of reliability. A Univariate linear regression analysis assesses the independent prognostic variables of PTB disease activity and significant variables in Univariate analysis inserted into a multivariate logistic regression model in order to investigate independent predictors of PTB disease activity.

Results

A total of 50 patients with APTB were enrolled in this study and 50 healthy controls. Demographic, clinical and laboratory characteristics of both groups were shown in Table 1. Compared to the healthy control, APTB patients had significantly lower BMI, Hb, HCT, absolute lymphocyte count, MPV, WBC/MPV, MLR, LMR, albumin, advanced lung cancer inflammation index (ALI), prognostic nutritional index (PNI) (P = 0.00001), and had significantly higher neutrophil count, monocyte count, RDW, NLR, PLR, combined NLR & PLR, ESR, CRP (P = 0.00001). However; there was no significant difference between the PTB cases and controls as regards the WBC, platelet counts, Table 2.

Table 1 clinical findings in the studied cases

Parameter		Number (percentage)		P-value
		Patient	Control	
Age (year) Mean ±SD		44.06±13.89	33.80±7.84	0.0001*
Male: female		21:29	12:38	0.0556
Disease duration (months) Mean ±SD		2.44±1.43	-	
Weight (kg)		53.42±10.461	71.60±8.266	0.0001*
BMI (kg/m²)		19.30±3.15	26.40±2.05	0.0001*
Temp		37.946±1.00	37.12±0.42	0.0001*
Heart rate		86.56±15.95	70.68±5.27	0.0001*
Respiratory rate		19.22±3.10	18.28±1.69	0.063
History of contact to active TB	Yes	23(46%)	-	0.0001*
	No	27(54%)	50(100%)	
Cough	Yes	47(94%)	-	0.0001*
	No	3(6%)	50(100%)	
Fever	Yes	20(40%)	-	0.0001*
	No	30(60%)	50(100%)	
Malaise	Yes	42(84%)	-	0.0001*
	No	8(16%)	50(100%)	
Weight loss	Yes	37(74%)	-	0.0001*
	No	13(26%)	50(100%)	
Night sweats	Yes	23(46%)	-	0.0001*
	No	27(54%)	50(100%)	
Smoking	Yes	14(28%)	8(16%)	0.227
	No	36(72%)	42(84%)	

*Significant

Citation: Fayed HM, Mohammed AE, Badawy MS, et al. The utility and validity of immunological, inflammatory, and nutritional-based scores and indices in active Pulmonary Tuberculosis. *Int Clin Pathol J.* 2018;6(6):199–213. DOI: 10.15406/icpjl.2018.06.00188

Table 2 laboratory findings in the studied subjects

Parameter	Mean ±SD		*P*-value
	Patient (N=50)	Controls (N=50)	
Hb (g/dl)	10.754±2.26	13.26±1.20	0.0001*
RBCs	5345.60±5795.60	4702.00±389.77	0.435
HCT	32.49±6.65	39.17±4.04	0.0001*
MCV	71.92±7.38	83.42±5.26	0.0001*
MCH	23.84±2.78	28.28±1.4109	0.0001*
MCHC	33.13±1.28	33.97±1.14	0.001*
RDW	18.15±1.64	12.04±1.16	0.0001*
Platelets (X10^9/L)	293±104	261±59	0.058
MPV (fl)	7.53±0.81	8.53±0.71	0.0001*
WBCs (X10^9/L)	10.018±6.291	7.648±2.103	0.013*
% Monocyte	9.56±4.60	5.61±2.18	0.0001*
Absolute Monocyte count (X10^9/L)	972.0±1008.34	410.2±121.69	0.0001*
% Neutrophil	64.79±14.08	57.11±8.55	0.001*
Absolute Neutrophil count (X10^9/L)	6.836±5.212	5.046±4.924	0.081
% lymphocyte	24.94±11.30	37.47±8.32	0.0001*
Absolute Lymphocyte count (X10^9/L)	2.198±1.134	2.954±985	0.001*
NLR	3.86±3.59	2.05±3.21	
• NLR <3:1 No(%)	28(56%)	46(92%)	0.009*
• NLR ≥3:1 No(%)	22(44%)	4(8%)	
DNLR	2.48±1.90	1.28±0.77	0.0001*
PLR	171.23±123.43	94.81±28.30	
• PLR <120: No(%)	16(32%)	41(82%)	0.0001*
• PLR ≥120:1 No(%)	34(68%)	7(14%)	
Neutrophil/platelet-lymphocyte ratio	59.16±63.65	57.67±53.22	0.07030
Combined NLR-PLR			
• NLR<3 and PLR < 120	13(26%)	40(80%)	
• NLR<3 and PLR > 120	15(30%)	6(12%)	< 0.00001*
• NLR>3 and PLR < 120	3(6%)	1(2%)	
• NLR>3 and PLR > 120	19(38%)	1(2%)	
MLR	0.46±0.30	0.15±0.06	0.0001*
LMR	3.06±1.90	7.57±2.50	0.0001*
ESR	93.48±27.43	11.90±6.344	0.0001*
CRP	109.25±47.30	3.15±0.82	0.0001*
Albumin	3.72±0.76	4.30±0.52	0.0001*
WBC/MPV	1348.86±877.39	906.43±276.51	0.001*
CRP/albumin ratio	31.40±16.76	0.73±0.18	0.0001*
ALI	33.24±27.84	88.98±79.09	0.0001*

Citation: Fayed HM, Mohammed AE, Badawy MS, et al. The utility and validity of immunological, inflammatory, and nutritional-based scores and indices in active Pulmonary Tuberculosis. *Int Clin Pathol J.* 2018;6(6):199–213. DOI: 10.15406/icpjl.2018.06.00188

Table Continued....

Parameter	Mean ±SD		*P*-value
	Patient (N=50)	Controls (N=50)	
GPS			
• CRP ≤10 mg/L+ albumin ≥35 g/L	0	50(100%)	
• CRP ≤10 mg/L +albumin <35 g/L	0	0	0.0001*
• CRP > 10 mg/L + albumin ≥35 g/L	30(60%)	0	
• CRP > 10 mg/L + albumin <35 g/L	20(40%)	0	
mGPS			
• CRP ≤10 mg/L+ albumin ≥35 g/L	0	50(100%)	
• CRP ≤10 mg/L + albumin <35 g/L	0	0	0.0001*
• CRP > 10 mg/L + albumin ≥35 g/L	30(60%)	0	
• CRP > 10 mg/L + albumin <35 g/L	20(40%)	0	
PNI	48.22±9.57	57.86±6.74	0.0001*

*significant Mann Whitney U test; ALI, Advanced lung cancer inflammation index; BMI, body mass index; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; MPV, mean platelet volume; NLR, Neutrophil Lymphocyte Ratio; PLR, Platelet Lymphocyte Ratio; MLR, Monocyte Lymphocyte Ratio; RDW, red cell distribution width.

The increase in the sputum Mycobacterium load was associated with significantly decreased BMI, albumin, PNI and significantly increased in the absolute neutrophil count, CRP, ESR, CRP/albumin ratio, ALI, GPS, mGPS and PLR, Table 3. The PTB patient with higher GPS and mGPS scores had significantly increased Mtb load, RDW, ESR, CRP, CRP/albumin ratio, as well had significantly lower BMI, Hb, albumin level, ALI, and PNI. No significant differences in relation to cellular-based inflammatory scores [NLR, dNLR, MLR, PLR, MPV, neutrophil/platelet-lymphocyte ratio and NPS], Table 4.

Table 3 Difference in laboratory data in relation to sputum Mtb load

Variables	Sputum Mtb load for AFB			*P value
Median (range)	+1 [23(46%)]	+2 [21(42%)]	+3 [6(12%)]	
BMI	20.96 (17.4-24.86)	17.3 (12.7-24.5	16.58 (14.2-23.67)	0.003*
Hb	11.5 (3.3-13.8)	11 (6.7-15.8)	10.25 (6.2-12.1)	0.369
RDW (%)	18 (15.2-21.4)	18.2 (15-20.9)	17.4 (16.8-21.3)	0.995
WBCs	7200 (2600-24900)	8600 (3700-22900)	12200 (5600-35100)	0.058
Absolute Neutrophil count ($X10^9$/L)	4900 (1300-14200)	6000 (2000-19600)	7450 (3400-30800)	0.0331
Absolute Lymphocyte count ($X10^9$/L)	2000 (1100-5400)	1900 (300-5200)	1800 (1400-5300)	0.388
Absolute Monocyte count ($X10^9$/L)	700 (200-6900)	800 (200-1500)	1300 (200-2500)	0.376
Platelets ($X10^9$/L)	255 (50-416)	292 (110-589)	275 (153-322)	0.200
MPV (fl)	7.4 (6.3-9.7)	7.4 (6.3-9.3)	7.15 (6.4-8.9)	0.766
WBC/MPV	963 (305.9-284.6)	1150.5 (500-3417.9)	1411.6 (875-5014.3	0.061
Neutrophil lymphocyte ratio (NLR)	2.33(0.83-8.59)	3.05(1.19-16.67)	3.28(1.72-17.11)	
• NLR <3:1=0 No (%)	17(34%)	9(18%)	4(8%)	0.064
• NLR ≥3:1=1 No (%)	6(12%)	13(26%)	2(4%)	
Platelet lymphocyte ratio (PLR)	133.89(45.45-268.67)	176.15 (67.57-750)	151.25(28.87-200)	
• PLR <150: No (%)	13(26%)	13(26%)	3(6%)	0.027*
• PLR ≥150:1 No (%)	10(20%)	8(16%)	3(6%)	

Variables	Sputum Mtb load for AFB			*P value
Median (range)	+1 [23(46%)]	+2 [21(42%)]	+3 [6(12%)]	
Neutrophil/platelet-lymphocyte ratio	2.33(0.83-8.55)	3.05(1.19-16.67)	3.29(1.72-17.11)	0.237
Combined NLR-PLR				
NLR < 3 and PLR < 120	10	3	1	
NLR < 3 and PLR > 120	7	5	2	0.182
NLR > 3 and PLR < 120	1	1	1	
NLR > 3 and PLR > 120	5	12	2	
Combined of Platelet count and NLR				
• Platelet count (>300 x10^3/ml)+ NLR (>3)	0	1	0	
• Platelet count (>300 x10^3/ml) or NLR (>3)	15	5	2	0.0629
• Platelet count (<300 x10^3/ml) & NLR (>3)	8	15	4	
Lymphocyte-monocyte ratio (LMR)	2.86 (0.78-8.75)	2.64 (0.67-5.2)	1.89 (0.72-8)	0.601
Monocyte-lymphocyte ratio (MLR)	0.35 (0.11-1.28)	0.37 (0.19-1.5)	0.53 (0.13-1.39)	0.346
ESR (mm/hr.)	75 (14-115)	105 (70-140)	130 (115-140)	< 0.0001*
CRP (mg/l)	75.3 (23.4-145.9)	132.2 (49.9-182.3)	183.3 (130.3-189.1)	< 0.0001*
Albumin (g/dl)	3.91 (2.94-5.92)	3.37 (2.74-5.43)	2.92 (2.61-3.91)	0.017*
CRP/albumin ratio	8.21 (5.48-34.33)	36.97 (9.2-63.1)	55.4 (42.34-71)	< 0.0001*
ALI= BMI x s albumin/NLR	35.87 (9.70-150.26)	18.16 (5.30-82.42)	13.58 (5.41-27.64)	0.005*
Prognostic index (PI):				
• CRP (≤1.0 mg/l) and WBC (≤11,000/µl)	0	0	0	
• CRP (≤1.0 mg/l) and WBC (>11,000/µl)	0	0	0	0.276
• CRP (>1.0 mg/l) and WBC (≤11,000/µl)	18	17	3	
• CRP (>1.0 mg/l) and WBC (>11,000/µl)	5	4	3	
Neutrophil platelets score (NPS)				
• #N ≤7.5 × 10^9/L & platelets ≤400 × 10^9/L	17	13	3	
• #N >7.5 × 10^9/L or platelets >400 × 10^9/L	5	7	3	0.413
• #N >7.5 × 10^9/L + platelets >400 × 10^9/L	1	1	0	
Prognostic nutritional index (PNI)	51.1(34.9-69.2)	44.7(28.9-72.7)	41.9(35.4-65.6)	
10 × Albumin + 0.005 × #L (/µl) ≥45	19	10	3	0.040*
10 × Albumin + 0.005 × #L (/µl)< 45	4	11	3	
GPS/mGPS				
• CRP≤10mg/L+ albumin ≥35g/L	0	0	0	
• CRP≤10 mg/L +albumin <35 g/L	0	0	0	0.0098*
• CRP>10 mg/L + albumin ≥35 g/L	19	9	2	
CRP > 10 mg/L + albumin <35 g/L	4	12	4	

ALI, advanced lung cancer inflammation index; BMI, body mass index; BNP, CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; Hb, hemoglobin; dNLR, derived neutrophil lymphocyte ratio; MPV, mean platelet volume; NLR, neutrophil lymphocyte ratio; PLR, platelet lymphocyte ratio; MLR, monocyte lymphocyte ratio; RDW, red cell distribution width

Citation: Fayed HM, Mohammed AE, Badawy MS, et al. The utility and validity of immunological, inflammatory, and nutritional-based scores and indices in active Pulmonary Tuberculosis. *Int Clin Pathol J.* 2018;6(6):199–213. DOI: 10.15406/icpjl.2018.06.00188

Table 4 The association between patient baseline characteristics and GPS/mGPS

Variables (Mean ±SD)	GPS/mGPS		*P value
	Score 1	Score 2	
Age (years)	45±14.2	42.5±13.7	0.4295
Male:Female	15:15	7:13	0.295
Disease duration (months)	2.36±1.60	2.55±1.14	0.3125
BMI	20.24±2.84	17.63±2.9	**0.001***
AFB smears:			
• **< 1+ (1-9 AFB/100 field)**	0	0	
• **1+ (10-99 AFB/100 field)**	19	4	**0.01***
• **2+ (1-10 AFB/field)**	9	12	
• **3+ (> 10 AFB/field)**	2	4	
ESR (mm/hr.)	83.63±27.79	108.25±19.96	**< 0.00001***
Hemoglobin (g/dl)	11.84±1.36	9.12±2.4	**< 0.00001***
RDW (%)	17.74±1.53	18.77±1.65	**0.033***
WBCs (X10^9/L)	8430±3631	12400±8485	0.1336
Absolute Neutrophil (X10^9/L)	5453±2899	8910±7047	0.059
Absolute Lymphocyte (X10^9/L)	2160± 971	2255±1369	0.952
Absolute Monocyte (X10^9/L)	817±514	1205±1457	0.418
Platelets (X10^9/L)	288±80	302±133	0.992
MPV	7.51±0.8	7.57±0.9	0.881
NLR	3.08±2.46	5.01±4.66	
• **NLR <3:1=0 No(%)**	19(38%)	12(24%)	0.067
• **NLR ≥3:1=1 No(%)**	11(22%)	8(16%)	
dNLR	2.12±1.53	3.02±2.29	0.075
LMR	3.15±1.72	2.93±1.20	0.294
PLR	162.44±91.99	184.42±161.46	
• **PLR <120:1**	9	7	0.803
• **PLR ≥120:1**	21	13	
Neutrophil/platelet-lymphocyte ratio	49.42±58.84	73.77±69.20	0.208
Combined NLR-PLR			
• **NLR < 3 and PLR < 120**	8	5	
• **NLR < 3 and PLR > 120**	11	4	0.486
• **NLR > 3 and PLR < 120**	1	2	
• **NLR > 3 and PLR > 120**	10	9	
CRP	96.06±46.20	129.04±42.74	**0.024***
Albumin	4.21±0.6	2.99±0.22	**<0.00001**
CRP/albumin ratio	23.25±11.72	43.64±15.91	**<0.00001**
ALI= BMI x s albumin/NLR	43.48±30.62	17.92±12.93	**0.0003***

Table Continued....

Variables (Mean ±SD)	GPS/mGPS		*P value
	Score 1	Score 2	
Prognostic nutritional index (PNI)	52.63±8.50	41.27±7.29	**< 0.00001**
Neutrophil-platelet score (NPS)			
• **#N ≤7.5 & platelets ≤ 400 ×10⁹/l**	23	10	0.1439
• **#N >7.5 or platelets > 400× 10⁹/l**	6	9	
• **#N >7.5 + platelets > 400× 10⁹/l**	1	1	

*significant; ALI, advanced lung cancer inflammation index; BMI, body mass index; CRP, C-reactive protein; dNLR, derived neutrophil lymphocyte ratio; ESR, erythrocyte sedimentation rate; Hb, hemoglobin; MPV, mean platelet volume; NLR, neutrophil lymphocyte ratio; PLR, Platelet Lymphocyte Ratio; MLR, monocyte lymphocyte ratio; RDW, red cell distribution width

Correlation analysis in PTB cases (Table 5) (Figure 1) showed that:

a) BMI positively correlated with PNI, ALI, and albumin but negatively correlated with ESR, CRP, and CRP/albumin ratio.

b) PNI positively correlated with BMI, Hb, lymphocyte count, ALI, albumin and negatively correlated with ESR, NLR, MLR, PLR, CRP, and CRP/albumin ratio.

c) WBC/MPV positively correlated with ESR, lymphocyte, monocyte, neutrophil count, NLR, CRP, CRP/albumin ratio, and negatively correlated with MPV, PLR, and ALI.

d) ALI positively correlated with BMI, Hb, lymphocyte count, PNI, albumin and negatively correlated with ESR, neutrophil count, NLR, MLR, PLR, WBC/MPV, CRP, and CRP/albumin ratio.

e) CRP/albumin ratio positively correlated with ESR, neutrophil count, NLR, MLR, WBC/MPV, CRP, and negatively correlated with BMI, Hb, PNI, ALI, and albumin

f) RDW had a negative correlation with Hb and albumin.

g) CRP positively correlated with ESR, neutrophil count, WBC/MPV, PNI, and negatively correlated with BMI, albumin, and ALI.

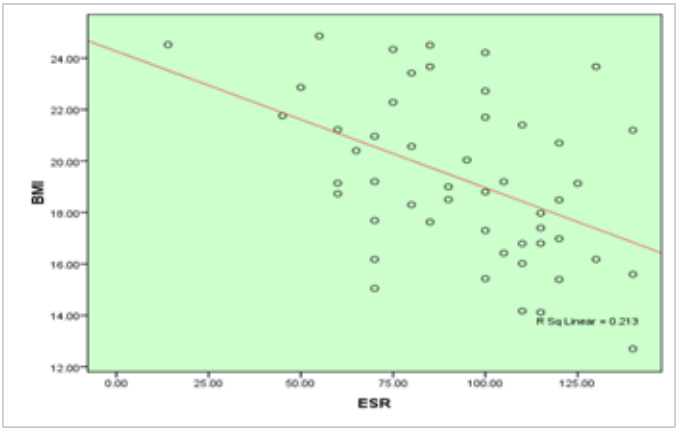
Table 5 Spearman's significant correlation in PTB cases

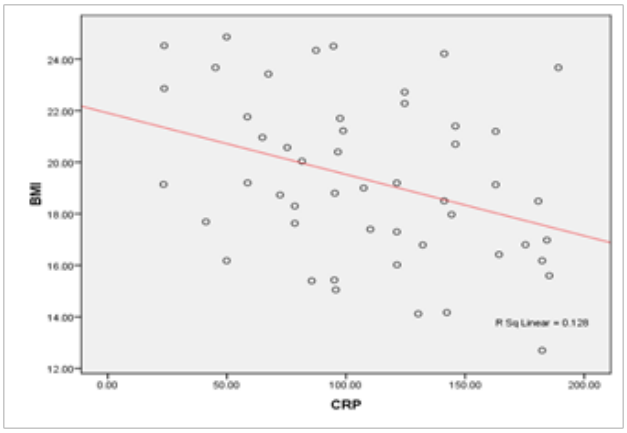
		Hb	RDW	MPV	#M	#N	#L	NLR	MLR	PLR	ESR	CRP	Albumin	WBC/MPV	CRP/alb	ALI	PNI
BMI	r	0.248									-0.461	-0.375	0.345		-0.769	0.391	0.519
	P	0.083									0.001	0.011	0.014		0.000	0.005	0.000
Hb	r	-	-0.625										0.546		0.590	0.368	0.566
	P	-	0.000										0.000		0.000	0.009	0.000
RDW	r		-														
	P		-														
MPV	r			-	0.296												
	P			-	0.037												
#M	r				-	0.469	0.547		0.590					0.527			
	P				-	0.001	0.000		0.000					0.000			
#N	r					-	0.327	0.541	0.411		0.329	0.379	-0.295	0.977	0.455	-0.470	
	P					-	0.020	0.000	0.003		0.019	0.007	0.037	0.000	0.001	0.001	
#L	r						-	-0.415		-0.606				0.427			0.599
	P						-	0.003		0.000				0.001			0.000
NLR	r							-	0.570	0.672		0.377		0.399	0.401	-0.568	-0.458
	P							-	0.000	0.000		0.007		0.004	0.004	0.000	0.001
MLR	r								-	0.301		0.315		0.351	0.320	-0.450	
	P								-	0.034		0.026		0.013	0.024	0.001	
PLR	r															-0.306	-0.388
	P															0.031	0.005
ESR	r										-	0.852	-0.375	0.328	0.828	0.483	
	P										-	0.000	0.007	0.020	0.000	0.000	
CRP	r											-	-0.334	0.323	0.928	-0.524	-0.308
	P											-	0.018	0.022	0.000	0.000	0.029

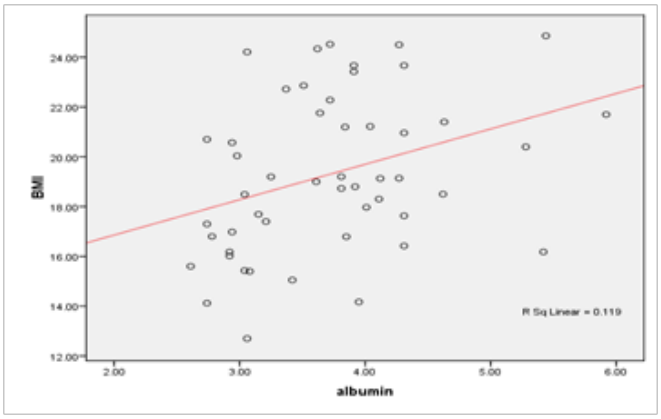
Table Continued...

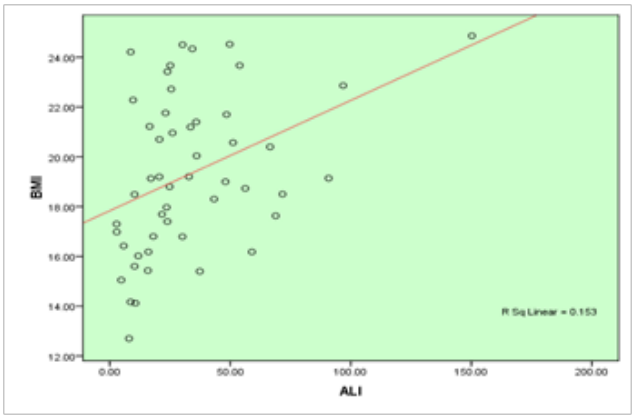
		Hb	RDW	MPV	#M	#N	#L	NLR	MLR	PLR	ESR	CRP	Albumin	WBC/MPV	CRP/alb	ALI	PNI
Albumin	r												-		**-0.610**	**0.567**	**0.806**
	P												-		**0.000**	**0.000**	**0.000**
WBC/MPV	r													-	**0.384**	**-0.393**	
	P													-	**0.006**	**0.005**	
CRP/alb	r														-	**-0.588**	**-0.514**
	P														-	**0.000**	**0.000**
ALI	r															-	**0.580**
	P															-	**0.000**

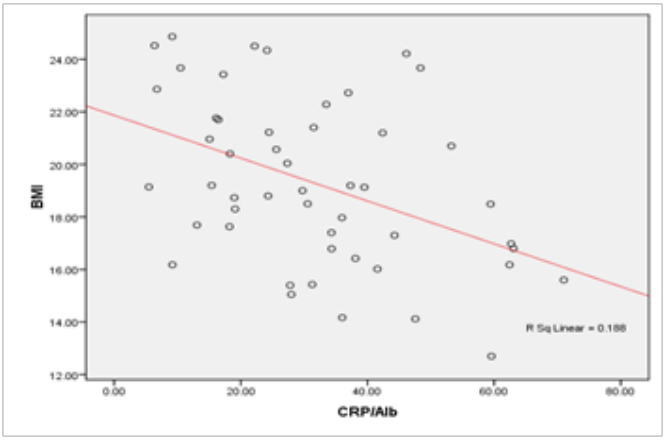
ALI, advanced lung cancer inflammation index; BMI, body mass index; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; Hb, hemoglobin; #M, absolute monocyte count; #N, absolute neutrophil count; # L, absolute lymphocyte count; MLR, monocyte lymphocyte ratio; MPV, mean platelet volume; NLR, neutrophil lymphocyte ratio; PLR, platelet lymphocyte ratio; RDW, red cell distribution width

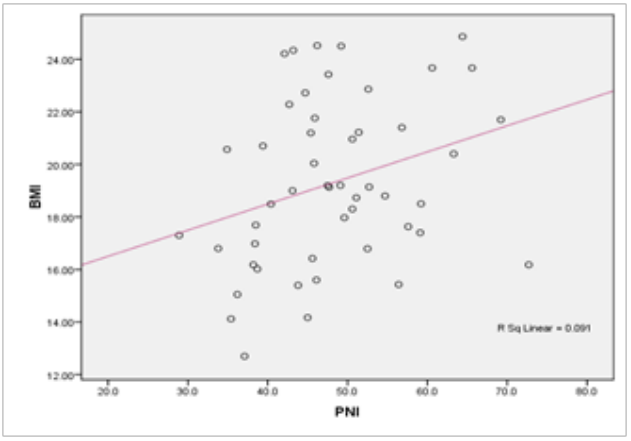












Citation: Fayed HM, Mohammed AE, Badawy MS, et al. The utility and validity of immunological, inflammatory, and nutritional-based scores and indices in active Pulmonary Tuberculosis. *Int Clin Pathol J.* 2018;6(6):199–213. DOI: 10.15406/icpjl.2018.06.00188

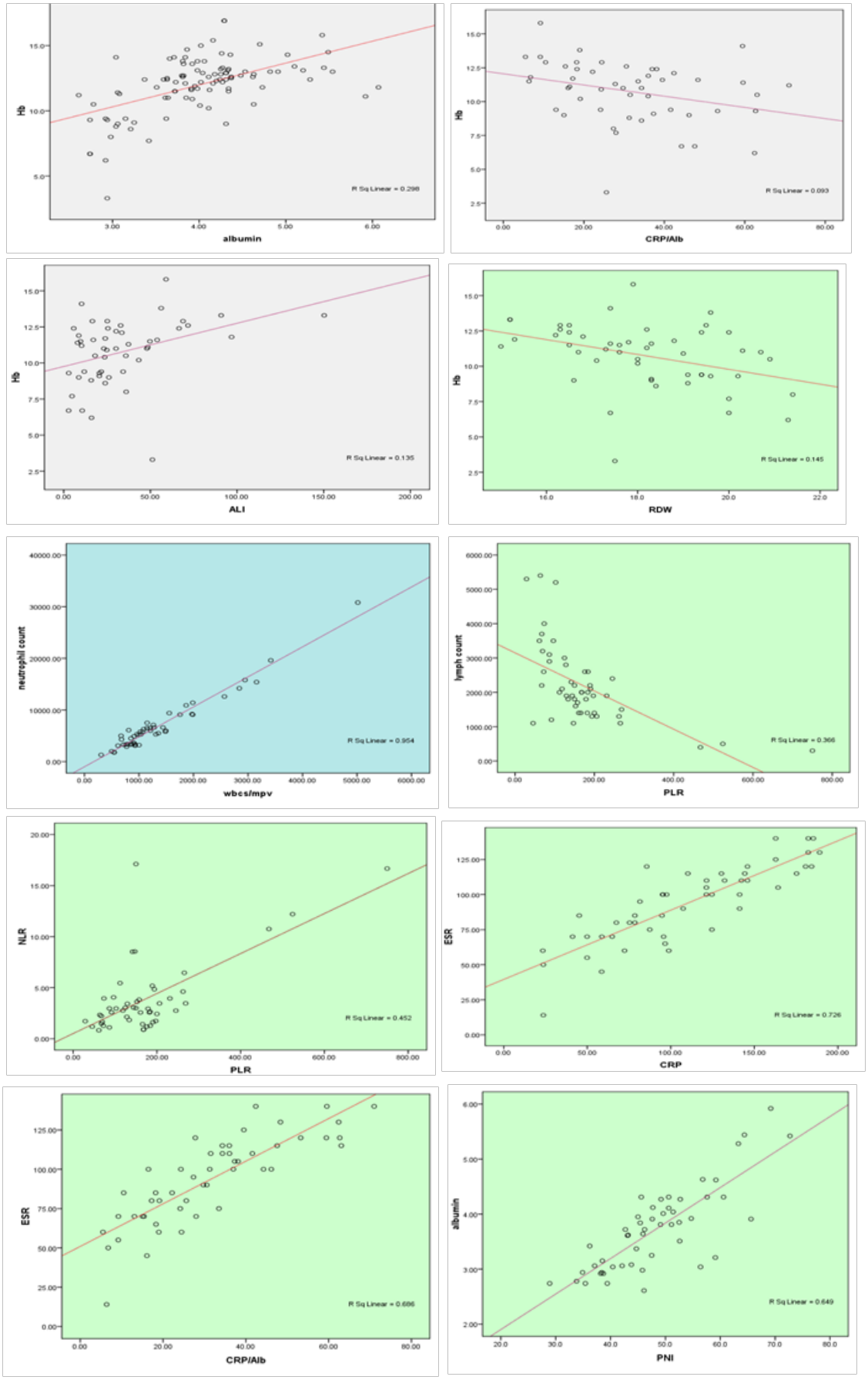


Figure 1 Correlation study between different inflammatory indices and/or markers.

Citation: Fayed HM, Mohammed AE, Badawy MS, et al. The utility and validity of immunological, inflammatory, and nutritional-based scores and indices in active Pulmonary Tuberculosis. *Int Clin Pathol J.* 2018;6(6):199–213. DOI: 10.15406/icpjl.2018.06.00188

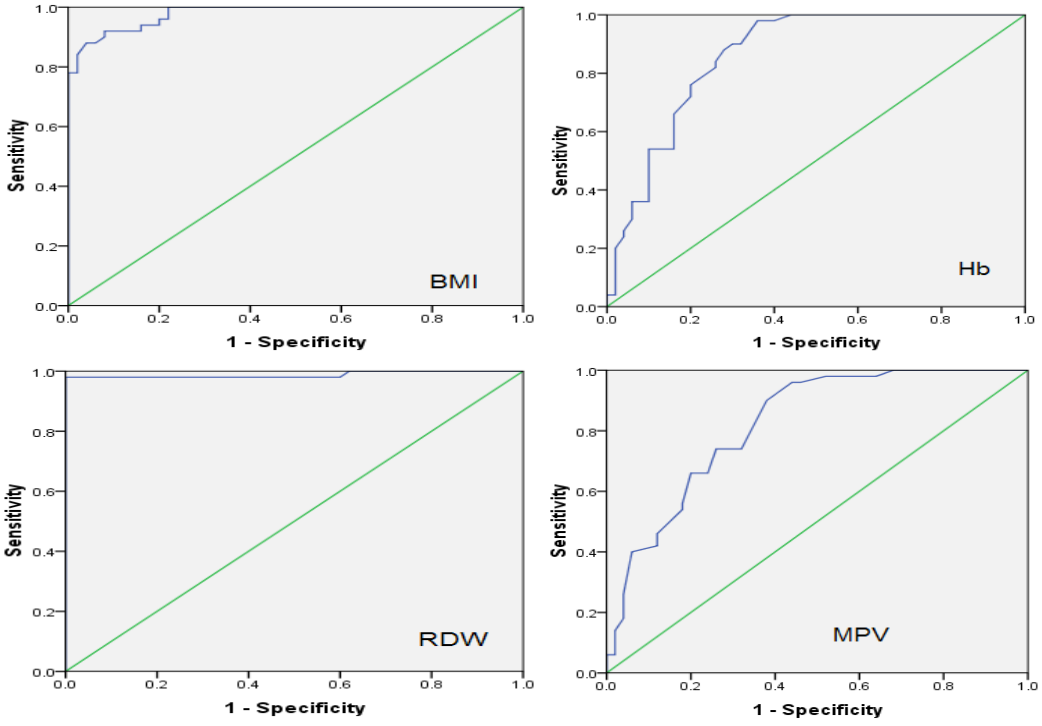
ROC curve analysis showed that the AUCs for [ESR (0.993), RDW (0.988), BMI (0.979), MLR (0.922), ALI (0.876), Hb (0.862), MPV (0.822), monocyte count (0.813), NLR (0.774), PLR (0.769), albumin (0.759) and lymphocyte count (0.728)] had a predictive value significantly superior to that of [WBC/MPV (0.658), CRP, neutrophil count and CRP/albumin ratio] and had a significant discrimination power that could differentiate PTB cases from controls.

ROC curve analyses defined the best cut off value that can discriminate PTB cases from healthy controls for MPV > (8.08 fl), serum albumin < (3.99 g/dl), BMI < (23.67 kg/m2), Hb < (12.3 g/dl), lymphocyte count < (2600×109/l), RDW > (14.8%), monocyte count > (550×109/l), and ALI < (53%). Regression analysis model confirmed that MPV, serum albumin level; BMI, Hb, lymphocyte count, and ALI had the highest odds ratio as predictors of PTB, (Table 6) (Figure 2).

Table 6 ROC curve analysis and Regression analysis for the diagnostic performance to discriminate BTB patient from healthy subjects

Parameter	Sensitivity	Specificity	Accuracy	AUC	Odds ratio	*P* value	Cut off	PPV (%)	NPV (%)
BMI (kg/m²)	86%	92%	89%	0.979	**3.178**	**0.0001***	23.67	91.49	86.79
Hb (g/dl)	74%	84%	79%	0.862	**3.151**	**0.0001***	12.3	82.22	76.36
RDW (%)	100%	98%	99%	0.988	0.159	**0.0001***	14.6	98.04	100
MPV (fl)	76%	66%	71%	0.822	**5.065**	**0.0001***	8.08	69.09	73.33
# Monocyte	68%	88%	78%	0.813	0.994	**0.0001***	550	85	73.33
# Neutrophil						0.114			
# Lymph	70%	56%	63%	0.728	**1.001**	**0.001***	2600	61.40	65.12
NLR	56%	90%	73%	0.774	0.765	**0.031***	2.70	70.18	67.16
LMR	80%	90%	85%	0.922	**2.000**	**0.0001***	0.24	88.89	81.82
PLR	68%	82%	75%	0.769	0.976	**0.0001***	117.57	79.07	71.93
WBC+MPV	50%	66%	58%	0.658	0.998	**0.004***	1040	59.52	56.90
ESR(mm/HR.)	98%	100%	99%	0.993	0.825	**0.0001***	27	100	98.04
CRP (mg/l)						0.986			
Albumin (g/dl)	68%	70%	69%	0.759	**4.165**	**0.0001***	3.99	69.39	68.63
CRP+albumin						0.983			
ALI	82%	72%	77%	0.876	**1.051**	**0.0001***	53	74.55	80

*significant; #, absluote; Alb, albumin; ALI, advanced lung cancer inflammation index= BMI+ serum albumin +NLR; AUC, Area under curve; BMI, body mass index; BNP, CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; Hb, hemoglobin; MPV, mean platelet volume; NLR, neutrophil lymphocyte ratio; PLR, platelet lymphocyte ratio; MLR, monocyte lymphocyte ratio; RDW, red cell distribution width



Citation: Fayed HM, Mohammed AE, Badawy MS, et al. The utility and validity of immunological, inflammatory, and nutritional-based scores and indices in active Pulmonary Tuberculosis. *Int Clin Pathol J.* 2018;6(6):199–213. DOI: 10.15406/icpjl.2018.06.00188

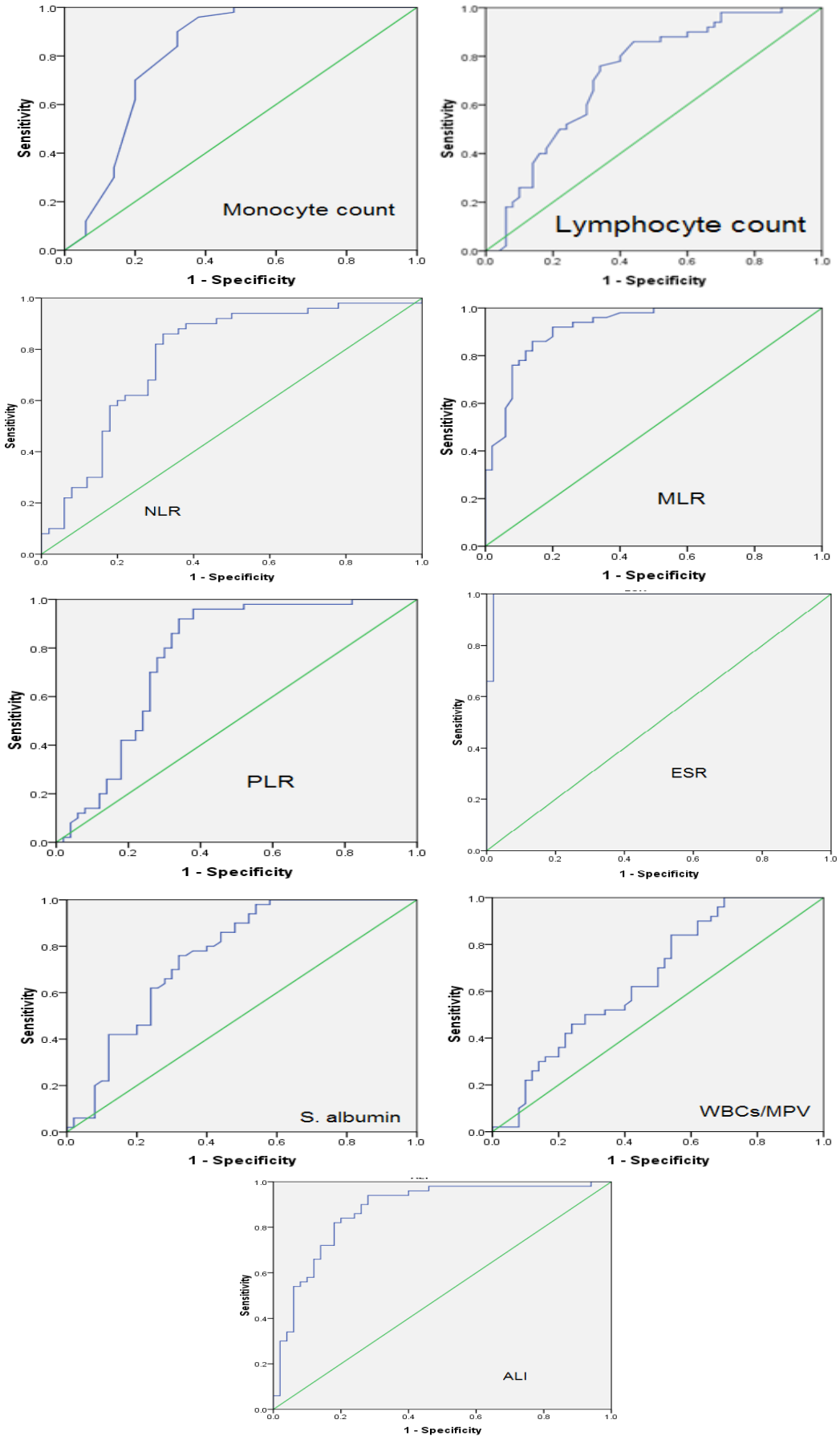


Figure 2 ROC curve diagnostic performance of inflammatory indices.

Citation: Fayed HM, Mohammed AE, Badawy MS, et al. The utility and validity of immunological, inflammatory, and nutritional-based scores and indices in active Pulmonary Tuberculosis. *Int Clin Pathol J.* 2018;6(6):199–213. DOI: 10.15406/icpjl.2018.06.00188

Discussion

In TB, the innate inflammatory immune response drives tissue destruction, morbidity, and mortality.[21] The main concern in patients with PTB is the inability of the host immune response to express bactericidal function and thus the extent of tissue pathology is related to bacillary burden and impairment of lung function.[22] In this study, ESR was significantly higher in the APTB patient s than controls, this was in agreement with other reports.[23,24] In the present study, we investigated the value of different inflammatory indices as predictive markers of APTB. We found that PTB cases had significantly higher in RDW, ESR, neutrophil and monocyte count, NLR, PLR, CRP and CRP/albumin ratio, and significantly lower BMI, Hb, lymphocyte count, MPV, MLR, LMR, and ALI but insignificant changes in WBC and platelet counts. This was consistent with many studies,[13,19,24-26] but partially consistent with Abakay and coworkers,[27] who reported lymphocytosis in active TB cases. In contrast; many studies reported leukocytosis and thrombocytosis in PTB patients with advanced stage.[28-32]

In this study, we found that TB cases had lower lymphocyte count with insignificant progressive decrease in lymphocyte count, increase in the monocyte count, platelets count, and neutrophil count with the increase in the sputum grade of infection, this was partially consistent with the finding of Deveci and co-workers[33] who found a progressive lymphopenia and reduction of T-lymphocytes in patients with more extensive pulmonary TB. Reactive thrombocytosis was reported in PTB by many authors and it was related to TB severity as an acute phase inflammatory reactant and as platelets could play important roles in TB pathogenesis by releasing chemokines associated with Th2 bias status in TB.[34,35]

In this study, we found cases of TB, had lower MPV this finding is in line with.[28,36] In contrast, Tozkoparan and his colleagues35 found significantly higher MPV in active TB patients than in inactive TB and Şahin and his colleagues reported an insignificant difference in the MPV values between TB patient group and non-TB subjects31. In this study, anemia was the most common hematological abnormality finding in PTB cases; it affects ~ 90% (of which 78 % were microcytic hypochromic and 22% were normocytic normochromic), this was in agreement with many reports.[19,25,26,30] Anemia is related to more severe forms of TB29 and associated with poorer TB outcomes,[37,38] and we found that RDW had a significant negative correlation with Hb and albumin.

In this study, PTB cases had significantly higher absolute neutrophil count; this was in contrast to Al-Omar and his colleagues, who found an insignificant higher count.[25] In this study, PTB cases had significantly lower BMI; this was in agreement with.[36] BMI showed significant correlation with inflammatory scores (positive with PNI, ALI, albumin and negative with ESR, CRP, and CRP/albumin ratio).

In our study, PTB cases had significantly increased RDW, ESR, neutrophil and monocyte count, NLR, PLR, CRP and CRP/albumin ratio, this was in agreement with.[27] This finding advocates the vital role of neutrophils in PTB as it contributes to the activation, regulation, and amplification of the immune responses.[39] As neutrophil infiltrate the inflammatory sites and phagocytose Mtb thereby inhibiting the bacillary spread initially until the accumulated macrophages get activated.[40] Thus neutrophil was considered as a probable surrogate marker in the assessment of lung inflammation and PTB disease severity.[41]

In this study TB cases had a higher ML ratio compared to healthy controls. This not significantly associated with sputum infection grade nor GPS and/or mGPS inflammatory scores. ML ratio positively correlated with neutrophil count, NLR, and N/PLR. This was in line with finding reported by Wang and his colleagues.[42]

In this study, CRP had a significant positive correlation with other inflammatory markers as ESR, neutrophil count, WBC/MPV, PNI, CRP/albumin ratio and a significant negative correlation with BMI, albumin, and ALI. This was consistent with the findings of other studies.[8,31,43-45] However; we did not find a correlation between ESR and CRP with MPV in contrast to the findings of Gunluoglu and his colleagues,[36] and Lee and his colleagues.[46]

In this study, PTB cases had significantly lower albumin level; this was in line with other studies.[47,48] PTB cases had significant albumin-based inflammatory scores as they had significantly higher (CRP/albumin ratio, GPS, mGPS), had significantly lower PNI and ALI ratios. These inflammatory scores display not only the inflammatory status but also the nutritional status of PTB patients. Therefore, might be a better predictor of the prognosis of PTB. In GPS and/or mGPS both were calculated, the serum CRP and albumin levels independently, which omitted the relationship between the two indexes. In contrast, the CRP/albumin ratio combined the two together, focusing on the interrelations between CRP and albumin; can be more convincing in practice.[49]

In this study, the CRP/albumin ratio was positively correlated with ESR, neutrophil count, WBC/MPV, NLR, MLR, CRP, and negative correlation with BMI, Hb, PNI, ALI, and albumin. This may indicate a progressive nutritional decline, ultimately clinical severity. This was consistent with the finding of low albumin and raised CRP concentration in most of PTB patients. This could specify that albumin level can impact the pathogenesis and prognosis of TB. As it was found that; people with low serum albumin levels were susceptible to TB,[50] and even they were susceptible to death.[43]

In this study, we found that PNI had a significant positive correlation with BMI, Hb, lymphocyte count, ALI, albumin, and negative correlation with ESR, NLR, MLR, PLR, CRP and CRP/albumin ratio. In this study, we found that WBC/MPV had a significant positive correlation with ESR, NLR, lymphocyte, monocyte, neutrophil count, CRP, CRP/albumin ratio, and negative correlation with MPV, PLR, and ALI. In this study, we found that ALI had a significant positive correlation with BMI, Hb, lymphocyte count, PNI, albumin, and negative correlation with ESR, neutrophil count, WBC/MPV, NLR, MLR, PLR, CRP, and CRP/ albumin ratio.

These sets of markers enable the inflammatory and nutritional factors to be merged, as it strongly influences the prognosis hence it may be used as an indicator of the extent of the inflammatory response.[51] However; Mendy and his colleagues proved that high CRP level is a good predictor of disease existence, but this was not correlated with chest radiological abnormalities.[52]

ROC curve analysis showed that ESR, RDW, BMI, MLR, ALI, Hb, MPV, monocyte, NLR, PLR, albumin, and lymphocyte count, have great judgment power that could differentiate APTB patients from healthy controls. However, Regression analysis model approved that MPV, serum albumin level; BMI, Hb, lymphocyte count, and ALI had the highest odds ratio as independent predictors of PTB. In the present study, we revealed that the GPS/mGPS had a prognostic value (along with ESR, CRP/albumin ratio, ALI, RDW, BMI, MLR, Hb, MPV, monocyte count, NLR, PLR, albumin, lymphocyte count, and PNI); as the rise of the GPS and/or mGPS score is associated with an increase in the sputum Mtb load. Therefore, they could help categorize patients with APTB.

The major limitation of this study: a small number of cases, the cross-sectional design; patients selected with a positive Mtb sputum sample; we did not correlate with other biochemical inflammatory markers, such as procalcitonin and IL-6 nor with chest radiological findings.

Conclusion

Inflammation is a major contributor associated with the PTB. Therefore, combining immunological, inflammatory and nutritional-based scores are valuable tools that reflect the degree of host inflammatory activity that promotes disease progression. These markers are not specific for TB; thus it is required for the combined use of other parameters such as clinical and radiological data.

Acknowledgments

Qena chest hospital staff members.

Author contributions

Conceived and designed the experiments: Hanan Mahmoud Fayed and Mohamed Shahat Badawy; Performed the experiments: Abdallah Elaiw Mohammed and Ayman Sabry Yassin; Wrote the original draft of manuscript and analyzed data: Hanan Mahmoud Fayed; reviewing the final draft: Mohamed Shahat Badawy, Abdallah Elaiw Mohammed and Ayman Sabry Yassin.

Conflicts of interest

The author declare no conflicts of interest.

References

1. Levinson W. Mycobacteria. In: Review of medical microbiology and immunology. New York: McGraw Hill companies; 2010. p. 150-154.
2. Ellkington PT, Friedland JS. Matrix metalloproteinases in destructive pulmonary pathology. *Thorax*. 2006;61(3):259–266.
3. Breen RA, Leonard O, Perrin FM, et al. How good are systemic symptoms and blood inflammatory markers at detecting individuals with tuberculosis? *Int J Tuberc Lung Dis*. 2008;12(1):44–49.
4. Donald PR, Diacon AH. The early bactericidal activity of anti-tuberculosis drugs: a literature review. *Tuberculosis (Edinb)*. 2008;88 Suppl 1:S75–83.
5. Ottenhoff TH. New pathways of protective and pathological host defense to mycobacteria. *Trends Microbiol*. 2012;20(9):419–428.
6. Flynn J L, Chan J. Macrophages, and control of granulomatous inflammation in tuberculosis. *Mucosal Immunol*. 2011;4(3):271–278.
7. Ong CW, Elkington PT, Friedland JS. Tuberculosis, pulmonary cavitation, and matrix metalloproteinases. *Am J Respir Crit Care Med*. 2014;190(1):9–18.
8. Caner SS, Köksal D, Ozkara S. et al. The relation of serum interleukin-2 and C-reactive protein levels with clinical and radiological findings in patients with pulmonary tuberculosis. *Tuberk Toraks*. 2007;55:238–45.
9. Kim MH, Ahn JY, Song JE, et al. The C-Reactive Protein/Albumin Ratio as an Independent Predictor of Mortality in Patients with Severe Sepsis or Septic Shock Treated with Early Goal-Directed Therapy. *PLoS ONE*. 2015;10(7):e0132109.
10. McMillan DC. An inflammation-based prognostic score and its role in the nutrition-based management of patients with cancer. *Proc Nutr Soc*. 2008;67(3):257–262.
11. Das B, Kashino SS, Pulu I, et al. CD271+ bone marrow mesenchymal stem cells may provide a niche for dormant Mycobacterium tuberculosis. *Sci Transl Med*. 2013;5(170):ra13–ra13.
12. Yodying H, Matsuda A, Miyashita M, et al. Prognostic significance of neutrophil-to lymphocyte ratio and platelet-to-lymphocyte ratio in oncologic outcomes of esophageal cancer: a systematic review ant meta-analysis. *Ann Surg Oncol*. 2016;23(2):646–654.
13. Naranbhai V, Kim S, Fletcher H, et al. The association between the ratio of monocytes: lymphocytes at age 3 months and risk of tuberculosis (TB) in the first two years of life. *BMC Med*. 2014;12:120.
14. Gideon HP, Flynn JL. Latent tuberculosis: what the host "sees"? *Immunol Res*. 2011;50(2-3):202–212.
15. World Health Organization. Treatment of Tuberculosis: Guidelines for National Programmes 2010. Geneva: WHO; 2010.
16. World Health Organization, Global Tuberculosis Control: WHO Report 2011, WHO. Geneva, Switzerland: WHO/HTM/TB/2011.16; 2011.
17. Laird BJ, Kaasa S, McMillan DC, et al. Prognostic factors in patients with advanced cancer: a comparison of clinicopathological factors and the development of an inflammation-based prognostic system. *Clin Cancer Res*. 2013;19(19):5456–5464.
18. World Health Organization (WHO). Laboratory Services in Tuberculosis Control Part II, 1998. Geneva: WHO, 1998.
19. Lee SW, Kang YA, Yoon YS, et al. The prevalence and evaluation of anemia associated with tuberculosis. *J Korean Med Sci*. 2006;21(6):1028–1032.
20. He X, Zhou T, Yang Y, et al. Advanced Lung Cancer Inflammation Index, a New Prognostic Score, Predicts Outcome in Patients With Small-Cell Lung Cancer. Clin Lung Cancer. 2015;16(6):e165–171.
21. Brilha S, Wysoczanski R, Whittington AM, et al. Monocyte Adhesion, Migration, and Extracellular Matrix Breakdown Are Regulated by Integrin αVβ3 in Mycobacterium tuberculosis Infection. *J Im munol*. 2017;199(3):982–991.
22. Hunter RL. Pathology of post primary tuberculosis of the lung: an illustrated critical review. *Tuberculosis (Edinb)*. 2011; 91(6):497–509.
23. Lawn SD, Obeng J, Acheampong JW, et al. Resolution of the acute-phase response in West African patients receiving treatment for pulmonary tuberculosis. *Int J Tuberc Lung Dis*. 2000;4(4):340–344.
24. Patience AA, Akpotuzor JO, Akwiwu C. Some Haematological Parameters of Tuberculosis (TB) Infected Africans: The Nigerian Perspective. *Journal of Natural Sciences Research*. 2012;2(1):50–57.
25. Al-Omar AI, Al-Ashban RM, Shah AH. Hematological abnormalities in Saudis suffering from pulmonary tuberculosis and their response to the treatment. *Research journal of Pharmacology*. 2009;3(4):78–85.
26. Sei W L, Ae Kang Y, Soon YY, et al. The Prevalence and Evolution of Anemia Associated with Tuberculosis. *J Korean Med Sci*. 2006;21(6):1028–1032.
27. Abakay O, Abakay A, Sen HS, et al. The relationship between inflammatory marker levels and pulmonary tuberculosis severity. *Inflammation*. 2015;38(2):691–696.
28. Baynes BMRD, Bothwell TH, Flax H, et al. Reactive thrombocytosis in pulmonary tuberculosis. *J Clin Pathol*. 1987;40(6):676–679.
29. Morris CD, Bird AR, Nell H. The haematological and biochemical changes in severe pulmonary tuberculosis. *Q J Med*. 1989;73(272):1151–1159.
30. Olaniyi JA, Aken'Ova YA. Haematological profile of patients with pulmonary tuberculosis in Ibadan, Nigeria. *Afr J Med Med Sci*. 2003;32(3):239–242.
31. Şahin F, Yazar E, Yıldız P. Prominent features of platelet count, plateletcrit, mean platelet volume and platelet distribution width in pulmonary tuberculosis. *Multidiscip Respir Med*. 2012;7(1):12–38.
32. Yaranal PJ, Umashankar T, Harish SG. Hematological profile in pulmonary tuberculosis. *IJHRS*. 2013;2(1):50–55.

33. Deveci F, Akbulut HH, Celik I, Muz MH, et al. Lymphocyte Subpopulations in Pulmonary Tuberculosis Patients. *Mediators Inflamm*. 2006;2006(2):89070.

34. Feng Y, Yin H, Mai G, et al. Elevated serum levels of CCL17 correlate with increased peripheral blood platelet count in patients with active tuberculosis in China. *Clin Vaccine Immunol*. 2011;18(4):629–632.

35. Tozkoparan E, Deniz O, Ucar E, et al. Changes in platelet count and indices in pulmonary tuberculosis. *Clin Chem Lab Med*. 2007;45(8):1009–1013.

36. Gunluoglu G, Yazar EE, Veske NS, et al. Mean platelet volume as an inflammation marker in active pulmonary tuberculosis. *Multidiscip Respir Med*. 2014;9(1):11.

37. Isanaka S, Mugusi FM, Urassa W, et al. Iron Deficiency and Anemia Predict Mortality in Patients with Tuberculosis. *J Nutr*. 2012;142(2):350–357.

38. Kourbatova EV, Borodulin BE, Borodulina EA, et al. Risk factors for mortality among adult patients with newly diagnosed tuberculosis in Samara, Russia. *Int J Tuberc Lung Dis*. 2006;10(11):1224–1230.

39. Mantovani A, Cassatella MA, Costantini C, et al. Neutrophils in the activation and regulation of innate and adaptive immunity. *Nat Rev Immunol*. 2011;11(8):519–31.

40. Pokkali S, Rajavelu P, Sudhakar R, et al. Phenotypic modulation in Mycobacterium tuberculosis infected neutrophil during tuberculosis. *Indian J Med Res*. 2009;130:185–192.

41. Gopal R, Monin L, Torres D, et al. S100A8/A9 Proteins Mediate Neutrophilic Inflammation and Lung Pathology during Tuberculosis. *Am J Respir Crit Care Med*. 2013;188(9):1137–1146.

42. Wang J, Yin Y, Wang X, et al. Ratio of monocytes to lymphocytes in peripheral blood in patients diagnosed with active tuberculosis. *Braz J Infect Dis*. 2015;19(2):125–131.

43. Kim CW, Kim SH, Lee SN, et al. Risk factors related with mortality in patient with pulmonary tuberculosis. *Tuberc Respir Dis*. 2012;73(1):38–47.

44. Muller BLA, Ramalho DM de P, dos Santos PFG, et al. Inflammatory and immunogenetic markers in correlation with pulmonary tuberculosis. *J Bras Pneumol*. 2013;39(6):719–727.

45. Peresi E, Silva SM, Calvi SA, et al. Cytokines and acute phase serum proteins as markers of inflammatory regression during the treatment of pulmonary tuberculosis. *J Bras Pneumol*. 2008;34(11):942–949.

46. Lee MY, Kim YJ, Lee HJ, et al. Mean Platelet Volume in Mycobacterium tuberculosis Infection. *Bio Med Research International*. 2016:7508763.

47. Sanchez A, Azen C, Jones B, et al. Relationship of Acute Phase Reactants and Fat Accumulation during Treatment for Tuberculosis. *Tuberc Res Treat*. 2011:346295.

48. Wang C, Wei LL, Shi LY, et al. Screening and identification of five serum proteins as novel potential biomarkers for cured pulmonary tuberculosis. *Scientific Reports*. 2015;5:15615.

49. Fairclough E, Cairns E, Hamilton J, et al. Evaluation of a modified early warning system for acute medical admissions and comparison with C-reactive protein/albumin ratio as a predictor of patient outcome. *Clin med*. 2009;9(1):30–33.

50. Cegielski JP, Arab L, Cornoni-Huntley J. Nutritional risk factors for tuberculosis among adults in the United States (1971–1992). *Am J Epidemiol*. 2012;176(5):409–422.

51. Ranzani OT, Zampieri FG, Forte DN, et al. C-reactive protein/albumin ratio predicts 90-day mortality of septic patients. *PloS one*. 2013;8(3):e59321.

52. Mendy J, Togun T, Owolabi O, et al. C-reactive protein, Neopterin, and Beta2 microglobulin levels pre and post TB treatment in The Gambia. *BMC Infect Dis*. 2016;16:115.

Citation: Fayed HM, Mohammed AE, Badawy MS, et al. The utility and validity of immunological, inflammatory, and nutritional-based scores and indices in active Pulmonary Tuberculosis. *Int Clin Pathol J.* 2018;6(6):199–213. DOI: 10.15406/icpjl.2018.06.00188