

## Association between clinical parameter, laboratorium and radiology along with validation of scoring system with lung tuberculosis status in adult HIV patients



Wayan Evie Frida Yustin<sup>1\*</sup>, I Ketut Agus Somia<sup>2</sup>, Ni Luh Putu Eka Arisanti<sup>1</sup>,  
I G N Bagus Ngurah Artana<sup>1</sup>, Ida Ayu Jasminarti Dwi Kusumawardani<sup>1</sup>,  
Ni Wayan Candrawati<sup>1</sup>, Ida Bagus Ngurah Rai<sup>1</sup>

### ABSTRACT

**Background:** Many obstacles are commonly found in diagnosing tuberculosis in HIV patients, increasing the risk of morbidity and mortality in patients. This study aimed to assess the association of several clinical, laboratory and radiological parameters to pulmonary TB status in adult HIV patients.

**Method:** This was an observational analytic study with cross-sectional design conducted in Bali from January to June 2021, involved patients with HIV. Bivariate analysis was performed with chi-square, while multivariate analysis with multiple logistic regression. The adjusted odds ratio indicates the association of each parameter with pulmonary TB status and used as the base to compile a score for adult TB.

**Results :** From 105 subjects, 92 subjects met the research requirements. The results of the multivariate analysis obtained several significant variables ( $p < 0.05$ ); cough (OR: 17.0), shortness of breath (OR: 21.0), fever (OR: 20.0), weight loss (OR: 5.5), night sweats (OR: 31.6), chest radiograph (OR: 80.0), geneXpert (OR: 27.8), neutrophils (OR: 6.2), NLR (OR: 10.7), MLR (OR: 11.3) and ESR (OR: 11.9). The results of pulmonary TB scoring in adult HIV patients with a value of  $> 55$  indicate pulmonary TB and  $< 55$  non-pulmonary TB with a significant validity test result ( $p$ -value  $< 0.001$ ).

**Conclusion:** Clinical, laboratory and radiological parameters have a significant relationship with TB status in adult HIV patients and can be used as complements to the gold standard if the results of the XpertMtb examination are doubtful or not in accordance with the patient's clinical course.

**Keywords:** Clinical, laboratorium, radiology, TB status, Human immunodeficiency virus (HIV), XpertMtb.

**Cite This Article:** Yustin, W.E.F., Somia, I.K.A., Arisanti, N.L.P.E., Artana, I.G.N.B.A., Kusumawardani, I.A.J.D., Candrawati, N.W., Rai, I.B.N. 2021. Association between clinical parameter, laboratorium and radiology along with validation of scoring system with lung tuberculosis status in adult HIV patients. *Bali Medical Journal* 10(3): 1085-1092. DOI: 10.15562/bmj.v10i3.2787

<sup>1</sup>Pulmonology and Respiratory Department, Faculty of Medicine, Universitas Udayana/Sanglah Hospital, Denpasar, Bali, Indonesia

<sup>2</sup>Tropical and Infectious Disease Division, Internal Medicine Department, Faculty of Medicine, Universitas Udayana/Sanglah Hospital, Denpasar, Bali, Indonesia

\*Corresponding:

Wayan Evie Frida Yustin; Pulmonology and Respiratory Department, Faculty of Medicine, Universitas Udayana/Sanglah Hospital, Denpasar, Bali, Indonesia; evie.youth@gmail.com

Received: 2021-10-13

Accepted: 2021-12-20

Published: 2021-12-30

### INTRODUCTION

Despite the progress Indonesia has made, the number of new tuberculosis cases in Indonesia is still ranked third in the world and is one of the biggest challenges, requiring attention from all stakeholders, since it provides a high burden of morbidity and mortality. Tuberculosis (TB) is the leading cause of death after ischemic heart disease and cerebrovascular disease. In 2017, the death rate from tuberculosis was 40/100,000 population (without TB-HIV) and 3.6 per 100,000 population (including TB-HIV).<sup>1,2</sup>

Human immunodeficiency virus (HIV) patients are one of the high-risk groups for pulmonary TB infection,

therefore screening is necessary. Clinically, the symptoms of HIV patients vary widely with atypical radiological features.<sup>3</sup> Chest X-rays may appear normal in severe HIV patients. Currently, the standard for diagnosis of pulmonary TB infection is the Xpert/MTB RIF examination, however it is not easily implemented.<sup>4,5</sup>

Lots of obstacles are commonly found, such as the difficulty of obtaining representative sputum and negative Xpert/MTB RIF results in severe HIV patients with CD4 counts  $< 200/\text{mm}^3$ , leads to underdiagnosis and delays in treatment. This will certainly increase the risk of morbidity and mortality in patients.

Another challenge in handling pulmonary TB infection is the availability

of Xpert MTB/RIF facilities as the gold standard for diagnosis of pulmonary TB in HIV patients, which is still very limited, especially in primary health care facilities and in peripheral hospitals in Indonesia. This will certainly be an obstacle for clinicians to establish a diagnosis of pulmonary TB which can cause delays in diagnosis, thereby increasing the risk of death in patients. An easier standard of diagnosis is needed to be able to detect pulmonary TB early in HIV patients.

Several parameters exist such as clinical, laboratory and radiological parameters that can be used as guidelines to support the diagnosis of pulmonary TB. This study aimed to determine the association of these parameters with pulmonary TB

status in adult HIV patients. Subsequently, we aimed to develop a systematic scoring system, utilizing the indicator of each parameter. The scoring system eases clinicians to determine the diagnosis of pulmonary TB in adult HIV patients.

## METHODS

This was an observational analytic study with cross sectional design. The study was conducted in Bali from January to June 2021. The sample was taken with simple random sampling method. Simple random sampling was chosen by making a list of patients diagnosed with HIV in the period January to June 2021. The patient list was made in Microsoft excel format and then the sample was entered in STATA from the minimum number of samples. The inclusion criteria in this study were HIV patients aged 18 years and over and seeking treatment at the hospital from January to June 2021. Subjects who refused to participate after good informed consent were HIV patients with severe comorbidities such as type 2 diabetes, Stage 5 CKD, stroke, malignancy and pregnancy were excluded from this study.

Based on the calculation of the sample size for the validity test, the minimum sample size is 92. All samples underwent a history and physical examination, then the results of laboratory tests, chest radiographs and geneXpert were obtained from medical records. The data collected will then be analyzed statistically with Statistical Package for Social Science (SPSS) 24.0 software. Univariate analysis presents data in the form of frequency, mean and standard deviation. Bivariate analysis was performed with Chi-Square, while multivariate analysis with multiple logistic regression.

The adjusted odds ratio indicates the strength of the association between the variables with pulmonary TB status and is used as a weighting factor to develop a score for pulmonary TB in adult HIV patients. Validity test was used to assess the ability of the score in diagnosing pulmonary TB in adult HIV patients. The validity test consisted of receiver operating curve (ROC) analysis to determine the cut-off point for detecting pulmonary TB in adult HIV patients and then calculated the sensitivity, specificity, negative predictive

value (NPV), positive predictive value (PPV) and accuracy of these scores.

## RESULTS

From the total of 105 subjects, 92 subjects met the research requirements, predominantly with male (79.3%), aged

26-50 years (79.3%) with a mean age of 37 years. The majority of samples have a high school education or equivalent (60.9%), and work in the private sector (66.3%). A total of 22 people (23.9%) were diagnosed with pulmonary TB, 22 (23.9%) had clinical TB and 48 people (52.2%) were not with TB (**Table 1**).

**Table 1. Baseline characteristic of subjects (n= 92)**

Variable	Mean	N	%
Age (years)	36.79±10.45		
18-25		12	13.0
26-50		73	79.3
51-80		7	7.6
Gender			
Male		73	79.3
Education			
Elementary school/junior high school		22	23.9
Senior high school		56	60.9
Graduate		14	15.2
Occupation			
Housewives		13	14.1
Private sectors		61	66.3
Civil worker		3	3.3
Army/police		3	3.3
Student		5	5.4
Not working		7	7.6
Family contact history			
Yes		4	4.3
Status			
Lung TB		44	47.8
Not lung TB		48	52.2

**Table 2. Main complaints of subjects (n= 92)**

Variable	n	%
Chief complaint		
Cough	33	35.9
Fever	7	7.6
Diarrhea	7	7.6
Weakness	8	8.7
Shortness of breath	10	10.9
Oral ulcer	7	7.6
Decrease of weight	6	6.5
Medical Check Up	5	5.4
Lump in anus	1	1.1
Melena	1	1.1
Dizzy	1	1.1
Lump in the chest	1	1.1
Itchy	3	3.2
Pain in swallowing	1	1.1
Lump in the neck	1	1.1

The main complaint of subjects when they came to the hospital in general was cough (35.9%), followed by shortness of breath (10.9%), weakness (9.7%), fever and diarrhea (7.6%) (Table 2).

The most common symptoms was fever (59.8%), followed by weight loss (83.7%), night sweats (44.6%), oral ulcer (62.0%), and pruritic papular eruption (PPE) (29.3%). A total of 6.5% had enlarged lymph nodes (Table 3).

The mean results of laboratory tests were  $7.15 \times 10^3/\text{mm}^3$  for leucocytes, 1.55% for lymphocytes, 5.49% for neutrophils, 0.76% for monocytes, 8.51 for neutrophil-to-lymphocytes (NLR) ratio, 0.88 for monocyte-to-lymphocytes (MLR) ratio, 55.88 for erythrocyte sedimentation rate (ESR), 11.54 g/dL for hemoglobin and 130.58 cells/ $\text{mm}^3$  for CD4. A total of 44.6% had a typical chest x-ray of pulmonary TB and 21.7% had a positive GeneXpert test result (Table 4).

The chest radiograph suggestive of TB obtained in the subjects consisted of 15 subjects with fibroinfiltrate, 16 subjects with consolidation, 3 subjects with miliary appearance, 2 subjects with multiple cavities, 3 subjects with pleural effusion and consolidation, 1 subject with fibroinfiltrates and cavities and 1 subject with multiple nodules and consolidation with thick-walled cavities. Cough, shortness of breath, fever, night sweats, anemia, chest radiograph and geneXpert were significantly related to the patient's pulmonary TB status (Table 5).

Cough was commonly found in pulmonary TB patients (39.1%), only 31.5% of patients with shortness of breath had TB. A total of 40.2% of patients with fever and 40.2% of patients who had decreased weight had pulmonary TB. A total of 35.9% of pulmonary TB patients experienced night sweats, while 40 people (43.6%) did not experience night sweats. Only one person had close contact with a pulmonary TB patient.

Subjects who experienced oral candidiasis generally did not have pulmonary TB (31.5%). Pruritus was also generally not experienced by subjects with pulmonary TB (14 people, 15.2%). Thoracic examination which was suggestive of TB made the patient diagnosed with pulmonary TB and almost

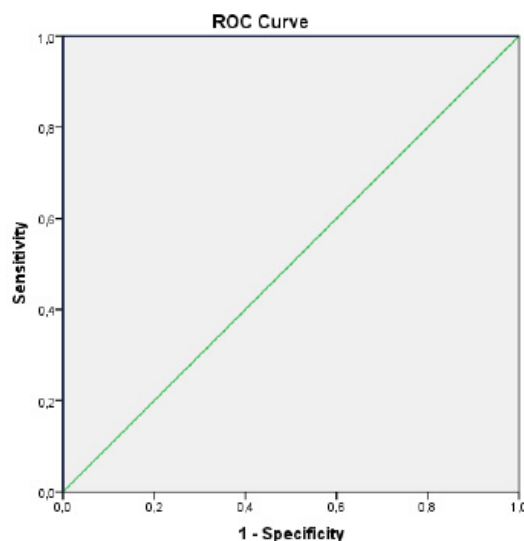
**Table 3. Symptoms of subjects (n= 92)**

Variable	n	%
Cough	55	59.8
Shortness of breath	38	41.3
Fever	55	59.8
Decrease of weight	77	83.7
Sweating at night	41	44.6
Oral candidiasis	57	62.0
Pruritic Papular Eruption (PPE)	27	29.3
Lymph node enlargement	6	6.5

**Table 4. Laboratorium parameters of subjects (n= 92)**

Variable	Mean	N	%
Hemoglobin (gr/dL)	11.54±2.45		
>10		67	72.8
<10		25	27.2
CD4 value (cells/ $\text{mm}^3$ )	130.48±110.70		
<200		71	77.2
200-400		15	16.3
>400		6	6.5
Leucocytes ( $\times 10^3/\text{mm}^3$ )	7.15±4.88		
Lymphocytes (%)	1.55±1.00		
Neutrophil (%)	5.49±3.47		
Monocyte (%)	0.76±0.48		
NLR	8.51±3.68		
MLR	0.88±0.43		
ESR	55.88±36.03		
Chest X-Ray			
Lung TB		41	44.6
Not lung TB		51	55.4
Sputum GeneXpert			
Yes		20	21.7
No		72	78.3

NLR: neutrophil-to-lymphocytes ratio, MLR: monocyte-to-lymphocytes ratio, ESR: erythrocyte sedimentation rate



**Figure 1.** Receiver operating curve analysis

all chest X-ray examinations which were not suggestive of TB did not lead to the diagnosis. All laboratory parameters analyzed with receiver operating curve (ROC) analysis to obtain the area under the ROC Curve (AUC) (Figure 1).

Several parameters were associated with TB status (AUC > 0.5); leukocytes (AUC = 0.59), neutrophils (AUC = 0.64), NLR (AUC = 0.74), MLR (AUC = 0.61), and ESR (AUC= 0.74). Those five parameters analyzed for sensitivity, specificity, negative predictive value

(NPV) and positive predictive value (PPV) tests (Figure 2). The optimal cut-off point (COP) of the five parameters is determined based on the AUC of each ROC.

Table 6 shows that neutrophils, NLR, MLR and ESR significantly associated with pulmonary TB status based on statistical tests. Leukocyte was not significantly associated with pulmonary TB status. The results of sensitivity, specificity, PPV and NPV tests for clinical and laboratory parameters depicted in Table 7.

Table 8 showed the results of the multivariate analysis by adjusting for

other factors in this study. The results of the multivariate analysis showed several significant variables based on statistical calculations, including cough (OR: 17.0,  $p < 0.001$ ), shortness of breath (OR: 21.0,  $p < 0.001$ ), fever (OR: 20.0,  $p < 0.001$ ), weight loss (OR: 5.5,  $p = 0.01$ ), night sweats (OR: 31.6,  $p < 0.001$ ), chest radiograph (OR: 80.0,  $p < 0.001$ ), geneXpert (OR: 27.8,  $p < 0.001$ ), neutrophils (OR: 6.2,  $p = 0.01$ ), NLR (OR: 10.7,  $p = 0.01$ ), MLR (OR: 11.3,  $p = 0.01$ ), ESR (OR: 11.9,  $p = 0.01$ ) and overall (OR: 85.9,  $p < 0.001$ ). A scoring system was developed based on the significant variables in Table 8. The description of the scoring system depicted in Table 9. The ROC curve based on the scoring system showed in Figure 3.

The above curve shows that the AUC was 1.00, which indicates that the scoring system can be used with a COP of 55.25 (100% sensitivity and 100% specificity). A 2 x 2 table was performed to measure the sensitivity, specificity, NPV and PPV of the scoring system.

This study showed that as many as 44 people or all patients with a score of >55 were diagnosed with pulmonary TB, while 48 people with a score of <55 were diagnosed with non-pulmonary TB ( $p < 0.001$ ). This scoring system had sensitivity, specificity, NPV and PPV of 100%.

**Table 5. Association between clinical manifestation, laboratory parameters and chest X-Ray with lung TB status**

Variable	Lung TB		Not Lung TB		OR	p-value
	n	%	n	%		
Cough						
Yes	36	39.1	19	20.7	6.8	< 0.001*
No	8	8.7	29	31.5		
Shortness of Breath						
Yes	29	31.5	9	9.8	8.3	< 0.001*
No	15	16.3	39	42.4		
fever						
Yes	37	40.2	18	19.6	8.8	< 0.001*
No	7	7.6	30	32.6		
Decrease of Weight						
Yes	41	44.6	36	39.1	4.5	0.18
No	3	3.3	12	13.0		
Night Sweats						
Yes	33	35.9	8	8.7	15.0	< 0.001*
No	11	12.0	40	43.6		
History of TB Contact						
Yes	1	1.1	3	3.3	0.3	0.35
No	43	46.7	45	48.9		
Oral Candidiasis						
Yes	28	30.4	29	57	1.1	0.74
No	16	17.4	19	35		
PPE						
Yes	13	14.1	14	15.2	1.0	0.96
No	31	33.7	34	37.0		
Anemia						
>10 (gr/dL)	26	38.8	41	61.2	4.05	< 0.001*
<10 (gr/dL)	18	72.0	7	28.0		
CD4						
<200 (cells/mm <sup>3</sup> )	38	41.3	33	35.9	4.1	0.12
200-400 (cells/mm <sup>3</sup> )	4	4.3	11	12.0		
>400 (cells/mm <sup>3</sup> )	2	2.2	4	4.3		
Chest X-Ray Suggestive of TB						
Yes	41	44.6	0	0	-	< 0.001*
No	3	3.3	48	52.2		
Sputum GeneXpert						
Yes	20	21.7	0	0	-	< 0.001*
No	24	26.1	48	52.2		
Lymph Node Enlargement						
Yes	5	5.4	1	1.1	6.0	0.07
No	39	42.4	47	51.1		

PPE: Pruritic Papular Eruption

## DISCUSSION

A total of 44 people (47.8%) were diagnosed with pulmonary TB and as many as 48 people (52.2%) were not. Most of the study subjects were male and age 26-50 years. Martino's study (2020) showed that the patients in their study were also predominantly male (58.7%) with a mean age of 35 years.<sup>6</sup> Similar characteristics were also demonstrated by the Canadian study.<sup>7</sup>

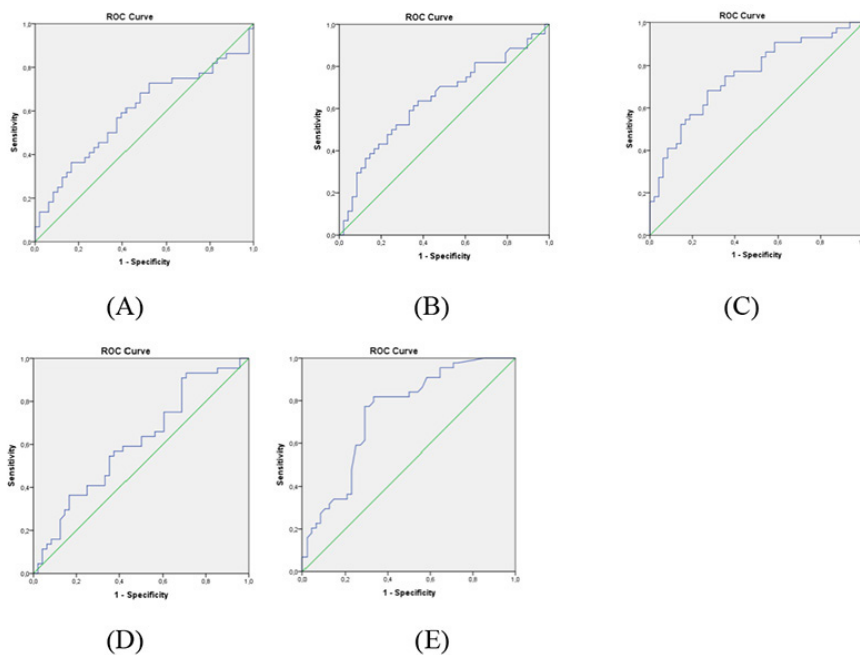
The majority of the subjects had a high school education (60.9%) followed by elementary/junior high school 23.9%. The subjects of this research mostly work in the private sector. The effects of housing status, education and race tend to have a general explanation in terms of low socioeconomic status. This is related to facing more pressing problems and reduced access to health services.<sup>8</sup> Lamria showed that participants with less than junior high school education had almost



**Table 6. Association between laboratorium parameters with pulmonary TB status**

Variable	Pulmonary TB		Not Pulmonary TB		OR	p-value
	n	%	n	%		
Leucocyte (x10 <sup>3</sup> /μL)						
>5.8	29	31.5	23	25.0	0.4	0.08
≤5.8	15	16.3	25	27.2		
Neutrophil (x10 <sup>3</sup> /μL)						
>3.0	28	30.4	18	19.6	0.3	<b>0.01*</b>
≤3.0	16	17.4	30	32.6		
NLR						
>2.27	34	37.0	21	22.8	0.2	<b>&lt; 0.001*</b>
≤2.27	10	10.9	27	29.3		
MLR						
>0.35	40	43.5	29	31.5	0.1	<b>&lt; 0.001*</b>
≤0.35	4	4.3	19	20.7		
ESR (mm/hours)						
>36	37	40.2	24	26.1	0.1	<b>&lt; 0.001*</b>
≤36	7	7.6	24	26.1		

NLR: neutrophil-to-lymphocytes ratio, MLR: monocyte-to-lymphocytes ratio, ESR: erythrocyte sedimentation rate

**Figure 2.** AUC for (A) leucocytes, (B) Neutrophils, (C) NLR, (D) MLR, and (E) ESR

1.5 times the risk of developing TB.<sup>9</sup>

HIV-infected people with pulmonary TB can have the classic symptoms of TB, but many pulmonary TB patients also have few or even less specific symptoms. A small proportion of HIV patients with pulmonary TB have minimal or no symptoms, especially in developing countries with high burdens of HIV and TB infection.<sup>10</sup>

The main complaints that made the subject come to the hospital in this study were cough (35.9%), followed by shortness of breath (10.9%), weakness (9.7%), fever and diarrhea (7.6%). While the complaints that were generally experienced by the subjects were 83.7% weight loss, 62.0% oral candidiasis, 59.8% fever, 44.6% night sweats, and 29.3% PPE. As many as 6.5% had enlarged lymph nodes. Mirambo et

al.<sup>11</sup> also showed that cough was the most common symptom (94.4%), followed by weight loss (69.3%), fever (68.7%), night sweats (36%), anorexia (23%). % and chest pain (8%).

Patel et al also showed that cough was the most common symptom in (94%) patients followed by fever, weight loss, and loss of appetite 86%, 78%, and 62%, respectively. Shortness of breath, chest pain and hemoptysis were found in 56%, 20%, and 14%, respectively. The mean duration of the most common symptom (cough) was 12 weeks, whereas fever and weight loss are between 14 and 12 weeks.<sup>12,13</sup>

The results of the multivariate analysis obtained several significant variables based on statistical calculations after adjusting for other variables, including cough, shortness of breath, fever, weight loss and night sweats. Salwani showed that fever and weight loss were clinical symptoms associated with the diagnosis of pulmonary TB in HIV in a multivariate analysis. The sensitivity and specificity of fever alone were 80% and 50% with PPV 41.4% and NPV 85.4%, respectively. The sensitivity for weight loss was 80%, specificity was 45.7%, PPV was 38.7%, and NPV was 84.2%. The ability to diagnose combined clinical symptoms for the diagnosis of pulmonary TB in HIV with an AUC value of 71.9% (p = 0.001; 95% CI = 0.60-0.82).<sup>14</sup>

The diagnosis of pulmonary TB in patients with HIV is difficult because the clinical manifestations of TB with HIV coinfection are non-specific, chest radiographs do not always show cavitary changes and patients can come with complications that interfere with the focus in making a diagnosis. Therefore, a high index of clinical suspicion and a systematic approach to diagnostic testing are needed to establish the diagnosis of TB in immunocompromised patients.<sup>15,16</sup>

Patients can be diagnosed with pulmonary TB even though the smear test results are negative based on the revision of the WHO regarding the elimination of suspected TB and becoming clinical TB. It defined as someone who does not meet the bacteriologically confirmed criteria but has been diagnosed as active pulmonary TB by a clinician or other medical practitioner who decides had complete administration

**Table 7. Association between laboratorium parameters with TB status**

Variable	Sensitivity	Specificity	PPV	NPV
Cough	81.82	60.42	65.45	78.38
Shortness of breath	65.91	81.25	76.32	72.22
Fever	84.09	62.50	67.27	81.08
Decrease of body weight	93.18	25.00	53.00	80.00
Night sweats	75.00	83.33	80.49	78.43
Chest X-Ray	93.18	100	100	94.12
GeneXpert	45.45	100	100	66.67
Leucocytes	65.91	52.05	55.77	62.50
Neutrophils	63.64	62.50	60.87	65.22
NLR	77.27	56.25	61.82	72.97
MLR	90.91	39.58	57.97	82.61
ESR	84.09	50.00	60.66	77.42

**Table 8. Multivariate analysis results after adjusted**

Variable	OR	p-value
Cough	17.0	< 0.001*
Shortness of breath	21.0	< 0.001*
Fever	20.7	< 0.001*
Decrease of body weight	5.5	0.01*
Night sweats	31.6	< 0.001*
History of TB contact	0.8	0.35
Oral candidiasis	0.1	0.75
PPE	0.0	0.96
Anemia	6.3	0.12
CD4	3.1	0.07
GeneXpert	27.8	< 0.001*
Chest X-Ray	80.0	< 0.001*
Lymph node enlargement	3.2	0.07
Leucocytes	3.0	0.08
Neutrophils	6.2	0.01*
NLR	10.7	0.01*
MLR	11.3	0.01*
ESR	11.9	0.01*
Overall	85.9	< 0.001*

**Table 9. Scoring system**

Variable	Score
<b>Clinical symptoms</b>	
Cough	8
Shortness of breath	9
Fever	9
Decrease of body weight	5
Night sweats	13
<b>Radiology</b>	
Chest X-Ray suggestive of pulmonary TB	35
<b>Laboratorium</b>	
Neutrophils >3	3
NLR >2,27	6
MLR >0,35	6
ESR >36	6
<b>Total</b>	<b>100</b>

of anti-TB drugs.<sup>17</sup>

Laboratory examination of the patients in this study found that the mean leukocytes of the patients were  $7.15 \times 10^3/\text{mm}^3$ , lymphocytes 1.55%, neutrophils 5.49%, monocytes 0.76%, NLR 8.51, MLR 0.88, ESR 55.88, Hb 11.54 g/dL and CD4 levels 130. Lee's study also showed that most TB patients were at an advanced stage of HIV infection, in which 93% had CD4 counts  $<200/\text{mm}^3$ .<sup>18</sup>

The results of laboratory tests conducted at H. Adam Malik Hospital (RSHAM), Medan showed that the levels of leukocytes, neutrophils, lymphocytes and NLR in patients with pulmonary TB were  $10.34 \times 10^3/\text{mm}^3$ , 67.67%, 18.75% and 4, respectively.<sup>19</sup> These indicate higher results compared the results obtained in this study.

The sensitivity, specificity, PPV and NPV for leukocyte levels were 65.91; 52.05; 55.77; and 62.50. The sensitivity, specificity, PPV and NPV for neutrophil levels were 63.64; 62.50; 60.87; and 65.22. Another study found that patients with TB had a mean absolute neutrophil count (ANC) of around  $3.4 \times 10^9/\text{L}$  (range 2.4-5.1), whereas those with negative TB cultures were only  $2.5 \times 10^9/\text{L}$  (range 1.8-3.4) with  $p < 0.0001$ .<sup>20</sup>

The sensitivity, specificity, PPV and NPV for chest X-ray were 93.18, 100, 100 and 94.12, respectively. Those were higher than study by Sorsa; chest X-rays had a sensitivity, specificity, PPV, and NPV of 67.9%, 77.3%, 43.8% and 90.3%, respectively. GeneXpert and CXR were good with kappa value 0.38.<sup>21</sup>

Other studies showed similar results, in which they used a COP of NLR 2.91, resulting in a sensitivity of 77%, specificity 50%, PPV 60.6%, and NPV 68.4%.<sup>22</sup> Study by Yongmei et al concluded that the NLR value before treatment can be used to determine the probability of treatment failure so that the patient requires repeat treatment. In this study, TB patients with NLR values of 2.53 had a greater chance of undergoing repeat treatment than  $\text{NLR} < 2.53$  (OR 1.99; 95%CI 1.11-3.56).<sup>23</sup>

This study used a COP of 0.35 for MLR examination and found that the sensitivity, specificity, PPV and NPV for MLR were 90.91; 39.58; 57.97; and 82.61. Another study showed that an  $\text{MLR} > 0.378$  identified children with confirmed

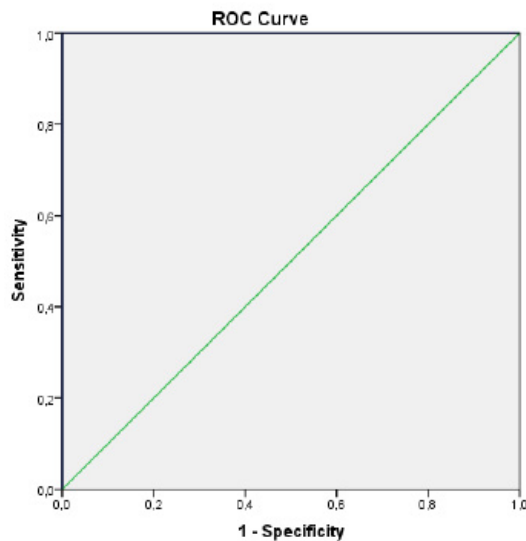


Figure 3. ROC analysis for the scoring system

Table 10. Association between scoring system and pulmonary TB diagnosis with HIV

Variable	Pulmonary TB		Not Pulmonary TB		p-value
	n	%	n	%	
Scoring					
< 55	0	0	48	52.5	< 0.001
> 55	44	47.8	0	0	

TB with a sensitivity of 77%, specificity 78%, PPV 24%, and NPV 97%. After TB treatment, the median MLR decreased in patients with confirmed TB.<sup>24</sup>

Our study used COP of 36 for ESR. This gives us the sensitivity, specificity, PPV and NPV for ESR of 84.09, 50.00, 60.66, and 77.42, respectively. Kumar's study showed that ESR was increased in 87% of patients with HIV TB, by a mean of 67.6 mm/hr with no statistically significant difference between pulmonary, extrapulmonary and disseminated TB.<sup>25</sup> This result is higher than what we found in this study.

A flow of pulmonary TB screening in HIV patients can be made in consideration with sensitivity and specificity of the results obtained. In HIV patients who will be screened for pulmonary TB, it is preceded by a symptom assessment; if the HIV patient has one of 5 symptoms consisting of cough, shortness of breath, fever, weight loss and night sweats, a chest x-ray examination is immediately carried out. If there are no symptoms, then proceed with laboratory tests consisting of neutrophils, NLR, MLR and ESR. If the results of

laboratory values increase, continue with a chest x-ray examination. Both chest X-rays with results suggestive of TB or non-TB must be subjected to GeneXpert examination as a standard for the diagnosis of pulmonary TB so that the results can be classified into bacteriologically confirmed pulmonary TB, clinical pulmonary TB and non-pulmonary TB.

This study has several limitations. First, this study did not identify the type of patient's TB case (whether pulmonary TB was a new case, old case, relapsed and others). Second, this study used clinical pulmonary TB classification, so patients with chest X-ray findings suggestive of pulmonary TB will definitely be included in the analysis as pulmonary TB patients. Third, this study did not use TB culture results as the gold standard. However, we resolved this by using the criteria for a positive pulmonary TB status diagnosis consisting of a positive smear or molecular rapid test (Xpert/MTB RIF) result or clinically confirmed pulmonary TB which showed improvement after one month of OAT administration.

## CONCLUSION

Clinical parameters of cough, shortness of breath, fever, night sweats and weight loss have a significant relationship with TB status in adult HIV patients. Laboratory parameters consisting of neutrophil, NLR, MLR and ESR and radiological also have a significant relationship with TB status in adult HIV patients. Clinical, laboratory and radiological parameters entered into the scoring system can be used as a complement to the gold standard if the results of the XpertMtb examination are doubtful or not in accordance with the patient's clinical course.

## CONFLICT OF INTEREST

There is no competing interest regarding the manuscript.

## ETHICS CONSIDERATION

The research was approved by the Ethics Committee, Faculty of Medicine Udayana University/Sanglah Hospital, with the number 1050/UN14.2.2.VII.14/LT/2021.

## FUNDING

None

## AUTHORS CONTRIBUTION

Conceptualization and methodology, WEFY, IKAS, IBNR; data collection WEFY, NLPEA, INGBNA, IAJDK, NWC; analysis and writing, WEFY, IKAS, IAJDK, NWC; review, IKAS, IBNR. All authors have read and agreed to publish the manuscript.

## REFERENCES

1. Kementerian Kesehatan Republik Indonesia. Riset Kesehatan Dasar [Internet]. Jakarta; 2018. Tersedia pada: [http://www.depkes.go.id/resources/download/infoterkini/materi\\_rakorpop\\_2018Hasil\\_Riskesdas\\_2018.pdf](http://www.depkes.go.id/resources/download/infoterkini/materi_rakorpop_2018Hasil_Riskesdas_2018.pdf)
2. World Health Organization (WHO). Global Tuberculosis Report 2019. 2019.
3. Kasper; Denis L; et al. Harrison's Principles of Internal Medicine 19th Edition. New York: McGraw-Hill Education; 2018.
4. Fishman JA, Grippi MA, Kotloff RM, et al. Fishman's Pulmonary Disease and Disorders Fifth Edition. New York: Elsevier Saunders; 2016.
5. Kemenkes RI. Pedoman Nasional Penanggulangan Tuberkulosis. Jakarta: Kementerian Kesehatan RI; 2014.

6. Martino RJ, Chirenda J, Mujuru H, et al. Characteristics Indicative of Tuberculosis/HIV Coinfection in a High-Burden Setting: Lessons from 13,802 Incident Tuberculosis Cases in Harare, Zimbabwe. *Am J Trop Med Hygiene*. 2020;103(1):214–20.
7. Wang GJ, Phipers M, Elis E. Demographic, laboratory and clinical characteristics of HIV-positive tuberculosis cases in Canada. *J Infect Public Health*. 2009;2(3):112–9.
8. Prado TN, Rajan JV, Miranda AE, et al. Clinical and epidemiological characteristics associated with unfavorable tuberculosis treatment outcomes in TB-HIV co-infected patients in Brazil: a hierarchical polytomous analysis. *Brazilian J Infect Dis*. 2017;21(2):162–70.
9. Pangaribuan L, Perwitasari D, Kristina, et al. Faktor-faktor yang memengaruhi kejadian tuberkulosis paru pada umur 15 tahun ke atas di Indonesia. *Bul Penelit Sist Kesehat*. 2020;23(1):10–7.
10. Sterling TR, Pham PA, Chaisson RE. HIV Infection—Related Tuberculosis: Clinical Manifestations and Treatment. *Clin Infect Dis*. 2010;50(3):223–30.
11. Mirambo MM, Hamis HK, Idd S, et al. Manifestations of Tuberculosis in TB-HIV co-infected patients: A retrospective study. *Tanzania Med J*. 2012;26(2):76–82.
12. Patel AK, Thakrar SJ, Ghanchi FD. Clinical and laboratory profile of patients with TB/HIV coinfection: A case series of 50 patients. *Lung India*. 2011;28(2):93–6.
13. Kementerian Kesehatan Republik Indonesia. *Pedoman Pengendalian TB Paru di Indonesia*. Jakarta: Kementerian Kesehatan RI; 2014.
14. Salwani D, Nasir UJ, Yuniastuti E, et al. Kemampuan Gabungan Gejala Klinis dan Pemeriksaan Radiologis serta Biakan MGIT 960 dalam Diagnosis Tuberkulosis Paru pada Pasien HIV. *J Penyakit Dalam Indones*. 2018;5(2):88–93.
15. Sharma SK, Mohan A, Sharma A. Challenges in the diagnosis & treatment of miliary tuberculosis. *Indian J Med Res*. 2012;135(5):703–30.
16. Sharma SK, Mohan A, Sharma A. Miliary tuberculosis: A new look at an old foe. *J Clin Tuberc Other Mycobact Dis*. 2016;3:13–27.
17. World Health Organization (WHO). *Guidance for national tuberculosis programmes on the management of tuberculosis in children*. Geneva: WHO Int; 2014.
18. Lee MP, Chan JW, Ng KK, et al. Clinical manifestations of tuberculosis in HIV-infected patients. *Respirology*. 2000;5(4):423–6.
19. Pane IDR. *Peran Rasio Netrofil Limfosit Count dalam Memberdakan antara TB Paru dan Pneumonia Komunitas*. Universitas Sumatera Utara; 2015.
20. Kerkhoff AD, Wood R, Lowe DM, et al. Blood Neutrophil Counts in HIV-Infected Patients with Pulmonary Tuberculosis: Association with Sputum Mycobacterial Load. *PLoS One*. 2013;8(7):67–9.
21. Sorsa A. The Diagnostic Performance of Chest-X-Ray and Erythrocyte Sedimentation Rate in Comparison with GeneXpert® for Tuberculosis Case Notification Among Patients Living with Human Immunodeficiency Virus in a Resource-Limited Setting: A Cross-Sectional Study. *Risk Manag Heal Policy*. 2020;13:1639–46.
22. Sormin DE, Siagian P, Sinaga BYM, et al. Neutrophyl Lymphocyte Ratio pada Pasien Tuberkulosis Paru dan Tuberkulosis Resistan Obat. *J Respir Indo*. 2018;38(3):177–80.
23. Yin Y, Kuai S, Liu J, et al. Pretreatment neutrophyllymphocyte ratio in peripheral blood was associated with pulmonary tuberculosis retreatment. *Arch Med Sci*. 2017;13:404–11.
24. Choudhary EK, Wall KM, Njuguna I, et al. Monocyte-to-Lymphocyte Ratio Is Associated With Tuberculosis Disease and Declines With Anti-TB Treatment in HIV-Infected Children. *J Acquir Imuune Defic Syndr*. 2019;80(2):174–81.
25. Mandal SK, Chavan L. Erythrocyte Sedimentation Rate Values in Cases of Active Tuberculosis without HIV Co-Infection. *J Med Sci Clin Res*. 2016;4(10).



This work is licensed under a Creative Commons Attribution