Sensitivity and Specificity of Monocyte-Lymphocyte Ratio to Predict Active Tuberculosis

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ABSTRACT

Objective: To determine the sensitivity and specificity of monocyte-lymphocyte ratio (MLR) to predict active pulmonary tuberculosis (TB), keeping X-PERT MTB/Rif as the gold standard.

Study Design: Validation study.

Place and Duration of the Study: Department of Pulmonology, Lady Reading Hospital, Peshawar, Pakistan, from September 2023 to March, 2024.

Methodology: A total of 121 patients with clinically suspected pulmonary TB were included. In all these patients, MLR and X-PERT MTB/Rif were performed. Based on this, a 2×2 contingency table was made to calculate diagnostic accuracy parameters.

Results: In this study, 121 patients were included. The median age was 44.00 (26) years. There were 94 (77.69%) male and 27 (22.31%) female patients. Median duration of disease was 2.00 (1.00) weeks. Median MLR was 0.50 (0.44). The frequency of patients who had MLR ≥0.47 was 67 (55.37%). The frequency of patients who had positive X-PERT MTB/Rif was 68 (56.20%). Sensitivity and specificity of MLR to predict active pulmonary TB, keeping X-PERT MTB/Rif as the gold standard, were 76.47% and 71.70%, respectively.

Conclusion: MLR is a useful tool in predicting the presence of active pulmonary TB.

Key Words: *Monocyte-lymphocyte ratio, Mycobacterium tuberculosis, Pulmonary tuberculosis, Sputum, Diagnostic accuracy*.

How to cite this article: Khan MM, Basit A, Khan MH, Sabahat S. Sensitivity and Specificity of Monocyte-Lymphocyte Ratio to Predict Active Tuberculosis. *J Coll Physicians Surg Pak* 2025; **35(07)**:19-22.

INTRODUCTION

Tuberculosis (TB) is caused by micro-organisms that belong to the genus *Mycobacterium*.[1] *Mycobacterium tuberculosis*, *Mycobacterium africanum*, and *Mycobacterium canetti* are the most common aetiologic agents of TB in humans, forming the *Mycobacterium tuberculosis* complex. On the other hand, *Mycobacterium bovis* is the most prevalent cause of TB in animals but can also cause TB in humans.[2] Global incidence of TB is quite high, and according to data compiled by the World Health Organisation (WHO), millions of people lost their lives due to TB, and this can be attributed to the high prevalence of multi drug resistant (MDR) TB reported at 11.6%.[3] Pulmonary TB is the most prevalent type of TB, and its prevalence, according to a study, was as high as 65.03%.[4]

For the purpose of diagnosing the presence of active TB, many laboratory tests are utilised in healthcare systems, including acid-fast bacilli (AFB) smear microscopy, Ziehl-Neelsen (ZN) smear staining, adenosine deaminase (ADA), and geneXpert Mycobacterium TB/rifampicin (MTB/RIF) assay.[5,6]

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Received: March 18, 2025; Revised: May 16, 2025; Accepted: May 16, 2025
DOI: https://doi.org/10.29271/jcpsp.2025.07.19

However, mycobacterial culture is the diagnostic gold standard for TB.[7] Another such method that has been hypothesised as an effective tool to predict the presence of active TB is the monocyte-lymphocyte ratio (MLR). In this instance, a study reported that the sensitivity and specificity of MLR to predict the presence of active TB were 79% and 87.4%, respectively.[8] In another study, the sensitivity and specificity of MLR in predicting pulmonary TB presence were reported at 95.1% and 70%, respectively.[9]

Lack of availability of sophisticated interventions such as X-PERT MTB/Rif, especially in health care centres located far from teaching hospitals, is a major problem. For this purpose, an easily available alternative should be researched that can be useful and accurate to predict the presence of active TB. One such method is MLR, which can be checked using just complete blood count (CBC). This study was thus conducted with the aim to determine the sensitivity and specificity of the MLR to predict active pulmonary TB.

METHODOLOGY

This validation study was conducted at the Department of Pulmonology, Lady Reading Hospital, Peshawar, Pakistan, from September 2023 to March, 2024, after getting approval from the Institutional Review Board of Lady Reading Hospital (Ref: No. 857/LRH/MTI). Sample size calculation was performed using the sensitivity and specificity sample size calculator by using a confidence level of 95%, precision of 10%, prevalence of

65.03%,[4] sensitivity of 79%[8] and 87.4%,[8] resulting in a sample size of 121. The participants were selected by using a non-probability consecutive sampling technique.

All male and female patients aged between 18 and 75 years who presented with clinically suspected pulmonary TB were included. Clinically suspected cases of pulmonary TB were defined as patients who had ≥2 weeks' history of low-grade fever (99-100.5˚C), persistent cough, and fatigue with/without an episode of haemoptysis. Patients who had widespread TB involving brain, bone marrow disease, febrile patients, patients with any signs of active infection, those using medications that could affect leucocyte count such as methotrexate, phenytoin or olanzapine, those currently using antibiotics, patients with history of immunodeficiency disorders, or those having history of autoimmune disorders were excluded.

Before inclusion in the study, written informed consent was obtained from every patient. After that, baseline characteristics including age (in years), gender, and duration of disease (in weeks) were documented. After this, a 3 ml blood sample was drawn by an expert phlebotomist, which was placed in a complete blood count (CBC) vial and brought to the haematology laboratory for performing differential leucocyte count (DLC) to calculate and document the MLR. A cut-off value of MLR as a predictor of active TB was set at ≥ 0.47. Additionally, for the confirmation of active pulmonary TB, sputum/bronchoalveolar lavage (BAL) was sent for X-PERT MTB/Rif. Based on the results of these tests, true positive and negative (TP and TN) and false positive and negative (FP and FN) patients were determined. A patient was labelled as TP if they had positive X-PERT MTB/Rif and MLR ≥0.47. A patient was labelled as FP if they had MLR ≥ 0.47, but the X-PERT MTB/Rif was negative. A patient was labelled as TN if they had negative X-PERT MTB/Rif and MLR <0.47. A patient was labelled as FN if they had MLR <0.47 but their X-PERT MTB/Rif was positive. Based on these data, a 2×2 contingency table was drawn to determine the sensitivity and specificity according to their standard formulae.

Data were analysed using the Statistical Package for Social Sciences (SPSS) version 22. Quantitative variables (age, body mass index [BMI], duration of disease, monocyte count, lymphocyte count, and MLR) were presented as median with interquartile range (IQR), as after checking the normality of data by Shapiro-Wilk's test, it was found that all quantitative variables were not distributed normally. Qualitative variables (gender and the presence of active PTB) were presented as frequencies and percentages. A 2×2 table was drawn in order to determine the sensitivity and specificity values using the following formula:

Sensitivity = (TP/TP+FN) × 100
Specificity = (TN/TN+FP) × 100

RESULTS

In this study, 121 patients were included. Median age was 44.00 (26.00) years. There were 94 (77.69%) male and 27 (22.31%) female patients. Median duration of disease was 2.00 (1.00) weeks. Median monocyte count was 480.00 (300.00)/mm^3. Median lymphocyte count was 960.00 (705.00)/mm^3. Median MLR was 0.50 (0.44). These baseline characteristics are tabulated below in Table I.

The frequency of patients who had MLR ≥0.47 was 67 (55.37%), while the frequency of MLR <0.47 was 54 (44.63%). The frequency of patients who had positive X-PERT MTB/Rif was 68 (56.20%), while 53 (43.80%) patients had negative X-PERT MTB/Rif. Based on these, there were 52 (42.98%) TP, 15 (12.40%) FP, 16 (13.22%) FN, and 38 (31.40%) TN cases. A 2×2 contingency table of TP, FP, FN, and TN cases is given below in Table II.

Based on this, the sensitivity and specificity of MLR to predict active pulmonary TB, keeping X-PERT MTB/Rif as the gold standard were 76.47% and 71.70%, respectively (Table III).

Table I: Baseline characteristics of all patients (n = 121).

Parameters	Median (IQR); n (%)
Median age	44.00 (26.00) years
Gender	
Male	94 (77.69%)
Female	27 (22.31%)
Median duration of disease	2.00 (1.00) weeks
Median monocyte count	480.00 (300.00)/mm^3
Median lymphocyte count	960.00 (705.00)/mm^3
Median MLR	0.50 (0.44)

Table II: The 2×2 contingency table of TP, FP, FN, and TN cases (n = 121).

	Positive X-PERT MTB/Rif	Negative X-PERT MTB/Rif
MLR ≥ 0.47	52 (42.98%)	15 (12.40%)
MLR <0.47	16 (13.22%)	38 (31.40%)

TP, True positive; FP, False positive; FN, False negative; TN, True negative.

Table III: Sensitivity and specificity of monocyte-lymphocyte ratio to predict active pulmonary tuberculosis (n = 121).

Diagnostic accuracy parameters	Percentage (%)
Sensitivity	76.47%
Specificity	71.70%

DISCUSSION

Pakistan is amongst those countries in the world that carry one of the highest burdens of infection caused by *Mycobacterium tuberculosis* and is ranked in the fifth position in this regard.[10,11] According to careful estimates, amongst all the new cases of TB diagnosed on the global scale, 70% of the incidence is found in the Pakistani population, making it a major public health concern.[12,13] It is therefore of utmost importance to explore every diagnostic option that can successfully predict the presence of active TB amongst patients who present with a high clinical suspicion of pulmonary TB. One such potential diagnostic tool is the MLR, which was the focus of the present study.

In the present study, the median age of all patients who presented with clinically suspected pulmonary TB was 44 years, with 77.69% of patients being males. This male predominance regarding the burden of pulmonary TB has been reported in

studies conducted by Mohammed *et al*. and Banti *et al*., who found that amongst all the pulmonary TB cases, the male population constituted 53.1% and 62%, respectively.[14,15] This male predominance can be attributed to multiple factors. One major factor is that a higher proportion of men have the habit of smoking.[16,17] Smoking causes significant damage to the lungs as well as causes certain changes in the immune system that make them more prone to chronic infections such as TB.[18,19] Other than this, hormonal and genetic variability amongst men and women also determine the probability of developing TB, and these variations make men more prone to develop TB.[20]

Upon analysis of the sensitivity and specificity of MLR, it was found that these values for MLR to predict active pulmonary TB, keeping X-PERT MTB/Rif as the gold standard, were 76.47% and 71.70%, respectively, exhibiting a moderate level of both the sensitivity and specificity of MLR in this regard. Compared to this, Liana *et al*.[9] conducted the study with the similar objective of finding the ability of MLR to predict active pulmonary TB presence but they found MLR to be a sensitive rather than a specific test. The reported sensitivity was also much higher as compared to the present study at 95.1% but the specificity was reported at 70% which was comparable to the present study.

In another study conducted by Sukson *et al*.,[8] sensitivity and specificity of MLR for successfully predicting the presence of active pulmonary TB were 79% and 87.4%, respectively, showing MLR to be a specific rather than a sensitive tool in this regard. Similar to the trend reported in the present study for MLR to be equally sensitive and specific for predicting the presence of active pulmonary TB, Adane *et al*. found that MLR was an equally sensitive and specific test in this regard, with the reported sensitivity and specificity of 79.5% and 80.2%, respectively.[21]

In another study conducted by Malik *et al*., it was found that the sensitivity of MLR to predict the presence of TB was 94%, which was much higher compared to the present study, while the reported specificity was only 48%, which was much lower compared to the present study.[22] One of the possible reasons for this major difference can be attributed to the difference in the cut-off value of MLR used by Malik *et al*.[22] compared to the present study. Additionally, differences from previous studies may also occur due to the differences in sample sizes, demographics, and geographical differences.

Importantly, the results of the present study validate the use of MLR as a screening tool to performing the definitive diagnostic tests for diagnosing TB in patients who present with clinical features suggestive of pulmonary TB. Additionally, owing to the availability of this simple test at the very basic level of healthcare, further supports its use in this regard. For this purpose, it is strongly recommended that patients who have clinical features suggestive of pulmonary TB and have MLR ≥0.47 should undergo definitive diagnostic evaluation for pulmonary TB.

One of the limitations of the present study was the lack of stratifying the patients based on their smoking habits, as smoking may impact MLR as well as the chances of getting infected by *Mycobacterium tuberculosis*. Therefore, further studies in this regard are warranted, with a focus on this particular group of population.

CONCLUSION

The sensitivity and specificity of MLR to predict active pulmonary TB, keeping X-PERT MTB/Rif as the gold standard, were 76.47% and 71.70%, respectively, making it a useful tool in this regard.

ETHICAL APPROVAL:

Ethical approval was obtained from the Institutional Review Board of Lady Reading Hospital, Peshawar, Pakistan (Ref No: 857/LRH/MTI).

COMPETING INTEREST:

The authors declared no conflict of interest.

PATIENTS' CONSENT:

Written informed consent was obtained from all the patients included in the study.

AUTHORS' CONTRIBUTION:

MMK, AB: Concept, study design, acquisition of the data, and manuscript writing.
MHK, SS: Analysis, interpretation, and acquisition of the data.
All authors approved the final version of the manuscript to be published.

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