

## The Ratio of Monocyte to Lymphocyte in Peripheral Blood as a Predictor of Tuberculosis

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Received 05 May 2024; Accepted 18 May 2024

### Abstract

#### Introduction

Tuberculosis is caused by mycobacterium tuberculosis and is the most contagious disease of developing countries. This infection causes many hematological changes, out of which, one is monocyte to lymphocyte count ratio alteration. Therefore, we did this research to prove that the ratio of monocytes to lymphocytes can be used as a predictor of tuberculosis diseases.

#### Method

A retrospective study was done in a tertiary care hospital between August 2022 to July 2023. A total of 76 subjects were included.

#### Result

Most of the subjects were in age group of 36-45 years (32%). Mean age  $\pm$  SD was 9.5 $\pm$ 4.5. The analyzed data showed a value of  $p < 0.0001$ . The cut off value was  $> 0.37$  with the sensitivity and specificity as 95.1% and 80% respectively.

#### Conclusion

The ratio of monocytes to lymphocytes cutoff point was 0.37, the sensitivity was 95.1% and specificity was 80%, the positive predictive value of 50.4% and negative predictive value of 92.1%.

Therefore we can conclude that the ratio of monocyte to lymphocyte can be used as early indicator for diagnosing tuberculosis.

#### Keywords

Tuberculosis, Monocytes, Lymphocytes, Culture, Acid fast bacilli

### I. Introduction

Tuberculosis is caused by mycobacterium tuberculosis and is the most contagious disease of developing countries. This infection causes many hematological changes, out of which, one is monocyte to lymphocyte count ratio alteration. Monocyte is a cellular immune response to granuloma of bacilli and it also mediates immune cells against bacteria containing granuloma which is mediated by cytokines. These cytokines are secreted by lymphocytes and phagocytes. **It is said that in tuberculosis there is increase in numbers of monocytes.** It was found that many cases had monocytosis and lymphocytopenia<sup>1</sup>.

Monocytes and lymphocytes are an important part of the immune response to tuberculosis infection, therefore the ratio of monocytes to lymphocytes (ML ratio) can show the immune response against tuberculosis infection. The ratio of monocytes to lymphocytes is expected to be the predictor marker of tuberculosis. Tuberculosis examination using sputum from tuberculosis patients is sometimes difficult to do because not all patients have a proper sputum for testing. Therefore having a simple and rapid predictor in distinguishing between tuberculosis and non tuberculosis is very useful. Monocytes and lymphocytes count is a simple, rapid and routine examination performed in patients with tuberculosis.

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Therefore, we did this research to prove that the ratio of monocytes to lymphocytes can be used as a predictor of tuberculosis diseases.

### **II. Method**

A retrospective study was done in a tertiary care hospital between August 2022 to July 2023. A total of 76 subjects were included. Data was obtained from their medical records. The subjects were all suspected cases of tuberculosis which came in the Department of Respiratory Medicine and in the Department of Internal Medicine. Inclusion criteria was all patients which were suspected cases of tuberculosis and came positive for tuberculosis by acid fast Bacilli (AFB) test and culture test. All patients who had conditions which can effect monocyte and lymphocyte count (like corticosteroid therapy, known case of leukemia, lymphopenia or aplastic anemia) were excluded.

Each patient's age, gender, comorbidities were noted. Peripheral blood monocytes and lymphocytes were noted and **MLR** was calculated from Complete blood count.

### **Data analysis**

Date was presented in descriptive and diagnostic tests was analyzed by SPSS 22.0.

### **III. Result**

In this study we included 106 patients with complete medical record and laboratory data. 40 patients were excluded due to cancer and chemotherapy treatment. 76 remaining patients were included in this study as research subjects.

**Table1- Distribution of subjects by age group (n=76)**

<b>Age (years)</b>	<b>Number</b>	<b>Percentage(%)</b>
5-11	1	1
12-16	2	3
17-25	4	5
26-35	9	12
36-45	24	32
46-55	12	16
56-65	21	27
>65	3	4
<b>Total</b>	<b>76</b>	<b>100</b>

Most of the subjects were in age group of 36-45 years (32%). Mean age  $\pm$  SD was  $9.5\pm 4.5$ . Oldest patient was 71 years old and youngest was 6 years old.

**Table 2- Distribution of subjects according to gender (n=76)**

<b>Gender</b>	<b>Number</b>	<b>%</b>
Male	56	74
Female	20	26
<b>Total</b>	<b>76</b>	<b>100</b>

Male:female ratio was 2.8:1. males were excluded more than females. The percentage of male patients was 74% and female patient was 26%.

**Table3- Distribution of subjects by acid fast bacilli grading (n=76)**

<b>AFB Positivity grade</b>	<b>Number</b>	<b>%</b>
1+	16	21
2+	16	21
3+	44	58
<b>Total</b>	<b>76</b>	<b>100</b>

44(58%) subjects had grade 3+ of AFB positivity. Grade 2 and grade 1 positivity was seen in equal number of patients (21%).

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Culture was done in all these negative and positive cases and showed positive culture in 54 cases and negative culture in 8 cases as shown in table 4.

**Table 4- Distribution of subjects by culture test(n=76)**

Culture	Number	%
Positive	68	89
Negative	8	11
<b>Total</b>	<b>76</b>	<b>100</b>

**Table5- Distribution of subjects by laboratory results**

Parameters		Culture results	
		Positive	Negative
Leukocytes( $10^3/mm^3$ )	Mean $\pm$ SD	12.57 $\pm$ 3.44	8.44 $\pm$ 3.77
Monocytes (%)	Mean $\pm$ SD	9.12 $\pm$ 3.14	7.34 $\pm$ 3.44
Lymphocytes(%)	Mean $\pm$ SD	10.11 $\pm$ 3.54	18.84 $\pm$ 6.31
Ratio of monocytes to lymphocytes	Mean $\pm$ SD	0.71 $\pm$ 0.41	0.32 $\pm$ 0.44

The analyzed data showed a value of  $p < 0.0001$ . the cut off value was  $>0.37$  with the sensitivity and specificity as 95.1% and 80% respectively.

**Table6- Distribution of subjects based on culture data and ratio of Monocyte to lymphocytes**

Ratio of monocytes to lymphocytes	Culture results		Total
	Positive	Negative	
$>0.37$	60	5	65
$<0.37$	8	3	11
<b>Total</b>	<b>68</b>	<b>8</b>	<b>76</b>

The distribution of tuberculosis subjects on the basis of culture and ratio of monocyte to lymphocytes can be seen in table 6. A total of 60 subjects with positive culture results had MLR ratio  $>0.37$  while 8 subjects had MLR ratio of  $<0.37$ .

A total of 5 subjects with negative culture had MLR ratio  $>0.37$  while 3 subjects had MLR ratio  $<0.37$ .

### IV. Discussion

The highest frequency of tuberculosis subjects at our hospital in between August 2022 to July 2023 was in the age group of 36-45 years, (32%). The mean age of the subjects was  $9.5 \pm 4.5$  years. These results are similar to the study done by Phey liana et al<sup>1</sup> they showed the mean age of the subjects was  $45.81 \pm 16$  years old. Another study conducted by Rakotosamimanana et al<sup>2</sup> also showed that the average age of tuberculosis patients was 34.7 years.

The study done by Tung et al<sup>3</sup> also showed similar results. He showed that the mean age was  $43 \pm 7.7$  years. He also stated that 43 years is a productive age group which means that this age group is most susceptible to tuberculosis bacteria because they interact more frequently with the surrounding environment, whether at community, school or work.<sup>4,5</sup>

This result is not in accordance with the study done by Wang et al<sup>6</sup> which found that the highest age group was at the age above 65 years. He stated that tuberculosis is more common in the elderly population because T lymphocytes function decreases with age due to changes in lipids structure in the cell membrane.<sup>7</sup>

In our study men were more affected than women(74% and 26% respectively). This finding is consistent with both Wang et al<sup>6</sup> which showed that 71.1% of 419 tuberculosis patients were male and Bashir et al<sup>8</sup> research which stated that out of 100 subjects 73% were male and 27% were female,

However in 2021 survey report of WHO stated that the tuberculosis incidence is higher in women than in men.<sup>9</sup>Nhamoyebonde et al<sup>10</sup> mentioned the relationship between tuberculosis and sex and stated that sex hormone is involved with the incidence of tuberculosis between women and men. T-helper 1 (Th1) is known as one of the most important immune systems in controlling the body's defenses against this infection but testosterone decreases the Th1 response whereas estrogen hormone increases the Th1 response to tuberculosis infection. The sex hormones also affect the response of macrophages to infection. Macrophages play an important role by directly killing the Mycobacterium tuberculosis bacteria and help in body's defence against this infection.. Estradiol or estrogen hormone can increase macrophage activation response to tuberculosis

infection, whereas testosterone can decrease macrophage activation by reducing TLR4 and result in alteration of defence mechanism.

Behavioral differences can also affect the different incidence of tuberculosis in men and women. Smoking decreases defense of the immune system against infection and are more commonly found in men than in women.<sup>10,11,12</sup>

Monocytes plays an important role in immunity against tuberculosis infection. Monocytes act as an antigen presenting cell that can activate and modulate adaptive immune responses and are cellular component of the innate immunity. Thus the factors that can interfere with function of monocytes can potentially affects individual's responses towards infection.<sup>3</sup> This study showed that tuberculosis patients who had positive culture report had a higher ratio of monocytes to lymphocytes than those patients with a negative culture report. Thus increasing the ratio of monocytes to lymphocytes in tuberculosis patients with positive cultures correlates with an increase monocytes count and decrease lymphocytes count.

The ratio of monocytes to lymphocytes sensitivity and specificity were 95,1% and 80%. . La Manna et al<sup>4</sup> in their study found that ratio of monocytes to lymphocytes sensitivity and specificity were 91.04% and 93.55%. respectively. This differences in both studies can be de to the differences in subject characteristics of the studies because La Manna et al<sup>4</sup> compared healthy patients with tuberculosis patients, while this study compared chronic symptomatic patients with AFB and positive and negative cultures. The other factors that can also cause the differences in both studies was the different hematology analyzer that was used to study the monocytes and lymphocytes.<sup>4</sup>

The sensitivity value of 95.1% which was seen in this study indicates that the ratio of monocytes to lymphocytes has a good diagnostic value therefore it can be considered as a screening marker of tuberculosis.

## V. Conclusion

The mean of monocytes(%), lymphocytes(%) and ratio of monocytes to lymphocytes in tuberculosis subjects with positive culture was  $9.12 \pm 3.14$ ,  $10.11 \pm 3.54$  and  $0.71 \pm 0.41$  respectively. The mean of monocytes(%), lymphocytes(%) and ratio of monocytes to lymphocytes in tuberculosis subjects with negative culture was  $7.34 \pm 3.44$ ,  $18.84 \pm 6.31$  and  $0.32 \pm 0.44$  respectively. The ratio of monocytes to lymphocytes cutoff point was 0.37, the sensitivity was 95.1% and specificity was 80% , the positive predictive value of 50.4% and negative predictive value of 92.1%.

Therefore we can conclude that the ratio of monocyte to lymphocyte can be used as early indicator for diagnosing tuberculosis.

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