ratio monosit to limfosit

by Phey Liana

Submission date: 29-Apr-2023 06:22PM (UTC+0700)
Submission ID: 2079118767
File name: rasio_monosit_limfosit_2019.pdf (684.53K)
Word count: 3045
Character count: 15978

The ratio of monocytes to lymphocytes accuracy as tuberculosis predictor

The ratio of monocytes to lymphocytes accuracy as tuberculosis predictor

Phey Liana[1,2], Brillia Brestilova[3], Kemas Yakub Rahadiyanto[1]

[1] Clinical Pathology Departement, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia
[2] Dr. Mohammad Hoesin Hospital, Palembang, Indonesia
[3] Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

E-mail : pheyliana@fk.unsri.ac.id

Abstract. Tuberculosis is one of the top ten death's causes in the world and even cause more deaths than HIV in 2015. In the same years, there are 10.4 million new TB case incidences with case notification rate is 142/100,000 population globally. Monocytes and lymphocytes play an important role in the body's defense mechanism against tuberculosis. Tuberculosis can induce increased monocytes and decreased lymphocytes. The ratio of Monocytes to lymphocytes is expected to be used as predictors of tuberculosis. Therefore, this study was conducted to determine the ratio of monocytes to lymphocytes accuracy as tuberculosis predictor. This diagnostic study was done at dr. Mohammad Hoesin General Hospital Palembang. Samples of this study had been taken from medical records which fulfilled the inclusion and exclusion criteria. The study was analyzed using SPSS version 22.0. The sample of the study was 101 tuberculosis subjects. Most of the subjects were men (70,3%) and were 36-45 years old group (25,7%). The cut-off value of 0,476 allowed the discrimination of tuberculosis with positive bacterial culture from negative bacterial culture, with a sensitivity of 95,1% and a specificity of 70%. Therefore, we concluded that the ratio of monocytes to lymphocytes can be considered as an early predictor marker of tuberculosis.

1. Introduction

Tuberculosis, commonly abbreviated as TB is caused by the bacteria *Mycobacterium tuberculosis* [1]. Tuberculosis is the most contagious infectious diseases in developing countries. Tuberculosis even is one of the top ten diseases in the world and by 2015 causes more deaths than HIV. There are 10.4 million new TB case incidents with a case notification number of 142/100,000 population globally in 2015. The number of deaths due to tuberculosis is 1.4 million people furthermore the other deaths in people with tuberculosis and HIV is 0.4 million people [2].

The incidence of TB in Indonesia is 395/100,000, the incidence of TB and HIV is 12/100,000, and the incidence rate of Multidrug resistance/Rifampicin resistance-tuberculosis (MDR/RR-TB) is 30/100.000 population in 2015. The TB death rate in Indonesia is 40/100.000 population and the death rate of TB with HIV is 10/100.000 population [2]. TB case notification number in South Sumatera is 116/100.000 population [1].

Mycobacterium tuberculosis infection can cause various hematological changes, one of them is a change in monocyte and lymphocyte count [3]. Pereira et al (2004) mentioned monocytes as a cellular immune response to granulomas of bacillus cell formation [4,5]. Monocytes mediate immune cells against bacteria containing granulomas regulated by cytokines. The cytokines are secreted by mononuclear phagocytes and lymphocytes [4]. There is a suspicion in tuberculosis that there is an

increase in monocytes or monocytosis. This is in line with research conducted by Bashir (2014) who found an increased of monocytes at tuberculosis patients center in Sudan. Monocytosis in some cases is believed to reflect that the illness is in active phase [3]. Lymphocytes are the main effector cells in the tuberculosis immune reaction [4]. Bashir (2014) mentioned that in tuberculosis there is an increase of lymphocytes or lymphocytosis, whereas based on the results of research by Bashir, there is a decrease in lymphocytes in tuberculosis patients. Research conducted by Wang et al (2015) obtained results in line with research conducted by Bashir, They obtained results that lymphocyte in tuberculosis patients is lower than normal people [6].

Monocytes and lymphocytes are an important part of the immune response to tuberculosis infection, therefore the ratio of monocytes to lymphocytes (ML ratio) can reflect the immune response against tuberculosis infection [6]. 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 to be tested. Therefore having a simple and rapid predictor in distinguishing between tuberculosis and nontuberculosis is very useful. Monocytes and lymphocytes count is a simple, rapid and routine examination performed in patients with tuberculosis.

La Manna et al (2017) mentioned that the predicted ratio of monocytes to lymphocytes in tuberculosis diseases was determined by ROC analysis with the cut-off value of 0.28, can accurately predict the incidence of tuberculosis with the sensitivity and specificity of 91.04% and 93.55 %, with p <0.0016 [7]. Therefore, we conduct this study to prove the ratio of monocytes to lymphocytes accuracy as a predictor of tuberculosis diseases.

2. Methods

The design research was the diagnostic study. Data were obtained from the medical record. The population and sample of this study were all suspect tuberculosis patients from the Internal Medicine Department wards of Dr. Mohammad Hoesin Hospital Palembang. Sampling was taken consecutively. This study was conducted from June until December 2017. The inclusion criteria of this study were all patients suspect as tuberculosis and have done a complete blood count and tuberculosis culture tests. The variables in this research are monocytes, lymphocytes, and the ratio of monocytes to lymphocytes, while the gold standard for tuberculosis diagnosis is sputum tuberculosis culture. Data were presented in the table descriptively. The diagnostic test was analyzed by SpSS 22.0.

3. Results

Patients with suspect tuberculosis recorded during the period 2015 to 2016 were 383 patients. There were 143 patients with complete medical record and laboratory data. A total of 42 patients were excluded due to cancer and chemotherapy treatment, 101 patients remained as research subjects.

Table 1. The distribution of subjects by age group (N = 101).

Age group (years)	N	Percentage (%)
5-11	2	2.0
12-16	1	1.0
17-25	11	10.9
26-35	10	9.9
36-45	26	25.7
46-55	19	18.8
56-65	25	24.8
> 65	7	6.9

The distribution of subjects by age group can be seen in table 1. Table 1 showed that most age group of tuberculosis subjects were in 36-45 years old. The mean age of the subjects was 45.81 ± 16 years old. The oldest patients were 83 years old and the youngest ones were 7 years old.

The distribution of subjects by sex can be seen in table 2. Figure 1 showed that male patients were more many than female patients. The percentage of male patients was 70.3%, while the percentage of female patients was 29.7%.

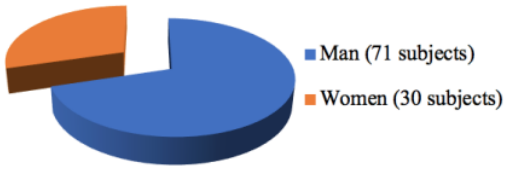

Figure 1. The distribution of subjects by sex (N=101).

The distribution of subjects by culture results can be seen in figure 2. Subjects with suspected tuberculosis who had negative culture results were 60 (59,4%), while subjects with positive bacterial culture result were 41 (40,6%).

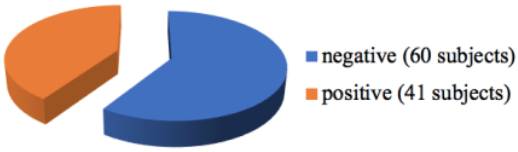

Figure 2. The distribution of subjects by culture results (N=101).

The distribution of subjects by laboratory results was shown in table 2. Tuberculosis patients with positive culture results had higher mean leukocytes, monocytes, and the ratio of monocytes to lymphocytes than patients with negative culture results. The lymphocytes count showed the opposite result, patients with negative culture results had higher lymphocytes count.

Table 2. The distribution of subjects by laboratory results.

Parameter		Culture results	
		Positive	Negative
Leukocytes (10^3/mm^3)	Mean (± SD)	12.87 ± 3.88	9.93 ± 4.76
	Median (min-max)	12,40 (6-21)	8.90 (3-28)
Monocyte (%)	Mean (± SD)	10.12 ± 3.74	8.34 ± 4.99
	Median (min-max)	10 (4-21)	8 (2-36)
Lymphocyte (%)	Mean (± SD)	11.83 ± 4.79	19.88 ± 8.47
	Median (min-max)	12 (2-28)	19 (3-43)
Ratio of monocytes to lymphocytes	Mean (± SD)	0.97 ± 0.51	0.57 ± 0.76
	Median (min-max)	0.85 (0.37-3)	0.38 (0.15-5.14)

The analyzed data showed Area Under Curve was 0.87 with a value of p <0.0001. The cut-off value was > 0.476 with the sensitivity and specificity are 95.1% and 70%, respectively (figure 3). The negative predictive value in this study was 95.45%, while the positive predictive value was 68.4%. Positive and negative probability values were 3.17 and 0.07 respectively.

The distribution of tuberculosis subjects based on the culture data and ratio of monocytes to lymphocytes can be seen in table 3. A total of 39 subjects with positive culture results had the ratio of monocytes to lymphocytes greater than 0.476, while the two other subjects had the ratio of monocytes to lymphocytes less than 0.476. A total of 18 subjects with negative culture results had the ratio of

monocytes to lymphocytes greater than 0.476, while 42 other subjects had the ratio of monocytes to lymphocytes less than 0.476 (table 3).

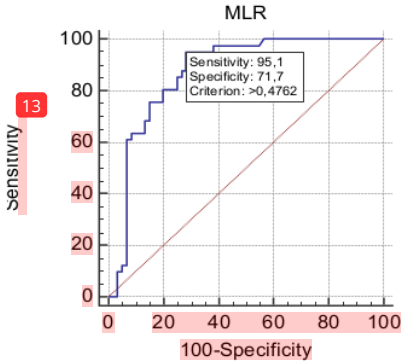

Figure 3. The ratio of monocytes to lymphocytes cut-off value in tuaberculosis.

Table 3. The distribution of subjects based on the culture data and ratio of monocytes to lymphocytes.

The ratio of monocytes to lymphocytes	Culture results		Total
	Positive	Negative	
> 0.476	39	18	57
≤0,476	2	42	44
Total	41	60	101

4. Discussions

The highest frequency of tuberculosis subjects at Dr. Mohammad Hoesin Palembang hospital in 2015-2016 was in the age group of 36-45 years, as much as 25.7%**.** The mean age of the subjects was 45.81 ± 15.99 years. These results are consistent with research conducted by Arrahmanda (2010) who found that the mean age of tuberculosis patients was 37.43 ± 13.24 years. Another study conducted by Rakotosamimanana et al (2015) in Antananarivo, Madagascar showed that the average age of tuberculosis patients was 34.7 years [8].

The research conducted by Tung (2013) in Taiwan also showed almost the same results. The mean age of tuberculosis patients obtained by Tung was 43 ± 7.7 years [5]. This age group is categorized as a productive age group. The productive age group is the age group most susceptible to tuberculosis bacteria because they interact more frequently with the surrounding environment, whether at work, school or community [7,9].

This result is not in accordance with the research conducted by Wang et al (2015) which found that the highest age group was at the age above 65 years [6]. Age 65 years and over is the elderly group. Tuberculosis is more common in the elderly because T lymphocytes have decreased function due to changes in lipids structure in the cell membrane [10]. The difference in the results of the study was caused by the differences between the characteristics and population of the study subjects.

More men suffer from tuberculosis than women (78% vs 22%). This finding was consistent with Wang (2015) and Bashir (2014) research results [3,6]. Wang et al study showed that 71.1% of 419 tuberculosis patients were male. Bashir stated that out of 100 research subjects, 73% were male and 27% were female. WHO also reports that the incidence of tuberculosis is higher in women than in men in the 2015 survey report.

Nhamoyebonde (2014) mentioned the relationship between the sex and tuberculosis. They found that sex hormone involved with the incidence of tuberculosis between men and women [11]. T-helper 1 (Th1) is one of the important immune systems in controlling the body's defenses against tuberculosis infection. Testosterone is known to decrease the Th1 response to tuberculosis infection, whereas

estrogen increases the Th1 response to tuberculosis infection. The sex hormones also affect the response of macrophages to infection. Macrophages play an important role in the body's defense against tuberculosis through its role in directly killing the *Mycobacterium tuberculosis* bacteria by active macrophages. Estradiol can increase macrophage activation response to tuberculosis infection, whereas testosterone can decrease macrophage activation by reducing TLR4.

Behavioral differences can also be a factor affecting the different incidence of tuberculosis in men and women. Smoking can decrease the body's defense of the immune system against infection. Smoking habits are more often found in men than in women [11–13].

Monocytes play an important role in immunity against tuberculosis. Monocytes are a cellular component of the innate immune response. Monocytes act as an antigen presenting cell that can activate and modulate adaptive immune responses. Therefore, all factors that may interfere with monocyte functions, potentially affecting individual responses during infection [5].

This study showed that tuberculosis patients with positive cultures had a higher ratio of monocytes to lymphocytes than those patients with a negative culture. Increasing the ratio of monocytes to lymphocytes in tuberculosis patients with positive cultures correlates with an increase in monocytes count and a decrease in lymphocytes count.

The ratio of monocytes to lymphocytes sensitivity and specificity were 95,1% and 70%. The Area Under Curve (AUC) of this study was 0.87 with P <0.001 and the cut-off point was > 0.476. This study obtained sensitivity value higher than La Manna study results (2007). On the other side, the specificity of this study was lower than La Manna study. La Manna obtained the ratio of monocytes to lymphocytes sensitivity and specificity were 91.04% and 93.55%. The differences in both studies were caused by the differences in subject characteristics of the studies. La Manna compared healthy patients and tuberculosis patients, while this study compared chronic cough patients with positive and negative cultures. The other factors that also caused the differences in both studies were the different hematology analyzer that was used to count the monocytes and lymphocytes [7]. The sensitivity value of 95.1% indicates that the ratio of monocytes to lymphocytes has a good diagnostic value so that it can be considered as a screening marker of tuberculosis.

5. Conclusions

The mean of monocytes (%), lymphocytes (%) and the ratio of monocytes to lymphocytes in tuberculosis subjects with positive cultures were 10.13 ± 3.74, 11.83 ± 4.79 and 0.97 ± 0.51, respectively. The mean of monocytes (%), lymphocytes (%) and the ratio of monocytes to lymphocytes in tuberculosis subjects with negative cultures were 8.34 ± 4.99, 19.88 ± 8.47 and 0.57 ± 0.76 respectively. The ratio of monocytes to lymphocytes cut-off point was 0.476 with AUC value of 0.87; the sensitivity of 95.1%; the specificity of 70%; the positive predictive value of 68.4%; the negative predictive value of 95.45%. Therefore we concluded that the ratio of monocytes to lymphocytes can be used as an early predictor for tuberculosis diagnosis.

6. References

[1] Kementerian Kesehatan R I 2016 Tuberculosis: Temukan Obati Sampai Sembuh *Jakarta: Pusadatin*
[2] World Health Organization and Others 2016 Global tuberculosis report 2016
[3] Bashir A B, Abufatima A S and Mohamedani A A 2014 Impact of Pulmonary Tuberculosis on Total and Differential Peripheral Blood Leukocytes Count *Int. J. Trop. Med.* **9** 33–7
[4] Pereira C B, Palaci M, Leite O H M, Duarte A J S and Benard G 2004 Monocyte cytokine secretion in patients with pulmonary tuberculosis differs from that of healthy infected subjects and correlates with clinical manifestations *Microbes Infect.* **6** 25–33
[5] Tung Y C, Ou T T and Tsai W C 2013 Defective Mycobacterium tuberculosis antigen presentation by monocytes from tuberculosis patients *Int. J. Tuberc. Lung Dis.* **17** 1229–34
[6] Wang J, Yin Y, Wang X, Pei H, Kuai S and Gu L 2014 Original article Ratio of monocytes to lymphocytes in peripheral blood in patients diagnosed with active *Brazilian J. Infect. Dis.* **19** 125–31
[7] La Manna M P, Orlando V, Dieli F, Di Carlo P, Cascio A, Cuzzi G, Palmieri F, Goletti D and

Caccamo N 2017 Quantitative and qualitative profiles of circulating monocytes may help identifying tuberculosis infection and disease stages *PLoS One* **12** e0171358
[8] Rakotosamimanana N, Richard V, Raharimanga V, Gicquel B, Doherty T M, Zumla A and Razanamparany V R Biomarkers for risk of developing active tuberculosis in contacts of TB patients : a prospective cohort study *Eur. Respir. J.* **46** 1095–1103
[9] Nurjana M A 2015 Faktor risiko terjadinya Tuberculosis paru usia produktif (15-49 tahun) di Indonesia *Media Penelit. dan Pengemb. Kesehat.* **25** 163–70
[10] Vasto S, Malavolta M and Pawelec G 2006 Immunity & Ageing Age and immunity **6** 1–6
[11] Nhamoyebonde S and Leslie A 2014 Biological differences between the sexes and susceptibility to tuberculosis *J. Infect. Dis.* **209** S100--S106
[12] Neyrolles O and Quintana-Murci L 2009 Sexual inequality in tuberculosis *PLoS Med.* **6** e1000199
[13] Narasimhan P, Wood J, MacIntyre C R and Mathai D 2013 Risk factors for tuberculosis *Pulm. Med.* **2013** 1–11

Acknowledgements
The authors would like to thank the Faculty of Medicine, Universitas Sriwijaya, Dr. Mohammad Hoesin Hospital and all those who helped in carrying out the research.

ratio monosit to limfosit

ORIGINALITY REPORT

19%	15%	17%	%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	repo-dosen.ulm.ac.id Internet Source	4%
2	journals.lww.com Internet Source	3%
3	eprints.whiterose.ac.uk Internet Source	2%
4	journal.kapin.org Internet Source	2%
5	Wei Wang, Li-fei Wang, Yan-yan Liu, Fang Yang, Lei Zhu, Xian-hui Zhang. "Value of the Ratio of Monocytes to Lymphocytes for Monitoring Tuberculosis Therapy", Canadian Journal of Infectious Diseases and Medical Microbiology, 2019 Publication	1%
6	Tiruneh Adane, Mulugeta Melku, Getnet Ayalew, Gezahegn Bewket, Melak Aynalem, Solomon Getawa. "Accuracy of monocyte to lymphocyte ratio for tuberculosis diagnosis and its role in monitoring anti-tuberculosis	1%

	treatment: Systematic review and meta-analysis", Medicine, 2022 Publication	
7	library.polmed.ac.id Internet Source	1 %
8	phd-dissertations.unizik.edu.ng Internet Source	1 %
9	Ella Amalia, Tia Sabrina, Yuwono, Venny Patricia, Radhiyatul Husna, Ayeshah Augusta Rosdah, Safyudin. "Identification of carbapenemases enterobacteriaceae producing gene blaVIM in clinical isolates", Journal of Physics: Conference Series, 2019 Publication	1 %
10	Natural Killer Cells, 2010. Publication	1 %
11	www.mdpi.com Internet Source	1 %
12	www.researchsquare.com Internet Source	1 %
13	www.transport-research.info Internet Source	1 %
14	Jun Wang, Yongmei Yin, Xuedong Wang, Hao Pei, Shougang Kuai, Lan Gu, Huiqin Xing, Yu Zhang, Qiusheng Huang, Bin Guan. "Ratio of monocytes to lymphocytes in peripheral	1 %

blood in patients diagnosed with active tuberculosis", The Brazilian Journal of Infectious Diseases, 2015
Publication

Exclude quotes	On	Exclude matches	< 1%
Exclude bibliography	On		