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# CORRELATION BETWEEN LESION EXTENT ON CHEST X-RAY AND POSITIVITY OF SPUTUM SMEAR WITH PLATELET PROFILE IN NEW CASE PULMONARY TUBERCULOSIS PATIENTS

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**ABSTRACT Background:** Pulmonary Tuberculosis (PTB) is an infection disease caused by bacilli bacteria called Mycobacterium Tuberculosis (MTB). Mycobacterium Tuberculosis invades the human body via droplet and induces pulmonary inflammation. Platelets play a role as inflammatory cells that contributed in chemotaxis, phagocytosis, complement activation and inflammatory mediators release. Platelet count and indices can be used to assess the PTB disease severity. **Objective:** To assess the correlation between lesion extent of chest x-ray and positivity of sputum smear with platelet profile in positive sputum smear new case PTB patients. **Methods:** This study was analytical study with cross-sectional design. Research subjects were 50 patients with positive sputum smear new case PTB. Lesion extent on chest x-ray was assessed and the platelet profile including platelet count, plateletcrit (PCT), Mean Platelet Volume (MPV) and Platelet Distribution Width were estimated. **Results:** Platelet count and PCT were significantly higher in PTB subjects with advanced lesion than minimal lesion ( $p < 0,001$ ) while MPV and PDW were lower in PTB subjects with advanced lesion than minimal lesion, but not significant ( $p > 0,05$  and  $p > 0,05$ ). According to the positivity of AFB smear sputum, platelet count was significantly higher in PTB subjects with sputum smear +2 than sputum smear +1 ( $p < 0,028$ ) while MPV and PDW were lowest in PTB subjects with sputum smear +3 and highest in PTB subjects with sputum smear +1, but not significant. **Conclusion:** Platelet count and PCT were significantly higher in PTB subjects with advanced lesion than minimal lesion, while MPV and PDW were lower in PTB subjects with advanced lesion than minimal lesion but not significant. According to the positivity of sputum smear, platelet count was significantly higher in PTB subjects with sputum smear +2 than sputum smear +1 while MPV and PDW were not significant.

**KEYWORDS** Pulmonary tuberculosis, Platelet, Plateletcrit, Mean Platelet Volume, Platelet Distribution Width

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**Table 1** Characteristic of PTB Subjects (n=50).

Variable		n	%
Gender	Male	28	56,0
	Female	22	44,0
Age (Years)	<30	16	32,0
	30-49	22	44,0
	>=50	12	24,0
Body Mass Index	Underweight	37	74,0
	Normoweight	13	26,0
Lesion extent	Advanced	19	78,0
	Minimal	11	22,0
Sputum Smear	+1	24	48,0
	+2	18	36,0
	+3	8	16,0

## Introduction

According to the World Health Organization (WHO) in 2016, there were 10,4 million people developed PTB disease, the most common incidence was in Southeast Asia (45%) and Africa (25%). Indonesia is the second country with the most significant number of PTB incidences after India.[1] Mycobacterium tuberculosis invades the human body via droplet and induces pulmonary inflammation. The inflammatory response is a body mechanism to survive from many common microorganisms invasion.[2]

Platelets play a role in immunology process of various pulmonary diseases including PTB. Platelets are possibly involved in microvascular thrombosis formation around tuberculous granuloma making occlusion and limiting MTB spread. Platelets also can act as inflammatory cells by undergoing chemotaxis, phagocytosis, complement activation and inflammatory mediators release.[3] The linkage of PTB and platelets was first time observed in 1987, showed an increase in some small megakaryocytes in bone marrow due to short platelet life span which induces the increasing of thrombopoiesis.[4] However a recent study in 2018 suggested the direct role of platelets in the inflammation process. Platelets interact with monocytes in cell regulation, cell maturation, cytokines and Matrix metalloproteinases (MMPs) release.[5]

The increase of platelet count in some studies showed a relation with disease activity and severity of lung destruction in PTB patients. Interleukin (IL)-6 release due to MTB infection increases thrombopoietin production in the liver, influences the thrombopoietic cell maturation and platelet secretion into circulation.[3,6] Change in platelet size in some studies also related to various inflammatory diseases including PTB. Platelet count and size can be used to assess the severity of PTB disease.[3,7]

**Table 2** Descriptive Statistic of Age, BMI, and Platelet Profile.

Variable	Min	Max	Mean	SD
Age	17	65	38,34	13,84
BMI	12,1	23,0	17,15	2,55
Platelet Count	343	825	497,68	117,98
PCT	0,30	0,68	0,43	0,09
MPV	7,7	10,9	9,02	0,72
PDW	7,5	12,7	9,44	1,06

## Materials dan Methods

This study was an analytical study with a cross-sectional design conducted at Wahidin Sudirohusodo Hospital in Makassar from November 2018 until December 2018. It has been approved by the ethical committee of Medicine Faculty with reference number: 998 / H4.8.4.5.31 / PP36-KOMETIK / 2018.

### A. Population

The population of this study were all inpatients and outpatients with positive sputum smear new case PTB at Wahidin Sudirohusodo Hospital in Makassar. The inclusion criteria were positive sputum smear new case PTB patients, patients have never consumed the tuberculosis therapy, patients with no Human Immunodeficiency Virus (HIV) infection, the age > 18 years old and sign the informed research consent.

### B. Methods and data collection

Sample collection was managed with consecutive sampling; patients who met all the inclusion criteria were eligible for participation. Subjects were divided into two categories according to the lesion extent on chest x-ray. Pulmonary tuberculosis with less lesion in one or two lungs which not exceeded the lung volume in chondrosternal junction from the second rib and processus spinosus of fourth or fifth thoracic vertebrae and no cavity is called "minimal lesion". Pulmonary tuberculosis with more advance than minimal lesion is called "advanced lesion". According to the positivity of sputum smear, subjects were divided into three categories, sputum smear +1, sputum smear +2 and sputum smear +3. The platelet count, PCT, MPV and PDW levels were compared with each category of lesion extent on chest x-ray and positivity of sputum smear.

### C. Statistical analysis

Data were analyzed using the Statistical Package for Social Science (SPSS) program version 22. The statistical analysis performed was the calculation of frequency distribution, Independent-t and ANOVA test. Statistical test results were significant if the value of  $p < 0,05$ .

## Results

During the two months of the study period, authors found 50 patients who met the inclusion criteria, Table 1 shows the characteristic of PTB subjects, PTB was more commonly found in male (56%), and the age range was 30-49 years old (44%). According to the lesion extent on chest x-ray, we found that most of the lesions were advanced lesion (78%), while based on the positivity of sputum smear most of the subject smears were sputum smear

**Table 3** Platelet Profile According to the Lesion Extent on Chest X-Ray.

Variable	Lesion Extent	n	Mean	SD	p
Platelet Count (x1000)	Advanced	39	531,90	110,79	0,000
	Minimal	11	375,91	26,06	
PCT	Advanced	39	0,46	0,08	0,000
	Minimal	11	0,33	0,02	
MPV	Advanced	39	8,94	0,77	0,147
	Minimal	11	9,30	0,41	
PDW	Advanced	39	9,34	1,14	0,199
	Minimal	11	9,81	0,64	

**Table 4** Platelet Profile According to the Positivity of Sputum Smear.

Variable	Sputum Smear	n	Mean	SD	p
Platelet Count (x1000)	+1	24	454,87*	107,48	0,028
	+2	18	551,22*	129,15	
	+3	8	505,00	72,47	
PCT	+1	24	0,41	0,09	0,091
	+2	18	0,47	0,09	
	+3	8	0,44	0,07	
MPV	+1	24	9,15	0,80	0,457
	+2	18	8,91	0,71	
	+3	8	8,88	0,40	
PDW	+1	24	9,62	1,13	0,516
	+2	18	9,31	1,15	
	+3	8	9,20	0,57	

\*significant difference

+1 (48%) and only a few subjects with sputum smear +3 (16%). Table 2 shows the age mean of the subject was 38,34+13,84 years old. Body Mass Index (BMI) was between 12,1-23,0, with the mean of BMI was 17,15+2,55, it shows that most of the subjects were underweight. Platelet count was between 343-825; PCT value was between 0,30-0,68; MPV value was between 7,7-10,9; and PDW value was between 7,5-12,7.

Table 3 shows the mean of platelet count and PCT were significantly higher in PTB subjects with advanced lesion than minimal lesion ( $p < 0,001$  and  $p < 0,001$ ). There was a significant correlation between higher platelet count and plateletcrit with the advanced lesion. The MPV and PDW value were lower in PTB subjects with advanced lesion than minimal lesion but not significant ( $p > 0,05$ ). Table 4 shows that the platelet count was significantly higher in PTB subjects with sputum smear +2 than Sputum smear +1 ( $p < 0,05$ ). There was a significant correlation between higher platelet count and the high positivity of sputum smear, while the PCT value was not significant ( $p > 0,05$ ). The MPV and PDW value were lowest in PTB subjects with sputum smear +3 and highest in PTB subjects with sputum smear +1, but not significant ( $p > 0,05$  and  $p > 0,05$ ).

## Discussion

Platelets play an essential role as pulmonary immune cells and have a contribution to the pathogenesis of some pulmonary diseases. Platelets are possibly involved in microvascular thrombosis formation around the tuberculous lesion. This mechanism can limit the distribution of MTB infection in the respiratory system.[3,8] Platelets are derived from the same myeloid stem cell as classic inflammatory cells and have a contribution in chemotaxis process, phagocytosis, complement activation and pro-inflammatory mediators including Platelet Factor (PF)-4 and Platelet Derived Growth Factor (PDGF) cause the interaction of platelets-monocytes and monocytes differentiation.[3,9] In vivo and in vivo studies also showed the IL-6 production could induce thrombopoiesis process.[10,11,12] Interleukin-6, as a hematopoietic cytokine with various biologic function, can induce thrombopoietin production in the liver, megakaryocyte maturation and secrete platelets into the blood circulation.[6]

In this study, authors divided the lesion extent on chest x-ray into two categories, minimal lesion and advanced lesion. Although all the subjects were new case pulmonary tuberculosis, most common subjects have an advanced lesion on their chest x-ray image (78%), so we suggested that maybe the disease process is already developed since a long time. According to the positivity of sputum smear, authors divided the subjects into three categories sputum smear +1, sputum smear +2 and sputum smear +3. The results of this study show that platelet count was significantly higher in PTB subjects with advanced lesion than minimal lesion ( $p < 0,001$ ) and significantly higher in PTB subjects with sputum smear +2 than sputum smear +1 ( $p < 0,028$ ). The PCT value was also significantly higher in PTB subjects with advanced lesion than minimal lesion ( $p < 0,001$ ). Plateletcrit is an analogue of hematocrit for platelet, reflects the presentation of platelet volume in blood circulation.[13] Sahin et al. found that platelet count and PCT were significantly higher in PTB subjects with the advanced lesion.[14] Tozkoparan et al. also showed that platelet count and PCT were significantly higher in PTB subjects with advanced lesion than minimal lesion.[3] Unsal et al. found that there was a significant correlation between thrombocytosis with lesion extent on chest x-ray in PTB subjects.[15] However, in our research, there was no significant difference between PCT

with the positivity of sputum smear ( $p>0,05$ ). Some references explained that although the sputum smear microscopy is a rapid, simple and inexpensive tool for diagnosing PTB, it has low and various sensitivity because of the high possibility occurring the sampling error or technical problems.[16,17]

Mean Platelet Volume reflects the size of platelets and has been shown to correlate with the platelets function or activation.[18] The MPV has been emphasised as an inflammation marker to assess the disease activity or the therapeutic response in some inflammatory diseases.[19] Platelet Distribution Width reflects the various size of platelets in circulation and also reflects the platelet activation.[3] In this research, we found that MPV and PDW value were lower in PTB subjects with advanced lesion than in minimal lesion, but not significant ( $p>0,05$  and  $p>0,05$ ). According to the positivity of sputum smear, we found that the MPV and PDW value were lowest in PTB subjects with sputum smear +3 and highest in PTB subjects with sputum smear +1, but not significant ( $p>0,05$  and  $p>0,05$ ). Research by Sahin et al. also found that MPV and PDW value were lower in PTB subjects with advanced lesion than a minimal lesion but not significant.[14] Fatimah et al. showed that the value of MPV and PDW were also lower in PTB subjects with advanced lesion than minimal lesion, but not significant.[20] However, Sadek et al. found that the MPV and PDW were significantly lower in PTB subjects with advanced lesion than minimal lesion.[21] Research by Baynes et al. in 1987 found that MPV value was lower in active PTB and suggested that even the thrombopoiesis is an increase in PTB patient, but the platelet's lifetime may have been shortened. Some references suggested that in PTB case, the MPV value can be obtained low due to the evidence of pro-inflammatory cytokines over-production and acute phase reactants can influence the thrombopoiesis process and decrease the platelet size from bone marrow.[4,22]

### Conclusion

Platelet count and PCT were significantly higher in PTB subjects with advanced lesion than minimal lesion, while MPV and PDW were lower in PTB subjects with advanced lesion than minimal lesion but not significant. According to the positivity of sputum smear, platelet count is significantly higher in PTB subjects with sputum smear +2 than sputum smear 1.

### Competing Interests

There were no financial supports or relationships between authors and any organization or professional bodies that could pose any conflict of interest.

### Funding

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### Ethics Committee

It has been approved by the ethical committee of Faculty of Medicine with reference number: 998 / H4.8.4.5.31 / PP36-KOMETIK / 2018.

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