

# **Pulmonary Tuberculosis CT-Scan Features and Sputum Smear in Tertiary Referral Hospital**

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## **ABSTRACT**

**Introduction:** Management of pulmonary tuberculosis (PTB) from primary and secondary health centers might affect the result of sputum acid-fast bacilli (AFB) smear and features of lung computed tomography scan (CT-scan) presented in tertiary hospitals. The study aims to investigate comparison between CT-scan features of PTB with sputum AFB smear in Wahidin Sudirohusodo Hospital as the top referral hospital in the Eastern part of Indonesia. **Methods:** This is a retrospective study of patients diagnosed as PTB by pulmonologist of nine months period. Patients with available CT-scan and sputum AFB smear results are included in the study. CT-scan features re-evaluated with RadiAnt DICOM viewer for standardized reading. The relationship between data obtained was analyzed with a chi-square test. **Results:** Sixty-one PTB patients were entered into the study. The three most common features found in CT were consolidation (93.4%) followed by Tree-in-bud (91.8%), and fibrosis calcification (85.2%). Relationship of CT features and sputum AFB smear was significant on cavity (*p*-value: 0.002) and pleural effusion (*p*-value: 0.020). However, unlike cavity (OR = 1.667), pleural effusion has opposite relationship (OR = 0.205) with sputum AFB smear. **Conclusions:** Pulmonary tuberculosis CT features seen in top referral hospitals can be very severe with consolidation and tree-in-buds as the most common

*features found in more than 90% of the cases. Feature of cavity may help radiologist to distinct highly active PTB with positive sputum AFB smear while presence of pleural effusion should raise the suspicion from pulmonologists to add further laboratory investigation.*

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## 1. INTRODUCTION

Pulmonary tuberculosis (PTB) is one of the world's leading diseases with Indonesia as the 2<sup>nd</sup> top endemic country with 842 thousand cases in 2017.<sup>1</sup> Vigorous efforts of TB prevention and treatment programs are available in primary health centers to tertiary hospitals. However, Indonesian Universal Health Insurance has a multi-tiered referral scheme where PTB cases should only be referred to higher referral centers when lower health centers cannot provide modalities needed to treat PTB.<sup>1,2,3,4</sup> Thus, widespread of anti-TB and antibiotic usage without sufficient laboratory confirmation may affect the manifestation shown in CT-scan and sputum acid-fast bacilli (AFB) presented in tertiary hospital.<sup>5</sup>

## 2. SUBJECT AND METHODS

This study was conducted in the Radiology Department of Wahidin Sudirohusodo Hospital located in South Sulawesi, Indonesia. The hospital has an A level accreditation from the government which is the highest level in terms of availability of subspecialists and facilities. Wahidin hospital serves as the top referral point from 43 hospitals located in the eastern part of Indonesia.<sup>6</sup>

This is a retrospective study. All patients diagnosed as PTB by pulmonologist that underwent CT scan examination from October 2018 to June 2019 (nine months period) were included in the study. Information about patients' demographic and Sputum AFB result was obtained from records available in the hospital's Electronic Medical Record (EMR). Only those with uncorrupted CT-scan DICOM images and clear sputum AFB smear result was included in the study.

Parenchymal lesion formed in the lung were recorded by reviewing DICOM images obtained from patients using RadiAnt DICOM Viewer (Medixant – Poland, 2009). The review was made by a team consist of two radiologists with more than 10 and 25 years of experience.

Variables recorded for this study are presence of consolidation, cavity, tree-in-bud, fibrosis and calcification, air-bronchogram sign (ABS), nodular lesion, pleural effusion, atelectasis, lymphadenopathy, bronchiectasis, and ground-glass opacity (GGO). These variables are decoded as binominal number (0 = not present and 1 = present). Relationship between sputum AFB smear and parenchymal lesions are tested with chisquare test using SPSS software for Windows (version 23. 2015, IBM Corporation, NY, USA) p-value of less than 0.05 are considered statistically significant. We also recorded risk analysis with odds ratio to determine the independent predictive factors for patients with positive and negative sputum smear results.

### 3. RESULTS

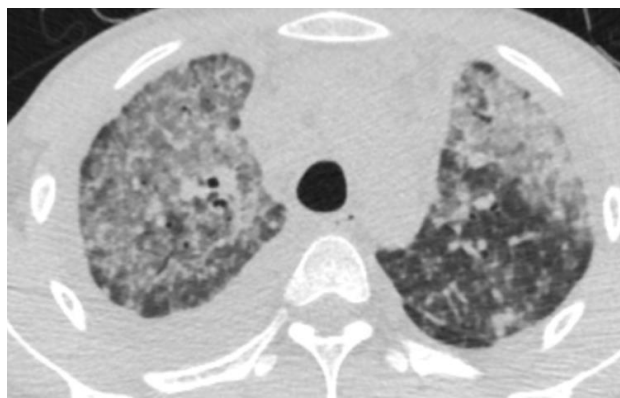
From October 2018 to June 2019, there were 115 patients diagnosed as pulmonary tuberculosis by pulmonologists who underwent lung CT-scan in Radiology Department of Wahidin Hospital. Of those, 20 patients (17.4%) did not have any sputum AFB smear result and 34 patients (29.6%) have corrupted DICOM files, leaving 61 patients (53.0%) available to be analysed.

The demographic distribution of gender is more predominant on male 39 (63.9%) compared to female 22 (30.1%). By age distribution, there are 42 (68.9%) patients above 40 years old with the oldest being 74 years old and the youngest being 6 years old at the time of study. The median age is recorded at 48 years old. Most cases are newly diagnosed as PTB (72.1%) despite the history of being filtered from previous primary and secondary health centers. There were 11 (18.0%) relapse cases, 2 (3.3%) Multiple Drug Resistance (MDR) cases, 1 (1.6%) case has mono-resistant PTB to isoniazid, 2 (3.3%) milliary TB, and 1 (3.3%) has drug allergy reaction (Table 1).

**Table 1.** Demographic and Pulmonary Tuberculosis Clinical Distribution

	N = 61	Sputum AFB Smear Result		p-value
		Positive (n = 16)	Negative (n = 45)	
Gender				
- Male	39 (63.9)	7 (43.7)	32 (71.1)	0.422
- Female	22 (30.1)	9 (56.2)	13 (28.9)	
Age distribution				
- < 40 yo	19 (31.1)	5 (31.1)	14 (31.1)	0.063
- ≥ 40 yo	42 (68.9)	11 (68.7)	31 (68.9)	
PTB diagnosis				
- New case	44 (72.1)	9 (56.2)	35 (77.8)	-
- Relapse case	11 (18.0)	3 (18.7)	8 (17.8)	
- MDR	2 (3.3)	2 (12.5)	0 (0)	
- Monoresistent	1 (1.6)	1 (6.2)	0 (0)	
- Miliary	2 (3.3)	0 (0)	2 (4.4)	
- Drug allergy	1 (1.6)	1 (6.2)	0 (0)	

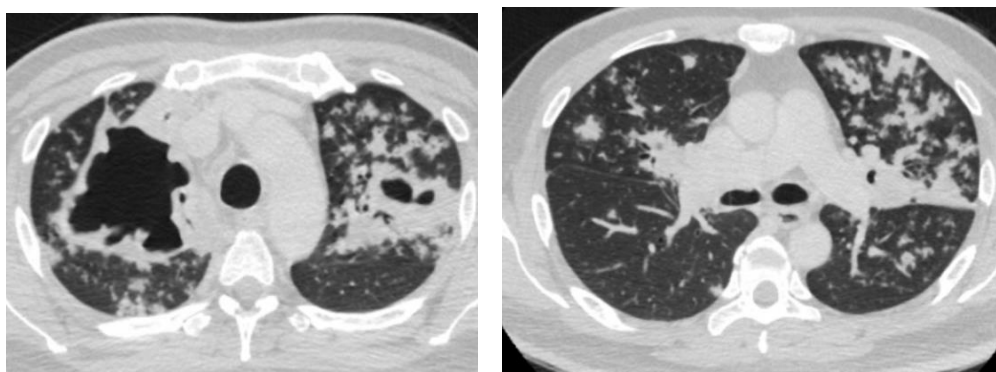
AFB = Acid-fast bacilli. PTB = pulmonary tuberculosis. MDR = Multiple drug resistance. yo = years old



**Figure 1.** Prominent features of consolidation, pleural effusion, ground-glass opacity and tree-in-bud in both lung parenchyma of a patient with negative sputum AFB smear and positive culture result.

In terms of AFB smear result, there were only 16 (26.2%) out of 61 that has positive AFB smear result. The rest of the patients 42( 68.9%) have negative results. However, looking at the culture result, there were 29 (47.5%) patients presented with positive culture results. Two of these patients are those diagnosed with millitary tuberculosis where sputum AFB smear was shown to be negative, but the culture was proved to be positive. This implies that established by other laboratory examinations, clinical symptoms, and response to anti-tuberculosis treatment according to pulmonologist in charge.

Figure 1 shows a case of negative sputum AFB smear results but presented with severe features of consolidation, GGO and tree-in-bud lesions in both lung parenchyma. This patient was then continued with culture examination which shown to be positive. Another case presents large multiple cavities with tree-in-bud lesions and positive AFB smear results. (Figure 2).



**Figure 2.** Multiple cavities with multiple nodules and tree-in-bud pattern were presented in a case with positive sputum AFB smear.

**Table 2.** Comparative chest CT scan features of positive and negative sputum AFB smear

CT scan features	N	Sputum AFB Smear		p-value
		Positive (n = 16)	Negative (n = 45)	
Consolidation	57 (93.4)	16 (26.2)	41 (67.2)	0.396
Cavity	40 (65.6)	16 (26.2)	24 (39.3)	0.002*
Tree-in-bud	56 (91.8)	15 (24.6)	41 (67.2)	1.000
Fibrosis and calcification	52 (85.2)	13 (21.3)	39 (63.9)	0.909
Air-bronchogram Sign	51 (83.6)	14 (22.9)	37 (60.6)	0.923
Nodules	51 (83.6)	15 (24.6)	36 (59.0)	0.377
Pleural effusion	36 (59.0)	5 (8.2)	31 (50.8)	0.020*
Atelectasis	35 (57.4)	11 (18.0)	24 (39.3)	0.437
Lymphadenopathy	29 (47.5)	7 (11.5)	22 (36.1)	0.950
Bronchiectasis	42 (68.8)	13 (21.3)	29 (47.5)	0.351
Ground glass opacity	50 (81.9)	14 (22.9)	36 (59.0)	0.771

Numbers in parentheses are percentages of presented lesion from total samples *Chi-Square test (continuity correction)*, \**p < 0.05*. AFB: Acid-fast bacilli. CT = computed tomography.

**Table 3.** Risk Analysis of Predictors for Sputum AFB Smear

CT Features	Odds ratio	95% CI	
Cavity	1.667	1.294 – 2.147	Favor positive AFB
Pleural Effusion	0.205	0.060 – 0.703	Favor negative AFB

AFB = Acid-fast bacilli. PTB = pulmonary tuberculosis

A comparison for each chest CT-scan features with the positivity of sputum AFB smear is presented in table 2. It is observed that the top three most presented features are consolidation 57 (93.4%), three-in-bud 56 (91.8%), and fibrosis-calcification 52 (85.2%). It is also noted that all cases with positive sputum smear have consolidation and cavity. When comparing CT-scan features between positive and negative sputum AFB smear, cavity and pleural effusion show statistically significant results with a *p-value* of 0.002 and 0.020 respectively. However, table 3 describes that the odds ratio for cavity is 1.667 favoring for positive sputum AFB smear while the odds ratio for pleural effusion is 0.205 favoring for negative sputum AFB smear.

#### 4. DISCUSSIONS

The study presents lung damages shown in chest CT features from a tertiary referral hospital that can be very severe. Features of nodules, air-bronchogram sign, ground-glass opacity, and fibrosis-calcification can be found in more than 80% of the patients. Even more, consolidation and tree-in-bud are presented in more than 90% of the patients. This finding might be related to the mandatory multi-tiered referral scheme from Indonesia universal health insurance. Referral scheme from the primary health center to hospital type D, C, and B, to finally reaching type A hospital can contribute to the delay of diagnosis and treatment, causing severe lung damages before the patient reach the top referral hospital. Previous study shown that delays in treatment for PTB mostly accounted from patients' and referral delays with average delays of 46.4 and 28.9 days respectively.<sup>7</sup> Adding to that, it is also shown that despite having to make multiple stops at lower-level health centre, 72% (n = 44) of the patients were still categorized as newly diagnosed cases in our centre. This implies the importance of increasing diagnostic capabilities to increase early detection rate for PTB in lower type health care centre.

Sputum AFB smear appears to be negative in most of the patients despite severe lung damages in this population. In this study, only 16 (26.2%) out of 61 patients are confirmed positive with sputum AFB smear. However, further laboratory tests with culture can only show 29 (47.5%) positive culture results in our patients. This finding is in concordance with previous study showing only 20.2% and 32.7% out of 5776 PTB patients in a TB centre showing positive result in sputum AFB smear and culture test respectively.<sup>8</sup>

A factor that can contribute to low findings of *Mycobacterium tuberculosis* (Mtb) in sputum AFB smear is because AFB smear method can only detect Mtb when there is at least 10,000 organisms per 1 ml sputum.<sup>8,9</sup> This finding implies that higher laboratory modalities such as culture combined with clinical assessment and image finding play a very important role in the diagnosis of PTB.

Computed tomography findings reported in our study are similar to previous studies showing cavity as the most important findings related to the positivity of sputum AFB smear.<sup>10</sup> Interestingly, the presence of pleural effusion is related significantly to negative, instead of positive AFB smear result with an odds ratio of 0.205. This finding implies that in the presence of negative AFB smear result combined with the presence of pleural effusion in CT scan, further evaluation with other modalities is needed. Previous study showed that 48 – 96% of sputum smear was negative on pleural

tuberculosis. Even with examination on pleural fluid samples, AFB stain remains negative in more than 90% of the patients.<sup>11,12</sup> Alternatively, some additional examination can be done to evaluate tuberculous pleural effusion such as examining the presence of lymphocyte-predominant exudative fluid with high adenosine deaminase (ADA) which has a positive predictive value for pleural tuberculosis of as high as 98%.<sup>13</sup> Another study suggests that a combination of multiple pathological examinations to detect presence of typical granulomas, AFB smears, and culture in tuberculosis with pleural effusion can yield positive results in 91% of the cases.<sup>14,15</sup>

Our study had several limitations that are worth noting. In this study, not all patients are confirmed with proven positive culture for tuberculosis but by a combination of imaging features, clinical symptoms and response to tuberculosis medication which might be affected by pulmonologist biases. This is also a retrospective study where CT scan files available for the study are not all standardized with contrast material but a mixture of both contrast-enhanced and non-contrast enhanced CT examination which might affect the appearance of CT scan features seen by our radiologist.

Population base for this study comes from patients with severe airway disease condition that was referred from multiple hospitals from lower-level health center. However, we did not control the patient based on what treatment they have been given from previous hospitals.

## **5. CONCLUSION**

Our results suggest that pulmonary tuberculosis found in a top referral hospital can be very severe with multiple lung parenchyma lesions seen in the CT features with consolidation and tree-in-buds as the most common features found in more than 90% of the cases. CT features can help to predict positive AFB smear from negative by checking on the presence of cavity which favor positive smear while the presence of pleural effusion favor negative smear results.

## **ACKNOWLEDGMENTS**

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