

Thoracic Radiography Findings of Multi-Drug Resistant Tuberculosis at Dr. Hasan Sadikin General Hospital Bandung

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Abstract

Background: The prevalence of multidrug-resistant pulmonary tuberculosis (MDR-TB) continues to increase, especially in Indonesia. Thoracic radiography examination plays a role in the TB diagnosis by providing findings of typical lesions in patients. The aim of the study was to determine the thoracic radiography findings in MDR-TB patients.

Methods: This was a cross-sectional retrospective descriptive study. This study had explored secondary data from medical records of patients who previously had a clinical diagnosis of MDR-TB and underwent thoracic radiography examinations at the Department of Radiology, Dr. Hasan Sadikin General Hospital, Bandung on July–August 2020.

Results: Of the 110 data collected, the average age was 37±12.6 years with male patients were predominantly prevalent and 65.5% had large lesions. The most frequent findings of lesions were calcification (94.5%) and fibrosis (90.9%). Other major findings were infiltration (88.2%), consolidation (55.5%), cavity (65.5%), ground-glass opacity (60.9%) while other were found in less than half of the cases such as, bronchiectasis (23%), nodule (34.5%), atelectasis (36.4%), lymphadenopathy (34.5%) and others. Interestingly, the miliary pattern was not found.

Conclusion: Large lesions, calcification, fibrosis, infiltration, consolidation, cavities, and ground-glass opacities are the main features of the radiographic findings in the majority of MDR-TB patients.

Keywords: Multi-drug resistant, thoracic radiograph, tuberculosis

Introduction

Tuberculosis (TB) is an infectious disease which is caused by *Mycobacterium tuberculosis*. This disease is one of the most common respiratory infections in the world, especially in developing countries such as Indonesia, with second highest incidence of TB cases.^{1,2} Multi-drug resistant tuberculosis (MDR-TB) is when *Mycobacterium tuberculosis* is resistant to at least Isoniazid and Rifampicin, which are the most effective first-line anti-TB drugs.¹ According to the World Health Organization (WHO), there were 24,000 MDR-TB cases in Indonesia in 2019 with 2.4% incidence and only 13% of cases have been treated. Data from the West Java Provincial Health Office has shown that there were over 1,500 MDR-TB

cases in West Java in 2018 of which 100 cases in Bandung, however, there was a slightly decrease. in 2019 with over 1,000 cases in West Java and less than 100 cases in Bandung.¹

Radiological examination plays an essential role in TB diagnosis. Radiological examination images show the location, area, and morphology of the lesions, such as cavity, consolidation, plural, effusion, and fibrosis. However, the radiological features are varied and not always distinctive. In addition, a chest radiograph is also useful in monitoring treatment response and detection of complications.³ A study found that MDR-TB contains multiple lung cavities, multiple nodules, bronchiectasis, and infiltration.³ Drug-sensitive tuberculosis (DS-TB) lesions are less common and the majority are infiltration, consolidation, cavity, and

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ground-glass opacity.⁴

In Indonesia, especially in West Java, there has been no study yet regarding the radiographic features of MDR-TB. The high incidence of MDR-TB in Indonesia encourages clinicians to be able early to detect this disease early to provide accurate and early therapy management. The objective of the study was to determine the thoracic radiography findings of MDR-TB patients at Dr. Hasan Sadikin General Hospital Bandung, the referral hospital for MDR-TB in West Java, particularly in Bandung.

Methods

This was a descriptive cross-sectional retrospective study. The study had used 110 samples of thoracic radiographs of patients who underwent chest radiography at the Department of Radiology, Dr. Hasan Sadikin General Hospital, Bandung for the period 15 July–31 August 2020 who were clinically diagnosed with MDR-TB based on rapid molecular test, bacterial culture, and drug sensitivity examinations according to standard diagnosis algorithm in Indonesia.⁵ Chest radiograph samples were obtained from the medical record and re-evaluated by an expert

radiologist.

This study has been approved by the Research Ethics Committee of Universitas Padjajaran no. 626/UN6.KEP/EC/2020 and from the Ethics Committee of Dr. Hasan Sadikin General Hospital Bandung no LB.02.01/X.2.2.1/19550/2020.

Data were analyzed using statistical software (Microsoft Excel 2019 and IBM SPSS version 22,0). Categorical data consisted of gender and lesion characteristics. Numerical data consisted of age which was stated as mean and standard deviation. Lesion characteristics were listed as percentages. Statistical calculations were carried out using the univariate method, statistical calculations using the frequency table of lesion characteristics.

Results

Of the 110 data collected, the most of patients with MDR-TB were male (66%) with a mean age of 37±12.6 years. Based on lesion area, most patients had large lesions (65.5%) and only small proportion of patients (5.5%) had minimal lesions (Table 1).

The most common findings on chest

Table 1 Radiologic Findings in Patients with Multi-drug Resistant Tuberculosis (MDR-TB)

Lesion characteristics	Proportion (n=110)
Area of the lesion, n (%)	
Minimal	6 (5.5)
Moderate	32 (29)
Large	72 (65.5)
Radiographic findings, n (%)	
Miliary pattern	0 (0)
Tree-in-bud nodules	7 (6.4)
Pleural effusion	11 (10)
Bullae	16 (14.5)
Bronchiectasis	26 (23.6)
Nodules	38 (34.5)
Lymphadenopathy	38 (34.5)
Atelectasis	40 (36.4)
Consolidation	61 (55.5)
Ground-glass opacity	67 (60.9)
Cavity	72 (65.5)
Infiltration	97 (88.2)
Fibrosis	100 (90.9)
Calcification	104 (94.5)



Figure 1 Large Lesion in the MDR-TB Patient

radiographs of patients were calcification (94.5%) as presented in Figure 1; whereas fibrosis (90.9%) and infiltration (88.2%) were also prevalent as shown in Figure 2. Other radiographic findings were in a lesser frequent such as cavity (65.5%), ground-glass opacity (60.9%), consolidation (55.5%). Interestingly, the miliary pattern was not found in radiographic findings of MDR-TB patients (Table 1).

Discussion

Our study has shown that MDR-TB patients

tend to be more common in men. Several other studies have similar result showing that males are more prevalent in MDR-TB cases. To date, there have been no conclusive studies explaining the relationship between the incidence of MDR-TB and gender. The higher proportion of male with MDR-TB might be based on individual behaviors affecting adherence to treatment as well as the risk of TB exposure.⁶

Another factor causing resistance to anti-TB drugs and MDR-TB is smoking. Smoking is an independent risk factor for MDR-TB. Smoking interferes with the alveolar macrophage



Figure 2 Cavity, Atelectasis, Infiltrate, and Fibrosis in MDR TB Patients

activity, decreases the immune response of pulmonary lymphocytes, and decreases the cytotoxic activity of natural killer cells, thereby increasing the likelihood of infection. Smoking also changes the metabolic clearance rate of anti-TB drugs by triggering the activity of cytochrome P450 CYP 1A1, CYP1A2, CYP2E1, and uridine 5'diphosphate (UDP) glucuronosyltransferase, thereby minimizing the effectiveness of treatment.⁷

In this study, the age range of the patients was 19–66 years (mean 37 years). Most MDR TB cases have occurred in the productive age, which might be related to high mobility and social interactions and thus might increase the risk of TB exposure and also decrease the effectiveness of TB treatment.⁸

Large lesions were found in 65.5% of cases and this is consistent with previous studies.^{5,9,10} The long duration of the disease is suspected to be the reason of the many large lesions found in MDR-TB patients.⁹ Furthermore calcification was the most common lesion in our study (94.5%), meanwhile in another retrospective study, the calcified lesion was found in only 46% of patients.¹¹ Calcification often occurred in long-term infections, such as TB. Calcification is one of the signs of TB which contains many components of *Mycobacterium tuberculosis*.¹² Another common lesion found in our study was fibrosis (90.9%). Fibrosis is formed during the healing or remodelling process which includes the activation and recruitment of fibroblasts, extracellular matrix materials, and distortion of normal tissue structures. Inflammatory cytokines IL-1 β , TGF- β , IFN- γ , IL-6, IL-8, and IL-12 regulate fibrosis formation leading to restrictive ventilatory defect in TB.¹³ Fibrosis appears to increase the risk of developing atelectasis which was found in 36.4% of cases.¹⁴

Another lesion found in high percentage in this study, is infiltration (88.2%). Infiltration at the onset of TB infection seems to cause significant damage in the future. Furthermore, the cavity was found in 65.5% of patients, similar percentage to another study.¹⁶ A cavity is formed when the area of caseous necrosis liquefies and communicates with the bronchi. Cavitory lesion is the primary mode of disease transmission due to the high bacterial content which allows the increase in drug-resistant mycobacteria. The cavitory lesion increases the likelihood of *Mycobacterium tuberculosis* resistance due to high oxidation and thick cavity walls which prevent the drug from penetrating the source of infection and reaching adequate concentrations.¹⁵

Additionally, most patients had ground-glass opacity (67%) and consolidation (61%) conform other study among MDR-TB patients.⁹ However, the presence of consolidation is not always specific to infection. Consolidation with ipsilateral hilar or paratracheal lymph node enlargement is predominant in TB patients.¹⁷

Other lesions are present in lower percentage such as the presence of nodules and lymphadenopathy (34.5%). In addition, in patients who were resistant to the anti-TB drugs, there was also an increase in cavitation of nodules.¹⁸ Bronchiectasis was found in 23.6% of patients and bronchiectasis was more frequent in MDR-TB than in DS-TB. In tuberculosis, bronchiectasis is caused by active inflammation and damage to the bronchial walls.¹⁹

Lesions that were rarely seen in this study were bullae (14.5%), pleural effusions (10%), and tree-in-bud nodules (6.4%). In contrary, studies showed that tree-in-bud nodules were one of the most common lesions found in MDR-TB patients. The tree-in-bud image results from the bronchogenic spread of necrosis and granulomatous inflammation.²⁰ Moreover, military lesion in our study was not found, consistent with another study that only found miliary lesions in 1% of patients.¹⁰

This study has several limitations, among others that this study did not include variables that could be comorbid with MDR-TB. Furthermore, as this study was conducted at one hospital in Bandung, the results obtained may not reflect the overall situation in the region.

To conclude, the main features of the radiographic findings in the majority of MDR-TB patients from Bandung are large lesions with calcification, fibrosis, infiltration, consolidation, cavities, and ground-glass opacities. Future studies examining the variables related to MDR-TB comorbidities and performing the study in several MDR-TB referral hospitals in Indonesia are of great interest.

References

1. WHO. Tuberculosis fact sheets. 2020 [cited 2020 February 16]. Available from: <https://www.who.int/news-room/fact-sheets/detail/tuberculosis>.
2. WHO. Global tuberculosis report 2020. Geneva: World Health Organization; 2020.
3. Laya BF, Sto. Domingo MCL, Javier XM, Sanchez M. Drug resistant tuberculosis: radiologic imaging manifestations. WFPI

- TB Corner. 2015;1(1):1-5.
- Majdawati A, Icksan AG, Lolong D. Comparison of chest x-ray lesion characteristics of multidrug-resistant tuberculosis and non-tuberculous mycobacterial infection. *Pol J Radiol*. 2019;84:e162-70.
 - Kementrian Kesehatan RI. Petunjuk teknis manajemen terpadu pengendalian tuberkulosis resistan obat. Jakarta: Direktorat Jenderal Pengendalian Penyakit dan Penyehatan Lingkungan Kementerian Kesehatan Republik Indonesia; 2018.
 - Yang Y, Zhou C, Shi L, Meng H, Yan H. Prevalence and characterization of drug-resistant tuberculosis in a local hospital of Northeast China. *Int J Infect Dis*. 2014;22:83-6.
 - Chiang YC, Lin YM, Lee JA, Lee CN, Chen HY. Tobacco consumption is a reversible risk factor associated with reduced successful treatment outcomes of anti-tuberculosis therapy. *Int J Infect Dis*. 2012;16(2):e130-5.
 - Mehari K, Asmelash T, Hailekiros H, Wubayehu T, Godefay H, Araya T, et al. Prevalence and factors associated with multidrug-resistant tuberculosis (MDR-TB) among presumptive MDR-TB patients in Tigray Region, Northern Ethiopia. *Can J Infect Dis Med Microbiol*. 2019;2019:2923549.
 - Icksan AG, Napitupulu MRS, Nawas MA, Nurwidya F. Chest X-ray findings comparison between multi-drug-resistant tuberculosis and drug-sensitive tuberculosis. *J Nat Sci Biol Med*. 2018;9(1):42-6.
 - Sulaiman SC, Handayani L, Suwandi MSY, Soedarsono S. Gambaran radiografi tuberkulosis paru multidrug-resistant. *J Respirasi*. 2018;4(3):71-5.
 - Zahirifard S, Amiri MV, Karam MB, Mirsaeidi M, Ehsanpour A, Masjedi MR. The radiological spectrum of pulmonary multidrug-resistant tuberculosis in HIV-negative patients. *Iran J Radiol*. 2003;1(3-4):161-6.
 - Iida T, Uchida K, Lokman N, Furukawa A, Suzuki Y, Kumasaka T, et al. Calcified granulomatous lung lesions contain abundant mycobacterium tuberculosis components. *J Mycobac Dis*. 2014;4(1):142.
 - Ravimohan S, Kornfeld H, Weissman D, Bisson GP. Tuberculosis and lung damage: from epidemiology to pathophysiology. *Eur Respir Rev*. 2018;27(147):170077.
 - Cherian RA, Lowrey B. Atelectasis. In: Kissane J, Neutze JA, Singh H, editors. *Radiology fundamentals: introduction to imaging & technology*. 6th ed. New York: Springer International Publishing; 2020. p. 89-97.
 - Barroso EC, Mota RMS, Santos RO, Sousa ALO, Barosso JB, Rodrigues JLN. Risk factors for acquired multidrug-resistant tuberculosis. *J Pneumologia*. 2003;29(2):89-97.
 - Wáng YXJ, Chung MJ, Skrahin A, Rosenthal A, Gabrielian A, Tartakovsky M. Radiological signs associated with pulmonary multi-drug resistant tuberculosis: an analysis of published evidences. *Quant Imaging Med Surg*. 2018;8:161-73.
 - Yeh JJ, Chen SC, Teng WB, Chou CH, Hsieh SP, Lee TL, et al. Identifying the most infectious lesions in pulmonary tuberculosis by high-resolution multi-detector computed tomography. *Eur Radiol*. 2010;20(9):2135-45.
 - Ballester AN. *Computed tomography features of multi-drug-resistant pulmonary tuberculosis in non-HIV-infected patients*. Tamil Nadu: SM Group; 2016.
 - Li D, He W, Chen B, Lv P. Primary multidrug-resistant tuberculosis versus drug-sensitive tuberculosis in non-HIV-infected patients: Comparisons of CT findings. *PLoS One*. 2017;12(6):e0176354.
 - Kim W, Lee KS, Kim HS, Koh WJ, Jeong BH, Chung MJ, et al. CT and microbiologic follow-up in primary multidrug-resistant pulmonary tuberculosis. *Acta Radiol*. 2016;57(2):197-204.