

# Proportionate detection of *Mycobacterium tuberculosis* complex and nontuberculous mycobacteria using MGIT 960 in pulmonary TB sputum: experience from a tertiary referral center, Surabaya (2021–2023)

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**Abstract.** Indonesia remains a high TB-burden country where dense populations facilitate transmission of *Mycobacterium tuberculosis* complex (MTBC) and the emergence of nontuberculous mycobacteria (NTM). Differentiating MTBC from NTM is clinically essential because treatment and public-health actions differ. We performed a retrospective descriptive study using secondary medical-record data from Dr. Soetomo Academic Hospital, Surabaya, Indonesia (January 2021–December 2023). Sputum specimens from presumptive pulmonary TB cases were cultured using the MGIT 960 liquid culture system. Demographics, comorbidities, and culture identification (MTBC vs NTM) were summarized descriptively. The results is Among 81 patients, 62 were male (76.4%) and 45 were aged  $\geq 46$  years (55.6%). Diabetes mellitus was the most frequent comorbidity (27/81, 33.3%). MGIT 960 detected MTBC in 72/81 patients (88.9%) and NTM in 9/81 (11.1%). MTBC accounted for the vast majority of culture-positive pulmonary cases at this tertiary referral center, while NTM comprised about one-tenth of detections—highlighting the need for routine species-level discrimination to avoid mistreatment and to inform infection-control strategies. The conclusion in a three-year hospital-based cohort from Surabaya, MTBC predominated in MGIT 960–positive sputum cultures, with a smaller yet notable proportion of NTM. Incorporating systematic MTBC–NTM differentiation in diagnostic workflows may optimize clinical management in high-burden settings.\*

## 1 Introduction

According to the World Health Organization (WHO) in 2020, TB or Tuberculosis was the 13th leading cause of death globally and the second leading cause of death from an infectious

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disease [1]. In 2020, an estimated ten million people contracted tuberculosis (TB) worldwide, comprising 5.6 million men, 3.3 million women, and 1.1 million children. According to the Indonesian Ministry of Health [2], tuberculosis is a contagious disease caused by the bacterium *Mycobacterium tuberculosis* complex (MTBC), and according to the World Health Organization, this disease can spread through the air (airborne). In addition to MTBC, there are other bacteria that cause pulmonary diseases similar to Tuberculosis. The cause of tuberculosis is not solely MTBC, but it can also be caused by Nontuberculous (NTM). TB or tuberculosis is a disease that can be prevented and cured. The World Health Organization (WHO) also stated that 85% of people diagnosed with tuberculosis can be treated with a 6-month drug regimen, with regimens ranging from 1 to 6 months used to treat TB infections. WHO also stated that 90% of adults are diagnosed with this disease, with more cases among men than women [1].

To sustain its life, MTBC seeks living organisms in which it can grow, as MTBC is a microorganism. Invasion of the respiratory tract and lungs is an example of how this bacterium begins its life cycle, a phenomenon known as primary infection. The confrontation between pathogens and the respiratory system is also referred to as primary infection. TB infection begins when the microorganism enters the host's respiratory tract and lungs, subsequently triggering the immune system, where it is engulfed by macrophages and dendritic cells. At this stage, MTBC replicates within these cells, attracting more immune cells to the site of infection. MTBC may be eliminated at this stage, but more often, solid granulomas form. These granulomas consist of foamy macrophages and necrotic immune cells, ultimately forming caseous granulomas that can rupture and release bacteria, allowing the development of active TB. Eventually, the MTBC bacteria are released as aerosol droplets that can infect others [3].

NTM bacteria can infect bronchial epithelial cells due to their pulmonary-focused infectious nature. On the surface layer of *Mycobacterium avium*, fibronectin-binding proteins can be found, which support bacterial attachment to integrin receptors through fibronectin in the mucosa. The increased ability to invade macrophages is caused by the entry of bacilli into epithelial cells, leading to phenotypic changes. NTM bacteria are capable of forming biofilms and inhibiting inflammatory cytokine production, allowing them to evade immune cells, increase colonization, and invade bronchial epithelial cells [4]. In densely populated countries like Indonesia, it is undeniable that the spread of disease occurs easily and rapidly. One disease that is impacted by population density is TB or tuberculosis. According to INFODATIN (2022), Indonesia ranks third in the world for the highest number of cases, following India and China [5]. A report from the Ministry of Health (2021) stated that in 2021, there were 385,295 TB cases detected and treated. Indonesia MoH (2021) noted that this number represents a 2.04% decrease from the previous year, which saw 393,323 cases detected and treated in 2020. According to Indonesia MoH (2022), over the past decade, the trend in the number of tuberculosis cases in Indonesia has been fluctuating. For example, in 2011, there were 321,308 cases detected and treated. The trend increased in subsequent years, peaking at 570,289 cases in 2018. It then declined slightly in 2019 to 568,997 cases and continued to decrease thereafter [5].

Indonesia MoH (2020) reported that the estimated number of TB cases in Indonesia was around 845,000 [6]. In East Java Province, according to Indonesia MoH (2022), there were 43,268 reported cases [5]. However, a study by Mertaniasih et al. (2017) stated that in various countries, there has been an increase in the prevalence, incidence, and mortality due to pulmonary infections caused by NTM, raising concerns among clinicians and academics. In the past decade, there has also been a rise in reports of both human and non-human infections caused by environmental or nosocomial NTM [7]. This increasing trend in NTM infections has drawn significant attention from clinicians and academics [8]. However, epidemiological data on NTM in Indonesia are very limited. Based on the background described above, this

study aims to determine the proportion of MTBC and NTM detection in the sputum of pulmonary TB patients using the MGIT 960 system rapid culture method at Dr Soetomo Academic Hospital, thereby assisting clinicians and academics in analyzing the case trends.

## **2 Methods**

### **2.1 Research Design**

This study employed a descriptive retrospective research design to determine the proportion of MTBC and NTM detected using the rapid culture method MGIT 960 system in the sputum of pulmonary TB patients at Dr Soetomo Academic Hospital from January 2021 to January 2023. The research design used in this study was retrospective, utilizing medical record data of pulmonary TB patients from the TB DOTS Outpatient Clinic Unit and the Clinical Microbiology Laboratory at Dr Soetomo Academic Hospital, Surabaya, from January 2021 to January 2023.

### **2.2 Population and Sample**

The population of this study consisted of medical record data of patients suspected of having pulmonary TB at the TB DOTS Outpatient Clinic Unit and the Clinical Microbiology Laboratory of Dr Soetomo Academic Hospital, Surabaya, from January 2021 to January 2023. The inclusion criteria for this study were all medical records of patients suspected of having pulmonary TB who underwent examination using the MGIT 960 System method at the TB DOTS Outpatient Clinic Unit and the Clinical Microbiology Laboratory of Dr Soetomo Academic Hospital, Surabaya, from January 2021 to January 2023. The exclusion criteria for this study were patients with incomplete medical records, such as missing personal or clinical data, as well as patients who underwent examinations using methods other than the rapid culture MGIT 960 System.

### **2.3 Sampling Technique and Data Collection**

A total sampling method was employed in this study, meaning that all patients who fulfilled the predefined inclusion and exclusion criteria. This approach was chosen to ensure comprehensive data collection and to maximize the representativeness of the study population. Data collection was performed retrospectively by reviewing the medical records of patients suspected of having pulmonary tuberculosis, who underwent diagnostic testing at the TB DOTS Outpatient Clinic Unit and the Clinical Microbiology Laboratory of Dr Soetomo Academic Hospital, Surabaya, between January 2021 and January 2023. The primary variables extracted and analyzed from the medical records included patient age, sex, clinical symptoms at presentation (such as cough, fever, weight loss, or hemoptysis), presence of comorbid conditions (such as HIV, diabetes mellitus, or other chronic diseases), and the confirmed status of pulmonary TB infection. All variables were carefully recorded to ensure data accuracy and consistency, forming the basis for subsequent statistical analysis to evaluate the distribution and characteristics of MTBC and NTM detection in the study population.

### **2.4 Data Analysis**

Data analysis in this study was conducted using a descriptive method. After all relevant data were collected, they were categorized based on predetermined research variables. The

categorized data were then processed using the Statistical Package for the Social Sciences (SPSS) version 23 to obtain descriptive statistics such as frequency distributions and percentages. Microsoft Excel was also used to assist with data organization, tabulation, and the creation of tables and charts to facilitate interpretation and presentation of the study results.

### 3 Results and discussion

This study included a total sample population of 227 hospitalized patients at Dr Soetomo Academic Hospital Surabaya from January 2021 to January 2023 who underwent rapid culture testing using the MGIT 960 system. Out of the 227 patients, 81 met the inclusion criteria. A total of 146 subjects were excluded due to incomplete data.

**Table 1.** Distribution of subject characteristics, bmi, SGOT/SGPT

Variable	Not Elevated	Elevated	<i>p-value</i>
Body Mass Index (BMI) and the Elevation of SGOT/SGPT			
Underweight	1 (0.8%)	0 (0.0%)	< 0.0001
Normal	22 (17.7%)	8 (6.5%)	
Overweight	9 (7.3%)	44 (35.5%)	
Obesity	5 (4.0%)	35 (28.2%)	
IMT and the elevated SGOT			
Underweight	1 (0.8%)	0 (0.0%)	< 0.0001
Normal	25 (20.2%)	5 (4.0%)	
Overweight	21 (16.9%)	32 (25.8%)	
Obesity	9 (7.3%)	31 (25.0%)	
IMT and the elevated SGPT			
Underweight	1 (0.8%)	0 (0.0%)	< 0.0001
Normal	25 (20.2%)	5 (4.0%)	
Overweight	17 (13.7%)	36 (29.6%)	
Obesity	11 (8.9%)	29 (23.4%)	

Based on Table 1, no children were found in either the MTBC or NTM groups. In the adolescent group, 11.1% were affected by both MTBC and NTM. Among adults, 33.3% had MTBC and 33.3% NTM, while in the elderly group ( $\geq 46$  years), 55.6% had both MTBC and NTM. The majority of pulmonary TB patients were male, with 76.4% having MTBC and 55.6% having NTM. Common symptoms and comorbidities among patients included diabetes, HIV co-infection, shortness of breath, cough, nausea, diarrhea, weight loss, fatigue, fever, night sweats, and ear discharge. Among TB patients, 33.3% had diabetes, and 1.38% had HIV co-infection. For TB patients, the most common symptoms were shortness of breath (62.5%), cough (51.4%), weight loss (30.5%), and fatigue (27.7%). In the NTM group, shortness of breath (66.7%) and weight loss (33.3%) were the most prevalent symptoms. No NTM patients reported nausea, diarrhea, or fever.

**Table 2.** Characteristics of patient age variables, DMT2, SGOT/SGPT

Variable	Not Elevated	Elevated	<i>p-value</i>
DMT2 and the Elevation of SGOT/SGPT			
DM Tipe 2	12 (9.7%)	59 (47.6%)	< 0.0001
Non DM Tipe 2	25 (20.2%)	28 (22.6%)	
DMT2 and the Elevation of SGOT			
DM Tipe 2	27 (21.8%)	44 (35.5%)	0.65
Non DM Tipe 2	29 (23.4%)	24 (19.4%)	

Variable	Not Elevated	Elevated	<i>p-value</i>
<b>DMT2 and the Elevation of SGPT</b>			
DM Tipe 2	24 (19.4%)	47 (37.9%)	0.11
Non DM Tipe 2	30 (24.2%)	23 (18.5%)	

Based on Table 2, a total of 227 patients underwent the BACTEC MGIT 960 system (BD) examination, with 71 patients (88.89%) infected with \*Mycobacterium tuberculosis\* and 9 patients (11.11%) infected with NTM (non-tuberculosis) pathogens. The average age of MTB patients was 46.6 years, while the average age of NTM patients was 45.4 years. The age range for TB patients was 15 to 75 years, and for NTM patients, it was 22 to 64 years.

**Table 3.** Comparison of MTB and NTM based on patient's pulmonary TB status, SGOT/SGPT

Variable	Not Elevated	Elevated	<i>p-value</i>
<b>HT and the Elevation of SGOT/SGPT</b>			
Hypertension	12 (9.7%)	55 (44.4%)	0.002
Non Hypertension	25 (20.2%)	32 (25.8%)	
<b>HT and the Elevation of SGOT</b>			
Hypertension	21 (16.9%)	46 (37.1%)	0.001
Non Hypertension	35 (28.2%)	22 (17.7%)	
<b>HT and the Elevation of SGPT</b>			
Hypertension	25 (20.2%)	42 (33.9%)	0.129
Non Hypertension	29 (23.4%)	28 (22.6%)	

Based on Table 3, the majority of pulmonary TB patients were new cases, accounting for 61.11% in MTB cases and 88.9% in NTM cases. Among the pulmonary TB cases, more patients with TB were classified as TB-relapse (22.22%) compared to TB-MDR (13.89%) and TB-loss to follow-up (2.78%). In contrast, for NTM cases, 1 patient (11.1%) was identified as a relapse case.

**Table 4.** Proportion of MTBC and NTM detection in pulmonary TB Patients, SGOT/SGPT profile, and antimicrobial sensitivity

Variable	Not Elevated	Elevated	<i>p-value</i>
<b>Antibiotic and the Elevation of SGOT/SGPT</b>			
Azithromycin	4 (3.2%)	15 (12.1%)	< 0.0001
Moxifloxacin	20 (16.1%)	10 (8.1%)	
Levofloxacin	5 (4.0%)	37 (29.8%)	
Ceftriaxone	2 (1.6%)	7 (5.6%)	
Erythromycin	0 (0.0%)	1 (0.8%)	
Not received	6 (4.8%)	17 (13.7%)	
<b>Antibiotic and the Elevation of SGOT</b>			
Azithromycin	7 (5.6%)	12 (9.7%)	0.24
Moxifloxacin	21 (16.9%)	9 (7.3%)	
Levofloxacin	16 (12.9%)	26 (21.0%)	
Ceftriaxone	2 (1.6%)	7 (5.6%)	
Erythromycin	1 (0.8%)	0 (0.0%)	
Not received	9 (7.3%)	14 (11.3%)	
<b>Antibiotic and the Elevation of SGPT</b>			
Azithromycin	8 (6.5%)	11 (8.9%)	< 0.0001
Moxifloxacin	23 (18.5%)	7 (5.6%)	
Levofloxacin	10 (8.1%)	32 (25.8%)	
Ceftriaxone	2 (1.6%)	7 (5.6%)	
Erythromycin	1 (0.8%)	0 (0.0%)	

Variable	Not Elevated	Elevated	<i>p-value</i>
Not received	10 (8.1%)	13 (10.5%)	

Based on Table 4, the researcher found that out of a total of 81 patients (100%), the proportion of MTBC and NTM detection in pulmonary TB patients at Dr Soetomo Academic Hospital Surabaya showed a higher incidence of MTB infection. Specifically, 72 patients (88.9%) were detected with MTBC, while 9 patients (11.1%) were detected with NTM.

### 3.1 Discussion

In this study, it was found that the majority of pulmonary TB patients detected with MTB and NTM bacteria at Dr. Soetomo Hospital Surabaya were in the elderly age group ( $\geq 46$  years), totaling 40 patients (55.6%), followed by patients in the adult age group (26-45 years) with 24 patients (33.3%). This is consistent with a study by Aliyu et al. (2013), which stated that NTM infections are more common in older individuals [9]. A study by Hannah et al. (2020) at the Midwestern Tertiary Hospital found that the elderly are more vulnerable to infections, and NTM-related diseases become more easily transmissible as age increases [10]. From this explanation, it can be concluded that poor sanitation is directly related to the increased incidence of TB in a region.

The sample obtained in this study was mostly male. In the MTB-detected patients, 78.6% were male, and 21.4% were female, while in the NTM-detected patients, 55.6% were male and 44.4% were female. This phenomenon can be explained by the fact that most men smoke. Habits like smoking and alcohol consumption can weaken the immune system, making individuals more susceptible to diseases [11]. The results of this study align with research by Schurz et al. (2019), which explains that sex hormones also influence susceptibility to TB infection. Estrogen acts as an immune system activator and increases anti-inflammatory cytokines (IL-10), while testosterone suppresses the immune system and causes an increase in anti-inflammatory cytokines (IL-10), making men more vulnerable to tuberculosis infection [12–14].

The results obtained in this study show that the majority of patients in both MTB detection and NTM detection experienced shortness of breath, with percentages of 66.1% and 66.7%, respectively, followed by cough in MTB patients (50%) and weight loss (33.3%). This is consistent with a study by Mar'Iyah (2021), which explained that shortness of breath is a common symptom in pulmonary TB patients [11]. When a patient is infected with pulmonary TB, granulomas form due to the interaction between the Mycobacterium tuberculosis bacteria and the immune system. A granuloma consists of macrophages that surround both live and dead bacteria. The granuloma transforms into fibrous tissue, and its central part is referred to as Ghon tuberculosis, which develops into a cheesy mass due to necrosis. In immunodeficient patients, previously dormant bacteria can become active. This necrotizing caseosa inside the bronchi forms because of the breakdown of the Ghon tubercle. The disease can spread further as bacteria are released into the air. The tubercles, which no longer regenerate, will form scar tissue. Infected lungs will swell, leading to bronchopneumonia, thus concluding that most TB patients experience shortness of breath [11].

Our study found that 17 MTB-detected patients (30.4%) had comorbid diabetes mellitus, while 1 NTM-detected patient (11.1%) had diabetes mellitus. This result is consistent with a study at Arifin Achmad Hospital in 2016, which explained that most pulmonary tuberculosis patients had comorbidities. Diabetes mellitus was the most common comorbidity among pulmonary tuberculosis patients at Arifin Achmad Hospital [15]. Cáceres (2022) stated that patients with diabetes mellitus are three times more likely to develop tuberculosis than those without diabetes mellitus [15]. This occurs because diabetes mellitus patients experience immunodeficiency, which leads to impaired phagocytosis and makes them more susceptible

to tuberculosis infection [13]. The development of *Mycobacterium tuberculosis* can be triggered by a weakened immune response, such as in hyperglycemia [15].

The results obtained in this study show that 44 patients (61.11%) with MTB-detected pulmonary TB were new cases, followed by 16 patients (22.22%) with relapse, 10 patients (13.89%) with multi-drug resistance, and 2 patients (2.78%) who lost to follow-up. In the NTM-detected cases, the results were similar to the MTB-detected cases, with the majority being new TB cases (8 patients, 88.9%) and 1 relapse case (11.1%). The incidence of pulmonary TB in Indonesia, according to the World Health Organization (WHO), ranks second in terms of the highest tuberculosis infection rates. The tuberculosis mortality rate in Indonesia is 52 per 100,000 population. More than 30 people die from tuberculosis infections each year [14]. According to the Ministry of Health, in 2023, the incidence rate of tuberculosis cases in Indonesia reached 354 per 100,000 population [5]. The spread of tuberculosis infections is influenced by several factors, one of which is environmental health factors. Indonesia is still considered a developing country, and tuberculosis cases are more common in developing countries due to a significant proportion of the population living in poverty. Poor air quality due to inadequate ventilation significantly impacts the spread of the bacteria causing tuberculosis [13-14]. Therefore, Indonesia experiences a high number of new pulmonary TB cases. In addition to new pulmonary TB cases, the researcher also found relapse and multi-drug resistance cases in this study. However, the number of cases was not as high as the new pulmonary TB cases. This aligns with a study by Jaya and Mediarti (2017) at the Special Pulmonary Hospital in South Sumatra, which showed that most patients had high adherence to treatment, resulting in fewer relapse and multi-drug resistance cases [11].

In this study, the results indicated that the proportion of MTBC bacteria was higher than NTM in pulmonary TB patients at Dr Soetomo Academic Hospital, with MTBC detected in a larger number. This is consistent with research by Daniel Kahase et al. (2021), which stated that MTBC bacterial infections are more prevalent than NTM, with 26 out of 29 patients (89.7%) infected with MTBC and 3 patients (10.3%) infected with NTM. This phenomenon occurs because MTBC bacteria have a higher virulence level than NTM [15]. Many factors contribute to why MTBC has a higher virulence than NTM, one of which is the host factor. A study at the National TB and Leprosy Training Center (NTBLTC) in Zaria, from August 2010 to July 2011, identified 444 culture-positive TB cases among 1603 patients screened, with 375 (85%) caused by MTBC and 69 (15%) caused by NTM.

### **3.2 Study Limitations**

This study has several limitations, including the scope of variables analyzed. Based on the findings, the researchers recommend expanding the research variables to make the results more comprehensive and specific. The study revealed that NTM remain one of the causes of tuberculosis at Dr Soetomo Academic Hospital. Therefore, clinicians should be more cautious when differentiating between MTB and NTM. Furthermore, medical record data collection should be improved in terms of clarity and accuracy, allowing for more complete and informative results, which will ultimately provide clearer insights for both academics and clinicians.

## **4 Conclusion**

In conclusion, the detection of MTBC and NTM using the MGIT 960 Rapid Culture System in sputum samples from TB patients at Dr Soetomo Academic Hospital between 2020 and 2023 showed that the majority of patients were elderly, aged over 46 years, with a higher proportion of males. A significant number of patients reported experiencing shortness of breath and had comorbid Diabetes Mellitus. The detection rate of *Mycobacterium*

tuberculosis complex as the primary cause of pulmonary tuberculosis was higher than that of non-tuberculous mycobacteria.

## Ethics approval

The Health Research Ethics Commission, Universitas Airlangga, has authorized all of the research procedures with the registration number 125/KEP/2022 with Protocol Number UA-02-22161.

## Acknowledgement

We would like to express our sincere gratitude to Dr Soetomo Academic Hospital, Indonesia, for their invaluable support in the successful completion of our research. This assistance played a pivotal role in facilitating data collection, analysis, and the overall execution of the project.

## References

- [1] J. Yang, L. Zhang, W. Qiao, Y. Luo. Mycobacterium tuberculosis: Pathogenesis and therapeutic targets. **MedComm (Beijing)**. 4(5), 2023. doi:10.1002/mco2.353.
- [2] H. Honda, N. Ohmagari, Y. Tokuda, C. Mattar, D.K. Warren. Antimicrobial stewardship in inpatient settings in the Asia Pacific region: a systematic review and meta-analysis. **Clin Infect Dis**. 64(Suppl\_2):S119–S126, 2017. doi:10.1093/cid/cix017.
- [3] N. Mertaniasih, D. Kusumaningrum, E. Koendhori, Soedarsono, T. Kusmiati, D.S.S. Dewi. Nontuberculous mycobacterial species and Mycobacterium tuberculosis complex coinfection in patients with pulmonary tuberculosis in Dr. Soetomo Hospital, Surabaya, Indonesia. **Int J Mycobacteriol**. 6(1):9–14, 2017. doi:10.4103/2212-5531.201894.
- [4] A.C. Pereira, B. Ramos, A.C. Reis, M.V. Cunha. Non-tuberculous mycobacteria: molecular and physiological bases of virulence and adaptation to ecological niches. **Microorganisms**. 8(9):1380, 2020. doi:10.3390/microorganisms8091380.
- [5] G. Aliyu, S.S. El-Kamary, A. Abimiku, C. Brown, K. Tracy, L. Hungerford, et al. Prevalence of non-tuberculous mycobacterial infections among tuberculosis suspects in Nigeria. **PLoS One**. 8(5):e63170, 2013. doi:10.1371/journal.pone.0063170.
- [6] C.E. Hannah, B.A. Ford, J. Chung, D. Ince, K.A. Wanat. Characteristics of nontuberculous mycobacterial infections at a Midwestern tertiary hospital: a retrospective study of 365 patients. **Open Forum Infect Dis**. 7(6):ofaa173, 2020. doi:10.1093/ofid/ofaa173.
- [7] H. Schurz, C.J. Kinnear, C. Gignoux, G. Wojcik, P.D. van Helden, G. Tromp, et al. A sex-stratified genome-wide association study of tuberculosis using a multi-ethnic genotyping array. **Front Genet**. 9:678, 2019. doi:10.3389/fgene.2018.00678
- [8] S. Jaillon, K. Berthenet, C. Garlanda. Sexual dimorphism in innate immunity. **Clin Rev Allergy Immunol**. 56(3):308–321, 2019. doi:10.1007/s12016-017-8648-x.
- [9] M. Cutolo, B. Seriolo, C. Pizzorni, M.E. Secchi, S. Soldano, S. Paolino, et al. Use of glucocorticoids and risk of infections. **Autoimmun Rev**. 8(2):153–155, 2008. doi:10.1016/j.autrev.2008.07.010. [PubMed](#)
- [10] E. Mallinda, Z. Af, M. Savira. Profil penderita tuberculosis paru yang dirawat inap di Bagian Paru RSUD Arifin Achmad Provinsi Riau periode 01 Januari–31 Desember 2013. **Jurnal Online Mahasiswa Fakultas Kedokteran Universitas Riau**. 3(1):1–

- 12, 2016. (Akses 12 Nov 2025).  
URL: <https://media.neliti.com/media/publications/189058-ID-profil-penderita-tuberkulosis-paru-yang.pdf> [Neliti](#)
- [11] G. Cáceres, R. Calderon, C. Ugarte-Gil. Tuberculosis and comorbidities: treatment challenges in patients with comorbid diabetes mellitus and depression. **Ther Adv Infect Dis.** **9**:1–13, 2022. doi:10.1177/20499361221086125. (DOI added for completeness)
- [12] C.B. Kartasasmita. Epidemiologi tuberkulosis. **Sari Pediatri.** **11**(2):124–129, 2009/2016 cetak ulang. (Tidak tersedia DOI; artikel berbahasa Indonesia).
- [13] B. Reis-Santos, R. Locatelli, B.L. Horta, E. Faerstein, M.N. Sanchez, L.W. Riley, et al. Socio-demographic and clinical differences in subjects with tuberculosis with and without diabetes mellitus in Brazil—A multivariate analysis. **PLoS One.** **8**(4):e62604, (2013). doi:10.1371/journal.pone.0062604. [PLOS](#)
- [14] WHO. Tuberculosis—key facts. 2021. (Akses 12 Nov 2025).  
URL: <https://www.who.int/news-room/fact-sheets/detail/tuberculosis>
- [15] CDC. How TB Spreads. 2022. (Akses 12 Nov 2025).  
URL: <https://www.cdc.gov/tb/topic/basics/howtbspreads.html>