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Knowing and Understanding the Tuberculosis (Tb) Disease of the Lung (Literature Review)

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Abstract

Tuberculosis is a highly prevalent disease among individuals. The bacteria may enter the human body with inhaled air, after which they will be taken into the lungs, and then might disseminate from the lungs into the other parts of the body via the circulatory system, lymphatic system, respiratory tract-bronchi, or by direct passage to other areas. The most affected organs with tuberculosis are the lungs, but it may also affect other organs, including the meninges, bones, superficial glands, and other organs. They include: India, 26%; Indonesia, 8.5%; China, 8.4%; the Philippines, 6%; Pakistan, 5.7%; Nigeria, 4.4%; Bangladesh, 3.6%; and South Africa, 3.6%. These eight countries account for two-thirds of the global cases put together. 8.2% of tuberculosis cases are co-infected with HIV. Targeted by the national tuberculosis control program is the elimination of tuberculosis by 2035 and attainment of a tuberculosis-free status by 2050. Methods: This study is based on a review of general clinical practice guidelines, research publications, websites, and textbooks on pulmonary tuberculosis. Findings and Analysis: There are various research writings about the clinical presentations of the condition, confirmatory investigations for Mycobacterium tuberculosis, the epidemiology of the patients, and risk conditions that predispose a patient to getting infected by the bacteria. Therapeutic interventions and pharmacological adverse effects. Conclusion Pulmonary tuberculosis is a communicable disease, and Indonesia still has a population that carries this infection. Thus, prevention of the disease should be done by every single individual in society by understanding and knowing the character of the disease.

Keywords: *Knowing and Recognizing, Pulmonary Tuberculosis Disease*

INTRODUCTION

It is among the oldest infectious diseases that have continued into modern times and has persisted through time. Pulmonary tuberculosis is an infectious disease caused by the bacterium Mycobacterium tuberculosis. The bacteria enter the human body when air is inhaled into the lungs and later spread to other parts of the body through the circulatory system, lymphatic system, respiratory tract or bronchus, and by direct transmission to other areas. It mainly affects the lungs but can spread to other organs such as the meninges, bones, superficial glands, and so on. Any individual infected with Mycobacterium tuberculosis does not necessarily develop the active form of the disease; it can, however happen in as short a period as between 2 to 20 weeks since the person got infected (Fitria & Rita, 2021).

According to the Global Tuberculosis Report 2020, the incidence of this disease was estimated at four cases in 2019. 10 million (range: 8.9 - 11 million) Deaths (HIV-negative): 1.2 million (1.1 - 1.3 million) HIV-positive deaths: 208,000 - range from 177,000 to 242,000 The highest proportion of cases occurred in Southeast Asia at 44%, Africa at 25%, and the Western Pacific area at 18%. These eight countries that contribute to two-thirds of the global burden include

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India, contributing about 26%, Indonesia 8.5%, China 8.4%, Philippines 6%, Pakistan 5.7%, Nigeria 4.4%, Bangladesh 3.6%, and South Africa 3.6%. About co-infection with HIV, 8.2% of those with tuberculosis are co-infected. In 2019, an estimated 3.3% of new pulmonary TB cases and 18% of pulmonary TB cases with a history of previous treatment will be MDR/RR TB cases, estimated at 465,000 new MDR/RR TB cases (range 400,000-535,000) (Indonesian Lung Doctors Association, 2021). The aim of the national TB control program is to eliminate TB in 2035 and to achieve a TB-free status by 2050. Based on the RAP 2020-2024, Indonesia is among the eight countries with the highest burden of pulmonary TB in the world and has shown an increasing trend each year. In 2017, the number reached 443,670, and in 2018, cases strongly increased to 565,869. By 2019, tuberculosis cases rose to 568,987. The incidence of tuberculosis cases in Indonesia decreased to 351,936 in the year 2020. In 2018, the five provinces were contributing factors to over 50% of pulmonary tuberculosis cases recorded in the country, respectively: West Java, with cases of 105,794; East Java, with 71,791; Central Java, with 65,014; DKI Indonesia with 41,441; and North Sumatra with 35,035. These five provinces are representatives of the most populous areas in Indonesia. Throughout 2021, Indonesia reported an increase in pulmonary tuberculosis cases, reaching a number of 393,323 cases (Sipayung et al., 2023). North Sumatra Province does have a relatively high population of pulmonary tuberculosis sufferers. In 2017, the incidence of pulmonary tuberculosis increased by 27,017 cases, but until the following year (2018), the total number of tuberculosis patients reached as many as 35,035. According to data from the Central Bureau of Statistics, five districts/cities in North Sumatra Province have the highest incidence of TB patients: Mandailing Natal Regency with 997 cases, Labuhan Batu Regency with 967 cases, Central Tapanuli Regency with 823 cases, Serdang Bedagai Regency with 820 cases, and Karo Regency with 806 cases. The Indonesian Health Profile 2019 reported the incidence rate of pulmonary tuberculosis to be 206/100,000 population in North Sumatra, with a treatment coverage rate of 47.4% and a treatment success rate of 92.4%. In 2020, the incidence of pulmonary tuberculosis was 138/100,000 individuals (Sipayung et al., 2023). Based on data from the Madiun City Health Office, the number of tuberculosis cases reported in 2022 had reached 753, already above the East Java Provincial Government's target for the city of Madiun of 600 cases.

Mycobacterium tuberculosis is an acid-fast straight or slightly curved rod without spores and capsules, 0.3 - 0.6 mm wide and 1 - 4 mm long, causing the disease and having a very complicated wall containing up to 60% of lipids. Mycolic acid, complex waxes, dimycolic trehalose referred to as cord factor, and mycobacterial sulfolipids are all the components comprising the bacterial cell wall and making the bacteria virulent. Mycolic acid is a long-chain fatty acid linked to arabinogalactan through glycolipid linkages, and to peptidoglycan through phosphodiester linkages. The cell wall of the bacterium also contains other components like polysaccharides: arabinogalactan and arabinomannan. The complex nature of this cell wall provides the bacteria with an ability of being acid-fast, thus, in case of staining, these bacteria will not easily be decolorized by acid-alcohol solution. Consequently, bacteria of the genus Mycobacterium are also known as Acid Resistant Bacteria, BTA, or acid-fast bacilli, AFB. The genome is composed of 4.41 Mb of base pairs and 4,009 genes; this characteristic makes it unique compared to other bacteria due to the high number of genes involved in lipogenesis and lipolysis, believed to be associated with the formation and maintenance of the bacterial cell wall. Approximately 52% of the proteins produced by these genes possess established activities. Genetic analysis reveals that M. tuberculosis possesses the capability to endure diverse environments, including those with minimal oxygen pressure, enabling the bacterium to remain dormant within the body under suboptimal conditions and to reactivate later if environmental

circumstances permit. My cobacterium has 120 species, including eight species within the M. TB complex: M. tuberculosis, M. bovis, M. caprae, M. Such as M africanum, M. microti, M. canneti, and M. pinnipedii (Perhimpunan Dokter Paru Indonesia, 2021).

The pathogenesis of M. tuberculosis depends on the resistance or immunity of the host. Tissue damage arising in TB is largely derived from the patient's immune response, for example, in the incidence of bronchial necrosis and cavities that are typically seen in the lungs of TB patients, for example, patients with an inadequate immune system, for example, in HIV patients, can show atypical signs and symptoms. Cavity formations in thoracic photographs are generally not found among TB-HIV patients, even though the immune response of the patient may not cause any, or minimal, damage to body tissue. The low level of immune response allows the bacteria that cause TB to more easily multiply and spread. This is evident by the billion photographs of thoracic TB commonly found in TB-HIV patients. Not every person who becomes exposed to the pathogenic bacterium of TB will have the disease. Schematically, it gives the percentage of people exposed to TB who will develop TB disease. About 30% of people exposed to TB germs will become infected with TB. Of patients infected with TB, about 3 - 10% will develop active TB within the first 1 year after infection. Dalam waktu 1 tahun, sekitar 3-5% pasien latent TB akan berkembang menjadi active TB, sedangkan sisanya akan tetap menjadi TB latent seumur hidup (Perhimpunan Dokter Paru Indonesia, 2021).

Primary pulmonary TB is caused by the transmission of the disease through airborne particles carried in the air-airborne particles called droplet nuclei, which measure between 1 to 5 microns, and these particles can survive for several hours depending on the surrounding environment. Aerodynamically, these particles may enter the airway through inspiration until they reach the respiratory bronchioles and alveoli. Deposited TB germs in the airway are immediately phagocytized and digested by the nonspecific immune system, namely macrophages, if the inhaled nuclei droplets are small. If the number of the deposited TB germs exceeds the ability to be phagocytized and digested by the macrophages, these TB germs will survive and multiply intracellularly in macrophages and cause localized tuberculous pneumonia. These germs multiply inside the macrophage and will leave when the macrophage does. The next step would then be a response by the immune system, in which it forms a sort of barrier in the infected area and forms a granuloma. If the infection is not controlled by the immune response, TB germs with the help of lymphatic and blood vessels can penetrate the barriers formed, which will spread to more distant tissues and organs such as lymphatic glands, lung apex, kidneys, brain, and bones. These germs, if they enter through the airway, will be lodged in the lung tissue and form nests of pneumony called primary foci. These may appear anywhere in the lung. In the primary focus, there may be inflammation of the lymph channels leading to the hilum-that is, local lymphangitis-and may be followed by enlarged lymph nodes in the hilum, regional lymphadenitis. The primary focus together with regional lymphangitis is called the primary complex. The following may happen to the primary complex: 1). Heal and leave no defect at all - restitution ad integrum 2). Heal and leave little trace - e.g. Ghon's nest, fibrotic streak, calcified nest in the hilum 3). May spread by: i). Percontinuate, disseminate to the surrounding area-an example is epituberculosis, it is an event of bronchial suppression, where the obstruction in the airway due to the compressed bronchus lobe medius by the enlarged hilum gland-can cause atelectasis. TB germs will travel along the obstructed bronchus to the atelectasised lobe and cause inflammation to the atelectasised lobe, which is known as epituberculosis. ii). Bronchogenous dissemination either within the lungs or to the contiguous lung or through ingestion. iii). Lymphogenous dissemination- The bacteria spread to the lymph

nodes, contiguous spread and may cause TB lymphadenitis. The lymphatic system of the lung thus provides a venue for the direct spread of M. tuberculosis from its initial focus of infection to the nearby lymph nodes, where an immune response would be subsequently established. This is due to the part of the lymph vessels that undergoes progressive inflammation in the course of the primary infection process. TB germ spreads in the lymph vessel channels at the onset of infection. This spread in immunodeficient hosts with both lung and lymph node lesions can be progressive. The extrapulmonary spread of infection begins with the spread to lymph nodes. Spread from the lymphatic system may progress to hematogenous spread via the thoracic duct. iv). Hematogenous spread is related to body resistance, number and virulence of germs. The resultant hives may heal spontaneously, but in the absence of adequate immunity, this dissemination will result in serious conditions such as miliary TB, TB meningitis, typhobacillosis Landouzy. A dissemination of M. tuberculosis can also cause TB in other body organs, such as bones, kidneys, kidneys, genitalia and so on. Complications of the germs and their spread might end with the recovery together with sequelae-for instance, retarded growth in children after obtaining encephalomeningitis, tuberculoma, or death (Perhimpunan Dokter Paru Indonesia, 2021).

The pathophysiology of secondary tuberculosis arises from the reactivation of dormant foci. Endogenous reactivation may occur in up to 5% of the tuberculosis-infected population several years post-primary infection. Tuberculosis reactivation typically transpires in the lung apex. The lesions at the apex are acquired via hematogenous dissemination following an initial infection several years prior. The apical and posterior portions of the superior lobe, together with the apical segment of the inferior lobe, are the predominant sites of reactivation due to their elevated oxygen tension relative to other lung regions. The lymphatic drainage system in these regions is inadequate. The lesion at the apex is a progression of the Simon focus that developed following the main infection. Upon reactivation, the lesions in Simon's focus will merge and undergo liquefaction and excavation. Reinfection may lead to secondary infection, albeit this is uncommon in patients residing in wealthy nations (Rahmani, 2020). The pathophysiology of tuberculosis involves the inhalation of M. tuberculosis bacteria, which subsequently infiltrate the alveoli via the airways, where they proliferate. Additionally, these bacteria can disseminate to other regions of the body, including the kidneys, bones, cerebral cortex, and various areas of the lungs, particularly the upper lobes, through the lymphatic system and bodily fluids. The immune system will react to the bacteria with an inflammatory response, phagocytizing or inhibiting the bacteria, whereas tuberculosis-specific lymphocytes will eliminate or lyse both the bacteria and normal tissue. This reaction results in exudate accumulation in the alveoli, potentially leading to bronchopneumonia. The interaction between M. tuberculosis bacteria and the immune system during the initial phase of infection results in the formation of granulomas, which are aggregates of viable and non-viable bacilli encased by macrophages. The granuloma subsequently evolves into a fibrous tissue mass, with the core region designated as Ghon tuberculosis, which undergoes necrosis to create a caseous necrotic mass. Sub-sequently, this condition will become rigid and ultimately develop into collagenous tissue, leading to the dormancy of the bacteria. Subsequent to the initial infection, an individual may manifest active disease due to immune system dysfunction or insufficient response, and the disease may also be triggered by reinfection and the reactivation of dormant bacteria. Rupture of the ghon tubercle results in necrotizing caseosa within the bronchi. Bacteria can become aerosolized, leading to an increased dissemination of the disease. Moreover, if the tubercle undergoes healing, it will result in the formation of scar tissue. The infected lung

becomes increasingly edematous, resulting in exacerbated bronchopneumonia (MAR'IYAH1 & ZULKARNAIN2, 2021).

The classification of tuberculosis is separated into two primary categories, namely: A. Bacteriologically confirmed tuberculosis patients, specifically those in whom evidence of infection with Mycobacterium tuberculosis is identified through bacteriological analysis, including: 1). Patients with pulmonary tuberculosis who test positive for BTA. Patients with pulmonary tuberculosis exhibiting positive Mycobacterium tuberculosis culture results. 3). Patients with pulmonary tuberculosis exhibiting positive results on the M. tuberculosis fast test. Bacteriologically verified extrapulmonary tuberculosis patients, identified using bacterial tissue analysis, culture, or quick testing of afflicted tissue samples. Pediatric tuberculosis identified using bacteriological analysis. B. Clinically diagnosed tuberculosis patients are those who do not fulfill the requirements for bacteriological confirmation; yet, based on other compelling evidence, they are nonetheless diagnosed and treated as tuberculosis by the attending physician, categorized into: BTA-negative pulmonary tuberculosis patients accompanied with corroborative thoracic images. Patients with BTA-negative pulmonary tuberculosis who exhibit no clinical improvement using non-OAT medications and possess risk factors for tuberculosis. Patients with extrapulmonary tuberculosis diagnosed using clinical, laboratory, and histopathological methods without bacteriological proof. Pediatric tuberculosis detected using the scoring system. Patients clinically diagnosed with tuberculosis who subsequently receive bacteriological confirmation should be classed as bacteriologically confirmed tuberculosis patients. Alongside bacteriologic testing, various more classifications exist to enhance communication among healthcare professionals and data documentation.

Alternative categories are predicated on: A. Site of infection: 1). Tuberculosis localized in the lung parenchyma. Miliary tuberculosis is classified as pulmonary tuberculosis because it involves lesions in lung tissue. Patients with both pulmonary and extrapulmonary tuberculosis are categorized as having pulmonary tuberculosis. 2). Extra-pulmonary tuberculosis: Tuberculosis that manifests in organs outside the lungs, potentially affecting the pleura, lymphatic glands, belly, urinary tract, gastrointestinal tract, skin, meninges, and bones. In cases of multiple extrapulmonary tuberculosis affecting various organs, classification is determined by identifying the organ most seriously impacted by the disease (Indonesian Lung Doctors Association, 2021). B. According to prior treatment history: 1) New cases of tuberculosis: instances that have never been administered anti-tuberculosis therapy (OAT) or have received OAT for a cumulative duration of less than 28 days. 2). Cases of previously treated tuberculosis: i). Relapse cases: instances that were previously proclaimed cured or completed treatment and are now re-diagnosed with tuberculosis. ii). therapy failure instances: instances that have undergone OAT and have not succeeded in the most recent therapy. iii) Drug withdrawal cases: instances when therapy has been suspended for a minimum of two continuous months. iv). Others: cases that have undergone OAT, although the outcomes of prior treatments remain unspecified (Perhimpunan Dokter Paru Indonesia, 2021).

Various classes of drug sensitization test outcomes: A. Drug-Sensitive Tuberculosis (TB-SO). B. Drug-Resistant Tuberculosis (TB-RO): 1). Monoresistant: bacteria exhibiting resistance to a singular form of first-line oral antimicrobial therapy. 2). Rifampicin-resistant tuberculosis (RR-TB): Mycobacterium tuberculosis exhibits resistance to Rifampicin, with or without concomitant resistance to other anti-tubercular agents (OATs). 3). Polyresistant: bacteria exhibit resistance to multiple first-line OATs, excluding simultaneous resistance to Isoniazid (H) and Rifampicin (R). 4). Multidrug-resistant tuberculosis (MDR-TB): resistant to both Isoniazid

(H) and Rifampicin (R) concurrently, with or without further resistance to other first-line anti-tuberculosis agents (Perhimpunan Dokter Paru Indonesia, 2021).

Various classes of pharmacological resistance: A.1) Pre-extensively drug-resistant (Pre-XDR TB): fulfills the criteria for multidrug-resistant tuberculosis (MDR TB) and exhibits resistance to at least one fluoroquinolone. Extensively drug-resistant tuberculosis (XDR TB) is multidrug-resistant tuberculosis (MDR TB) that exhibits resistance to at least one fluoroquinolone and at least one agent from group A, which includes levofloxacin, moxifloxacin, bedaquiline, or linezolid. B. Classification according to HIV status: HIV-positive tuberculosis. 2). Tuberculosis with HIV negative status.3). Tuberculosis with indeterminate HIV status (Perhimpunan Dokter Paru Indonesia, 2021).

Several definitions of cases are: 1.) A suspected case of tuberculosis (TB) is characterized by the presence of symptoms or signs indicative of the disease, primarily a cough with sputum lasting two weeks or longer. Additional symptoms may include hemoptysis, dyspnea, asthenia, anorexia, weight loss, malaise, nocturnal hyperhidrosis without exertion, and a fever persisting for over one month. In HIV-positive individuals, cough is frequently not a characteristic symptom of tuberculosis, hence cough symptoms may not always need to persist for 2 weeks or longer. Definitive tuberculosis refers to a TB patient in whom Mycobacterium tuberculosis complex has been identified from clinical specimens (such as tissues, bodily fluids, throat swabs, etc.) and cultures. In nations with restricted laboratory capabilities for identifying M. tuberculosis, a diagnosis of pulmonary TB can be confirmed if one or more BTA-positive sputum samples are detected, or if a patient is diagnosed with TB by a physician or healthcare worker following a corroborative examination and subsequently receives a complete regimen of treatment (Perhimpunan Dokter Paru Indonesia, 2021).
Risk factors for pulmonary tuberculosis include host variables, microbial agents, and environmental conditions. The environment comprises external factors that include both the internal and external living environments, encompassing the physical environment (such as water, air, soil, weather, food, heat, light, radiation, and shelter), as well as biological and social elements that are closely associated with disease transmission (Sipayung et al., 2023). The risk factors influencing tuberculosis are: 1) Gender. This condition is predominantly observed in men, perhaps attributable to their greater engagement in outside activities, such as employment, which increases their susceptibility to exposure to tuberculosis pathogens. 2). Age. The condition is predominantly observed in individuals of productive age, who engage in numerous activities involving extensive social interaction. However, it is occasionally noted in the elderly, potentially attributable to a reduction in resilience, rendering this demographic more vulnerable to illness. In underdeveloped nations, the majority of individuals infected with tuberculosis are still of working age. 3) In individuals who are malnourished, the condition correlates with diminished immunity, encompassing phagocytosis, cellular proliferative response, and the synthesis of T lymphocytes and cytokines, among others. 4). Alcohol consumption can induce direct or indirect toxic effects via deficiencies in macronutrients and micronutrients, leading to immune system impairment characterized by diminished T and B lymphocyte functionality, disrupted macrophage activation with a reduced capacity for antigen presentation to T cells, and an attenuated macrophage response to cytokines. This results in a shift towards Th2 cell predominance, inhibiting the proliferation of Th1 cells, which are crucial for the eradication of M. tuberculosis pathogens. Smoking is a contributing factor that elevates the risk of pulmonary tuberculosis by hindering mucosal secretion clearance. The nicotine present in cigarettes diminishes the production of TNF-α, which is essential for activating

macrophages and CD4+ lymphocytes, thereby impairing the immune response. This results in a reduction of the phagocytic capacity of alveolar macrophages and a further decline in immune response and CD4+ lymphocytes, facilitating the colonization of tuberculosis pathogens (LESTARI, 2020; Rahmani, 2020). 6). Comorbidities that compromise the human immune system. In immunocompromised states, such as those affecting patients with Human Immunodeficiency Virus (HIV), individuals exhibit diminished CD4+ T cell counts and elevated viral loads, alongside impaired macrophage and monocyte functions, with CD4 cells and macrophages contributing to the body's defense against Mycobacterium tuberculosis pathogens. In Diabetes Mellitus (DM), an immune deficiency diminishes the functionality of neutrophils, impairing their chemotaxis and oxidative killing capabilities. This results in reduced bactericidal activity, mobilization, chemotaxis, and phagocytic functions of polymorphonuclear (PMN) cells, attributed to hyperglycemic conditions and a diminished capacity to detect microorganisms, likely due to a decrease in both the sensitivity and quantity of receptors on monocytes. The socioeconomic level correlates with malnutrition as a result of inadequate employment or income. A humid environment resulting from insufficient ventilation and sunlight, when UV light contributes to transmission. 9). Education correlates with treatment adherence; it is anticipated that individuals with higher education levels possess knowledge and comprehension regarding pulmonary tuberculosis (Rahmani, 2020), (LESTARI, 2020).

Anamnesis: primary symptom: productive cough lasting over two weeks, accompanied by other symptoms: hemoptysis, dyspnea, asthenia, anorexia, involuntary weight loss, malaise, nocturnal diaphoresis without exertion, subfebrile temperature persisting for more than one month, and thoracic pain. Symptoms may not be characteristic in individuals with HIV co-infection. In addition to understanding the symptoms of tuberculosis, it is essential to consider the patient's medical history to identify risk factors, including prior close contact, living in crowded conditions, and occupational environment. The manifestations of extrapulmonary tuberculosis are contingent upon the affected organ; for instance, TB lymphadenitis presents as a gradual and painless enlargement of lymph nodes, TB meningitis exhibits discernible symptoms of meningitis, and TB pleurisy is characterized by dyspnea, occasionally accompanied by chest pain on the side of the pleural cavity with effusion (Perhimpunan Dokter Paru Indonesia, 2021). II). Clinical assessment: In pulmonary tuberculosis, the abnormalities are contingent upon the degree of lung structural impairment. Initially, it is challenging to identify these abnormalities, which are typically situated in the superior lobe, particularly in the apical region and posterior segment (S1 and S2), as well as the apical area of the inferior lobe (S6).1. Physical examination of pulmonary tuberculosis: bronchial breath sounds, amphoric noises, diminished breath sounds, coarse or fine crackles, and/or indications of pulmonary, diaphragmatic, and mediastinal retraction.2. Physical examination of tuberculosis pleurisy: the extent of fluid in the pleural cavity influences percussion findings, which may be faint or dull; auscultation reveals diminished to inaudible breath sounds on the affected side with fluid accumulation (Perhimpunan Dokter Paru Indonesia, 2021). 3. Examination of TB lymphadenitis reveals swollen lymph nodes, predominantly in the cervical region (consider the potential for tumor spread), occasionally in the axillary region, and may develop into a “cold abscess” (Perhimpunan Dokter Paru Indonesia, 2021) .III). Examination support: used materials include sputum, pleural fluid, cerebrospinal fluid, bronchial lavage, gastric lavage, bronchoalveolar lavage (BAL), urine, feces, and tissue biopsy (including fine needle biopsy/BJH). By: A. Bacteriological analysis: Two sputum samples, including at least one collected in the morning. In the TCM or Molecular Rapid Test assessment, a single sputum

examination suffices, with the specimen from BJH prepared as a dry smear on a glass slide. For culture and sensitivity assays, NaCl 0.9% is utilized. 3-5 ml may be added before to dispatch to the microbiology and anatomical pathology laboratories ((Perhimpunan Dokter Paru Indonesia, 2021).

B. Standard microscopic examination: Ziehl-Nielsen staining, fluorescent microscopy: auramine-rhodamine staining, and evaluation using the IUATLD (International Union Against Tuberculosis and Lung Disease) scale as suggested by WHO: 1). No BTA detected within a 100-degree field of vision; classified as negative. Identified 1-9 BTA within a 100 field of view and recorded the quantity of bacilli observed. 3). Identifying 10-99 BTA within a 100-degree field of vision is designated as + (1+). 4). Identified 1-10 BTA in a single visual field, designated as ++ (2+). Identified more than 10 BTA in one visual field, designated as +++ (3+) (Indonesian Society of Pulmonology, 2021). In Ziehl Nielsen or Kinyoun Gobbet (BTA positive): i). S (during): sputum is obtained when the suspected tuberculosis patient initially presents at the healthcare facility. Upon discharge, the suspected patient provides a sputum container to collect morning sputum on the following day. ii). P (Morning): Sputum is obtained at home on the morning of the second day, shortly upon awakening. The pot is delivered to the personnel at the healthcare center. iii). S (during): Sputum is collected at the health facility on the second day, coinciding with the submission of the morning sputum (Rahmani, 2020).

C. Examination of bacterial culture is the definitive method for recognizing Mycobacterium tuberculosis (MTB). For therapeutic applications, it is conducted using two varieties of culture medium, specifically: I). Liquid medium (Mycobacteria Growth Indicator Tube/MGIT). II). Solid media (Lowenstein-Jensen). The evaluation utilizing culture media exhibits greater sensitivity than microscopic examination. Cultural investigation can identify 10 to 1000 mycobacterium per milliliter, utilizing both solid and liquid media. Lowenstein-Jensen media is a solid medium composed of egg-based components initially formulated by Lowenstein and then refined by Jensen in the 1930s, and it continues to be enhanced by subsequent researchers. Lowenstein-Jensen media is utilized for the isolation and growth of Mycobacteria species, offering excellent sensitivity and specificity, and serves as a diagnostic instrument in tuberculosis prevention initiatives. The Mycobacteria Growth Indicator Tube (MGIT) is a simple, efficient, and economical method for culturing Mycobacterium tuberculosis (MTB). Upon seeing colony growth in the culture, the identification of the MTB species is conducted using the Rapid TB Test Ag MPT64. Positive culture outcomes may then undergo resistance testing for first and second line OAT (Indonesian Lung Doctors Association, 2021). Rapid Molecular Test (TCM) to diagnose MTB, alongside a medication sensitivity test that detects genetic material indicative of resistance. The frequently utilized test is GeneXpert MTB/RIF (sensitivity test for Rifampicin). Additional TCM assessments are increasingly prevalent, if not yet broadly acknowledged. GeneXpert MTB/RIF Xpert MTB/RIF is an automated, cartridge-based diagnostic test capable of detecting Mycobacterium tuberculosis and resistance to Rifampicin. Xpert MTB/RIF utilizes the Cepheid GeneXPert platform, a moderately sensitive and user-friendly nucleic acid amplification test (NAAT). This approach cleanses, concentrates, amplifies (by real-time PCR), and detects nucleic acid sequences within the TB genome. The duration for test management to completion is 1 to 2 hours. This technique is effective for the fast evaluation of suspected TB-RO cases using sputum examination samples. The test exhibits a sensitivity and specificity of approximately 99% (Perhimpunan Dokter Paru Indonesia, 2021). IV. Alternative molecular assays: 1). MTBDRplus (sensitivity assay for Rifampicin and Isoniazid). 2). MTBDRsl (sensitivity

assay for ethambutol, aminoglycosides, and fluoroquinolones). Molecular beacon assay (sensitization test for R) 4). PCR-Based Techniques for IS6110 Genotyping 5) Spoligotyping 6). Restriction Fragment Length Polymorphism (RFLP) 7). MIRU/VNTR Examination PGRS RFLP 9). Analysis of Genomic Deletions 10). Genoscholar: a. PZA TB II (sensitization assay for Z) b. NTM+MDRTB II (sensitization assay for Mycobacterium species identification and H+R sensitization test) c. FQ+KM-TB II (fluoroquinolone and kanamycin susceptibility test). 11). The MTBDRplus and MTBDRsl assays (Hain Lifescience) can identify mutations in the rpoB, katG, and inhA genes that confer resistance to rifampicin and isoniazid. Interferon-Gamma Release Assays (IGRAs) are diagnostic instruments for identifying Mycobacterium tuberculosis infection, encompassing both active tuberculosis and latent tuberculosis. 13). Nucleic Acid Amplification Test (WHO Recommendation) to swiftly ascertain the resistance profile of the invading pathogen (establish the OAT therapy) given. Molecular fast tests are suggested as the primary diagnostic tool for patients suspected of HIV co-infected tuberculosis or tuberculosis resistant organisms, superseding conventional microscopy, culture, and tuberculin testing, based on high-quality evidence (Perhimpunan Dokter Paru Indonesia, 2021).

D. Radiologic evaluation is the usual protocol for pulmonary tuberculosis (posteroanterior projection/PA). Additional clinical indications include lateral projection thoracic radiographs, top-lordotic views, oblique imaging, and CT scans. Radiologic characteristics are presumed to be: Active tuberculosis lesions are located: i). Cloudy or nodular opacities in the apical and posterior segments of the upper lobe of the lung and the superior segment of the lower lobe. ii). Cavities, particularly many ones, encircled by hazy or nodular opaque shadows. Miliary spot shadows. iv) Unilateral pleural effusion (often) or bilateral pleural effusion (occasionally). 2). Inactive tuberculosis lesions: i). Fibrosis ii). Calcifications 3). Schwarte or pleural hypertrophy Severely damaged lung tissue, clinically referred to as lung destruction.The radiological depiction of lung destruction includes: i) atelectasis, ii) multicavities, and iii) fibrosis of the lung parenchyma.The evaluation of lesion activity in this disease is challenging when relying just on radiological imaging; nonetheless, bacteriological analysis is essential for confirming the disease process's activity (Perhimpunan Dokter Paru Indonesia, 2021).. E. Additional supportive examinations: I.) Analysis of pleural fluid:1). Rivalta test for pleural effusion in individuals with pleural fluid. The diagnosis of tuberculosis is indicated by a positive Rivalta test, revealing exudative fluid characterized by a predominance of lymphocyte cells and a reduced glucose concentration. The adenosine deaminase (ADA) test is utilized to assist in diagnosing tuberculosis pleural effusion. Adenosine deaminase is an enzyme synthesized by lymphocytes that is involved in purine metabolism. ADA levels are heightened in the exudative fluid generated in tuberculosis pleural effusions. II). Histopathological evaluation of tissue. Material or tissue is obtained through biopsy or autopsy, namely: 1). Fine needle aspiration biopsy (FNAB) of the lymph nodes (LN). Pleural biopsy (performed using thoracoscopy or utilizing Abram, Cope, and Veen Silverman needles). Lung tissue biopsy methods include transbronchial lung biopsy (TBLB) via bronchoscopy, transthoracic needle aspiration (TTNA), and open lung biopsy. 4). Biopsy or aspiration of extrapulmonary organ lesions suspected of tuberculosis. The biopsy examination requires two preparations: one is placed in saline solution and dispatched to the microbiology laboratory for culture, while the second is fixed for histological analysis (Perhimpunan Dokter Paru Indonesia, 2021). A positive tuberculin test indicates the presence of a TB infection. In Indonesia, where tuberculosis is quite prevalent, the tuberculin test serves as a diagnostic tool, however it holds diminished significance in adulthood. The tuberculin test is significant when there is conversion, a nodule, or substantial induration size. The criterion for a positive outcome varies based on the patient's medical

history, wherein: Induration ≥5 mm is deemed positive if: i) Patients are HIV positive. History of direct exposure to individuals with active tuberculosis. iii). Patients exhibiting characteristic tuberculosis manifestations on chest radiographs. iv). Patients exhibiting immunosuppression. v) Patients undergoing prolonged corticosteroid treatment. Patients with end-stage renal failure. Induration ≥10 mm is deemed positive in: i) Patients residing in or arriving from countries with high tuberculosis prevalence within the last five years. Injecting drug users. iii) Patients residing in high-density environments (e.g. correctional facilities). Microbiology laboratory personnel. v) Patients at high risk (e.g., diabetes, renal failure, chronic malabsorption syndrome), and vi) children under the age of five. Induration of ≥15 mm is deemed positive in all individuals. The tuberculin test may yield false negative findings in individuals with malnutrition and HIV infection (Perhimpunan Dokter Paru Indonesia, 2021).

The objective of tuberculosis treatment is to cure patients and enhance their productivity and quality of life. 2. Avert mortality and/or disability or its subsequent consequences. 3. Avert recurrence. Minimize the risk of tuberculosis transmission 5. Prevent OAT resistance and transmission, as it is the most effective method to inhibit transmission. A. The principles of effective tuberculosis treatment are: Treatment consists of a pharmacological combination of at least four medications to avert resistance to OAT. OAT is administered in the appropriate dosage. iii). OAT is ingested consistently under the supervision of a drug swallowing supervisor (PMO) until the conclusion of the treatment term. OAT is administered for an adequate duration, encompassing both the first intensive phase and the advanced stage (Perhimpunan Dokter Paru Indonesia, 2021). B. Duration of treatment for pulmonary tuberculosis: 1) Absence of problems and comorbidities for a duration of six months. In extrapulmonary tuberculosis and tuberculosis with comorbidities, treatment duration may exceed six months.In the initial stage/intensive phase, OAT is administered daily. The primary objective of OAT administration is to swiftly diminish the quantity of TB bacteria in the patient's system and decrease the likelihood of transmission. If OAT is ingested consistently at the appropriate dosage, the risk of transmission is typically reduced after the initial two weeks of treatment. The initial therapy also seeks to reduce the impact of a minor fraction of TB bacteria that may have developed resistance to OAT prior to the commencement of treatment. The treatment regimen for drug-sensitive tuberculosis (TB-SO) commences with an initial phase lasting two months, succeeded by a continuation phase designed to eradicate any residual TB bacilli not eliminated during the initial phase, hence mitigating the risk of recurrence. The advanced stage lasts from 4 to 6 months (Perhimpunan Dokter Paru Indonesia, 2021).
Patients with SO-TB receive treatment with first-line OAT. i). Rifampicin (R), Dosage (mg/kg body weight): 10 (range 8-12), Maximum dosage (mg): 600. Isoniazid (H), Dose (mg/kg body weight): 5 (4-6), Maximum dose (mg): 300. Pyrazinamide (Z), Dosage (mg/kg body weight): 25 (range: 20-30).iv). Ethambutol (E), Dosage (mg/kg body weight): 15 (15-20). v). Streptomycin, Dosage (mg/kg body weight): 15 (12-18) 2. First-line OAT recommendations use Fixed Dose Combination/KDT (to enhance treatment adherence), administered daily, and dosed as follows:1). Initial phase: For a duration of 8 weeks: daily administration of KDT RHZE (150/75/400/275): a). 2 tablets of 4KDT: for body weight of 30 - 37 kg. Three pills of 4KDT: for body weight 38 - 54 kg, c). Four pills of 4KDT: for those weighing 55 kg or more. 2). Continuation phase daily with KDT RH (150/75) for a duration of 16 weeks: a). Two pills for those weighing 30 to 37 kilograms. Three pills for those weighing between 38 and 54 kg, c). Four pills for those weighing 55 kg or more (Kosasih et al., 2021).
Effective treatment of pulmonary tuberculosis heals patients and prevents the emergence of drug-resistant tuberculosis. The formulation of a DOTS (Directly Observed Treatment

Shortcourse) strategy to mitigate the tuberculosis epidemic is a paramount goal for the WHO. The International Union Against Tuberculosis and Lung Disease (IUALTD) and WHO advocate for the substitution of single-drug/release combinations with KDTs in the primary treatment of tuberculosis since 1998. The benefits of KDT encompass: 1). Streamlined management and reduced prescribing errors. Enhanced patient adherence and acceptance with minimal inadvertent medication errors. Enhanced compliance among healthcare professionals with proper and established management protocols. Enhanced medication management resulting from a reduced variety of drugs. 5). Mitigating the danger of single drug overuse and the emergence of drug resistance resulting from diminished reliance on monotherapy. The determination of the dosage for the 4-drug Fixed Dose Combination therapy, as established by the WHO dose range, is classified as an effective dose or remains within the therapeutic and non-toxic limits. Patients undergoing OAT KDT must be directed to a hospital, lung specialist, or an appropriate facility if they encounter severe adverse effects (Perhimpunan Dokter Paru Indonesia, 2021).

The OAT combination with regular TB treatment is categorized into: A. For new patients: the recommended regimen is 2HRZE/4HR with daily administration. B. In the context of first-line tuberculosis treatment: it is advisable to base the regimen on sensitivity testing results. Healthcare facilities must perform drug sensitivity testing, and patients may receive category 1 OAT while awaiting these results. Treatment is modified based on the outcomes of personalized sensitivity testing. Drug sensitization tests must be conducted; patients may receive category 1 OAT while awaiting the results of these testing. Subsequent treatment is modified based on the outcomes of the sensitivity test (Kosasih et al., 2021). The treatment protocol for pulmonary and extrapulmonary tuberculosis is identical; however, the duration of treatment varies. Tuberculous meningitis requires a treatment length of 9 to 12 months due to the associated risks of disability and fatality. Ethambutol ought to be substituted with Streptomycin. 2). Tuberculosis of the spine, therapy period 9 to 12 months. 3). Tuberculous lymphadenitis for six months, with a potential extension to twelve months. Variations in gland size (either hypertrophy or atrophy) are not indicative of therapy duration. Corticosteroids are administered for tuberculosis meningitis, severe miliary tuberculosis, and tuberculosis pericarditis (Perhimpunan Dokter Paru Indonesia, 2021). Adverse effects of OAT include: 1). Dermatological and hypersensitivity reactions, specifically: If a medicine is determined to induce an allergic reaction, it should be discontinued. ii). The drug desensitization procedure is a viable option, particularly when the patient exhibits allergies to first-line and second-line medications or when no superior alternatives are available. The procedure is conducted based on the intensity of the allergic reaction. In cases of minor allergic reactions, desensitization may be achieved with a gradual daily increase in dosage.2). Drug-Induced Hepatitis (DIH) occurs: i). If clinical signs of nausea or vomiting occur, OAT is discontinued. ii). If clinical symptoms are observed alongside an elevation in SGOT and/or SGPT over three times the normal level, then OAT is discontinued (Perhimpunan Dokter Paru Indonesia, 2021). iii). OAT is discontinued if no clinical symptoms are present and laboratory findings indicate bilirubin levels exceeding 2 or SGOT and SGPT levels beyond five times the normal range. If SGOT and SGPT exceed three times the normal levels, treatment will proceed under observation. Proposed method for OAT administration: Cease the hepatotoxic OAT (RHZ) and persist in monitoring clinical and laboratory indicators. If clinical and laboratory parameters normalize (bilirubin, SGOT, SGPT), initiate a gradual re-administration of rifampicin to the full dosage, while closely observing clinical symptoms and conducting laboratory assessments. Upon achieving normal clinical and laboratory parameters on the full rifampicin

dosage, introduce INH with a gradual increase in dosage to the full amount, adjusted according to body weight. The OAT combination may be administered separately following re-initiation or rechallenge. In icteric individuals, it is advised to exclude pyrazinamide from the pharmacological regimen. If rifampicin is intolerable: 2HES/10HE; if INH is intolerable: 6-9 RZE (Indonesian Lung Doctors Association, 2021).

OAT protocols in specific situations, specifically in: Miliary tuberculosis: the treatment regimen is identical to that of pulmonary tuberculosis (2RHZE/4RH), and corticosteroids are not routinely administered; they are reserved for certain conditions such as the presence of meningitis symptoms, dyspnea, toxic manifestations, or high fever. 2) Pulmonary tuberculosis with diabetes mellitus: The treatment regimen and duration remain same to those for pulmonary tuberculosis without diabetes mellitus, contingent upon regulated blood glucose levels. If blood sugar levels remain uncontrolled, treatment may extend for a length of up to 9 months. 3) Pulmonary tuberculosis with pregnancy, lactation, and hormonal contraceptive usage: All first-line tuberculosis medications are safe for use during pregnancy, with the exception of streptomycin. Rifampicin diminishes the efficacy of hormonal contraceptives. 4). Pulmonary tuberculosis in renal impairment: the OAT regimen consists of 2RHZE/4RH, necessitating dosage modification of pyrazinamide and ethambutol (administered three times weekly at an altered dosage). 5). Pulmonary tuberculosis with hepatic impairment: if the SGPT level exceeds three times the normal value, the severity of hepatic disease dictates the selection of less hepatotoxic OAT, with the following options: RHE nine months 2RHES/6RH 2HES/10HE ES + Ofloxacin / Levofloxacin for a duration of 18-24 months (Perhimpunan Dokter Paru Indonesia, 2021).

Symptomatic supportive treatment in: A. Ambulatory patients: Treatment of tuberculosis patients must consider their clinical status. If the clinical situation is stable and hospitalization is unwarranted, the patient may receive outpatient treatment. 3). In conjunction with OAT, supplementary or supportive treatment is required to enhance endurance or alleviate symptoms/complaints. 4). High-calorie, high-protein nutrition (animal protein is superior to plant protein for immune function) and micronutrients include zinc, vitamins D, A, C, E, B6, iron, and folate (essential for cellular immunity against TB infection).5). Symptomatic medications: mucolytics, expectorants, antipyretics, analgesics, antiemetics, bronchodilators, etc.6). Corticosteroids in severe tuberculosis (meningitis, pericarditis, life-threatening conditions). Management of adverse events resulting from opioid agonist therapy (OAT).8). Management of adverse effects resulting from OAT.9). Cessation of smoking.10) Infection Control.11). Surveillance of pharmaceutical consumption (PMO). B. Hospitalized patients: I. Pulmonary tuberculosis with associated conditions/complications, specifically: 1) Profuse hemoptysis.2). Suboptimal overall condition Pneumothorax.4) Empyema.Extensive bilateral pleural effusion 6). Acute dyspnea (not attributable to pleural effusion). II. Life-threatening extrapulmonary tuberculosis: 1). Miliary pulmonary tuberculosis.2) Tuberculous meningitis.Supportive or symptomatic treatment is administered based on the clinical condition and care indications (Kosasih et al., 2021; Perhimpunan Dokter Paru Indonesia, 2021).

Surgical intervention for tuberculosis (TB): A. Unconditional indication 1). Patients expectorating copious amounts of blood that cannot be managed conservatively Patients with bronchopleural fistula and empyema that cannot be treated conservatively. B. Relative Indications Patients with sputum-negative results exhibiting recurrent hemoptysis Unilateral lung or lobe impairment accompanied by symptoms 3). Enduring residual cavities. C. Invasive procedures aside from surgery, namely: 1) Bronchoscopy Pleural puncture.3). Installation of

water-sealed drainage (WSD). Surgery is employed for the treatment of extrapulmonary tuberculosis and the management of sequelae, including hydrocephalus, uropathic blockage, constrictive pericarditis, and nerve involvement in spinal tuberculosis. Drainage or aspiration/incision constitutes a therapeutic and diagnostic intervention for extensive, fluid-filled tuberculosis lymphadenitis (Kosasih et al., 2021). Assessment of treatment for tuberculosis patients encompasses: A. Clinical evaluation: patients have periodic assessments at a minimum frequency of once per month, encompassing complaints, weight fluctuations, and physical examinations.B. Assessment of treatment efficacy and the existence or non-existence of adverse medication reactions and disease-related problems C. Bacteriological assessment (0 - 2 - 3 * - 6 /8 months of treatment) is essential in identifying the presence or absence of sputum conversion. D. Microscopic analysis and assessment, specifically: 1). Prior to the commencement of treatment.2) Following two months of treatment (subsequent to the intensive phase). In the third month, if the microscopic results from the second month remain positive.4). Upon conclusion of treatment If a culture facility exists, a culture examination and sensitivity test are conducted.F. Radiological assessment (0 - 2 - 6/8 months of therapy) Assessment and analysis of thoracic images are conducted on: 1) Prior to treatment. 2). Following two months of treatment (one month of treatment is permissible in cases of cancer). 3). Patients deemed cured at the conclusion of treatment must be assessed at the 3rd, 6th, and 12th months post-treatment to ascertain recurrence. Evaluated elements include clinical circumstances, sputum BTA microscopy, and thoracic imaging, contingent upon indications or the presence of tuberculosis symptoms (Perhimpunan Dokter Paru Indonesia, 2021).

Complications in tuberculosis patients, occurring prior to therapy, throughout the treatment phase, and following the conclusion of treatment. Potential issues that may occur include: Coughing up blood Pneumothorax Respiratory failure Heart failure In cases of problems, referral to a suitable facility is necessary (Kosasih et al., 2021). Prognosis of pulmonary tuberculosis. 1. In the context of daily life, the function of doubt serves to enhance well-being. 2. For recovery or relapse / To healing: Doubts towards good. 3. To ensure survival or in life-threatening situations / Ad vitam: The optimal cure is typically attained and may enhance with appropriate OAT administration; however, the prognosis can be unfavorable in cases such as delayed treatment, elderly individuals, infants and children, those with compromised immunity or comorbidities, and patients with multidrug-resistant tuberculosis (MDR-TB) (Kosasih et al., 2021). PUPK 2021 Preventive education is conducted in: I). Individual (patient or family): may be conducted in the outpatient unit (at the pharmacy during medication collection or during treatment), II). Group: executed in collectives (patients, patients' families, or the community) of hospital visitors. Instructions for execution:1) Impart information regarding pulmonary tuberculosis tailored to their comprehension level. 2) Facilitate opportunities for inquiries, employ accessible language, and utilize instructional materials (e.g., brochures, flip sheets, or pamphlets). The PMO must comprehend the information to communicate it to the patient and family on tuberculosis, specifically: i). Induced by pathogens, rather than being a genetic disorder or malediction. ii). Can be remedied with consistent treatment. iii) The modes of transmission, associated symptoms, and preventive measures. iv) Methods for medication administration (intense and advanced phases). v). Optimal oversight to ensure patients adhere to their treatment regimen. vi). Risks that emerge if treatment is incomplete (Perhimpunan Dokter Paru Indonesia, 2021).

METHODS

This document is a literature review that synthesizes information from many credible articles regarding pulmonary tuberculosis (TB) sickness. The sources utilized in this literature review comprise systematic searches of digital databases, including research journals, review articles, and books. The author synthesizes key elements from each article, aligning them with the central issue to compose a discourse on pulmonary tuberculosis, a lung illness.

RESULTS and DISCUSSION

This study examines pulmonary tuberculosis (TB), including its causes, incidence rates, common symptoms, demographic features (gender, age, education, and occupation), risk factors, diagnostic exams, treatment options, side effects, and recurrence rates.

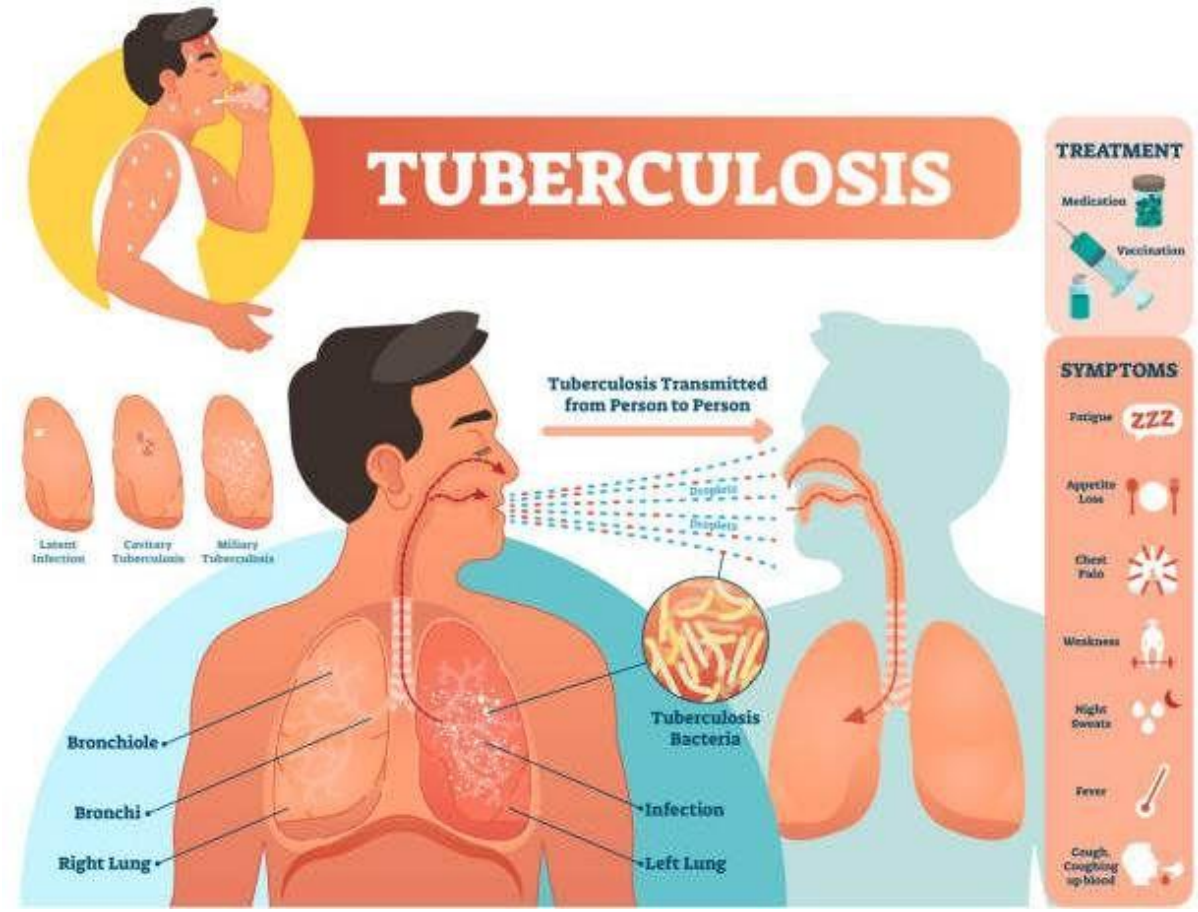

Figure 1. Tuberculosis

Source: Medicastore (2023)

Tuberculosis (TB) is an illness induced by Mycobacterium tuberculosis, which comprises eight species: M. tuberculosis, M. bovis, M. caprae, M. africanum, M. microti, M. canneti, and M. pinnipedii (Perhimpunan Dokter Paru Indonesia, 2021). Pulmonary tuberculosis (TB) is a pulmonary illness induced by the bacterium Mycobacterium tuberculosis, belonging to the Actinomycetales order and Mycobacteriaceae family, also referred to as acid-resistant bacteria (BTA) (Mahulae & Suandy, 2020). The dissemination of Mycobacterium tuberculosis can lead to tuberculosis in several organs, including bones, kidneys, and genitalia, with the lungs being the most commonly affected (Perhimpunan Dokter Paru Indonesia, 2021). The transmission of this disease occurs readily between individuals, particularly via the respiratory tract by the

ingestion or aspiration of sputum (droplets) that contain viable bacilli, either directly or indirectly. The risk of transmission is heightened as individuals may be unaware of their pulmonary tuberculosis status and can disseminate the pathogens to others prior to diagnosis (S, 2020). Mycobacterium tuberculosis germs induce pulmonary tuberculosis, which readily infects individuals with HIV/AIDS, those with inadequate nutritional status, and is affected by the individual's immune system. Transmission occurs when individuals with BTA-positive pulmonary tuberculosis talk, sneeze, or cough, releasing around 3,000 aerosolized sputum droplets containing pathogens into the air. These pathogens disseminate to others by transmission or airborne particles (sputum droplets, BTA positive) (Nanda, 2020) The absence of therapy will result in an elevated mortality rate, making it one of the ten principal causes of death globally. Prior to the coronavirus (COVID-19) pandemic, pulmonary tuberculosis was the foremost cause of mortality attributable to a single infectious agent, surpassing HIV/AIDS. Approximately 90% of individuals who get the condition are male adults rather than females. Approximately 25% of the global population is infected with M. tuberculosis (WHO, 2020) (Fitria & Rita, 2021).

The Human Immunodeficiency Virus (HIV) epidemic has significantly impacted the rise of pulmonary tuberculosis (TB) globally, leading to an escalation in the incidence of TB cases within communities. Patients with tuberculosis with HIV have an elevated mortality risk compared to those with tuberculosis alone. The HIV status remains indeterminate because numerous pulmonary TB patients decline HIV testing and referral to the HIV section. In individuals with HIV, there is a steady decline in both the quantity and functionality of CD4 cells, alongside compromised activity of macrophages and monocytes, which play a crucial part in the body's defense against mycobacterium. The cytokine tumor necrosis factor alpha, released by active macrophages during granuloma tissue formation in pulmonary tuberculosis, is one of the activators of HIV replication in lymphocyte cells associated with the disease (Rismayanti et al., 2023).

Table 1. Prevalence of TB Cases in Different Countries

Country	**Number of TB Cases (latest year)**	**Global Percentage (%)**	**TB Cases with HIV Positive (%)**
India	26%	2.6 million	8.2%
Indonesia	8.5%	850,000	3.5%
China	8.4%	840,000	2.0%
Philippines	6%	600,000	4.5%
Pakistan	5.7%	570,000	5.3%

According to WHO Global Tuberculosis data (2020) and (Perhimpunan Dokter Paru Indonesia, 2021), Indonesia ranks third among the eight Southeast Asian countries with the highest incidence or prevalence of pulmonary tuberculosis. Approximately 10 million individuals globally are afflicted with active pulmonary tuberculosis. Data indicates elevated morbidity and mortality rates in tuberculosis patients following the completion of treatment. The mortality rate of tuberculosis patients is elevated by 3-6 times in high-income nations relative to the general population (Rusmini, 2023). Eight nations comprise two-thirds of new tuberculosis cases: India, Indonesia, China, the Philippines, Pakistan, Nigeria, Bangladesh, and South Africa. In 2019, tuberculosis resulted in the deaths of 1.4 million individuals, including 208,000 who were also infected with HIV. Tuberculosis is among the ten foremost causes of mortality globally

and is the primary cause attributable to a single infectious agent. In 2019, approximately 10 million individuals contracted tuberculosis globally. 5.6 million males, 3.2 million females, and 1.2 million children. (World Health Organization, 2020) (Baliasa et al., 2020). Its frequency in males is three times greater than in females globally. The incidence rate is higher in men, perhaps because to increased exposure to risk factors such as smoking and non-compliance with sociodemographic and other medications. Epidemiologically, pulmonary tuberculosis is prevalent throughout Asia, accounting for 55% of the total estimated cases in 2007, with seven economies in Central and West Asia, including Kazakhstan, Tajikistan, and Uzbekistan, reporting a rise in tuberculosis prevalence. In 2007, the three nations with the highest overall number of tuberculosis infections were India (2.0 million), China (1.3 million), and Indonesia (0.53 million), all located within the Asian Development Bank (ADB) region. The ADB Strategy 2020, established in 2008, acknowledges the interrelationship between health, poverty, and social development (Nanda, 2020).

Common complaints and symptoms identified in various studies include: persistent coughing with phlegm or dryness over the past few days, a cough with phlegm or dryness lasting more than two weeks, expectoration of blood mixed with mucus or blood alone, excessive nocturnal sweating, and unintentional weight loss over the past three months (Madona et al., 2023). Persistent cough with sputum lasting over two weeks, accompanied by prevalent symptoms of weight loss and dyspnea (Ismah & Novita, 2017). New cases of pulmonary tuberculosis present with respiratory tract disorders, including a productive cough lasting ≥ 2 weeks, hemoptysis, dyspnea, and chest pain, accompanied by systemic symptoms such as fever, night sweats, anorexia, and weight loss (Aida et al., 2022; Mahulae & Suandy, 2020; S, 2020).

Table 2. Common Clinical Symptoms of Pulmonary TB

Clinical Symptoms	Frequency (%)
Cough with phlegm ≥ 2 weeks	85%
Hemoptysis (coughing blood)	40%
Shortness of breath	65%
Chest pain	45%
Fever	55%
Night sweats	50%
Weight loss	70%

The predominant clinical manifestations observed in patients with pulmonary tuberculosis include cough, dyspnea, hemoptysis, and thoracic discomfort, typically accompanied by low-grade fever, nocturnal diaphoresis, and unexplained weight loss (S, 2020). The immune response of the body is activated to thwart Mycobacterium tuberculosis infection, leading to an elevation in body temperature. This triggers the secretion of fluids from the sweat (sudoriferous) and sebaceous glands, resulting in symptoms of fever and perspiration. If unaddressed, this can lead to dehydration, disrupting metabolic processes and causing malaise due to nutritional deficiency (Aida et al., 2022; Perhimpunan Dokter Paru Indonesia, 2021). Several research indicate that the characteristics of lung patients predominantly include men over women (Mahulae & Suandy, 2020; Rismayanti et al., 2023; Sari et al., 2022; Yakob et al., 2023). Several research indicate that tuberculosis patients are predominantly female (Madona et al., 2023; Monita & Fadhillah, 2021). Similarly, pulmonary tuberculosis co-infected with HIV/AIDS predominantly occurs in males (Abdillah et al., 2022).

Numerous studies indicate that pulmonary tuberculosis predominantly affects men, attributed to the immunosuppressive effects of smoking and alcohol consumption, which increase susceptibility to the bacteria responsible for the disease (Arisandi et al., 2023; Syafefi et al., 2015). Data from the Ministry of Health of the Republic of Indonesia's information center in 2013 indicated that the figure was 16 times higher for men than for women. Besides pulmonary tuberculosis, smoking can lead to further ailments like cerebrovascular illness, coronary heart disease, lower respiratory tract infections, chronic obstructive pulmonary disease (COPD), and lung cancer. Cigarette smoke contains around 4,500 compounds, which exhibit toxic, mutagenic, and carcinogenic properties, affecting numerous components in both cellular and extracellular environments, including water-soluble particles and gases. Numerous compounds are carcinogenic and cytotoxic; nevertheless, tar and nicotine have demonstrated immunosuppressive effects by impairing the host's innate immune system and heightening vulnerability to infections. Increased amounts of tar and nicotine correlate with a more significant impact on the immune system. Ceasing smoking can diminish the incidence of pulmonary tuberculosis by about two-thirds (Namuwali, 2019). The Indonesian Ministry of Health reports that men experience a higher incidence of pulmonary TB co-infection compared to women. Risk factors for pulmonary tuberculosis in HIV-TB patients may arise from behavioral and socioeconomic habits or unhealthy lifestyles, including smoking (which can impair ciliary function in the respiratory tract), alcohol consumption, promiscuity (which can enhance transmission), and excessive workloads (Abdillah et al., 2022). Men engage in numerous social interactions and exhibit elevated work activities relative to women, potentially resulting in a heightened incidence of tuberculosis (TB) infection or relapse. Additionally, smoking and alcohol consumption can compromise the immune system, facilitating the entry of pulmonary TB pathogens into the body. Furthermore, extensive external interactions and activities increase the likelihood of exposure to individuals infected with TB. Relapsed pulmonary tuberculosis is observed in individuals aged 18-59, perhaps due to the increased mobility and activity associated with this demographic, which facilitates re-exposure to tuberculosis bacteria (Saraswati et al., 2022). The World Health Organization reports that the prevalence of pulmonary tuberculosis is 2.3 times higher in men than in women, attributed to men's greater involvement in social activities and increased exposure in workplace environments, facilitating transmission to family members (S, 2020).The individual's mobility and outdoor activity, due to his role as the head of the household and family support, increase his exposure to tuberculosis pathogens in the workplace, educational institutions, and his residential surroundings (Latifah et al., 2023; Saraswati et al., 2022). Numerous studies indicate that a significant number of pulmonary TB cases occur in women (Madona et al., 2023; Monita & Fadhillah, 2021). This may result from women being more prompt in seeking healthcare than males, as they exhibit greater concern for their health and their obligations as homemakers to care for their children and families everyday. Other studies indicate that women are more vulnerable to tuberculosis due to a higher prevalence of passive smoking among them (Madona et al., 2023).

The predominant clinical manifestations observed in patients with pulmonary tuberculosis include cough, dyspnea, hemoptysis, and thoracic discomfort, typically accompanied by low-grade fever, nocturnal diaphoresis, and unexplained weight loss (S, 2020). The immune system's response is activated to thwart Mycobacterium tuberculosis infection, leading to an elevation in body temperature. This triggers the secretion of fluids from the sweat (sudoriferous) and sebaceous glands, resulting in fever and perspiration. If unaddressed, this can lead to dehydration, disrupting metabolic processes and causing malaise due to nutritional deficiency

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Numerous studies indicate that pulmonary tuberculosis predominantly affects men, attributed to the detrimental effects of smoking and alcohol consumption on the immune system, rendering them more susceptible to the bacteria responsible for the disease (Syafefi et al., 2015; Arisandi et al., 2023). Data from the Ministry of Health of the Republic of Indonesia's information center in 2013 indicated a prevalence 16 times more in men than in women. Besides pulmonary tuberculosis, smoking can lead to further ailments like cerebrovascular illness, coronary heart disease, lower respiratory tract infections, chronic obstructive pulmonary disease (COPD), and lung cancer. Cigarette smoke contains about 4,500 compounds that exhibit toxic, mutagenic, and carcinogenic properties, affecting numerous components in both cellular and extracellular compartments, including water-soluble particles and gases. Numerous compounds are carcinogenic and cytotoxic; nevertheless, tar and nicotine have demonstrated immunosuppressive effects by impairing the host's innate immune system and heightening vulnerability to infections. Increased amounts of tar and nicotine correlate with a more significant impact on the immune system. Ceasing smoking can diminish the incidence of pulmonary tuberculosis by about two-thirds (Namuwali, 2019). The Indonesian Ministry of Health reports that men experience higher rates of pulmonary TB co-infection compared to women. Risk factors for pulmonary tuberculosis in HIV-TB patients may arise from behavioral and socioeconomic habits or detrimental lifestyles, including smoking (which can impair ciliary function in the respiratory tract), alcohol consumption, promiscuity (which can enhance transmission), and excessive workloads (Abdillah et al., 2022). Men engage in numerous social interactions and exhibit higher work-related activities than women, potentially resulting in a heightened incidence of tuberculosis (TB) infection or relapse. Additionally, smoking and alcohol consumption can compromise the immune system, facilitating the entry of pulmonary TB pathogens into the body. Furthermore, extensive external interactions and activities increase the likelihood of exposure to individuals infected with TB. Relapsed pulmonary tuberculosis occurs in people aged 18-59, likely due to the increased mobility and activity associated with this demographic, which facilitates re-exposure to tuberculosis bacteria (Fajriah Saraswati et al., 2022). The World Health Organization reports that the prevalence of pulmonary tuberculosis is 2.3 times higher in males than in women, attributed to men's greater involvement in social activities and direct exposure in workplace environments, facilitating transmission to family members (S, 2020).The individual's mobility and external activity, due to his role as the head of the household and the family's cornerstone, increase the likelihood of exposure to tuberculosis pathogens in the workplace, educational institutions, and the surrounding community (Fajriah Saraswati et al., 2022; Latifah et al., 2023). Numerous research indicate that a significant number of pulmonary tuberculosis cases occur in women (Madona et al., 2023; Monita & Fadhillah, 2021). This may result from women being more prompt in seeking healthcare than males, as they tend to be more vigilant about their health and their obligations as homemakers in caring for their children and families everyday. Other studies indicate that women are more vulnerable to tuberculosis due to a higher prevalence of passive smoking among them (Madona et al., 2023).

Table 3. Characteristics of Pulmonary TB Patients by Gender, Age, and HIV Status

Characteristic	Number of Cases	Percentage (%)
Gender		
- Male	650,000	65%
- Female	350,000	35%
Age		
- 15-24 years	200,000	20%
- 25-34 years	300,000	30%
- 35-44 years	250,000	25%
- ≥45 years	250,000	25%
HIV Status		
- HIV Positive	150,000	15%
- HIV Negative	850,000	85%

The characteristics of pulmonary patients, as indicated by several research on pulmonary tuberculosis, exhibit variation across different age groups, with the highest prevalence observed in a specific age category. 15 to 25 years (Arisandi et al., 2023; Madona et al., 2023). The majority are aged 17 and 72 years (Mahulae & Suandy, 2020). Predominantly those aged beyond 38 years (Yakob et al., 2023).The majority are in early adulthood, specifically aged 21 to 35 years (Ismah & Novita, 2017; Monita & Fadhillah, 2021; Pradana et al., 2020). The majority are aged between 26 and 45 years (Namuwali, 2019). Additionally, the highest prevalence occurs between the ages of 49 and 61 years (Ismah & Novita, 2017). The highest prevalence occurs in those aged 56 to 65 years (Sari et al., 2022). Numerous studies indicate that people with pulmonary tuberculosis are typically of working age. In individuals with HIV/AIDS co-infection, pulmonary tuberculosis is predominantly observed in the age group of 26-35 years (Abdillah et al., 2022).

The age demographic, particularly the productive age group, influences the prevalence of pulmonary tuberculosis. Data from the Indonesian Ministry of Health in 2022 indicates that tuberculosis predominantly affects those aged 15 to 54 years. This is due to the significant mobility of individuals during a productive age, which increases the likelihood of exposure to tuberculosis pathogens (Latifah et al., 2023). At this age, patients frequently engage with others, exhibit significant mobility, and facilitate transmission to individuals in their vicinity (Ismah & Novita, 2017; Syafefi et al., 2015). The productive age refers to an age group characterized by elevated activity levels, during which individuals allocate substantial time and energy to employment or social interactions (Herawati & Purwanti, 2018; Syafefi et al., 2015). Consequently, diminished rest periods may provide a danger of decreasing endurance (Monita & Fadhillah, 2021). Research indicates that the elevated prevalence of relapsed pulmonary tuberculosis in adults aged 26 to 59 is attributable to their increased activity and mobility, stress, insufficient rest following extensive physical exertion, and inconsistent adherence to medication, which facilitates re-exposure to tuberculosis pathogens (Saraswati et al., 2022). Research in Europe indicates that the majority of second occurrences occur among the elderly, as older patients are more susceptible to therapeutic failure due to diminished drug absorption linked to age-related physiological changes. As age increases, individuals become more adept at disease prevention; nevertheless, the immune system also diminishes, resulting in a heightened susceptibility to illness (Nanda, 2020; Saraswati et al., 2022). The World Health Organization indicates that individuals under 45 years of age constitute the demographic most affected by

tuberculosis in Indonesia. Research at RSPI Jakarta indicated that the number of pulmonary TB patients under 45 years of age exceeded that of patients aged 45 years and over. Co-infection of HIV and pulmonary tuberculosis is prevalent among individuals under 45 years of age, particularly those with high mobility, as this demographic encompasses the highest risk category, including sexually active individuals and those who use injectable medications. This is probably attributable to the impact of sexual activity prevalent during a productive age, environmental factors, and occupational impacts (Abdillah et al., 2022) .According to Law No. 13 of 2003, Chapter I, Article 1, Paragraph 2, an individual is permitted to work between the ages of 15 and 64 years (Pradana et al., 2020).

Studies indicate that patients with pulmonary tuberculosis exhibit varying educational levels, with the majority possessing a high school or equivalent education (Arif et al., 2022; Madona et al., 2023; Monita & Fadhillah, 2021). The majority are in junior high school (Sari et al., 2022). The majority in elementary school education (SD) (Namuwali, 2019; Palele et al., 2022). The majority in higher or graduate study (Yakob et al., 2023). The majority of tuberculosis relapses occur among those with a high school education (Saraswati et al., 2022).

The amount of education influences the learning process; higher education is essential for acquiring knowledge about pulmonary tuberculosis (Monita & Fadhillah, 2021). A deficient degree of education will result in restricted public awareness of pulmonary tuberculosis (Syafefi et al., 2015). At the elementary school education level (SD), there is a deficiency in knowledge and health information on pulmonary tuberculosis (Anni, 2022; Palele et al., 2022). Individuals with lower educational attainment are at a heightened risk of contracting pulmonary tuberculosis, as education significantly influences knowledge regarding treatment options. Furthermore, education is a critical determinant in making informed decisions about healthy lifestyle choices; thus, higher educational levels correlate with enhanced knowledge (Namuwali, 2019). Education is essential for self-development, as a higher level of education facilitates the acquisition and advancement of knowledge and technology (Pradana et al., 2020). A person's limited educational attainment does not preclude their aspiration to recover from pulmonary tuberculosis, and they consistently adhere to health workers' medication recommendations. Despite their low educational levels, TB patients frequently acquire information from television, radio, newspapers, and other media, thereby enhancing their understanding. It is unreasonable to expect patients with limited education to possess extensive knowledge regarding the dangers of pulmonary tuberculosis (Nanda, 2020). The extent of knowledge acquired through education influences patient adherence to treatment for a minimum of six months, with PMOs serving a crucial role in facilitating treatment success, as guided by technical officers in disseminating information about TB disease and its management (Arisandi et al., 2023; Monita & Fadhillah, 2021). Patients possess adequate awareness regarding pulmonary tuberculosis, including its transmission, signs and symptoms, prevention, treatment, PMO, treatment monitoring, management, and drug side effects. The questionnaire indicates that patients receive information from several sources in their environment, including newspapers, periodicals, the internet, neighbors, family, and posters in health services (Herawati & Purwanti, 2018). All educational levels can be affected by TB bacteria; however, primary and secondary education may be more susceptible, potentially due to insufficient understanding and information on the transmission of TB (Arif et al., 2022).

Characteristics based on occupation in patients with pulmonary tuberculosis indicate that a significant proportion are employed as private employees and housewives, as evidenced by multiple research (Madona et al., 2023; Rismayanti et al., 2023; Yakob et al., 2023). In other

research, the majority were privately employed or self-employed (Arif et al., 2022; Arisandi et al., 2023; Namuwali, 2019). Conversely, another study indicated that the majority of individuals with pulmonary tuberculosis were unemployed (Ismah & Novita, 2017).

Work is an endeavor undertaken to generate income, and the work environment may expose an individual to illness. An adverse work environment is more likely to result in lung tuberculosis infection among individuals such as drivers, laborers, and pedicab operators, in contrast to those employed in office settings; occupational conditions are closely associated with poverty and insufficient money. Families lacking income experience diminished purchasing power, hindering their ability to fulfill dietary requirements, which frequently results in malnutrition and subsequently weakens the immune system.Employment can influence an individual's knowledge in contrast to those who are unemployed, exemplified as individuals working in a medical setting as opposed to those outside of it (Monita & Fadhillah, 2021). The risk of exposure to tuberculosis is influenced by the work environment and socio-economic conditions, particularly in indoor settings with inadequate sunlight and poor ventilation (Arisandi et al., 2023)). A contributing factor to pulmonary tuberculosis is insufficient sunshine exposure, while another is the physical exertion experienced by manual laborers, which can lead to exhaustion, diminished immunity, and increased vulnerability to infection (Ismah & Novita, 2017). Self-employed individuals are more susceptible to tuberculosis (TB) due to their work environment, as frequent interactions with others can elevate the risk of transmission from those afflicted with TB (Herawati & Purwanti, 2018). Pulmonary tuberculosis is invariably linked to poverty. According to the WHO (2003), 90% of tuberculosis patients globally belong to groups with vulnerable or impoverished socioeconomic status. Affluent families will be more capable of sustaining household cleanliness, ensuring proper nutritional intake, and financing necessary healthcare services. Individuals in low socioeconomic conditions experience inadequate nourishment, substandard housing, and limited access to services. The quality of life of tuberculosis patients is a significant metric for evaluating treatment efficacy (Namuwali, 2019). In the investigation of pulmonary tuberculosis recurrence, a significant portion of the cohort consisted of individuals who were unemployed, including housewives, while the second largest demographic comprised self-employed individuals (Saraswati et al., 2022). A person infected with pulmonary tuberculosis may experience relapse due to elevated work activity levels, as well as environmental factors including home humidity, ventilation conditions, window status, and natural lighting (Saraswati et al., 2022). The characteristics of each patient's work type may not provide immunity from pulmonary tuberculosis, as workplace toxins also play a significant role; however, patients who are unemployed may still contract the disease via their home environment (Arif et al., 2022).

The risk factors for pulmonary tuberculosis are influenced by the interplay of three components: host, agent, and environment. The host's susceptibility to tuberculosis infection is significantly affected by the immune system; individuals with HIV/AIDS or those with inadequate nutritional status and compromised immunity are more prone to tuberculosis infection (Kemenkes RI 2018) (Diantara et al., 2022). Smoking is prevalent among men who do not adhere to a healthy lifestyle (Madona et al., 2023). Smoking is recognized to impair pulmonary function and inhibit personal adaptive immunity. Impaired immunity, resulting from undernutrition or malnutrition and anemia (attributable to alterations in blood leptin and inhibition of erythropoiesis), affects patient response to treatment (Ismah & Novita, 2017).

Residential environmental elements impact occupancy density, ventilation, lighting, humidity, flooring, and wall conditions, which in turn determine the prevalence of tuberculosis (Sipayung

et al., 2023). The workplace environment poses a risk for tuberculosis transmission, as individuals encounter a larger number of people, increasing the likelihood of infectious diseases such as pulmonary tuberculosis, particularly in BTA positive cases (Arisandi et al., 2023; S, 2020). Environmental factors, including unsanitary and overcrowded living conditions, as well as poorly ventilated and sunlit rooms, further exacerbate this risk (Latifah et al., 2023). Another element is sanitation in residential areas (Diantara et al., 2022). Residential density can expedite the transmission of pulmonary tuberculosis when the size of a dwelling is incongruent with the number of occupants. This circumstance renders the inhabitants of the dwelling ill due to insufficient oxygen intake. Transmission of an infectious disease, particularly tuberculosis, among family members residing in the same household is highly probable if one individual is infected. Moreover, occupancy density is governed by the Regulation of the Minister of Health of the Republic of Indonesia Number 1077 / Menkes / Per / V / 2011, which pertains to Guidelines for Air Health in Residential Spaces, identifying occupancy density as a risk factor for the transmission of contagious infectious diseases (Sipayung et al., 2023). Home ventilation functions to expel contaminated air (bacteria, CO2) from the residence and substitute it with fresh, clean air or facilitate air movement that allows ultraviolet radiation to penetrate. Ventilation serves to regulate indoor air humidity; insufficient ventilation can elevate humidity levels, leading to the accumulation of water vapor from skin evaporation or external sources. Humid domestic environments provide an optimal setting for the proliferation of harmful bacteria, including those responsible for tuberculosis, which may endure in dark and moist conditions. Illumination is a critical element in residential environments. As per the Indonesian Minister of Health Decree No. 829 / Menkes / SK / VII / 1999 about health standards for residential properties, homes must possess sufficient illumination during both daytime and nighttime (Sipayung et al., 2023). The condition of the home floor influences the prevalence of pulmonary tuberculosis; uneven and hard-to-clean flooring might retain moisture, hence promoting the transfer of TB pathogens by adherent droplets (Aulia et al., 2021; Sipayung et al., 2023). Risk factors for pulmonary tuberculosis include cleanliness and the home environment. Mycobacterium tuberculosis bacteria pose a lung TB risk three times higher than residences devoid of TB bacteria. A house in poor physical condition that fails to satisfy standards poses a risk of pulmonary tuberculosis three times larger than that of a building in satisfactory condition (Diantara et al., 2022).Environmental issues, specifically a polluted and congested living space, as well as a room characterized by inadequate air circulation and insufficient sunlight (Latifah et al., 2023). Based on the supporting examinations conducted, several studies indicate that several tests can be performed to diagnose pulmonary tuberculosis, including: Interferon Gamma Release Assays (IGRA) are conducted on healthcare professionals to assess the prevalence of latent tuberculosis (Angelia et al., 2020) The majority of HIV patients exhibit negative BTA results upon microscopic examination, although thoracic imaging reveals severe lesions (Abdillah et al., 2022). The outcomes of the bacteriological sputum examination are variable, with some results being positive and others negative (S, 2020). At present, each Puskesmas conducts microscopic examinations for BTA (Acid-Fast Bacilli) and TCM (Molecular Rapid Tests). The supporting examination findings indicated the highest number of BTA examinations, specifically Positive 1, while the thoracic X-ray examinations revealed only minimum lesions and comorbidities, predominantly diabetes mellitus (Mahulae & Suandy, 2020). Numerous patients with HIV/AIDS co-infection and pulmonary tuberculosis exhibit diminished hemoglobin levels, as this anemic condition is a significant risk factor linked to malnutrition, which can exacerbate immune deficiency and triple the likelihood of bacteriologically confirmed tuberculosis (Abdillah et al., 2022)..

In supporting investigations, atypical clinical symptoms, sputum analysis, and radiographic findings may indicate a reduced CD4 count (Abdillah et al., 2022). The negative BTA test results from diminished immunity in advanced HIV patients. The sensitivity of BTA sputum examination in HIV patients is approximately 50%, and this sensitivity diminishes with chronic immunosuppression. BTA-negative sputum correlates with elevated death rates due to postponed access to OAT (Abdillah et al., 2022). Widespread lesions observed in thoracic pictures may indicate a significant decline in the patient's immune resistance (severe immunocompromise), as evidenced by the presence of widespread lesions in the imaging (Abdillah et al., 2022). Bacteriological investigation is a crucial assessment for diagnosing tuberculosis in both children and adults. Bacteriological investigation is a crucial assessment for diagnosing tuberculosis in both children and adults.The supporting examination in youngsters revealed that the majority of results from BTA, Mantoux, and x-rays were negative (Rita & Qibtiyah, 2020). The tuberculin test aids in diagnosing tuberculosis in children, particularly when the history of exposure to TB patients is ambiguous; nonetheless, a negative result does not definitively exclude the possibility of pulmonary tuberculosis. The analysis of thoracic radiographs in pediatric patients reveals that the radiographic presentation of tuberculosis is atypical, with the exception of miliary tuberculosis (Ernirita et al., 2020; Rita & Qibtiyah, 2020). The PCR approach for detecting Mycobacterium tuberculosis in pleural effusion fluid exhibits greater sensitivity than the microscopic Ziehl Neelsen examination, hence facilitating a more accurate diagnosis of tuberculosis (Rita & Qibtiyah, 2020). Elevated BTA test findings correlate with an increased risk of transmission to others and a systemic effect, wherein the patient gradually transmits the condition to individuals in close proximity, particularly family members (S, 2020).

Treatment administered to patients with pulmonary tuberculosis, as indicated by several research on tuberculosis management, typically include family PMOs, category 1 treatment, and new cases (Aida et al., 2022; Sari et al., 2022). Typically, OAT consumption occurs in pulmonary TB patients who adhere to treatment consistently and comprehensively (Arif et al., 2022; Saraswati et al., 2022; Sari et al., 2022). Patients recover from new tuberculosis with treatment (Arisandi et al., 2023).

Treatment for pulmonary tuberculosis is administered based on the patient's disease status, utilizing the First Line category (category 1) for individuals with newly diagnosed pulmonary TB in the early phase (2HRZE) and advanced phase (4H3R3). The Fixed Dose Combination (FDC) formulation simplifies medication adherence by allowing patients to take many medications in a single dosage form (Arif et al., 2022). Several factors influence the success of treatment, including treatment history, drug side effects, patient characteristics, medication, the national TB program, inadequate therapy, resistance to OAT, patient motivation, the distance of healthcare facilities from the patient's residence, and treatment-related monotony due to duration and expense. Additionally, patients are required to adhere to the treatment regimen for six to nine months, uphold environmental sanitation, follow the PMO by consistently taking medication punctually, manage the side effects of OAT, administer the correct dosage at the appropriate times, conduct sputum examinations to assess disease progression, ensure sufficient rest, and consult health services if symptoms worsen the condition (Herawati & Purwanti, 2018). The PMO is a crucial entity that facilitates the success of treatment overseen by technical officers at each patient's healthcare facility (Arisandi et al., 2023). Compliance with tuberculosis therapy not only diminishes mortality but also mitigates extended illness, transmission to others, and the emergence of multidrug-resistant tuberculosis (Diantara et al.,

2022).Patients who comply with therapy are those who consistently and thoroughly finish the regimen without interruption for a duration of six to nine months. Patients are considered neglectful if they fail to attend appointments between three days to two months from the scheduled date, and they are deemed to have dropped out if they do not seek treatment for more than two consecutive months after being contacted by health workers (Depkes RI, 2010). (Baliasa et al., 2020) Pulmonary tuberculosis may relapse if the patient exhibits symptoms of the disease after being deemed cured of treatment. The symptoms typically mirror those observed after first infection with pulmonary tuberculosis, specifically a prolonged cough, dyspnea, nocturnal diaphoresis, and fever. Recurrence of pulmonary tuberculosis can be attributed to various factors, including incomplete treatment leading to bacterial resistance to antitubercular medications, proximity to untreated infectious sources, and a compromised immune system (Kemenkes RI. 2022) (Latifah et al., 2023).Post-tuberculosis sequelae is a condition resulting from complications arising from prior pulmonary tuberculosis. Upon recovery from tuberculosis, an individual will exhibit a 2-4 fold increase in enduring spirometry score abnormalities indicative of obstruction and restriction, compared to those without tuberculosis. This is accompanied by detectable parenchymal and airway abnormalities on radiographic imaging, along with symptoms of respiratory distress and diminished quality of life. Residual effects of tuberculosis have frequently been neglected as a contributor to chronic illness throughout the last five decades, resulting in the absence of established protocols for the identification and treatment of post-TB patients (Rusmini, 2023).
In the management of pulmonary tuberculosis patients, comorbidities such as diabetes mellitus must be considered, as this chronic condition is linked to compromised immune function, rendering patients more vulnerable to infections, including pulmonary tuberculosis. Therefore, active collaboration for monitoring is essential (Latifah et al., 2023; Rohman, 2018). Alongside diabetes mellitus, comorbidities associated with poor lifestyles and diets include HIV.In a study including pulmonary tuberculosis patients co-infected with HIV (CD4 < 100, hemoglobin levels < 10) (Abdillah et al., 2022). Alongside HIV and diabetes mellitus, the hepatitis C virus, cancer, cardiovascular disease, and chronic obstructive pulmonary disease (COPD) significantly contribute to the incidence of pulmonary tuberculosis (Arif et al., 2022). The adverse effect of anemia, commonly associated with zidovudine first-line ART regimens, is crucial to monitor for the onset of tuberculosis in these patients (Abdillah et al., 2022).
The patient received government-provided FDC TB medications to enable their administration. FDC TB medications serve as first-line treatments for newly infected tuberculosis patients and are coupled with Vitamin B6 to mitigate the negative effects associated with Isoniazid. Management of co-morbid conditions: 1). The HIV regimen, comprising Duviral/NRTI (Lamivudine 150 mg and Zidovudine 300 mg) and Efavirenz, has been demonstrated in multiple studies to be highly effective in achieving complete viral suppression in adults undergoing concurrent rifampicin-based tuberculosis treatment, with the standard adult dosage of efavirenz being 600 mg daily alongside two NRTIs (Arif et al., 2022). 2). DM, specifically Metformin in conjunction with tuberculosis fixed-dose combination medications. Metformin is the primary pharmacological agent for type 2 diabetes and typically does not induce hypoglycemia. Metformin is not processed by cytochrome P450 enzymes pharmacokinetically. Pharmacodynamically, Superoxide Dismutase (SOD) is a crucial element in preventing isoniazid resistance, indicating that metformin may enhance the efficacy of OAT. Metformin therapy is linked to enhanced management of pulmonary tuberculosis bacterial infection and reduced disease severity. Gastric disturbances Antacid medications used with tuberculosis fixed-dose combination pharmaceuticals. Pharmaceuticals that elevate stomach pH impede the absorption

of isoniazid. Antacids with aluminum hydroxide impede the absorption of rifampicin. Antacids do not impede the absorption of pyrazinamide. Antacids can diminish the peak concentration of ethambutol by 28%. Consequently, medications must to be administered at extended intervals. Omeprazole, when used with tuberculosis fixed-dose combination (FDC) medications, particularly rifampicin, influences the hepatic metabolism of the enzyme CYP2C19, resulting in reduced serum levels of omeprazole (Arif et al., 2022). The interaction mechanism between isoniazid and omeprazole involves isoniazid influencing the hepatic metabolism of the enzyme CYP2C19, hence enhancing the effects of omeprazole. 4). Heart illness, namely the medication Nitroglycerin in conjunction with TB FDC package medications, is recognized for lacking pharmacological interactions owing to variations in the administration route. The sublingual delivery of nitroglycerin, an organic nitrate, bypasses first-pass metabolism by the liver, resulting in rapid onset and a brief duration of action of approximately 15-30 minutes. The more rapidly the drug attains therapeutic concentrations in the system, the more swiftly it is removed from the body. Cardiac comorbidities utilize simvastatin together tuberculosis fixed-dose combination medications. Pharmacokinetics indicates that rifampicin can influence the efficacy of statins by activating cytochrome P450 enzymes. The administration of acetylsalicylic acid alongside TB FDC package medications pharmacodynamically demonstrates that M. tuberculosis's exposure to salicylates enhances resistance to isoniazid, streptomycin, rifampicin, and ethambutol, hence usually increasing H37Ra susceptibility (Arif et al., 2022).

The World Health Organization (WHO) asserts that the cornerstone of an effective tuberculosis control program is the implementation of the Directly Observed Treatment Short Course (DOTS) strategy, which has also been adopted by our nation. Consequently, comprehending DOTS is crucial for effectively addressing tuberculosis. In cases where pulmonary tuberculosis does not respond to therapy, patients are directed to a pulmonary specialist, whereas TB-RO cases are sent to the TB-RO referral center (Indonesian Lung Doctors Association, 2021).

In Indonesia, tuberculosis drug guidelines encompass the number of cases that require retreatment, including instances of relapse. The Community Lung Health Center (BKPM) is a health agency that implements the DOTS strategy to address pulmonary tuberculosis. The adverse effects of recurrent pulmonary tuberculosis include diminished production, mortality, heightened transmission within the community, and an increase in multidrug-resistant (MDR) strains. The relapse of pulmonary tuberculosis poses a significant challenge to the tuberculosis control program, potentially obstructing the attainment of treatment and control objectives for pulmonary tuberculosis (Saraswati et al., 2022)). Moreover, for OAT treatment to be sufficient: Treatment involves a pharmacological combination of a minimum of four different medications to avert resistance to OAT. ii). The OAT is administered at the appropriate dosage. iii). The OAT is ingested consistently under the supervision of a drug swallowing supervisor (PMO) until the conclusion of the treatment term. iv). OAT must be administered for an adequate duration, encompassing both the initial/intensive phase and the continuing phase, to avert relapse (S, 2020).

Table 4. Side Effects and Management of Anti-Tuberculosis Drugs (OAT)

Drug Type	Common Side Effects	Management if Side Effects Occur
Rifampicin	Cutaneous reactions, hepatitis	Discontinue drug, desensitization if necessary
Isoniazid	Hepatitis, neuropathy	Provide vitamin B6, monitor liver function

Ethambutol	Visual impairment	Discontinue use if impairment is severe
Streptomycin	Ototoxicity	Regular hearing monitoring

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CONCLUSION

Understanding pulmonary tuberculosis is essential, as it is caused by the bacterium Mycobacterium tuberculosis, which infects the human body via inhalation into the lungs. Subsequently, the pathogen disseminates from the lungs to other body regions through the circulatory system, lymphatic system, respiratory tract (bronchi), or direct transmission to other areas. Tuberculosis mostly impacts the lungs, but it can also involve other organs, including the meninges, bones, superficial glands, and others. The symptoms of pulmonary tuberculosis include a persistent cough with phlegm lasting two weeks or longer, potentially accompanied by additional manifestations such as hemoptysis, dyspnea, asthenia, anorexia, weight loss, malaise, nocturnal hyperhidrosis without exertion, and fever persisting for over one month. The most frequently conducted supplementary assessments are bacteriological or BTA analysis and radiological imaging. The most recognized treatment is OAT, and according to the WHO, the cornerstone of an effective tuberculosis control program is the implementation of the Directly Observed Treatment Short Course (DOTS) method, which has also been adopted by our nation. Supportive and symptomatic treatment, along with PMO, is essential for the effectiveness of the treatment. Furthermore, it is imperative to understand the aspects associated with pulmonary tuberculosis, including the necessity for patients to consistently pursue regular treatment, cease both active and passive smoking, prevent direct contact with those infected with tuberculosis, and uphold health by adopting a clean and healthy lifestyle, among other considerations.Participation in all societal components and collaboration with external agencies beyond the health sector are essential for the effective decrease of TB incidence.

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