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# *Sensitivity of Spontaneous Sputum and Induced Sputum in Molecular Rapid Test (TCM) Examination in Pulmonary Tuberculosis Patients*

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## Abstract

Pulmonary tuberculosis (TB) is an infectious disease caused by Mycobacterium tuberculosis and remains a significant global health issue, with a high incidence rate in Indonesia. Early detection of TB is crucial to prevent its spread and improve treatment success rates. The Rapid Molecular Test (TCM) based on GeneXpert has become an effective diagnostic method for detecting Mycobacterium tuberculosis DNA, including rifampicin resistance. This study aims to compare the sensitivity of spontaneous sputum and induced sputum in TCM testing for pulmonary TB patients Based on a literature review, spontaneous sputum showed a higher positive ratio (73%) than induced sputum (60%). However, there was no significant difference in effectiveness between the two methods. The study also found that sputum quality, such as mucopurulent consistency, affects the accuracy of TCM results. Additionally, induced sputum proved to be more effective in detecting TB in children compared to spontaneous sputum. Therefore, the choice of sputum collection method should be tailored to the patient's condition to enhance the sensitivity and specificity of TB diagnosis.

## INTRODUCTION

Pulmonary tuberculosis (TB) is an infectious disease caused by the bacteria *Mycobacterium tuberculosis*. Transmission occurs through the air, especially when people cough, sneeze or spit, allowing the bacteria to spread easily from one person to another. The bacteria that cause TB are bacilli and have a very strong resistance, so treatment takes a long time. Although it can infect various organs of the body, the lungs are the most commonly affected organ, making pulmonary TB the most common type of TB found in Indonesia (Mar'iyah & zulkarnain, 2021).

According to a World Health Organization (WHO) report in 2021, there were 10.6 million cases of TB worldwide, with 6.4 million patients already on treatment, while the other 4.2 million were undiagnosed. Indonesia ranks second only to India in the number of TB cases, with a total of 969,000 cases, an increase of 17% over the previous year. TB cases in Indonesia reached 354 cases per 100,000 population with a mortality rate of 150,000 cases and increased by 60% compared to 2020. However, only 45.7% of cases were detected and reported, while the other 54.3% remained undiscovered, indicating major challenges in TB detection and treatment efforts in Indonesia (Atanai et al., 2025).

Despite numerous treatment and prevention efforts, TB remains a significant global health problem. Treatment discrepancies or incomplete treatment can lead to drug resistance (DR) and may worsen the situation. In Indonesia, despite continuous awareness raising and early detection, the number of undiagnosed cases is still high indicating gaps in the health system. This is due to limited access to health services, lack

of community knowledge, and stigma towards people with TB. The increasing mortality rate through TB cases indicates the need for more attention to detection, appropriate treatment, and addressing social and economic factors that can influence the spread of the disease. Therefore, collaboration between the government, health workers, and the community is essential to reduce TB cases (Making et al., 2023).

One method that is increasingly being applied to improve the early detection and accuracy of pulmonary TB diagnosis is the Rapid Molecular Test (TCM). TCM is a molecular-based diagnostic technology that is able to detect the presence of *Mycobacterium tuberculosis* (M.tb) DNA directly in sputum samples. Sputum samples can be obtained in 2 ways, namely spontaneous sputum and induced sputum. Spontaneous sputum can be obtained by removing it directly without requiring any assistance. Whereas induced sputum can be obtained by requiring assistance, such as inhaling hypertonic saline (up to 6%) to cough, nasopharyngeal suction using a sterile catheter to collect samples with a mucus trap, or through nasopharyngeal aspiration (nasopharyngeal swab) (Olbrich et al., 2023).

TCM uses the fluorescence signal measurement method to semiquantitatively detect the amount of M.tb in the sample, which is measured through the Cycle threshold (Ct) value. TCM is also able to identify resistance to antibiotics, such as rifampicin. The positivity level of TCM results is divided into four categories based on the range of Ct values, namely high (Ct < 16), medium (Ct 16-22), low (Ct 22-28), and very low (Ct > 28). The lower the Ct value, the higher the amount of M.tb detected, indicating the severity of infection in the body. Patients with high positivity results are 5.40 times more likely to experience treatment failure. This positivity rate is one of the important variables affecting the success of treatment therapy, as the quantity of M.tb can be determined directly and gives an idea of the severity of the infection. With TCM, the process of TB detection and treatment can be carried out more quickly and accurately, which in turn can increase the cure rate and reduce the spread of the disease (Kurniati et al., 2023).

## METHOD

The method in this research is literature review. Literature review is a systematic and comprehensive review of various literature sources relevant to the research topic or study. The purpose of this study was to analyze the comparison of spontaneous sputum with induced sputum in TCM examination in patients with pulmonary TB. The journals used in this study are national and international journals obtained from scientific databases such as Science Direct, PubMed, and Google Scholar. Journals selected for literature review are journals published in 2018 - 2025.

## RESULTS AND DISCUSSION

Table 1 shows the sensitivity data of spontaneous sputum and induced sputum in the Rapid Molecular Test (TCM) examination in patients with pulmonary tuberculosis. This literature review aims to evaluate the effectiveness of both sampling methods in detecting *Mycobacterium tuberculosis* infection. High sensitivity in TCM testing is essential for early diagnosis and appropriate treatment, thereby reducing morbidity and mortality from tuberculosis.

**Table 1.** Sensitivity Data of Spontaneous Sputum and Induced Sputum in Molecular Rapid Test (TCM) Examination in Patients with Pulmonary Tuberculosis Literature Review

| | Researcher | Year | Country | Respondents | Design | Finding |
|---|---|---|---|---|---|---|
| 1. | Pratama, M. K., Pandu, E., & Anggita, D | 2023 | Indonesia | 60 sputum samples from patients with suspected pulmonary TB | Cross sectional | The result of the comparison between spontaneous sputum and induced sputum found the following results: Which is more positive in spontaneous sputum, which is 55%. Based on the chi-square statistical test, the results showed that there was no evidence of significant effectiveness between spontaneous sputum and induced |

| | Researcher | Year | Country | Respondents | Design | Finding |
|---|---|---|---|---|---|---|
| | | | | | | sputum in TCM examination using GeneXpert in patients with suspected pulmonary tuberculosis. |
| 2. | Susilawati, T. N., Saptawati, L., Damayanti, K. E., & Larasati, R. | 2018 | Indonesia | 471 sputum samples from patients with suspected pulmonary TB | Analytical observational study with a retrospective cohort approach | High sensitivity was obtained in the GeneXpert MTB/RIF examination using raw sputum samples, which was 93.62%. Previous studies using sputum pellets obtained sensitivities of 80% and 82.3%. It appears that the GeneXpert MTB/RIF examination using raw sputum samples is more sensitive in diagnosing TB compared to sputum pellets. This is in line with previous studies which found that the sensitivity of the GeneXpert MTB/RIF examination using raw sputum samples was 87.5%. 13 In addition to being more sensitive, the use of raw sputum as an examination sample is more practical because it does not need to go through the dilution stage, decontamination with N-acetyl-l-cysteine and sodium hydroxide (NALC/NaOH), and the centrifugation process. |
| 3. | Mohsenpour, B., Reshadmanesh, N., Bagheri, K., & Afrasiabian, S. | 2015 | Iran | 27 patients treated with suspected pulmonary TB | Cross sectional | According to the research results, the diagnostic value of induced sputum in diagnosing TB is higher than the spontaneous sputum method. In addition, the quality of sputum produced through induction is higher than spontaneous sputum and does not cause any special complications. This method is recommended for use in patients suspected of having TB. |

| | Researcher | Year | Country | Respondents | Design | Finding |
|---|---|---|---|---|---|---|
| 4. | Olbrich, L., Smith, Z. F., Larsson, L., Sabi, I., Ntinginya, N. E., Khosa, C., Banze, D., Niiwasa, M., Corbett, E. L., Semphere, R., Verghese, V. P., Michael, J. S., Ninan, M. M., Saathoff, E., McHugh, T. D., Razid, A., Graham, S. M., Song, R., Nabeta, P., Trollip, A., … RaPeed-AIDA-TB consortium | 2025 | Germany | 102 children under 5 years old detected with M tuberculosis | Secondary analysis of data from RaPeed-TB, a multicenter diagnostic accuracy study evaluating new diagnostic methods and testing approach | According to related literature reports, the results of the study showed that of 102 children under 5 years of age who were detected with M tuberculosis, 78% of them were positive in sputum. Of the children who were positive in sputum, the majority (80%) only showed positive results in sputum itself. Induced sputum was more effective, with 95% of them being positive in induced sputum, while only 3% were positive in spontaneous sputum, and 2% were positive in both. This suggests that induced sputum is a better method for detecting tuberculosis in young children. |
| 5. | Cuong, N. K., Ngoc, N. B., Hoa, N. B., Dat, V. Q., & Nhung, N. V. | 2021 | Vietnamese | 123 pulmonary TB patients | Cross sectional conducted in 3 hospitals | According to literature reports, induced sputum is more effective in detecting TB and (MDR-TB) cases compared to spontaneously expelled sputum using the TCM Xpert MTB/RIF method. This study has several strengths, including a significant sample size and optimization of sample quality through the use of spontaneous and induced sputum. However, there are methodological limitations such as retrospective data and constraints in sequencing in patients with inconsistent result |

Based on the review of study 1, the comparison of spontaneous and induced sputum in patients with suspected TB pneumonia showed that out of 60 patients (44 males and 16 females), males had a better ratio (44.73%) and most were adults (70%). Results from the TCM GeneXpert strategy showed that from spontaneous sputum, 23 were positive and 8 were negative, with a positive ratio of 73%. Meanwhile, from induced sputum, 18 were positive and 12 were negative, with a positive ratio of 60%. The comparison showed more positive results in spontaneous sputum (55%). However, there was no significant evidence of effectiveness between the two strategies. Further studies should use better plans, such as case-control studies or cohort studies, and consider other factors that affect sputum quality, such as comorbid infections and smoking tendencies (Pratama et al., 2023).

Research in article 2 shows that the sensitivity of GeneXpert MTB/RIF examination using raw sputum samples reaches 93.62%, higher than the use of sputum pellets which have a sensitivity of around 80% to 82.3%. The use of raw sputum is more practical because it does not require a dilution and decontamination

process. However, the specificity of raw sputum was only 27.17%, much lower than that of sputum pellets which reached 100% and 73.3%. This low specificity may be due to several factors, including PCR inhibitors and the influence of anti-tuberculosis (OAT) drugs with unknown history (Susilawati et al., 2018).

The number of TB cases was dominated by men (288 cases) compared to women (183 cases). This study has limitations, such as the lack of data on the patient's disease history and treatment, as well as variations in the number of samples per year that may affect the results of the analysis. The quality of samples taken at different times is also a factor that affects the accuracy of the results (Susilawati et al., 2018).

The research in article 3 shows that the diagnostic value of induced sputum in TB diagnosis is higher than the spontaneous sputum method. In addition, the quality of sputum produced through induction is higher than spontaneous sputum and does not cause any special complications. This method is recommended for use in patients with suspected TB (Mohsenpour et al., 2015).

According to literature report 4, showed that out of 102 children under 5 years old detected M tuberculosis, 78% were sputum positive. Of the sputum-positive children, the majority (80%) were positive only on the sputum itself. Induced sputum was more effective, with 95% of those positive on induced sputum, while only 3% were positive on spontaneous sputum, and 2% were positive on both. This suggests that induced sputum is a better method for detecting tuberculosis in young children (Olbrich et al., 2025).

According to literature reports 5, Xpert MTB/RIF performs well in the diagnosis of tuberculosis (TB) and multidrug-resistant tuberculosis (MDR-TB), with induced sputum collection being more effective in detecting TB cases than spontaneously expelled sputum.

Tuberculosis, known as a chronic infectious disease, is a health condition caused by infection with the bacterium *Mycobacterium tuberculosis*. This bacterium has a rod shape and is resistant to acid staining, so it is commonly known as Acid Resistant Bacillus (BTA). In most cases, these tuberculosis-causing bacteria invade the lung parenchyma, leading to a form of the disease called pulmonary TB. However, the bacteria also have the ability to invade and spread to other organs outside of the lungs, known as extra-pulmonary TB, with infection sites that can include the pleura (lining of the lungs), lymph nodes, bones, and other organs. Scientifically, there are five types of bacteria known to be closely associated with tuberculosis infection, namely: *Mycobacterium tuberculosis*, *Mycobacterium bovis*, *Mycobacterium africanum*, *Mycobacterium microti*, and *Mycobacterium cannettii*. However, of the five types of bacteria, *Mycobacterium tuberculosis* (M.TB) is the type most commonly found in human TB cases and is known to spread from one individual to another mainly through airborne transmission (Cuong et al., 2021).

Human-to-human transmission of tuberculosis generally occurs when a person with pulmonary or laryngeal tuberculosis releases tiny droplet nuclei, less than 5 microns in size, during activities such as coughing, sneezing, or talking. They can also be released into the air during certain medical procedures that produce aerosols, such as sputum induction, bronchoscopy, or during manipulation of infected tissue, either during diagnosis or laboratory sample processing. These micro airborne particles are between 1 and 5 microns in size, and although they are small, they can carry between 1 and 5 highly infectious bacilli. They are also highly resilient, as they can remain airborne for up to four hours, and because they are so small, they can enter the lower respiratory tract and reach the alveolar spaces in the lungs, where the bacteria then multiply and replicate (Silalahi & Banjarnahor, 2022).

TB transmission is more likely to occur in enclosed spaces that are poorly lit and ventilated, as such conditions allow the germs to survive in the air for longer periods of time. In contrast, exposure to direct sunlight can quickly kill tuberculosis bacilli, so these bacteria will not survive for long in bright, open environments. Close and prolonged contact with individuals infected with active TB significantly increases one's risk of contracting the disease, especially when it takes place in unsanitary and crowded environments. However, not everyone exposed to the bacteria that cause TB will progress to active TB disease. The development of the disease is greatly influenced by the condition of the individual's immune system. In people with good immunity, about 90% of them will not develop active disease, but will only experience latent infection. Conversely, the remaining 10% are at risk of progression to active TB, with half of these cases appearing a short time after initial infection, and the other half progressing slowly and appearing later in life. The first two years after initial infection is the most critical period, as this is when the risk of latent TB progressing to active TB is highest. Population groups at highest risk of contracting and progressing to active TB include children under the age of five and older individuals, as both groups tend to have immune systems that are more susceptible to infection. (Silalahi & Banjarnahor, 2022).

Spontaneous sputum and induced sputum are two different methods for collecting sputum specimens in the diagnosis of tuberculosis. In spontaneous sputum, the patient is asked to produce sputum naturally

through coughing at a specific time, such as after waking up. The quality of the sputum produced may vary, with the aim of producing purulent or mucopurulent sputum. In contrast, induced sputum involves techniques to stimulate sputum discharge, such as using a device called a nebulizer, 5% hypertonic saline is converted into small particles by ultrasonic waves after inhaling these particles, the airway becomes irritated and causes coughing. Although it can speed up specimen collection, the quality of sputum produced is better than spontaneous sputum. Therefore, spontaneous sputum is not recommended as the primary method for the initial diagnosis of tuberculosis. The main difference between these two methods lies in the collection method and sampling conditions (Mohsenpour et al., 2015).

Molecular rapid tests, which include methods such as PCR (Polymerase Chain Reaction) or technology-based diagnostic devices such as GeneXpert, are a new technique for detecting pathogens, including *Mycobacterium tuberculosis* that causes tuberculosis (TB). The method works by detecting pathogen genetic material directly from clinical specimens such as sputum. The process begins with DNA or RNA extraction from the specimen, followed by amplification of the target gene using PCR enzymes. The amplification results are analyzed to confirm the presence of the pathogen's genetic material. The main advantages of molecular rapid tests are their accuracy in diagnosing TB, including drug-resistant forms (MDR-TB), as well as their ability to provide results in a short period of time, usually less than two hours. This is critical for rapid intervention and epidemic control, as it enables rapid identification and treatment of patients, reducing the risk of transmission. The test is also able to identify the type of bacterial strain, which helps in the management of treatment. However, this test requires specialized equipment and training of medical personnel, and tends to be more expensive than traditional examination methods such as microscopy (Susilawati et al., 2018).

## CONCLUSION

A literature review revealed differences in sensitivity between spontaneous and induced sputum in diagnosing tuberculosis (TB). Two studies indicated that spontaneous sputum was more sensitive, while three others indicated that induced sputum was more sensitive. Induced sputum is considered to produce better sample quality without complications and is recommended for patients suspected of having TB. However, the effectiveness of this method is still low due to the influence of sputum quality, sampling time, and unknown history of anti-TB drug use, which can reduce the accuracy of Rapid Molecular Test (TCM) results.

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