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Description of Bronchial Wash (BW) as a diagnostic procedure for presumptive pulmonary tuberculosis with sputum scarce at Mataram Regional Hospital

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ABSTRACT

Background: Some patients with presumptive TB cannot be bacteriologically confirmed because sputum is scarce. Improvement in the diagnostic value of using bronchoscopy for specimen collection has been reported. Due to its high sensitivity and specificity, PCR examination is recommended as an initial diagnostic test in all individuals suspected of pulmonary TB. This study aims to describe the results of the BW examination using the PCR GeneXpert MTB/RIF test in these populations treated at Mataram Regional General Hospital.

Methods: A descriptive study with secondary data collection from medical records at Mataram Regional General Hospital was conducted from July to December 2023. Statistical analysis was carried out using SPSS 26. Data on age, gender, examination results, and rifampicin sensitivity levels were described as proportions.

Results: A total of 143 patients were included in the analysis. Gender males (61.5%) and those aged 40-60 years (44.8%) were reported in this study. Of this examination, 89 (61.5%) patients reported positive, 52 (37.1%) negative, and 2 errors (1.4%). Based on the level of cycle threshold, it was reported that 16 patients (17.9%) were high, 12 patients (13.5%) were medium, 21 patients (23.6%) were low, and 40 patients (44.9%) were very low. No rifampicin resistance was reported in this study.

Conclusion: More than 50% of presumptive pulmonary TB patients with sputum scarce were reported positive through the BW and GeneXpert MTB/RIF examinations. This examination is recommended especially for these populations to get faster antituberculosis treatment.

Keywords: Presumptive pulmonary TB, Negative AFB, Bronchial Wash, BW, GeneXpert MTB/RIF.
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INTRODUCTION

Tuberculosis (TB) is the 10th leading cause of death worldwide and is the main cause as a single infectious agent. Every year, around 10 million new cases of TB are diagnosed, and 1.4 million die cases are reported. Most TB cases reported from Southeast Asia and Indonesia included 8 countries contributing to 2/3 of TB cases globally. Indonesia is also the second-highest-ranked country in terms of estimated incidence per year. Based on data from the World Health Organization (WHO), the proportion of patients with bacteriologically confirmed pulmonary TB was around 57% in 2019. Although the number of new TB cases has increased, there is still a large gap between the reported number and estimates, possibly due to underreporting, and diagnosis still needs to be improved. Effort needs to be made to increase the bacteriological confirmation of pulmonary TB using diagnostic tools recommended by WHO.[1]

Bacteriological diagnosis of pulmonary TB is confirmed by good-quality sputum performed on two consecutive sputum specimens. Microscopic examination of acid-fast bacilli (AFB) is still the first choice in diagnosing TB, but its sensitivity is low and variable (16-60%).[2] This may be related to several conditions, such as poor-quality sputum specimens or a low number of organisms in the specimen, so they cannot be detected. Apart from that, some patients are also scarce in sputum.[3] In this group of patients, several techniques must be used to provide good-quality sputum so diagnosis and therapy can be carried out more quickly and precisely. Good-quality sputum is reported to be able to improve the diagnostic quality of pulmonary TB.[4]

Several modalities, such as sputum induction, gastric lavage, and bronchoscopy, were reported in many studies. Bronchoscopy is reported to be safe and effective as a method to help diagnose TB. This procedure can be performed to collect sputum in patients with sputum scarcity, even after sputum induction, such as children and HIV patients. Several studies also report the benefits of this technique in patients with negative

smear tests.[4,5] Further examinations such as smears and cultures can be carried out with specimens from bronchial aspirate or bronchial wash (BW), bronchoalveolar lavage fluid (BALF), bronchial brush, post-bronchoscopy sputum, or tissue biopsy examination with cytopathological and histopathological examination.[6,7]

Since 2010, WHO has recommended the Xpert MTB/RIF examination, which 2014 was expanded to include this modality as an initial diagnostic test in all patients suspected of pulmonary TB. This examination is reported to have a sensitivity of 80-93% in patients with positive cultures.[8]

Based on those mentioned above, this study aims to evaluate the results of the GeneXpert examination on bronchial wash samples from patients with presumptive pulmonary TB with sputum scarce who were undergoing treatment in the inpatient ward at Mataram Regional Hospital, West Nusa Tenggara.

METHODS

This study is a retrospective descriptive study of adult patients (over 18 years) who underwent bronchoscopy examination and sputum sampling via BW and were treated from July to December 2023 at Mataram Regional Hospital, West Nusa Tenggara. The inclusion criteria for this study are:

1. Presumptive TB patient (combination of ≥2 clinical symptoms for > 2 weeks) with one radiological finding suggestive of pulmonary TB)
   a. Clinical symptoms include cough, fever (above 37.5^{0}C), night sweating and shortness of breath, physical examination with RR above 20 times/minute, and weight loss of <5% of initial body weight within 6-12 months.
   b. The radiological picture shows consolidation, cavities, nodular opacities
2. Patients with scarce sputum (unable to produce good quality or sputum production < 1 ml).

Patients with a suspected diagnosis of extrapulmonary TB and patients with HIV or immunocompromised conditions were excluded from the study.

The data obtained is secondary data from manual and electronic medical records after requesting approval from the ethics committee at Mataram Regional Hospital. Sampling was carried out using the consecutive sampling method, taking all data on patients who underwent examination within the specified time. Some of the data taken includes patient demographic data such as age and gender, GeneXpert examination results from BW samples, and the final diagnosis from the pulmonary specialist who treated the patient.

The bronchoscopy procedure used an optical sheath bronchoscope with an internal tube insertion diameter of 6.2 mm. The bronchial tree is then visualized. The BW procedure is carried out by placing a bronchoscope in the airway in the affected lung lobe. Sample collection is carried out after the instillation of 1-3 aliquots of 10 ml of sterile normal saline. Any complications in the procedure (hypoxemia, desaturation, fever, etc.) will be recorded and reported in the study results.

PCR inspection was carried out on BW samples, which were then transferred to the Xpert® MTB/RIF version G4 cartridge according to the manufacturer's specifications. The examination results include MTB not detected (negative) and MTB detected (positive). The positive detection rate is reported according to the cycle threshold value, namely negative, very low (>28), low (22-28), medium (16-21) or high (<16). In positive samples, whether the sample is sensitive or resistant to rifampicin will be further reported.

The data was then collected using Microsoft Excel 2016 software and analyzed statistically using SPSS 26 for Windows. Quantitative descriptive data is described in frequency with percentages, tables, and graphs.

RESULTS

Table 1 describes the demographic characteristics of research subjects resulting from TCM examinations from the BW sample. Of the 143 samples with suspected pulmonary TB, male gender (61.5%) and an age range of 40-60 years (44.8%) were predominantly reported.

Figure 1 describes the GeneXpert results of BW samples. Of the 143 samples with suspected pulmonary TB, the following results were obtained: positive for 89 samples (62%), negative for 52 samples (36%) and error results for 2 samples (2%). Of all these samples, there were no rifampicin-resistant samples.

Figure 2 describes the positive GeneXpert examination results from BW samples based on cycle threshold values. Of the 89 samples with suspected pulmonary TB, the following results were obtained: 16 samples were high, 12 samples were medium, 21 samples were low, and 40 samples were very low.

DISCUSSION

Several studies have been reported comparing bronchoscopy examination modalities as a diagnostic tool. There are several different reports regarding the superiority of using the bronchoscopy technique.[9,10] The combination of the GeneXpert examination can increase the diagnostic value of the examination (from 29.5% to 68.2%) as an initial diagnostic test for pulmonary TB patients, having a high diagnostic value and the results are indifferent even if the transthoracic biopsy examination procedure is added. Biopsy examination can be avoided in diagnosing pulmonary TB, considering several complications that can occur, such as pneumothorax and bleeding.[11] This study reports the results of bronchial wash with the GeneXpert examination as the diagnostic method for pulmonary TB performed at Mataram Regional Hospital.

This study reported that the proportion of BW samples that were positive through the GeneXpert examination was 61.5%, which means that more than 50% of patients with sputum scarcity showed positive results. This proportion is still within the range of several similar studies published in the last 10 years (11.1-69.2%).[9,12-20] In 2021, eight countries, based on the number of TB cases, contributed to 2/3 of TB cases globally, including India, Indonesia, China, Philippines, Pakistan, Nigeria, Bangladesh, and Congo. The proportion of results of this study similar to the report by Zuberi FF et al. Studies from Mohammadi J et al. and Kanade S et al. reported different results. This is because the study reported two bronchoscopy methods, namely BAL and

Table 1. Demographic Characteristics of Research Subjects

Characteristics	n (%)
Gender	
• Male	88 (61.50)
• Female	55 (38.50)
Age (year)	
• <40	19 (13.20)
• 40-60	64 (44.80)
• >60	60 (42.00)

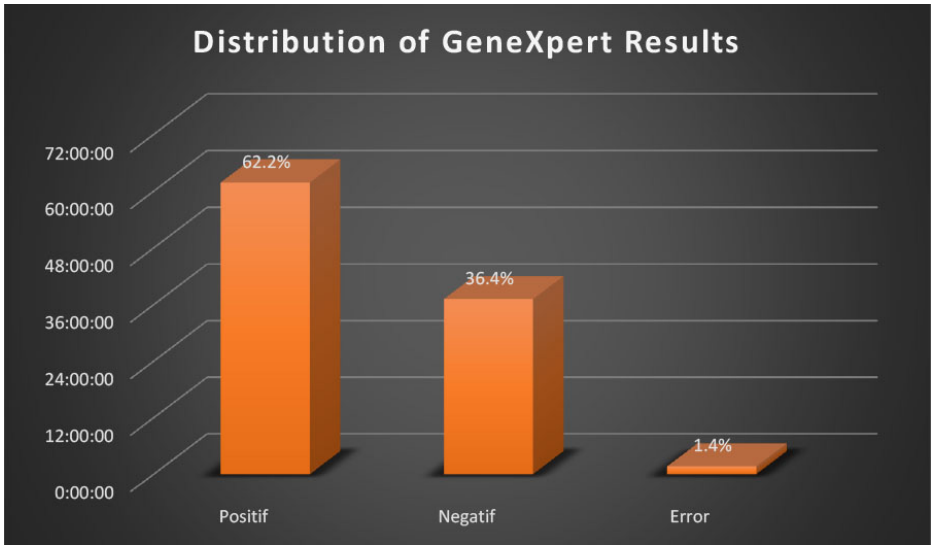

Figure 1. Distribution of GeneXpert Results.

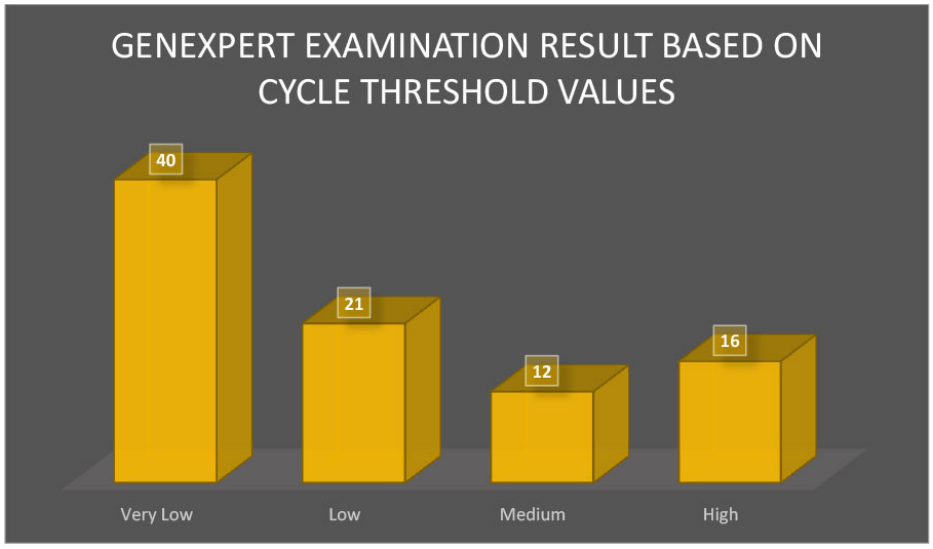

Figure 2. GeneXpert Examination Result based on Cycle Threshold Values.

BW, and was mostly carried out using the BAL technique. However, the proportion of MTB detection itself is also low. Palud P et al. reported a low proportion compared to other studies, possibly due to geographic factors.

This study also reported that most of the samples showed results at low and very low levels. Barnard et al. reported slightly different results, with the proportion of medium levels slightly higher than in the study. Yang J et al. (BAL was carried out in the study) reported results that were not much different, where of the 293 positive samples, there were 109 (37.2%) with very low results and 131 (44.7%) with low results. It was further reported that the majority (96%) had positive culture values in high and medium samples.[21]

Based on existing studies, this examination has sensitivities above 80% for culture as the gold standard assay.[9,14,17-20] Yang J et al. reported that adjustments were made where the low and very low rifampicin sensitivity categories were categorized as negative results, and an increase in the specificity value and a decrease in sensitivity were obtained.[21] Meanwhile, for the final diagnosis as a gold standard assay (a combination of clinical, radiological, and bacteriological), GeneXpert shows slightly better sensitivity values than culture.[9,14,17-20] This requires paying attention to the possibility of false positives from the GeneXpert examination.

Mok Y et al. reported false-positive results where the sample had a history of having received pulmonary TB therapy in the last 2 years before the examination.[11] Barnard DA et al. reported false-positive examination results for 7 samples, of which 3 were treated as suspicious for pulmonary TB. Another consideration for samples that are not confirmed as pulmonary TB is a history of previous pulmonary TB and a history of having undergone pulmonary TB therapy. Examination based on the amplified DNA polymerase chain reaction can also come from dead pathogens, so to diagnose this population, it is necessary to consider other examinations. It is also not clear whether the bacterial load in samples with latent infection or previous exposure can reach the examination threshold, thereby potentially resulting in a very low result.[19] De Brito reported in his study that there were false positives where the cycle threshold value for the sample was higher (26.6- 30.9; probes A-E) which implies a low DNA concentration is a possible reason why other tests used in the study (AFB staining and culture) gave negative results.[22,23]

The finding highlighted in this study is that more than 50% of patients with negative BTA smear results showed positive results with the BW + GeneXpert examination. There are several limitations in this study, such as the small sample size and the fact that it was conducted at one health center only. The other limitation is that culture tests were not carried out as the gold standard, so the sensitivity and

specificity cannot be estimated, and its possible superiority compared to culture, as in several other studies, is not possible. No follow-up was carried out after establishing the diagnosis with similar examination modalities.

Recommendations for further study are: multicenter study should be conducted in the future to be more representative of a larger population. Future studies should compare with the gold standard and other definitive diagnoses; care must be taken in interpreting examination results, especially in patients with a previous history of pulmonary TB, and considering clinical and other modalities in determining whether the patient will receive pulmonary TB therapy. The last follow-up is necessary to increase understanding of the modality of bronchial washing and GeneXpert as an examination for tuberculosis.

CONCLUSION

Based on the results of this study, it was concluded that more than 50% of presumptive patients with pulmonary TB with sputum scarcity had positive results based on the BW+GeneXpert examination. Patients with sputum scarcity can benefit from this examination because rapid detection can help speed up the patient's access to antituberculosis drug services. Apart from that, this examination is also safe for patients.

CONFLICT OF INTEREST

We declare that there was no conflict of interest in this study.

ETHICAL CONSIDERATIONS

The Institutional Review Board of Mataram Regional Hospital, West Nusa Tenggara, Indonesia, approved the study with protocol number 003/E.PEN/II/2024.

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AUTHOR CONTRIBUTION

All authors contributed equally to the study from the conceptual framework, data acquisition, and data analysis until the results were reported through publication.

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