IJTID. Volume 13 No 1 January-April 2025 e-ISSN: 2356-0991; p-ISSN:2085-1103
Sinta 2 (Decree No: 105/E/KPT/2022) Available online at https://e-journal.unair.ac.id/IJTID

Article Review

IJTID
(INDONESIAN JOURNAL OF TROPICAL AND INFECTIOUS DISEASE)
Scientific Journal of Tropical and Infectious Disease

Diagnosis Approach of Endobronchial Tuberculosis: Literature Review

Mario Oktafiendi Ginting[1,*], Sri Indah Indriani[1], Elvando Tunggul Mauliate Simatupang[1]

[1]Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Riau University, Arifin Achmad General Hospital, Pekanbaru

OPEN ACCESS

ARTICLE INFO

Received: July 15, 2024
Accepted: October 24, 2024
Published: April 30, 2025
Available online: April 30, 2025

*) Corresponding author:
E-mail: mariogintingdr@gmail.com

Keywords:
Tuberculosis
EBTB
Stenosis
Bronchoscopy
Mtb

Abstract

Pulmonary tuberculosis (PTB) remains a global health problem and the leading cause of death from infectious diseases. Indonesia as an endemic country and the second highest contributor of PTB cases in the world provides support and attention to PTB case finding and treatment success. Endobronchial tuberculosis (EBTB) is problematic PTB because the lesions are often not detected by sputum examination and chest X-ray. Clinically, there is no significant difference in symptoms between TB and EBTB. In general, EBTB gives a more severe clinical appearance due to airway stenosis. Bronchoscopy and thoracic computed tomography scan (CT scan), along with microbiological investigations, are the most useful diagnostic tools for confirming and evaluating tracheobronchial stenosis. In addition, bronchoscopy can also be used as a long-term treatment in cases of EBTB due to airway stenosis. The goals of treatment are the eradication of *Mycobacterium tuberculosis* (Mtb) bacilli with antituberculosis drugs (ATD) and the prevention of airway stenosis. Intervention of bronchoscopic techniques and surgery are required for those patients who develop severe tracheobronchial stenosis that causes significant symptoms, including dyspnea, repeated post-obstructive pneumonia or bronchiectasis. The most common complications of EBTB are airway stenosis, atelectasis, hemoptysis and shortness of breath accompanied by wheezing despite the administration of ATD. Bronchoscopic intervention can support the acceleration of EBTB treatment, prevent repeated hospitalizations and improve the quality of life of patients. Acceleration of diagnosis and administration of ATDs in a complete and routine way is expected to reduce morbidity and even mortality rates in EBTB cases.

Cite this as: Ginting, M. O., Indriani, S. I., and Simatupang, E. T. M. (2025). Diagnosis Approach of Endobronchial Tuberculosis: Literature Review. *Indonesian Journal of Tropical and Infectious Disease*, 13(1) : 39–48. https://doi.org/10.20473/ijtid.v13i1.60257

INTRODUCTION

Pulmonary tuberculosis (PTB) continues to be a global health issue and is the main cause of mortality of infectious diseases. In 2021, the World Health Organization (WHO) reported 10.6 million cases of PTB, which amounts to about 134/100.000 individuals.[1] The incidence of PTB has shown 3.6% increase, leading to a mortality rate of within the period of 2020-2021. Indonesia is the second-highest contributor of PTB cases in 2021, after India, which is the greatest contributor globally.[2]

Endobronchial tuberculosis (EBTB) is defined as *Mycobacterium tuberculosis* (Mtb) infection of the tracheobronchial tract that is microbiologically or histopathologically confirmed tuberculosis with or without parenchymal involvement. This case is a form of PTB infection that is tricky to diagnose because of the infectious lesions can often be underdetected on sputum examination and chest X-ray. Active PTB patients represent 10-40% of EBTB cases, and bronchial stenosis occurs > 90% of cases. The incidence of EBTB is underdetected and unknown due to a bronchoscopy and thoracic computed tomography scan (CT scan) being rarely used for routine examinations in cases of PTB.[3]

EBTB is defined as an infection of the tracheobronchial tract with *Mycobacterium tuberculosis* that has been microbiologically or histopathologically confirmed, with or without lung parenchymal disease. Richard Morton, a doctor in England, was the first to report the involvement of the trachea and bronchi in PTB infection in 1698. Delays in treatment are often the result of issues in identifying EBTB. Bronchoscopy and thoracic CT scan can be recommended for follow-up examinations to confirm the diagnosis and examine bronchial lesions, including obstruction or stenosis.[4]

The main goals of EBTB treatment are the prevention of bronchial stenosis and the elimination of tubercle bacilli. EBTB cases show improved responses to the use of antituberculosis drugs (ATD). In some cases, the histopathologic appearance of endobronchial lesions does not always display the classic granuloma appearance of tuberculosis, despite the negative results of acid-fast bacilli (AFB) sputum. The diagnosis of EBTB can be difficult to determine related to the absence of classic PTB systemic symptoms, such as anorexia, weight loss, and nocturnal sweats.[5]

PATHOGENESIS

The exact pathogenesis of EBTB is still not completely known. Generally, there are five mechanisms of Mtb infection in EBTB: Direct spread of infection to the lung parenchyma, direct spread of Mtb from infected sputum, hematogenous spread, lymph node (LN) erosion into the bronchi, and flow of LN from the parenchyma to the peribronchial area.[6] EBTB infection can impact any layers of the tracheobronchial wall, including the muscularis lamina and cartilage. Ulcers, granulomas, fibroplasia, mucosal and submucosal infiltration, and tracheobronchial stenosis are among the various pathological changes (Figure 1).[7]

There are two phases in the pathophysiology of EBTB: the early and advanced stages. Hyperemia occurs in the mucosa during the early stage, and it shows in the submucosa when the next stage as the result of the infiltration of inflammatory cells, particularly lymphocytes.[8] EBTB can affect all branches of the bronchi during its course,

with the primary locations with the main bronchi, bilateral superior lobes, and middle lobe. The left bronchus is the location most likely to be infected with EBTB because infection in the LN spreads more quickly in the left bronchus than the right bronchus. This is because the LN is structurally located in the mediastinum and aortic arch nearer to the left bronchus.[9]

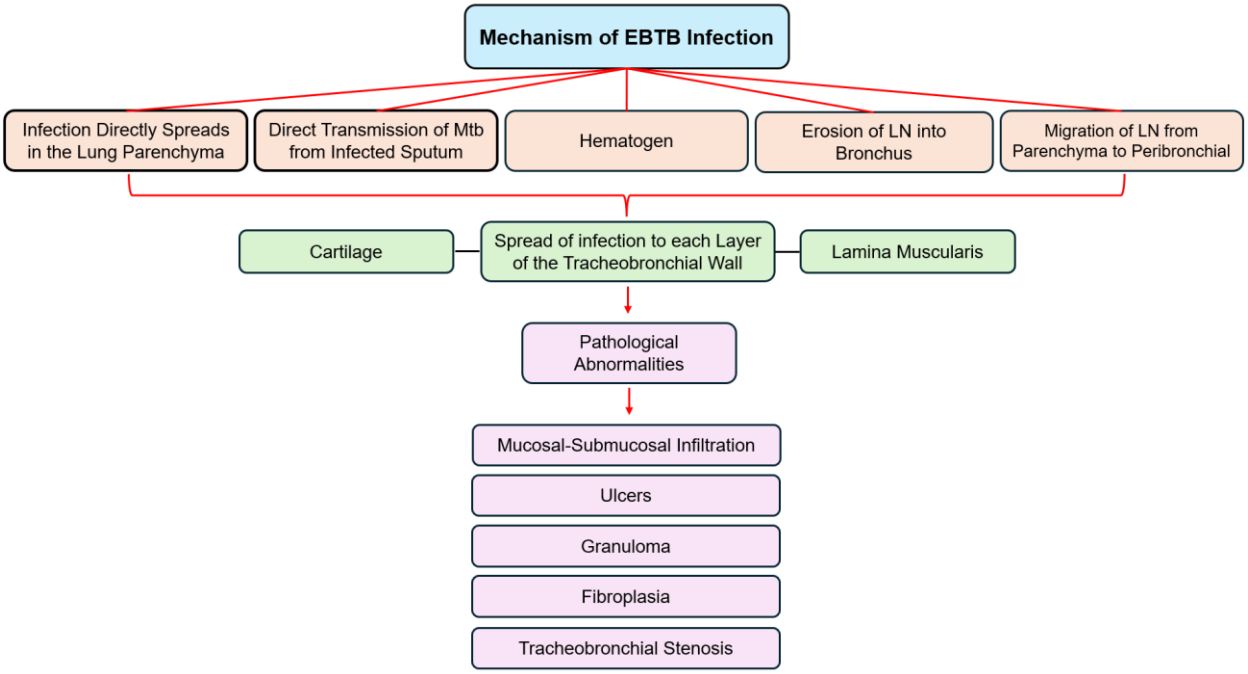

Figure 1. Pathological Abnormalities of EBTB[6,7]

The formation of an EBTB nodule is followed by the development of a caseous necrosis within the nodule and, finally, mucosal ulceration. The ulcer can either progress to the tracheobronchial wall and develop into an internal ulcer or become an inflammatory hyperplastic polyp that extends into the tracheobronchial lumen, like a tumor.[8] The incidence of tracheobronchial stenosis will reach 68% within 4-6 months and will continue to rise as the disease progresses, leading to the development of fibrous hyperplasia and contracture in the advanced stages. In addition to local factors, the development of EBTB is a complex phenomenon that is significantly affected from a variety of cytokines.[9]

The pathogenesis and progression of EBTB are also influenced by elevated levels of transforming growth factor-β (TGF-β) and interferon gamma in fluid of bronchoalveolar lavage (BAL). The development of bronchial stenosis through the course of the disease is associated with the alterations in TGF-β levels observed in serum after treatment.[9] The classification of EBTB by Jung et al. depends on the variety of levels involved. Single-level EBTB is characterized by the involvement of a single major tracheal or bronchial location. Multiple EBTB is defined as EBTB that affects two or more bronchi, and central EBTB has the potential to extend from the proximal to the bronchial lobe, potentially causing stenosis signs (Figure 2).[10]

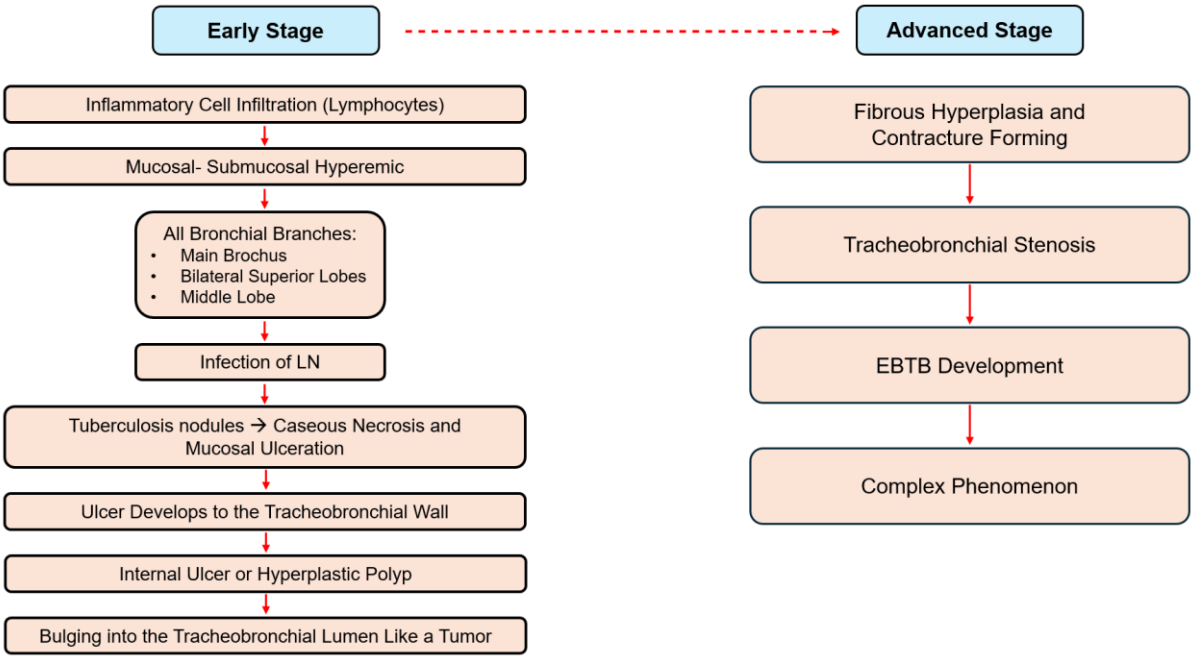

Figure 2. Mechanism of EBTB Occurrence[9,10]

DIAGNOSIS

Anorexia, fatigue, and weight loss belong to the symptoms of EBTB, which are as various as the systemic symptoms of PTB. It is reported that these symptoms manifest in more than 50% of patients.[11] Cough is the most common symptom in 70-80% of patients. When EBTB develops in cavitary PTB, dry cough or bronchorrhea is a common symptom. EBTB is indicated by a persistent cough that is responsive to concurrent steroid treatment with ATD but is not responsive to antitussives. While fever is present, coughing is typically moderate and may be associated with hemoptysis.[12]

Painful or dull chest pain at the sternum or parasternal is a symptom of ruptured LN. In certain lung areas, physical examination reveals decreased breathing noises, as well as ronchi and wheezing. Respiratory failure and lung collapse may result from symptoms of EBTB that involve the trachea. Liu et al. reported that pleural effusion may be a clinical symptom in EBTB cases as an outcome of delayed treatment. Central airway obstruction and failure of endotracheal intubation are life-threatening consequences of EBTB that can result in mortality.[13]

The diagnosis of EBTB is more complex compared to that of PTB. This is due to the fact that the indicators and symptoms of EBTB are not typical. A complete clinical examination of EBTB is extremely useful for the early identification and offering of appropriate treatment. Sputum examination and AFB culture are essential diagnostic procedures for patients suspected with EBTB. Bronchoscopy and thoracic CT scan are used as the main indicators are used as the main indicators to diagnose and assess bronchial involvement and surgical intervention.[14] In patients with EBTB, lung function evaluations are mainly restrictive. It's the result of chronic inflammation and modifications in parenchymal injury that extend above the stenosis.[15]

Sputum Examination

The AFB sputum examination is the most significant and frequently used method for the diagnosis of EBTB, despite the low diagnostic result. AFB sputum positivity

rates in EBTB are variable and with some studies showing that these numbers range from 16-53% of cases. In addition, early detection of EBTB should also be considered by clinical and physical examination even if AFB sputum examination is negative. Ulceration and mucosal involvement in EBTB patients are associated with a higher positive sputum result. In comparison to AFB sputum examination, AFB culture examination has a higher positivity rate. Therefore, it may be considered.[8]

Radiology

The diagnosis of EBTB can be difficult to establish because of a fact that chest X-rays usually produce normal results in about 10-20% of patients. For 10-40% of patients with active PTB, bronchial stenosis is identified. Infiltrates that are unevenly distributed in the affected lobe are common abnormalities on chest X-ray. Bronchostenosis, calcifications, cavities, bronchiectasis, intrathoracic lymphadenitis, and pleural effusion are some of the other chest X-ray findings that are based according to the severity.[16] Lee et al. showed that consolidation and atelectasis occurred in approximately 83.4% of chest X-ray for EBTB. The results for chest X-ray are one of the limiting factors in the diagnosis of EBTB, as it can be difficult to differentiate from asthma and lung cancer (LC) among older people.[17]

A thoracic CT-scan gives more detailed information than chest X-rays, including mediastinal lymphadenopathy, pleural effusion, nodules, and stenosis. Other results include endobronchial obstruction, fibrosis, and segmental bronchial narrowing with wall thickening.[17,18] Multiple lobar lesions, exudative shadows, and atelectasis are the most prevalent radiologic features, as noted by Qingliang et al. The goal of the examination is to present visualization before bronchoscopy. Patients with thoracic CT scan examination results that indicate EBTB images need to have bronchoscopy or a microbiology examination (Figure 3).[19]

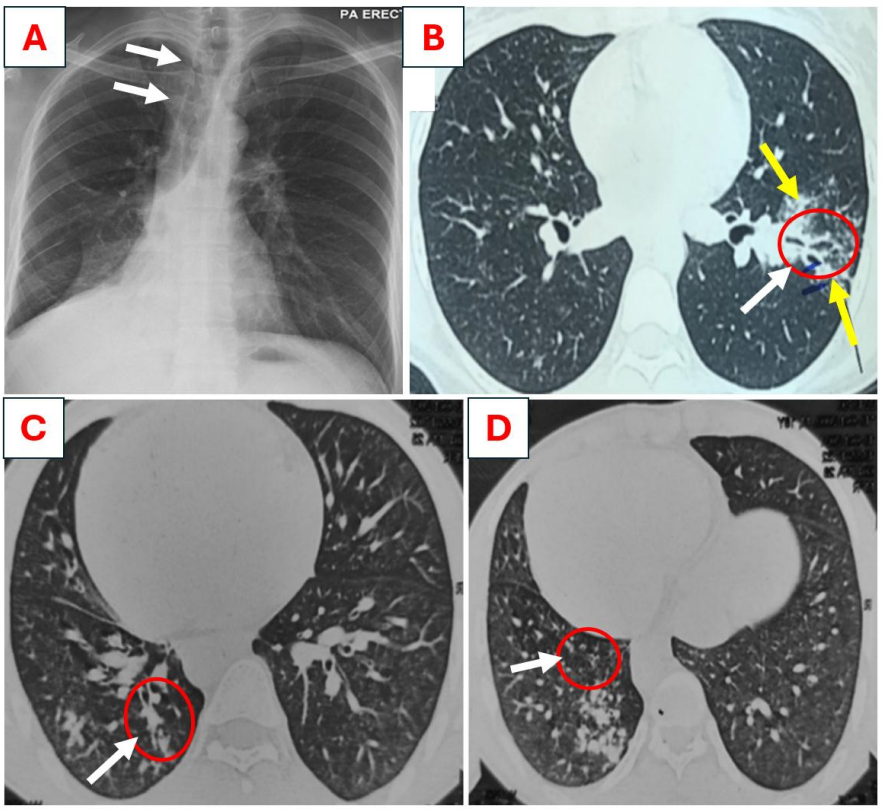

Figure 3. Radiologic Findings of EBTB. (A) Atelectasis of the Right Lung on Chest X-Ray; (B) Left Lung Nodules and Bronchiectasis on Thoracic CT Scan ; (C) Features of Tree in Buds on right Lower Lobe with High-Resolution Computed Tomography (HRCT); (D) Right Lower Lobe Nodules on HRCT

Bronchoscopy

Bronchoscopy is the most important technique for identifying the initial diagnosis and assessing the prognosis of EBTB. Several bronchoscopic procedures, including biopsy, bronchial brushing, bronchial washing, needle aspiration, bronchoalveolar lavage and endobronchial ultrasound (EBUS), are indicated as the most effective methods for identifying EBTB. Also, bronchoscopy is employed to exclude other concurrent or underlying diseases, such as malignancy. Studies conducted in China have indicated that bronchial brushing has a sensitivity of 84.88%, while bronchial washing has a positivity rate that ranges from 10-37.5%.[20]

Bronchoscopic specimen collection is important for the successful diagnosis of EBTB, as indicated by the presence of sputum examination and AFB culture positivity rate > 90%, while needle aspiration can be employed to obtain specimens from lobe segments that are inaccessible to biopsy instruments. EBTB is visualized through bronchoscopy to facilitate the differential diagnosis of other conditions. In addition, EBTB is classified according to bronchoscopic visualization, which comprises seven subtypes (Table 1).[18,19]

Table 1. Classification of Bronchoscopic Visualization of EBTB[19]

Subtype	Description
Active Caseous	Tracheobronchial mucosal wall is edematous, hyperemic and coated with a cheese-like yellowish-white coating
Hyperemic Edema	Edematous and hyperemic tracheobronchial mucosa
Non-specific Bronchitis	Tracheobronchial mucosa appears mild to moderate edema and hyperemic mucosa
Granular	Tracheobronchial mucosa is highly inflamed with rice grain-like nodules
Ulcerative	Tracheobronchial mucosa ulcers appearance
Tumorous	Hyperplastic focal tissue forms, tumor-like intraluminal masses
Fibrostenosis	Tracheobronchial lumen constricted by hyperplasia and fibrosis

The prospective study by Chung and Lee investigated the progression of EBTB by serial bronchoscopy, from the period of diagnosis to the conclusion of ATD treatment. The initial non-specific form of bronchitis is followed by the formation of submucosal tubercles. Next, the hyperemic granular and edematous type develops. The subsequent stage is identified by caseous necrosis, which results in the formation of tuberculous granulomas on the mucosal surface. Then, ulcers are formed and coated by caseous material as the inflammation extends through the mucosa.[8,19]

Hyperplastic inflammatory polyps develop from bronchial mucosal ulcers, and endobronchial tuberculous lesions resolve through fibrostenosis.[21-23] The erosion of tuberculous LN into the bronchus can occur in tumor-type EBTB.[24-26] The best prognosis is associated with the active caseous type and hyperemic edema type, which will result in fibrostenosis in patients. Granular, ulcerative, and non-specific forms of EBTB have an almost better prognosis (Figure 4).[19,27-29]

This form of tumor features a complex clinical course with a variety of progressions. The development of bronchial stenosis can be caused by such unpredictable modifications, despite the availability of adequate treatment.

The degree of progressing disease correlates strongly with the classification features of EBTB, with a distinctive appearance.[30-32] The management of EBTB through bronchoscopy encompasses balloon dilatation, stenting, laser, cryotherapy, and airway reconstruction.[33-35] Expertise in usage of both rigid and flexible bronchoscopy is necessary for the management of endobronchial lesions.[8]

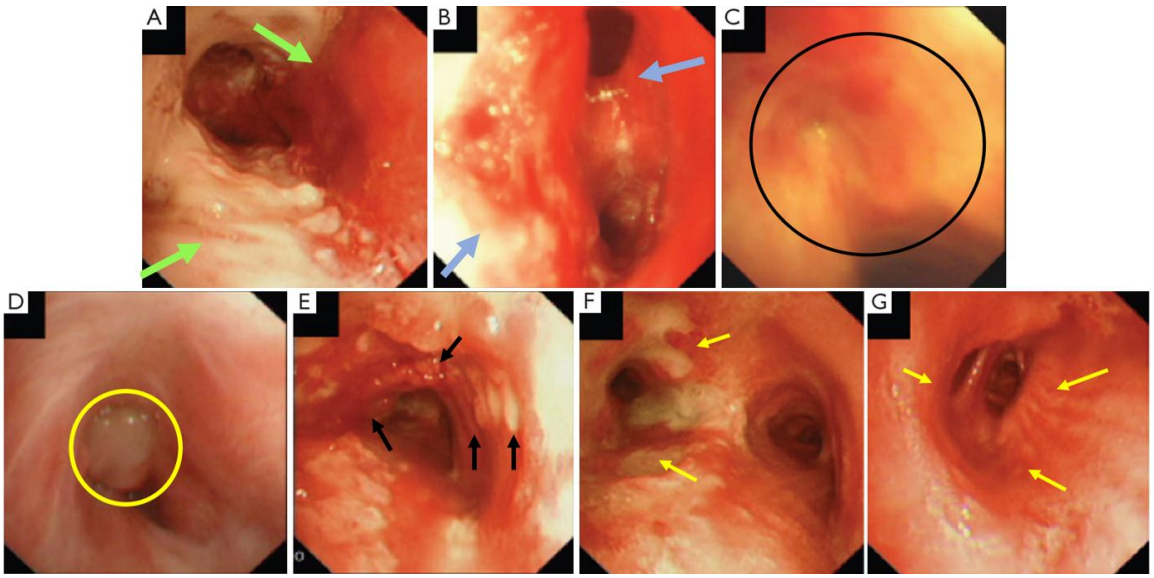

Figure 4. Bronchoscopic Visualization of EBTB. (A) Active Caseous; (B) Hyperemic Edema; (C) Fibrostenosis; (D) Tumorous; (E) Granular; (F) Ulcerative; (G) Non-specific Bronchitis.[19]

STRENGTH AND LIMITATION

This study can provide information related to the acceleration of diagnosis and the provision of complete and routine OAT which is expected to reduce morbidity and even mortality in EBTB cases. The limitation of this study is that it only focuses on Endobronchial tuberculosis.

CONCLUSION

PTB is a prevalent disease globally. The non-specific clinical symptoms of this form of EBTB demand special attention, as they have the potential to develop into severe complications of bronchial stenosis and delay the diagnosis of EBTB. Tracheobronchial stenosis can be prevented by early diagnosis and aggressive treatment with ATD treatment in the management of EBTB. Radiology, microbiology, and histopathology examinations are recommended along with bronchoscopy as the main diagnostic tool. Furthermore, the classification and prognosis of EBTB can be explained by the results of bronchoscopic visualization. Further research is needed to identify the disease's pathogenesis and progression in more detail.

ACKNOWLEDGMENT

None

FUNDING

This study did not receive any funding.

CONFLICT OF INTEREST

The authors confirm that they have no conflict of interst.

AUTHOR CONTRIBUTION

Writer, literature searcher, collecting data from literature: MOG and SII. Review and supervisio: ETMS.

REFERENCES

1. World Health Organization (WHO). Global Tuberculosis Report 2022. Geneva; 2022.
2. Laporan Program Penanggulangan Tuberkulosis Tahun 2022 KEMENTERIAN KESEHATAN REPUBLIK INDONESIA TAHUN 2023. Available from: https://tbindonesia.or.id/wpcontent/uploads/2023/09/Laporan-Tahunan-Program-TBC-2022.pdf
3. Siow WT, Lee P. Tracheobronchial tuberculosis: a clinical review. J Thorac Dis [Internet]. 2017 [cited 2024 Jul 10];9(1):E71. Available from: /pmc/articles/PMC5303096/
4. Su Z, Cheng Y, Wu Z, Zhang P, Chen W, Zhou Z, et al. Incidence and Predictors of Tracheobronchial Tuberculosis in Pulmonary Tuberculosis: A Multicentre, Large-Scale and Prospective Study in Southern China. Respiration [Internet]. 2019 Jan 30 [cited 2024 Jul 10];97(2):153–9. https://dx.doi.org/10.1159/000492335.
5. Ip. MS, Lam WK, So SY, Mok CK. Endobronchial Tuberculosis Revisited. Chest. 1986 May 1;89(5):727–30.
6. Rikimaru T, Kinosita M, Yano H, Ichiki M, Watanabe H, Shiraisi T, et al. Diagnostic features and therapeutic outcome of erosive and ulcerous endobronchial tuberculosis. Int J Tuberc Lung Dis. 1998 Jul;2(7):558-62.
7. Murgu AD, Colt HG, Mukai D, Brenner M. A Multimodal Imaging Guide for Laser Ablation in Tracheal Stenosis. Laryng, 2010;120(9): 1840-6.
8. Kim S, Eom JS, Mok J. Bronchoscopic Strategies to Improve Diagnostic Yield in Pulmonary Tuberculosis Patients. Tuberc Respir Dis (Seoul). 2024 Jul;87(3):302-8.
9. Schulte SC, Fischer S. Management of Tracheobronchial Stenoses. Zentralbl Chir. 2023 Jun; 148(3): 293-303.
10. Jung SS, Park HS, Kim JO, Kim SY. Incidence and Clinical Predictors of Endobronchial Tuberculosis in Patients with Pulmonary Tuberculosis. Respirology. 2015: 20(3):488-95.
11. Hoseini SHA, Ghalenavi E, Amini M. Clinical and Para-Clinical Presentation of Endobronchial Tuberculosis. J Cardiothorac Med .2015;3(4):371-4.
12. Samardzic N, Jovanovic D, Denic L, Milenkovic MR. Clinical Features of Endobronchial Tuberculosis. Vojno Pregled. 2014;71(2):156-60.
13. Liu X, Xu L, Jiang G, Huang S. Pleural Effusion Resulting from Bronchial Tuberculosis. Medic. 2018; 97(40). 1-4.
14. Moon SM, Lee WY, Shin B. Clinical characteristics and drug resistance profile of patients with endobronchial tuberculosis in South Korea: single-center experience. Ann Palliat Med. 2023

May; 12(3):487-95.
15. Li Z, Mao G, Gui Q, Xu C. Bronchoplasty for Treating The Whole Lung Atelectasis Caused by Endobronchial Tuberculosis in Main Bronchus. J Thorac Dis. 2019;20(1): 71-7.
16. Natarajan A, Beena PM, Devnikar AV, Mali S. A systemic review on tuberculosis. Indian J Tuberc. 2020 Jul;67(3):295-311.
17. Lee P. Endobronchial tuberculosis. Indian J Tuberc. 2015 Jan1;62(1):7–12.
18. Akamatsu T, Shimoda Y, Saigusa M, Yamamoto A, Morita S, Asada K, et al. Use of virtual bronchoscopy to evaluate endobronchial TB. Int J Tuberc Lung Dis. 2021 Feb 1; 25(2): 145-7.
19. Martins J, Carvalho C, Freitas F, Monteiro P. Endobronchial tuberculosis. Port J Card Thorac Vasc Surg. 2022 Apr 11;29(1):83.
20. Kashyap S, Solanki A. Challenges in endobronchial tuberculosis: From diagnosis to management. Pul Medi. 2014;(2014): 1-8.
21. Cary C, Jhajj M, Cinicola J, Evans R, Cheriyath P, Gorrepati VS. A rare case of fibrostenotic endobronchial tuberculosis of trachea. Ann. Med. Surg. 2015;4(4):479-482.
22. Shahzad T, Irfan M. Endobronchial tuberculosis-a review. J. Thorac. Dis. 2016 Dec;8(12):3798-3802.
23. Panigrahi MK, Pradhan G, Mishra P, Mohapatra PR. Actively caseating endobronchial tuberculosis successfully treated with intermittent chemotherapy without corticosteroid: a report of 2 cases. Adv. Respir. Med. 2017;85(6):322-327.
24. Ahmad Z, Masood I, Baneen U, Ejaz S, Rehman S. Endobronchial growth: tumor or tuberculosis. J. Family Med. Prim. Care. 2024 Mar 6;13(2):792-796.
25. Esa NYM, Othman SK, Zim MAM, Ismail TST, Ismail AI. Brochoscopic features and morphology of endobronchial tuberculosis: A Malaysian tertiary hospital experience. J. Clin. Med. 2022 Jan 28;11(3):676
26. Kassam NM, Aziz OM, Somji S, Shayo G, Surani S. Endobronchial tuberculosis: A rare presentation. Cureus. 2020 May 8;12(5):e8033.
27. Peng S, Zhang G, Hong J, Ding H, Wang C, Luo J, Luo Z. Clinical and bronchoscopy features of tracheobronchial tuberculosis in children. Zhongguo Dang Dai Er Ke Za Zhi. 2023 Apr 15;25(4):381-387.
28. Dey A, Shah I. Infantile endobronchial tuberculosis. J. Family Med. Prim. Care. 2019 Jan;8(1):299-301.
29. Idrees F, Kamal S, Irfan M, Ahmed R. Endobronchial tuberculosis presented as multiple endobronchial vesicular lesions. Int. J. Mycobacteriol. 2015 Jun;4(2):154-7.
30. Rezaeetalab F, Farrokh D. Endobronchial tuberculosis in anthracotic bronchitis. Pneumologia. 2016 Jan-Mar;65(1):10-3.
31. Jioa A, Sun L, Liu F, Rao X, Ma Y, Liu X, Shen C, Xu B, Shen A, Shen K. Characteristics and clinical role of bronchoscopy in diagnosis of childhood endobronchial tuberculosis. World J. Pediatr. 2017 Dec;13(6):599-603

32. Nguyen-Ho L, Tran-Van N, Le-Thuong V. Central versus peripheral lesion on chest X-ray: A case series of 31 endobronchial tuberculosis patients with negative sputum smears. Int. J. Mycobacteriol. 2021 Jan-Mar;10(1):89-92.
33. Wahyuni TD, Alatas MF, Siahaan SS, Muljadi R, Carolline C. Bronchoscopic ballon dilatation for tuberculosis-related bronchial stenosis: A rare case. Respiratory Science. 2024;4(2):133-138.
34. Hanaoka J, Ohuchi M, Kuku R, Okamoto K, Ohshio Y. Bronchoscopic ballon dilatation combined with laser cauterization of high and long segmental tracheal stenosis secondary to endobronchial tuberculosis: A case report. Respir. Med. Case Rep. 2019 Jul 30;28:100917
35. Ichikawa Y, Kurokawa K, Furusho S, Nakatsumi Y, Yasui M, Katayama N. An effective case of bronchoscopic ballon dilatation for tuberculous bronchial stenosis. Respirol. Case Rep. 2023 Jul 18;11(8):e01191