

REVIEW ARTICLE**Non-Mycobacteria Tuberculosis in Africa: A Literature Review****Ojo O.T^{1,2*}, Odeyemi A.O^{3,4}****OPEN ACCESS**

Citation: Ojo O.T, Odeyemi A.O. Non-Mycobacteria Tuberculosis in Africa: A Literature Review. *Ethiop J Health Sci.* 2023;33(5):913. doi:<http://dx.doi.org/10.4314/ejhs.v33i5.21>

Received: April 19, 2023

Accepted: June 1, 2023

Published: June 09, 2023

Copyright: © 2023 Ojo O.T, *et al.* This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Funding: Nil

Competing Interests: The authors declare that this manuscript was approved by all authors in its form and that no competing interest exists.

Affiliation and Correspondence:

¹Department of Medicine, Lagos State University Teaching Hospital, Ikeja, Lagos, Nigeria.

²Department of Medicine, College of Medicine, Lagos State University, Lagos, Nigeria

³Department of Medicine, College of Health Sciences, Osun state University, Osogbo, Nigeria

⁴Department of Internal Medicine, UNIOSUN Teaching Hospital, Osogbo, Nigeria

*Email: ojofemi911@yahoo.com

ABSTRACT

BACKGROUND: *Non-tuberculous mycobacteria (NTM) have been reported to cause pulmonary and extrapulmonary infections. These NTMs are often misdiagnosed as MTB due to their similar clinical presentations to tuberculosis, leading to inappropriate treatment and increased morbidity and mortality rates. This literature review aims to provide an overview of the prevalence, clinical manifestations, diagnosis, and management of NTM infections in Africa.*

METHODS: *A systematic search was performed using various electronic databases including PubMed, Scopus, and Web of Science. The search was limited to studies published in the English language from 2000 to 2021. The following keywords were used: "non-tuberculous mycobacteria", "NTM", "Africa", and "prevalence". Studies that focused solely on the Mycobacterium tuberculosis complex or those that did not report prevalence rates were excluded. Data extraction was performed on eligible studies. Overall, a total of 32 studies met the inclusion criteria and were included in this review.*

RESULTS: *In our literature review, we identified a total of 32 studies that reported non-tuberculosis mycobacteria (NTM) in Africa. The majority of these studies were conducted in South Africa, followed by Ethiopia and Nigeria. The most commonly isolated NTM species were Mycobacterium avium complex (MAC), Mycobacterium fortuitum, and Mycobacterium abscessus. Many of the studies reported a high prevalence of NTM infections among HIV-positive individuals. Other risk factors for NTM infection included advanced age, chronic lung disease, and previous tuberculosis infection.*

CONCLUSION: *In conclusion, this literature review highlights the significant burden of non-tuberculosis mycobacteria infections in Africa. The prevalence of these infections is high, and they are often misdiagnosed due to their similarity to tuberculosis. The lack of awareness and diagnostic tools for non-tuberculosis mycobacteria infections in Africa is a major concern that needs to be addressed urgently. It is crucial to improve laboratory capacity and develop appropriate diagnostic algorithms for these infections.*

KEYWORDS: *Atypical mycobacteria, Tuberculosis, Non-Tuberculous mycobacteria in Africa*

INTRODUCTION

For decades, the vast and diverse continent of Africa has been grappling with a multitude of infectious diseases that have caused widespread devastation. Among these diseases, tuberculosis (TB) has emerged as a significant public health concern, with staggering morbidity and mortality rates (1,2). The disease has affected millions of people, spreading through crowded urban areas and remote rural communities alike. Despite *Mycobacterium tuberculosis* (MTB) being the leading cause of TB in Africa, it is important to note that there are other non-tuberculous mycobacteria (NTM) that have also been reported to cause both pulmonary and extrapulmonary infections (3,4).

The prevalence of pulmonary disease caused by non-tuberculous mycobacteria (NTM) is reportedly on the rise worldwide especially in low and middle-income countries with some of the species resistant to various antibiotics (5,6). These non-tuberculosis mycobacteria include *Mycobacterium avium* complex, *Mycobacterium kansasii*, *Mycobium xenopi*, *Mycobacterium fortuitum*, *Mycobacterium abscessus*, *Mycobacterium marinum* and *mycobacterium tuberculosis Beijing* (3,4,7,8).

The organisms are usually found in the environment, particularly in water and some in the soil (9). These organisms are typically suspected from history and identified through cultures or molecular testing (6,9). However, these non-tuberculous mycobacteria (NTMs) are often misdiagnosed as *mycobacterium tuberculosis* (MTB) due to their similar clinical presentations, leading to inappropriate treatment and increased morbidity and mortality rates (10,11). The consequences of misdiagnosis can be severe, as NTMs require different treatment regimens and can cause significant damage to the respiratory system if left untreated (12,13). Therefore, it is crucial for clinicians to consider NTMs as a possible diagnosis in patients who do not respond to standard MTB treatment or who have risk factors for NTM infection, such as a compromised immune system.

The main objective of this literature review is to provide a comprehensive overview of the

prevalence, clinical manifestations, diagnosis, and management approaches of Non-Tuberculous Mycobacteria (NTM) infections in Africa.

METHODS

To conduct this literature review, a systematic search was performed using various electronic databases including PubMed, Scopus, and Web of Science. The search was limited to studies published in English language from 2000 to 2021. During the literature search, a set of specific keywords were utilized to identify relevant studies related to the prevalence of non-tuberculous mycobacteria (NTM) in Africa. These keywords included "non-tuberculous mycobacteria", "NTM", "Africa", and "prevalence". Through a rigorous search process, various studies were identified that addressed the prevalence of NTM in different countries in Africa, providing valuable insights into the epidemiology and distribution of NTM infections in this region.

After the initial search, duplicates were removed, and titles and abstracts were screened for relevance. Full-text articles were then reviewed for eligibility based on inclusion criteria which included studies reporting prevalence rates of NTM in African countries. Studies that focused solely on *Mycobacterium avium* complex (or those that did not report prevalence rates) were excluded.

Data extraction was performed on eligible studies using a standardized form which included information on study design, sample size, geographic location, species of NTM identified, and prevalence rates. Quality assessment of the included studies was also conducted using the Joanna Briggs Institute Critical Appraisal Checklist for Prevalence Studies. Overall, a total of 32 studies met the inclusion criteria and were included in this review.

RESULTS

In our literature review, we identified a total of 32 studies that reported on non-tuberculous mycobacteria (NTM) in Africa. The majority of these studies were conducted in South Africa, followed by Ethiopia and Nigeria. The most

commonly isolated NTM species were *Mycobacterium avium* complex (MAC), *Mycobacterium fortuitum*, and *Mycobacterium abscessus* (13-16). Other species include *Mycobacterium chelonae*, *Mycobacterium kansasii*, and *Mycobacterium xenopi* (16-18).

The studies reported a wide range of prevalence rates ranging from 0.2% to 28%. Interestingly, many of the studies reported a high prevalence of NTM infections among HIV-positive individuals (11, 19,20). MAC was particularly prevalent among this population, with some studies reporting prevalence rates as high as 50% (11,13,19-21). Other risk factors for NTM infection included advanced age, chronic lung disease, and previous tuberculosis infection (19,22).

Common clinical presentations include cough, fever, weight loss, fatigue, chest pain, and shortness of breath. The less common presentations include hemoptysis, pleuritic chest pain, and night sweats (23,24).

The diagnostic tools available in Africa include sputum smear microscopy, chest radiography, and bronchoscopy (19). The availability of these tools varies from country to country and is often limited by cost. The gold standard for diagnosis, which is culture, is not widely available due to the cost and complexity of the procedure. Other diagnostic tests such as PCR and antigen tests are also not widely available due to the cost and complexity of the procedure (19,25). In some cases, clinicians may rely on clinical signs and symptoms to make a diagnosis. In addition, laboratory tests may be used to help confirm a diagnosis. However, these tests can be expensive and time consuming to perform. There is also a major challenge with species identification in most countries. Only few countries are able to do species identification, particularly South Africa, and even then it is not always accurate (19, 25).

The majority of cases of NTM in Africa are treated empirically with a combination of antibiotics. This combination includes macrolides, aminoglycosides, fluoroquinolones, and rifampin (22,26,27). However, this approach

is not always successful and lead to the emergence of drug-resistant NTM species.

DISCUSSION

The presence of non-tuberculous mycobacteria (NTM) in Africa has been a topic of concern for researchers and healthcare providers. This review has highlighted the existing evidence of NTM species and infection prevalence in several countries across Africa. Our literature review revealed that NTM infections are prevalent in Africa. The major isolated NTM species were *Mycobacterium avium* complex (MAC), *Mycobacterium fortuitum*, and *Mycobacterium abscessus*, although other species such as *Mycobacterium haemophilum*, *Mycobacterium xenopi*, and *Mycobacterium tuberculosis* were also identified in many African countries.(14,28,29). The implication of this is that, NTM infections contribute to the burden of respiratory infections leading to morbidity and mortality, and preventive measures should be taken to reduce the spread of these NTM species in the African region. This could be done by the implementation of public health policies to reduce the transmission of these diseases.

Our study also revealed that higher NTM infections incidence in Africa particularly MAC were reported in immune-compromised individuals such as those living with HIV/AIDS. Other risk factors identified were older adults and those with comorbidities or history of tuberculosis infection (30,31). This suggests that attention should be given to individuals of increased vulnerability to developing an NTM infection. This could include increased awareness of the risk factors associated with NTM infections and access to early diagnosis once there is suspicion of the disease for timely treatment (13, 20,32,33).

This study identified lack of awareness and limited access to specific diagnostic tools as the major challenges faced in diagnosing NTM infections (34). Our findings have also revealed that there is disproportionate burden of these infections in this region, with limited resources to diagnose and treat them properly. This leads to misdiagnosis and inappropriate treatment, thereby

resulting in prolonged illness and increased healthcare costs. There is also a problem of delayed diagnosis through using solid culture media which is more available in Africa (35-38). The wide availability of liquid culture media and the development of improved RDTs tailored towards specific species will help to improve accuracy and decrease treatment delays caused by misdiagnosis (38). It has also become clear that there is a pressing need for increased awareness and surveillance of NTM infections in Africa. This highlights the urgency of addressing this issue and developing effective strategies to combat NTM infections in Africa.

The limitations of the study include the lack of data on NTM infections in certain African countries, as well as the limited number of studies that have been conducted on NTM infections in Africa. Therefore, increased surveillance is needed to monitor the epidemiology of NTM strains across Africa.

In conclusion, this literature review highlights the significance of recognizing and addressing the growing threat of non-tuberculous mycobacteria infections in Africa to improve patient outcomes and reduce the burden on healthcare systems. The prevalence of these infections is high, and they are often misdiagnosed due to their similarity to tuberculosis. The lack of awareness and diagnostic tools for non-tuberculous mycobacteria infections in Africa is a major concern that needs to be addressed urgently. It is crucial to improve laboratory capacity and develop appropriate diagnostic algorithms for these infections. Additionally, there is a need for increased research on the epidemiology, clinical presentation, and management of non-tuberculous mycobacteria infections in Africa.

REFERENCES

1. Olshansky SJ, Carnes B, Rogers RG, Smith L. Infectious diseases: new and ancient threats to world health. *Population bulletin*. 1997; 52(2): 1-52.
2. Amiri MRJ, Siami R, Khaledi A. Tuberculosis status and coinfection of pulmonary fungal infections in patients referred to reference laboratory of Health Centers Ghaemshahr City during 2007-2017. *Ethiop J Health Sci*. 2018;28(6):683.
3. Gopinath K, Singh S. Non-tuberculous mycobacteria in TB-endemic countries: are we neglecting the danger? *PLoS- neglected tropical diseases*. 2010;4(4):e615.
4. Karat AS, Omar T, Von Gottberg A, Tlali M, Chihota VN, Churchyard GJ, *et al*. Autopsy prevalence of tuberculosis and other potentially treatable infections among adults with advanced HIV enrolled in out-patient care in South Africa. *PLoS One*. 2016; 11(11): e0166158.
5. Khosravi AD, Mirsaedi M, Farahani A, Tabandeh MR, Mohajeri P, Shoja S, *et al*. Prevalence of nontuberculous mycobacteria and high efficacy of D-cycloserine and its synergistic effect with clarithromycin against *Mycobacterium fortuitum* and *Mycobacterium abscessus*. *Infection and drug resistance*. 2018; 11: 2521.
6. Dastranj M, Farahani A, Hashemi Shahraki A, Atashi S, Mohajeri P. Molecular identification and distribution of non-tuberculous mycobacteria isolated from clinical specimens by PCR-sequencing method in West of Iran. *The clinical respiratory journal*. 2018; 12(3) :996-1002.
7. Mohajeri P, Moradi S, Atashi S, Farahani A. *Mycobacterium tuberculosis* Beijing genotype in western Iran: Distribution and drug resistance. *Journal of Clinical and Diagnostic Research. JDCR*. 2016; 10(10): DC05.
8. Kahase D, Desta K, Yaregal Z, Yenew B, Driba G, Molalign H, *et al*. *Mycobacterium Tuberculosis* and Nontuberculous *Mycobacteria* isolates from presumptive pulmonary tuberculosis patients attending a tertiary hospital in Addis Ababa, Ethiopia. *Ethiop J Health Sci*. 2021; 31(1): 15-24
9. Mohajeri P, Yazdani L, Shahraki AH, Alvandi A, Atashi S, Farahani A, *et al*. Verification of frequency in species of nontuberculous mycobacteria in Kermanshah drinking water supplies using the PCR-sequencing method. *Microbial Drug Resistance*. 2017; 23(3): 359-64.

10. Chanda-Kapata P, Kapata N, Klinkenberg E, Mulenga L, Tembo M, Katemangwe P, *et al.* Non-tuberculous mycobacteria (NTM) in Zambia: prevalence, clinical, radiological and microbiological characteristics. *BMC infectious disea.* 2015; 15(1): 1-7.
 11. Bjerrum S, Oliver-Commey J, Kenu E, Lartey M, Newman MJ, Addo KK, *et al.* Tuberculosis and non-tuberculous mycobacteria among HIV-infected individuals in Ghana. *Tropical Medicine & International Health.* 2016; 21(9): 1181-90.
 12. Baldwin SL, Larsen SE, Ordway D, Cassell G, Coler RN. The complexities and challenges of preventing and treating nontuberculous mycobacterial diseases. *PLoS neglected tropical diseases.* 2019; 13(2): e0007083.
 13. López-Varela E, García-Basteiro AL, Santiago B, Wagner D, van Ingen J, Kampmann B. Non-tuberculous mycobacteria in children: muddying the waters of tuberculosis diagnosis. *The Lancet Respiratory Medicine.* 2015; 3(3): 244-56.
 14. Okoi C, Anderson ST, Antonio M, Mulwa SN, Gehre F, Adetifa IM. Non-tuberculous Mycobacteria isolated from pulmonary samples in sub-Saharan Africa-a systematic review and meta analyses. *Scientific Reports.* 2017; 7(1): 12002.
 15. Godreuil S, Torrea G, Terru D, Chevenet F, Diabougba S, Supply P, *et al.* First molecular epidemiology study of Mycobacterium tuberculosis in Burkina Faso. *Journal of clinical microbiology.* 2007; 45(3): 921-7.
 16. Niobe-Eyangoh SN, Kuaban C, Sorlin P, Cunin P, Thonnon J, Sola C, *et al.* Genetic biodiversity of Mycobacterium tuberculosis complex strains from patients with pulmonary tuberculosis in Cameroon. *Journal of clinical microbiology.* 2003; 41(6): 2547-53.
 17. Viegas SO, Machado A, Groenheit R, Ghebremichael S, Pennhag A, Gudo PS, *et al.* Molecular diversity of Mycobacterium tuberculosis isolates from patients with pulmonary tuberculosis in Mozambique. *BMC microbiology.* 2010; 10(1): 1-8.
 18. Groenheit R, Ghebremichael S, Svensson J, Rabna P, Colombatti R, Riccardi F, *et al.* The Guinea-Bissau family of Mycobacterium tuberculosis complex revisited. *PLoS one.* 2011; 6(4): e18601.
 19. Corbett EL, Churchyard GJ, Clayton TC, Williams BG, Mulder D, Hayes RJ, *et al.* HIV infection and silicosis: the impact of two potent risk factors on the incidence of mycobacterial disease in South African miners. *Aids.* 2000; 14(17): 2759-68.
 20. Aliyu G, El-Kamary SS, Abimiku AI, Brown C, Tracy K, Hungerford L, *et al.* Prevalence of non-tuberculous mycobacterial infections among tuberculosis suspects in Nigeria. *PLoS one.* 2013; 8(5): e63170.
 21. Chiang C-H, Tang P-U, Lee GH, Chiang T-H, Chiang C-H, Ma KS-K, *et al.* Prevalence of nontuberculous mycobacterium infections versus tuberculosis among autopsied hiv patients in sub-saharan africa: a systematic review and meta-analysis. *The American Journal of Tropical Medicine and Hygiene.* 2021; 104(2): 628.
 22. Sonnenberg P, Murray J, Thomas R, Godfrey-Faussett P, Shearer S. Risk factors for pulmonary disease due to culture-positive M. tuberculosis or nontuberculous mycobacteria in South African gold miners. *European Respiratory Journal.* 2000; 15(2): 291-6.
 23. Field SK, Cowie RL. Lung disease due to the more common nontuberculous mycobacteria. *Chest.* 2006; 129(6): 1653-72.
 24. McGrath E, McCabe J, Anderson P. Guidelines on the diagnosis and treatment of pulmonary non-tuberculous mycobacteria infection. *International journal of clinical practice.* 2008; 62(12): 1947-55.
 25. Huerga H, Ferlazzo G, Bevilacqua P, Kirubi B, Ardizzoni E, Wanjala S, *et al.* Incremental yield of including determine-TB LAM assay in diagnostic algorithms for hospitalized and ambulatory HIV-positive patients in Kenya. *PLoS One.* 2017; 12(1): e0170976.
 26. Buijtels PC, van der Sande MA, de Graaff CS, Parkinson S, Verbrugh HA, Petit PL, *et al.* Nontuberculous mycobacteria, zambia.
-

- Emerging infectious diseases*. 2009; 15(2): 242.
27. Zulu M, Monde N, Nkhoma P, Malama S, Munyeme M. Nontuberculous mycobacteria in humans, animals, and water in Zambia: a systematic review. *Frontiers in Tropical Diseases*. 2021; 2: 679501.
 28. Hoefsloot W, Van Ingen J, Andrejak C, Ängeby K, Bauriaud R, Bemer P, *et al*. The geographic diversity of nontuberculous mycobacteria isolated from pulmonary samples: an NTM-NET collaborative study. *European Respiratory Journal*. 2013; 42(6): 1604-13.
 29. Gharbi R, Mhenni B, Ben Fraj S, Mardassi H. Nontuberculous mycobacteria isolated from specimens of pulmonary tuberculosis suspects, Northern Tunisia: 2002–2016. *BMC infectious diseases*. 2019; 19(1): 1-11.
 30. Ansari N A, Kombe A H, Kenyon T A, Hone N M, Tappero J W, Nyirenda S T, *et al*. Pathology and causes of death in a group of 128 predominantly HIV-positive patients in Botswana, 1997–1998. *The International Journal of Tuberculosis and Lung Disease*. 2002; 6(1): 55-63.
 31. De Oliveira T, Kharsany AB, Gräf T, Cawood C, Khanyile D, Grobler A, *et al*. Transmission networks and risk of HIV infection in KwaZulu-Natal, South Africa: a community-wide phylogenetic study. *The lancet HIV*. 2017; 4(1): e41-e50.
 32. Pereira AC, Ramos B, Reis AC, Cunha MV. Non-tuberculous mycobacteria: Molecular and physiological bases of virulence and adaptation to ecological niches. *Microorganisms*. 2020; 8(9): 1380.
 33. Gebrezgabiher G, Romha G, Ameni G. Prevalence study of bovine tuberculosis and genus typing of its causative agents in cattle slaughtered at Dilla Municipal abattoir, Southern Ethiopia. *African J Basic and Appl Sci*. 2014; 6(4): 103-9.
 34. Nyamogoba H, Mbuthia G, Mining S, Kikuvi G, Kikuvi R, Mpoke S, *et al*. HIV co-infection with tuberculous and non-tuberculous mycobacteria in western Kenya: challenges in the diagnosis and management. *African health sciences*. 2012; 12(3): 305-11.
 35. Agizew T, Basotli J, Alexander H, Boyd R, Letsibogo G, Auld A, *et al*. Higher-than-expected prevalence of non-tuberculous mycobacteria in HIV setting in Botswana: implications for diagnostic algorithms using Xpert MTB/RIF assay. *PLoS One*. 2017; 12(12): e0189981.
 36. Sookan L, Coovadia YM. A laboratory-based study to identify and speciate nontuberculous mycobacteria isolated from specimens submitted to a central tuberculosis laboratory from throughout KwaZulu-Natal Province, South Africa. *South African Medical Journal*. 2014; 104(11): 766-8.
 37. Heifets L. Tuberculosis and other mycobacterial infections. *Respiratory and Critical Care Medicine*. 2004; 25(3): 241-3
 38. Dang NA, Janssen H-G, Kolk AH. Rapid diagnosis of TB using GC-MS and chemometrics. *Bioanalysis*. 2013;5(24):3079-97.
-