

Prevalence and Distribution of Non – Tuberculous Mycobacteria (NTM) Among MDR-TB Suspected Patients in Northern Malawi

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Abstract

Background

Non-tuberculosis *Mycobacteria* (NTM) are increasingly being recognized as human pathogens, causing substantial morbidity and mortality in progressive lung disease, immunosuppressed, the elderly and the youth. Similarity of clinical symptoms with MTB, coupled with limited diagnostic capacities in tuberculosis (TB) endemic developing countries has led to misdiagnosis of NTM pulmonary disease. The study aimed at establishing the prevalence and distribution of NTM among Multi-Drug Resistance Tuberculosis (MDR-TB) suspected patients in Northern Region of Malawi based on laboratory culture records from 2015 to 2018 conducted at Mzuzu Central Hospital.

Methods

The study used a retrospective cross-sectional design. All culture positive underwent MTB confirmatory test using the SD-Bio line TB Ag MPT64 Kit to confirm MTB or to suspect for NTM. Data was analysed for descriptive statistics in SPSS version 20 and presented using frequency tables, charts and graphs.

Results

Out of 170 culture positive reports reviewed, 30 (18%) were NTM. Much as there were generally more males (69.4%) who were MDR-TB suspected patients, the proportion of NTM patients was female predominant 13/52 (25%) as compared to 17/118 (14%) for males while the age range of 30-49 was the most (22%) affected. Twenty-nine (97%) of the NTM cases were previously treated for MTB.

Conclusions

The high prevalence of NTM among MDR-TB suspected patients shows that the disease is a serious public health problem. This therefore calls for urgent attention from Ministry of Health and partners, health workers and all stakeholders involved in policy making so that NTM diagnosis should have a clear algorithm to avoid wastage of resources as well as for good patient care.

Background

Non-tuberculous *Mycobacteria* (NTM) are environmental mycobacterium species other than *Mycobacterium tuberculosis* complex (MOTT), *Mycobacterium leprae* and *Mycobacterium Ulcerans* [1]. These rarely cause disease in healthy adult humans but their increase in prevalence likely due to HIV/AIDS and other immune-suppression conditions is a great concern for clinicians as well as microbiologists. NTM were discovered in 1950s, they cause morbidity and mortality in progressive lung disease, immunosuppressed, the elderly and the young [2]. The clinical and molecular epidemiology of NTM in low- and middle-income countries, which are also endemic for pulmonary tuberculosis, is less known. This is mainly because pulmonary tuberculosis and other disease manifestations pose a diagnostic challenge for NTM [3].

Globally, published reports on speciation and geographical distribution of NTM isolated from pulmonary samples are limited and more so in Africa. However, unlike in developed countries where the prevalence and distribution of pulmonary and extra pulmonary NTM disease is considerably well documented [4], very little data is available on the prevalence and distribution of NTM and its clinical importance in resource-limited settings [5].

In a study conducted by Shao, et al., (2015) [6] in China the prevalence of NTM was 3.37% among 1779 smear positive clinical isolates. However, reports from some sub-Saharan settings have been indicating that the prevalence of NTM among mycobacteria culture positive ranges from 4 to 9% [1]. Furthermore, a prospective study conducted in Nigeria reported that the prevalence of NTM among tuberculosis suspects was 15.5% [7].

In most cases NTM is resistant to Mycobacterial tuberculosis drugs, this makes it to be misdiagnosed as multidrug - resistant M. tuberculosis (MDR-TB) and Extreme drug resistant (XDR) TB [8]. In most poor resource settings Malawi inclusive, sputum smear examination for acid-fast bacilli (AFB), is still the main diagnostic tool for pulmonary tuberculosis (PTB) diagnosis [3] and like MTB, NTM stain acid-fast, making the two indistinguishable by this method hence posing a critical clinical challenge on diagnosis for proper TB case management.

In Malawi there is little to no clinical data on the prevalence of NTM among MDR-TB suspected patients. However, the prevalence of MTBC in Malawi is among the highest in sub-Saharan countries. This clearly pose a clear question which needed to be investigated and establish as to what could be the extent of prevalence of NTM among MDR-TB suspected patients in Malawi especially in this era of high HIV/AIDS prevalence. Therefore, this study was conducted to determine the prevalence and distribution of non-tuberculous Mycobacteria among MDR-TB suspected patients in Northern Region of Malawi.

Methodology

Study Design and Period

This was a laboratory based cross-sectional retrospective study. The design was being considered because TB culture samples are not in huge numbers as such accumulation of the samples for some years was considered good approach. This involved collating patients' records for 4 years from 2015-2018.

Study Settings

This study was conducted at Mzuzu Central Hospital (MZCH) TB culture Laboratory in Mzuzu City, Mzimba District in Northern Region of Malawi. MZCH TB laboratory is a government (public) institution under the Ministry of Health. It is mandated to act as a regional reference laboratory for diagnosis of TB through the provision of microscopy, mycobacterium culture and drug sensitivity testing (DST) services for patient care and management. This laboratory was selected because it offers specialized TB testing

with modern sensitive and specific techniques such as the BACTEC™ MGIT™ (Mycobacteria Growth Indicator Tube), gene Xpert. Positive cultures are confirmed as MTBC using the SD-Bioline TB Ag MPT64 Kit and when the SD-Bioline is Negative, NTM is confirmed using Ziehl Neelsen microscopy.

Study Population

The study population involved all TB patient's samples which had MGIT positive culture results reports kept in the laboratory at Mzuzu Central Hospital (MZCH) from January 2015 to December 2018. As per local National Tuberculosis Programme diagnostic guidelines, only samples suspected to be MDR-TB are cultured whilst the rest of the samples are tested using microscopy or GeneXpert [9].

Sampling Method

We used census study approach where all reports were considered.

Inclusion Criteria

All patient reports on culture samples kept in the laboratory which were positive on MGIT™ 960 machine from January 2015 and December 2018

Exclusion Criteria

All patient records with incomplete information.

Data Collection Tool

A data collection checklist was used which contained the following variables; date and patient code, age and sex. The checklist also captured laboratory results on cultures on the MGIT 960 and AFB by ZN and TB immune-chromatographic assay (SD-Bioline Ag MPT64 Rapid TM assay).

Data Analysis

The data collected from records were manually checked for missing, irrelevant and inaccurate information. The data was analyzed using Statistical Product and Service Solution (SPSS) version 20 where it was cleaned and checked for completeness to determine prevalence of NTM. Distribution of NTM by gender, age and clinical history. Data was presented in form of tables, graphs, pie chart and bar chart.

Ethical Consideration

The patient's data was treated with respect where by only ID numbers were used and not actual names. Data was secured by the use of password on the personal computer so that no other person apart from the researcher could access it. All the patient's information during data collection process were kept confidential by the researcher under lock and key. Permission to conduct this study was issued by the

Mzuzu University Ethical Committee through the Biomedical Sciences department under the faculty of Health Sciences and Research Committee of Mzuzu Central Hospital.

Results

One hundred and seventy-eight (178) reports were found but the analysis was conducted on 170 reports because the other eight were incomplete representing 95.5%.

Table 1: Demographic Characteristics of patients (N=170)

Characteristics		Frequency	Percentage
Gender	Male	118	69.4%
	Female	52	30.6%
Age (Years)	0-29	32	18.8%
	30-49	96	56.5%
	50-79	33	19.4%
	80+	9	5.3%

There were more males who were suspected of having MDR-TB as compared to females and the most active population group (30-49 years) was the most affected (56.5%)

Prevalence of NTM among MDR-TB suspected patients (N=170)

The Figure 1 above shows that the prevalence of NTM among MDR-TB suspected patients (N=170) was 18% and MTBC was 82%.

The figure 2 above shows the point prevalence of NTM from the year 2015 to 2018. More NTM were isolated in 2017 where of the 47 isolates in 2017 13 (28%) were NTM.

Table 2: Distribution of NTM according to Demographic Characteristics (gender and age) of patients

Characteristics	Frequency	Percentage (95% CI)
Gender		
Male	17/118	14% (8.6-22.1)
Female	13/52	25%(14.0-38.9)
Age		
10-29	3/32	9% (2.0-25.0)
30-49	21/96	22% (14-31.5)
50-79	6/33	18% (7.0-35.1)
80+	0/9	0% (0.0-33.6)

Table 2 above shows that, out of 30 NTM cases 13 were females representing 25% while 21 of the NTM being within the age (30-49) years representing 22% among this age range.

Figure 2: Distribution of NTM according to treatment category (presumptive or retreatment cases) (N=30)

Figure 2 above shows that out of 30 cases of NTM 29 were those of first line treatment failure and scheduled for retreatment representing 97%.

Discussion

Non-tuberculous mycobacteria (NTM) have been shown to be significant contributors to TB like disease in pulmonary cases [10, 11]. This study presents a first attempt to quantify NTM prevalence in assumed MTBC cases in Malawi.

This study found that the prevalence of NTM among MDR TB suspected patients was 18%. This prevalence is relatively higher compared to reports from other studies in India, Zambia and Nigeria which were 15%, 15.1% and 7.5% respectively. However, the findings of our study are much lower compared to those conducted in other parts of Nigeria and Zambia which were 30% and 56% respectively [7, 10]. It is more likely that geographical interference could be part of the aspect that brings about dynamics that same countries may produce different results in terms of prevalence of NTM.

In a study of patients with pulmonary NTM in the USA, Adjemian, et al, (2012) [14] found a higher prevalence of pulmonary NTM in the Asian and pacific Islander population with a male predominance. In contrast with the white population where the prevalence is lower and female patients form the predominant group. This predominance of male patients affected with NTM disease was also seen in study conducted in Singapore [13]. This is in contrast with this study which shows a higher proportion in females than males even though the total MDR TB suspected patients in our study shows higher proportion of males. Other studies conducted in Zambia and Botswana have shown an increase in

females than males. According to them they suggested that the number could have been small in males because men delay in seeking care or are unwilling to seek care [1, 10]. The findings vary geographically due to different predisposing factors such as immune status, occupation and life style and possibly climatic conditions.

Out of the 30 NTM cases isolated 1 (3%) was presumptive case while 29 (97%) were retreatment cases. These results are in contrast with a study conducted in Kenya which found that 4(%) of the NTM disease were previously treated for TB while 11(%) were presumptive cases [15]. In a study conducted in Iran also found a large percentage of presumptive cases where 15.1% NTM. Six were misdiagnosed as MDR-TB and the rest were TB suspects [16]. This shows that those patients seeking TB care for the first time are also mismanaged as MTB. Furthermore, in this study the high rate of NTM in patients with suspected MDR-TB due to TB treatment failure has important implications for healthcare economics, epidemiology and antimicrobial stewardship especially the care and quality of life of the individual patient. The high costs to the patient and society should lead health care providers to consider NTM in all patients suspected of having TB. [17]. The World Health Organization (WHO) recommends National Tuberculosis Control Programs to obtain sputum culture only in new patients if the smear is positive in the end of month 3 of treatment [18]. However, this is not followed in many resource-limited countries [19]. Identifying NTM frequency and alerting physicians to this problem may increase awareness, help better understanding of the epidemiology, putting patients on appropriate therapy sooner, and decrease the stigma and cost of care more especially in the resources limited settings.

Conclusion

This study found relatively higher prevalence of NTM in MDR TB suspected patients at regional referral hospital in Malawi. Even though there were generally more males among MDR-TB suspected patients, NTM cases were more among female and those in the ages group of 30- 49 years. It also found that NTM is more prevalent in retreatment cases than presumptive cases. To our best knowledge, this is the first report on prevalence of NTM in Northern Region of Malawi and probably the whole country. Therefore, this study has demonstrated that there is need to establish a deliberate policy that can be used to diagnose NTM and rule them out possibly before TB treatment begins so as to identify the NTM faster and timely. Likely, NTM is also one of the neglected diseases of poverty as it is not reported in our routine clinical and laboratory diagnostic systems. The high prevalence of NTM among symptomatic participants found in this study demonstrates that NTM is a public health problem.

Limitations of the Study

The results from this study cannot be generalized for the whole country because the study was conducted in one region of the country. Furthermore, the laboratory procedures lacked the required resources such as genotyping (molecular procedures) to categorize NTM into different species. Scarcity of literature in Malawi made the comparison of results difficult nationally.

Abbreviations

AFB	Acid fast bacilli
ATS	American Thoracic Society
LAM	Lipoarabinomannin
MAC	Mycobacterium Avium complex
MDR-TB	Multi-Drug-Resistant Tuberculosis
HIV	Human Immunodeficiency Virus
PLHIV	People living with HIV
IQR	Interquartile range
MGIT	Mycobacterium Growth Indicator Tube
MOTT	Mycobacterium Other Than Tuberculosis
MTB	Mycobacterium Tuberculosis
MTBC	Mycobacterium Tuberculous Complex
MPT64	Mycobacterium tuberculosis protein 64
NTM	Non-Tuberculous Mycobacterium
NTRL	National Tuberculosis Reference Laboratory
TB	Tuberculosis
LPA	Line Probe Assay
USA	United States of America
MZCH	Mzuzu Central Hospital
ZN	Ziehl Neelsen

Declarations

Ethics approval and consent to participate

Ethical approval for the study was obtained from Mzuzu University Research Ethics Committee. No consent was obtained from participants since this was a retrospective study

Consent for publication

None

Availability of data and materials

All data related to this study can be accessed at Mzuzu Central Hospital through the hospital authorities and the corresponding author.

Competing interests

None

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Authors' contributions

Study conception: MC, MN, GCM, ; study design: MC, GCM, MN, ; data collection: MC, GCM MN,; data analysis: MC, AK, PSK, GCM, BMC, ; manuscript preparation: MC, GCM, MN, PSK, TM, BMC, AK. All the authors contributed adequately towards the completion of this study. Their career background played important roles. All authors read and approved the manuscript.

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Figures

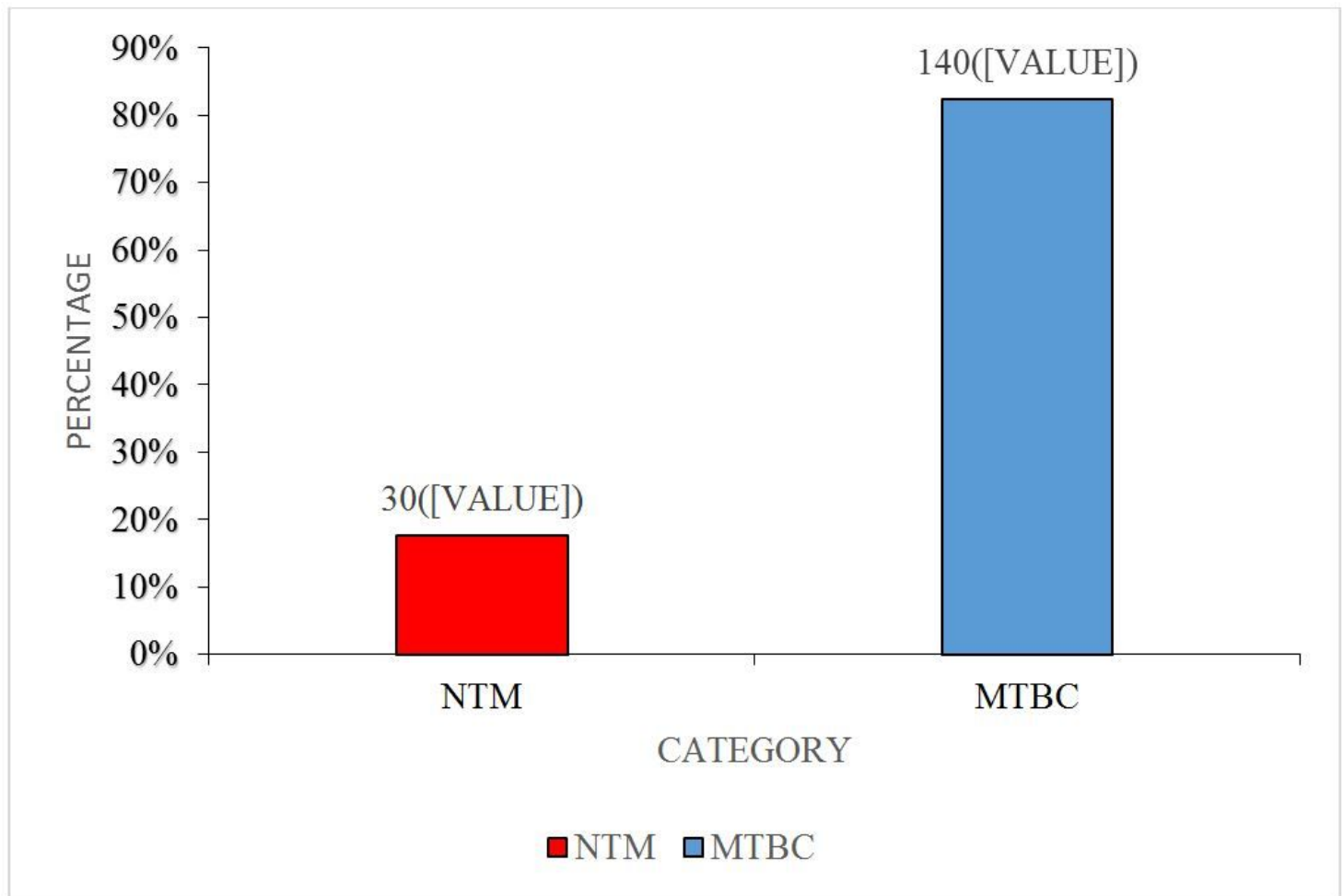


Figure 1

Period Prevalence of NTM

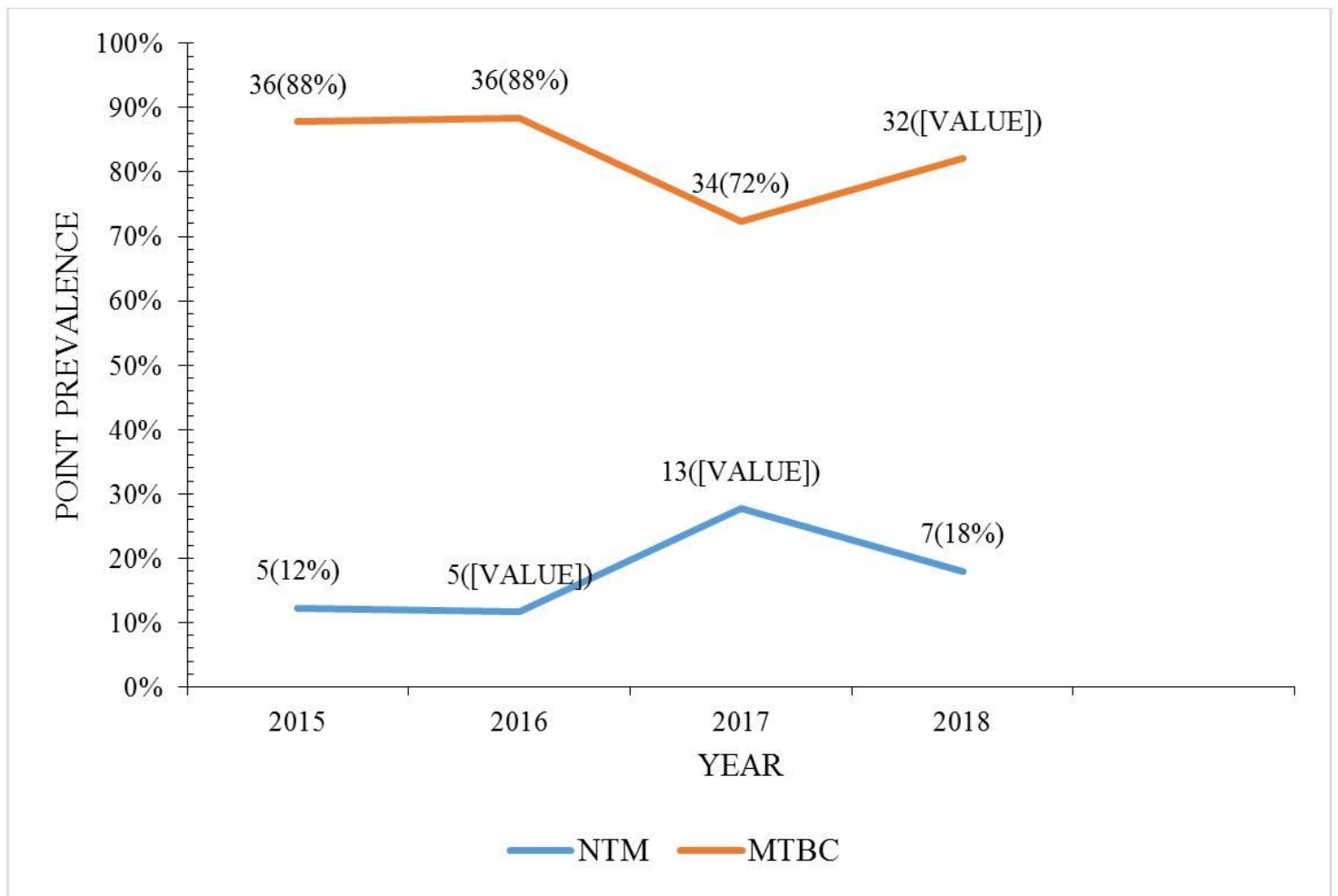


Figure 2

Point prevalence.

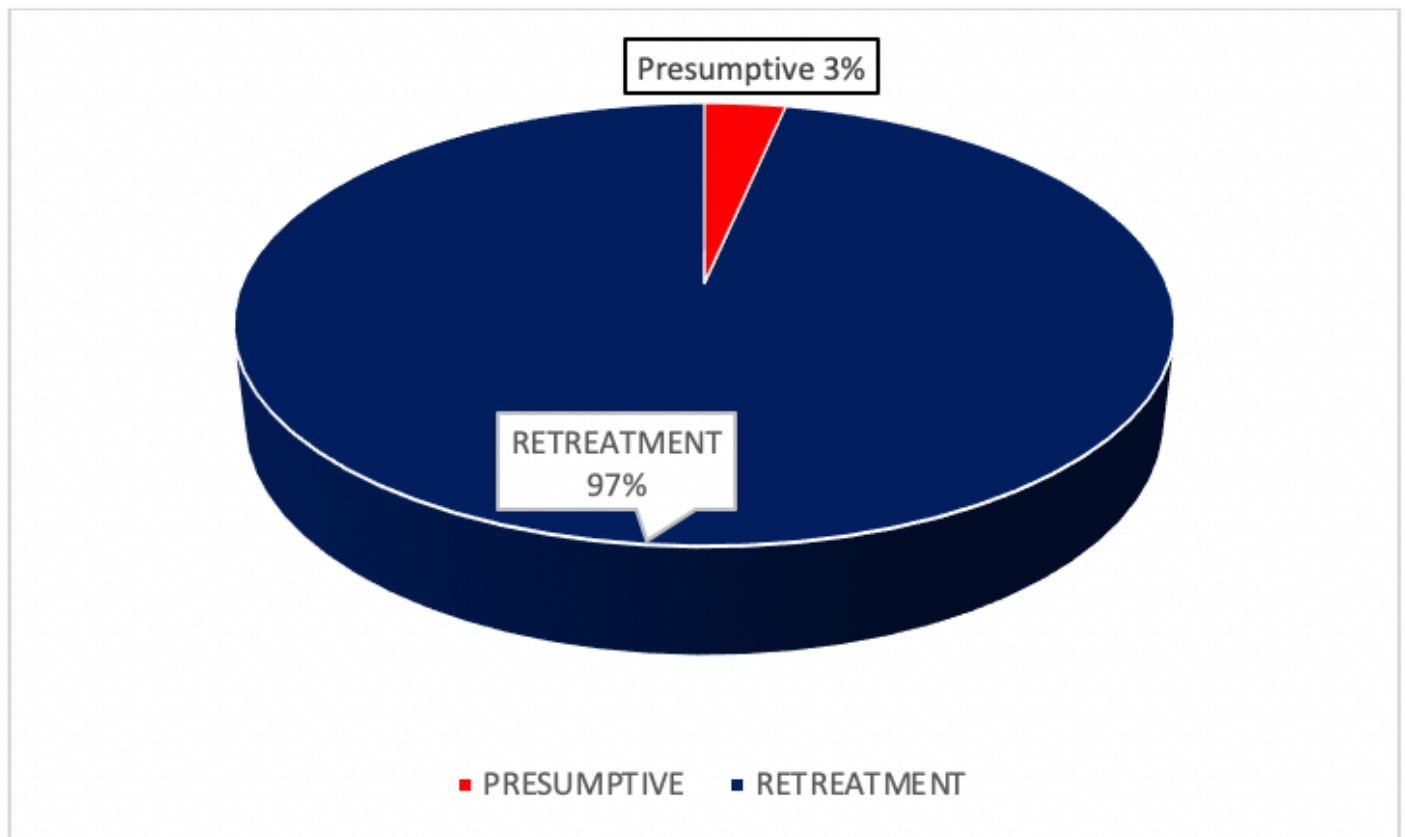


Figure 3

Figure 2: Distribution of NTM according to treatment category (presumptive or retreatment cases) (N=30)