ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

DEPARTMENT OF DERMATOVENEREOLOGY

CLINICAL OUTCOME MORPHOLOGIC INDEX AND ASSOCIATED FACTORS IN MULTIBACILLARY LEPROSY PATIENTS AT COMPLETION OF MULTIDRUG THERAPY AT ALERT HOSPITAL, ADDIS ABABA, ETHIOPIA

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Clinical outcome, morphologic index and associated factors in multibacillary leprosy patients at completion of multidrug therapy at ALERT Hospital, Addis Ababa, Ethiopia

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Acronyms/Abbreviations

ALERT	All African Leprosy Rehabilitation Training
BI	Bacteriological Index
MB	Multibacillary
MDT	Multi-Drug Therapy
PB	Paucibacillary
PD	Physical Disability
SPSS	Statistical Package for Social Science
SSS	Slit Skin Smear

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Abstract

Background: Although Ethiopia has substantially reduced its leprosy burden, new cases persist, and management challenges, such as poor patient adherence, limited education, and inadequate healthcare training, continue to impact treatment outcomes. However, clinical outcomes and morphologic indices in multibacillary leprosy patients upon multidrug therapy completion remain undocumented in the Ethiopian context.

Objective: To assess clinical outcome morphological indices and associated factors in multibacillary leprosy patients at completion of multidrug therapy (MDT) at ALERT Hospital, in Addis Ababa, Ethiopia

Methods: The study was a facility based cross-sectional study conducted in ALERT Hospital. All patients diagnosed with multibacillary leprosy and given the advised MDT in ALERT Hospital between November 1, 2020, and November 30, 2025, were followed up. The data were analyzed and inputted in SPSS version 26. The demographic and clinical characteristics were summarized by descriptive analysis. BI/MI change was tested using Wilcoxon signed-rank, bivariate (p[?]0.25) and multivariate logistic regression determined the outcome poor predictors. The outcome of the development of new and progressive lesions, active lesions or a continuance of active lesions, the BI persistence and a severe reaction after 12 months of MDT are considered poor outcome. The p-value of less than 0.05 was counted as significant. Results were presented using texts, tables and figures.

Results: In total, 107 MB leprosy patients were included. The median (IQR) age was 30 (25–36) years. Young adults (25–44 years: 67.2%) and males (65.4%, n=70) predominated. One third 33.6% had poor clinical outcomes and three-fourths, 83.2%, had persistent MI at the end of MDT. BI ($z = -7.85$, $p < 0.001$) and MI ($z = 7.01$, $p < 0.001$) were significantly reduced at end of MDT. End MDT- MI (1–10%) in 86.0%. High BI at diagnosis [AOR=11.7 (95% CI 1.44- 93.66)] and High MI at diagnosis [AOR = 5.13(95% CI: 1.94-13.57), p=0.001] were independently associated with poor clinical outcome. High BI at diagnosis was associated persistent MI at end of MDT [AOR=12 (95% CI: 3.53–42.28), p=0.001].

Conclusions: One third of the patients had poor clinical outcome, and more than three-fourths had persistent MI at the end of Fixed 12-month MDT. We found discordance between achieved dermatological cure and suboptimal bacteriological clearance in the high-BI Ethiopian cohort. Post-MDT smear monitoring is recommended for lepromatous cases.

Keywords: Multibacillary leprosy, MDT, bacteriologic index, morphological index, ALERT Hospital

1. Introduction

1.1 Background

Leprosy or Hansen disease is a chronic infectious disease that is usually caused by the acid-fast bacillus Mycobacterium leprae and in a few cases by the Mycobacterium lepromatosis (1). This is a disease of antiquity and is associated with several parts of the body such as the skin, peripheral nerves, as well as the mucosal lining of the upper respiratory tract and the eyes (2-4).

The primary modes of transmission of leprosy are through respiratory droplets which are released through the nose and mouth of untreated persons when there is a prolonged close contact, coughs, and sneezes are the major methods of transmission. Nevertheless, leprosy is not thought to be very contagious; it needs close and prolonged contacts to be transferred not by an incidental contact (1,5,6).

Diagnosis of leprosy is mainly clinical but some cases might require laboratory-based services. The diagnosis of leprosy is based on the presence of either or all of the following cardinal signs: (1) Definite loss of sensation in a pale (hypopigmented) or reddish area of the skin, (2) Thickened or enlarged peripheral nerve, and (3) microscopic identification of bacilli in a slit-skin smear (5,7).

According to the above-mentioned criteria, there are two types of leprosy cases that can be treated, such as Paucibacillary (PB) and Multibacillary (MB). The former is known to have one to five skin lesions, and the absence of bacilli in a skin smear, whereas the latter is known to have an over five skin lesions, nerve involvement (pure neuritis), or the presence of bacilli in a slit-skin smear with or without the skin lesions (5,7).

Treatment of leprosy should include a combination of three drugs, namely, dapsone, rifampicin, and clofazimine. Such a treatment program is referred to as multi-drug therapy (MDT). The treatment period of chemotherapy is normally six months in the case of PB and twelve months in the case of MB. MDT is good at destroying the bacteria that cause leprosy and it leads to the healing of the patient (8).

The Morphological Index (MI) is defined as the percentage of solid-staining acid-fast bacilli observed in skin smears, indicating the proportion of viable M. leprae capable of replication. This index is calculated by examining a standardized number of bacilli from multiple sites, with a higher MI suggesting a greater presence of potentially viable organisms. The MI

serves as a sensitive marker for assessing treatment response and has been suggested as an early indicator of drug resistance, particularly when clinical symptoms persist post-therapy (9,10). High Bacteriological Index (BI) and persistent MI positivity post-MDT may indicate potential treatment failure and the need for further investigation into resistance patterns (11,12).

Despite the availability of effective MDT, which has been shown to significantly reduce the burden of MB leprosy, this chronic infectious disease continues to present complex clinical and microbiological challenges. This thesis aims to investigate the clinical outcomes in MB leprosy patients upon completion of MDT at ALERT Hospital in Addis Ababa, Ethiopia.

1.2 Statement of the problem

Although this disease has been eradicated in most areas of the globe, the problem of leprosy continues to be a major healthcare issue, especially in endemic developing nations (13,14). It is still present in more than 120 countries and its geographical distribution is very wide and uneven (14), not to mention that than 200,000 fresh cases are reported each year (15). Although significant progress has been made in curbing the occurrence of leprosy, the WHO reports show that Ethiopia is among the twenty three nations which record between 1,000 and 10,000 new cases annually (16,17).

Naturally, neglected infectious diseases such as leprosy are one of the foremost causes of peripheral neuropathy, disability and irreversible deformities in the world, commonly leading to social stigma and marginalization in case of non-treatment (2,18-20).

Management of MB leprosy is a challenging task to undertake especially in the realization of both high clinical outcome and full bacteriological clearance post the use of MDT. The pathogenic bacterium is able to withstand the effect of the antibiotic treatment and may exist in the body in a dormant state making it difficult to eliminate them. The cell-mediated immunity in patients with MB leprosy is usually weak, that is why they cannot eliminate the infection fully. As a result, chronic clinical symptoms and slow elimination of the bacilli could happen many years after treatment (21,22). Indeed, recent debates in the leprosy community have cast doubts in the sufficiency of the current 12-month MDT regimens in managing MB leprosy patients with the view that such regimens could negatively impact the effective management of the disease (23).

The dilemma of the diagnosis of leprosy is based on a number of factors. Clinically, leprosy is dependent on identifying symptoms, signs and microscopic analysis of skin smears, but these approaches are not always specific and sensitive enough, particularly in the initial symptoms of leprosy. The onset of the symptoms may take months or even years resulting in a lot of delays in diagnosis and initiation of treatment. Moreover, subclinical cases, in which people are infected but do not show any signs, are also an additional problem of the early detection, which can influence the final clinical result (24,25).

Interestingly, delayed clearance increases the fear of the possible occurrence of relapses that is significant in long-term leprosy management. As an example, the number of cases that needed retreatment in India alone grew by 23.4% between 2016 and 2019, which is 11,881 to 15,517 (21). It is worth mentioning that in the article by Gupta et al., roughly 29.4 percent of patients had viable bacilli 12 months post-treatment (26).

Resource-limited environments create a further burden on leprosy through delays in diagnosis that are affected by stigma, ignorance and insufficient healthcare facilities. The problems are preventing proper leprosy control practices especially in such a country as Ethiopia where trained staff and diagnostic equipment are scarce. The effect of this insufficiency is that it affects early detection programs and makes the treatment adherence and management of the disease as a whole more difficult, which adds to the increased concern of resistance to first-line medications used to treat Mycobacterium leprae (6,13,27). Further, as far as we could determine, no data exists that compares the clinical outcomes of MDT after treatment of leprosy in Ethiopia, especially in MB. This knowledge gap prevents knowledge of the effectiveness of the treatment and the management of the disease in the local situation in the long term. Considering this background, the current study was meant to help to assess the clinical outcome of MB leprosy patients after they completed the multidrug therapy at ALERT Hospital and Addis Ababa, Ethiopia.

1.3 Significance of this study

This study is hoped to contribute Ethiopian-specific empirical data on leprosy morphological indices and clinical outcomes after completion of MDT, informing customized patient management for healthcare providers.

For Healthcare Providers: Findings will be of valuable contribution in the tailored treatment strategies incorporating clinical outcomes and morphological correlations, improving clinical decision-making and patient outcomes.

For Institutions: Results are hoped to support optimized resource allocation and local leprosy management guidelines, enhancing institutional capacity.

For Health Bureaus: Evidence will highlight treatment regimen effectiveness and limitations, guiding revisions to national control programs for better population health.

For Policymakers: The data generated will inform policy updates and resource prioritization to advance leprosy elimination as a public health concern.

For Researchers: It will provide a foundation for future studies in similar low-resource, high-burden settings, building on global literature.

2. Literature review

2.1 Clinical outcome in multibacillary leprosy patients at completion of multidrug therapy

Global literature establishes MDT as highly effective for MB leprosy, achieving cure rates of 98% with relapse rates <1% annually in controlled settings. A 2023 meta-analysis of 60 trials (n=9,256) confirmed MDT efficacy (OR 1.06–1,255,584) but noted potential insufficiencies for high-bacillary-load cases, where adjuncts like Pefloxacin and ofloxacin enhance outcomes (28). Systematic reviews report post-MDT smear negativity in 98.7% at 6-year follow-up, though reactions occur in 20–50% and drug resistance prevalence reaches 11.7% globally (29).

A retrospective study was done involving a total of 1210 patients who were registered at the leprosy clinic of India between 199 9 and 2010. In this, 730 MB patients were administered a 12 months MDT MBR during this period. The proportion of patients with a high BI (>3+) among the studied patients was high (42.8%), and 54.9% had a lepra reaction during the treatment or after it. Recurrent erythema nodosum leprosum (ENL) was only seen in 14 patients and this means that although the reactions are prevalent, it can be controlled in terms of frequency and intensity. Moreover, there was strong association between clinical and histological result in approximately 49.5 percent of cases, which supports the relevance of extensive evaluations in the treatment process (30).

Patil et al. conducted a retrospective observational study in India on 345 clinically suspected cases of leprosy in a period of one year. There were 160 cases (46.38%) of MB. These cases were 1.9:1 male to female. The majority of patients were rural and represented lower or middle social classes as they were mostly in the third and fourth decades of age. At all three locations, the smear tests were positive in 112 cases, which composed 70% of the total. A BI of 1+ was observed in 66 cases (41.25%). A single case (0.62) had a BI of 6+, which shows that there are over 1,000 bacilli on average in each field of oil immersion. Concerning the morphological index, the morphological index in 70 cases (43.75%), was lower than 25. On the other hand, the morphological index was over 50 in 14 cases (8.75%), (9).

The long-term follow-up data suggest that while most patients show complete clinical recovery, a small subset may experience relapses or persistent lesions. Previous reviews indicate that relapses typically occur several years post-treatment, often linked to initial high

BI levels (23). For instance, a Brazilian study reported a low relapse rate of 0.07/100 person-years, emphasizing that extended treatment durations may not be necessary for all patients.

The study was a retrospective cohort study and survival analysis based on previously diagnosed cases of leprosy in Caceres, a hyperendemic municipality in the state of Mato Grosso, Brazil, and the newly released cases of leprosy patients between the years of January 1, 2000, and December 31, 2017. The findings showed that the mean time to physical disability (PD) grade advancement of both PB and MB leprosy patients was 162 and 151 months respectively. The survivorship analysis indicated that 15 years after the initiation of treatment (release), probability of PD grade progression was around 35 percent, without any significant difference between patients of PB and MB as well as patients of various ages. It is worth noting that leprosy responses and medical complaints reported during treatment became crucial risk factors on PD progression with hazard ratio of 1.6 and 1.8 respectively (32).

2.2 Morphological indices in multibacillary leprosy patients at completion of multidrug therapy

A study done in Indian patients who were affected by MB leprosy utilizing three various genes showed that of the 36 patients, 20/36 with esxa, 22/36 with hsp18, and 24/36 with 16S rRNA cases, the viability of the M. leprae was seen at the end of 12 months treatment under medicated with multidrugs. These positive patients were all histopathologically active and bacillary indexes of 3+ up to 4+. However, histopathological studies also showed that in these patients, the cells continued to be active and had granulomas, which meant that they could still be infectious even after they showed improved clinical results (33).

The study was a retrospective study that was performed in a tertiary hospital located in Surabaya, Indonesia, and the results were analyzed through the use of medical records of patients in that period between January 2018 and December 2020 in order to assess the effectiveness of slit skin smear (SSS) before and after treatment. The research was carried with 49 patients, diagnosed with MB leprosy, having a positive SSS, and having undergone MDT. In the study, the BI score at the end of the MDT was 0 among 71.4% of patients, which is significant to reduce the load of bacteria. Also all patients had an MI score of 0% showing that the morphological signs of leprosy were entirely resolved in this cohort (34).

In India, between February 2022 and December 2022, a total of eighteen leprosy cases were evaluated for antimicrobial resistance (AMR) to assess resistance against rifampicin, dapsone, and ofloxacin. In this cohort, twelve patients (66.7%) exhibited a high BI of ≥4+ based on SSS examination. Out of the eighteen cases, fifteen patients demonstrated positive MI results on SSS. Notably, fourteen patients maintained positive MI after completing one year of MDT with high rate of drug resistance proposing MI could be an early and sensitive indicator for AMR even in the absence of clinical relapse. (10).

A Brazilian study highlighted that patients receiving a 12-month regimen experienced significantly fewer relapses compared to those on a shorter 6-month regimen (21). This finding supports the WHO's recommendation for a minimum treatment duration of one year.

In a Brazilian retrospective series (2016–2023), 131 MB patients completing 24-month MDT at SEINPE underwent post-treatment evaluation via histopathology, SSS (BI/MI), qPCR, and drug-resistance sequencing. Active disease or bacillary persistence occurred in 50.4% histologically (62/123) and 64.4% by mouse footpad inoculation (29/45); qPCR was positive in 95.1% (96/101). Resistance mutations affected 2.3% (2/88). Despite 67.9% lesion resolution (89/131), neurological impairment rose from 53.4% (70/131) to 87.0% (114/131), with Grade 2 disability increasing from 5.0% (5/100) to 23.1% (27/117) (35).

A systematic review indicated that relapse rates after 12 months of MDT are approximately 0.2% annually, which is comparable to those observed after 24 months. However, higher relapse rates have been recorded among patients with high initial BI (≥ 4+), with some studies reporting cumulative relapse frequencies ranging from 17% to 39%. (22). Notably, patients with a high BI may continue to harbor viable bacilli post-treatment, raising concerns about disease transmission and the necessity for extended follow-up care (33).

The datum of morphological index (MI) is not fully exploited that could assist in monitoring the possible relapses. It is the proportion of solid stained bacilli (live/viable), which have been counted after observation of 200 red pink staining elements that are lying singly. Such index determines the current and responsive treatment of the leprosy in the patient, or whether the patient has missed his treatment or created resistance to the bacteria used in therapy. (49)

2.2 Conceptual framework

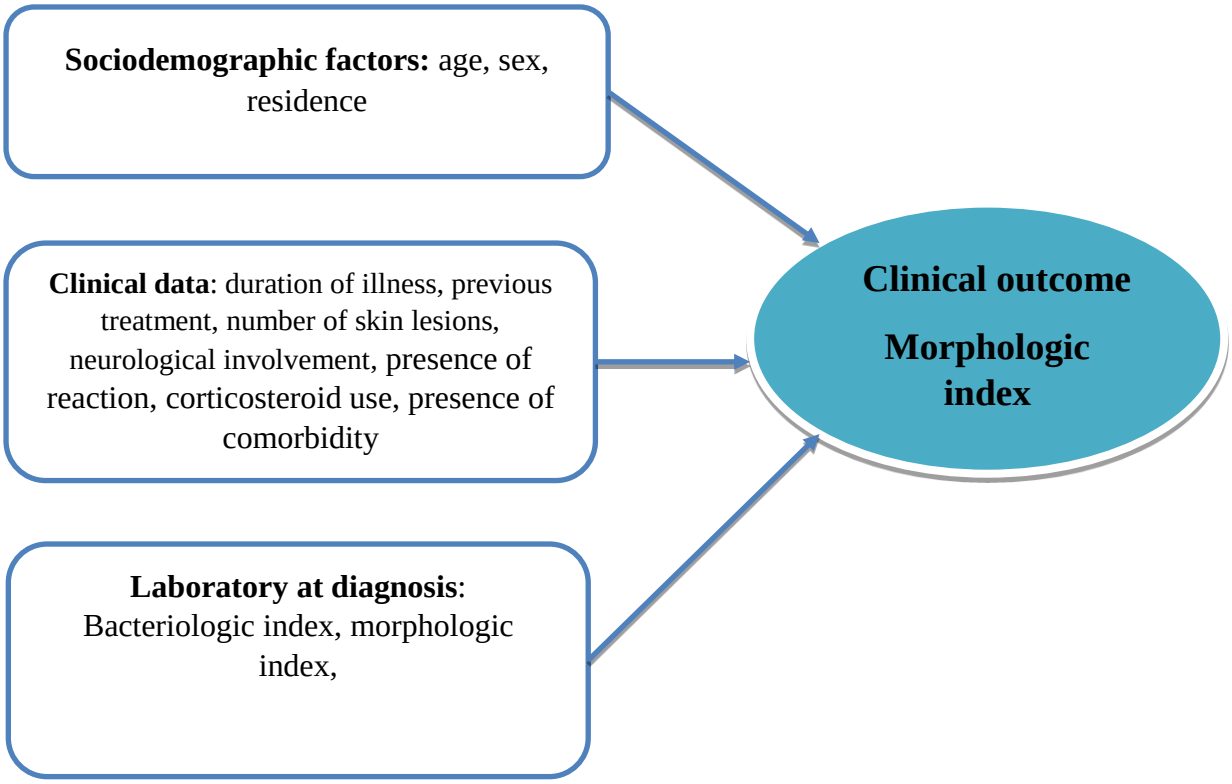

Figure 1. Factors potentially associated with clinical outcome and morphologic index in multibacillary leprosy patients

3. Objective of the study

3.1 General objective

- To evaluate clinical outcome, morphologic indices and other related variables in patients of multibacillary leprosy at the end of multidrug therapy at ALERT Hospital, Addis Ababa, Ethiopia.

3.2 Specific objectives

1. To determine clinical outcome among patients of multibacillary leprosy on completion of multidrug therapy in ALERT Hospital, Addis Ababa, Ethiopia.
2. To determine Morphologic index of multibacillary leprosy on completion of multidrug therapy in ALERT Hospital, Addis Ababa, Ethiopia.
3. To determine variables linked with clinical outcome among multidrug therapy patients of multibacillary leprosy at the end of treatment in ALERT Hospital, Addis Ababa, Ethiopia.
4. To determine variables associated with persistent MI at discharge of MDT at ALERT Hospital, Addis Ababa, Ethiopia.

4. Methods and Materials

4.1 Study setting

The research was carried out at the All Africa Leprosy, Tuberculosis, and Rehabilitation Training Center (ALERT) Hospital which was founded in 1932 by a philanthropist as a leprosy treatment facility. In Addis Ababa, the ALERT is one of the biggest government hospitals in Zenebework, Kolfe Keraniyo subcity that serves the millions of people in the city in different parts of Ethiopia. It has been acting as a referral and teaching hospital having a bed population of over 240 beds and it has a department of dermatology, ophthalmology, surgery and orthopaedics.

ALERT Hospital is a leading training and research hospital in diseases like tuberculosis, HIV/AIDS, leprosy, leishmaniasis as well as other diseases that affect the other parts of the world. The hospital offers a full scope of clinical services such as inpatient and outpatient medical services.

ALERT excels in leprosy management through its 32-bed treatment unit, handling approximately 470 new cases annually referred from all regions of the country via dermatovenereologists and specially trained nurses. Laboratory technicians are proficient in BI and MI readings using standard Ziehl-Neelsen staining and microscopy protocols, supported by the institution's Armauer Hansen Research Institute (founded 1970) for advanced leprosy diagnostics, training, and research.

4.2 Study design

The cross-sectional type of study was used by the research team based on facilities. The method entailed a gathering and analysis of data at one point in time of a given clinical setting.

4.3 Study period

The period of active data collection occurred between November 21 and December 21, 2025. The data reference period also happened to be the treatment period that was longer in length. This was a long-term period of time since November 1, 2020, up to November 30, 2025, which is the entire treatment period of the subjects under study.

4.4 Population

4.4.1 Source population

The population of interest was all the patients who were diagnosed with multibacillary (MB) leprosy and currently receiving the recommended multidrug therapy (MDT) at ALERT Hospital.

4.4.2 Study population

The study population was a certain section of the source population. It was comprised of all patients diagnosed with MB leprosy who not only took but also completed successfully a full course of prescribed MDT during the stated period of time in the ALERT Hospital.

4.5 Eligibility criteria

4.5.1 Inclusion criteria

The participants of the study were selected under the following conditions:

- Patients diagnosed with multibacillary leprosy.
- Patients that completed all of the scheduled multidrug therapy.
- Patients aged 15 years and above during the period.

4.5.2 Exclusion criteria

This was a condition in which the potential participants were excluded in the study:

- Patients with incomplete medical records. This was specifically the case with records lacking necessary clinical and laboratory data required to conduct the analysis.

4.6 Sample size determination and sampling technique

The authors used the non-probability purposeful sampling method. These were all medical records of all the patients who qualified to the specific study criteria. These were patients with multibacillary leprosy and who had undergone their MDT in the range of November 1, 2020, to November 30, 2025. A calculated sample size was not conducted with probabilistic sampling because the study sought to cover all the records which were eligible during the same period.

4.7 Data collection tools and procedures

Secondary data were collected from patients' medical records using a structured data collection checklist specifically designed for this study, which has been adapted from previous similar studies (30,36–40). The data collection format consists of eleven items divided into three parts: demographic information, which include details such as age, sex, and

residence; clinical history, which covered the duration of illness, previous treatments, corticosteroid use, and presence of comorbidity; baseline characteristics, which assessed the number of skin lesions, neurological involvement, bacteriologic indices and morphological indices. Bacteriologic and morphologic indices were determined through slit-skin smear microscopy, disability grading based on WHO classification, and characteristics of skin lesions (size, number, location).

Patients' data were retrieved from standard leprosy registry logbooks used throughout the country. These logbooks contain essential information such as the patient's name, age, sex, address, smear result, category, disability grade at diagnosis, and after treatment.

To facilitate this process, two experienced onsite healthcare workers were recruited and trained in the data collection procedures.

4.8 Study variables

4.8.1 Dependent variables

- Clinical outcome (dichotomized as poor and good)
- Morphologic index

4.8.2 Independent variables

- **Demographic information**: age, sex, residence
- **Clinical data**: history of treatment, duration of symptoms, highest site BI at diagnosis, highest site MI at diagnosis, number of skin lesions, neurologic involvement, disability grade at diagnosis, presence of comorbidity, use of systemic steroid

4.9 Operational definitions

Multibacillary leprosy: ≥6 skin lesions, or multiple nerve involvement, or smear positive. (15)

Completion of MDT: Patient has taken 12 supervised monthly doses of MB-MDT within a maximum period of 18 months (15)

Few skin lesions: is defined as <5 skin lesions

Many skin lesion: is defined as skin lesions of 5 or more

Resolution of skin lesions: clinical improvement characterized by marked improvement in existing lesion either healing completely or showing substantial regression (loss of erythema, infiltration and flattening of plaques) (8,22).

Persistent or worsening lesions: The presence of new skin lesions or failure to achieve significant healing in existing lesions after the completion of treatment (23,30).

Neurological function recovery is indicated by the improvement of sensory and motor functions, as well as a reduction in neuropathic pain (8,22).

Bacteriological Index (BI): Logarithmic measure of the number of Mycobacterium laprae in slit skin smear of leprosy patients (8,22)

Bacteriological clearance: a sustained reduction in bacillary load as evidenced by slit-skin smear examinations conducted at regular intervals during and after treatment (8,22)

Increased bacterial index: An increase in the BI. A rise in BI by 2+ or more from previous measurements would also denote treatment failure (23,30).

Morphological index is defined as the percentage of solid-staining acid-fast bacilli observed in skin smears, indicating the proportion of viable M. leprae (9).

A **positive MI** is declared when solid-staining AFB are detected in the smears, indicating the presence of viable bacilli (10,42).

A **negative MI** is observed when no solid-staining AFB are found, indicating that the bacilli are non-viable or have been effectively eradicated by the treatment (10,42).

Persistent positive MI is defined as positive MI at completion of MDT. (11)

Clinical outcome: encompass resolution of skin lesions, recovery of neurological function, bacteriologic profile after completion of MDT treatment (23,30,41).

A **good clinical outcome** is defined as improvement of existing skin lesions, absence of new lesions, improved sensory or motor function, and non-increased BI following completion of MDT (23,30,41).

A **poor clinical outcome** is defined as the development of new or worsening of lesions, or worsening or no improvement of sensory and motor impairment, or increased BI by log of 2 at completion of MDT(23,30,41).

4.10 Data quality management

To ensure the reliability and integrity of the data collected for this study on clinical outcomes of MB leprosy patients, a comprehensive data quality management strategy was implemented. An English version checklist, developed after an extensive literature review,

served as the primary tool for data collection after pretesting with 10 patients excluded from the main study.

Before the commencement of data collection, a brief training session focusing on the data collection process was conducted for the two experienced health professionals designated as data collectors. Close supervision was maintained throughout the data collection phase to monitor adherence to protocols.

To enhance data quality, all filled checklists underwent a rigorous verification process. The data collectors and the principal investigator double-checked the completed checklists daily for consistency and completeness.

4.11 Data processing and analysis

Microsoft Excel version 2016 was used to enter data, code it, and cleaning, whereas SPSS (Statistical Package for the Social Sciences) version 26 was used to conduct statistical analysis. The missing values and the evaluation of variables were checked with the help of sorting and cross-tabulation methods. Descriptive statistics such as mean +- standard deviation and median (interquartile range) was used to summarize the demographic and clinical characteristics of the patients with continuous variables and percentages and frequencies with categorical variables.

The best site (BI) and Mi were paired before and after MDT and the Wilcoxon signed-rank test was used to test the differences. Bivariate logistic regression filtered independent variables to be associated to poor clinical outcome (p[?]0.25). Important variables were added to multivariate logistic regression (enter method) to estimate adjusted odds ratio (AOR) and confidence intervals and $p<0.05$ was used as the significant level. The Hosmer-Lemeshow test was used to measure model fit ($p= 0.986$). Findings were represented in the forms of narratives, tables and figures.

4.12 Ethical consideration

Data was also collected after ethical approval had been obtained at the College of Health Sciences at Addis Ababa University. To help in data collection, a letter of support was offered to the leprosy treatment unit by the Dermatovenereology Department. The information obtained was anonymous and confidential. Providing a waiver of informed consent is being sought because the given project is going to have the secondary analysis of the existing data, which means that the given project will be a minimal-risk retrospective chart review, and no interaction with patients is to be provided.

4.13 Dissemination of the study findings

The research outcomes of this project were presented to the Department of Dermatovenereology of AAU as a partial requirement of the specialty degree in Dermatovenereology. The results of this research were also published in the Dermatovenereology annual conference. Moreover, as the results were likely to act as inputs to the health policymakers, the attempts were made to inform the critical stakeholders of the Federal ministry of health (FMoH) and the Armauer Hansen Research Institute (AHRI) about the broad view of the study findings. Lastly, the paper was sent to reputable scientific journals where possible publication would be done.

5. Results

5.1 Demographic profile of patients

There were 107 multibacillary (MB) leprosy patients who took part in the study. Their demographic traits were analyzed and the following findings were made.

Most of the respondents, which is 67.2 percent (n=72), were of the young adult group with 25-44 years. All the participants were aged 30 years, with an interquartile range (IQR) of between 25 and 36 years.

The study population was more prevalent in males who constituted 65.4% (n=70) of the participants. The rest of the 34.6% (n=37) were females giving a ratio of males to females an approximation of 1.9 to 1.

In terms of geographical distribution, the majority of patients were born out of the Oromia and Amhara regions. Precisely, the patients who lived within the Oromia region were 41.1% (n=44) and the patients who lived in the Amhara region were 35.5% (n=38). The most common residence of the participants was the capital city, Addis Ababa, with 15.9 per cent (n=17). Table 1 below is a detailed presentation of these demographic details.

Table 1: Demographics of multibacillary leprosy patients who were prescribed multidrug therapy and attended ALERT Hospital on November 1, 2020-November 30, 2025 (n=107).

Variable	Frequency	Percent (%)
Age category		
15–24 years	24	22.5
25–44 years	72	67.2
45-59 years	8	7.5
>60 years	3	2,8
Sex		
Male	70	65.4
Female	37	34.6
Residence		
Addis Ababa	17	15.9
Tigray	4	3.7
Amhara	38	35.5
Oromia	44	41.1
Other	4	3.7

5.2 Clinical data of patients

Nearly all study participants (97.2%, n=104) had no prior treatment history. Most presented with symptoms lasting 1–5 years (72.9%, n=78), while 15.9% (n=17) had symptoms for less than one year (Table 2).

At diagnosis, highest site Bacterial Index (BI)—was predominantly high, with 69.1% (n=74/107) of patients scoring 3+ or greater on the Ridley logarithmic scale. Highest site Morphological Index (MI) predominantly indicated low viability: 43.0% (n=46) of patients had low viability (0–10%), while 30.8% (n=33) showed moderate viability (11–25%). High (26–50%) and very high viability (>50%) were less frequent, at 7.5% (n=8) and 18.7% (n=20), respectively (Table 2).

The majority of patients (87.9%, n=94) presented with numerous skin lesions at diagnosis, while a few lesions were observed in 8.4% (n=9), and single or no lesions in 1.9% (n=2). Regarding disability, Grade 1 was predominant (77.6%, n=83), followed by Grade 2 (16.8%, n=18) and Grade 0 (5.6%, n=6). Comorbidities were rare (2.8%, n=3), with cases of chronic rheumatic valvular heart disease, diabetes mellitus, and rheumatoid arthritis.

Variable	Frequency	Percent (%)
History of treatment		
No	104	97.2
Yes	3	2.8
Duration of symptoms		
<1 year	17	15.9
1–5 years	78	72.9
>5 years	12	11.2
Highest site BI at diagnosis		
1+	9	8.4
2+	13	12.1
3+	29	27.1
4+	30	28.0
5+	15	14.0
6+	11	10.3
Highest site MI at diagnosis		
1–10% (low viability)	46	43.0
11–25% (moderate viability)	33	30.8
26–50% (high viability)	8	7.5
>50% (very high viability)	20	18.7
Number of skin lesions		
No	2	1.9
Single	2	1.9

Few	9	8.4
Many	94	87.9
Impariment of Sensory test		
Yes	103	96.2%
No	4	3.8%
Impairment of VMT		
Yes	102	95.3
No	5	4.7%
Disability grade at diagnosis		
Grade 0	6	5.6
Grade 1	83	77.6
Grade 2	18	16.8
Presence of comorbidity		
No	104	97.2
Yes*	3	2.8

*Comorbidities included chronic rheumatic valvular heart disease, diabetes mellitus, and rheumatoid arthritis.

Table 2. Baseline clinical characteristics at diagnosis among multibacillary leprosy patients who completed recommended multidrug therapy at ALERT Hospital, 1 November 2020 to 30 November 2025 (n=107)

5.3 Post-treatment details of patients

In this study, the poor clinical outcome at the treatment completion was 33.6% (n=36), while 63.4% (n=71), had good clinical outcomes.

Following treatment, disability was predominantly Grade 1 (55.1%, n=59), followed by Grade 0 (38.3%, n=41) and Grade 2 (6.5%, n=7). Most patients showed positive clinical responses: skin lesion reduction (93.3%, n=98/105), sensory improvement (56.1%, n=56/103), and motor function improvement (61.8%, n=63/102).

Immunological reactions occurred in 25.2% (n=27) of patients, predominantly Type 2 (59.3% of reactions). Steroids were used to manage reactions in 18.7% (n=20) of the total cohort.

At the end of Multidrug Therapy (MDT), the highest Bacterial Index (BI) was (2+ to 3+) in 50.5% (n=54) of patients. The highest Morphological Index (MI) indicated low bacterial viability (1–10%) in the majority of cases (69.2%, n=74) (Table 3).

Variable	Frequency	Percent (%)
Disability grade at the end of MDT		
Grade 0	41	38.3
Grade 1	59	55.1
Grade 2	7	6.5
Reduction in skin lesions (n=105)		
No	7	6.7
Yes	98	93.3
Worsening in sensory function (n=103)		
Yes	47	43.9
No	56	56.1
Worsening in voluntary motor function (n=102)		
Yes	39	38.2
No	63	61.8
Highest BI at the end of MDT		
0+	18	16.8
1+	20	18.7
2+	25	23.4
3+	29	27.1
4+	11	10.3
5+	4	3.7
Highest site MI at the end of MDT		
0% (no viable bacilli)	18	16.8
1–10% (low viability)	74	69.2
11–25% (moderate viability)	13	12.1
>25% (high viability)	2	1.9
History of immunological reaction		
No	80	74.8
Yes	27	25.2
Type of immunological reaction (n=27)		
Type 1	11	40.7
Type 2	16	59.3
History of steroid use		
No	87	81.3
Yes	20	18.7
Persistent MI at end of MDT		
Yes	89	83.2
No	18	16.8
Overall clinical outcome		
Good	55	51.4
Poor	52	48.5

Persistent MI at the end of MDT was found in 83.2% (n=89) of patients. (Table 3)

ALERT Hospital: All Africa Leprosy Rehabilitation and Training Hospital, MDT: Multidrug therapy BI: Bacterial Index, MI: Morphological Index

Table 3. Post-treatment characteristics among multibacillary leprosy patients who completed recommended multidrug therapy at ALERT Hospital, 1 November 2020 to 30 November 2025 (n=107)

5.4 Changes in bacterial and morphological indices

Among 107 MB leprosy patients, the highest site BI showed a significant decline from diagnosis to MDT completion (Wilcoxon signed-rank test: $z = -7.85$, $p < 0.001$). Most transitioned from high baseline BI (e.g., 4+ in 28/107, 5+ in 12/107) to lower levels. Specifically, 14/28 baseline 4+ cases were reduced to 3+, and 12/28 to 2+. Similarly, the highest site MI improved markedly ($z = -7.01$, $p < 0.001$), with 74/107 shifting to 1–10% post-MDT (30/46 from baseline 1–10%, 15/20 from >50%). However, in 5/20 (25%) with baseline >50% declined to (11-25%) (Table 4).

Variable		Highest BI at the end of MDT						Test value*	P value
		0+	1+	2+	3+	4+	5+		
Highest site BI at diagnosis	1+	7	1	0	0	1	0	-7.85	**<0.001**
	2+	5	6	1	1	0	0		
	3+	5	7	7	6	4	0		
	4+	0	2	12	14	1	1		
	5+	1	3	3	4	2	2		
	6+	0	1	2	4	3	1		
		Highest site MI at the end of MDT							
		0%	1–10%		11–25%		>25%		
Highest site MI at diagnosis	0–10%	13	30		3		0	-7.01	**<0.001**
	11–25%	3	24		4		2		
	26–50%	2	5		1		0		
	>50%	0	15		5		0		

Table 4. Changes in bacterial and morphological indices from diagnosis to multidrug therapy completion among multibacillary leprosy patients at ALERT Hospital, November 2020–November 2025 (n=107)

BI: Bacterial Index, MDT: Multidrug therapy, MI: Morphological Index

5.5 Factors potentially associated with clinical outcome

Among all tested variables, the highest-site Morphologic Index (MI) and Bacteriologic Index (BI) at diagnosis were selected for inclusion in the multivariable regression model based on a univariate screening criterion of $p < 0.25$.

In the univariate analysis, a Morphologic Index (MI) greater than 25% was significantly associated with poor clinical outcome, with 6.10 times the odds of a poor outcome (95% CI: 2.39 to 15.54; p=0.001). Similarly, a Bacteriologic Index (BI) at diagnosis of 3–6+ was

significantly associated with poor clinical outcome, with an odds ratio of 14.7 (95% CI: 1.89 to 114.42; p=0.01).

In the multivariable model, both factors remained independently associated with poor clinical outcome. Patients with an MI >25% had 5.13 times the odds of a poor outcome (95% CI: 1.94 to 13.57; p=0.001) compared to those with an MI of 0–25%. Patients with a BI of 3–6+ had 11.7 times the odds of a poor outcome (95% CI: 1.44 to 93.66; p=0.021) compared to those with a BI of 0–2+

Table 5. Factors associated with poor clinical outcome among multibacillary leprosy patients who completed recommended multidrug therapy at ALERT Hospital, 1 November 2020 to 30 November 2025 (n=107)Only variables with p value <0.25 in binary logistic regression are shown here

MI: Morphological Index BI: Bacteriologic Index

1: reference category

Variable	Clinical outcome		COR (95%CI)	p-value	AOR (95%CI)	P value
	Poor (%)	Good (%)				
Highest MI at diagnosis						
0-25%	18(22.8)	61(77.21)	1		1	
>25%	18(64.3)	10(35.1)	6.10(2.39,15.54)	0.001	5.13(1.94,13.57)	0.001
Highest BI at Diagnosis						
0-2 +	6(19.34)	15(80.64)	1			
3-6+	29(33.72)	57(66.28)	14.7(1.89,114.42)	0.01	11.7(1.44,93.66)	0.021

5.6 Factors potentially associated with persistent MI at completion

Among all the tested variables, —age category, sex, highest-site MI and BI at diagnosis, and history of steroid use were selected for inclusion in the multivariable regression model based on a univariate screening criterion of $p < 0.25$.

Only the highest-site BI at diagnosis showed a statistically significant association with Persistent MI at the end of MDT in the final model. Compared to patients who had BI less than 3+, those who had an initial BI of $\geq$3+ had 12-fold higher odds of persistent MI at the end of treatment [AOR=12.22 (95% CI: 3.53–42.28), p=0.001] (Table 6).

Table 6. Factors associated persistent MI among multibacillary leprosy patients who completed recommended multidrug therapy at ALERT Hospital, 1 November 2020 to 30 November 2025 (n=107)

Only variables with p value <0.25 in binary logistic regression are shown here
MI: Morphological Index BI: Bacteriologic Index
1: reference category

6. Discussion

This study assessed clinical outcome, Morphologic indices, and associated factors among MB leprosy patients who completed multidrug therapy at ALERT Hospital, Addis Ababa, Ethiopia. In this study, the poor clinical outcome at the treatment completion was 33.6% (n=36), while 63.4% (n=71), had good clinical outcomes. 83.2% of patients had positive MI at the end of MDT. High Morphologic Index (MI) at diagnosis (> 25%) and High BI (> +3) at diagnosis were found to be independently associated with poor clinical outcome. High BI (> +3) at diagnosis was found to be an independent predictor of positive MI at completion of MDT among multibacillary leprosy patients.

The patients in this study experienced poor clinical outcomes after using fixed 12 months standard MDT with a percentage of 33.6. A study conducted in India in the cross-sectional format revealed the Burden of Fixed WHO-MDT non-responders at 17% (49); which is significantly affected by male gender (p value 0.013) and grade 1 disability (p value: 0.034). This discrepancy may be due to the fact that the study has included paucibacillary leprosy patients and the ratio of to Multibacillary leprosy patients.

Although there was significant clinical improvement, a recent Brazilian retrospective study found poor outcome at the end of the treatment (24 months). Clinically, 68 percent of the patients had no visible lesions in their skin at discharge, and 87 percent of patients had neural worsening, 50 percent of the patients had active M. leprae on histological/microbiological examination (35). A series of cases in Brazil of 10 multibacillary leprosy patients that had initially high bacillary indices, after receiving twelve doses of MDT; all reported clinical improvements, including flattening, repigmentation and reduction of the size of skin lesions. On completion of treatment, there was a decrease in the index of bacilli in all the patients but viable bacilli were observed in 30% of cases. (51). The majority of clinical outcome assessments that are used to evaluate the clinical outcomes after MDT use the surveillance and the long term follow up. The poor clinical outcome among the study population was relatively more and should be explained by the long natural history of the disease considering sluggish recovery of nerve functions.

In this trial, even with a significant improvement in skin lesions, as well as a significant reduction in BI and MI during the initiation and termination of treatment, even with low viability (1-10) representing a significant proportion -69%, 83.2% patients had positive MI at the end of treatment. In Indian cases series; Among 18 patients, 15 patients reported positive

MI after 1-year of MDT and poor clinical profile in 11 patients and general rate of resistance to rifampicin amongst MI-positive cases was 33.3% proposing MI might be an early and sensitive predictor of antimicrobial resistance (10). In a Brazilian study conducted in 73 patients with multibacillary, it was discovered that 20.54% patients had positive MI with standard 12 dose of MDT. Such patients were treated until 24 months (50). However, unlike in our study, in an Indian study demonstrated that persisters using molecular studies were only 29.4% even after 12 months MDT (26). There was a retrospective study in Indonesia that was conducted in the year 1998, 49 MB patients were found to have a positive SSS examination and had completed multidrug therapy (MDT) MI score of 0% in all patients ($p<0.05$) compared to the finding of this study.

Even though MI remained positive in 83% of patients after completion of MDT, 74(69%) had low Vialbility (1-10%). Additionally measurement of MI is liable for observer variations. (9)

These discordant clinical and microbiologic findings challenge the national program definition of MDT completion as "cure" irrespective of bacteriologic parameters, as it can be demonstrated that clinical improvements can mask subclinical activity undetectable by skin clearance alone. The observed higher rate of persistent viable bacilli, and poor outcome in 33.6% of patients underscores the limitations of uniform fixed-duration MDT for Multibacillary patients in Ethiopian settings. Time-based discharge criteria alone is inadequate to confirm cure and signals the rationale for treatment continuation beyond the standard duration in the clinical practice.

The negative findings of this study may be attributed to the relatively small sample size and retrospective design.

7. Strengths and Limitations

7.1 Strengths

- This study was conducted at ALERT Hospital, Ethiopia's leading leprosy referral center with the highest caseload and demographic diversity, featuring a specialized unit ensuring high-quality slit-skin smear interpretation and standardized MDT delivery.

7.2 Limitations

- The retrospective design relied on secondary medical record data, introducing risks of incomplete data and selection bias toward treatment completers.

- BI and MI assessments were subject to inter-observer variability inherent in technician-dependent smear interpretation, despite standardized training.
- The sample size (n=107) from a single center limited statistical power for subgroup analyses (e.g., reactions, n=27; comorbidities, n=3) and generalizability beyond the study hospital.

8. Conclusions and Recommendations

8.1 Conclusions

This study demonstrated that fixed 12-month MDT for MB leprosy at ALERT Hospital achieved significant reductions in bacterial index (BI) and morphological index (MI), alongside high rates of skin lesion resolution. However, more than one third (33.6%) of the patients exhibited poor clinical outcomes defined based on composite outcome measure and majority (83.2%) showed persistent MI at the end of treatment. This study highlights that treatment completion does not necessarily translate into optimal clinical recovery.

8.2 Recommendations

Based on the key findings obtained in this study, the following recommendations can be forwarded.

For Healthcare Providers,

- Continue strong Implementation serial and post-MDT slit-skin smear monitoring (BI/MI) giving emphasis to patients with baseline BI ≥3+ or MI >25%, considering therapy extension if persistence of viable bacilli.
- Standardize composite outcome assessment (BI, MI, clinical) beyond skin clearance to detect subclinical persistence early.

For Local Policymakers,

- Consider revising national guidelines to incorporate bacteriological criteria and molecular testing alongside fixed 12-month MDT completion for MB release, addressing the high burden of poor outcomes.
- Allocate resources for regional screening camps targeting high-prevalence areas such as Oromia and Amhara, and train peripheral health workers in smear microscopy.
- Support molecular resistance surveillance given persistent viable bacilli, integrating with Ethiopia's TB/leprosy control programs.

For Future Researchers

- Conduct the same study in a prospective study design
- Conduct prospective multi-center studies with long-term relapse in high bacillary load.

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Annex

Annex I: Information sheet

Addis Ababa University

College of Health Sciences

Department of Dermatovenereology

This note will be read for medical director of the hospital before collecting any information from the registries.

Greetings. My name is Dr. Hanna Bekele and I am a postgraduate student in Dermatovenereology at Addis Ababa University.
This tertiary hospital was selected to conduct the proposed study entitled **"Clinical outcome and associated factors in multibacillary leprosy patients at completion of multidrug therapy at ALERT Hospital, Addis Ababa, Ethiopia"** as it is the leading public hospital where the highest number of individuals with leprosy disease can be recruited, and it represents patients from various parts of the country.

I am respectfully seeking your great office to allow me to carry out the mentioned study in this hospital. Further explanation is given below:

Study procedure: to meet the intended aim of this study, the socio-demographic data, and clinical history and course of management of the patients will be collected in medical records of patients. The data collectors shall be using a checklist to get the data required with the help of the medical records of the patients in case your respected institution does not have an issue with the undertaking of the study. The questions in the checklist will be concerning social-demographic and clinical data and laboratory data of the patients. I would greatly like to ask you to assist me in this research.

Risks and benefits: It is assumed that the outcome of the study will contribute to advancement of such specific group of patients care by responsible body and allow to optimize clinical care in the target population.

Confidentiality: The whole information that will be gathered will be held in confidentiality and will be utilized by the purpose of research. The information to be collected will not be accessible to anybody other than the members of the research team. Any report will not notify the name and/or any other personal information of patients. Any paper and computer documents of the study will be stored in an secured location under lock key when not in use.**Contact Address of the principal investigator**

Name**:** Dr. Hanna Bekele

Mobile Phone**:** 0913593190

Annex II: Data collection format

001. Data collector: code ____/___/___ Name _____

002. Date of data collection ____/___/____ Time _____

003. Checked by Supervisor: Signature _____day _____month _____ year____

I. Background data			
SN	**Question**	**Response**	**Skip**
101	Age in years		
102	Sex	1. Male 2. Female	
103	Region of residence	_____	
Section 2: Clinical variables			
201	Bacteriological Index at diagnosis: Scale from 0 to 6	_____	
202	Morphological index at diagnosis in percent		
203	Number of skin lesions at diagnosis	_____	
204	Disability grade at diagnosis:	0. Grade 0: No disability 1. Grade 1: Some disability 2. Grade 2: Severe disability	
205	Presence of chronic medical illness	1. Yes 2. No	
Section 3: Treatment and outcome related variables			
301	Disability Grade at Completion	Grade 0 Grade 1 Grade 2	
302	Clinical Improvement Indicators:	Reduction in skin lesions: Yes No	
		Improvement in sensory function (test): Yes No	
		Improvement in voluntary motor function: Yes No	
303	Bacteriological Index at completion: Scale from 0 to 6	_____	
304	Morphological index at completion in percent	_____	
305	History of immunological reaction	Yes No	
308	Additional corticosteroids Received	Yes No	