JAMBI MEDICAL JOURNAL
Jurnal Kedokteran dan Kesehatan
Vol. 13 No 2 November 2025
DOI: 10.22437/jmj.v13i2.48898
Journal homepage: https://online-journal.unja.ac.id/kedokteran
p-Issn : 2339-269x
e-Issn : 2580-6874

Original Article

Correlation of IL-10 Levels with the Bacterial Index in Multibacillary Leprosy

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Article History:

Submit: Sept 2025
Accepted: Nov 2025

Keyword:

multibacillary leprosy; bacterial index;
IL-10;

ABSTRACT

Background: Multibacillary (MB) leprosy is characterised by a high bacillary burden and a tolerogenic immune profile. Interleukin-10 (IL-10) is a key immunoregulatory cytokine that may reflect bacillary load. Objective: To compare bacillary burden and IL-10 between MB patients and controls and to examine the correlation between the Bacterial Index (BI) and IL-10 among MB patients.

Methods: A comparative cross-sectional study included 68 participants (MB n=34; controls n=34). Categorical variables were analysed using Chi-square tests, and medians were used with Mann–Whitney U tests. Spearman's rank correlation was used to assess the BI–IL-10 relationship in MB.

Results: Age distribution was similar between groups (p=0.451), whereas occupation (p=0.040) and education (p=0.027) differed. BI was markedly higher in MB than in controls (median 2.5 [IQR 4] vs 0 [0]; p<0.001). IL-10 concentrations were also higher in MB (1.96 [4.03] pg/mL) than in controls (1.12 [1.94] pg/mL; p=0.029). Among MB patients, BI correlated positively with IL-10 (ρ = 0.358; p = 0.038).

Conclusion: MB leprosy shows substantially greater bacillary burden and elevated IL-10 relative to controls. The positive association between BI and IL-10 supports the role of an immunoregulatory milieu linked to bacillary load. These findings highlight IL-10 as a potential biomarker for disease burden in MB leprosy and warrant validation in larger, adjusted cohorts.

INTRODUCTION

Leprosy, also known as Hansen's disease, is a chronic infectious disease caused by *Mycobacterium leprae*, a slow-growing, obligate intracellular bacillus primarily affecting the skin and peripheral nerves.[1,2] Despite effective multidrug therapy (MDT) programs, multibacillary (MB) leprosy cases remain prevalent. They are responsible for the majority of transmission and disability due to their high bacillary load and immunosuppressive host responses.[3,4]

Recent global analyses suggest a shift in disease classification, with the proportion of paucibacillary (PB) cases decreasing from approximately 80% in the 1980s to around 40% in recent years—implying a substantial increase in MB cases worldwide.[5] In Asia, this trend is particularly pronounced. For example, in China, a 2020 surveillance report revealed that 93.3% of newly diagnosed leprosy patients were classified as MB.[6] Similarly, a retrospective multicenter study in Indonesia conducted across 13 hospitals between 2018 and 2020 found that 86.2% of leprosy cases were of the multibacillary type, reflecting the predominant clinical pattern in endemic regions.[7] Although official WHO reports do not always disaggregate MB and PB in regional prevalence data, Southeast Asia remains the global epicentre of leprosy burden, accounting for nearly half of all newly reported cases annually.[4] These figures emphasise the urgent need to understand the immunopathological mechanisms underlying MB leprosy better.

Multibacillary (MB) leprosy is immunologically distinct from its paucibacillary counterpart, primarily due to a dominant T-helper 2 (Th2) response and a suppressed T-helper 1 (Th1)-mediated cellular immune response. This immune deviation impairs the host's ability to mount an effective intracellular defence, allowing *Mycobacterium leprae* to persist and proliferate. A key contributor to this immunological profile is the elevated production of anti-inflammatory or regulatory cytokines, especially interleukin-10 (IL-10). IL-10 is produced by several immune cells, including monocytes, dendritic cells, and $CD4^+CD25^+$ regulatory T cells, in response to *M. leprae* antigens. Functionally, IL-10 inhibits macrophage activation and downregulates pro-inflammatory mediators such as IL-12 and interferon-gamma (IFN-γ), thereby limiting phagosome maturation and antigen presentation, which are essential for adequate microbial clearance.[8-10]

The Bacterial Index (BI) remains a fundamental diagnostic and prognostic tool in leprosy management, especially for multibacillary (MB) cases. It quantifies the bacillary load from Ziehl-Neelsen-stained slit-skin smears, graded 0-6+ based on the number of acid-fast bacilli observed. A high BI correlates with active bacillary replication, increased transmission risk, and a greater probability of reactional episodes or relapse after treatment. Recent studies reaffirm its critical role: for instance, a 2025 cross-sectional study in the Comoros found that only MB patients with a BI ≥1 yielded *Mycobacterium leprae* DNA from novel diagnostic sites such as the tongue dorsum, supporting BI's association with systemic bacillary burden.[11,12] Bacillary counts increased over time in an experimental in vitro model using dental pulp stem cells, suggesting that BI can also reflect pathogen viability in host-cell environments.[13] These findings underscore the BI's value not only in routine diagnostics but also in advancing experimental models for *M. leprae* biology and immunopathogenesis

Several studies have highlighted that IL-10 is elevated in MB leprosy and may correlate with disease severity, bacillary index (BI), and neuropathy progression.[14,15] Moreover, IL-10 may serve as a potential biomarker of bacillary burden, aiding in assessing therapeutic response or risk of relapse.[16,17] Understanding this immunoregulatory axis is essential for developing host-targeted diagnostic and monitoring tools, particularly in resource-limited endemic settings.

Therefore, this study aims to assess the relationship between serum IL-10 levels

and bacillary index in patients with multibacillary leprosy and to evaluate the diagnostic relevance of IL-10 as a surrogate marker for bacillary burden.

METHODS

Study Design and Setting

This study was an cross-sectional, observational comparative study conducted in Sukajadi Primary Health Centre, Banyuasin Regency, South Sumatra, Indonesia. The investigation aimed to analyse the correlation between serum interleukin-10 (IL-10) levels and the bacterial index (BI) in patients with multibacillary (MB) leprosy. The study was conducted in accordance with the Declaration of Helsinki; the protocol was approved by the Ethics Committee of the Faculty of Medicine and Health Sciences, Universitas Jambi (No. 2352/UN21.8/PT.01.04/2025), and written informed consent was obtained from all participants.

Study Population and Sampling

Participants were recruited using a consecutive sampling method until the target number was achieved. The case group consisted of newly diagnosed or existing MB leprosy patients with positive slit-skin smear (SSS) results, aged between 18 and 60 years, and who provided informed consent. The control group included individuals without a history or clinical signs of leprosy. Exclusion criteria included individuals with severe lepra reactions, pregnancy or lactation, autoimmune diseases, or atopic conditions. The minimum sample size, calculated using the two-proportion hypothesis test, was at least 25 participants per group; however, this study enrolled 34 participants in each group, exceeding the required minimum.

Data Collection

Sociodemographic data were collected through structured interviews. Clinical diagnosis of MB leprosy was made by a certified dermatologist according to WHO clinical criteria and confirmed by slit-skin smear microscopy. BI was determined using the Ridley logarithmic scale (0 to +6) after Ziehl-Neelsen staining of smears obtained from skin and nasal mucosa samples, following WHO guidelines.[18]

Measurement of IL-10

Venous blood (3 mL) was aseptically collected from all participants into sterile red-top tubes and allowed to clot at room temperature. After centrifugation at 1000 rpm for 15 minutes, the serum was separated and stored at –80°C until analysis. IL-10 levels were quantified using high-sensitivity ELISA (Human IL-10 ELISA Kit, 96-well format, detection range: 0.78–50 pg/mL) at the Biotechnology Laboratory, Faculty of Medicine, Universitas Sriwijaya.

Data Analysis

Univariate analyses were conducted to describe the distributions of sociodemographic variables, IL-10 concentrations, and BI scores. Between-group comparisons (control vs. MB leprosy) were performed using the chi-square and Mann–Whitney U tests, with $p < 0.05$ as the significance threshold. The correlation between IL-10 levels and the Bacterial Index was assessed using Spearman's rank correlation; $p < 0.05$ was considered significant. Correlation strength was categorised as very weak ($\rho < 0.20$), weak (0.20–0.39), moderate (0.40–0.59), strong (0.60–0.79), and very strong (≥ 0.80).

RESULT AND DISCUSSION

Sixty-eight participants were analysed (control n=34, multibacillary [MB] leprosy n=34). Between-group comparisons (control vs. MB leprosy) were conducted and presented in Table 1. Age distribution (18–44 vs 45–70 years) did not differ between groups (p=0.451, chi-square). In contrast, occupation differed significantly (p=0.040, chi-square), with a higher proportion of traders/farmers/labourers in the MB group. Education level also differed (p=0.027, chi-square), with elementary/junior high school more frequent in MB than in controls.

Table 1. Demographic, Clinical, and Immunologic Characteristics with Group Comparisons

Variables	Control (n=34)	Multibacillary Leprosy (n=34)	p-value
Age, n (%), years			
18-44	20 (29.4)	23 (33.8)	0.451[a]
45-70	14 (20.6)	11 (16.2)	
Occupation, n (%)			
Civil servant/Private sector	17 (25.0)	7 (10.3)	0.040[a/*]
Trader/Farmer/Labourer	11 (16.2)	18 (26.5)	
Housewife/Unemployed	6 (8.8)	9 (13.2)	
Education, n (%)			
Elementary/Junior HS	15 (22.1)	24 (35.3)	0.027[a/*]
Senior HS/Higher Education	19 (27.9)	10 (14.7)	
Bacterial Index, median [IQR]	0 [0]	2.5 [4]	0.000[b/**]
IL-10, median [IQR], pg/mL	1.12 [1.94]	1.96 [4.03]	0.029[b/*]

Notes. *Group differences tested using: [a]Chi-square; [b]Mann–Whitney U.*
*Significance codes: ** p < 0.01; * p < 0.05 (two-tailed).*

Disease-related markers showed clear between-group contrasts (Table 1). The Bacterial Index was markedly higher in MB (median 2.5 [IQR 4]) than in controls (0 [0]; p<0.001, Mann–Whitney U). IL-10 concentrations were also higher in MB (median 1.96 [4.03] pg/mL) compared with controls (1.12 [1.94] pg/mL; p=0.029, Mann–Whitney U).

Table 2. Spearman's Rank Correlation Matrix of Study Variables in Patients with Multibacillary Leprosy

Variables		BI ρ (p-value)	IL-10 ρ (p-value)
Multibacillary Leprosy (n=34)	BI	1.000	1.000
	IL-10	0.358 (0.038)*	

Notes. *Spearman's rank correlation (ρ).*
*Significance codes: ** p < 0.01; * p < 0.05 (two-tailed).*

Based on Table 2, Spearman's rank correlation in multibacillary leprosy patients (n=34) shows a positive association between IL-10 and the Bacterial Index (ρ = 0.358, p = 0.038), indicating a weak-to-moderate association. Still, a statistically significant relationship: higher IL-10 levels are associated with greater bacillary burden.

In this comparative cross-sectional study, multibacillary (MB) leprosy showed the expected pattern of markedly greater bacillary burden and higher circulating IL-10 compared with controls. Beyond this between-group contrast, we observed a positive correlation between IL-10 and the Bacterial Index (BI) among MB patients (ρ=0.358, p=0.038), indicating that individuals with higher IL-10 tended to harbour a greater bacillary load. Although the effect size falls in the weak-to-moderate range, the direction and statistical significance are biologically coherent and align with the immunoregulatory phenotype classically described in MB disease.

Mechanistically, IL-10 functions as a central anti-inflammatory cytokine, suppressing Th1-driven immunity and thereby compromising the host's ability to eliminate *Mycobacterium leprae*. It downregulates antigen presentation by dendritic cells, inhibits macrophage activation, and blocks the production of critical pro-inflammatory mediators, such as IL-12 and interferon-gamma (IFN-γ), which are essential for adequate bacillary clearance.[19,20] Within multibacillary (MB) leprosy lesions, the immune milieu is characterised by increased IL-10 secretion—particularly by regulatory T cells (Tregs)—which promotes a tolerogenic environment that favours bacillary persistence.[21,22]

Our findings, showing systemic IL-10 elevation in MB patients and a positive correlation with the bacterial index, are consistent with this immunosuppressive model. Rather than acting as a passive bystander, IL-10 may actively sustain *M. leprae* survival by reinforcing immunological anergy, limiting Th1 responsiveness and phagocyte-mediated killing. This underscores IL-10's role not only as a biomarker of disease severity but also as a potential immune checkpoint in leprosy immunopathogenesis.

Sociodemographic differences between groups (occupation and education) likely reflect underlying socioeconomic determinants of health and access to care. While these variables are not the focus of the present work, they underscore the importance of considering social context when interpreting immunological markers. Age distribution and marital status were comparable, reducing concern that these factors confounded the main findings.

From a clinical perspective, interleukin-10 (IL-10) shows promise as an adjunct biomarker to the bacterial index (BI) for stratifying bacillary burden in multibacillary (MB) leprosy, particularly in settings with limited slit-skin smear facilities. IL-10’s elevation correlates with bacillary load and immune suppression, suggesting it could help track treatment response when direct bacilloscopic methods are unavailable or less sensitive in early follow-up phases.[23] However, its modest correlation with BI implies that IL-10 cannot function as a stand-alone diagnostic tool but may instead serve as part of a multi-marker panel, combining with other host-derived immune or inflammatory signatures to enhance clinical decision-making. This approach mirrors recent trends in infectious disease management, where composite cytokine panels have demonstrated superior prognostic value compared with single markers.[24] Additionally, AI-based platforms are being developed to integrate such biomarker data into real-time decision-support tools, further enhancing their diagnostic and monitoring capacity.[25]

This study has several limitations. First, the cross-sectional design precludes causal inference; we cannot determine whether elevated IL-10 drives bacillary accumulation or primarily reflects host response to higher bacterial load. Second, although the sample size exceeds the calculated minimum, it still limits precision around correlation estimates. Third, we did not adjust for potential confounders (e.g., treatment status, nutritional state, comorbid infections) in multivariable models, and BI—being ordinal—reduces measurement granularity. Fourth, in the final analysis, biomarkers were restricted to IL-10; broader cytokine/mediator profiling and cellular phenotyping would clarify mechanistic pathways. Finally, single-centre recruitment may limit generalizability.

Future work should adopt longitudinal designs to track IL-10 and BI dynamics throughout MDT, evaluate temporal coupling (e.g., whether declines in IL-10 parallel bacteriological clearance), and test partial correlations or ordinal regression controlling for relevant covariates. Multi-marker panels (e.g., IL-10 with other immunoregulatory or inflammatory mediators) and external validation across centres would strengthen translational relevance.

CONCLUSION

Multibacillary (MB) leprosy was characterised by a substantially higher bacillary burden and elevated circulating IL-10 compared with controls. Within the MB group, IL-10 showed a positive, statistically significant association with the Bacterial Index, indicating that higher IL-10 levels are associated with greater bacillary load. These findings support the concept of a tolerogenic immune milieu accompanying bacillary proliferation in MB disease. Although IL-10 is unlikely to replace direct bacteriological measures, it may serve as an adjunct biomarker—potentially as part of a composite host-marker panel—to inform risk stratification and monitoring. Validation in larger, longitudinal, and covariate-adjusted cohorts is warranted to determine the clinical utility and temporal dynamics of this therapy alongside multidrug therapy.

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