Morphological indices and patterns of acid-fast bacilli from multiple sites were not correlated with IL-10, PGE2, and IL-35 levels in multibacillary leprosy patients

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Abstract : Multibacillary leprosy is characterized by a high bacterial load and a tolerogenic immune profile involving interleukin-10 (IL-10), prostaglandin E2 (PGE2), and interleukin-35 (IL-35). Previous studies relied solely on the aggregate bacterial index, without accounting for bacillary distribution across body sites or viability, reflected in the morphological index. This study analyzed relationships between the morphological index and acid-fast bacilli (AFB) patterns at six sites and serum IL-10, PGE2, and IL-35 levels in multibacillary leprosy patients in Banyuasin Regency, South Sumatra, using a cross-sectional design. The morphological index and AFB grade at both ears, hands, and feet were examined via skin scraping. IL-10 and PGE2 levels were measured in 30 patients, and IL-35 levels in 29 patients. Five bacteriological metrics were correlated with the three immune markers using Spearman's correlation, with P values corrected using the Benjamini-Hochberg method. Of the fifteen pairs tested, none were significant after correction (corrected P 0.96-0.97). The strongest correlation was between the number of positive smear sites and PGE2 (rho -0.27, P = 0.16), with a confidence interval crossing zero. The morphological index and multisite AFB patterns were not associated with IL-10, PGE2, or IL-35. Larger studies are needed to confirm these associations.

Keywords : Leprosy, Lepromatous; Mycobacterium leprae; Interleukin-10; Dinoprostone; T-Lymphocytes

Abstrak *: Lepra multibasiler ditandai beban basil tinggi dan profil imun tolerogenik yang melibatkan interleukin-10 (IL-10), prostaglandin E2 (PGE2), dan interleukin-35 (IL-35). Penelitian terdahulu hanya mengandalkan Indeks Bakteri agregat, tanpa memperhitungkan sebaran basil antar lokasi tubuh atau viabilitas basil yang tercermin pada Morfologi Indeks. Penelitian ini menganalisis hubungan Morfologi Indeks dan pola basil tahan asam (BTA) pada enam lokasi dengan kadar serum IL-10, PGE2, dan IL-35 pada pasien lepra multibasiler di Kabupaten Banyuasin, Sumatra Selatan, memakai desain potong lintang. Morfologi Indeks dan derajat BTA pada kedua telinga, tangan, dan kaki diperiksa melalui kerokan kulit. Kadar IL-10 dan PGE2 diukur pada 30 pasien, kadar IL-35 pada 29 pasien. Lima metrik bakteriologis dikorelasikan dengan ketiga penanda imun memakai uji Spearman, nilai P dikoreksi dengan metode Benjamini-*

Hochberg. Dari lima belas pasangan yang diuji, tidak satu pun bermakna setelah koreksi (P terkoreksi 0,96 sampai 0,97). Korelasi terbesar ditemukan antara jumlah lokasi BTA positif dengan PGE2 (rho -0,27, P = 0,16), dengan interval kepercayaan melewati nol. Morfologi Indeks dan pola BTA multilokasi tidak berhubungan dengan IL-10, PGE2, atau IL-35. Studi lebih besar diperlukan untuk memastikan hubungan tersebut.

Kata Kunci *: Kusta Tipe Lepromatosa; Mycobacterium Leprae; Interleukin-10; Dinoprostone; Limfosit T*

INTRODUCTION

Leprosy remains a public health problem in tropical regions, with Indonesia ranking third worldwide in terms of the number of new cases after India and Brazil (Deps et al., 2025). The Indonesian government aims to eliminate leprosy through the "Zero Leprosy" national action plan; however, active transmission continues in several endemic pockets, including Banyuasin Regency, South Sumatra (Sebong et al., 2025). Multibacillary leprosy is a clinical form with the highest bacterial burden and is characterized by the dominance of regulatory T cells that suppress the cellular immune response and facilitate the persistence of *Mycobacterium leprae* in host tissues (Silva et al., 2024; Grijsen et al., 2024). Interleukin-10, prostaglandin E2, and interleukin-35 are the primary mediators in this immunosuppressive environment. Interleukin-10 suppresses the expression of MHC class II molecules and the production of interleukin-12 in macrophages and dendritic cells (Couper et al., 2008). Prostaglandin E2, synthesized via the cyclooxygenase pathway, inhibits interferon-gamma-mediated macrophage activation while increasing interleukin-10 secretion (Chen et al., 2023; Wang et al., 2025). Interleukin-35, produced by regulatory T cells, plays a role in the expansion of these cells and the suppression of Th1 and Th17 responses (Tarique et al., 2017). The same research group in this cohort reported that the bacterial index, which reflects bacterial density, is positively correlated with interleukin-10 levels in patients with multibacillary leprosy (Fitriyanti et al., 2025), while the interleukin-10 promoter variant at position -819 T/C modulates interleukin-10 levels independently of prostaglandin E2 (Fitriyanti et al., 2026).

All bacteriological correlations in the aforementioned previous studies relied on a single aggregate bacterial index value per patient derived from the average of skin scraping examinations. This aggregate approach obscures two distinct bacteriological pieces of information beyond mere bacterial density. First, the distribution of bacteria across anatomical sites, since standard testing covers six sites including both earlobes, both hands, and both feet whose severity can vary significantly within the same patient. Second, the proportion of viable bacteria, which is reflected in the morphology index through the calculation of bacteria that fully absorb the stain compared with fragmented or granular bacteria (Malhotra & Husain, 2022). The bacterial index and the morphology index measure two distinct bacteriological dimensions the former describing quantity and the latter describing viability and thus neither can replace the other in assessing disease activity.

As of the writing of this manuscript, there have been no reports examining whether the morphology index and distribution patterns of acid-fast bacilli (AFB) across locations are associated with the levels of interleukin-10, prostaglandin E2, or interleukin-35-. This gap warrants further investigation because the morphology index is clinically used to monitor the response to multidrug therapy, but the immunological mechanisms underlying the reduction in bacilli viability during therapy remain poorly understood. If bacillary viability and its distribution patterns are associated with these immunosuppressive mediators, these findings could enhance our understanding of the relationship between the host's immune response and the biological state of the bacilli rather than merely their quantity.

This study aimed to analyze the relationships between the morphology index and smear patterns at six anatomical sites and serum levels of interleukin-10, prostaglandin E2, and interleukin-35 in multibacillary leprosy patients in Banyuasin Regency, South Sumatra. The results of this study provide an empirical basis for the role of the morphology index and multilocalized

smear patterns as complementary bacteriological variables to the bacterial index in future research on the immunopathogenesis of leprosy.

METHODS

This was an analytical cross-sectional study conducted as a follow-up analysis of a cohort of multibacillary leprosy patients who were recruited at Rivai Abdullah Regional General Hospital and Sukajadi Community Health Center, Banyuasin Regency, South Sumatra, from January to July 2025. Examination of acid-fast bacilli by anatomical site and morphology index was performed on July 28, 2025; these data were then combined with previously obtained serum measurements of interleukin-10, prostaglandin E2, and interleukin-35 from the same cohort. Laboratory analysis for enzyme-linked immunosorbent assay (ELISA) testing was performed at the Biotechnology Laboratory, Faculty of Medicine, Sriwijaya University, Palembang. The study population consisted of patients with multibacillary leprosy who received treatment at Rivai Abdullah Regional General Hospital and the Sukajadi Community Health Center. The inclusion criteria included being at least 18 years of age, having a diagnosis of multibacillary leprosy based on the World Health Organization's clinical criteria accompanied by a positive skin scraping result, not having received multidrug therapy or having started it less than one month prior, and being willing to participate in the study by signing a written informed consent form. The exclusion criteria included autoimmune diseases, malignancies, or other severe infections that could affect serum cytokine levels; the use of immunosuppressants, systemic corticosteroids, or nonsteroidal anti-inflammatory drugs within the past 30 days; pregnancy or breastfeeding; and incomplete laboratory data. Samples were collected via consecutive sampling from all patients who met the inclusion criteria during the recruitment period. The number of patients analyzed in this study was 30 for interleukin-10 and prostaglandin E2 and 29 for interleukin-35, with smaller subsets of 20 and 19 patients, respectively, for the morphology index, as this index is defined only in patients with positive acid-fast bacilli results.

Acid-fast bacilli testing was performed via skin scrapings at six standard sites, namely, the right and left earlobes, the backs of the right and left hands, and the backs of the right and left feet, plus one site of active skin lesion if identified. Smears were stained using a modified Ziehl–Neelsen technique and evaluated by trained laboratory personnel. The bacterial index at each site is expressed on a Ridley logarithmic scale ranging from negative to 5+ on the basis of the available data, and the morphological index is calculated as the percentage of bacilli that take up the stain completely reflecting viable bacilli out of the total number of bacilli observed in positive smears (Malhotra & Husain, 2022). Venous blood samples were collected from each participant for serum separation. Interleukin-10 and prostaglandin E2 levels were measured using an enzyme-linked immunosorbent assay (ELISA), while interleukin-35 levels were measured using a method similar to that used in a previous study in this cohort. All laboratory tests were performed by personnel who were unaware of the detailed clinical status of the samples being tested. Morphological index data and patterns of acid-fast bacilli results per site were extracted from examination records dated July 28, 2025. From these data, five bacteriological metrics were derived for each patient: the morphology index; the number of sites with positive acid-fast bacilli among the six standard sites; the average acid-fast bacilli grade across all six sites; the maximum grade among the six sites; and the range of grades between the site with the highest result and the site with the lowest result. These data were then combined with data on interleukin-10 and prostaglandin E2 levels using laboratory test sample serial numbers, while data on interleukin-35 levels were combined by matching patient identities to previous test records in the same cohort. Patients who did not have a confirmed match for any of the immune markers were excluded from the analysis.

Basic sample characteristics are presented as medians and interquartile ranges for numerical variables and as frequencies and percentages for categorical variables. The relationships between each bacteriological metric and each immune marker were tested using Spearman's rank correlation. The 95% confidence interval for the correlation coefficient was calculated using the bootstrap method with 2,000 resampling iterations. Since fifteen pairs of correlations were tested simultaneously, the P values from all tests were collectively corrected using the Benjamini–

Hochberg method to control the false discovery rate. P values less than 0.05 were considered to indicate statistical significance, with the primary interpretation being based on the corrected P values. All data analysis and figure creation were performed using R software version 4.3, with the dplyr, readxl, ggplot2, and patchwork packages.

RESULT AND DISCUSSION

In this study, 30 patients with multibacillary leprosy were analyzed for correlations with interleukin-10 and prostaglandin E2, and 29 patients were analyzed for correlations with interleukin-35. The baseline characteristics of the two sample groups are presented in Table 1. The median age in the interleukin-10 and prostaglandin E2 groups was 41.5 years (interquartile range 23.25), with 17 men and 13 women. The median age in the interleukin-35 group was 42 years (interquartile range 21), with 17 men and 12 women. Among the 30 patients in the first group, 20 patients tested positive for acid-fast bacilli at least one site and had a calculable morphology index, with a median of 9% (interquartile range 12, overall range 3 to 35%). A total of 18 out of 30 patients tested positive at all six examination sites, while 10 patients tested negative at all sites.

Table 1. Baseline characteristics of the analyzed sample

Characteristics	IL-10/PGE2 Group (n=30)	IL-35 Group (n=29)
Age, median (IQR), years	41.5 (23.25)	42 (21)
Male, n (%)	17 (56.7)	17 (58.6)
Female, n (%)	13 (43.3)	12 (41.4)
Negative sputum smear results at 6 sites, n (%)	10 (33.3)	-
Positive sputum smear results at 6 locations, n (%)	18 (60.0)	-
Calculated morphological index (positive BTA), n	20	19
Morphological Index (%), median (RIK)	9 (12)	-
IL-10 (pg/mL), median (RIK)	2.06 (4.69)	-
PGE2 (pg/mL), median (RIK)	1,244.02 (456.32)	-
IL-35 (pg/mL), median (RIK)	-	3.47 (20.95)

IQR = interquartile range; AFB = acid-fast bacilli.

Table 2 presents the results of the Spearman's correlation test for all 15 pairs of bacteriological variables and immunological markers. The correlation coefficients ranged from -0.27 to 0.18. Before correction for multiple testing, the P values ranged from 0.15 to 0.97. After Benjamini–Hochberg correction, all corrected P values fell within the range of 0.96–0.97, indicating that none of the correlation pairs were statistically significant. The correlation coefficient with the greatest magnitude was found between the number of acid-fast bacilli-positive sites and prostaglandin E2 ($\rho = -0.27$, P = 0.157, 95% confidence interval −0.559 to 0.066) and between the mean degree of acid-fast bacilli and prostaglandin E2 ($\rho = -0.27$, P = 0.154, 95% confidence interval −0.533 to 0.090), as shown in Figure 3. For interleukin-10, the highest correlation coefficients were found for the mean degree of acid-fast bacilli (rho 0.16, P= 0.406) and the maximum degree of acid-fast bacilli (rho 0.12, P 0.523); both were positively correlated but with confidence intervals that crossed zero, as shown in Figure 2.

For interleukin-35, the highest correlation coefficients were found for the intersite degree range (rho = −0.17, P = 0.387), followed by the morphology index (rho = −0.10, P = 0.685); both were also nonsignificant, as shown in Figure 1. All correlation coefficients in a single correlogram are summarized in Figure 4, revealing inconsistent directional patterns among the three immune

markers: prostaglandin E2 tends to correlate negatively with nearly all metrics of acid-fast bacilli severity, whereas interleukin-10 tends to correlate positively, albeit weakly, and interleukin-35 does not show a clear directional pattern.

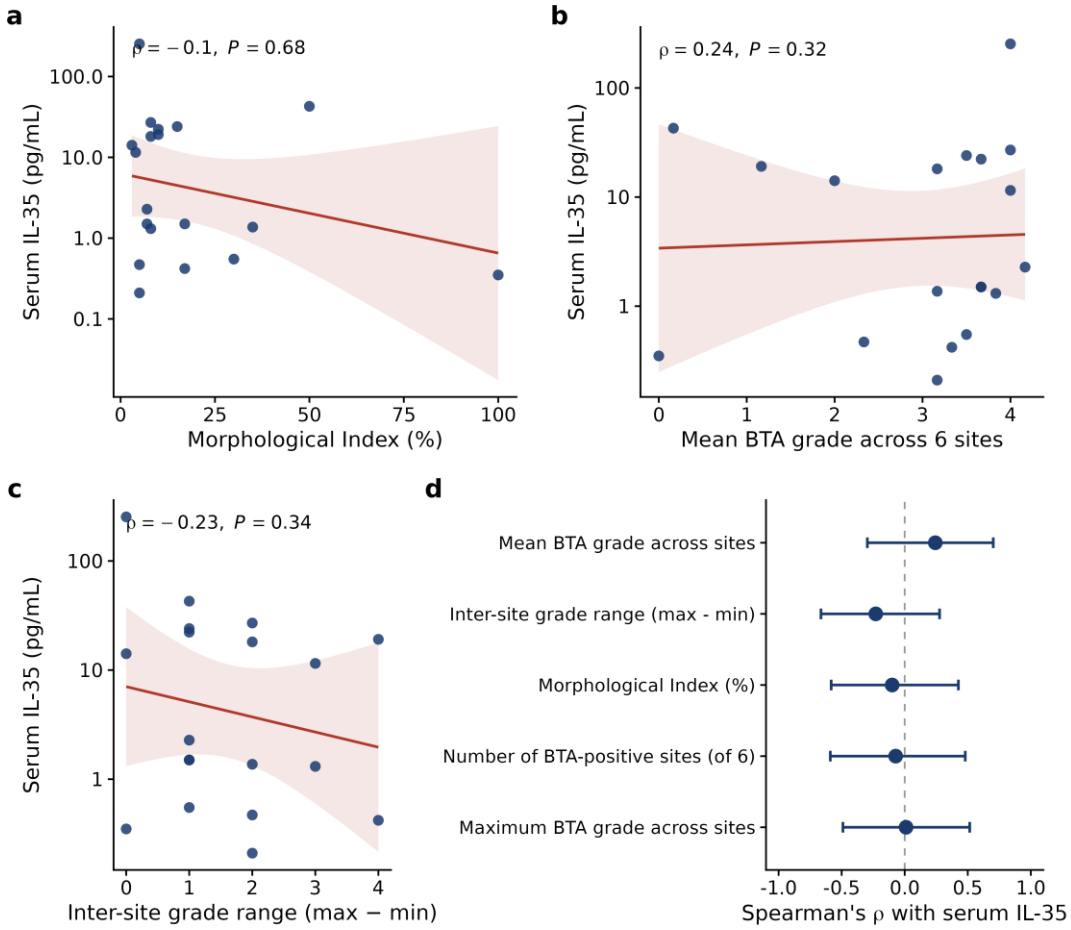

Figure 1. Correlation between morphological indices and acid-fast bacilli patterns by location and IL-35 concentration. (a–c) Scatter plots of the three bacteriological metrics with the highest coefficients of determination against IL-35; red lines indicate linear regression with 95% confidence intervals. (d) Summary of Spearman's correlation coefficients for the five metrics, along with 95% bootstrap confidence intervals.

Table 2. Spearman's correlation between bacteriological metrics and immune markers

Bacteriological metrics	Immune Markers	n	rho	95% CI	P	P-FDR
Cross-site average BTA score	IL-10	30	0.16	-0.23 – 0.50	0.406	0.960
Maximum BTA across locations	IL-10	30	0.12	-0.24 – 0.49	0.523	0.960
Morphological Index	IL-10	20	~0.04	-0.53 – 0.45	0.869	0.960
Degree range between locations	IL-10	30	~0.04	-0.43 – 0.37	0.839	0.960
Number of BTA-positive sites	IL-10	30	0.04	-0.35 – 0.42	0.843	0.960

Bacteriological metrics	Immune Markers	n	rho	95% CI	P	P-FDR
Degree range between locations	IL-35	29	~0.17	-0.53 – 0.22	0.387	0.960
Morphological Index	IL-35	19	~0.10	-0.59 – 0.44	0.685	0.960
Cross-site average BTA score	IL-35	29	0.07	-0.30 – 0.44	0.704	0.960
Number of BTA-positive sites	IL-35	29	~0.05	-0.44 – 0.35	0.805	0.960
Maximum BTA across locations	IL-35	29	~0.03	-0.39 – 0.32	0.896	0.960
Cross-site average BTA score	PGE2	30	~0.27	-0.53 – 0.09	0.154	0.960
Number of BTA-positive sites	PGE2	30	~0.27	-0.56 – 0.07	0.157	0.960
Maximum BTA across locations	PGE2	30	~0.18	-0.47 – 0.14	0.351	0.960
Morphological Index	PGE2	20	0.14	-0.41 – 0.62	0.568	0.960
Degree range between locations	PGE2	30	0.01	-0.40 – 0.40	0.966	0.966

Remarks: 95% CI = 95% confidence interval (bootstrap method, 2,000 resamples); P-FDR = Benjamini–Hochberg-corrected P value.

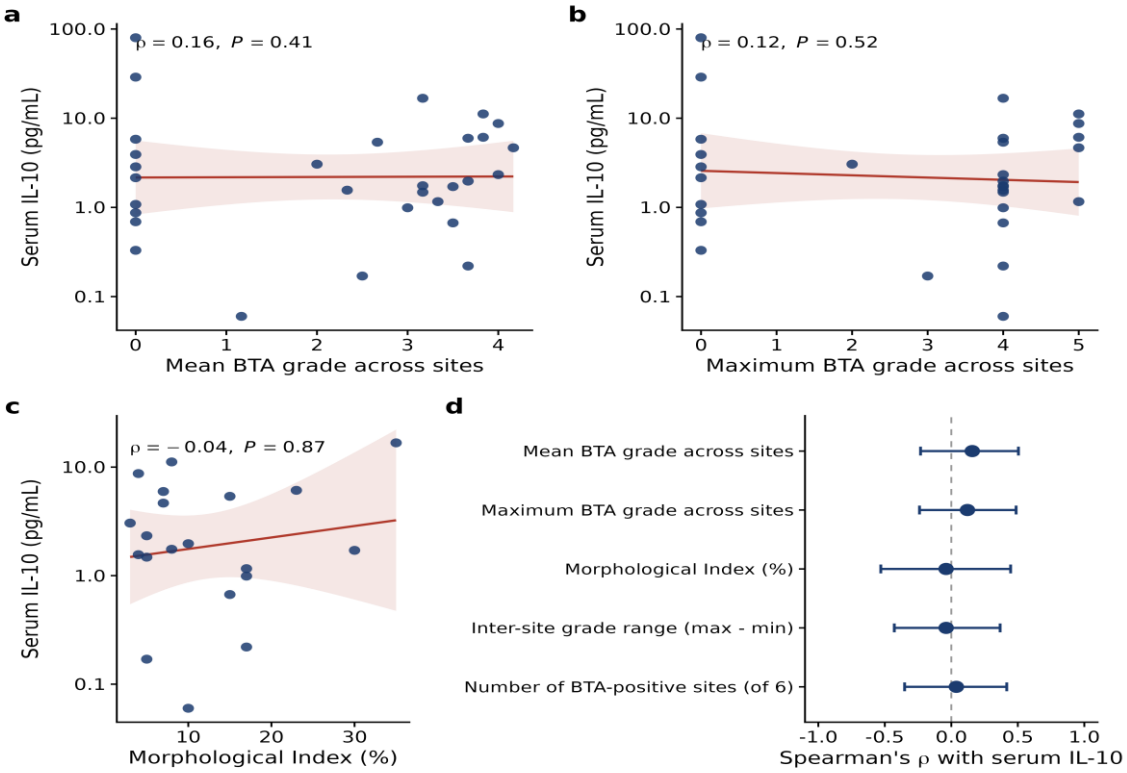

Figure 2. Correlation between morphological indices and acid-fast bacilli patterns by location and IL-10 concentration. (a–c) Scatter plots of the three bacteriological metrics with the highest

coefficients of determination for IL-35; red lines indicate linear regression with 95% confidence intervals. (d) Summary of Spearman's correlation coefficients for the five metrics, along with 95% bootstrap confidence intervals.

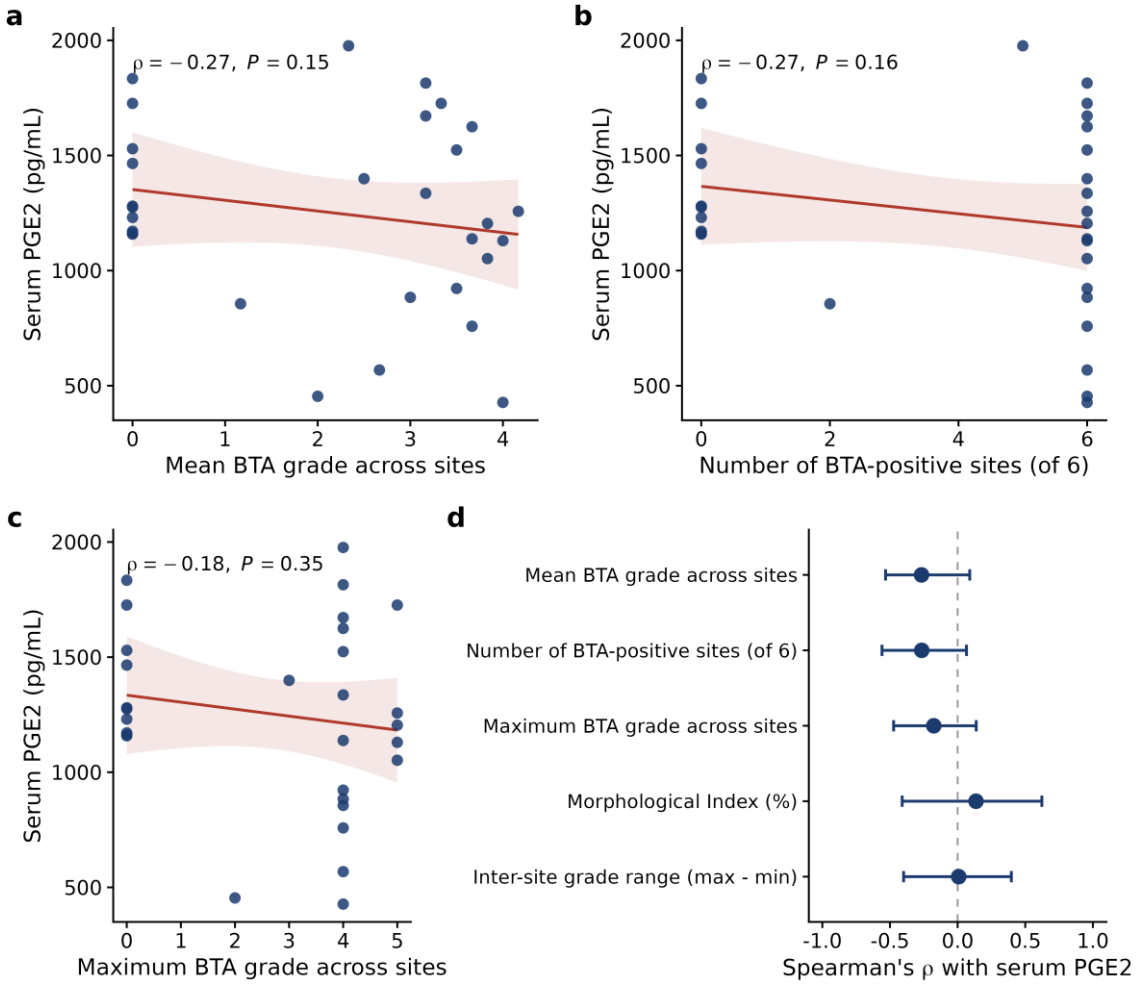

Figure 3. Correlation between morphological indices and acid-fast bacilli patterns per location with PGE2. (a–c) Scatter plots of three bacteriological metrics with the highest coefficient of determination for IL-xml-ph-0000@deepl.internal35; the red line indicates linear regression with a 95% confidence interval. (d) Summary of Spearman's correlation coefficients for the five metrics, along with 95% bootstrap confidence intervals.

This study examined whether the morphology index and pattern of acid-fast bacilli at six anatomical sites were associated with serum levels of interleukin-10, prostaglandin E2, and interleukin-35 in patients with multibacillary leprosy. Of the 15 correlation pairs tested, none remained statistically significant after correction for multiple testing. These findings suggest that, in the available sample, bacilli viability and their distribution patterns across body sites cannot be distinguished from the absence of a relationship with these three immunosuppressive mediators.

Interleukin-10 in this cohort was previously reported to be positively correlated with the aggregate bacterial index in patients with multibacillary leprosy (Fitriyanti et al., 2025), which is consistent with the general model in which interleukin-10 suppresses effector T-cell activity, thereby allowing *Mycobacterium leprae* to replicate more freely (Couper et al., 2008). In this study, interleukin-10 levels did not correlate with the morphology index, the number of positive sites, or the mean smear grade. This difference in pattern is biologically plausible if interleukin-10 production is more strongly influenced by the total systemic antigenic load than by the spatial distribution or proportion of viable bacilli at specific examination sites. Macrophages and dendritic

cells, which are the primary sources of interleukin-10, are distributed throughout all compartments of infected tissue (Chen et al., 2023); thus, serum levels likely reflect the accumulation of signals from multiple foci of infection rather than the condition at a single examination site. This explanation is provisional and requires confirmation in a study design that allows for the measurement of interleukin-10 in local tissue, not just serum.

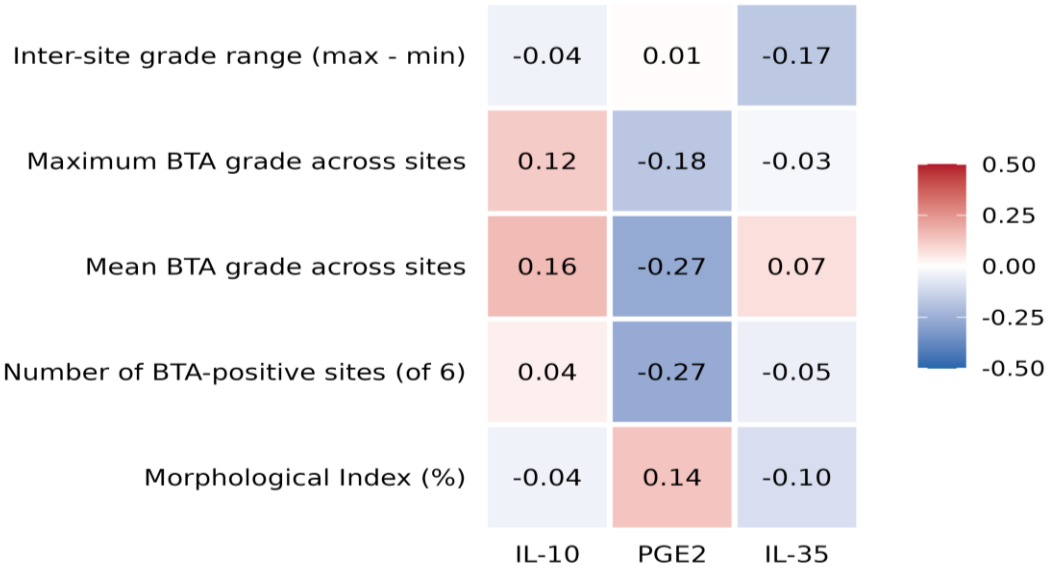

Figure 4. Correlogram of Spearman's correlation coefficients between the five bacteriological metrics (rows) and three immune markers (columns). An asterisk indicates $P < 0.05$ before correction for multiple tests.

Prostaglandin E2 had the highest correlation coefficient among the three mediators, although it remained statistically insignificant, with a negative relationship with the number of BTA-positive sites and the mean BTA score. This negative relationship contradicts the simple assumption that immunosuppressive mediators increase with increasing bacterial load. Prostaglandin E2 plays a dual role in tissue biology: on the one hand, it suppresses interferon-gamma-mediated macrophage activation; on the other hand, it contributes to postinflammatory tissue regeneration and repair (Wang et al., 2025). If part of the measured prostaglandin E2 levels originates from tissue repair processes at the site of skin lesions rather than solely from a response to bacterial density, then this weak negative pattern can be understood as a reflection of local metabolic activity that is not directly proportional to the number or distribution of bacteria. A previous study in the same cohort also revealed no correlation between the aggregate bacterial index and prostaglandin E2; thus, the findings of this study reinforce the pattern that prostaglandin E2 consistently shows no measurable association with bacterial load in this population, regardless of how that load is operationalized. Another possibility to consider is the pharmacokinetic characteristics of prostaglandin E2 itself, which has a very short half-life and is prone to degradation during sample processing; thus, technical variations in blood collection could introduce measurement noise that obscures the biological relationship that actually exists.

Interleukin-35 in this cohort was previously reported to be elevated in the multibacillary leprosy group compared with the healthy control group, but it did not correlate with the aggregate bacterial index. This study extends this null pattern to the morphology index and all BTA location pattern metrics. This pattern differs from that in the report by Tarique et al. (2017) on a cohort in India, in which a positive correlation between the proportion of interleukin-35-producing regulatory T cells and the bacterial index in patients with late-stage disease was detected. This discrepancy in results most likely stems from differences in tissue compartments and measurement methods; the study by Tarique et al. measured the frequency of interleukin-35-producing cells via flow cytometry on peripheral blood mononuclear cells, whereas this study measured the

concentration of free interleukin-35 in serum via ELISA. The frequency of cells producing a cytokine does not always correlate directly with the concentration of free cytokines circulating in the blood, as factors such as secretion, degradation, and binding to soluble receptors can influence serum levels independently of the number of source cells. Differences in genetic background and disease stage across populations are also potential explanatory factors that cannot be separated from these methodological differences.

When viewed as a whole, neither the five bacteriological metrics tested in this study nor the aggregate bacterial index tested in a previous study of the same cohort showed a consistent and significant association with these three immune mediators. This recurring pattern suggests that the levels of immunosuppressive mediators in multibacillary leprosy are determined more by a relatively stable immunoregulatory equilibrium in each individual, reflecting the commitment of regulatory T-cell lineages and the host's genetic background (Nath, 2016), rather than by fluctuations in the number or viability of bacilli at the time of examination. This interpretation is consistent with a model of relatively stable T-cell anergy at the lepromatous pole, which posits immune dysregulation as a preexisting condition rather than a mere reaction to daily variations in bacillary load.

The above interpretation must still account for the possibility that the sample size of this study, which ranged from nineteen to thirty patients depending on the metric tested, was not large enough to detect weak-to-moderate correlations, even if such relationships did exist in a broader population. The confidence intervals for all correlation pairs extend beyond zero in both directions; therefore, these findings should most appropriately be interpreted as insufficient evidence to conclude whether a relationship exists rather than as definitive evidence of its absence. The combination of a limited sample size and high interindividual biological variability in cytokine levels, as reflected in the wide interquartile ranges for all three immune markers, results in low statistical power for this study to detect effects that are more subtle than the previously reported differences between patient and control groups.

The recurring null results in this study are also consistent with those of a recent systematic review on the immunopathogenesis of leprosy, which identified the dysregulation of regulatory T cells and an immunosuppressive cytokine network as relatively uniform features across all the lepromatous patients, without a clear gradation corresponding to variations in bacterial load among multibacillary patients (Silva et al., 2024; Grijsen et al., 2024). In other words, the bacterial load threshold separating the lepromatous from the tuberculoid phenotypes appears to determine an individual's immune profile more strongly than variations in the number or viability of bacteria within the lepromatous phenotype itself. If so, studies comparing multibacillary patients with healthy controls are more likely to find sharp differences in cytokine levels, while studies correlating bacteriological variations among multibacillary patients themselves, such as the present study, tend to find weak or no associations because the range of immunological variation within the multibacillary group is much narrower than the range of differences between the multibacillary group and the control group.

This explanatory framework is also relevant for understanding why macrophages infected with *Mycobacterium leprae* tend to polarize toward the M2 phenotype, which is permissive toward the pathogen immediately after chronic infection develops itself, rather than changing gradually in response to fluctuations in bacilli counts over time (Cabral et al., 2022). This relatively stable macrophage polarization also helps explain why regulatory T cells, which are the primary source of interleukin-35 and influence transforming growth factor beta levels in this cohort, appear to be more strongly affected by a cell differentiation program established early in the disease course than by more dynamic bacteriological signals (Liu et al., 2016). Consequently, the search for immunological biomarkers that are truly sensitive to changes in bacterial load or viability may need to focus on markers that directly reflect cellular activity, such as gene expression in regulatory T cells, rather than the concentration of free cytokines in serum, which undergo multiple layers of regulation before they can be measured.

From a field practice perspective, these results are relevant to how leprosy control programs in Indonesia should prioritize bacteriological testing. The national program has long relied on the

aggregate bacterial index as the primary marker for classification and treatment monitoring, given the limited laboratory resources in many primary health care facilities in endemic areas (Lubis et al., 2022; Sebong et al., 2025). The absence of a detected association between the morphology index or multilocation BTA patterns and the three immune markers in this study suggests that simplifying the assessment to a single aggregate bacterial index value at least for the purpose of estimating systemic immunological activity does not appear to result in a significant loss of information that could be captured through per-location testing or the more time- and labor-intensive calculation of the morphology index.

Moving forward, exploring the relationship between bacillary viability and immunosuppressive mediators in multibacillary leprosy will be more informative if a longitudinal study is designed to track the decline in the morphology index during multidrug therapy alongside serial measurements of interleukin-10, prostaglandin E2, and interleukin-35 levels in the same patients. Such a design would allow for an assessment of whether changes in bacilli viability over time rather than values at a single point in time are associated with changes in the immune profile. The addition of measurements at the cellular level, such as the frequency of interleukin-35-producing regulatory T cells via flow cytometry or FOXP3 mRNA expression via real-time PCR, which were not yet performed in this cohort, would complement the picture currently derived solely from serum concentrations. Multicenter studies with larger sample sizes are needed to determine whether the consistent "zero" pattern observed in the Banyuasin cohort also applies to multibacillary leprosy populations in other endemic regions of Indonesia.

Clinical And Public Healts Implications

In clinical practice, the examination of morphological indices and acid-fast bacilli patterns by site remains relevant as a tool for bacteriological monitoring and assessing the response to multidrug therapy, regardless of the results of this study, because these two examinations assess different biological aspects of the bacilli as opposed to their immunological functions. However, the lack of an association with interleukin-10, prostaglandin E2, or interleukin-35 indicates that these two tests cannot yet be relied upon as substitutes for or simple predictors of a patient's systemic immunological status. With respect to public health programs in endemic areas with limited laboratory resources, these findings support the feasibility of retaining the aggregate bacterial index as the primary bacteriological marker for program classification and monitoring without the loss of significant immunological information compared with site-specific tests, which are more operationally complex.

Limitations

The sample size ranged from nineteen to thirty patients depending on the metric tested, resulting in limited statistical power to detect weak- to moderate-strength correlations. The cross-sectional design with a single time point of measurement does not allow causal or temporal conclusions to be drawn between bacterial viability and immune mediator levels. Bacteriological data and immunological serum data were obtained from examination visits that were not always concurrent; thus, variations between collection times could add measurement noise. Interleukin-35 levels were available only for some patients through identity matching with previous examination records, rather than through direct laboratory sample numbers, as was the case for interleukin-10 and prostaglandin E2 levels. This study also included a single district; therefore, caution is needed when the results should be generalized to multibacillary leprosy populations in other endemic regions.

CONCLUSION AND SUGGESTION

This study found no statistically significant associations between morphological indices or multilocalised acid-fast bacilli patterns and serum levels of interleukin-10, prostaglandin E2, or interleukin-35 among patients with multibacillary leprosy in Banyuasin, South Sumatra. These findings indicate that the bacteriological parameters examined were not significantly associated with the selected systemic immune mediators in this study population. However, the findings do not exclude potential relationships that may emerge through longitudinal assessment or the examination of additional immunological markers.

Future research should involve larger samples, longitudinal designs, repeated bacteriological and immunological measurements, and cellular markers such as regulatory T-cell frequencies to clarify the relationship between bacillary characteristics and immunosuppressive profiles. Clinicians should continue using morphological indices and acid-fast bacilli assessments for bacteriological monitoring and treatment-response evaluation, rather than treating them as substitutes for immunological assessment. Public health authorities should support integrated bacteriological and immunological research in diverse endemic settings to strengthen the evidence base for leprosy monitoring and inform context-appropriate clinical and public health strategies.

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