

A STUDY OF HISTOMORPHOLOGICAL SPECTRUM OF ON TREATMENT CASE OF LEPROSY AT TERTIARY CARE CENTER OF CENTRAL GUJARAT

Pathology

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ABSTRACT

Background: Leprosy is one of the ancient disease, still India continue to bear highest burden of leprosy worldwide, remains an important public-health concern. Histopathological assessment during multidrug therapy (MDT) can help distinguish resolving lesions from persistent activity, lepra reactions, relapse, and inactive lesions histologically. Clinical improvement and tissue-level resolution do not always occur in parallel. **Aim and Objective:** To describe histomorphological spectrum of progression or regression of leprosy disease in paired pre-treatment and on-treatment skin biopsies, with emphasis on epidermal and dermal changes, inflammatory infiltrates, and bacillary index. **Methods:** This retrospective observational study was conducted in the Department of Pathology, Medical College and S.S.G. Hospital, Vadodara, Gujarat, from October 2023 to September 2025. Fifty paired pre-treatment and on-treatment biopsies were reviewed. Haematoxylin and eosin (H&E)-stained sections were assessed for histomorphological features and Ridley–Jopling subtype; Fite–Faraco staining was used to evaluate acid-fast bacilli and bacillary index. **Results:** The mean age was 40.1 ± 15.1 years and 64% of participants were male. Lepromatous leprosy was the most frequent pre-treatment subtype (30%), followed by borderline tuberculoid (24%), tuberculoid (22%), borderline lepromatous (20%), and borderline-borderline leprosy (4%). Bacillary-index-negative biopsies increased from 62% pre-treatment to 88% on-treatment. Histopathological regression was recorded in 45/50 cases (90%); progression in 3 (6%); erythema nodosum leprosum in 1 (2%); and relapse in 1 (2%). Treatment-associated patterns included reduced inflammatory infiltrates and granulomas, increased basal-layer pigmentation, intradermal edema, dermal sclerosis, fibroplasia, fibromyxoid change, and telangiectasia. **Conclusion:** Paired biopsies histopathological assessment, interpreted alongside clinical findings, treatment history, and bacillary morphology, can provide useful evidence of tissue response during MDT.

KEYWORDS

Bacillary Index; Fite–faraco Stain; Leprosy; Multidrug Therapy.

INTRODUCTION

Leprosy is a chronic infection caused mainly by *Mycobacterium leprae* and primarily affects the cooler tissue of body, especially the skin and peripheral nerves. Delayed diagnosis or management of neuritis can result in permanent disability. The clinical and histological expression of infection is shaped substantially by host cell-mediated immunity, producing a spectrum from tuberculoid disease, with well-formed granulomas and few bacilli, to lepromatous disease, with sheets of foamy macrophages containing numerous bacilli.^[1-6] The Ridley–Jopling classification remains useful for clinicopathological interpretation.^[7-10]

Histology is particularly valuable when clinical features are equivocal, when borderline lesions show reactional change, or when lesions persist during or after MDT. H&E staining demonstrates the pattern of inflammation, granuloma formation, neural and adnexal involvement, and tissue repair. Fite–Faraco staining helps identify bacilli in tissue and supports assessment of the bacteriological index using Ridley's logarithmic scale.^[8,11] The global strategy to interrupt transmission and reduce leprosy-related disability underscores the importance of timely diagnosis and appropriate follow-up.^[12,13]

Treatment does not immediately erase all tissue-level evidence of infection. In paucibacillary disease, inflammation and granulomas may regress relatively quickly, whereas foamy macrophages and fragmented bacillary remnants can persist in multibacillary disease. Treated lesions may show fibrosis, sclerosis, fibromyxoid stromal change, altered basal pigmentation, and sparse lymphoplasmacytic inflammation. These changes may be mistaken for other dermatoses if the history of leprosy and treatment is not available.^[14-17] Conversely, persistent or new lesions may reflect a lepra reaction, active progression, or relapse, each of which has different clinical implications and may create clinical dilemma.^[2,8,18]

This study describes histological patterns in paired pre-treatment and on-treatment biopsies from a tertiary care centre in Central Gujarat, with attention to tissue with regression or progression of disease, bacillary persistence, and findings that warrant clinicopathological reassessment.

Materials and Methods

Study design and setting

A retrospective observational study was conducted in the Department of Pathology, Medical College and S.S.G. Hospital, Vadodara, Gujarat, India, from October 2023 to September 2025. The study included 50 paired skin-biopsy sets comprising pre-treatment and on-treatment biopsies from the same participants who attended the dermatology outpatient clinic.

Eligibility and data collection

Adequately preserved skin biopsies from patients with leprosy, including pre-treatment and on-treatment biopsies, were included. Inadequate, necrotic, or poorly preserved skin biopsies were excluded. Demographic details, clinical information, biopsy site, treatment status, histopathological classification, and available laboratory findings were abstracted retrospectively from pathology registers, requisition forms, reports, and archived records.

Histopathological assessment

Haematoxylin and eosin (H&E)-stained sections were reviewed for epidermal and dermal changes in the pre-treatment biopsy and compared with the corresponding follow-up biopsy. Fite–Faraco staining was assessed for the presence and morphology of acid-fast bacilli, and the bacillary index.

RESULTS

Demographic and clinical profile

The study included 50 paired pre-treatment and on-treatment skin-biopsy sets. The mean age was 40.1 ± 15.1 years, and the largest age group was 31–40 years (30%). Males accounted for 64% of participants and females for 36%. The back was the most common biopsy site (40%), followed by the forearm (34%). At on-treatment assessment, 49 participants (98%) attended for follow-up; one participant (2%) had new skin lesions over the back.

Pre-treatment Ridley–Jopling spectrum

Lepromatous leprosy (LL) was the most frequent pre-treatment subtype (15/50; 30%), followed by borderline tuberculoid leprosy (BT; 12/50; 24%), tuberculoid leprosy (TT; 11/50; 22%), borderline lepromatous leprosy (BL; 10/50; 20%), and borderline-borderline leprosy (BB; 2/50; 4%). Thus, the pre-treatment biopsies represented the full Ridley–Jopling spectrum, with LL as the largest subgroup.

Bacillary index pre-treatment and post-treatment

As shown in Table 1, bacillary-index-negative biopsies increased from 31/50 (62%) pre-treatment to 44/50 (88%) on-treatment. Pre-treatment, higher bacillary-index grades included 2+ in 8%, 3+ in 6%, 4+ in 12%, 5+ in 10%, and 6+ in 2%. During treatment, recorded categories included grade 1+ (4%), grade 1+ with fragmented bacilli (2%), grade 4+ (4%), and grade 5+ (2%); grades 2+, 3+, and 6+ were not recorded. Overall, the distribution shifted towards negative or lower bacillary-index categories, although bacillary morphology and inflammatory activity remain important to interpretation.

The epidermal and dermoepidermal changes observed in paired biopsies. Increased basal-layer melanin pigmentation was recorded in 43/50 on-treatment biopsy (86%), compared with 7/50 pre-treatment biopsy (14%). Rete ridges were described as starting to reappear in 21/50 on-treatment specimens (42%), while loss of rete ridges decreased from 66% pre-treatment to 36% on-treatment. Melanophages at the dermoepidermal junction were also more frequent during treatment (20% versus 4%). On assessment of dermal features, the proportion of biopsies with mild or scanty inflammatory infiltrates increased, while dense or moderate infiltrates decreased. Granulomas were absent in 72% of on-treatment specimens compared with 52% of pre-treatment specimens. Dense and moderate perineural inflammation decreased, whereas mild or scanty inflammation was more frequent. Dermal remodelling features recorded during treatment included intradermal oedema (60%), fibromyxoid change (68%), fibroplasia (82%), dermal sclerosis (78%), and telangiectasia (64%). Representative paired histomorphological appearances are shown in Figures 1–3.

Overall histopathological interpretation

Overall histopathological interpretation is summarised in Table 2. Regression was recorded in 45 cases (90%), progression in three cases (6%), erythema nodosum leprosum (ENL) in one case (2%), and relapse in one case (2%). These are descriptive interpretations of the reviewed records and should be correlated with clinical findings and treatment history.

DISCUSSION

This paired-biopsy series describes a broad histomorphological spectrum of leprosy during treatment and illustrates tissue response.

Morphological indicators of regression

The findings summarised in Table 2 and illustrated in Figures 1–3 show a reduction in dense inflammatory infiltrates, fewer well-formed granulomas and Virchow cells, and a shift towards mild or scanty perivascular, periadnexal, and perineural inflammation during treatment. Recurrent epidermal findings included increased basal-layer melanin pigmentation and reappearance of rete ridges. Dermal changes—including oedema, fibroplasia, dermal sclerosis, and telangiectasia—were more frequent in on-treatment biopsies. These observations accord with descriptions of treated leprosy in which reparative dermal remodelling and residual pigmentary changes may persist after active inflammation has diminished.^[8,10,14–17]

These features are useful clues rather than individually definitive markers. Dermal sclerosis and mucin may mimic morphea or connective-tissue disease, while foamy histiocytes may resemble xanthomatous processes. Interpretation should integrate lesion distribution, prior diagnosis, treatment duration, neural/adnexal involvement, and Fite–Faraco findings. In the correct clinical context, a relatively flat epidermis with increased basal melanin, sparse

inflammation, and fibrosclerotic stroma may support treated, less-active leprosy.^[8,10]

Interpreting bacillary persistence

The increase in bacillary-index-negative specimens from 62% to 88% (Table 1) supports an overall decline in demonstrable bacillary load. Higher grades were mostly confined to pre-treatment biopsies, while low-grade and fragmented bacilli were observed in some on-treatment biopsies. This is plausible because MDT kills bacilli, but clearance of bacillary remnants and lipid-rich macrophage contents may lag behind clinical improvement.^[14,16,17,19]

The bacillary index is a semiquantitative measure of bacillary density, not a direct viability assay. Fragmented or granular bacilli are not equivalent to solid-staining bacilli. Suspected relapse warrants comparison with previous clinical and bacteriological findings, assessment for new or progressive lesions and renewed activity, review of adherence and treatment history, and drug-resistance testing where available.^[8,18,20]

Reactional disease and diagnostic separation

Lepa reactions may occur during or after MDT and can produce marked inflammation without necessarily indicating bacillary multiplication. Type 1 (reversal) reactions typically show edema and increased granulomatous inflammation, often with nerve involvement; erythema nodosum leprosum (ENL) may show neutrophils, vasculitis, and panniculitis in the context of multibacillary disease.^[2,8–10,21] The single ENL case in this study highlights the need to identify reactional pathology separately from simple regression or progression of disease. Histology should be interpreted with symptom timing, nerve-function changes, systemic features, and dermatological assessment.

Clinical implications

A structured reporting approach can improve consistency: (1) state the pattern and estimated activity of inflammation; (2) describe granuloma formation and neural/adnexal involvement; (3) document bacillary presence and morphology; (4) record reparative features; and (5) provide a cautious integrated interpretation, such as findings favouring regression, persistent activity, reaction, or relapse. Clinical follow-up and assessment of barriers to attendance are also important, as stigma and social factors can affect engagement with care.^[12,13,22] Biopsy findings should complement rather than replace clinical assessment and established programme guidance.

CONCLUSION

The present study demonstrate multidrug therapy was associated with characteristic histomorphological changes in leprosy lesions. Reduction in inflammatory infiltrates and granulomas, reparative stromal changes, and increased basal-layer melanin pigmentation were common findings. Lepromatous leprosy was the predominant pretreatment subtype. Most cases showed histological regression, while a small proportion showed progression, ENL, or possible relapse.

The most consistent treatment-associated findings were reduced inflammation, dermal sclerosis and fibroplasia, and increased basal-layer melanin pigmentation. H&E examination together with Fite–Faraco staining and assessment of bacillary morphology remains useful for evaluating tissue response. These findings should be interpreted in conjunction with clinical course, treatment history, and programme guidance.

The principal diagnostic lesson is that treated lesions may retain bacillary remnants and distinctive stromal or pigmentary changes even when disease activity is regressing. Reliable interpretation requires clinicopathological correlation and careful assessment of bacillary morphology; persistent or new lesions merit targeted clinical reassessment rather than automatic retreatment.

Declarations

Ethics approval: The study was conducted only after obtaining permission from the local research advisory committee, scientific committee and the institutional ethics committee for biomedical and health research of medical college and ssg hospital, vadodara.

Informed consent: All patients has provided informed consent for the publication.

Author contributions:

Author 1: Methodology, investigation, and writing – original draft.
 Author 2: Data collection, formal analysis, and writing – original draft.
 Author 3: Data curation, formal analysis, and writing – review and editing.
 Author 4: Formal analysis, critical review, manuscript and image editing.
 Author 5: Supervision, guidance, critical review, and editing of the manuscript.
 Author 6: Study design, conceptualization, senior supervision, project administration, guidance, and final review of the manuscript.

Data availability: De-identified data may be made available from the corresponding author subject to institutional approval and privacy requirements, if accurate.

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Tables and figures

Table 1. Distribution of bacillary index categories in pre-treatment and on-treatment skin biopsies.

Bacillary Index category	Pre-treatment n (%)	On-treatment n (%)
Negative	31 (62.0)	44 (88.0)
Grade 1+	0 (0.0)	2 (4.0)
Grade 1+ with fragmented bacilli	0 (0.0)	1 (2.0)
Grade 2+	4 (8.0)	0 (0.0)
Grade 3+	3 (6.0)	0 (0.0)
Grade 4+	6 (12.0)	2 (4.0)
Grade 5+	5 (10.0)	1 (2.0)
Grade 6+	1 (2.0)	0 (0.0)
Total	50 (100.0)	50 (100.0)

Table 2. Overall histopathological interpretation of paired pre-treatment and on-treatment biopsies.

Histopathological conclusion	n	%
Regression	45	90.0
Progression	3	6.0
Erythema nodosum leprosum	1	2.0
Relapse	1	2.0
Total	50	100.0

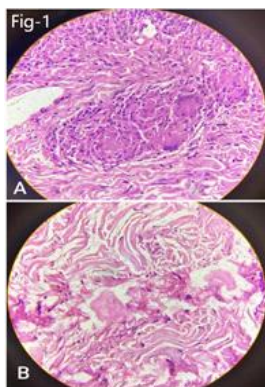


Figure 1. Histomorphological changes in tuberculoid leprosy before and during treatment.

(A) Pretreatment tuberculoid leprosy (40x): well-formed granulomas with a moderate inflammatory infiltrates. (B) On-treatment tuberculoid leprosy (40x): absence of granulomas with a scanty inflammatory infiltrates, intradermal oedema, fibroplasia, and fibromyxoid stromal changes.

Figure 2. Histomorphological changes in borderline lepromatous leprosy before and during treatment.

(A) Pre-treatment borderline lepromatous leprosy (40x): ill-defined granuloma formation with a moderate inflammatory infiltrate. (B) On-treatment borderline lepromatous leprosy (40x): increased basal-layer melanin pigmentation, absence of granulomas, mild inflammatory infiltrates, intradermal edema and fibroplasia.

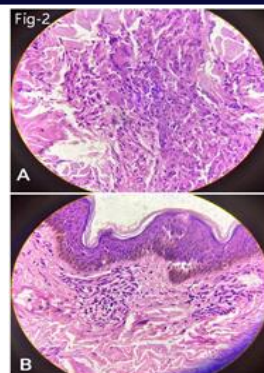
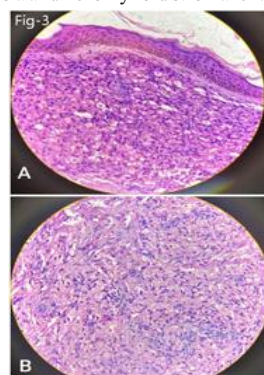


Figure 3. Histomorphological changes in lepromatous leprosy before and during treatment.

(A) Pretreatment lepromatous leprosy (40x): dense inflammatory infiltrate with numerous Virchow cells. (B) On-treatment lepromatous leprosy (40x): reduced inflammatory infiltrate and fewer Virchow cells, with fibroplasia and fibromyxoid stromal changes.

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