Research Article

Clinico-Histopathological Correlation in Leprosy: A Cross-Sectional Study of Ridley-Jopling Concordance At A Tertiary Care Centre

Madadi Pragnya[1], Asma Anjum[2], Bandaru Sougandhika[3], Kanakam Varun[4]*

[1] Assistant Professor, Department of Dermatology, Venereology and Leprosy (DVL), Kanachur Institute of Medical Sciences, Mangalore, Karnataka, India.
[2] Assistant Professor, Department of Dermatology, Venereology and Leprosy (DVL), Government Medical College, Narsampet, Telangana, India.
[3] Consultant Dermatologist, Samanvi Skin Clinic, Hyderabad, Telangana, India.
[4] Assistant Professor, Department of Pathology, Prathima Institute of Medical Sciences, Karimnagar, Telangana, India.

Corresponding Author: Dr. Madadi Pragnya, Email: madadi.pragnya20@gmail.com

Abstract

Leprosy is placed along the Ridley-Jopling spectrum using clinical, histopathological and bacteriological criteria, and agreement between clinical and histopathological typing guides treatment and case detection. Thirty consecutive untreated patients attending a tertiary care dermatology outpatient department were typed clinically and by skin biopsy, and slit-skin smears provided the bacteriological index. Patients were aged 10 to 70 years, and 53% were 21 to 40 years old, with a male-to-female ratio of 1.7:1. Borderline tuberculoid was the commonest type both clinically and histopathologically. Anaesthesia and hypopigmented patches were the leading clinical features, and the bacteriological index was positive in half the patients. Exact clinico-histopathological agreement was 70% (Cohen's kappa 0.59), complete for lepromatous disease and lowest for the mid-borderline and borderline lepromatous groups. Grouped into paucibacillary and multibacillary categories, agreement rose to 94.1% and 76.9% (kappa 0.72). Clinical and histopathological typing agree in most cases but diverge across the immunologically unstable borderline spectrum. Combining clinical examination, histopathology and bacteriological index classifies leprosy most reliably and lowers the risk of undertreating an infectious patient.

Keywords: Hansen's disease; Mycobacterium leprae; skin biopsy; bacteriological index; immunological spectrum.

Introduction

Leprosy is a chronic infectious disease caused by Mycobacterium leprae, with clinical effects concentrated in the skin and peripheral nerves. The organism is still not cultivable in vitro, and untreated disease causes nerve damage, deformity and lasting social stigma (Scollard et al., 2006). Global case numbers fell sharply after multidrug therapy was introduced, yet the annual count of new cases has plateaued rather than declined (Rao & Suneetha, 2018).

India carries a large share of the global burden. After the country declared elimination as a public health problem in 2005, indicators of new case detection, disability and childhood disease have shown little further improvement (Rao & Suneetha, 2018). Accurate early diagnosis is the basis of control, because undiagnosed multibacillary patients sustain transmission in the community (Reibel et al., 2015).

Ridley and Jopling described a five-group spectrum anchored by cell-mediated immunity: tuberculoid (TT), borderline tuberculoid (BT), mid-borderline (BB), borderline lepromatous (BL) and lepromatous (LL), with indeterminate (I) leprosy as an early unclassified form (Ridley & Jopling, 1966). Clinical classification captures the gross appearance of lesions. Histopathological classification uses defined tissue criteria together with the immunological response, which lets it separate types that overlap clinically (Moorthy et al., 2001).

Diagnosis of early and borderline lesions is difficult even for experienced clinicians, and the two methods do not always agree (Moorthy et al., 2001). Studies that pair clinical and histopathological typing, supported by the bacteriological index, have reported concordance across a wide range (Giridhar et al., 2012). Where rural services lack biopsy and smear facilities, treatment often starts on clinical grounds alone, and this risks both over-treatment and under-treatment.

This study typed 30 leprosy patients clinically and histopathologically by Ridley-Jopling criteria, measured the agreement between the two methods, and examined the bacteriological index alongside them.

Materials and Methods

Study design and setting

This cross-sectional observational study was carried out in the Department of Dermatology, Venereology and Leprology of a tertiary care teaching hospital over a two-year period. The study was approved by the Institutional Ethics Committee and written informed consent was obtained from every participant.

Participants
Thirty consecutive patients with clinically suspected leprosy attending the outpatient department were enrolled. Patients of any age and either sex were eligible. Patients already receiving multidrug therapy and those who declined biopsy were not included.

Clinical assessment
Each patient underwent a full history and cutaneous and neurological examination. The number, distribution and morphology of lesions, sensory impairment and peripheral nerve thickening were recorded, and a clinical Ridley-Jopling type was assigned (Ridley & Jopling, 1966). For treatment purposes patients were also grouped by the WHO operational classification, in which five or fewer skin lesions define paucibacillary disease and six or more define multibacillary disease (WHO, 1988).

Histopathology
A skin biopsy was taken from the most active or infiltrated lesion. Sections were stained with haematoxylin and eosin and examined for epidermal change, granuloma type, cellular infiltrate, subepidermal grenz zone and nerve involvement. A modified Fite-Faraco stain was used to demonstrate acid-fast bacilli. Each biopsy was assigned a histopathological Ridley-Jopling type on the basis of granuloma composition (epithelioid cells, lymphocytes, macrophages and giant cells) and bacillary load.

Bacteriological index
Slit-skin smears were graded on the Ridley logarithmic scale from 0 to 6+. Smear positivity was defined as any grade above 0.

Outcome definitions
Anaesthesia was recorded when a lesion showed loss of temperature, pain or touch sensation on bedside testing. Nerve thickening was assessed by palpation of the ulnar, common peroneal, radial cutaneous and greater auricular nerves. Grade-2 disability followed the WHO definition of visible deformity or damage. A hypopigmented patch was defined as a well or ill-defined area of reduced pigmentation with altered sensation.

Statistical analysis
Data and measurements were summarised as frequencies and percentages. Agreement between clinical and histopathological typing was expressed as exact-type concordance and Cohen’s kappa, computed unweighted across the six categories and linearly weighted across the ordered five-group spectrum. A paucibacillary versus multibacillary agreement analysis was also performed. Kappa values were read using standard thresholds, where 0.41 to 0.60 indicates moderate and 0.61 to 0.80 substantial agreement.

Results

Demographic and clinical profile
The 30 patients were aged between 10 and 70 years. Most (16, 53.3%) were in the 21 to 40 year group, followed by the 41 to 60 year group (11, 36.7%). Nineteen patients (63.3%) were male and 11 (36.7%) female, a male-to-female ratio of 1.7:1. One child aged under 15 years was included. Twenty-one patients (70%) belonged to the low-income group and nine (30%) to the middle-income group. Manual labourers formed the largest occupational group (10, 33.3%), followed by farmers and housewives (6, 20% each). Disease duration was 1 to 5 years in 11 patients (36.7%) and 6 to 11 months in 9 (30%). The demographic and clinical profile is shown in Table 1.

Table 1. Demographic and baseline clinical profile of the study population (n = 30).

Variable	Category	n	%
Age group (years)	≤20	2	6.7
	21 to 40	16	53.3
	41 to 60	11	36.7
	61 to 80	1	3.3
Sex	Male	19	63.3
	Female	11	36.7
Socioeconomic status	Low income	21	70.0
	Middle income	9	30.0
Occupation	Manual labourer	10	33.3
	Farmer	6	20.0
	Housewife	6	20.0
	Student	4	13.3
	Other	4	13.3
Duration	<6 months	8	26.7
	6 to 11 months	9	30.0
	1 to 5 years	11	36.7
	>5 years	2	6.7

Clinical morphology and lesion distribution

Upper limbs were involved in 20 patients (66.7%) and lower limbs in 16 (53.3%), followed by the trunk and abdomen in 15 (50%). Anaesthesia was the commonest clinical feature (22 patients, 73.3%), followed by hypopigmented patches (14, 46.7%). Nerve thickening and nodules were each present in 10 patients (33.3%). The ulnar and common peroneal nerves were most often thickened. Two patients (6.7%) had trophic ulcers, and no other grade-2 disabilities were seen. The distribution of clinical features across Ridley-Jopling types is given in Table 2, and the clinical and immunological profile of the cohort is summarised in Figure 1.

Table 2. Clinical morphology and lesion-site distribution across Ridley-Jopling types (n = 30). Values are numbers of patients.

Feature	TT	BT	BB	BL	LL	I	Total (%)
Single lesion	2	3	0	0	0	1	6 (20.0)
Multiple lesions	1	10	3	3	7	0	24 (80.0)
Anaesthesia	3	11	2	2	4	0	22 (73.3)
Hypopigmented patch	2	9	2	1	0	0	14 (46.7)
Nerve thickening	1	6	1	1	1	0	10 (33.3)
Nodules	0	0	0	3	7	0	10 (33.3)
Combined lesions	0	1	2	1	3	0	7 (23.3)
Infiltration	0	0	1	1	5	0	7 (23.3)
Erythematous patch	0	4	0	0	0	0	4 (13.3)
Xerotic patch	1	2	0	0	0	1	4 (13.3)
Trophic ulcer	0	1	0	0	1	0	2 (6.7)
Site: upper limb	2	7	1	3	7	0	20 (66.7)

Feature	TT	BT	BB	BL	LL	I	Total (%)
Site: lower limb	0	6	1	1	7	1	16 (53.3)
Site: trunk/abdomen	0	3	2	3	6	1	15 (50.0)
Site: face	1	2	2	2	2	0	9 (30.0)

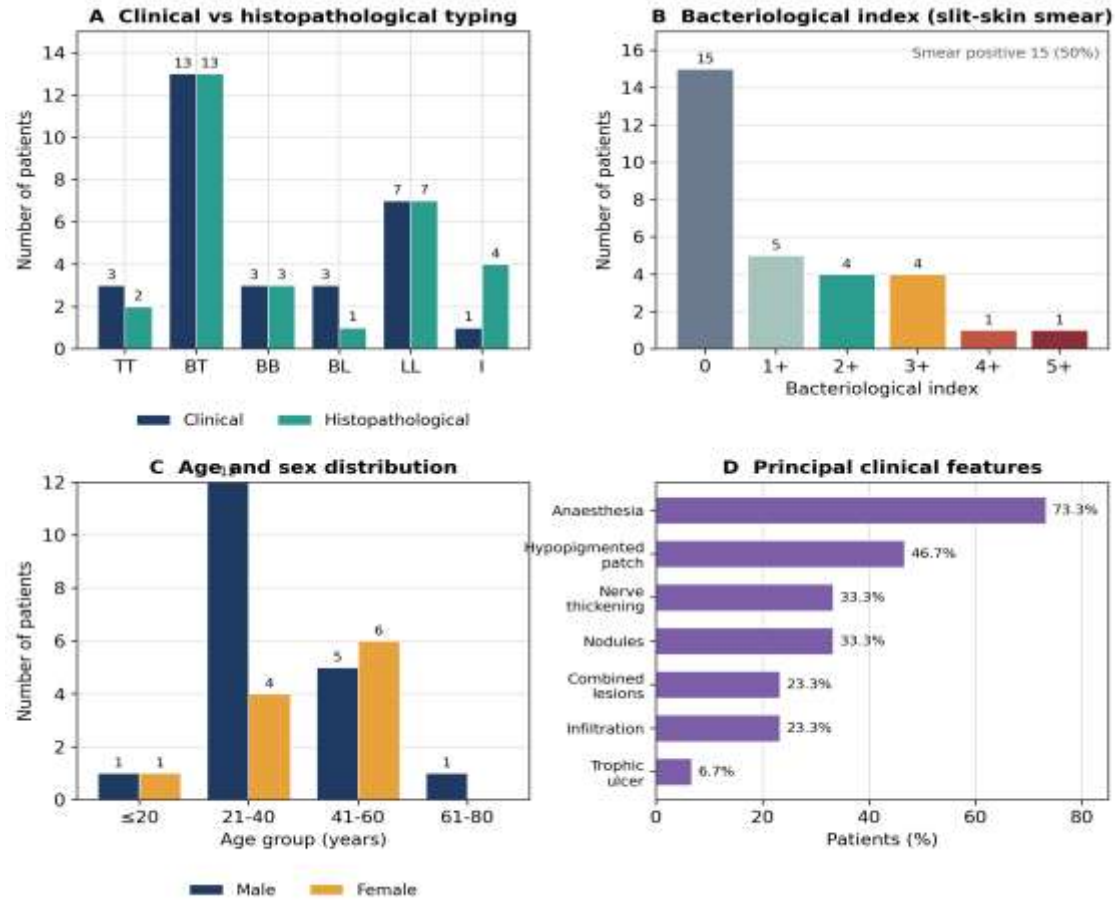


Figure 1. Clinical and immunological profile of the cohort (n = 30). (A) Clinical versus histopathological Ridley-Jopling type distribution. (B) Bacteriological index on slit-skin smear. (C) Age and sex distribution. (D) Frequency of the principal clinical features. TT, tuberculoid; BT, borderline tuberculoid; BB, mid-borderline; BL, borderline lepromatous; LL, lepromatous; I, indeterminate.

Histopathology and bacteriological index

Borderline tuberculoid was the commonest histopathological type (13, 43.3%), followed by lepromatous (7, 23.3%) and indeterminate (4, 13.3%). Epidermal atrophy was seen in 8 biopsies. Granulomas were present in 19 biopsies, foamy macrophages in 10 and a subepidermal grenz zone in 5 lepromatous biopsies. The bacteriological index was positive in 15 patients (50%), and high loads of 3+ or above were confined to lepromatous and borderline lepromatous cases. Histopathological features and the bacteriological index across types are shown in Table 3.

Table 3. Histopathological features and bacteriological index across Ridley-Jopling types (n = 30). Values are numbers of patients.

Parameter	TT	BT	BB	BL	LL	I	Total
Cases (histopathological)	2	13	3	1	7	4	30
Epidermal atrophy	1	4	1	1	1	0	8
Granuloma	2	13	2	1	1	0	19

Parameter	TT	BT	BB	BL	LL	I	Total
Giant cells	1	7	0	0	0	0	8
Foamy macrophages	0	0	2	1	7	0	10
Grenz zone	0	0	0	0	5	0	5
Perineural infiltrate	0	10	2	0	5	0	17
Perivascular infiltrate	1	7	1	1	7	4	21
Bacteriological index 0	3	10	1	0	0	1	15
Bacteriological index 1+ to 2+	0	3	2	2	2	0	9
Bacteriological index ≥3+	0	0	0	1	5	0	6

Clinico-histopathological correlation

Clinical and histopathological types matched exactly in 21 of 30 patients (70%), with a Cohen's kappa of 0.59. Concordance was complete for lepromatous (7 of 7, 100%) and indeterminate (1 of 1) types, high for borderline tuberculoid (9 of 13, 69.2%) and tuberculoid (2 of 3, 66.7%), and low for mid-borderline and borderline lepromatous (1 of 3, 33.3% each). Most discordant borderline tuberculoid cases were reclassified histopathologically as indeterminate (3) or mid-borderline (1). Grouped into paucibacillary and multibacillary treatment categories, agreement rose to 94.1% (16 of 17) for paucibacillary and 76.9% (10 of 13) for multibacillary cases, with a kappa of 0.72. The full correlation matrix is shown in Table 4 and Figure 2, and representative clinical and histopathological features are shown in Figure 3.

Table 4. Clinico-histopathological correlation by Ridley-Jopling type (n = 30). Rows show clinical diagnosis and columns show histopathological diagnosis; the diagonal (bold) shows concordant cases.

Clinical ↓ / HPE →	TT	BT	BB	BL	LL	I	Total
TT	**2**	1	0	0	0	0	3
BT	0	**9**	1	0	0	3	13
BB	0	2	**1**	0	0	0	3
BL	0	1	1	**1**	0	0	3
LL	0	0	0	0	**7**	0	7
I	0	0	0	0	0	**1**	1
Total	2	13	3	1	7	4	30

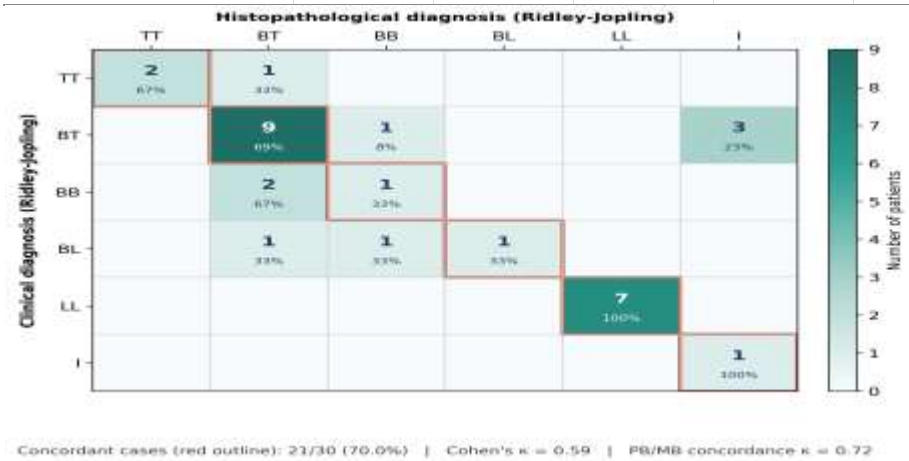


Figure 2. Clinico-histopathological concordance matrix. Colour intensity encodes the number of patients; concordant cells lie on the diagonal (red outline). Exact agreement across all six types was 21 of 30 (70.0%), with Cohen's kappa 0.59 for six-type agreement and 0.72 for the paucibacillary versus multibacillary grouping.

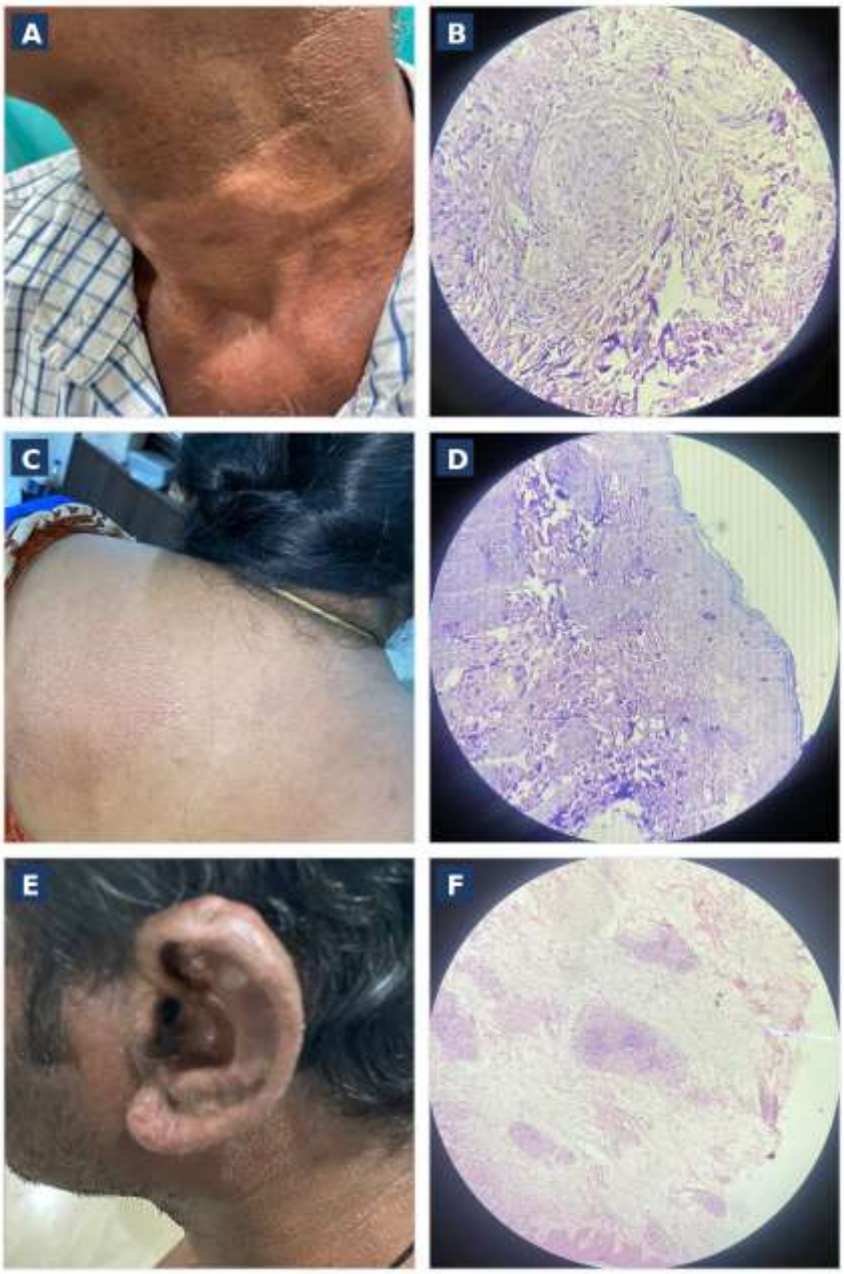


Figure 3. Representative clinical and histopathological features across the spectrum. (A) Tuberculoid pole: well-defined hypopigmented plaque. (B) Tuberculoid pole: dermal epithelioid-cell granuloma (haematoxylin and eosin). (C) Borderline disease: infiltrated plaque of the trunk. (D) Borderline disease: subepidermal granuloma with perineural and perivascular infiltrate (haematoxylin and eosin). (E) Lepromatous pole: nodular and infiltrative involvement of the ear. (F) Lepromatous pole: diffuse macrophage infiltrate with a subepidermal grenz zone (haematoxylin and eosin).

Discussion

This study found exact clinical and histopathological agreement in 70% of leprosy cases, with a moderate Cohen's kappa of 0.59. Agreement was strongest at the poles of the spectrum and weakest across the borderline groups. The

same pattern runs through the published literature and has direct consequences for how cases are classified and treated in field settings.

The disease clustered in the 21 to 40 year group, matching the profile that Lathiya et al. (2022) and Joshi et al. (2022) reported from other Indian tertiary centres. Male predominance of 1.7:1 is consistent with the figures of Agarwal and Bhuptani (2018), who attributed the excess in men to greater occupational exposure and more complete clinical examination. One childhood case points to continuing transmission in the community.

Most patients came from low-income households. This agrees with the ecological findings of Kerr-Pontes et al. (2004), who tied leprosy to poverty and crowding in Northeast Brazil. Manual labourers predominated, as Nardi et al. (2012) also described, probably because outdoor work increases both exposure and skin trauma.

Borderline tuberculoid was the commonest clinical type. Nirmala Devi et al. (2021) and Jindal et al. (2009) reported the same predominance, though the exact mix of types shifts between centres with local awareness and referral pathways. A third of patients presented one to five years after onset. van Brakel et al. (2005) recorded similarly long intervals in a north Indian multibacillary cohort, and late presentation raises the risk of nerve damage.

Upper and lower limbs were the commonest sites, as Roy et al. (2019) and Patel et al. (2022) found, because exposed parts are more prone to trauma and contact. Anaesthesia and hypopigmented patches led the clinical features, matching Moorthy et al. (2001) and Verma (1976). Sensory loss over a hypopigmented patch is the clinical signature of the disease.

Borderline tuberculoid also dominated the histopathological picture, in keeping with Vasaikar et al. (2017) and Kamle et al. (2021). The preponderance of borderline forms fits the unstable immunology of this part of the spectrum, where cases shift with time and treatment.

Half the patients were smear-positive, close to the proportion that Patil et al. (2020) recorded. Slit-skin smear has limited sensitivity, because bacilli in the deep dermis escape sampling and blood can obscure the smear. Bhushan et al. (2008) showed that the bacterial index of the granuloma detects multibacillary status more reliably than smear or clinical lesion count. Kumaran et al. (2015) reached the same conclusion and argued for tissue-based indices in doubtful cases.

Just over half the patients were multibacillary by the WHO operational classification. Daniel et al. (2009) and Relhan et al. (2016) linked rising multibacillary proportions to late reporting and the shift from active to passive case detection after programme integration. A high multibacillary share points to a reservoir of infectious cases that sustains transmission.

The overall concordance of 70% matches the 68.3% that Ridley and Jopling (1966) reported in their original series and the range of later Indian studies. Kalla et al. (2000) and Jerath and Desai (1982) found comparable overall agreement with the same pole-to-centre gradient. Chadha et al. (2021) described the same discordance and a spectral shift toward the lepromatous side.

Agreement was lowest in the mid-borderline and borderline lepromatous groups. Bommakanti et al. (2016) attributed this to the continuously changing immunity of borderline patients. Ganapati and Desikan (1974) showed that different lesions in the same patient can yield different histology, which is a strong argument for biopsying the most infiltrated lesion. Lepromatous cases, by contrast, showed complete agreement, in keeping with their fixed histology and stable immunology.

Collapsing the six types into paucibacillary and multibacillary groups raised agreement to 94.1% and 76.9%. For treatment the error that matters is a multibacillary case being classified and treated as paucibacillary, which undertreats an infectious patient and encourages relapse and resistance. Adding histopathology and the bacteriological index to clinical typing reduces that error.

The two methods are complementary rather than interchangeable. Histopathological examination of the most infiltrated lesion, read with the clinical picture and the bacteriological index, gives the most accurate placement on the spectrum and the safest treatment decision. Where the more advanced finding sits nearer the lepromatous pole, cases are best classified and treated accordingly.

Limitations

The sample was small and drawn from a single centre, and treatment follow-up was not available, so changes in histology and bacteriological index with therapy could not be assessed. Type allocation rested on a single biopsy per patient. Larger multicentre studies with serial sampling would test these findings and refine the classification criteria.

Conclusion

Clinical and histopathological typing agreed in 70% of leprosy cases, with near-complete agreement at the tuberculoid and lepromatous poles and clear divergence across the borderline spectrum. Clinical classification captures lesion morphology, histopathology captures the tissue and immunological response, and the bacteriological index measures the infectious load. Used together they classify leprosy more accurately than any single method and lower the chance of misclassifying an infectious case. Histopathological examination of the most infiltrated lesion, with clinico-pathological correlation and bacteriological index, is recommended for all leprosy patients at tertiary care settings.

References

1. Agarwal S, Bhuptani N (2018). Clinico-histopathological concordance in leprosy patients: a study of 200 cases. Indian Journal of Leprosy 90:147-153.
2. Bhushan P, Sardana K, Koranne RV, Choudhary M, Manjul P (2008). Diagnosing multibacillary leprosy: a comparative evaluation of diagnostic accuracy of slit-skin smear, bacterial index of granuloma and WHO operational classification. Indian Journal of Dermatology, Venereology and Leprology 74(4):322-326.
3. Bommakanti J, Putta S, Gokhale S (2016). Histopathological relevance in the clinical spectrum of Hansen's disease. Journal of Medical Science and Clinical Research 4(6):14678-14684.
4. Chadha A, Dongre A, Khopkar US (2021). A single-centre cross-sectional study of clinicopathological correlation in leprosy: discordance and spectral shift. Indian Journal of Leprosy 93:143-156.
5. Daniel S, Arunthathi S, Rao PS (2009). Impact of integration on the profile of newly diagnosed leprosy patients attending a referral hospital in South India. Indian Journal of Leprosy 81(2):69-74.
6. Ganapati R, Desikan KV (1974). Simultaneous occurrence of different types of leprosy in a patient: a case report. Leprosy in India 46(2):148-151.
7. Giridhar M, Arora G, Lajpal K, Chahal KS (2012). Clinico-histopathological concordance in leprosy: a clinical, histopathological and bacteriological study of 100 cases. Indian Journal of Leprosy 84(3):217-225.
8. Jerath VP, Desai SR (1982). Diversities in clinical and histopathological classification of leprosy. Leprosy in India 54(1):130-134.
9. Jindal N, Shanker V, Tegta GR, Gupta M, Verma GK (2009). Clinico-epidemiological trends of leprosy in Himachal Pradesh. Indian Journal of Leprosy 81(4):173-179.
10. Joshi K, Rizvi G, Kaushik A, Kandwal P, Ahmad S (2022). A five-year retrospective study of the profile of leprosy patients in a teaching tertiary care centre in Uttarakhand. Indian Journal of Leprosy 94:141-152.
11. Kalla G, Salodkar A, Kachhawa D (2000). Clinical and histopathological correlation in leprosy. International Journal of Leprosy and Other Mycobacterial Diseases 68(2):184-185.
12. Kamle A, Awasthi P, Rawat N, Sabale V, Bhake A (2021). Clinicopathological diagnosis of leprosy: comparative evaluation of three staining methods for acid-fast bacilli in slit-skin smears and biopsy specimens. Indian Journal of Leprosy 93:15-27.
13. Kerr-Pontes LR, Montenegro AC, Barreto ML, Werneck GL, Feldmeier H (2004). Inequality and leprosy in Northeast Brazil: an ecological study. International Journal of Epidemiology 33(2):262-269.
14. Kumaran SM, Bhat IP, Madhukara J, Rout P, Elizabeth J (2015). Comparison of bacillary index on slit-skin smear with bacillary index of granuloma in leprosy and its relevance to present therapeutic regimens. Indian Journal of Dermatology 60(1):51-54.
15. Lathiya SL, Makwana VR, Patel ZR, Gandha KM, Nerurkar SP (2022). A study on clinical profile and disability and deformity among newly diagnosed leprosy patients attending a tertiary care institution. Indian Journal of Leprosy 94:1-11.
16. Moorthy BN, Kumar P, Chatura KR, Chandrasekhar HR, Basavaraj PK (2001). Histopathological correlation of skin biopsies in leprosy. Indian Journal of Dermatology, Venereology and Leprology 67(6):299-301.
17. Nardi SM, Ikehara E, Pedro HS, Paschoal VD (2012). Characterization of the profession or occupation of individuals affected by leprosy and the relationship with limitations in professional activities. Indian Journal of Leprosy 84:1-8.
18. Nirmala Devi P, Arunkumar B, Judith Joy S, Vijayabhaskar C (2021). Clinicopathological profile of cases attending the leprosy clinic in a tertiary care hospital of South Tamil Nadu and its correlation with current leprosy trends under NLEP. Indian Journal of Leprosy 93:329-340.

19. Patel K, Modi R, Vaghela M, Italiya S (2022). A study of the histopathological spectrum of leprosy at a tertiary care hospital. Indian Journal of Pathology and Oncology 9(1):16-20.
20. Patil AS, Nayak SV, Kumar V, Bhat RM (2020). A study of indices in smear-positive leprosy in the post-elimination era: experience at a teaching tertiary care centre. MAMC Journal of Medical Sciences 6(3):211-215.
21. Rao PN, Suneetha S (2018). Current situation of leprosy in India and its future implications. Indian Dermatology Online Journal 9(2):83-89.
22. Reibel F, Cambau E, Aubry A (2015). Update on the epidemiology, diagnosis, and treatment of leprosy. Medecine et Maladies Infectieuses 45(9):383-393.
23. Relhan V, Ghunawat S, Tenani A, Garg VK (2016). Trends in the profile of leprosy cases reporting to a tertiary care centre in Delhi during 2006-2015. Indian Journal of Leprosy 88:217-225.
24. Ridley DS, Jopling WH (1966). Classification of leprosy according to immunity: a five-group system. International Journal of Leprosy and Other Mycobacterial Diseases 34(3):255-273.
25. Roy P, Dhar R, Patro P, Hasan Z, Ganguly S (2019). Histopathological study of leprosy patients in a tertiary care hospital in Navi Mumbai. International Journal of Health Sciences and Research 9(2):6-12.
26. Scollard DM, Adams LB, Gillis TP, Krahenbuhl JL, Truman RW, Williams DL (2006). The continuing challenges of leprosy. Clinical Microbiology Reviews 19(2):338-381.
27. van Brakel WH, Nicholls PG, Das L, Barkataki P, Suneetha SK, Jadhav RS, et al. (2005). The INFIR Cohort Study: investigating prediction, detection and pathogenesis of neuropathy and reactions in leprosy. Methods and baseline results of a cohort of multibacillary leprosy patients in north India. Leprosy Review 76(1):14-34.
28. Vasaikar MS, Ahmed SS, Halwai VK (2017). A study of histological types of leprosy along with clinico-histopathological correlation in a tertiary centre from North Maharashtra region. Annals of Pathology and Laboratory Medicine 4(3):A272-278.
29. Verma OP (1976). Some epidemiological features of leprosy in a rural area in Hooghly district. Leprosy in India 48(4):371-381.
30. World Health Organization (1988). WHO Expert Committee on Leprosy: sixth report. Geneva: World Health Organization. Technical Report Series No. 768.