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Histopathological spectrum of leprosy with clinicopathologic correlation

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Abstract
Introduction: Leprosy is a chronic infectious disease involving skin and peripheral nerves and certain other tissues. It is classified into five groups based on clinical, histopathological, and bacteriological criteria tuberculoid (TT), borderline tuberculoid (BT), mid-borderline (BB), borderline lepromatous (BL), lepromatous (LL) according to Ridley-Jopling classification. Clinical classification gives recognition only to the gross appearance of lesions, while histopathological classification parameters are well-defined and precise thus, it provides confirmatory information for suspect cases which might be missed clinically. This study is conducted to correlate between clinical and histopathological diagnosis of leprosy.
Material and Methods: This research was **a** retrospective study of three years from August'20 to July'23. A total of 100 cases were studied in the Histopathology Laboratory, Department of Pathology, SIMS, Hapur
Result: There was a total of 100 cases; out of which 68 (68%) were males. Most cases were in the age group 15-30 years comprising 44 % males. Maximum number of patients clinically belonged to borderline lepromatous leprosy in 44% of cases. Histologically, borderline tuberculoid leprosy was the most common type in 36% of cases. The maximum clinical-histopathological correlation was seen in LL (100%) followed by TT (92.1%), BT (81.8%), and BL (50%).
Conclusion: Clinical features in leprosy indicate morphological changes due to underlying pathology while the histopathological features indicate accurate response of the tissues. Classification of leprosy requires attention to histopathological criteria and correlation with clinical information to facilitate accurate therapy according to the proper treatment category and to prevent complications.

Keywords: Leprosy, histopathology, clinical features, correlation

Introduction
Leprosy is a chronic granulomatous infectious disease caused by noncultivable Mycobacterium leprae [1]. Although there has been a significant reduction in the prevalence of Hansen's disease (HD) worldwide since the mid-1980s to elimination levels, new cases continue to arise in several Southeast Asian countries, particularly India and Indonesia, indicating continuous transmission [2].
Many classifications for leprosy have been proposed based on clinical, bacteriological, immunological, and histological status, for example, Madrid classification, Ridley and Jopling classification, and Indian classification [3]. In the 1960s, Ridley and Jopling proposed a histological classification for leprosy as indeterminate (I) leprosy, tuberculoid (TT), borderline tuberculoid (BT), mid-borderline (BB), borderline lepromatous (BL), and lepromatous (LL) leprosy [4]. However, in 1982, the World Health Organization classified leprosy as multibacillary (MB) and paucibacillary (PB) based on the bacillary index (BI). I, TT, and BT cases of leprosy were classified as PB, and BB, BL, and LL cases of leprosy were classified as MB [5].
Polar forms (TT and LL) are the most stable and the Borderline forms (BB) are most labile [6]. Clinical diagnosis is done based on the visual appearances of the lesions and nerve sensation, while the histopathological diagnosis is done on the basis of presence or absence of granuloma, bacterial load (BI), distribution of lymphocytes, involvement of nerves, and the presence or absence of the subepidermal grenz zone and epidermal changes. Histopathology gives a confirmatory diagnosis for suspect cases which can be missed by clinicians or

epidemiological studies and helps in exact typing. Also, histopathology helps in the indication of progression and regression of disease under treatment [7].

Ridley Jopling Classification

Immune Response	High Resistance		Unstable Resistance		Little or No Resistance
Clinical Spectrum	Polar Tuberculoid (TT)	Borderline Tuberculoid (BT)	Mid Borderline (BB)	Borderline Lepromatous (BL)	Polar Leprosy (LL)
No. of skin lesions	Few usually single	Few	Few or many	Many	Many
Bacillary load (slit smear skin test)	0 or rarely, +1	+1	+2	+3	+4
Lepromin Test	Positive	Positive	Positive, doubtful, no response	Doubtful or no response	No response
Histology	Epithelioid granulomas ringed by lymphocytes found around dermal appendages and nerve in both papillary and reticular dermis, extending up to the epidermis, caseation necrosis may occur. Nerve edema infiltration by AFB bacilli or destruction	Epithelioid granulomas by moderate number of lymphocytes. Langhans giant cell can be present. Rare infiltration of the subepidermal zone. Nerve edema and infiltration by AFB bacilli and destruction.	Granulomas consist of foamy macrophages. Number of lymphocytes in granuloma are generally less. Langhans cell absent. Dermal nerve shows Schwann cell proliferation. Infiltration by lymphocytes, foamy macrophages.	Increasing histiocytes and fewer epithelioid cells and lymphocytes. Foamy macrophages. Lipid laden granulomas with grenz zone. Nerve bundle damaged.	Massive granulomas or diffuse sheets of foamy lipid-laden granuloma with grenz zone present. Multiple even large multinucleated globi. Nerve bundle damaged

The diagnosis of leprosy is based on different clinical parameters involving detailed examination of skin lesions and peripheral nerves, slit-skin smear examination, histopathological examination, and demonstration of acid-fast bacilli.

Leprosy causes lesions and anesthesia of skin, along with enlarged and thickened peripheral nerves [7]. Due to clinical diversity and ability to mimic other skin diseases, it is very difficult to diagnose it clinically in early stages [8]. Thus, histopathological examination of skin biopsies plays a pivotal role in early diagnosis, categorization, and treatment of disease.

The study aims to describe the histopathological spectrum of leprosy with its clinicopathologic correlation.

Materials and Methods

This retrospective study was conducted in the Department of Pathology, Saraswathi Medical College, Hapur involving 100 patients. All the clinically diagnosed and/ or suspected patients of leprosy from August 2020 to July 2023 were enrolled in the study. All patients with different clinical spectrums of leprosy were included in the study and graded as per the Ridley-Jopling classification. The data were retrieved from the records maintained in the department including age, sex, clinical diagnosis, and histopathological findings.

Study Design: Retrospective study

Study Period: August'2020 to July'2023

Inclusion Criteria: Newly diagnosed leprosy patients with hypopigmented patches with loss of sensation were included in the s.tudy.

Exclusion Criteria: Patients who had taken anti-leprosy treatment in the past, patients who were on anti-leprosy treatment, and inadequate biopsy samples were excluded from the study.

Sample size: A total of 100 samples of leprosy received during the study period in the histopathology laboratory, Department of Pathology, Saraswathi Institute of Medical Sciences, Hapur, Uttar Pradesh were studied.

Results

A total of 100 patients were studied, out of which 68 were males and 32 were females. The ages of the patients ranged from 15 to 70 years.

On clinical evaluation Tuberculoid Leprosy (TT) was diagnosed in 38%, Borderline Tuberculoid leprosy (BT) in 44%, Lepromatous Leprosy (LL) in 11%, Borderline Lepromatous (06%) and not specified (? Hansen) in 1% patients.

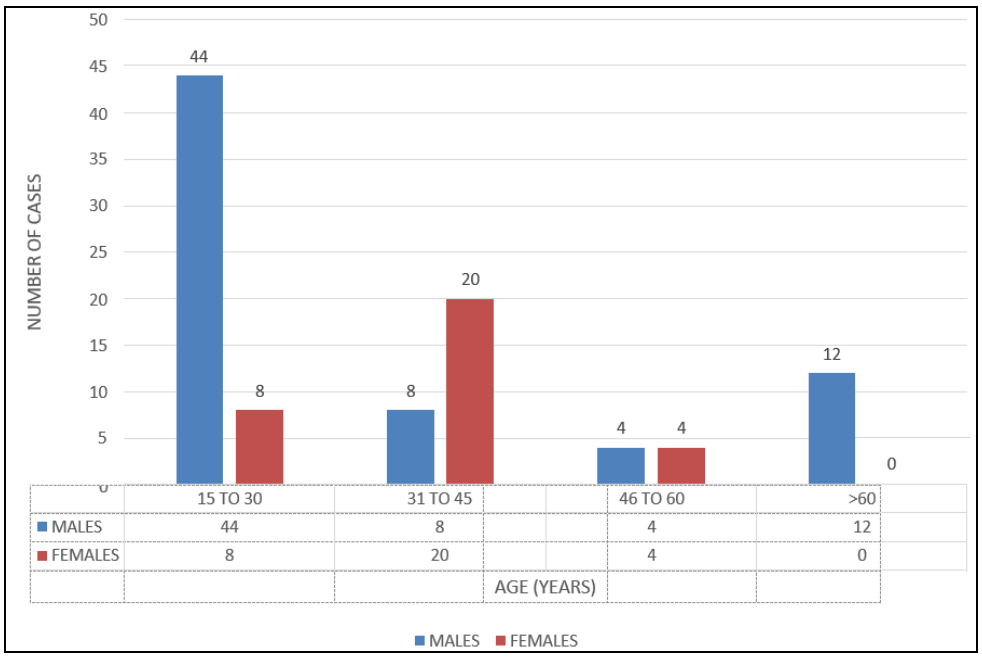


Fig 1: Age Distribution

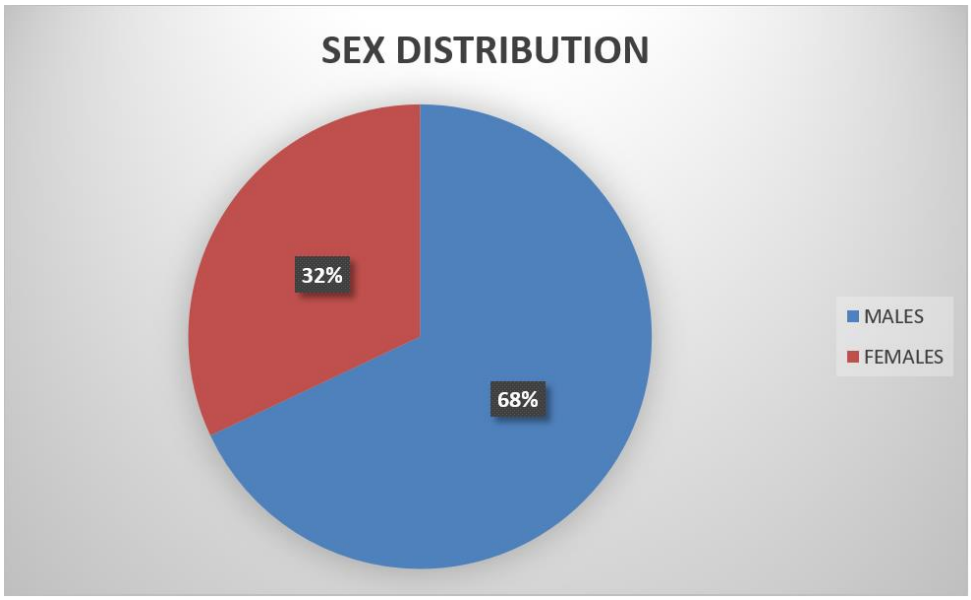
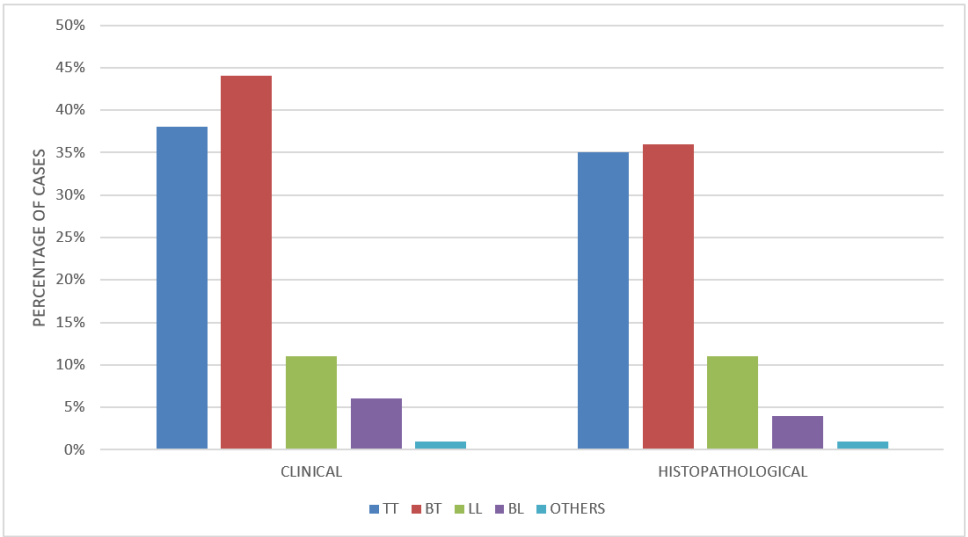


Fig 2: Distribution of Cases of Different Types of Leprosy Based on Clinical and Histopathological Criteria



Distribution of Leprosy Type on the basis of Clinical and Histopathological Criteria

Types of leprosy	Clinical diagnosis	Histopathological diagnosis
TT	38%	35%
BT	44%	36%
LL	11%	11%
BL	06%	03%
Other than Hansens	1%	1%

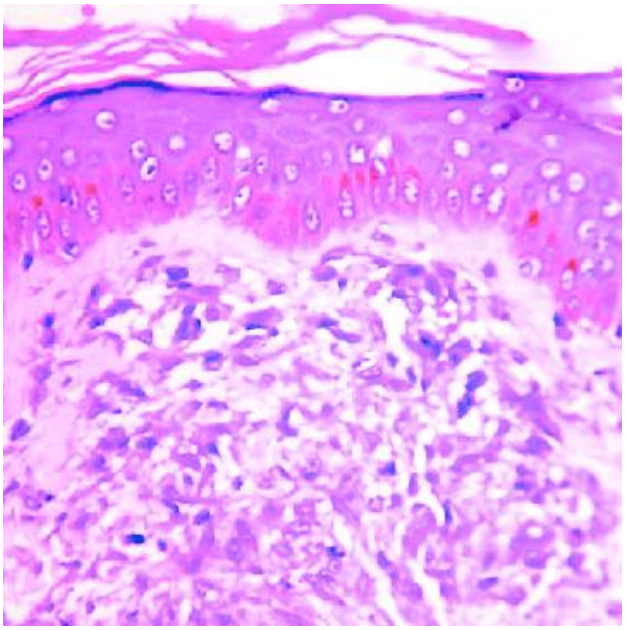


Fig 3: Lepromatous leprosy: Grenz zone (H and E, ×400)

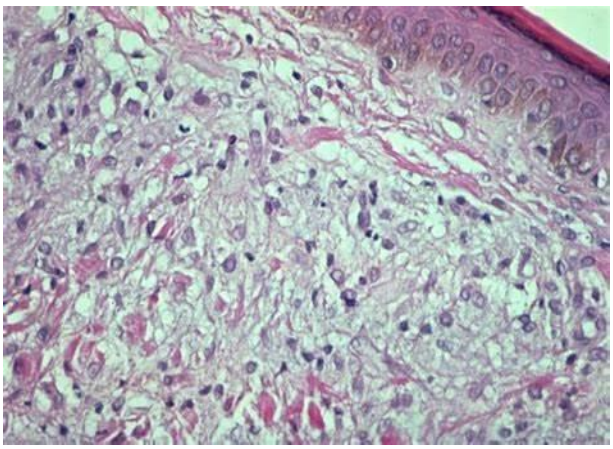


Fig 4: Histopathology of Leprosy (H & E, X400)

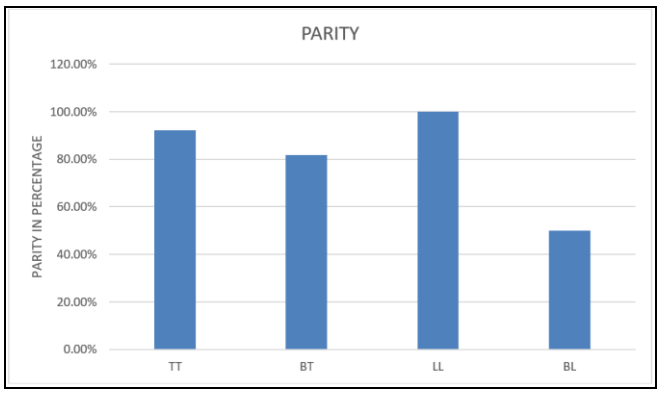


Table 1: Correlation between Clinical and Histopathological Diagnosis

Clinical Diagnosis	Histopathological Diagnosis						
	Tt	Bt	Ll	Bl	Indeterminate	Other Than Hansens	(Correlation) Parity
TT 38%	35	0	0	0	03	0	92.1%
BT 44%	0	36	0	0	08	0	81.8%
LL 11%	0	0	11	0	0	0	100%
BL 06%	0	0	0	03	03	0	50%
Others 01%	0	0	0	0	0	01	100%

Fite farraco stain was done to demonstrate acid-fast bacilli. It was positive in BL and LL types of leprosy

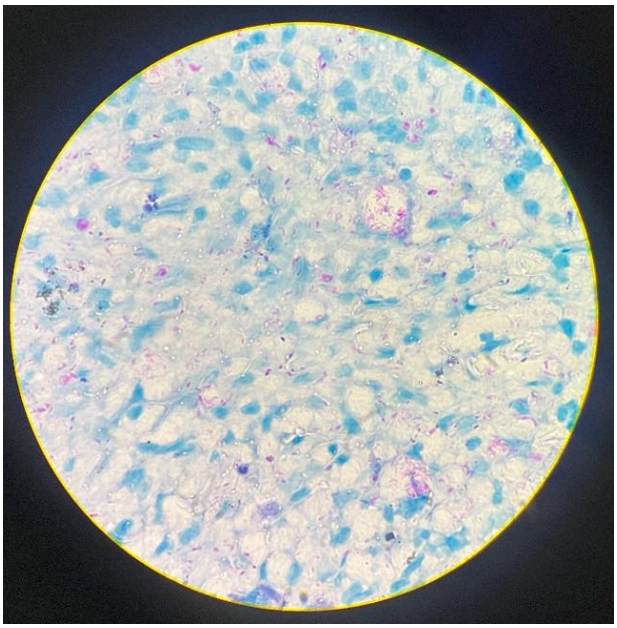


Fig 3: FITE FARRACO STAIN: positive for Acid Fast Bacilli (100X)

Discussion

Leprosy is a chronic contagious disease with various clinical presentations, which can mimic many diseases. A definitive diagnosis of leprosy cases cannot be reached based on clinical examination alone [6]. So, histopathological examination continues to be an important tool in the correct diagnosis and classification of leprosy and remains the gold standard. During the study period of three years 100 skin biopsies were clinically diagnosed as leprosy. In our study majority of cases were male (68%) and the male: female ratio was (2:1). These findings were correlated with the findings of other studies [11-13].

The possible causes of male predominance of leprosy are environmental, more chances of contact, urbanization, and industrialization. Leprosy can be seen in any age. In our study, the maximum cases were in the 15-30 years of age group. Most of the studies showed maximum cases in the same age group [12, 14]. In our study, the least number of cases (4%) were reported in 45-50 years. This may be due to the longer incubation period of lepra bacilli [15].

The eldest case in our study was a 74-year-old while a 15-year-old boy was the youngest case. Most of the patients were presented with hypopigmented patches (72%) and the remaining with erythematous macules and papules. Similar studies were seen in some other studies also [13, 14, 16].

A comparison of clinical and histopathological diagnoses is presented in Table: 1

Clinically, out of 100 cases, BT was found to be the most seen in 44% of cases followed by TT (38%); LL was seen in 11%, BL in 06% whereas Hansens? in 01%. We did not encounter even a single case of non-reactional BB leprosy (Table 1).

On histopathological examination, BT (36%) was the most common, followed by TT (35%), LL (11%), BL (03%), Indeterminate (14%), and other than Hansen's (1%).

The disparity found between clinical and histopathological correlation is because histopathological diagnosis is done based on microscopic findings while clinical diagnosis gives a gross appearance of lesions due to underlying pathological changes [3, 16].

We found a statistically significant correlation of FF (FITE-FARACO STAIN) positivity with the histopathological diagnosis.

Conclusion

In Leprosy, histopathological features indicate accurate response of tissues whereas clinical features indicate morphological changes due to underlying pathology. There is some degree of overlap in all types of leprosy in confirming the clinical diagnosis as well as therapeutic guide of leprosy, skin biopsy plays an important role. Clinical detection and histopathological diagnosis of borderline lesions remains challenging hence the need for interpretation along with clinical findings.

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