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Original Article

Spectrum of Leprosy with Clinicopathological Correlation in a tertiary Care Hospital: A Retrospective and Prospective Study

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Abstract

Background: Leprosy is a disease of antiquity and was well-recognized in the oldest civilizations of Egypt, China, and India. The first known written record of leprosy appeared in an Egyptian papyrus document written around 1550 BCE. The disease has been shrouded in significant stigma, often misconstrued as a condition afflicting the cursed or unfortunate or mistakenly attributed to genetic factors.

Methods: This was a retrospective and a prospective study. The data consisted of approximately 62 cases over two years. Non-probability sampling/convenience sampling was performed. Modified Fite-Faraco staining and Ziehl-Neelsen (ZN) staining were done to identify the lepra bacilli.

Results: Out of 62 cases, 34 were male and 28 were female. Lepromatous leprosy (LL) was more prevalent in males, and borderline lepromatous (BL) leprosy was more prevalent among females. The 31–40 years age group was the most commonly affected. The incidence of various types of leprosy was as follows: BL leprosy (35.48%) followed by borderline tuberculoid (BT) leprosy (27.42%), LL (22.58%) and tuberculoid leprosy (TL) (12.90%). Macules and plaque were the most common clinical presentations associated with BL and LL, respectively.

Conclusion: The most common clinical presentation of leprosy is anesthetic hypopigmented lesions. Modified Fite-Faraco stain is the staining of choice as it has higher chances of identifying the bacilli than the ZN stain. More research needs to be done for a more expedited and swift modality of investigation to identify the bacilli.

Keywords: Leprosy, Histopathology, ZN stain, Fite-Faraco stain, Skin biopsy

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Introduction

There has been substantial debate about whether leprosy originated in ancient Eastern Africa or India centuries ago; however, the origins will likely never be known with any degree of certainty. Early written records giving clinical descriptions generally accepted as being true leprosy date from 600 BC to possibly as early as 1400 BC in India, when a disease called Kushta was distinguished from vitiligo (1). In 1873, Norwegian physician Gerhard Hansen saw the leprosy bacillus under the microscope and proved that leprosy was an infectious disease and not a curse (2).

The overall prevalence of leprosy in India declined from 5.27/10 000 in the year 2000 to 0.66/10 000 in the year 2016, but still, it continues to be a sizable public health problem (3). Leprosy is a disease that is chronic and communicable. It is caused by leprosy bacillus, a rod-shaped acid-fast bacillus. The condition affects the skin, peripheral nerves, upper respiratory tract mucosa, and eyes (4,5).

With the availability of multiple drug therapy (MDT) as a cure for leprosy, the National Leprosy Eradication Program (NLEP) was launched in 1983–1984. The NLEP's mission is to supply quality leprosy services free of cost to many sections of the population with easy accessibility through the integrated healthcare system, including disability management post-cure of the disease (6).

India represents approximately 60% of the global burden. The clinical correlation between Hansen's disease and histology helps in understanding the disease. Histopathological diagnosis and demonstration of bacilli using different stains such as Ziehl-Neelsen (ZN) and Fite-Faraco confirm the diagnosis (7). Ridley and Jopling's histological classification includes polar tuberculoid (TT), borderline tuberculoid (BT), mid-borderline (BB), borderline lepromatous (BL), and polar lepromatous (LL). (8) The classification was done according to various features and their subdivisions by the bacteriologic index

(BI) on a logarithmic scale, scored from 0 to ≥6. (8) Clinical classification is based on the gross appearance of the lesion. In contrast, histopathological classification is based on the correlation between the underlying disease progression and regression features (8,9).

This study aimed to correlate the clinical diagnosis of leprosy cases with the histopathological diagnosis through skin biopsies.

Objectives

- To study the histomorphological features of various types of leprosy and categorize them according to the Ridley Jopling Classification.
- To assess the various lesions with regard to frequency, age, and sex distribution.
- To compare the efficacy of modified Fite-Faraco staining with ZN staining in diagnosing leprosy in tissue sections.

Methods

This was an observational and analytical study spanning over two years. For the retrospective cases, all the cases registered in the pathology department database for the previous year were considered. All the new cases received after acquiring the IEC clearance were included as prospective cases.

Inclusion criteria

All clinically diagnosed cases of leprosy and patients who consented to biopsy were included.

Exclusion criteria

Patients with the following cases were excluded from the study:

- Cases with inadequate biopsies, which did not include full depth of the dermis.
- Patients already treated with anti-leprosy medication.
- Cases showing features of reactional leprosy
- HIV-positive cases and pregnant women.
- Patients on immunosuppressive drugs, such as corticosteroids.
- Patients not giving consent for biopsy.

Sample size

All the existing specimens of leprosy and specimens that arrived during the study period were taken as study samples, reaching a total of 62 patients. For the retrospective study, patient clinical data were collected from the medical records, followed by histopathology requisition forms containing clinical information. All the paraffin blocks and slides were retrieved and reviewed for the record. Patients who met the inclusion criteria and gave written informed consent were included for the prospective study.

History and clinical examination of the patient regarding location, morphology, number, size, color, anesthesia, satellite lesions, central clearing of skin lesions, and the involvement of peripheral and cutaneous nerves were noted. The results of the slit skin smear stained with hematoxylin and eosin, ZN stain, and modified Fite-Faraco stain were noted. Based on Ridley's logarithmic scale, BI was calculated.

The clinical classification of leprosy done by dermatologists was also noted. The skin biopsies obtained were kept in 10% formalin. The specimens underwent routine histopathological processing in the histopathology lab. The Ridley and Jopling criteria were utilized to diagnose and classify these cases histopathologically. The patients' clinical data were collected from the medical records for the retrospective study. Histopathology requisition forms containing clinical information and all the paraffin blocks and slides were retrieved and reviewed for the record.

Statistical Analysis

Data were entered in Microsoft Excel, and analysis was done in percentages and presented in tables.

Results

The results obtained after staining the biopsy slides with Hematoxylin and eosin (H & E), ZN, and modified Fite-Faraco staining were analyzed for all 62 cases. In the present study, Table 1 shows the distribution of lesions according to age and sex in comparison to the clinical diagnosis of the patients. There were 34 males and 28 females. The male-to-female ratio was 1.2:1.

The majority of the patients were aged between 31–40 years (29%), followed by 51–60 years (25.8%) and 21–30 years (19.4%). There was no case in the 0–10 year age group.

BL and BT leprosy were more prevalent among females, whereas LL and TT were more prevalent in males. The most commonly diagnosed type was BL leprosy, comprising (35.48%) of cases, followed by BT leprosy (27.42%) and LL (22.58%). TL comprised (12.90%) of cases.

Table 2 shows the common clinical presentations in various types of leprosy. The hypopigmented lesions were more common in BL, followed by BT leprosy. Meanwhile, erythematous lesions were more common in LL. Anesthesia was present in the majority of the histological types of leprosy.

Overall, the total concordance between clinical and histological diagnoses was 77.4%. Maximum concordance was observed for LL (92.8 %), followed by BL (81.8%) and BT (70.5%). The concordance was lower in TL (62.5%). Details of the correlation between the clinical and histological diagnosis are covered in Table 3.

The most commonly observed site of the lesions was the limbs (35.48%), followed by the trunk and back (30.65%). However, 16.13% of the patients had lesions in multiple

Table 1. Distribution of lesions according to age and sex across clinical diagnoses of the patients

Age	Gender	LL	BL	BB	BT	TT	Negative for Hansen's
0–10	Male	0	0	0	0	0	0
	Female	0	0	0	0	0	0
11–20	Male	2	1	0	2	0	0
	Female	0	1	0	0	0	0
21–30	Male	3	1	0	2	0	0
	Female	1	5	0	2	1	0
31–40	Male	1	1	0	2	5	0
	Female	1	4	0	2	1	0
41–50	Male	0	2	0	0	0	1
	Female	0	1	0	2	1	0
51–60	Male	2	3	0	0	3	2
	Female	0	1	0	1	1	0
61–70	Male	2	0	0	0	0	0
	Female	0	0	0	1	0	0
>70	Male	0	0	0	0	0	1
	Female	0	0	0	0	0	0

Table 2. Distribution of clinical features present in various types of leprosy

Clinical features	LL	BL	BB	BT	TT	Negative for Hansen's	Total
Hypo-pigmented	2	16	0	14	5	2	39
Erythematous	10	4	0	0	6	1	21
Hyper-pigmented	0	0	0	0	1	0	1
Skin colored	0	0	0	0	0	1	1
Anesthesia	10	19	0	12	10	3	54

Table 3. Correlation between the clinical diagnosis and histopathological diagnosis

Clinical diagnosis	Histological diagnosis						Total	% Agreement
	TT	BL	BB	BL	LL	Negative for Hansen's		
TT	5	1	0	0	0	2	8	62.5%
BT	0	12	0	4	0	1	17	70.5%
BB	0	0	0	0	0	1	1	0%
BL	0	1	0	18	3	0	22	81.8%
LL	0	0	0	1	13	0	14	92.8%
Total	5	14	0	23	16	4	62	

sites, and 17.74% had lesions on the face and neck.

The most common clinical presentation in LL and BL leprosy was in the form of papules and macules. For TL and BT cases, the most common presentation was plaques. Hypopigmented lesions were more common in BL, followed by BT leprosy, whereas erythematous lesions were more common in LL. Anesthesia was present in the majority of the histological types of leprosy. Atrophy was the most common finding in all LL cases and almost all BL cases. Epidermal changes were unremarkable in 9 cases of BT, 7 cases of TT, and 4 cases of BL.

Histopathological findings

The presence of grenz zones was characteristic of LL, seen in all (100%) cases. The other predominant histological changes were the presence of foamy macrophages and lymphocytes around appendages. The characteristic feature in TT was the presence of epithelioid granuloma or epithelioid cells (100%) (Figure 1). In BL, a prominent finding was the presence of macrophages and lymphocytic infiltration, as seen in Figure 2. All (100%) LL and B L leprosy cases were positive by Fite-Faraco staining, and 4 out of 14 cases of BT and 2 out of 12 cases of TT were positive on staining. LL leprosy showed a BI of +6, while most of the cases in BT leprosy and TL leprosy showed a BI of 0 by ZN staining. Figures 3 and 4 show the presence of *Mycobacterium leprae* bacilli in the ZN stain and Fite-Faraco stain, respectively.

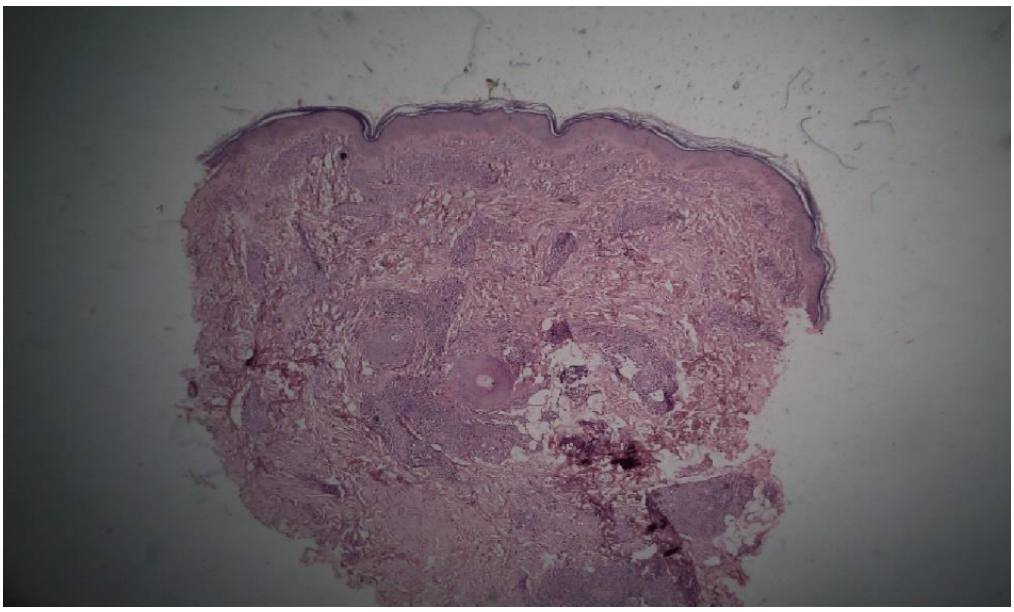

Figure 1. Lymphocytes and epithelioid cells (H&E) (10×)

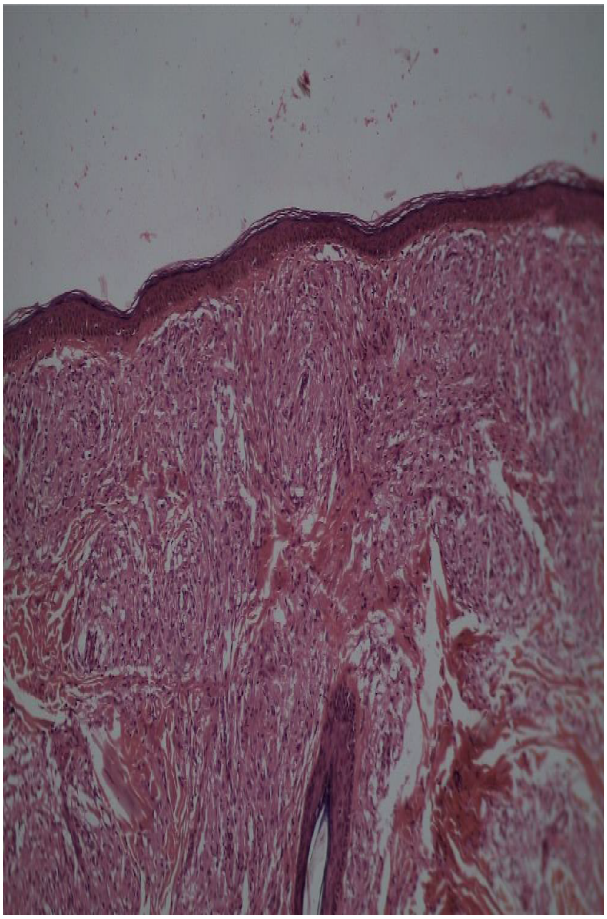

Figure 2. Atrophied epidermis with loss of rete ridges; dermis showing macrophages and few lymphocytes (H&E) (10×)

Discussion

Leprosy is a chronic infectious disease. Diagnosing promptly and precisely is the mainstay for control of leprosy, proper patient management, disease transmission, and preventing deformity (5). Histopathological examination of skin lesions is still the gold standard in diagnosis and classification (10). In the present study, we analyzed the distribution of cases according to clinical diagnosis. Clinically, the most commonly diagnosed type was BL leprosy (35.48%), followed by BT leprosy (27.42%), LL (22.58%), and TL leprosy (12.90%). There was one patient with BL leprosy. Other authors have noted a similar predominance of cases in the borderline group (11-15).

The distribution of cases according to histological diagnosis found that the most common type of leprosy was BL leprosy (32.26%), followed by BT leprosy (22.58%). There was no patient with BL leprosy. Thus, the borderline group, which included the BL and BT types, constituted the major part of the spectrum, as confirmed by the findings of other authors (16-19).

Maximum concordance is seen in LL (92.8 %), followed by BL (81.8%) and BT (70.5%) leprosy. Studies done by and Shirazi et al (13), Mohan et al (14), Mathur et al (15), Bijjaragi et al (16) also showed a maximum clinical-histopathologic correlation in the LL subtype of leprosy.

In early cases, clinical signs and symptoms are more prominent than changes at the tissue level. Discordance between the clinical and histological observations is likely in an early biopsy. Multiple parameters influence the histopathological diagnosis, such as quality of the histopathological section, duration of the lesion, depth of biopsy, immune status of the patient, number of sections stained with ZN stain, and any previous treatment taken by the patient (17-20).

Leprosy can occur at all ages. The current study had no case in the 0–10 age group. This was comparable to the results of Shirazi et al (13). The highest number of cases in our study were in the 31–40 age group. In contrast with our findings, Kumar et al (18), Mathur et al (15), and Hazarika

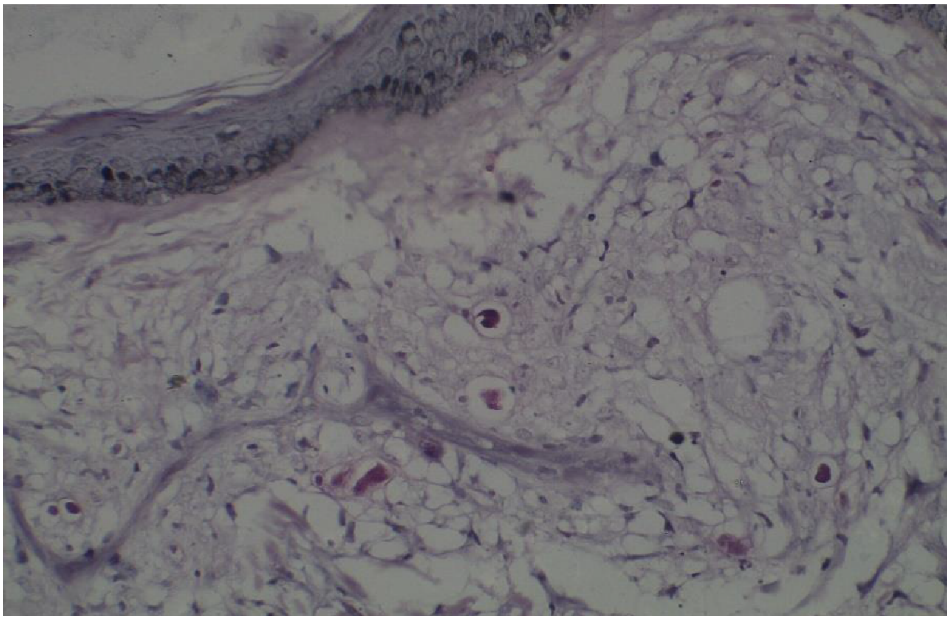

Figure 3. ZN stain showing small rod-like bacilli red in color

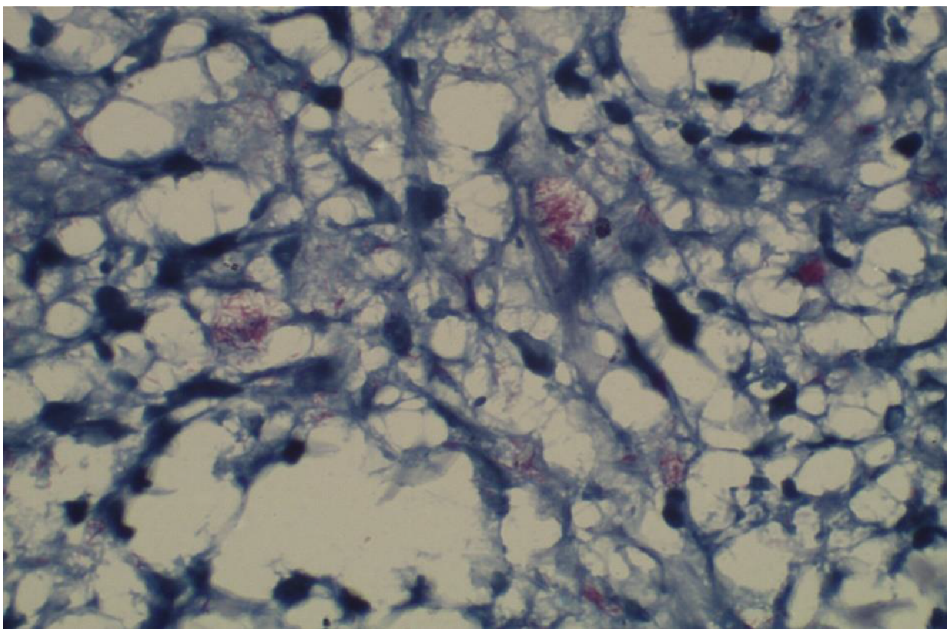

Figure 4. Fite-Faraco stain showing magenta bacilli in globi formation; picture showing solitary erythematous plaque over the left lower back

et al (12) reported that most cases were in the 20–29 years' age group. The most probable reason is that third-world countries' working age is usually up to 50 years.

The male-to-female ratio was 1.21:1 in the present study. Gender distribution shows male preponderance over female patients. The predilection of the disease in males observed in the present study is similar to other studies. In other studies, higher ratios have been reported, ranging from 2.2 to 3:1, possibly because those studies were done over a more extended period and had more cases.

The most commonly observed sites of the lesion were limbs (35.48%) followed by the trunk and back (30.65%), similar to Atram et al (21), who noted that the most common site of the lesion was the upper limbs, followed by the lower limbs, trunk, and face. The most common presentation was papules, followed by macules, which is comparable to other studies (22-26).

The positive histological presence of Hansen's disease and grenz zones was characteristic of LL, seen in 100% of cases. The other predominant histological change in this category was the presence of macrophages and lymphocytes around appendages. The characteristic feature of TT was the presence of epithelioid granuloma and epithelioid cells in 100% of cases (27,28). In BT, granulomas have fewer lymphocytes and more giant cells, and epidermal erosion is not seen. Erosion into the epidermis without a grenz zone is a useful feature in differentiating TT from BT (15,29). In BL, granuloma

rich in foamy histiocytes and few epithelioid cells is seen, and LL is characterized by diffuse sheets of foamy histiocytes with a grenz zone. Dermal edema is one of the characteristic features of leprosy. Histopathologically, it is seen most predominantly as an inflammatory infiltrate. In indeterminate leprosy, neurovascular bundles, erector pili muscles, and sweat glands show mild lymphocytic infiltration around them (23,27,28,30).

The Fite-Faraco stain was positive in 61.3% of subjects and negative in 38.7% of subjects, comparable to the studies done by others (27,31,32).

Conclusion

Leprosy is still prevalent in third-world countries. Although various national programs are in progress, more awareness is needed, especially in rural communities. Clinical and histopathological diagnosis of leprosy cases is still one of the best methods of identifying the lesion. There is an increasing need to evaluate newer techniques for detecting *M. leprae* to ensure rapid screening and reduce observer fatigue while increasing sensitivity and specificity.

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Authors' Contribution

Conceptualization: Nancy Mourya.
Data curation: Nancy Mourya.
Investigation: Nancy Mourya.
Methodology: Jyoti Namdev, Jai Bawane.
Project administration: Puja Singh.
Supervision: Puja Singh.
Validation: Meena Singrol, Jyoti Namdev.
Visualization: Meena Singrol, Jai Bawane.
Writing–original draft: Nancy Mourya.
Writing–review & editing: Puja Singh.

Competing Interests

None declared.

Ethical Approval

This study was approved by the Institutional Ethical Committee, LN Medical College & Research Centre and JK Hospital (Registration number ECR/1190/INST/MP/2019).

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