

A Clinical and Histopathological Correlation among Leprosy Patients (in this Post Elimination Era) Attending Tertiary Referral Centre

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Abstract

Background: Leprosy is caused by *Mycobacterium leprae*, which chiefly affect skin and peripheral nerves. Leprosy expresses itself in different clinicopathological forms depending upon underlying immunity of the host. Histopathology is considered gold standard for accurate diagnosis especially in early disease, however, clinicopathological correlation is a must for appropriate diagnosis and classification of disease that will in-turn affect the treatment and overall prognosis of the patient. The present study of clinicohistopathological correlation among leprosy patients in this post elimination era was undertaken. **Aims and objectives:** To study the clinical and histopathological correlation among leprosy patients. **Materials and Methods:** Present study consists of 54 patients of newly diagnosed leprosy cases at Department of Dermatology, Venerology and Leprology from November 2016 to October 2018. Skin punch biopsy and slit skin smear taken from patients. Histopathological examination by staining with H&E and Fite-Faraco stain for tissue AFB and Ziehl-Neelsen staining of SSS for presence of AFB. **Results:** In this study, 35 cases (64.81%) showed clinicohistopathological concordance and 19 cases (35.19 %) were discordant according to Ridley-Jopling spectrum. **Conclusion:** Histology should be performed in all suspected patients of leprosy if feasible, for exact allocation of the patient across the spectrum for accurate treatment and to identify the vulnerable patients in borderline spectrum as they are prone for reactions, neuritis and thus deformities and it also aids in achieving terminal goal of leprosy elimination.

Keywords: Clinicohistopathological Concordance, Leprosy, Ridley-Jopling Classification

1. Introduction

Leprosy is infectious and treatable disease which commonly affects the skin and the peripheral nerves. It also affects eyes, upper respiratory tract mucosa, testis, kidney, smooth muscles, reticuloendothelial system, vascular endothelium and bones¹. It surprisingly spares female reproductive system, central nervous system and lungs. The discovery of *leprae bacillus* by Gerhard Henrik Armauer Hansen in 1873 opened a new vista in the understanding of the disease². *M. leprae* is a Gram positive rod shaped; intracellular

obligatory bacillus^{3,4}. Diagnosis of leprosy depends on cutaneous examination and examination of peripheral nerves and AFB in slit skin smears by Ziehl-Neelsen's stain and histologic diagnosis and demonstration of AFB in histology sections⁵⁻⁸. Clinical classification considers only gross appearances of the lesions, whereas histology classification parameters are unique and specific and it also includes immunological manifestations. In suspected cases, histopathology provides confirmatory information⁹. Ridley and Jopling divided leprosy into 5 types based on an immunology; tuberculoid (TT), borderline tuberculoid

(BT), midborderline (BB), borderline lepromatous (BL) and lepromatous (LL)¹⁰.

Although the prevalence of leprosy is declining, the annually newly diagnosed cases are stable. This paradox need to be addressed with the best scientific methods¹¹. So, histopathological examination is quite necessary for confirmatory diagnosis of doubtful leprosy cases. The present study was conducted to study the clinical and histopathological correlation among leprosy patients.

2. Materials and Methods

This is cross-sectional, descriptive qualitative study carried out at Outpatient Department (OPD) of Dermatology, Dr. Vasantrao Pawar Medical College, Hospital and Research Centre, Nashik for two years duration from November 2016 to October 2018. New cases of leprosy were selected and recruited purely on clinical ground (World Health Organization (WHO) criteria) attending Dermatology Out-patient department¹². Total 54 cases were finally analyzed.

2.1 Inclusion Criteria: Patients satisfying any of the following criteria irrespective of age and gender

- Hypopigmented or erythematous cutaneous lesions with anesthesia.
- Involvement of peripheral nerves (as demonstrated by thickening with anesthesia)

2.2 Exclusion Criteria

- Patient who has taken anti-leprosy treatment in the past/old cases.
- Patient who is on anti-leprosy treatment.
- Patient not willing to participate in the study.
- Patient presenting in Type 1 and Type 2 Lepra reactions.

To determine incidence, patients were enlisted and records were maintained about clinical diagnosis of all patients. After this initial screening, thorough clinical evaluation was done. Then, all clinically confirmed cases of leprosy were enlisted. Then these patients were subjected to slit skin smear examination taken from four standard sites and two from anesthetic or hypoesthetic, hypopigmented and/or erythematous patch. Slit skin smear was stained by modified ZN stain. Skin biopsy was taken from lesions and stained by Haematoxylin and Eosin stain (H & E) and Fite-Faraco stain¹³.

2.3 Examination of Slides

The processed and stained sections were examined for the following features:

1. Atrophy of the epidermis.
2. Invasion of the epidermis with/without erosion.
3. Subepidermal free zone (Grenz zone).
4. Character and extent of granuloma (formed, diffuse, pedunculated, epithelioid, macrophage)
5. Density & distribution of lymphocytes, histiocytes, foam cells, epithelioid cells, giant cells & other cellular elements.
6. Infiltration of the nerves, blood vessels and adnexae.
7. Bacterial load.

Histopathological classifications of sections were done on the basis of the scheme put forth by Ridley (1974) and later it was correlated with the clinical classification across the Ridley-Jopling spectrum to evaluate the concordance among two.

2.4 Bacteriological Index (BI) on Slit Skin Smear was Calculated Using Ridley's Score¹³

- 1+: 1 to 10 bacilli per 100 Oil Immersion Field
- 2+: 1 to 10 bacilli per 10 Oil Immersion Field
- 3+: 1 to 10 bacilli per Oil Immersion Field
- 4+: 10 to 100 bacilli per Oil Immersion Field
- 5+: 100 to 1000 bacilli per Oil Immersion Field
- 6+: more than 1000 per Oil Immersion Field or many clumps or globi of bacilli in average microscopic field.

3. Results

Out of total 24,239 dermatological cases attended during the two year period from 1 November 2016 to 31 October 2018; 54 were new cases of leprosy were studied for clinicohistopathological concordance. This suggests an incidence rate of 0.2% amongst dermatology outdoor attendances.

Maximum number of patients belonged to the age group of 21-30 years (n=15, 27.78%) followed by 31-40 years (n=14, 25.93%) and 41-50 years (n=8, 14.81%). Thus, the majority of patients (n=37) were in their 3rd to 5th decades of life; accounting 68.52% of the study population. The lowest incidence was seen at extremes of age – 3.70% in 0-10 years and 5.56% in 61-70 years age group.

Overall, males (n=31, 57.40%) outnumbered females (n=23, 42.59%) by a ratio of 1.35:1. This ratio was highest in the age group of 11-20 years (4:1) followed by 61-70 years (3:0). All cases were male gender in age group of 61-70 years and female in age group of 0-10 years as shown in (Table 1 and figure 1).

Table 1. Age and gender distribution

Age (years)	Number of patients			
	Male	Female	Total	%
0-10	0	2	2	3.70
11-20	4	1	5	9.26
21-30	10	5	15	27.78
31-40	7	7	14	25.93
41-50	3	5	8	14.81
51-60	4	3	7	12.96
61-70	3	0	3	5.56
Total	31	23	54	100

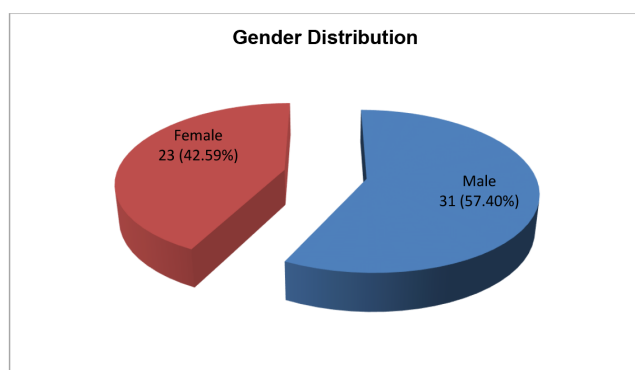


Figure 1. Pie diagram showing gender distribution.

Out of total 54 patients, 32 patients (59.26%) hailed from rural areas and rest i.e. 22 (40.74%) were residing in urban areas.

The majority of patient's duration of disease is less than a year (n=42, 77.78%). Amongst them majority had duration of less than 6 months. 3 patients (5.56%) had duration of more than 3 years. On clinical examination, there were 10 (18.52%) cases of tuberculoid leprosy, 13(24.07%) cases of borderline tuberculoid, 4(7.41%) cases of mid-borderline leprosy, and so on as shown in Table 2.

Table 2. Distribution of clinical profile

Clinical diagnosis	Number of patients	%
TT	10	18.52
BT	13	24.07
BB	04	07.41
BL	06	11.11
LL	16	29.63
IL	05	09.26
Total	54	100.00

Histopathological diagnosis of the patients reveals the features of tuberculoid leprosy in 12 (22.22%), borderline tuberculoid in 14 (25.93%), mid-borderline leprosy in 6 (11.11%), borderline lepromatous leprosy in 3 (5.56%), lepromatous leprosy in 14 (25.93%) patients, while 5 (9.26%) cases showed features of indeterminate leprosy as depicted in Table 3.

Table 3. Distribution of histopathological diagnosis

Histopathological diagnosis	Number of patients	Percentage (%)
TT	12	22.22
BT	14	25.93
BB	06	11.11
BL	03	05.56
LL	14	25.93
IL	05	09.26
Total	54	100.00

Histopathological features of 35 cases showed agreement with its clinical diagnosis, giving overall concordance rate of 64.81%. Disparity was observed in 19 cases accounting for 35.19% discordant rate as shown in Table 4.

Table 4. Overall clinicohistopathological concordance and discordance

Total cases	Concordant cases	Concordance (%)	Discordant cases	Discordance (%)
54	35	64.81	19	35.19

The pattern of concordance between the clinical and histopathological classification across the Ridley-Jopling spectrum was analysed. The highest rate of concordance was seen in lepromatous leprosy (81.25%) where 13 out of 16 patients showed agreement between clinical and histopathological diagnosis followed by tuberculoid leprosy (80%) with as many as 8 out of 10 and indeterminate leprosy, (80%) where 4 out of 5 patients showed clinic-histopathological concordance.

On the other hand, borderline leprosy cases exhibited great disparity between their clinical findings and histopathology. The clinicohistopathological correlation was lowest in mid-borderline leprosy i.e., just 25% - with only 1 case out of 4 showing parity. Concordance was seen in 33.33% cases of borderline lepromatous leprosy (n=2/6) and 53.85% cases of borderline tuberculoid leprosy (n=7/13) as depicted in Table 5.

Table 5. Concordance pattern across the Ridley-Jopling spectrum

Clinical diagnosis	Clinically diagnosed cases	Histological diagnosis						Concordance (%)
		TT	BT	BB	BL	LL	IL	
TT	10	08	02	-	-	-	-	80.00
BT	13	02	07	03	-	-	01	53.85
BB	04	01	02	01	-	-	-	25.00
BL	06	-	02	01	02	01	-	33.33
LL	16	-	01	01	01	13	-	81.25
IL	05	01	-	-	-	-	04	80.00
Total	54	12	14	06	03	14	05	64.81

The pattern of discordance across the Ridley-Jopling spectrum is highlighted in the Table 6. Overall 35.19% of discordance was observed. The majority of the 19 discordant cases, were seen in the borderline part of the spectrum (n=13) with the maximum i.e. 6 number of cases found in borderline tuberculoid cases, followed by 4 cases in BL group.

Table 6. Discordance pattern across the Ridley-Jopling spectrum

	Number cases						Discordance (%)
	TT	BT	BB	BL	LL	Total	
Discordance	02	06	03	04	03	19	35.19

4. Discussion

In India; Bihar, Chhattisgarh, Odisha, Lakshadweep and Dadra and Nagar Haveli are states and UT's with the maximum patients of leprosy. (NLEP – Monthly Progress card for the year 2016-17)¹⁴

In Maharashtra, a total of 15012 new cases were detected during the year 2016-17. District wise break-up of these cases revealed that Palghar district contributed maximum number of cases (1365), followed by Chandrapur district (1165) and Jalgaon district (1108). In capital city, Mumbai, a total of 450 new leprosy cases were detected. In Nashik, a total of 968 new leprosy cases were detected¹⁴.

The present study comprises of 54 newly diagnosed leprosy cases among 24,239 of total OPD attendance giving an incidence of 0.2% with 1.85% of the subjects in the age group 0-9 year age group at our institute. The percentage of new child leprosy cases at national level is 8.70%, whereas in Maharashtra state it is 10.18% (NLEP – Monthly progress report card for the year 2016-2017)¹⁴.

The maximum number of patients in our study were males (n=31, 57.41%), whereas females accounted (n=23, 42.59%).

In India, females accounted for 39.17% of 1,35,485 new leprosy cases registered for treatment as of March, 2017¹⁴. The incidence of female cases was 45.11% amongst the new cases detected in Maharashtra during the year 2016-17¹⁴.

Noorden SK observed that the higher incidence of leprosy in males¹⁵. 32 out of 54 patients i.e. 59.26% hailed from rural areas, while remaining 40.74% were from urban areas.

The present study showed an overall clinicohistopathological concordance of 64.81% with 35 out of the total 54 cases. In literature there are several studies were done to evaluate the correlation between clinical findings and histological features of leprosy. The various concordance rates noted in these studies were 56.54% (Nitesh Mohan et al, 2013)¹⁶, 62.9% (Kumar et al, 2014)¹⁷, 57.3% (Bajjaragi et al., 2013)¹⁸, 61.8% (Nadia et al, 2015)¹⁹, 65% (K L Shobha et al., 2015)²⁰. From the above data it's evident that clinicohistopathological concordances of most of the studies are more or less similar to our study. The little variation observed is may be due to the difference in sample size.

The present study noted discordance rate of 35.19%. The clinicohistopathological discordance observed in different studies are 43.46% (Nitesh Mohan et al., 2013)¹⁶, 37.1% (Kumar et al., 2014)¹⁷, 42.7% (Bajjaragi et al., 2013)¹⁸, 38.2% (Nadia et al., 2015)¹⁹, 35% (K L Shobha et al., 2015)²⁰. Thus the rate of discordance observed in our study is in congruence with study done by K L Shobha et al.,²⁰

4.1 Concordance Pattern

The highest rate of concordance was observed in lepromatous leprosy which is 81.25% i.e., 13 out of 16 patients showed parity between clinical and histopathological finding. Our study shows concordance with the studies done by Mathur MC et al.,²¹, Shivaswamy KN et al.,²², Bijjaragi S et al.,¹⁸, Giridhar M et al.,²³ and Manandhar U et al.,²⁴ which also showed highest clinicohistopathologic correlation in LL subtype of leprosy, 95.2 %, 84.2%, 76.9%, 93.8% and 57.1% respectively.

The lowest concordance was found in mid-borderline leprosy cases. Only 25% i.e., 1 out of 4 patients showed correlation among clinical and histological findings in BB leprosy.

4.2 Discordance Pattern

The present study observed discordance rate of 35.19%. Majority of the 19 discordant cases, were seen in the borderline part of the spectrum i.e. 13 (68.42%) with the maximum i.e., 6 (31.57%) number of cases found in borderline tuberculoid cases.

These findings are in conformity with different studies like 43.46% (Nitesh Mohan et al., 2013)¹⁶, 37.1% (Kumar et al., 2014)¹⁷, 42.7% (Bajjaragi et al., 2013)¹⁸, 38.2% (Nadia et al., 2015)¹⁹ and 35% (K L Shobha et al., 2015)²⁰.

Early stage biopsy may result into more chances of clinical and histological discordance. Also inter observer variation in clinical and histopathological examination may lead to overlap between different types of leprosy (Bhatia et al.)²⁵.

5. Conclusion

This study highlights the importance of histological examination in assessing the leprosy cases as the clinical examination only reflects the gross morphology of the lesions; whereas the specific histopathologic features in leprosy which are well defined and precise and indicate the accurate response of the tissue, while taking into account the immunologic manifestations. Due to variable CMI, there is variable tissue response in the disease spectrum of leprosy, and thus it results into disparity between the clinical and histopathological features, which is evident in our study. In this era of elimination, clinically misdiagnosed case of multibacillary leprosy may help in spreading of disease in due course, moreover there will be danger of drug resistance.

To conclude, in-depth studies with large sample size are required to reassess the criteria, taking into consideration of clinical examination and histopathological parameters, for the prompt and accurate diagnosis of leprosy.

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