

# Clinical and Histopathological Correlation in Hansen's Disease

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## ABSTRACT

**Background:** The present study was carried out to correlate clinical diagnosis of new leprosy cases with that of histopathological diagnosis of skin biopsies stained with Haematoxylin and Eosin followed by Fite Faraco stain.

**Method:** Skin biopsies of 70 newly diagnosed leprosy patients were fixed in 10% formalin and routine histopathological examination done followed by special stain (Fite Faraco) to evaluate the bacterial index.

**Results:** From this study it was observed that, the commonest age group affected by leprosy was 31 to 50 years, males are twice more commonly affected than females (M:F = 1.9 : 1) and the most commonest clinically diagnosed spectrum was Tuberculoid leprosy (TT). The commonest histopathologically diagnosed spectrum was Indeterminate leprosy (IL). It was observed that there was complete agreement between clinical diagnosis and histopathological diagnosis in 62.85% cases and disagreement was observed in 37.15% cases.

**Conclusion:** In case of confirmed discrepancy, the more advanced findings (ie. towards the lepromatous pole) should be given greater weightage and the case is to be classified and treated accordingly.

**Keywords:** Clinical Diagnosis, Histopathological Diagnosis, Leprosy, Fite Faraco Stain, Agreement, Disagreement

## Introduction

Leprosy (Hansen's disease), is a chronic infectious disease that primarily affects the skin & the peripheral nerves. Leprosy is one of the oldest diseases of mankind<sup>[1]</sup>. Even though tremendous progress has been made in the field of leprosy, it still continues to be a global health problem.

Despite an extensive global drug programme for leprosy, implemented by the WHO, leprosy is endemic in many countries with approximately 211,000 new cases reported every year.

The overall prevalence of leprosy in India has declined from 5.27/10000 in the year 2000 to 0.66/10000 in the year 2016, but still it continues to be a sizable public health problem<sup>[2]</sup>. India represents approximately 60% of the global burden<sup>[3]</sup>.

Leprosy expresses itself in different clinico- pathological forms depending on the immune status of the host. Diagnosis of leprosy is based on different clinical parameters which involves detailed examination of skin lesions and peripheral nerves. Demonstration of acid- fast bacilli in slit skin smears by modified Ziehl- Neelsen's staining also aids in the diagnosis of leprosy. A reliable diagnosis hinges around a good histopathological work up and demonstration of bacilli in histopathological sections.

Fite - Faraco staining procedure has proved most valuable in demonstrating lepra bacilli in tissue sections.

Ridley and Jopling were the first to suggest a subclassification of leprosy based on immunological aspects, as five types; Tuberculoid (TT), Borderline Tuberculoid (BT), Mid borderline (BB), Borderline Lepromatous (BL) and Lepromatous Leprosy (LL)<sup>[4]</sup>. Later, they correlated clinical and bacteriological findings in each group with respective immunological and histological findings.

## Materials and Methods

The study was conducted on the skin biopsies of patients newly registered at the Department of Dermatology, Venerology & Leprosy and subsequently reported to the Histopathology section of the Department of Pathology, Government Vellore Medical College & Hospital, Vellore, over a period of 2 years from January 2015 to Dec 2016. Newly diagnosed leprosy patients aged between 15 to 65 years with hypopigmented patches with loss of sensation were included in the study. Patients younger than 15 years and older than 65 years, old treated cases and those who were on multi drug therapy (MDT) were excluded from the study.

After informed consent, enrolled patients were subjected to general and dermatological examination regarding

the morphology, number, size, site, colour, anaesthesia, margins, surface, satellite lesion and central clearing of skin lesions as well as the involvement of peripheral nerves and cutaneous nerves was done. Reactions and deformities were also noted.

Skin biopsy was done from the margin of the skin lesion and fixed in 10% formalin. The specimen was processed routinely in the histopathology lab and sections were stained with Haematoxylin and Eosin.

Haematoxylin and Eosin stained sections of the skin biopsies of all the cases of leprosy included in the study were examined for : a) Epidermal atrophy, epithelioid granulomas, number and distribution of lymphocytes, histiocytes & foam cells. b) Infiltration of nerves, blood vessels and adnexa. c) Grenz zone.

Sections stained with Fite- Faraco stain were examined for lepra bacilli. The following Fite Faraco staining procedure was carried out : 4 micron thick sections were kept in the incubator for 10 to 20 minutes to dewax the sections. The slides were kept in a mixture of xylene and oil (liquid paraffin) in the ratio of (3:2) for 40 minutes. The slides were drained, blotted, dried and rinsed in water for 1 minute, followed by this the sections were covered with carbol fuschin for 40 minutes. The slides were rinsed in water, decolourised with 5% sulphuric acid for 5 minutes. The slides were washed in water, counter stained with haematoxylin for 3 minutes. Followed by this, slides were washed in water, air dried and mounted with DPX. The stained slides were observed under microscope, mycobacterium appears as pink to red rods in a blue background. Based on Ridley's logarithmic scale, bacterial index (BI) was done. Histopathological findings were graded into tuberculoid (TT), borderline tuberculoid (BT), mid borderline (BB), borderline lepromatous (BL) and lepromatous leprosy (LL) according to Ridley & Jopling scale. Sections showing scattered non specific lympho-histiocytic infiltration with cellular reaction within the dermal nerve or presence of bacilli in arrector pilorum muscle / dermal nerve were classified as indeterminate leprosy and also included in the study for the purpose of analysis.

**Table 1: Histological Types of Leprosy**

HISTOLOGICAL TYPE	NUMBER OF CASES	PERCENTAGE
TT	16	22.85%
BT	4	5.72%
BB	4	5.72%
BL	6	8.57%
LL	12	17.14%
HISTOID	4	5.72%
IL	24	34.28%

Clinical diagnosis of leprosy cases (as provided by Department of Dermatology, Venerology & Leprosy) using Ridley & Jopling scale was correlated with the results of histopathological examination of their respective biopsies.

## Results

During the study period of 2 years from January 2015 to Dec 2016, 70 skin biopsy specimens of clinically diagnosed new untreated cases of leprosy were studied, which included 46 males and 24 females (M : F = 1.9 : 1) aged between 15 to 65 years.

Histopathological examination of the skin biopsies of 70 patients revealed that, the maximum histopathological cases were seen in IL (Indeterminate) type followed by TT and LL (with its variant Histoid type). Maximum number of cases were seen in the polar spectrum ie). TT & LL (including its variant Histoid) and indeterminate type.

Based on the Ridley & Jopling logarithmic scale, bacteriological index (BI) was studied on Fite Faraco stained slides. BI observed was 0 (zero) in case of TT and 5+ / 6+ in cases of LL and its variant Histoid leprosy.

The distribution of 70 cases on clinical leprosy spectrum based on Ridley & Jopling scale revealed maximum cases in polar spectrum: TT - 28 cases (40 %), LL and its variant Histoid - 18 cases (14 + 4) (25.71 %), borderline (BT + BB + BL) - 20 cases (28.57 %) and the least in IL - 4 cases (5.72%). Complete agreement of clinical and histological diagnosis was seen in Histoid Hansen's (variant of LL) (100%) and IL (100%) followed by LL (85.71%) & TT (57.14%). Least agreement of clinical and histopathological diagnosis was observed in borderline spectrum (BT, BB, BL). Most number of cases which had disparity between clinical and histopathological diagnosis showed histological features of IL (20 cases) due to the absence of granuloma.

In the present study the histopathological characteristics were consistent with the clinical diagnosis in 44 cases out of 70 cases. Complete agreement between clinical diagnosis and histopathology was observed in 62.85 % and disagreement was seen in 37.15% cases.

**Table 2: Correlation of Hpe Diagnosis and Bacteriological Index ( Fite Faraco Stain).**

HPE DIAGNOSIS	BACTERIOLOGICAL INDEX ( BI )
TT	0
BT	1+
BB	2+ / 3+
BL	3+ / 4+
LL	5+
HISTOID	5+ / 6+
IL	0 / 1+

**Table 3: Clinico- Histopathological Correlation**

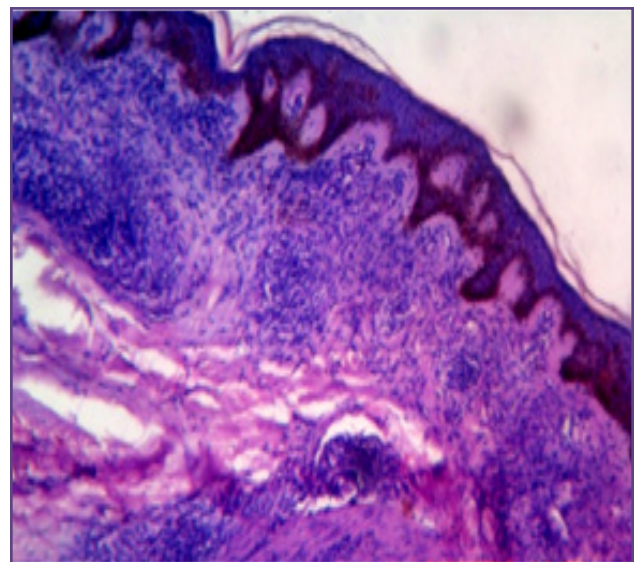
CLINICAL DIAGNOSIS	HISTOPATHOLOGICAL DIAGNOSIS							PARITY PERCENTAGE
	TT	BT	BB	BL	LL	HISTOID	IL	
TT (28)	16	-	-	-	-	-	12	57.14%
BT (8)	-	2	2	-	-	-	4	25%
BB (4)	-	-	2	-	-	-	2	50%
BL (8)	-	2	-	4	-	-	2	50%
LL (14)	-	-	-	2	12	-	-	85.71%
HISTOID(4)	-	-	-	-	-	4	-	100%
IL(4)	-	-	-	-	-	-	4	100%

**Table.4. Complete Agreement - Clinical Diagnosis & Histopathology**

TYPES	CLINICAL CASES		COMPLETE PARITY ( HPE )	
	NUMBER		NUMBER	PERCENTAGE
TT	28		16	57.14%
BT	8		2	25%
BB	4		2	50%
BL	8		4	50%
LL	14		12	85.71%
HISTOID	4		4	100%
IL	4		4	100%
<b>TOTAL</b>	<b>70</b>		<b>44</b>	<b>62.85%</b>



**Fig.1: Borderline lepromatous leprosy. Multiple bilateral more or less symmetrical copper coloured shiny anaesthetic patches.**



**Fig. 2: Borderline lepromatous leprosy : Atrophic epidermis, clear subepidermal grenz zone, collection of macrophages and lymphocytes.**

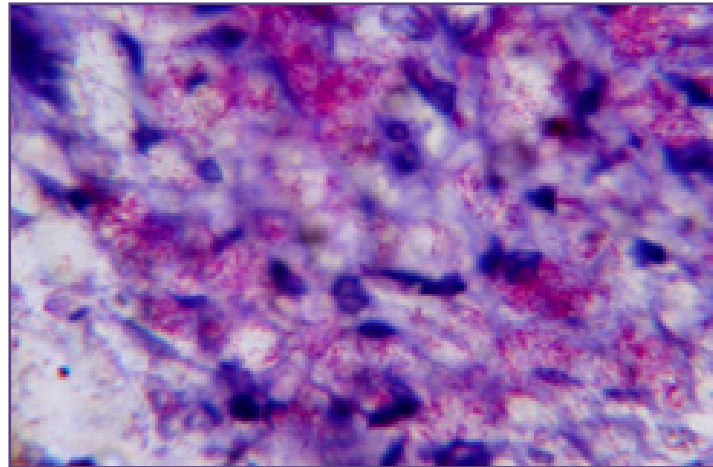


Fig. 3: Borderline lepromatous leprosy. Fite- Faraco stain. Bacterial Index ( BI ) = 4+.

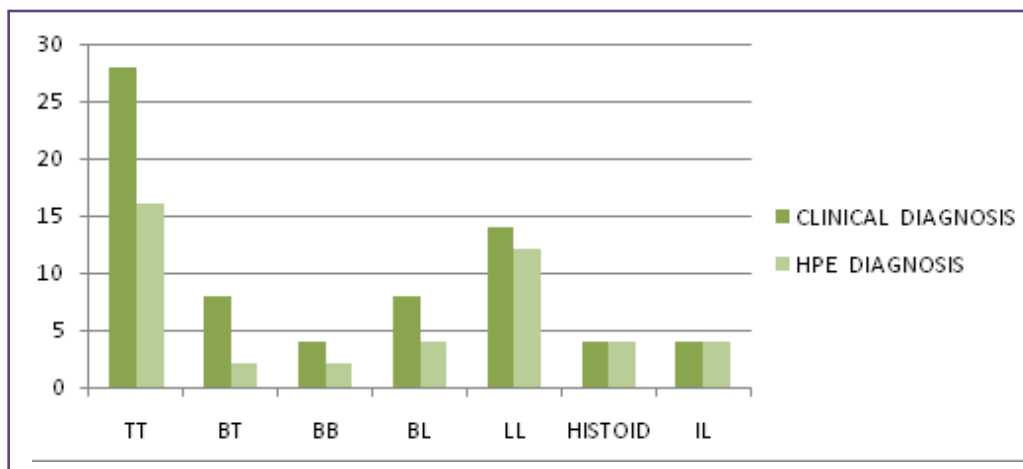


Fig. 4: Clinico - Histopathological correlation of various types of leprosy. Y- axis denotes the number of patients.

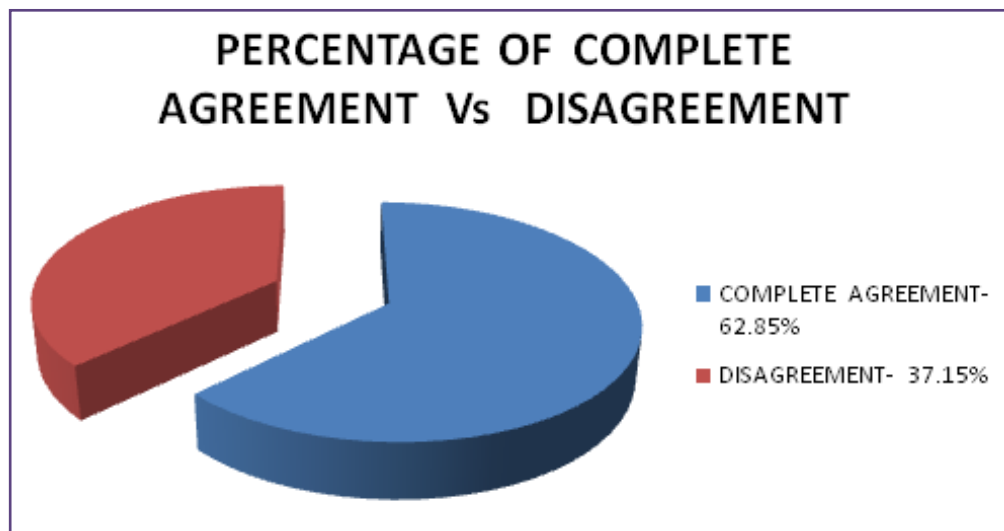


Fig. 5: Percentage of complete agreement of histopathological diagnosis with clinical diagnosis and percentage of disagreement.

## Discussion

A chronic disease like leprosy needs appropriate classification because of its varied manifestations. The most commonly accepted classification by research workers is that of Ridley & Jopling<sup>4</sup> which is primarily based on immunity but has been correlated with clinical, histopathological and bacteriological findings.

Despite having such an accurate classification, there are diversities between the clinical and histopathological features. Clinical spectrum of leprosy in the present study revealed maximum cases in polar spectrum - TT (40%), followed by LL and its variant Histoid (25.71%), borderline (ie) BT, BB, BL (28.57%) and IL (5.72%). Similar predominance of cases in polar spectrum was observed by Kalyani mitra et al<sup>5</sup>. In the present study the histopathological characteristics were consistent with the clinical diagnosis in 44 cases out of 70 cases (62.85%), similar to the observation made by Nadia et al<sup>6</sup>. Lepromatous cases (including its variant Histoid) seem to present the least problem in classification. Similar highest percentage of agreement between clinical and histopathological diagnosis of lepromatous leprosy cases was also observed by Shenoi & Sidappa<sup>7</sup>, Pandey & Tailor<sup>8</sup>, Bhatia et al<sup>9</sup>, Kalla et al<sup>10</sup> and Shanker Naryan et al<sup>11</sup> in their respective studies.

Least agreement was seen in cases of borderline spectrum (BT, BB, BL) in this study, which is in concordance with observations recorded by Shenoi & Siddappa<sup>7</sup>, Nadkarni & Rege<sup>12</sup>, Bhatia et al<sup>9</sup> and Singhi et al<sup>13</sup>. Maximum discordance (37.15%) between clinical and histopathological diagnosis was observed in borderline spectrum cases (BT, BB, BL) of the present study and the same was also noted by Singhi et al<sup>13</sup> and Sandeep et al<sup>14</sup>. Borderline spectrum particularly midborderline leprosy is immunologically the least stable and a variety of clinical lesions of different morphology may be found in the same patient. It is therefore necessary to relate the histological features with the clinical characteristics presented by the particular morphological lesion subjected to biopsy. If this is done carefully, it may be possible to achieve a better clinical correlation with the histological changes.

Tuberculoid and borderline tuberculoid leprosy often overlap clinically, histologically and immunologically but differ only in the degree and the same is true for borderline lepromatous and lepromatous leprosy.

In the present, study, 24 cases (34.28%) were diagnosed as indeterminate leprosy histologically as against 4 cases (5.72%) clinically. Nadkarni & Rege<sup>12</sup> and Kalyani

mitra et al<sup>5</sup> had also diagnosed a sizeable proportion of the cases as indeterminate leprosy histopathologically, who were clinically classified as cases of TT, BT, BB or BL leprosy. Indeterminate leprosy is one which cannot be classified within the Ridley & Jopling spectrum due to lack of distinguishing features and this happens more often histologically (due to the failure to find a granuloma) than clinically. In the present study, the high percentage of indeterminate leprosy noted histologically in clinical cases of TT, BT & BB groups could have been due to immunological differences in host responses.

The disparity between clinical and histological observation was anticipated because the parameters used for the histopathological classification are well-defined, precise and also take into account the immunologic response of the tissue, while the clinical classification gives recognition only to the gross appearances of the lesions, which is due to the underlying pathological changes. Moreover, a sizable proportion of leprosy cases (BT, BB, BL) are in a continuously changing immunological spectrum and the histological classification gives a better indication for any recent shift of a case position in the spectrum.

In some early cases, clinical signs and symptoms may precede the presently known characteristic tissue changes, or vice versa<sup>9</sup>. If a biopsy is taken at an early stage, there is likely to be discordance between the clinical and histopathologic observation. As disparity depends upon the lesion biopsied at the time of study, biopsy from the lesion which is morphologically suggestive of clinical diagnosis, serial biopsies from the same lesion or from paired lesions should be studied for better clinico - pathological correlation.

### From the present study it was observed that :

- The commonest age group affected by leprosy was 31 - 50 years.
- Males are twice more commonly affected by leprosy than females. (M : F = 1.9 : 1).
- The most commonest clinically diagnosed spectrum was tuberculoid leprosy (TT).
- The commonest histopathologically diagnosed spectrum was IL, followed by TT & LL with its variant histoid leprosy.
- It was observed that there was complete agreement between clinical diagnosis and histopathological diagnosis in 62.85% cases.
- Disagreement between histopathological diagnosis and clinical diagnosis was observed in 37.15 % cases.

- If there is discrepancy between clinical and histopathological classification, both the findings should be reviewed by independent experienced observers.
- In case of confirmed discrepancy, the more advanced findings (ie. towards the lepromatous pole) should be given greater weightage and the case is to be classified and treated accordingly.
- In all cases of leprosy, in order to type the exact spectrum of disease for appropriate treatment, skin biopsy of the lesions with histopathological examination followed by special stain (Fite -Faraco) is recommended.

### Conclusion

In clinical practice a case of leprosy is to be classified as per clinical criteria. Skin biopsy has to be taken from the most active site of the lesion. This will help in the confirmation of diagnosis and classification. If there is discrepancy between clinical and histopathological classification both the findings should be reviewed by independent experienced observers. In case of confirmed discrepancy the more advanced findings (ie. towards the lepromatous pole) should be given greater weightage and the case is to be classified and treated accordingly. This will prevent inadequate treatment of a particular case.

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