

Original Article**Clinico-Histopathological Correlative Study of Leprosy at a Rural Hospital**

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Abstract**Objectives**

1. To analyze the clinico-histopathological correlation in different types of leprosy.
2. To study histopathological spectrum of skin lesions in leprosy.
3. To observe disparity between clinical and histopathological features in different types of leprosy.

Methods: The history and complete clinical examination of 197 patients coming to Dr. Bhausaheb Sardesai Hospital, Talegaon-Dabhade was noted, with reference to skin lesions, nerves and sensory disturbances. Relevant past and family history was taken. Biopsies were taken from most active skin lesions including margins of lesion by Department Of Dermatology & samples were sent to the Department Of Pathology in 10% formalin. The tissue section was stained routinely by Hematoxylin and Eosin. Special stain like Modified Fite Faraco was done to demonstrate lepra bacilli. Histopathological findings were graded into Tuberculoid (TT), Borderline-Tuberculoid (BT), Midborderline (BB), Borderline-Lepromatous (BL), and Lepromatous (LL), according to Ridley and Jopling scale. Clinico-Histopathological correlation was done.

Results: Out of 197 suspected cases of Leprosy which are biopsied, 135(68.52%) cases showed histological features consistent with one type of leprosy. A comparison of histopathological findings with that of clinical pattern revealed that maximum correlation was seen with TT(83.33%) followed by BT(79.76%), BL(54.16%), LL(50%) & BB(25%). There were 3 cases of Histoid Leprosy which showed 100% correlation.

Conclusions: As there can be some degree of overlap between different types of leprosy, both clinically and histopathologically, correlation of clinical and histopathological features along with bacteriological index appears to be more useful for accurate typing of leprosy than considering any one of the single parameters alone.

Key Words: Leprosy, BT, BL, TT, LL.

INTRODUCTION

Leprosy is one of the leading cause of physical disabilities which contribute to social stigma.

Leprosy is a chronic infectious disease caused by Mycobacterium leprae¹ affecting the cooler parts of the body i.e. skin, upper respiratory tract,

anterior segment of the eye, superficial portions of peripheral nerves and testes.²

Leprosy is widely prevalent in India. There were 0.86 lakh leprosy cases as on 1st April 2016 with a prevalence rate 0.66/10000 population.³

Leprosy is a disease which, apart from causing awful disfiguration, physical pain and hardship, leads to isolation, rejection and social stigma that still characterize attitudes towards leprosy.⁴

Histopathological study of leprosy is very important in understanding the disease, its varied manifestation and complications. For accurate and adequate treatment the diagnosis must be made early & it should be accurate. So clinicopathological correlation is very important in patient care and management.

Since exact typing of leprosy is sometimes clinically not possible, added to this the poor results obtained by slit skin smear leads to false negative diagnosis. Hence histopathological examination of skin provides confirmatory information in suspected case and gives indication of progression and regression of disease under treatment.⁵

This study was undertaken to know the histopathological features of leprosy in skin biopsies in suspected cases of leprosy and to categorise these into various types based on microscopy, bacteriological index and to correlate with clinical presentation whenever possible

AIMS AND OBJECTIVES

1. To analyze the clinico-histopathological correlation in different types of leprosy.
2. To study histopathological spectrum of skin lesions in leprosy.
3. To observe disparity between clinical and histopathological features in different types of leprosy.

MATERIALS & METHODS

The present study was conducted mainly to analyse the clinico-histopathological correlation in different types of leprosy. The present study was a prospective study conducted in department of

pathology, at MIMER, Medical College & Hospital located in rural area, during the period of May 2012 to July 2014.

The histopathological study has been carried out in collaboration with Department of Dermatology in the same institute.

Inclusion criteria: Untreated leprosy patients.

Exclusion criteria: Patients who were on treatment for leprosy were excluded from the study.

197 new cases of Hansen's disease were selected for the study.

Method of Collection of Data:

Histopathological study of skin biopsy specimens from clinically suspected leprosy patients was done.

A detailed clinical history, examination findings indicating signs and symptoms of the skin lesions and provisional clinical diagnosis were collected.

Skin punch biopsies measuring 0.5cmx0.5cm from the representative lesion were taken by the Dermatologists, and dispatched in plastic containers containing 10% formalin solution.

Following fixation for 12-24 hours the tissues were processed embedded in paraffin and serial sections of 4-5 microns were obtained, which were stained with Hematoxylin and Eosin for morphological assessment and with Fite-Faraco for identification of the bacilli.

After studying the histopathological features and noting the bacteriological status, the diagnosis of leprosy was confirmed and classified according to Ridley and Jopling classification.

H & E stained sections were studied to observe the various changes that occurred in the epidermis, papillary, reticular, deep dermis, neurovascular bundles and adnexa.

The procedure followed for FiteFaraco Stain was Wade-Fite method for *M.leprae* in paraffin section.

The sections which were stained with the above modifications were observed under oil immersion using 100 x objectives. The bacteriological index was assessed in exactly the same way as the one

followed for smear. The entire dermis was observed to assess the logarithmic index of bacilli. Following was the scale used to calculate the bacteriological index (BI).

0 No bacilli seen.

1+ 1 to 10 bacilli per 100 oil immersion fields.

Examine 100 oil

2+ 1 to 10 bacilli per 10 oil immersion fields.

immersion fields.

3+ 1 to 10 bacilli per oil immersion field.

4+ 10 to 100 bacilli per oil immersion field.

Examine 25 oil

5+ 100 to 1000 bacilli per oil immersion field.
immersion fields.

6+ > 1000 bacilli per oil immersion field.

After studying the histopathological features and noting the bacteriological status, the diagnosis of leprosy was done according to Ridley and Jopling classification and clinico-pathological correlation was done.

OBSERVATIONS AND RESULTS

Out of 197 suspected cases of Leprosy which are biopsied, 135(68.52%) cases showed histological features consistent with one type of leprosy.

The remaining 62(31.47%) cases showed scant perivascular lymphocytic infiltrate. There was no evidence of granulomas and nerve infiltration by lymphocytes. Acid fast bacilli were not detected

on Fite-Faraco stain and in slit-skin smears. Hence these cases were diagnosed as non-specific dermatitis on histopathology.

In present study age of the patients ranged from 8 years to 85 years. Amongst them majority 65 (48.14%) of the patients were in 3rd and 4th decade of life.

There were 75 (55.55%) male patients and 60 (44.44%) female patients, with male to female ratio (M: F) of 1.2:1.

47 (34.81%) cases presented with upper extremities as primary site of the lesion followed by face 40(29.62%), trunk 20(14.81%), lower extremities 16(11.85%), head & neck 8(5.92%) and back 4 (2.96%).

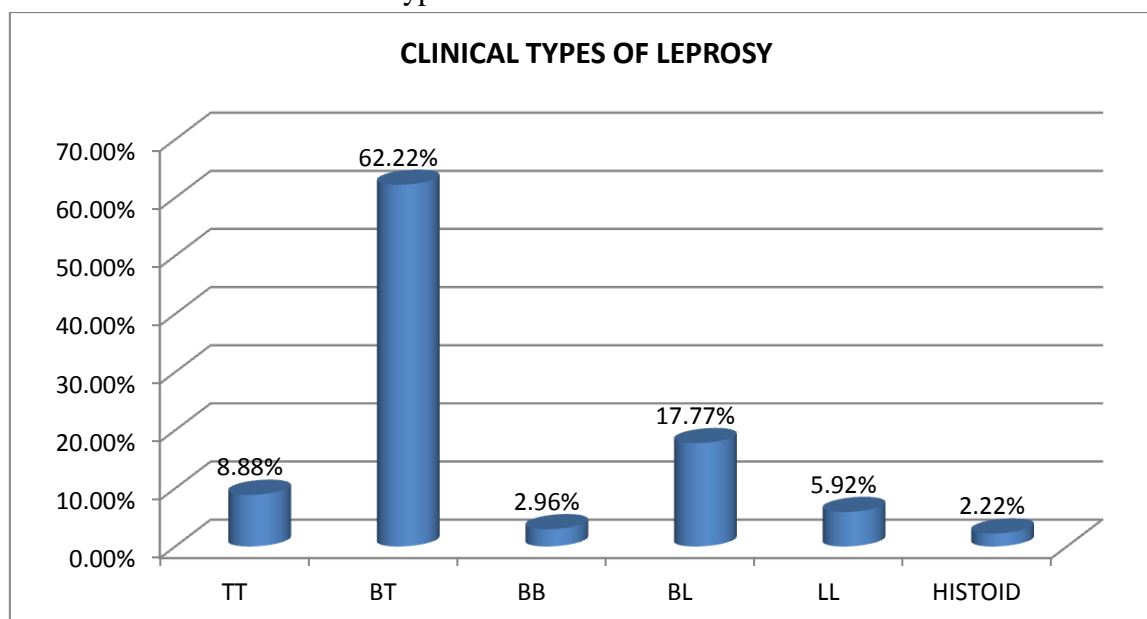
91 (67.40%) cases presented with hypo pigmented lesion and 44 (32.60%) cases presented with erythematous lesion.

Out of 135 cases, 105 (77.77%) patients presented with loss of sensation and 30(22.23%) patients had intact sensation.

Macules, nodules, patches and plaques were the skin lesions most frequently biopsied.

Macules/patches were the skin lesions most frequently biopsied 101(74.81%) and in these skin biopsy features of TT, BT were frequently found. Out of 34(25.18%) nodules/plaques, biopsied most of cases showed features of BL, LL.

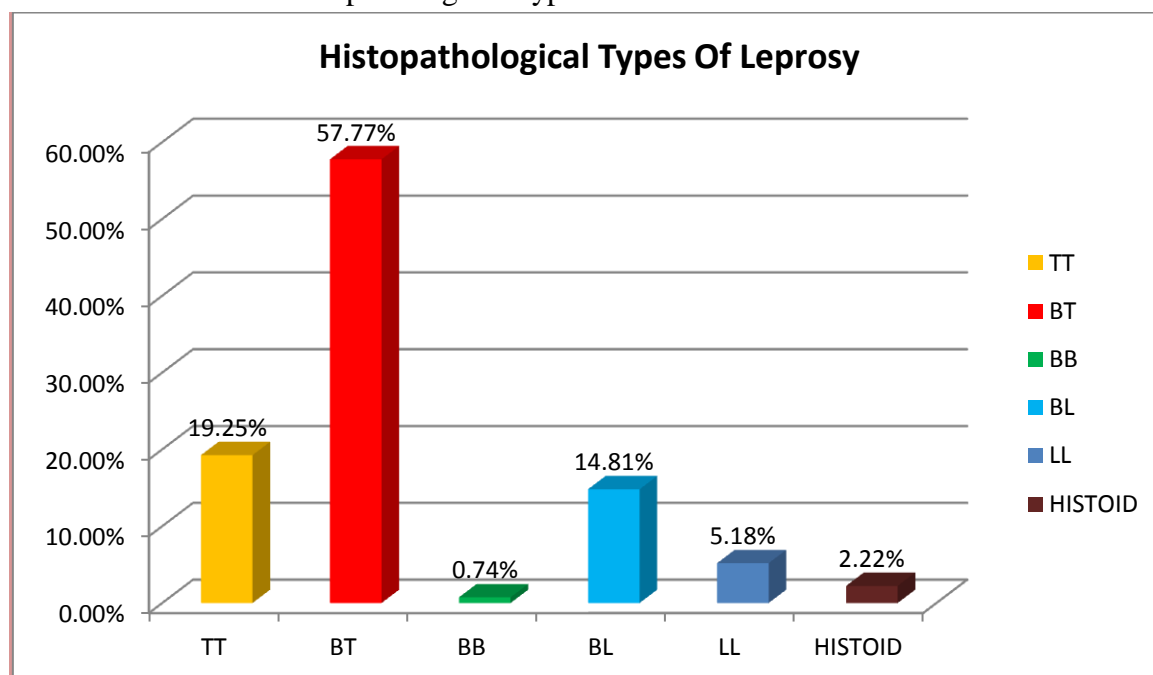
Graph No. 1: Distribution of Clinical Types of LEPROSY



Clinical spectrum of 135 cases revealed maximum 84(62.22%) cases of BT, followed by BL 24 (17.77%), TT 12(8.88%), LL 08(5.92%) and BB

04(2.96%). There were 3 (2.22%) cases of Histoid leprosy.

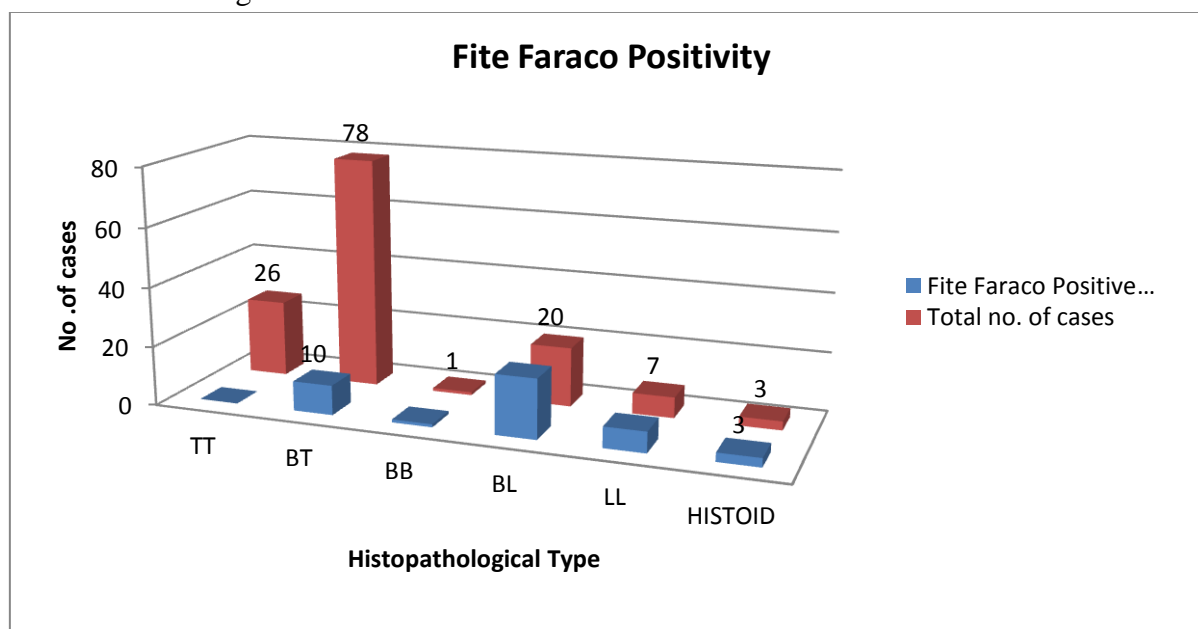
Graph No. 2: Distribution of Histopathological Types of LEPROSY



Histopathologically most common subtype was BT 78 (57.77%), followed by TT 26 (19.25%), BL 20(14.81%), LL 07(5.18%) and BB 01 (0.74%).

There were 3 cases of Histoid leprosy constituting 2.22%.

Graph No. 3: Bacteriological Index

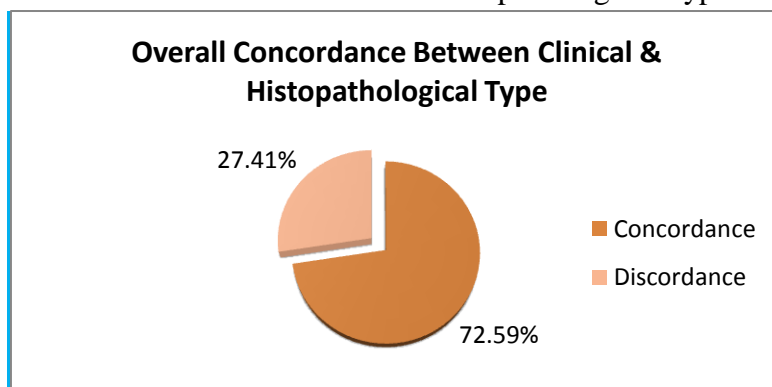


Out of 135 cases, 94(69.62%) cases were of paucibacillary leprosy and 41(30.37%) were of multibacillary leprosy.

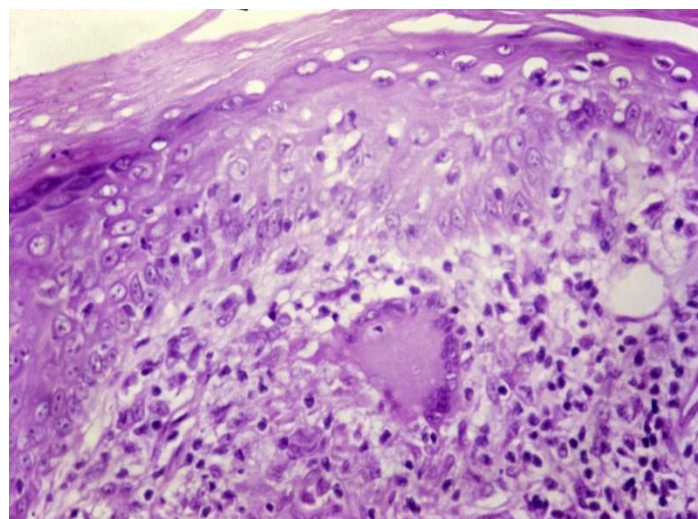
Table 1: Clinico-Histopathological Correlation

Clinical types		Histopathological Diagnosis						Aggregate (%)
Type	→	TT	BT	BB	BL	LL	HISTOID	
↓	No.	26	78	01	20	07	03	
TT	12	10	01	00	01	00	00	83.33
BT	84	14	67	00	03	00	00	79.76
BB	04	00	03	01	00	00	00	25
BL	24	01	07	00	13	03	00	54.16
LL	08	01	00	00	03	04	00	50
HISTOID	03	00	00	00	00	00	03	100

Maximum correlation was seen with TT (83.33%) followed by BT (79.76%), BL (54.16%), LL (50%) & BB (25%). In Histoid leprosy 100% correlation was found.

Graph No. 4:- Overall concordance between Clinical & Histopathological Types

Overall clinico-histopathological correlation was observed in 98(72.59%) of cases.

BORDERLINE TUBERCULOID LEPROSY**Figure 1-**Clinical photograph showing well-defined erythematous plaque**Figure 2-**Microphotograph showing well defined granuloma composed of epithelioid cells, lymphocytes and Langhan's giant cell in dermis. (H &E X40)

TUBERCULOID LEPROSY

Figure 3- Clinical photograph showing well-defined erythematous patch

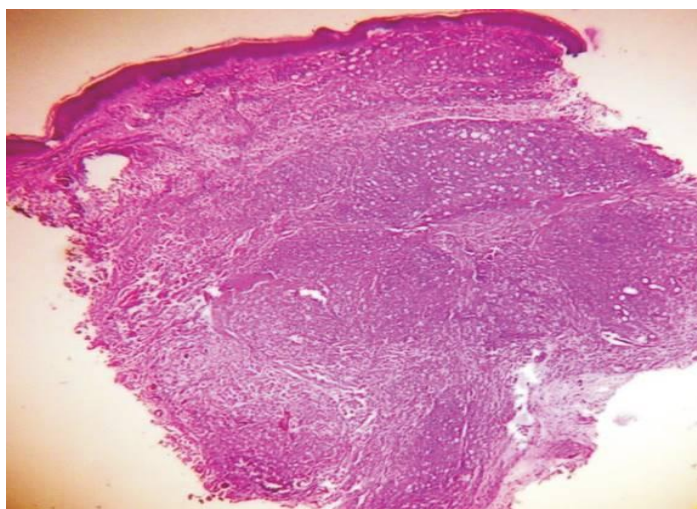


Figure 4- Microphotograph showing granulomas eroding the epidermis (H & E X10)

BODERLINE LEPROMATOUS LEPROSY

Figure 5- Clinical photograph showing ill-defined raised plaque

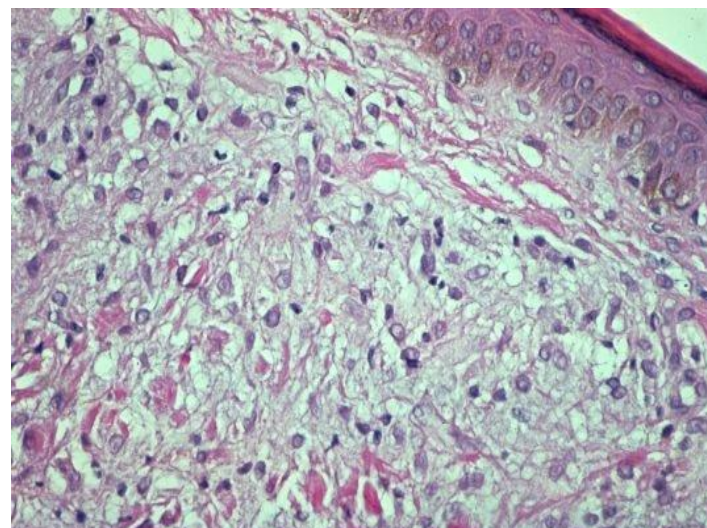


Figure 6- Microphotograph showing foamy macrophages, lymphocytes and few epithelioid cells in dermis with a clear Grenz zone at dermoepidermal junction (H & E X40)

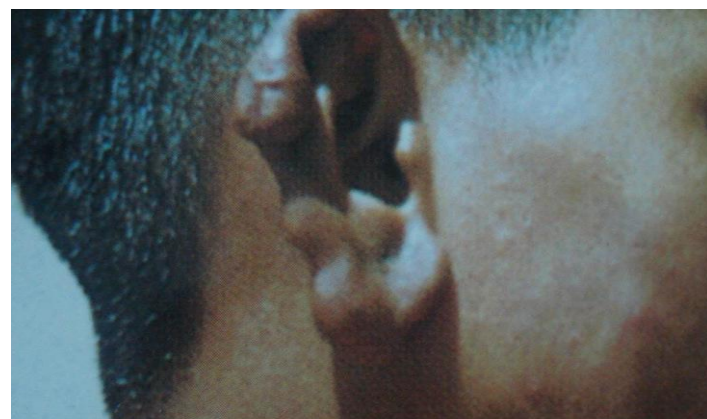
LEPROMATOUS LEPROSY

Figure 7- Clinical photograph showing nodules

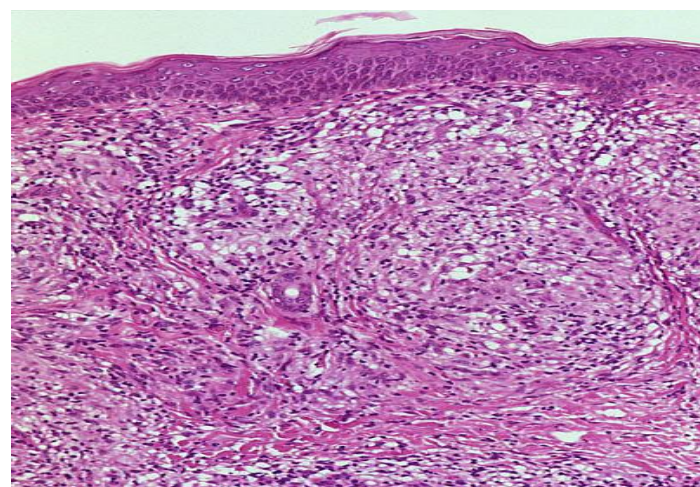


Figure 8- Microphotograph showing sheets of foamy macrophages in dermis with a clear Grenz zone at dermoepidermal junction (H & E X40)

Histoid leprosy

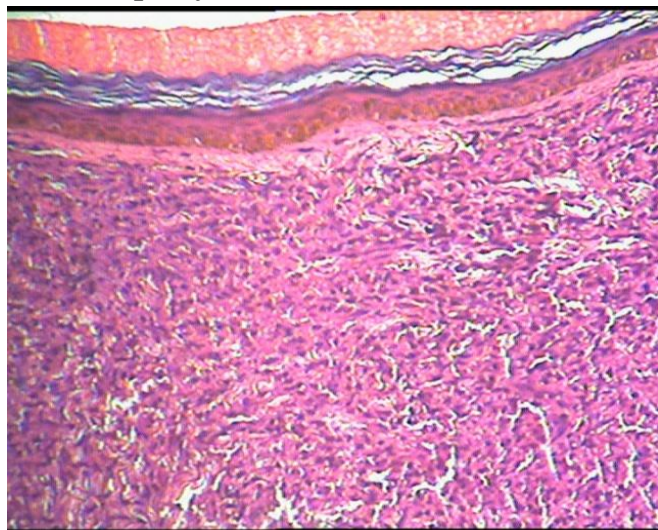


Figure 9- Microphotograph showing clear zone at dermoepidermal junction and spindle shaped histiocytes in the dermis (H & EX40)

Fite Faraco Stain

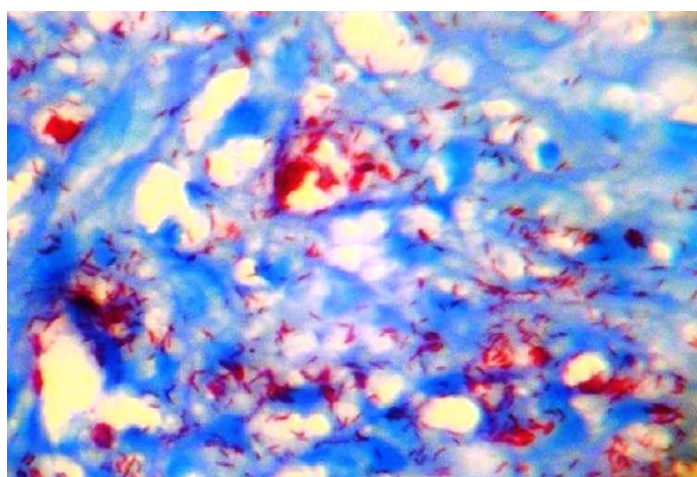


Fig 10- Microphotograph showing Lepra cells with AFB forming globi (Fite Faraco X100)

DISCUSSION

Leprosy or Hansen's disease is a chronic granulomatous, slowly progressive infection caused by *Mycobacterium leprae* affecting the skin and peripheral nerves. It is exclusively a disease of human and only source of infection is a patient suffering from leprosy. Leprosy still continues to be an important public health problem.

Accurate diagnosis is of fundamental importance to all aspects of leprosy epidemiology, management and prevention of disability. Under diagnosis

will lead to continued transmission of disease and much needless sufferings.

Histopathological study of leprosy is very important in understanding the disease, its varied manifestation and complication. For the accurate and adequate treatment the diagnosis must be made early and it should be accurate.

The present study was undertaken in the Department of Pathology, MIMER, Medical College, Talegaon-Dabhade, over a period of 27 months from May 2012 to July 2014. The aim was to study histopathological features of leprosy in skin biopsies and to categorize them into various types based on microscopy and to correlate with clinical presentations whenever possible.

All skin biopsies were from patients who were clinically diagnosed as new cases of leprosy.

AGE WISE CORRELATION-

Disease occurrence in leprosy is often related to age at detection rather than age at onset of disease. It is known to occur at all ages ranging from infancy to very old age.⁶

Out of 135 patients in the present study, 34 (25.18%) patients with age group of 20-29 years (3rd decade) were affected most and patients below 9 yrs were affected least. Similar observations were made by majority of authors likea Guha et al,⁷ Sehgal et al,⁸ Mathur MC et al.⁹ However Kaur et al¹⁰ observed 4th decade as major age group. Although exact reason cannot be given for this age distribution, variable and long incubation period may be responsible for this age distribution.¹¹

SEX DISTRIBUTION

The attitude of society, methods of case detection, type of personnel carrying out survey, methods and frequency of examination, the criteria adopted for diagnosis, type of classification of disease, are some variables that affect the description of the condition. Generally, leprosy is believed to be more common in males than in females.¹²

There were 75 (55.55%) male patients and 60 (44.44%) female patients, with male to female ratio (M: F) of 1.2:1 which is similar to findings made by other authors like Kar PK et al¹³ and Nadkarni & Rege.¹⁴

Male predominance may be because of many factors like industrialization, urbanization and more opportunities for contact in males. Social customs and taboos may account for the smaller number of females reporting for treatment to the hospital.¹⁵

Comparison of Histopathological types

Table 2-

Authors	Type of Leprosy						Total
	TT	BT	BB	BL	LL	IL	
Moorthy BN et al ¹⁶	39 (10.48%)	203 (54.56%)	8 (2.15%)	86 (23.11%)	23 (6.18%)	13 (3.49%)	372
Sharma A et al ¹⁷	19 (7.69%)	83 (33.6%)	83 (33.6%)	17 (6.88%)	29 (11.74%)	16 (6.47%)	247
Shivamurthy Veena et al ¹⁸	3 (1.5%)	145 (72.5%)	5 (2.5%)	21 (10.5%)	11 (5.5%)	15 (7.5%)	200
Shivaswamy KN et al ¹⁹	25 (18.4%)	53 (39.9%)	2 (3.6%)	15 (11%)	19 (13.9%)	22 (16.1%)	136
Present Study	26 (19.25%)	78 (57.77%)	01 (0.74%)	20 (14.81%)	07 (5.18%)	-	135

Out of 197 suspected cases of Leprosy which are biopsied, 135(68.52%) cases showed histological features consistent with one type of leprosy.

The remaining 62(31.47%) cases diagnosed as non-specific dermatitis on histopathology. These cases were followed clinically for a period of 6 months and the follow-up was uneventful.

Out of 135 cases, the most common subtype histologically was BT 78(57.77%) followed by TT 26(19.25%), BL 20(14.81%), LL 07(5.18%) and BB 1(0.74%).

Borderline group constituted the major spectrum (73.33%), similar to findings of other authors.^{16,17,18,19}

A sizable portion of leprosy patients are in a continuously changing immunological spectrum, i.e., BT, BB and BL. Immunological instability in these borderline cases makes them move in either direction along the borderline spectrum. With treatment, they move towards tuberculoid pole while without treatment they tend to move towards lepromatous pole. Biopsy from a case recognized at an earlier stage may show BT while that from a case recognized at a later stage may show BL.^{15,20}

Increased awareness of the people to leprosy owing to national programmes makes them present at an earlier stage to leprosy clinics, which may contribute to increased number of borderline group of leprosy.^{15,20}

BACTERIOLOGICAL INDEX-

Demonstrating AFB is still considered important for diagnosis, classification and management of leprosy. The specificity of slit-smears is almost 100% as it directly demonstrates the presence of acid-fast bacilli (AFB) but the sensitivity is low and varies from 10-50%.

As observed in the studies by other authors like S Veena et al²¹ & Bhushan P et al,²² maximum cases were of paucibacillary leprosy.

In the present study too, majority of the patients were of 94 (69.72%) paucibacillary leprosy and the rest were of multibacillary leprosy 41(30.37%). Majority of the biopsies of BT were of paucibacillary leprosy. All the cases of BL and LL were of multibacillary leprosy.

The difference can be attributed to regional variation and different socio-economic and immune status in population studied.¹⁵

Clinico-Histopathological Correlation-**Table 3-**

Authors	Clinico- Histopathological Correlation						
	TT	BT	BB	BL	LL	IL	Total
Shenoy, Siddappa ²³	77.80%	62.20%	20%	14.40%	100%	85.70%	47%
Nadkarni, Rege ¹⁴	88%	80.7%	69.9%	81.3%	95.3%	93%	81.8%
BijaragiS et al ²⁴	75%	57.3%	16.7%	40%	76.9%	66.7%	57.3%
Bhushan P et al ²²	100%	83.13%	50%	65.22%	100%	-	74.47%
Singh Arjun et al ⁵	100%	83.3%	75%	94.7%	70%	75%	81.5%
Mathur et al ⁹	73.2%	89.74%	64.7%	72.4%	95%	-	80.4%
Kakkad K et al ²⁵	100%	83%	50%	60%	93%	-	84%
Present study	83.33%	79.76%	25%	54.16%	50%	-	72.59%

- Overall complete clinico-histopathological parity was noted in 72.59% cases which is similar to other authors studies.
- Maximum correlation was seen with TT (83.33%) followed by BT (79.76%), BL (54.16%), LL (50%) & BB (25%) which is comparable to other studies.
- When we combined TT and BT cases in one tuberculoid group and LL and BL cases in single lepromatous group, we noted a better clinico-histopathological correlation. Similar rise in clinico-histopathological concordance of tuberculoid group and lepromatous group was also noted by Sharma et al²⁶.

CONCLUSION

The spectrum of leprosy manifestations is very wide and there is considerable overlap between different types of leprosy so both clinical and histopathological features along with bacteriological index are more useful than any single parameter in arriving at a definitive diagnosis and classification of the disease.

Histopathological examination should be carried out for all cases for proper classification of leprosy which may be helpful for the better allocation of the patients to the treatment categories.

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