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Histopathological analysis of Leprosy cases in a tertiary care centre

Akshaya Mandloi [1], Amit V. Varma [2], Navin Jain [3], Kamal Malukani [4], Ekta Patidar [5], Shilpi Singh [6]
[1, 6] PG Resident, [2] Professor and Head, [3] Associate Professor, [4] Professor
Department Of Pathology, Sri Aurobindo Medical College and P.G. Institute, Indore (M.P.),
[5] Consultant Pathologist, Sampurna Diagnostics, Indore (M.P.)

***Corresponding Author:**

Amit V Varma
Add: R.H 19, Ashirwad Villas, Near Delhi Public School, Nipania, Indore, M.P 452010

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ABSTRACT

Background: Leprosy also known as Hansen's disease is a chronic granulomatous, slowly progressive infectious disease caused by Mycobacterium leprae which can present itself in different clinical and pathological forms depending on host's immunity. A reliable diagnosis pivots around an accurate histopathological diagnosis along with demonstration of bacilli in histopathological sections.

Aim: To detect the Lepra bacilli and bacterial index in the biopsies received from clinically diagnosed Leprosy cases, classify the cases as per Ridley–Jopling scale along with inclusion of Indeterminate, Histoid and Pure Neuritic types and to associate clinical and histopathological diagnosis.

Material & Methods: The present study was conducted on skin and/or nerve biopsy of 141 clinically diagnosed patients of leprosy in the department of Pathology in Sri Aurobindo Medical College & Post Graduate Institute over a period of 18 months (from Jan 2017-June 2018).

Results: In the present study, age of patients ranged from 9 years to 82 years with maximum cases (28.37%) belonging to 31-40 years age group. Male preponderance with a male to female ratio of 1.9:1 was observed. Both clinically (35.46%) and histopathologically (39%), BT constituted the predominant group. Out of 141 biopsies, 67 (47.52%) showed positive results with Fite-Faraco staining. 39 (27.66%) biopsies demonstrated features suggesting Lepra reactions. 28.2% cases showed type I and 71.8% cases showed type II Lepra reactions. Most of the biopsies were paucibacillary type 74 (52.48%). The overall concordance between the clinical and histopathological classification was observed in 73% cases.

Conclusion: The clinical manifestations of leprosy are very varied and diverse so, histopathological study of leprosy is very important for timely management and proper treatment of patients.

Keywords: Hansen's disease, Fite Faraco, Bacillary Index, Lepra Reaction

INTRODUCTION

Leprosy also known as Hansen's disease and 'Kushtarog' is one of the oldest disease known to mankind.[1] Leprosy is a chronic granulomatous, slowly progressive infectious disease caused by Mycobacterium leprae which mainly affects peripheral nervous system and skin. Fite-Faraco method is used for demonstration of lepra bacilli and it gives information about the infective status and also quite helpful in deciding the treatment. Leprosy is still widely prevalent in India despite being declared eliminated in 2015. Leprosy is considered important mainly because of its potential to cause permanent and progressive physical deformities with serious social and economic consequences.[2] Leprosy can present itself in different clinical and pathological forms depending on host's immunity.[3] Exact typing of leprosy is sometime clinically not possible and results obtained by slit skin smear are not satisfactory. A reliable diagnosis pivots around an accurate histo-pathological diagnosis along with demonstration of bacilli in histopathological sections.[4]

AIM: To study histopathology of the biopsies received from clinically diagnosed cases of Leprosy.

OBJECTIVES: To classify leprosy cases on histo-pathological basis and to detect the Lepra bacilli in the biopsy. To determine the bacterial index and associate it with the diagnosis. To associate clinical and histopathological diagnosis as per Ridley–Jopling scale along with inclusion of indeterminate, histoid and pure neuritic types.

Inclusion Criteria: All biopsies received in histopathology department from clinically suspected cases of leprosy were included in this study.

Exclusion Criteria: Cases where leprosy was not confirmed histopathologically and the cases with inadequate biopsies were excluded from present study.

Material and Methods: After approval from institutional ethical committee, this observational study was conducted on 141 clinically diagnosed patients of leprosy who underwent skin and/or nerve biopsy at Sri Aurobindo Hospital, associated with Sri Aurobindo Medical College & Post Graduate Institute over a period of 18 months (Jan 2017-June 2018).

The biopsies were stained with H&E and Fite-Faraco stain. Bacterial index was calculated. The collected data was further distributed and tabulated according to gender, age, clinical type, histopathological type, Fite-Faraco staining pattern and presence of lepra reactions. The final diagnosis was made according to the Ridley- Jopling Classification along with inclusion of Indeterminate, Histoid and Neural forms. Clinico-histopathological correlation was established using the 1 proportion Z- test.

RESULTS:

Distribution Of Leprosy Cases According To Age Group and Gender: The age of patients ranged from 9 years to 82 years. Mean age was 38.68 years. Majority of cases were seen in 31-40 yrs age group followed by 21-30 yrs. Out of total 141 cases, there were 93 (65.96%) male and 48 (34.04%) females with a male: female ratio of 1.9:1

Results of Fite Faraco staining in Hansen's disease: Out of all 141 cases, 74 (52.48%) cases were Paucibacillary while remaining 67 (47.52%) were Multibacillary.**Results of Fite Faraco staining in different morphological categories of Hansen's disease:** 10 (18.18%) cases of BT, 1 (7.70%) case of BB, 19 (70.37%) cases of BL, 32 (94.12%) cases of LL, 2 (100%) cases of neural and all the 3 (100%) cases of Histoid leprosy showed positive staining results with Fite-Faraco stain ;while all the 6 cases (100%) of TT and the only case of IL (100%) showed negative staining result.

Table 1: Results of Fite Faraco staining in different morphological categories of Hansens disease

Type of Leprosy	FF POSITIVE		FF NEGATIVE		
	No. of cases	%	No. of cases	%	TOTAL
TT	0	0	6	100	**6**
BT	10	18.18	45	81.82	**55**
BB	1	7.70	12	92.30	**13**
BL	19	70.37	8	29.63	**27**
LL	32	94.12	2	5.88	**34**
HISTIOD	3	100	0	0	**3**
IL	0	0	1	100	**1**
NEURAL	2	100	0	0	**2**
TOTAL	**67**	**47.52**	**74**	**52.48**	**141**

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Distribution of cases with lepra reactions: Out of 141 biopsies, total 39 (27.66%) biopsies demonstrated features suggesting lepra reactions. Out of the total cases showing lepra reactions 11 (28.2%) cases showed type I and 28 (71.8%) cases showed type II lepra reactions

Table 2: Distribution of cases with lepra reactions as per histological type of leprosy

TYPE OF LEPROSY	NUMBER	LEPRA REACTIONS		
		TYPE I	TYPE II	TOTAL
TT	**6**	**0**	**0**	**0**
BT	**55**	**5**	**3**	**8**
BB	**13**	**0**	**0**	**0**
BL	**27**	**5**	**5**	**10**
LL	**34**	**1**	**20**	**21**
IL	**1**	**0**	**0**	**0**
HISTOID	**3**	**0**	**0**	**0**
NEURAL	**2**	**0**	**0**	**0**
TOTAL	**141**	**11**	**28**	**39**

Maximum positive cases (21) belonged to LL type constituting 53.8% of the total cases showing Lepra reactions, followed by 10 cases of BL and 8 cases of BT. Lepra reactions were not seen in other types of leprosy. Out of 21 positive biopsies of LL type, 20 showed features of type-II reaction while 1 showed features of type-I reaction. Out of the 10 positive biopsies of BL type half were reported type-I and half type-2 reaction. In positive cases of BT 5 cases showed type-I reaction.

Correlation between clinical and histomorphological type of Leprosy

Table 3: Correlation between clinical and histomorphological type of Leprosy

Clinical Types	Histopathological Types								
	TT	BT	BB	BL	LL	IL	HIS	NEU	TOTAL
TT	**2**	2	1	2	0	0	0	0	**7**
BT	4	**43**	2	1	0	0	0	0	**50**
BB	0	2	**6**	0	0	0	0	0	**8**
BL	0	4	3	**19**	2	0	0	0	**28**
LL	0	4	0	5	**29**	0	0	0	**38**
IL	0	0	0	0	1	**0**	0	0	**1**
HIS	0	0	0	0	2	0	**3**	1	**6**
NEU	0	0	1	0	0	1	0	**1**	**3**
Total	**6**	**55**	**13**	**27**	**34**	**1**	**3**	**2**	**141**

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Out of 7 clinically diagnosed cases of TT, histopathology confirmed 2 cases as TT,. 28.57% concordance was observed between the clinical and histopathological diagnosis. Out of 50 clinically diagnosed cases of BT, histopathology confirmed 43 cases as BT. Maximum (86%) concordance between the clinical and histomorphological diagnosis was seen in BT. Out of 8 clinically diagnosed BB cases, 6 came out to be BB. Concordance observed was 75%.Out of 28 cases suspected to be BL clinically, histopathology confirmed 19 cases as BL. Out of 38 clinically suspected LL cases,29 cases histologically came out to be LL. Concordance observed between the clinical and histopathological type was 76.31%.The only case clinically suspected to be IL came out to be LL. Hence, 100% discordance was seen between the clinical and histomorphological diagnosis. Out of 6 clinically suspected histioid leprosy cases, histology proved 3 cases as histioid (50 % concordance),Out of 3 cases suspected as neural clinically , one case (33.33% concordance) came out to be neural.

.**Table 4: Concordance and discordance between clinical and histomorphological type of Leprosy**

Clinical Types	**% of Concordance**	**% of Discordance**	****P value**
TT	28.57%	71.43%	<0.001
BT	86%	14%	<0.001
BB	75%	25%	0.003
BL	67.86%	32.14%	<0.001
LL	76.31%	23.69%	<0.001
IL	0	100%	0.01
HIS	50%	50%	<0.001
NEU	33.33%	66.67%	<0.001

Test applied: 1Proportion Z test

**{Null Hypothesis : H0: Clinical types accuracy = Histopathological types

Alternate Hypothesis: Ha: Clinical types accuracy < Histopathological types

Confidence interval = 95% (α=0.05)}

Of all the subtypes, maximum (86%) concordance was observed in BT Hansens, followed by LL Hansens (76.31%) and BB Hansens (75%). 100% discordance was observed in IL Hansens.

In all the histopathological categories of leprosy cases studied, the typing of cases was significantly accurate by histopathological examination as compared to the clinical typing.

The overall parity between the clinical and histopathological diagnosis, irrespective of the type of leprosy, was observed in 73% cases. Disparity was noted in 27% of cases.

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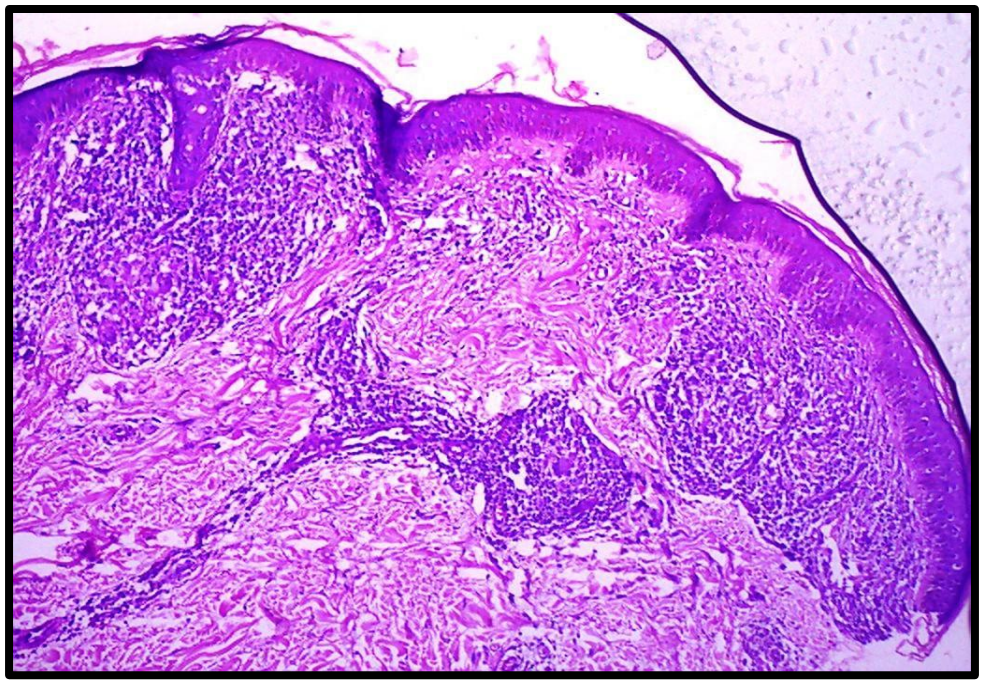

Figure1: Borderline Tuberculoid Leprosy. Photomicrograph showing numerous epithelioid cell granulomas with peripheral lymphocytes and occasional Langhans type of giant cells. (H&E stain, 100x).

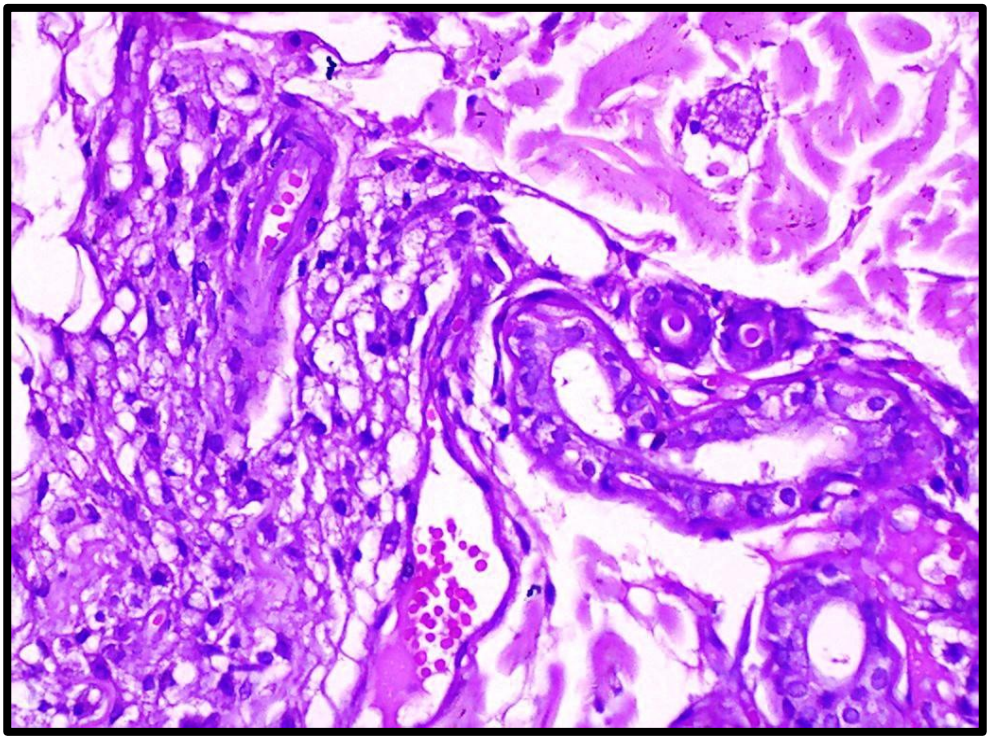

Figure 2: Borderline Lepromatous Leprosy. Photomicrograph showing perivascular and periadnexal infiltrate of histiocytes and foamy macrophages corresponding to BL Hansens. (H&E, 400x)

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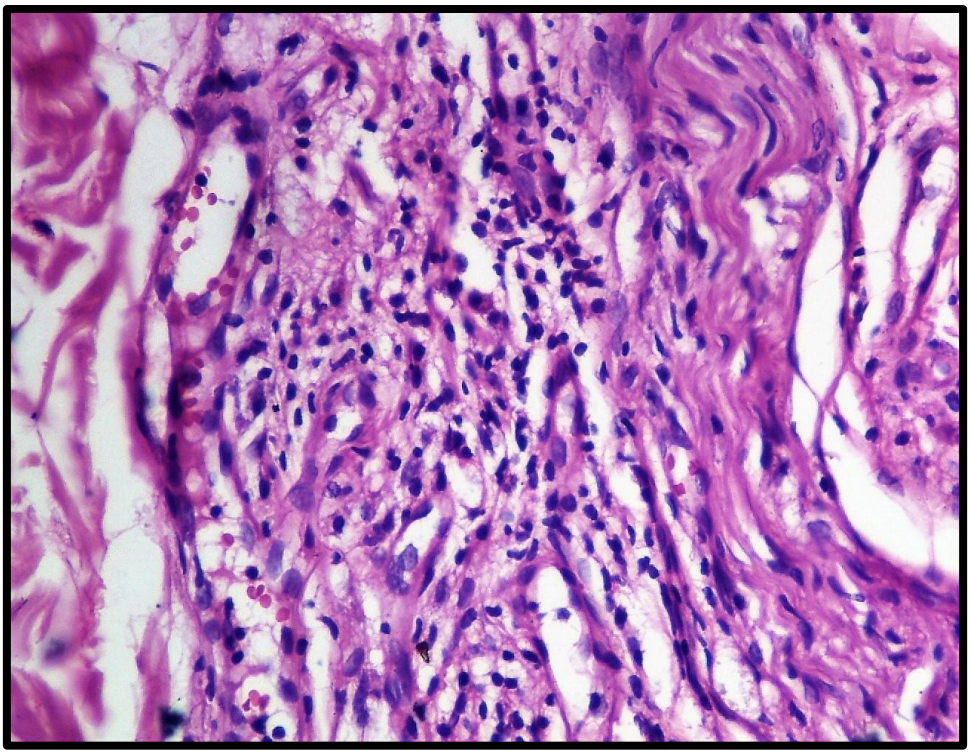

Figure 3: Neural Hansen's. Photomicrograph showing perineural infiltrate of Lymphocytes and histiocytes. (H&E, 400x).

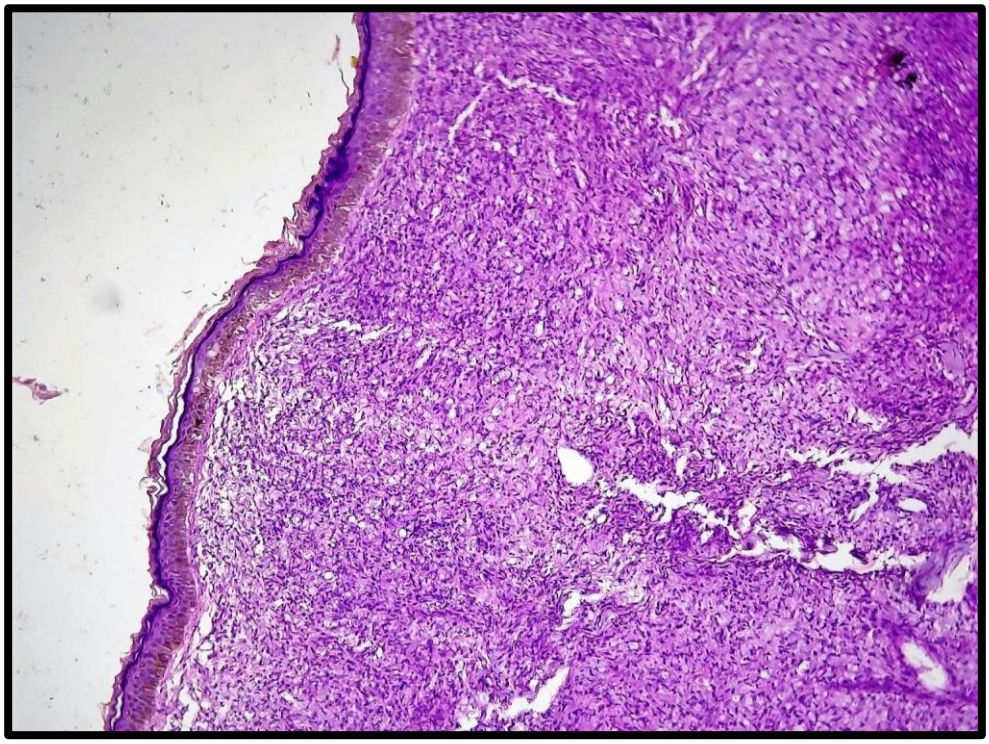

Figure 4: Histoid Leprosy. Photomicrograph showing atrophy of epidermis. Dermis show spindle shaped histiocytes forming whorling and simulating as fibrous histiocytes.(H&E, 100x)

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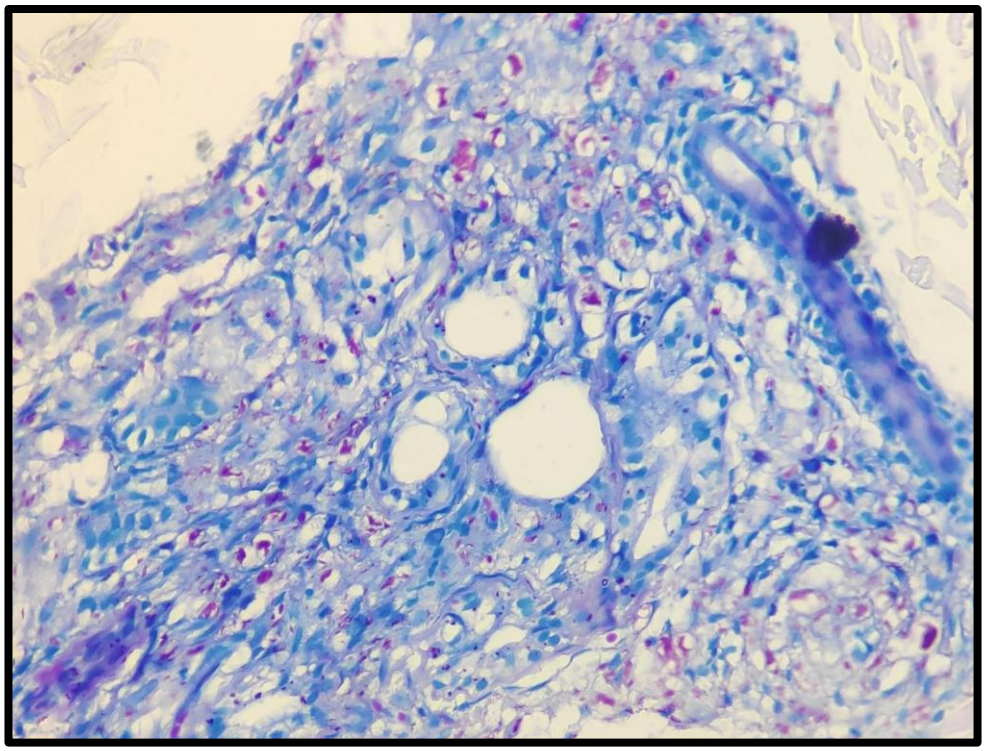

Figure 5: Demonstration of Acid Fast Bacilli. (BI 6+). (Fite Faraco, 400X).

Discussion

Comparison of Age Incidence of various previous studies with present study:

In the present study majority (28.37%) of the cases were in 31-40 years age group followed by 23.41% in 21-30 years age group while least number of cases belonged to the age group 71-80 years and <10 years respectively. The age of patients ranged from 9 years to 82 years and mean age of this study was 38.82 years. These findings were similar to that observed by Moorthy BN *et al.*[5], Nadia *et al.*[6] and Rekam A *et al.*[7], whereas Kumar A *et al.*[8] and Deora MS *et al.*[9] reported maximum incidence in 21-30 years age group.

GENDER WISE DISTRIBUTION

Comparison of gender-wise distribution of leprosy cases in different population

The result of present study are comparable with the studies of Moorthy BN *et al.*[5], Mathur MC *et al.*[10], Mehta B *et al.*[11], Shivaswamy KN *et al.*[12], Nadia S *et al.*[6], Rekam A *et al.*[7], Manandhar *et al.*[13] , Kumar *et al*[8]. And Badhan R *et al.*[14] In present study majority (65.96%) of the cases were male and 34.04% were females, with a male to female ratio of 1.9:1. The results of these studies are in congruence with the results of the present study having sex ratio more than one in favour of males.

COMPARISON OF HISTOPATHOLOGICAL TYPES

Table 5: Comparison of histopathological types

Histopathological types	Nandkarni *et al.* (1999)[15]	Moorthy *et al.* (2001)[5]	Pandya AN *et al.* (2008)[16]	Mathur MC *et al.* (2011)[10]	Shivaswamy *et al.* (2012)[12]	Thapa DP *et al.* (2013)[17]	Kumar A *et al.* (2014)[8]	Present study (2018)

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TT	460 (17.4%)	26 (6.98%)	2 (4.00 %)	43 (30.7%)	25 (18.4%)	14 (29.2%)	80 (18.91 %)	6 (4.25%)
BT	969 (36.7%)	269 (72.31 %)	11 (22.0%)	39 (27.86 %)	53 (39.9%)	14 (29.2%)	40 (9.45%)	55 (39%)
BB	326 (12.3%)	2 (0.53%)	3 (6.00%)	7 (5%)	2 (3.6%)	00	106 (52.06 %)	13 (9.21%)
BL	300 (11.4%)	40 (10.70 %)	6 (12.0%)	22 (15.71 %)	15 (11%)	2 (4.1%)	30 (7.09%)	27 (19.15 %)
LL	165 (6.3%)	10 (2.69%)	10 (20.0%)	21 (15%)	19 (13.9%)	4 (8.3%)	42 (9.92%)	34 (24.11 %)
IL	420 (15.9%)	25 (6.72%)	15 (30.0%)	8 (5.71%)	22 (16.1%)	12 (25%)	34 (8.04%)	1 (0.7%)
HIS	-	-	3 (6.0%)	-	-	-	15 (3.55%)	3 (2.12%)
NEU	-	-	-	-	-	2 (4.1)	-	2 (1.4%)
Oth	-	-	-	-	-	23 (32.4%)	76 (17.96 %)	-

His=Histioid ; Neu= pure Neural Hansen's ; Oth=others

In the present study, histologically the most common type of leprosy encountered was BT (39%), followed by LL (24.11%), BL (19.15%), BB (9.21%), TT (4.25%), Histoid (2.12%), Neural (1.4%) and Indeterminate Hansen's (0.7%).

Similar to the present study, Nandakarni *et al.*[15], Moorthy N B *et al*[5]., Mathur MC *et al.*[10] and Shivaswamy KN *et al*[12] found BT as the most common subtype of leprosy.

In contrast to this study, studies done by Kumar *et al.*[8] found BB and that done by Pandya *et al.*[16] found IL as the most common subtype of leprosy.

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LOGARITHMIC INDEX OF BACILLI IN BIOPSIES

Table: 6 Logarithmic indexes of bacilli in biopsies

Type	Moorthy NB *et al.* (2001)[5]		Anusha KS *et al.* (2017)[18]		Present Study (2018)	
	BI=0	**BI≥ 1+**	**BI=0**	**BI≥ 1+**	**BI=0**	**BI≥ 1+**
TT	26 (100%)	0	04 (100%)	0	6 (100%)	0
BT	269 (99.62%)	1 (0.37%)	11 (100%)	0	45 (81.8%)	10 (18.2%)
BB	0	2 (100%)	2 (40%)	3 (60%)	12 (92.3%)	1 (7.7%)
BL	0	40 (100%)	8 57.2%)	6 (42.8%)	8 (29.6%)	19 (70.4%)
LL	0	10 (100%)	3 (20%)	12 (80%)	2 (5.9%)	32 (94.1%)
IL	25 (100%)	0	11 (78.6%)	3 (21.4%)	1 (100%)	0
HISTIOID	-	-	-	-	-	3 (100%)
NEURAL	-	-	-	-	-	2 (100%)
TOTAL	**319 (85.75%)**	**53 (14.24%)**	**39 (62%)**	**24 (38%)**	**74 (52.5%)**	**67 (47.5%)**

PB- Paucibacillary (BI=0) ; Multibacillary (BI ≥ 1+)

In the present study, majority (52.5%) cases were paucibacillary while 67 (47.5%) cases were multibacillary type. Similar observations were made by Moorthy NB *et al.*[5] and Anusha KS *et al.*[18]

In the present study, all the 6 cases (100%) of TT, the only case of IL and majority cases of BT (81.8%) were of paucibacillary type while majority cases of BL (70.4%) and LL (94.1%) were multibacillary. Studies done by Moorthy NB *et al.* [5] and Anusha KS *et al.* [18] also showed majority TT and BT Hansens cases to be of paucibacillary type and majority BL and LL cases to be of multibacillary type.

CLINICOPATHOLOGICAL CORRELATION

Table 7: Comparative study of clinicopathological correlation by different authors

AUTHOR	NUMBER OF CASES	CLINICO-HISTOPATHOLOGICAL CORRELATION

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Bhatia S *et al.*(1993)[19]	1272	69%
Moorthy BN *et al.*(2001)[5]	372	62.63%
Mathur MC *et al.*(2011)[10]	156	80.4%
Bijjaragi S *et al.*(2012)[20]	171	57.3%
Chauhari B *et al.*(2012)[21]	120	70.83%
Manandhar U *et al.*(2013)[13]	75	45.33%
Kumar A *et al.*(2014)[10]	423	62.90%
Badhan R *et al.*(2014)[14]	60	75%
Nadia S *et al.*(2015)[6]	118	61.8%
Anusha R *et al.*(2016)[7]	52	57.69%
Bhanushree CS *et al.* (2016)[22]	107	79.44%
Deora MS *et al.*(2018)[9]	121	80%
Present study (2018)	141	73.05%

The results of present study are comparable with studies of Bhatia S *et al.*[19], Chuahari B *et al.*[21], Badhan R *et al*[14]., Bhanushree CS *et al*[22]., and Deora MS *et al*[9].

Percentage of overall concordance between clinical and histopathological diagnosis by different authors ranged from 45.3% to 80%. In the present study, concordance between the clinical and histopathological diagnosis was observed in 73.05% cases which is comparable to the studies mentioned above. Concordance observed in present study was better than the studies of Manandhar U *et al.*[13], Bijjaragi S. *et al.*[20], Moorthy BN *et al.*[5], Kumar A *et al.*[8] and Nadia S *et al*[6].

CONCLUSION

Leprosy can present itself in different clinical and pathological forms depending on host's immunity. The clinical manifestations of leprosy are very varied and diverse and can mimic variety of unrelated diseases. Also, exact typing of leprosy is sometime clinically not possible. As per our study, maximum numbers of cases were found to be in the age-group of 31-40 years. Majority of the affected cases were males. In our study, Borderline Tuberculoid (BT) was the most common clinical and histopathological form observed. Most of the biopsies were paucibacillary type. 39 biopsies demonstrated features suggesting Lepra reaction. Out of all the cases showing reactions, majority were showing type II reaction.

Out of 141 cases, typing of 103 cases correlated clinically and histopathologically (73.05%). Maximum correlation was observed in BT type followed by LL type. Statistical analysis showed that histopathological typing of Leprosy cases was significantly accurate than clinical typing in all the studied types.

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