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Original Article

Demographic profile and clinicopathologic concordance of leprosy in the North-West part of Rajasthan, India: A 2 years prospective study

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Abstract

Background: Leprosy is a chronic granulomatous disease caused by *Mycobacterium leprae* principally affecting the skin and peripheral nerves. *M. leprae* is an obligate intracellular bacillus (0.3–1 μ wide and 1–8 μ long) that is acid-fast. Leprosy exhibits a spectrum of clinical characteristics that correlate with the histopathological changes and the immunological status of the individual. There is a range of varied clinicopathologic manifestations, and the diagnosis is made from adequate clinical information combined with histopathology. The aim of the study was to classify leprosy according to the Ridley–Jopling classification and perform the clinicopathological correlation.

Materials and Methods: A prospective study was conducted on 184 cases of skin biopsies clinically diagnosed with leprosy, received in the Department of Pathology, Government Medical College, Kota from July 2015 to July 2017. Adequate clinical history was taken and biopsies were stained with hematoxylin and eosin and modified Fite Faraco stain. The Ridley and Jopling classification was followed in both clinical and histopathological diagnosis.

Results: This study included 184 patients diagnosed clinically with leprosy. Skin biopsy revealed evidence of leprosy in 158 cases. A maximum number of patients clinically belonged to indeterminate leprosy which constituted 57 (30.9%) cases followed by borderline tuberculoid (BT) 41 cases (22.2%). On the contrary, histologically, although indeterminate leprosy was the most common with 51 cases (32.2%), the second most common was borderline lepromatous (BL) with 28 cases (17.7%) cases. Twenty-six cases of clinically diagnosed leprosy showed no features of leprosy histologically. The clinical and histopathological correlation was seen in 158 cases (85.3%the). The correlation was highest in BL (89.2%) followed by lepromatous and BT leprosy. Fite-Farraco stain was positive in 85 cases (53.7%).

Conclusion: The classification of leprosy requires attention to the histopathological criteria and correlation with clinical information and bacteriological examination to facilitate accurate therapy.

Keywords: Clinicopathologic concordance, demographic profile, leprosy

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INTRODUCTION

Leprosy or Hansen's disease is a chronic granulomatous disease caused by *Mycobacterium leprae* principally affecting the skin and peripheral nerves. *M. leprae* is an obligate intracellular bacillus (0.3–1 μ wide and 1–8 μ long) that is acid-fast, indistinguishable microscopically from other mycobacteria and ideally detected in tissue sections by

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modified Fite stain.[1] Ridley and Jopling devised a diagnostic classification of leprosy based on immunopathologic data. Five objective histopathologic criteria form the microscopic basis for classification: granuloma cell type, bacterial load, number and distribution of lymphocytes, pathologic changes in nerves, and the presence or absence of encroachment of the subepidermal Grenz zone and epidermis.[2] Leprosy exhibits a spectrum of clinical characteristics that correlate with the histopathological changes and the immunological status of the individual. At one end of the spectrum is tuberculoid leprosy (TT), which is a highly resistant form with few lesions and a paucity of organisms (paucibacillary leprosy). At the other end is lepromatous leprosy (LL), in which there are numerous lesions with myriad bacilli (multibacillary leprosy) and an associated defective cellular immune response. In between two poles are borderline-tuberculoid (BT), borderline (BB), and borderline lepromatous (BL).[3] TT clinically presents as one to few asymmetrical scattered hypopigmented well-demarcated anesthetic plaques. Occasionally, these plaques may reveal erythema, central clearing, and more peripheral induration. Histopathology reveals large epithelioid cells arranged in compact granulomas along with neurovascular bundles, with dense peripheral lymphocyte accumulation. LL clinically presents as erythematous papules, nodules, and plaques with widespread and symmetrical distribution mostly on the face, buttock, and lower extremities. Histopathology reveals dense infiltrate mainly consisting of foam cells admixed with lymphocytes and plasma cells, Grenz zone is also identified. In borderline, TT also granulomas are seen, BL show poorly to moderately defined granuloma, and in mid-borderline, the macrophages are uniformly activated to epithelioid cells but are not focalized into distinct granulomas, and the lymphocytes are scanty. Lepra bacilli are usually not identified in the TT but rarely can be seen in the periphery of the lesion but are easily identified in LL.[4] Fite Faraco stain may be used for identification of lepra bacilli. A distinctive variant of LL, the histoid type, first described in 1963 by Wade, is characterized by the occurrence of well-demarcated cutaneous and subcutaneous nodules. The appearance of histoid LL in children has been reported. It may be caused by drug-resistant strains of *M. leprae*.[5]

Cardinal signs of leprosy are as follows– anesthesia, thickened peripheral nerves, skin lesions, the presence of acid-fast bacilli (AFB) in slit skin smear. For the diagnosis of leprosy, at least two of the three cardinal signs or demonstration of AFB is essential.[6]

Clinical evaluation and skin smear examination are required for early diagnosis and adequate treatment. However in some early and borderline cases of leprosy, it is difficult to label cases only on clinical basis. Thus, histological examination is a must for confirmation of diagnosis in leprosy. Moreover, correct labeling of paucibacillary and multibacillary cases is a prerequisite due to the difference in treatment regimens. Hence, clinico-histopathological correlation of leprosy cases is must for early diagnosis and proper subtyping of the cases.

MATERIALS AND METHODS

A prospective study was conducted on 184 cases of skin biopsies clinically diagnosed with Leprosy, received in the Department of Pathology, Government Medical College, Kota from July 2015 to July 2017. History of patients was recorded. The clinical history, age, sex, duration of disease, location, type of lesion, and clinical diagnosis were noted. Skin biopsies were fixed, processed and stained with hematoxylin and eosin stain and modified Fite Faraco stain. The Ridley and Jopling classification was followed in both clinical and histopathological diagnosis.

RESULTS

This study included 184 patients diagnosed clinically as leprosy. Skin biopsy revealed evidence of leprosy in 158 cases. Table 1 illustrates the clinical presentation of leprosy in accordance with sex distribution and a number of males and females overall in the present study. Lesions more commonly presented as hypopigmented patch corresponding to 100 cases (45.4%) with 69 males (37.5%) and 31 females (16.8%) followed by erythematous patches in 70 cases. Other presentations seen were a necrotic lesion, verrucous plaque, ulcerative plaques, and nodules. Out of total 184 clinical cases of leprosy, 119 (64.6%) were male and 65 (35.3%) were female, respectively. Majority of the biopsies were taken from lower limb with 54 cases (29.3%); followed by upper limb with 50 cases (27.1%); followed by back 30 cases (16.3%); chest and abdomen 26 cases (14.1%) followed by the face and neck 24 cases (14.1%).

Table 2 shows the clinical distribution of subtypes of leprosy. Maximum number of cases were from indeterminate leprosy corresponding to 57 cases (30.9%) with 39 males (21.1%) and 18 females (9.7%), followed by

Table 1: Clinical presentation of leprosy with sex-wise distribution

Clinical presentation of leprosy	Number of cases (%)		
	Male	Female	Total
Hypopigmented patch	69 (37.5)	31 (16.8)	100 (45.4)
Erythematous patch	40 (21.7)	30 (16.3)	70 (31.8)
Other presentation	10 (5.4)	4 (2.1)	14 (6.3)
Total	119 (64.6)	65 (35.3)	184 (100)

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borderline TT corresponding to 41 cases (22.2%). LL had 31 total cases with 22 males (11.9%) and 9 females (4.8%). Least common cases were from histoid leprosy having 4 male (2.1%) and 3 female (1.6%) cases.

Table 3 shows the histopathological spectrum of leprosy with age-wise distribution. Maximum incidence of leprosy was seen in the age group of 21–40 years corresponding to a total of 73 cases (46.2%) followed by the age group of 41–60 years corresponding to total 50 cases (31.6%). Most common subtype of leprosy in the age group of 21–40 years was of the indeterminate type having 21 cases (13.2%) followed by the lepromatous type of leprosy having 16 cases (11.3%).

Table 4 shows the histological spectrum of leprosy with sex-wise distribution. There was a male preponderance showing 104 male patients (65.8%) and 54 female patients (34.1%). Males most commonly showed the indeterminate type of leprosy (32 cases) followed by LL (22 cases). Table 5 shows the presence of lepra bacilli in different subtypes of leprosy. Out of total 158 cases, the presence of lepra bacilli was seen in 85 cases (53.7%) and 73 cases (46.2%) showed no lepra bacilli. Furthermore in the case of TT 100% of cases showed absent bacilli whereas in mid-borderline, BL, lepromatous and histoid leprosy 100% showed the presence of bacilli.

Table 6 shows the various histopathological diagnoses given for clinically diagnosed subtypes of leprosy in the present study and thus the clinicopathological correlation. Maximum concordance was seen in case of borderline LL (86.2%) in which out of 29 clinically diagnosed cases 25 cases showed concordance histopathologically. Clinically, maximum cases-57 cases were of IL, of which histologically IL was seen in 39 cases and rest 18 cases turned out to be nongranulomatous and thus 68.4% concordance. Similarly, in clinically 41 cases of BT, 23 cases were histologically BT, whereas 7 turned out to be IL, 2 TT, 1 BB, 1 BL, 1 LL, and 6 nongranulomatous. Thus, concordance in the case of BT was 56%. In the case of LL, out of 31 clinically diagnosed cases, 24 were histologically confirmed LL, 2 were BL, 2 were HL, 1 of BT, 1 IL, and 1 was nongranulomatous. Thus, concordance for LL was 77.4%. Concordance in cases of TT was 80%, HL was 85.7%, and BB was 50%.

DISCUSSION

In our study, majority of the patients were in the age group of 21–40 years with 73 cases (46.2%) and least affected were in the age group of 0–10 years with 12 cases (7.5%).

Table 2: Clinical distribution of subtypes of leprosy

Clinical diagnosis of leprosy	Number of cases (%)		
	Males	Females	Total
TT	6 (3.2)	9 (4.8)	15 (8.1)
BT	23 (12.5)	18 (8.1)	41 (22.2)
BB	3 (1.6)	1 (0.5)	4 (2.1)
BL	22 (11.9)	7 (3.8)	29 (15.7)
LL	22 (11.9)	9 (4.8)	31 (16.8)
IL	39 (21.1)	18 (9.7)	57 (30.9)
HL	4 (2.1)	3 (1.6)	7 (3.8)
Total	119 (64.6)	65 (35.3)	184 (100)

TT: Tuberculoid leprosy, BT: Borderline-tuberculoid, BB: Borderline, BL: Borderline lepromatous, LL: Lepromatous leprosy, IL: Indeterminate leprosy, HL: Histoid leprosy

Table 3: Spectrum of histological diagnosis of leprosy with age wise distribution

Spectrum of histological diagnosis for leprosy	Age group Number of cases (%)				
	0-20	21-40	41-60	>60	Total
TT	1 (0.6)	8 (5.0)	5 (3.1)	0 (0)	14 (8.8)
BT	1 (0.6)	9 (5.6)	10 (6.3)	6 (3.7)	26 (16.4)
BB	0 (0)	1 (0.6)	1 (0.6)	1 (0.6)	3 (1.8)
BL	3 (1.8)	14 (8.8)	7 (4.4)	4 (2.5)	28 (17.7)
LL	1 (0.6)	16 (11.3)	5 (3.1)	5 (3.1)	27 (17.0)
IL	5 (3.1)	21 (13.2)	19 (12.0)	6 (3.7)	51 (32.2)
HL	1 (0.6)	4 (2.5)	3 (1.8)	1 (0.6)	9 (5.6)
Total	12 (7.5)	73 (46.2)	50 (31.6)	23 (14.5)	158 (71.8)

TT: Tuberculoid leprosy, BT: Borderline-tuberculoid, BB: Borderline, BL: Borderline lepromatous, LL: Lepromatous leprosy, IL: Indeterminate leprosy, HL: Histoid leprosy

Table 4: Spectrum of histological diagnosis for leprosy with sex-wise distribution

Sex wise histological diagnosis	Number of cases (%)		
	Male	Female	Total
TT	6 (3.7)	8 (5.0)	14 (8.8)
BT	17 (10.7)	9 (5.6)	26 (16.4)
BB	3 (1.8)	0 (0)	3 (1.8)
BL	19 (12.0)	9 (5.6)	28 (17.7)
LL	22 (13.9)	5 (3.1)	27 (17.0)
IL	32 (20.2)	19 (12.0)	51 (32.2)
HL	5 (3.1)	4 (2.5)	9 (5.6)
Total	104 (65.8)	54 (34.1)	158 (100)

TT: Tuberculoid leprosy, BT: Borderline-tuberculoid, BB: Borderline, BL: Borderline lepromatous, LL: Lepromatous leprosy, IL: Indeterminate leprosy, HL: Histoid leprosy

Majority patients were in the age group of 21–30 years and 0–10 age group was least affected. Almost similar results were seen in the study conducted by Moorthy *et al.* and the majority of patients were found to be in the age group of 21–30 years (20.70%).[7] Similarly, in a study conducted by Nadkarni and Rege the majority were in the age group 20–40 years.[8] Kalla *et al.* also found that maximum numbers of cases (56%) were between the age group of 21 and 40 years among 893 cases.[9]

In our study, out of 158 histologically confirmed cases, there were 104 male patients (65.8%) and 54 female patients (34.1%). These results were also comparable to the

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Table 5: Percentage positivity of lepra bacilli in different histological subtypes of leprosy

Percentage lepra bacilli Type of leprosy	Number of cases (%)		
	Positive	Negative	Total
TT	0	14 (100)	14
BT	7 (26.9)	19 (73.0)	26
BB	3 (100)	0	3
BL	28 (100)	0	28
LL	27 (100)	0	27
IL	11 (21.5)	40 (78.4)	51
HL	9 (100)	0	9
Total	85 (53.7)	73 (46.2)	158

TT: Tuberculoid leprosy, BT: Borderline-tuberculoid, BB: Borderline, BL: Borderline lepromatous, LL: Lepromatous leprosy, IL: Indeterminate leprosy, HL: Histoid leprosy

Table 6: Correlation between clinical and histopathological spectrum of leprosy

Clinical diagnosis	Number of cases	Histopathological diagnosis								Percentage of agreement
		TT	BT	BB	BL	LL	IL	HL	NG	
TT	15	12	-	-	-	-	2	-	1	80.0
BT	41	2	23	1	1	1	7	-	6	56.0
BB	4	-	1	2	-	-	-	1	-	50.0
BL	29	-	1	-	25	1	2	-	-	86.2
LL	31	-	1	-	2	24	1	2	1	77.4
IL	57	-	-	-	-	-	39	-	18	68.4
HL	7	-	-	-	-	1	-	6	-	85.7
Total	184	14	26	3	28	27	51	9	26	

TT: Tuberculoid leprosy, BT: Borderline-tuberculoid, BB: Borderline, BL: Borderline lepromatous, LL: Lepromatous leprosy, IL: Indeterminate leprosy, HL: Histoid leprosy, NG: Non granulomatous

above three studies by Moorthy *et al.*[7] Nadkarni and Rege,[8] and Kalla *et al.*[9] In our study, the most common clinical presentation was as hypopigmented patches/macules which was similar to the study by Mittal *et al.*[10]

Majority of the biopsies were taken from lower limb with 54 cases (29.3%); followed by upper limb with 50 cases (27.1%); followed by back 30 cases (16.3%); chest and abdomen 26 cases (14.1%) followed by the face and neck 24 cases (14.1%). Similar results were seen in a study done by Vargas-Ocampo in which maximum 40% of skin biopsies were taken from the upper limb.[11]

In the present study, out of total 158 cases diagnosed histopathologically with leprosy, the presence of lepra bacilli was seen in 85 cases (53.7%), and 73 cases (46.2%) showed no lepra bacilli. Furthermore in the case of TT 100% of cases showed absent bacilli while in mid-borderline, BL, lepromatous and Histoid leprosy 100% showed the presence of bacilli. Similar results were observed in the study by Bhushan *et al.* where no AFB was seen in cases of TT, whereas 34.94% of cases of BT showed AFB. On the contrary, only 66.67% of BB, 78.26% of BL, and 83.3% of LL cases revealed AFB.[12]

This study included 184 patients diagnosed clinically as leprosy. Skin biopsy revealed evidence of leprosy in 158 cases thus an overall concordance of 85.8%. Coming to subtypes of leprosy, clinically maximum cases-57 cases were of IL, out of which histologically IL was seen in 39 cases and rest 18 cases turned out to be nongranulomatous and thus 68.4% concordance. Similarly, in clinically 41 cases of BT, 23 cases were histologically BT while seven turned out to be IL, 2 TT, 1 BB, 1 BL, 1 LL, and 6 nongranulomatous. Thus, concordance in the case of BT was 56%. In the case of LL, out of 31 clinically diagnosed cases, 24 were histologically confirmed LL, 2 were BL, 2 were HL, 1 of BT, 1 IL, and 1 was nongranulomatous. Thus concordance for LL was 77.4%. Similarly, out of 29 clinical cases of BL 25 cases were histologically BL with a concordance of 86.2%. Concordance in cases of TT was 80%, HL was 85.7%, and BB was 50%. Maximum concordance was seen in case of borderline LL (86.2%). Results were comparable with following studies.

In study by Pandya and Tailor complete parity between clinical type and histopathological type was noted in 58% of cases and parity for individual type of leprosy was found to be TT (66.7%), BT (53.3%), BB (0%), BL (36.3%), LL (83.3%), and IL (87.5%).[13] Similar study by Kumar *et al.*, clinicohistological correlation was established in 37 (60.6%) cases. A positive correlation was found in 2 (50%) cases with IL, 28 (58.3%) with BT, 5 (100%) with BL and 2 (66.6%) with LL leprosy.[14] In a study by Singh *et al.*, overall concordance was observed in 58.6%.[15] In a study by Mittra *et al.* on 92 cases, complete agreement was found between clinical and histopathological diagnosis in 53 cases (7.61%) and disparity in 39 cases (42.39%).[16]

Ridley and Jopling in their study of 82 cases found complete agreement between clinical and histological types in 56 patients (68.3%).[3] Kar and Arora in their study observed total parity in 70%. They also observed the highest parity in stable poles i.e., TT (87.5%) and LL (71.4%) followed by IL (81.2%), BT (60.9%), BB (54.5%), and BL (53.8%).[17] Kalla *et al.* in a study on 736 patients observed the highest parity in LL and TT group (76.7% and 75.6%), respectively, followed by BT (44.2%), BL (43.7%), and BB (37%).[18] Jerath and Desai in a study of 130 cases found complete agreement in 89 cases (68.5%). The figures for individual groups were TT (74.5%), BT (64.7%), BB (53.8%), and BL (28.5%), LL (61.5%) and indeterminate leprosy (88.8%).[19] In a study by Bhatia *et al.*, histopathological and clinical diagnosis of classification of leprosy coincided in 69% of the cases. Concordance between the clinical and histopathological diagnosis of different types of leprosy were as follows: indeterminate (IL) = 36%, tuberculoid (TT) = 50%, BT = 77%, borderline (BB) = 26%, BL = 43% and

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lepromatous (LL) = 91%.[20] In a study by Bhushan *et al.*, the overall concordance in clinical and histological diagnosis was observed in 105 (74.47%) cases. The concordance was maximum in LL (12) and TT (3) cases with 100% agreement and was 69 (83.13%) in BT, 6 (50%) in BB, and 15 (65.22%) in BL cases.[12]

CONCLUSION

Leprosy presents in different clinicopathological forms, depending on the immune status of the host. The study of pathological changes in leprosy lesions has contributed a great deal in understanding the disease and clinico pathological correlation studies have provided further insights into the disease, its varied manifestations and complications. Clinical evaluation and skin smear examination is required for early diagnosis and adequate treatment to make the patient non infectious, but in some early and borderline cases of leprosy it is difficult to label only on clinical basis, so histopathological examination is must for confirming the diagnosis in doubtful cases of leprosy. Moreover, correct labeling of paucibacillary and Multibacillary cases is a prerequisite. No multibacillary case should be treated as paucibacillary case, thus clinico-histopathological correlation of leprosy cases assumes a pivotal role for early diagnosis and for proper labeling of a case. Pathological examination helps to confirm a presumptive clinical diagnosis and also helps for extra typing.

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Conflicts of interest
There are no conflicts of interest.

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