Research Article

Clinicopathological correlation in leprosy

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ABSTRACT

Background: Leprosy is a chronic granulomatous disorder that is caused by *Mycobacterium leprae*. It mostly affects skin and peripheral nerves. The disease has varied clinical and pathological manifestations depending on the immune response of the patient. Histopathology helps in confirming the diagnosis for clinically suspicious cases and helps in exact typing which, in turn, influences treatment plan. **Objectives:** The objectives of this study were to study the incidence of different subtypes of leprosy and to evaluate the correlation of clinical subtype with the histopathological subtype. **Materials and Methods:** This was a cross-sectional comparative study done over a period of 1.5 years from August 1, 2017, to January 31, 2019, of skin biopsies of patients newly diagnosed with leprosy using routine and special stains along with clinicopathological correlation. **Results:** A total of 41 patients were studied between 11 and 80 years of age with a mean age of 32.64 years. Male-to-female ratio was 1.56:1. The majority of patients (41.46%) belonged to the age group of 21–30 years. Histopathologically, tuberculoid leprosy (19.51%) was the most common type followed by lepromatous leprosy and erythema nodosum leprosum (17.07% each). Clinical and histopathological concordance was seen in 65.8% of cases. The concordance was highest (100%) in histoid leprosy, indeterminate leprosy, and Type 1 lepra reaction. The most common presenting lesion was a hypopigmented macule (41.46%) followed by nodules (29.26%). Fite-Faraco positivity was 41.46%. **Conclusion:** Cumulative clinical, histopathological, and bacteriological diagnoses help in accurate typing of leprosy, thus facilitating appropriate therapy to prevent complications.

KEY WORDS: Leprosy; Clinicohistopathological Correlation, Skin Biopsy

INTRODUCTION

Leprosy is a granulomatous skin lesion caused by *Mycobacterium leprae* that predominantly affects cooler tissues such as skin and peripheral nerves. The bacilli are shed from nose, upper respiratory tract, and skin.[1] Leprosy has been declared eliminated (prevalence rate <1/10,000 population) as a public health problem in our country on January 1, 2006, still cases are being reported with varying prevalence in various states of our country.[2] Physical disabilities caused due to leprosy often evoke severe social stigma that leads to prejudice against patients and their families.[3] Clinical presentation, disabilities associated with the disease and its management differs in different types of leprosy. Histopathological examination of skin biopsies taken from the affected parts helps in accurate identification of the type of leprosy. Hence, studying entire spectrum of the disease using routine and special stains is significant to understand distribution and frequency of various leprosy types, to identify emerging patterns of disease distribution if any, and to throw light on clinical and histopathological concordance or discordance. Hereby, we conduct histopathological examination of various types of leprosy to study the distribution of various types of leprosy within the disease spectrum, to evaluate frequency in relation with the age and gender, and to correlate with clinical presentation of the disease and with primary clinical impression of the disease.

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MATERIALS AND METHODS

The Department of Pathology at GMERS Medical College and Hospital, Sola, Ahmedabad, received 137 skin biopsies over a period of 1.5 years, from August 1, 2017, to January 31, 2019; skin biopsies of 41 patients diagnosed with leprosy were included in our study. The Institutional Ethics Committee approval was obtained before starting the study. The skin biopsies were fixed in 10% formalin and then they were subjected to processing in automated tissue processor followed by embedding and section cutting for preparation of slides. The slides were stained with routine hematoxylin and eosin and Fite-Faraco stain whenever necessary. History, clinical details of patient (site of involvement and type of lesion), and other investigations were recorded. Histopathologically confirmed cases of leprosy were then divided according to Ridley and Jopling classification, into tuberculoid (TT), borderline tuberculoid (BT), midborderline (BB), borderline lepromatous (BL), and lepromatous leprosy (LL). Skin biopsies with morphological features suggestive of other subtypes of leprosy such as indeterminate leprosy (IL), histoid leprosy (HL), Type 1 lepra reaction, and erythema nodosum leprosum (ENL) (Type 2 lepra reaction, ENL) were also reported and included in the study.

RESULTS

This study included a total of 41 skin biopsies received from dermatology department and reported as leprosy on histopathological examination. The age of the patients varied from 11 years to 80 years with mean age of 32.64 years. The peak incidence (41.46%) was in 21–30 years of age followed by 21.95% incidence in 31–40 years of age. The least affected were those in the age group of 71–80 years (2.44%) [Table 1]. Of the 41 cases, 25 cases (60.97%) were males and 16 cases (39.02%) were females with male-to-female ratio of 1.56:1 indicating a male preponderance [Figure 1]. On histopathological study of all the 41 study cases, Tuberculoid leprosy (TT) with 8 cases (19.51%) was found to be most dominant group followed by LL leprosy and ENL with 7 cases (17.07%) of each [Table 2]**.** All skin biopsies of 41 leprosy cases were subjected to Fite-Faraco stain, 17 cases (41.46%) were positive for acid-fast bacilli. BL, LL leprosy, and HL showed 100% positivity, while ENL showed 71.42% Fite-Faraco positivity [Table 3]. Bacillary index (BI) was 0–1 in the TT leprosy cases while in LL leprosy it was three or >3. BI in type 1 lepra reaction ranged from 0 to 3, whereas in most of the type 2 lepra reactions, it was four or >4 [Table 4]. The most common presenting complaint was a hypopigmented macule (41.46%) followed by nodules (29.26%). The extremities were affected most commonly (46.34%) [Table 5]. The overall correlation between clinical and histopathological diagnoses was 65.8%. Maximum concordance (100%) was seen in HL, IL, and Type 1 lepra reaction followed by 87.5% concordance in ENL while there was no concordance in BB and BL leprosy cases [Table 6].

Table 1: Age distribution of cases

Age group (in years)	Number of cases (%)
11–20	04 (9.75)
21–30	17 (41.46)
31–40	09 (21.95)
41–50	05 (12.20)
51–60	03 (7.32)
61–70	02 (4.88)
71–80	01 (2.44)

Table 2: Distribution of cases on histopathological examination (*n*=41)

Etiology	Number of cases (%)
TT leprosy	8 (19.51)
BT leprosy	6 (14.63)
BB leprosy	2 (4.88)
BL leprosy	2 (4.88)
LL leprosy	7 (17.07)
IL	4 (9.76)
Type 1 reaction	3 (7.32)
ENL	7 (17.07)
HL	2 (4.88)

TT: Tuberculoid, BT: Borderline tuberculoid, BB: Midborderline, BL: Borderline lepromatous, LL: Lepromatous leprosy, HL: Histoid leprosy, IL: Indeterminate leprosy, ENL: Erythema nodosum leprosum

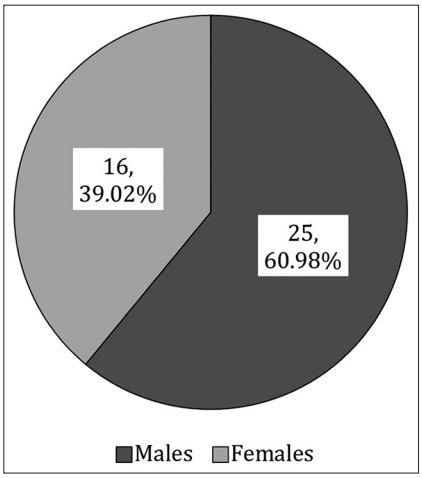

Figure 1: Sex distribution

DISCUSSION

Leprosy is a chronic dermal granulomatous condition caused by *M. leprae*. This disease has different clinical and histopathological presentations based on the immune status of the host. The aid provided by histopathological examination in correct diagnosis is important for all facets of leprosy

such as epidemiology, treatment, and averting disability. Misdiagnosis can directly lead to increased transmission of the disease. The outlook of society, disease detection methods used, technique used for examination, frequency of analysis, kind of personnel conducting the study, the standards adopted for diagnosis, and type of classification of disease are few variables that influence the description of the condition.[4]

Table 3: Percentage distribution of Fite-Faraco stain positivity among various types of leprosy

Type	Number of cases	Number of positive cases (%)
TT	8	1 (12.5)
BT	6	0 (00)
BB	2	0 (00)
BL	2	2 (100)
LL	7	7 (100)
HL	2	2 (100)
IL	4	0 (00)
Type 1 reaction	3	2 (66.67)
ENL	7	5 (71.42)

TT: Tuberculoid, BT: Borderline tuberculoid, BB: Midborderline, BL: Borderline lepromatous, LL: Lepromatous leprosy, HL: Histoid leprosy, IL: Indeterminate leprosy, ENL: Erythema nodosum leprosum

This study included a total of 41 skin biopsies of patients between 11 years and 80 years with mean age of 32.64 years, the highest incidence (41.46%) in 21–30 years of age and male-to-female ratio of 1.56:1 indicating a male preponderance [Table 1 and Figure 1]. TT leprosy was found to be most dominant histopathological group (19.51%) followed by LL leprosy and ENL (17.07% of each) [Table 2]. Overall, Fite-Faraco positivity was 41.46% with BL, LL and HL showing 100% positivity [Table 3]. BI was 0–1 in the TT leprosy cases while in LL leprosy, it was three or >3 [Table 4]. The most common presenting complaint was a hypopigmented macule (41.46%) and the extremities were affected most commonly (46.34%) [Table 5]. The overall clinicohistopathological correlation was 65.8% [Table 6].

Table 4: BI in various histopathological subtypes

Diagnosis										
BI	**IL**	**TT**	**BT**	**BB**	**BL**	**LL**	**HL**	**Type 1**	**Type 2**	**Total**
0	4	7	6	1	-	-	-	1	2	21
1+	-	1	-	-	-	-	-	1		2
2+	-	-	-	-	-	-	-	-	-	-
3+	-	-	-	-	-	2	-	1	-	3
4+	-	-	-	-	2	2	-	-	2	6
5+	-	-	-	-	-	-	1	-	2	3
6+	-	-	-	-	-	3	1	-	1	5
Inconclusive	-	-	-	1	-	-	-	-	-	1
Total	4	8	6	2	2	7	2	3	7	41

TT: Tuberculoid, BT: Borderline tuberculoid, BB: Midborderline, BL: Borderline lepromatous, LL: Lepromatous leprosy, HL: Histoid leprosy, IL: Indeterminate leprosy, ENL: Erythema nodosum leprosum

Table 5: Clinical characteristics of leprosy lesions

Diagnosis	Shape of lesion					Site of lesion				
	Nodule/ papule	**Plaque**	**Hypopigmented macule**	**Hyperpigmented patch**	**Others**	**Face**	**Extremities**	**Trunk**	**Multiple**	**Others**
HL	2	-	-	-	-	-	1	1	-	-
LL	3	2	2	-	-	-	3	1	3	-
BL	-	-	-	-	2	-	-	-	2	-
BB	-	-	2	-	-	-	-	-	2	-
BT	-	-	5	-	1	-	4	1	1	-
TT	1	1	4	2	-	-	4	-	3	1
IL	-	-	4	-	-	-	3	1	-	-
Type 1 reaction	1	2	-	-	-	-	-	-	3	-
ENL	5	1	-	-	1	1	4	2	-	-
Total	12	6	17	2	4	1	19	6	14	1

TT: Tuberculoid, BT: Borderline tuberculoid, BB: Midborderline, BL: Borderline lepromatous, LL: Lepromatous leprosy, HL: Histoid leprosy, IL: Indeterminate leprosy, ENL: Erythema nodosum leprosum

Table 6: Correlation of clinical and histopathological classification in leprosy cases

Type	Clinically diagnosed cases	Histopathological classification									Agreement (%)	Disagreement (%)
		TT	BT	BB	BL	LL	IL	Type 1 reaction	ENL	HL		
TT	8	6	2	-	-	-	-	-	-	-	75	25
BT	4	-	3	1	-	-	-	-	-	-	75	25
BB	3	-	1	-	1	-	1	-	-	-	00	100
BL	2	-	-	1	-	-	-	1	-	-	00	100
LL	11	2			1	7	1	-	-	-	63.6	36.4
IL	1	-	-	-	-	-	1	-	-	-	100	0
Type 1 reaction	1	-	-	-	-	-	-	1	-	-	100	0
ENL	8	-	-	-	-	-	-	1	7	-	87.5	12.5
HL	2	-	-	-	-	-	-	-	-	2	100	0
Total	41	8	6	2	2	7	4	3	7	2	65.8	34.2

TT: Tuberculoid, BT: Borderline tuberculoid, BB: Midborderline, BL: Borderline lepromatous, LL: Lepromatous leprosy, HL: Histoid leprosy, IL: Indeterminate leprosy, ENL: Erythema nodosum leprosum

Table 7: Comparison of spectrum of leprosy by various authors with the present study

Type	Present study (%)	Tiwari *et al*.[6] (%)	Kumar *et al*.[5] (%)	Nadia *et al*.[9] (%)	Mathur *et al*.[7] (%)
TT	19.5	7.5	18.9	14.4	27.56
BT	14.63	41.5	9.4	34.7	25
BB	4.88	5.7	25.0	16.1	4.48
BL	4.88	15	7.0	5.9	14.10
LL	17.07	3.8	9.9	21.1	13.46
IL	9.76	26.4	8.0	4.2	5.12
Type 1 reaction	7.32	0	0	0	0
ENL	17.07	0	17.9	0	0
HL	4.88	0	3.5	3.4	0
Total	41	53	423	118	156

TT: Tuberculoid, BT: Borderline tuberculoid, BB: Midborderline, BL: Borderline lepromatous, LL: Lepromatous leprosy, HL: Histoid leprosy, IL: Indeterminate leprosy, ENL: Erythema nodosum leprosum

Table 8: Comparative study of overall clinicopathological correlation with different authors

Studies	Number of cases studied	% correlation
Nadkarni and Rege[14]	2640	81.8
Moorthy *et al*.[15]	372	62.6
Bhatia *et al*.[16]	1272	69
Jerath and Desai[12]	130	68.5
Kar and Arora[13]	120	70
Kalla *et al*.[17]	736	64.7
Sindhushree and Vernekar[11]	280	33.70
Present study	41	65.8

In the present study, spectrum of patients with leprosy ranged from 11 to 80 years with a mean age of 32.64 years which was concordant with studies done by Kumar *et al*.[5] (40.1 years) and Tiwari *et al*.[6] (32.66 years). Maximum frequency (41.46%) was found in the age group of 21–30 years which was comparable to the results of Kumar *et al*.,[5] Mathur *et al*.,[7] and Manandhar *et al*.[8] while our findings contrasted with Nadia *et al*.[9] (Dehradun) who reported maximum cases in the age group of 31–40 years. This could be due to better health-care facilities in our area, leading to early diagnosis compared to Dehradun. The male preponderance observed in the present study (1.56:1) is similar to studies done by Tiwari *et al*.[6] (1.4:1), Nadia *et al*.[9] (1.8:1), and Taviyad *et al*.[10] (1.75:1). Sindhushree and Vernekar,[11] Kumar *et al*.,[5] and Manandhar *et al*.[8] also reported male preponderance; however, in these studies, the ratio was higher ranging from 2.2 to 3:1. Tuberculoid leprosy (TT) was the most common type of leprosy in our study which was concordant with the study done by Mathur *et al*.[10] In our study, LL leprosy and ENL were the second most common cause. The frequency of LL was much higher compared to Tiwari *et al*.[6] (3.8%) and Kumar *et al*.[5] (9.9%) while it was comparable to Nadia *et al*.[9] and Mathur *et al*.[7] The frequency of ENL in our study was similar to the results of Kumar *et al*.[5] [Table7]. This might be due to increased occurrence of leprosy (0.98/10,000) in Gujarat in comparison to other regions, as LL leprosy cases that have high infectivity are more common in Gujarat including the area of our study. Fite-Faraco stain revealed

Table 9: Comparative study of clinicopathological correlation of different studies

Studies	IL (%)	TT (%)	BT (%)	BB (%)	BL (%)	LL (%)	HL (%)	Type 1 (%)	ENL (%)
Nadkarni and Rege[14]	93	97	95	89	43	91	-	-	-
Moorthy *et al*.[15]	20	46.15	66.54	50	70	80	-	-	-
Bhatia *et al*.[16]	36	50	77	26	43	91	-	-	-
Jerath and Desai[12]	88.8	74.5	64.7	53.8	28.5	61.5	-	-	-
Kar and Arora [13]	81.2	87.5	60.9	54.5	53.8	71.4	-	-	-
Kalla *et al*.[17]	-	76.7	44.2	37	43.7	75.6	-	-	-
Sindhushree and Vernekar[11]	100	25	37.89	8.33	12.50	33.33	57.14	33.33	31.57
Present study	100	75	75	00	00	63.6	100	100	87.5

TT: Tuberculoid, BT: Borderline tuberculoid, BB: Midborderline, BL: Borderline lepromatous, LL: Lepromatous leprosy, HL: Histoid leprosy, IL: Indeterminate leprosy, ENL: Erythema nodosum leprosum

lepra bacilli in 17 of 41 leprosy cases (42.46%). All cases of LL leprosy, BL leprosy, and HL and five of seven cases of ENL were positive for lepra bacilli. One case of TT leprosy was also positive for lepra bacilli; however, the BI was low (BI-1). Fite-Faraco positivity in our study was somewhat lower than other studies done by Taviyad *et al*.[10] and Tiwari *et al*.[6] who reported 64.33% and 55% positivity, respectively, while it was considerably higher than Manandhar *et al*.[8] and Nadia *et al*.[9] Extremities were most commonly affected (46.34%) in our study. Clinically, the most common presenting lesion was a hypopigmented macule (41.46%) which was comparable to the study done by Nadia *et al*.,[9] Sindhushree and Vernekar,[11] and Tiwari *et al*.[6] Manandhar *et al*.[8] reported plaque as the most common presenting lesion, while hypopigmented macules was the second most common lesion.

The present study showed correlation between clinical and histopathological diagnoses in 27 cases (65.8%) which was comparable with other studies [Table 8]. Dividing leprosy into its subtypes is sometimes difficult due to overlapping features. Different studies thus showed variable clinicohistopathological concordance. The maximum correlation was seen in HL, IL, and type 1 lepra reaction (100%) followed by ENL (87.5%), TT and BT (75% each), and LL (63.6%). In our study, maximum disagreement (100%) was seen in BB and BL cases [Table 9].

The discrepancy between clinical diagnosis and histopathological subtype occurred due to the fact that clinical diagnostic type was assigned based on Ridley and Jopling classification even when histopathological examination had been pending. Multiple parameters influence the histopathological diagnosis such as duration of lesion, depth of biopsy, number of cases of each type, quality of the histopathological section, number of sections stained with Ziehl–Neelsen stain, different criteria used to select the cases, immune status of the patient, and any previous treatment taken by the patient. Biopsy taken early in the course of the disease can lead to higher clinicohistopathological discordance. Clinical and histopathological interobserver variation is also a significant contributing factor to the overlap that occurs between various leprosy subtypes.[12] The limitation of the present study is that it was conducted in a single tertiary care center in our region and its small sample size compared to other studies.

Clinical, histopathological, and immunological coincidences are often observed among various subtypes of leprosy. Thus, to increase the accuracy in subtyping of leprosy, it is crucial to correlate clinical diagnosis with histopathological features as well as with bacteriological index as it will be more reliable than considering a single parameter.[13]

CONCLUSION

Although leprosy has been declared as eliminated from India in 2006, incidences of this disease are still reported from our region. Histopathological examination remains a gold standard for diagnosis and subtyping of leprosy cases. Due to the overlapping histopathological appearances of various leprosy subtypes, appropriate clinical data can help in good clinicopathological correlation, thus leading to accurate subtyping of leprosy. The clinician must provide detailed clinical information including the age and sex of the patient, site/s of lesion, type of lesion, a clinical diagnosis, or a list of differential diagnosis. The biopsy findings are affected by factors such as site of the biopsy, morphology of lesion, and immune status of the individual; these factors may play a role in the clinicopathological discordance. This study emphasizes the importance of clinicopathological correlation in arriving at a proper diagnosis. For better preventive measures and proper treatment, early clinical diagnosis, accuracy in assigning histopathological subtype, as well as correlation with BI are important which, in turn, will help in controlling the transmission of leprosy.

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