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Analysis of histomorphological study in Hansen's disease: A hospital based study done in rural population

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Abstract
Leprosy, also known as Hansen's disease is a chronic infectious disease caused by Mycobacterium Leprae. It still continues to be a major public health problem in India.
AIM: The study was aimed at analysing the histomorphological features of leprosy in skin biopsies and based on histological findings they were categorised according to Ridley-Joplings classification. Clinical correlation was also done wherever possible.
Materials and methods: After adequate fixation of skin biopsies with 10% formalin, routine processing was done and tissue embedded in paraffin section of 5µ thickness and then stained with Hematoxylin and Eosin (H&E) and Fite-Faraco stain, subsequently studied under microscope.
Results: Total of 35 skin biopsies were studied, with the mean age of presentation ranging from 14-72 years, showing male predominance. Boderline tuberculoid (37.14%) was the most common type. Atrophic epidermis was seen only in 9 cases but Grenz zone was present in all 12 cases of Lepromatous leprosy. Epithelioid granuloma is the commonest finding in Boderline Tuberculoid type. Clinico histomorphological correlation was made in 23 cases and discoherence was found in remaining 12cases.
Conclusion: Correlation of clinical and histopathological features along with bacteriological index plays a pivotal role for accurate typing and for prognostication. Clinicopathological concordance is highest in polar forms, and being least in Indeterminate Leprosy (IL).

Keywords: Histopathological features, clinical presentation, Ridley-Jopling classification, leprosy

Introduction
Leprosy is a non fatal, chronic infectious disease caused by *Mycobacterium leprae*, with different clinicopathological forms, depending on the immune status of the patient [1]. WHO implementation of Multidrug therapy has contributed leprosy to be a less prevalent infection with less than one case per 10,000 population with 90% of its endemic countries [2]. In India the prevalence rate has reduced from 57 per 10,000 in 1981 to 0.84 per 10,000 in 2000 [3]. Clinical presentation includes Skin lesion such as hypo pigmented macules, erythematous plaques, papules and nodules. Neural involvement include numbness, loss of sensation, neuritis and disability. Major cause of morbidity in leprosy are its unique tropism of *M. leprae* for the peripheral nerves (from large nerve trunks to microscopic dermal nerves) and certain immunologically mediated reactional states. When left untreated, the tendency of disease progression to characteristic deformities and the recognition in most cultures that the disease is communicable from person to person have historically resulted in profound social stigma. Clinical diagnosis is confirmed by histopathological examination of skin biopsy & determination of Bacterial index (BI) [4]. The gold standard for diagnosis of leprosy is by histological examination [5]. The Patients in lepromatous group is the main source of infection and discharged into environment through oronasal secretion and from skin ulceration. The nasal mucosa plays the main role as the entry and exit of leprosy bacilli is through the nasal mucosa [6]. The categorization of leprosy was done according to Ridley-Jopling classification (1966). It is based on immunological, histological and microbiological parameters, grouped as: Tuberculoid (TT), Borderline tuberculoid (BT), Borderline borderline (BB), Borderline lepromatous (BL), Lepromatous leprosy (LL) [7].

This study was done to understand the various histomorphological features of leprosy in received skin biopsies with an attempt in correlating the same with its different clinical manifestations and finally to categorize them based on Ridley-Jopling classification.

Aim and objectives

1. To analyse the histomorphological features of leprosy in skin biopsy and to categorise them according to Ridley-Jopling classification.
2. To correlate the same findings with different clinical manifestation wherever possible.

Materials and Methods

A retrospective study on skin biopsies was conducted in the Department of Pathology at Sri Manakula Vinayagar Medical College & Hospital (SMVMCH), Puducherry, a rural tertiary care level hospital for a period of one year (December 2018-December 2019). A total number of 35 skin biopsies of clinically suspected leprosy patients were included in the study. Demographic and clinical parameters such as age, gender, clinical history, examination findings and provisional clinical diagnosis were analysed along with histomorphological findings using Hematoxylin and eosin (H&E) stain and Fite-faraco stain. The skin punch biopsies from the representative lesion were taken and fixed in 10% formalin solution. The tissues were processed and embedded in paraffin sections and serial sections of 4-5 microns were obtained. Hematoxylin and Eosin and with Fite-Faraco stain used for morphological assessment and identification of the bacilli respectively [8].

The sections were examined for presence of Grenz zone, epidermal atrophy, granuloma, and infiltrates of lymphocytes, histiocytes, foam cells, infiltration of nerves, blood vessels and adnexa. They were histopathologically categorized as per the Ridley and Jopling classification and then a correlation was made between the histopathologic and clinical findings.

Results

Fig 1: In a total 35 cases, 24 cases were male and 11 cases were female.

Fig 2: 18 cases (51.42%) presented with patches, 13 patients (37.14%) developed plaque, 5 cases (14.28%) with macule and 3 cases (8.5%) with nodule.

Fig 3: Correlation between clinical & Histological types.

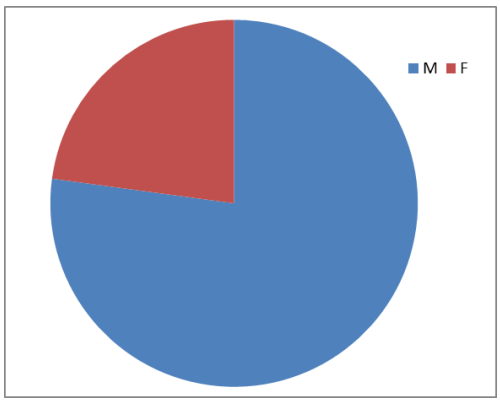

Fig 1: Gender distribution

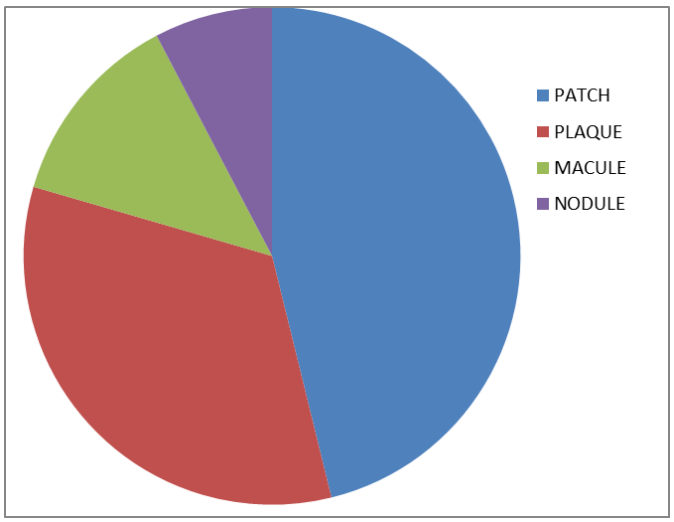

Fig 2: Clinical presentation

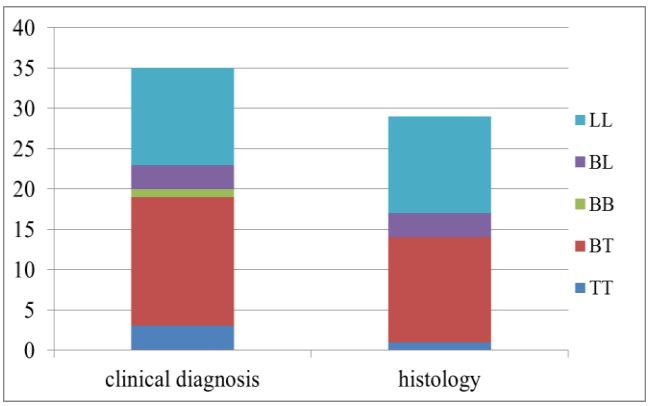

Fig 3: Correlation between clinical & histological types

Table 1: Histological types

Histology types	No: of cases	Percentage
TT	1	2.8%
BT	13	37.14%
BB	-	-
BL	3	8.5%
LL	12	34.2%
IL	5	14.5%
HL	1	2.8%

Table 2: Correlation between clinical and histological diagnosis

CD	TT	BT	BB	BL	LL	IL	HL	Correlates (%)
TT(3)	1	-		-		2	-	33.3
BT(17)	-	13		-	3	1	--	76.4
BL(3)	-	1		1		1	-	33.3
LL(12)	-	-		2	8	1	1	66.6
Total	1	14	-	3	11	5	2	35

Histological changes

Table 3: Epidermal changes

Epidermal changes	TYPES	TT	BT	BB	BL	LL	IL	HL	Total
	NO	1	13	-	3	12	5	1	35
Unremarkable	0	0	8	0	1	3	1	1	14(40%)
Atrophic	0	1	3	0	2	9	4	0	19(54.28%)
Ulcerated	0	0	2	0	0	0	0	0	2(5.71%)

Table 4: Dermal changes

Clinical features	Type	TT	BT	BL	LL	IL	HL	Total
	NO	1	13	3	12	5	1	35
Grenz zone		0	0	2(66.6%)	12(100%)	0	0	12(34.28%)
Lymphocytes around Arrector pilorum		1(100%)	6(46.15%)	0	0	0	0	7(20%)
Adnexa		1(100%)	12(92.30%)	1(100%)	10(83.3%)	5(100%)	0	29(82.85%)
NV bundles		1(100%)	11(84.61%)	1(100%)	12(100%)	5(100%)	0	30(85.71%)
Macrophages around Arrector pilorum		0	2(15.38%)	1(33.3%)	10(83.3%)	0	1(100%)	14(40%)
Adnexa		1(100%)	4(30.76%)	2(66.6%)	12(100%)	1(20%)	1(100%)	21(60%)
NV bundles		1(100%)	7(53.84%)	3(100%)	12(100%)	1(20%)	0	24(68.57%)
Giant cells		1(100%)	9(69.23%)	1(33.3%)	0	0	0	12(34.28%)
Granulomas		1(100%)	11(84.61%)	2(66.6%)	0	0	0	14(40%)

Discussion

Leprosy is a chronic infectious disease caused by Mycobacterium leprae. It is a serious, mutilating disease in many parts of the world. The most important strategy for its control is the early diagnosis and therapy [9]. Important tool that aids in accurate diagnosis and classification is by histopathological examination [10]. It is an important public health problem in India [10]. The keystone of leprosy control is timely and accurate diagnosis, as it is helpful in case management, transmission of disease and prevention of deformity. Hence, it is vital to have clarity regarding the diagnosis and classification of leprosy cases at the field level [11]. The aim of this study was to assess the histomorphological features of leprosy and to categorise them into various types based on histological findings and to correlate them with the clinical diagnosis.

Out of 512 skin biopsies received, 35 biopsies were diagnosed with leprosy, which constitutes about 6.8%. According to statistics of National Health Mission Tamil Nadu, Department of Health and Family welfare, the prevalence rate of leprosy is 0.43 per 10,000 population as on 2017. There is always a relation between the disease occurrence and the age of detection of leprosy. It occurs at any age ranging from infancy to old age [12].

Leprosy is believed to show male predominance [13]. In this study there was male preponderance with 68% of them being male and 31% being female. Male preponderance was seen in this study which is similar to studies like Manandhar *et al.* and Vargas-Ocampo. The same finding was reflected in the study by Khan *et al.* and Bijjaragi *et al.* which showed male preponderance [14, 15]. Method of case detection depends on the attitude of society, method of examination, criteria of diagnosis and the classification of disease, believed to affect the description of disease. In a study by Noorden SK [12] stated that there is male dominance, due to lifestyle and is associated with higher risks of acquiring the infection. The under detection of leprosy in female is also due to the social taboos and customs which account for lesser number of female report to the hospital for treatment.

In the present study, BT was the most common clinically diagnosed form of leprosy similar to studies like Manandhar *et al.* and Sharma *et al*. The most common type of leprosy encountered was borderline type 37.14% and the second most common being lepromatous leprosy which was found in about 34.2% of cases. In this study, Least type was identified to be Tuberculoid type. Major type constitutes borderline type which is also similar and concordant with other studies [16, 17, 18]. The accuracy of clinical diagnosis of leprosy was 52.4% almost similar to the studies conducted by Sharma *et al.* The polar forms TT and LL comprises 37% of cases. Boderline types were the majority which comprises of about 45.19% of cases. Indeterminate type 14.5% of cases and Histioid type 2.8% of cases. (Table 7)

The common clinical presentation in order of higher frequency were hypo pigmented patches, plaques, macule and nodule in 18 cases,13 cases,5 cases and 3 cases respectively. These findings were in concordance with the study done by Verma *et al.* [17] where the most common clinical presentation was found to be hypo pigmented patches (97%) and Moorthy *et al.* [19] reported that hypo pigmented lesion were the most common clinical presentation (80.91%) as the common habitats of lepra bacillus are skin and nerve. The signs and symptoms related to them are also common. (Table 5)

Atrophic epidermis was present in 19 out of 35 skin biopsies which constitutes about 54.34%. Grenz zone was present in all 12 biopsies (100%) of lepromatous leprosy. Lymphocytic aggregates around the adnexa and neurovascular bundles were found to be a characteristic feature in indeterminate leprosy. Epithelioid granulomas were seen in (84.61%) BT followed by (66.66%) in BL. Lymphocytic aggregates and ill-formed granulomas around adnexa and neurovascular bundles were mostly found in BT and BL and LL Biopsies showed macrophages along with few lymphocytes. In a study done by Maheswari KH [20] *et al.*, atrophy was the most common finding in LL, other cases had unremarkable epidermis. Clear Grenz zone was seen in 75% of cases of LL. Indeterminate leprosy was a characterized by the presence of lymphocytic aggregates around adnexa and neurovascular bundles. Epithelioid granuloma was most commonly seen in BT, along with lymphocytic aggregates and ill-formed granulomas. BL and LL showed macrophage aggregates with a few lymphocytes. The study also showed overall histopathological correlation of about 59.01%. (Table 6)

In a study done by Mohanraj *et al.* Diagnosis of leprosy is made on the basis of active nerve destruction by granulomatous inflammation in skin biopsy using S-100 immunostaining. Nerve destruction was seen in entire spectrum of leprosy and also found a relationship between Bacillary index and dendritic cell population in lepromatous leprosy [20]. This study also implies that, future studies should be carried out to demonstrate nerve destruction using S-100 immunohistochemistry stain.

Table 5: Comparative study of Clinico-Pathological correlation

Ridley *et al.*	Sharma *et al.*	Kar *et al.*	Present study
68.3%	53.5%	88.4%	52.4%

Table 6: Comparison of Epidermal and Dermal changes

	Maheswari KH *et al.*	Present study
Total cases	**61**	**35**
Grenz zone	8(13.1%)	12(34.28%)
Lymphocytes around Arrector pilorum	17(27.9%)	7(20%)
Adnexa	51 (83.6%)	29(82.85%)
NV bundles	54 (88.5%)	30(85.71%)
Macrophages around Arrector pilorum	6 (9.8%)	14(40%)*
Adnexa	23 (37.7%)	21(60%)*
NV bundles	33 (54.1%)	24(68.57%)
Giant cells	19 (31.1%)	12(34.28%)
Granulomas	37 (60.7%)	14(40%)

Table 7: Comparison of histopathological types in various studies

Type	Verma *et al.*	Moorthy *et al.*	Mohanraj *et al.*	Present study
TT	18.52%	6.99%	6.6%	8%
BT	37.04%	72.31%	60.7%	37.14%
BB	3.70%	0.54%	6.6%	-
BL	18.52%	10.72%	14.8%	8.5%
LL	22.22%	2.68%	6.6%	34.2%
IL	-	6.72%	4.9%	14.5%

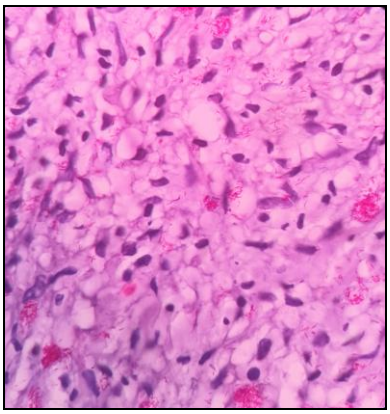

Fig 4: AFB stain: 100x: Showing numerous bacilli

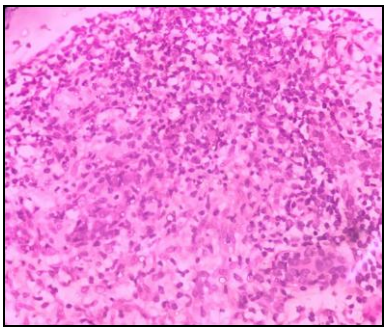

Fig 5: H&E Stain: High power view showing admixture of histiocytes and lymphocytes

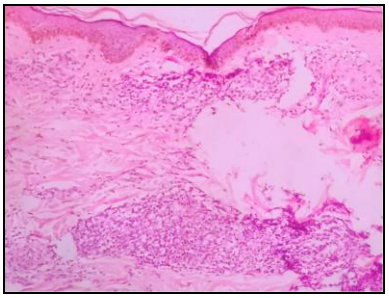

Fig 6: H&E Stain: 4x view showing clear Grenz zone and granuloma

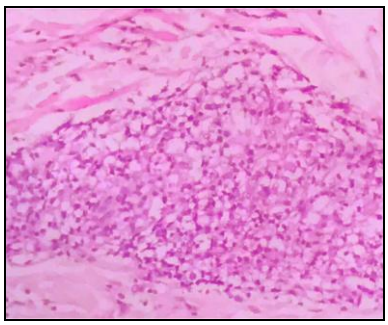

Fig 7: H&E stain: High power showing well defined granuloma

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Conclusion

Mean age group of patients affected by leprosy ranges from 14-72 years and showed male predominance. Most commonly patients presented with hypopigmented patches. Boderline tuberculoid (BT) was the most commonest type of leprosy and the second common being lepromatous type. 35 skin biopsies were taken for the study and its dermal and epidermal changes were also noted. Atrophic epidermis was present in 54.34% of cases. Grenz zone was present in all skin biopsies of lepromatous leprosy. Lymphocytic aggregates around the adnexa and neurovascular bundles were found to be a characteristic feature in indeterminate leprosy. Epithelioid granulomas were seen in BT (84.61%) followed by BL (66.66%). Lymphocytic aggregates and ill-formed granulomas around adnexa and neurovascular bundles were mostly found in BT and BL Biopsies of LL showed macrophages around nerve bundles and arrector *pilorum muscle*. Lepra reactions were not seen in any of the cases. The overall clinico-histopathological correlation was possible in 23 cases and discoherence was found in remaining 12 cases.

There is always some degree of overlapping among the types of leprosy and so it is mandatory to correlate clinical and histopathological features in leprosy. Correlation of clinical and histopathological features along with bacteriological index plays a pivotal role for accurate typing and for prognostication.

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