Retrospective Study of Histopathological Spectrum in Leprosy from a Tertiary Care Hospital, Odisha, India

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ABSTRACT

BACKGROUND
Skin lesions are common in all countries, but it varies greatly with wide histological variation. Leprosy has been officially eliminated from India since December 2005. But even now high prevalence of the disease is being reported from different parts of the country. Leprosy is a chronic, curable infectious disease mainly causing skin lesion & nerve damage. The study was planned to evaluate the histopathological pattern of leprosy cases attending tertiary care hospital, their treatment & outcome.

METHODS
Records of 108 patients who were diagnosed as leprosy in the department of pathology of Hi-Tech Medical College, Bhubaneshwar, between 2014 -2019 were studied.

RESULTS
9.25% were children. M:F ratio was 2.7:1. Most common type was borderline tuberculoid.

CONCLUSIONS
It is seen that despite statistical elimination, multibacillary disease, leprosy reaction & deformities are seen although in less number than before. More active elimination strategy is needed.

KEYWORDS
Leprosy, Multibacillary, Skin Lesion, Nerve Damage

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BACKGROUND

Skin lesions occur on any part of your body & may cover a tiny or large area. Skin lesion can be singular or multiple, confined to one specific area of your body or distributed widely. It may be due to many causes as harmless as scrape or as serious as skin cancer. Leprosy is one of oldest, chronic, granulomatous, infectious disease having a prolonged incubation period that affects mainly skin & peripheral nerves. It can also affect muscles, eye, bones, testis, & internal organs.[1] It is caused by a slow growing mycobacterium, *Mycobacterium leprae*. The bacteria were discovered by Hansen in 1837. It is also known as Hansen's disease. Interestingly, the organism cannot be cultured.[1,2]

Exact mechanism of transmission of leprosy is not known; the most widely held belief was by contact between the leprosy patient & healthy person & transmission by the respiratory route. It is also a cause of permanent disability in the world. Hence control of communicable disease is based on identifying and destroying or attacking the causative organism.[2] The disease is now readily treatable with MDT. Disability & disfigurement can be avoided if the disease is treated early. It can be diagnosed by clinical, microbiological & histopathological study. Clinically leprosy cases presented as poorly defined with hypopigmentation or erythematous papules, nodules & some are with a single or few lesions as macules or plaques with well-defined edges. Leprosy show clinical diversity as well as its ability to mimic other diseases, leprosy is sometimes difficult to diagnose clinically, that's why histopathological examination a helpful diagnostic tool to confirm the diagnosis.[3,4]

Ridley & Jopling classified leprosy as the basis of clinical, histological, immunological & bacteriological findings.[3,5,6] In leprosy due to clinical diversity, it mimics to other diseases, so sometimes it's difficult to diagnose clinically. To confirm the diagnosis H.P study is most important, as well as demonstration of AFB is proved to be the most valuable in tissue sections. Even though Government declared leprosy eliminated from India, still considered as big health problem with social stigma.

METHODS

A retrospective 5 years hospital based study was conducted in the pathology department, Hi Tech Medical College, Bhubaneswar in the period 2014-2019. All cases of leprosy diagnosed on skin biopsy specimen in the department were included in the study. Patients of all age groups are included in study. Relevant clinical details were obtained from each patient in the proforma. Patients whose data was incomplete, patients unwilling for a punch biopsy were excluded from the study.

Punch biopsy was obtained in each case & was received at the Department of pathology for histopathological examination. Punch biopsy was given thin sections whatever appropriate & processed as per standard protocol. Formalin fixed & paraffin embedded sections were stained routinely with H.E. technique. Special stains like Wade Fite stain were applied whenever necessary. Final H.P. diagnosis was given in each case correlating with clinical findings. The results obtained were tabulated & analysed.

Procedure of Wade Fite Staining

1. Warm sections and de-paraffinize in a mixture of two parts xylene/one part vegetable oil for 15 mins.
2. Blot dry and wash in water.
3. Filter on carbol fuchsin solution, DO NOT HEAT, for 20 mins.
4. Wash in running tap water.
5. Differentiate in 10.0% sulphuric acid for 2 mins.
6. Wash well in running tap water, rinse distilled water.
7. Counterstain in 0.25% methylene blue for 20 seconds.
8. Wash and blot dry. DO NOT DEHYDRATE IN ALCOHOL.
9. Clear in xylene. Repeat the blotting-xylene treatment until section is clear.
10. Mount in a DPX type mountant.

RESULTS

Total no of cases included in study were 499 cases of skin lesion, out of which 108 cases were leprosy. Distribution of leprosy cases according to age group, among them the youngest age group is 7 years & oldest age group is 75 years. There was young to adult age group predominance with M:F is 2.7:1. Most common clinical presentation was hypopigmented patch/plaque & nodule. Most cases of lepromatous leprosy had multiple skin lesions, other cases had only single lesion. Most common histopathological diagnosis is Non-specific inflammatory lesion, followed by Hansen disease; followed by non-specific dermatitis & followed by lichenoid lesion & psoriasis.

A detailed clinical history was included for every cases. Among all the lesions most cases were non specific inflammatory lesion.the cases who were diagnosed as leprosy were 22% of all skin lesions in this 5 years. Most common age group affected were 20- 50 yrs. The maximum number of male and female patients was between this group. Total no of male is 79, total female are 29. The male to female ratio is 2.7:1. The youngest patient was 7 years old & the oldest one was 75 years. Children age groups are reported mostly to be tuberculoid as paucibacillary disease.

Sl. No.	Name of Disease	No. of Cases	% of Cases
1	Non-specific inflammatory lesion	205	41.8%
2	Hansen's disease	108	22%
3	Lichenoid lesion	49	10%
4	Psoriasis	21	4.2%
5	Pityriasis Rosea	14	2.8%
6	Non-specific dermatitis	65	13.2%
7	DLE	2	0.4%
8	Morphea	21	4.2%
9	Pemphigus	14	2.8%

Table 1. Distributions of Different Skin Lesions

Wade Fite stain done in all cases. M. leprae is a non-motile, non-spore forming acid fast bacilli, when it stained with Wade Fite it appears as red rod shaped organism, shorter, beaded or granular shape. The sensitivity of

detection of acid-fast bacilli by histologic means remains poor, because about 1000 bacilli per cubic centimeter of tissue must be present. The bacterial index follows Ridley's logarithmic scale. This table shows almost all cases of lepromatous & histoid were 100% Wade Fite positivity.

Sl. No.	Age Group	No. of Cases	Male	Female
1	1- 10	8	5	3
2	11- 20	6	5	1
3	21 -30	21	16	5
4	31 -40	28	18	10
5	41 -50	23	14	9
6	51 -60	7	5	2
7	61 -70	10	6	4
8	71 -80	5	3	2

Table 2. Distribution of Leprosy Cases among Males and Females

Sl. No.	Histopathological Diagnosis	No. of Cases	% of Cases
1	Lepromatous leprosy	13	12.03%
2	Borderline leprosy	28	25.9%
3	Histioid leprosy	2	1.85%
4	Mid borderline leprosy	3	2.7%
5	Borderline tuberculoid leprosy	45	41.66%
6	Tuberculoid leprosy	14	12.96%
7	Indeterminate leprosy	3	2.77%
8	Lepra reaction	0	

Table 3. Distribution of 108 Cases According to Histopathological Type

Age Group (Yrs.)	LL	BT	TT	BL	Histoid	IL	BB	Lepra Reaction
1-10	0	3	4	0	0	0	1	0
11-20	2	4		1	0	0	0	0
21-30	4	10	2	6	1	1	0	0
31-40	1	10	3	3	0	0	0	0
41-50	3	8	2	8	0	0	1	0
51-60	2	7	1	5	1	0	0	0
61-70	1	2	0	3	0	1	1	0
71-80	0	1	2	1	0	1	0	0

Table 4. Distribution of Leprosy Cases According to Age Groups

Histological Type of Leprosy	No. of Cases	Wade Fite Stain Positive Cases	% of Cases
TT	14	0	0%
BT	40	10	25%
BL	25	20	80%
LL	12	12	100%
IL	2	0	0
Histioid	3	3	100%

Table 5. Wade Fite Positivity in Individual Histological Type of Leprosy

DISCUSSION

Over last three decades WHO has been coming out with various action plans outlining the strategies required for control of leprosy. The present strategy of leprosy control is to reduce the load of infection in society by detecting the cases & providing adequate treatment. However, the rate of case detection & prevalence rate from 2014 -2019 which clarify that transmission of leprosy still continued.[5] Accurate diagnosis is of fundamental importance to all aspects of leprosy epidemiology, management and prevention of disability. There will chances of continued transmission of disease and many sufferings due to under diagnosis.

The retrospective study conducted in a tertiary care hospital in Bhubaneswar included 108 cases & confirmed histopathologically. Age of patient vary from 5- 80. Maximum cases were observed in the age group of 21 -50. Similar findings seen in Singh et al (2016).[7] Youngest patient was 7 years and oldest patient was 75 years. These findings are similar to the findings of other studies like Singh et al (2016) and Bandhan et al (2014).[8] These finding show increased number of cases in younger age group, while decreased number of cases in children age group. Usually leprosy show male predominance, present study was observed male predominance, M:F - 2.7:1 similar findings noted by other studies including Park JE et al (1991)[1] and Jindal N et al in (2009).[9] Male predominance may be because of many factors such as industrialization, urbanization and there are more opportunities for contact in males,

Vasaikar et al (2017) have noted a slightly higher number of females in their study, with male to female ratio being 0.8:1.[10] Present study indicates it may be due to occupation and more chance of contact in males. Histopathological examination is required even if the case is easily diagnosed clinically to classify the exact type of leprosy. Thus, histopathological study is the gold standard for the accurate diagnosis of leprosy.[11] Sometimes lesion on face do not show anaesthetic that time. These lesions can be missed if we completely depend on clinical basis. In tuberculoid & indeterminate both the cases lepra bacilli are fewer compared to lepromatous form.

The clinical categorization of leprosy cases into paucibacillary and multibacillary based on the number of lesions counted in a patient by World Health Organization (WHO) in 1994. More than 5 lesions counted is said to be multibacillary; a count of less than or equal to 5 lesions is typed as paucibacillary. Present study show paucibacillary 70% and 30% multibacillary. However, this method is unreliable as there may be miscounting and misreporting of cases. Thereby, histopathology is a best method of diagnosis.

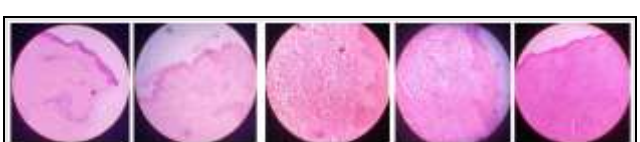

Figure 1. Histopathological Spectrum of Leprosy Presented in the Upper Panel, (40x) in H & E Stained Sections

Figure 2. Fite Stained Showing Lepra Baclii in the Lower Panel. (100x)

The histopathological diagnosis were classified on the basis of histopathological features to borderline leprosy (BL), mid borderline leprosy (BB), lepromatous leprosy (LL), histioid leprosy, borderline tuberculoid leprosy (BT), tuberculoid leprosy (TT) & indeterminate leprosy (IL).[12] Histopathological criteria used for clinical correlation was the flattening of epidermis, involvement of sub-epidermal zone, character and extent of granuloma formation, density of lymphocytic infiltrate, nerve involvement, presence of M. Leprae and epithelioid cells and other cellular elements in

biopsy sections.[5] Most common age group affected are 21 - 50 years which is similar study of Manadhar et al (2013)[13] and Jindal et al (2009). Most common site affected were back, arm, thigh, leg, & face presented with single or multiple lesion with sensation loss over the affected area.

Histological patterns observed in our study were epidermal changes in the form of thinning and atrophy, followed by normal epidermis and ulcerative changes. BL type usually showed lymphocytes more prominent and there is tendency for activated macrophages to form poorly defined to moderately formed granulomas. Foamy macrophages may not be conspicuous and globi (numerous bacilli clumped in macrophages) are usually not seen. Perineural fibroblast proliferation was found. LL type in our study showed extensive cellular which is separated from the flattened epidermis by a narrow grenz zone which is a clear space of normal collagen without any cellular infiltrate. Dermis is filled with plenty of foamy macrophages and contained mixed population of solid and fragmented bacilli. Globi are often present and there is absence of granulomas, though diffuse plasma cell infiltration is present.[14]

In case of Histoid leprosy it showed the cells become spindle shaped and arranged in a storiform pattern. It showed highest load of bacilli. Histoid leprosy, coined by Wade in 1963. All LL cases and 80% BL cases showed AFB positivity. BT type typically showed granuloma with peripheral lymphocytes with infiltration of neurovascular bundles, sweat gland and erector pili muscles by lymphocytes. Granulomas and Langhans giant cells are present. Few AFB may be demonstrated. Presence of Langhans giant cell. They do not infiltrate up to epidermis. Acid Fast bacilli are scanty. TT type typically showed large epithelioid cells arranged in compact granuloma with dense lymphocytes accumulation. Langhans giant cell was absent. Acid Fast bacilli rarely found.[14]

Cases of Indeterminate leprosy are also difficult to diagnose due to the nonspecific histology of the lesions. It also depends on factors such as nature and depth of biopsy, the acid-fast-stained sections examined, and the interobserver variation in both clinical and histopathological examinations. In the present study, two cases were diagnosed as indeterminate leprosy both clinically and histopathologically with the aid of Fite-Faraco stain. But in case of Indeterminate leprosy this is an early, transitory lesion seen in patients with variable immunological status. It showed mild lymphocytic and macrophage accumulation around neurovascular bundles, dermal vessels, sweat glands

Epithelioid cell granuloma and giant cells were more common towards tuberculoid pole whereas foamy macrophages with clear sub epidermal grenz zone were more common towards lepromatous pole. But the other histopathological findings like the granulomas & neural involvement were the criteria most useful for the typing of the tuberculoid forms. The indeterminate forms were obviously problematic histopathologically due to the nonspecific histopathological findings but then the clinical correlation was recommended for the final diagnosis. In this study borderline tuberculoid was the most common form with male predominant.[15]

Most cases in our study is BT type. This is comparable to studies Prerona et al (2019), Thapa et al (2013), Mandhar et al (2013), Giridhar et al (2012) and Kadam YR et al (2016).[3,4,16] Khamankar et al (2016)[17] found LL to be the commonest histological type followed by BL. Pokhrel et al (2017) found BT to be the least common and TT to be the most common type. TT was the second commonest type in our study. Many patients showed a continuous immunological progression with treatment. Immunological instability in these borderline cases makes them move in either direction along the borderline spectrum. Most of cases move towards tuberculoid pole with treatment, or they tend to move towards lepromatous pole without treatment. If the disease is recognized at an earlier stage and biopsy is taken, it will be in BT stage or if the disease is recognized at a later stage, it may be in BL stage.

CONCLUSIONS

The predominance of borderline spectrum and paucibacillary leprosy could be due to lower socioeconomic status, poor sanitary conditions, overcrowding, and illiteracy. Accurate diagnosis is required for proper treatment, preventing deformities, and drug resistance. For accurate diagnosis, histopathological examination is the gold standard and combining with Wade Fite staining is important for classifying leprosy group especially where there is limited clinical history. Early diagnosis & treatment of leprosy is required. History of contact in the study subject was not common, & presence of leprosy in paediatric age group indicates continued transmission. However, there is a need for strong follow-up system for defaulters. Training the health care workers in diagnosing nerve thickening and nerve function impairment will prevent the progression of deformity or any new case.

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