ORIGINAL RESEARCH

Evaluation of histopathological changes in Hansen's disease spectrum: A cross-sectional study from central India

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Received: 18 February, 2023 Accepted: 24 March, 2023

ABSTRACT

Background: Hansen's disease is still considered to be a severe threat to the health of people all over the globe, particularly in developing nations such as India. Due to the lengthy incubation period of Hansen's illness, the excessive reliance on clinical competence, and the absence of a quick and easy diagnostic instrument, patients who are afflicted with the condition might be misdiagnosed for an extended period of time. **Aim**: The purpose of this study is to evaluate the histopathological alterations that occur throughout the range of Hansen's disease.

Material and methods: A cross-sectional observational study including all newly diagnosed instances of Hansen's disease over a duration of one year,that had a clinical suspicion associated with them were included in the research. After receiving the institutional ethics approvaland written informed consent of the patient, a comprehensive clinical history and examination was done. After which skin biopsy samples were obtained from the most active portion of the lesion and sent for histopathological evaluation. **Results:** A total of 35 patients were studied with age group ranging between 27 to 72 years. Out of 35 patients, 19 were males and 16 were females with male to female ratio being 1.88:1. Histopathologically, borderline lepromatous was the commonest (48.57%) followed by borderline tuberculoid (25.71%). On histopathological assessment, the most common epidermal change observed was atrophy and flattened rete ridges (60%) and was found most commonly in borderline lepromatous type. The commonest dermal change was peri appendageal lympho-histiocytes (45.71%) and was found most frequently in borderline lepromatous followed by borderline tuberculoid. The common inflammatory infiltrates were foamy histiocytes (51.43%), found frequently in borderline lepromatous Hansen's disease. **Conclusion:** We concluded that the detailed histopathological evaluation of Hansen's disease spectrum mark decisive role to identify stages of disease activity and ongoing shifts in various forms and toformulate the first line management.

Keywords: Hansen's disease, Histopathology, borderline lepromatous.

INTRODUCTION

Leprosy, also known as Hansen's disease, is a chronic inflammatory mycobacterial illness. It has a long history of being one of the most stigmatised diseases, perhaps because of concerns of its contagiousness and disfiguring effects. From the beginning of human society, it has been a source of misery for people everywhere. It continues to be a problem for mankind, creating new difficulties, and continuing to pique our interest. In spite of the fact that we know a lot about Hansen's illness, it is continued to be a significant threat to the public's health in underdeveloped nations for centuries. The World Health Organization (WHO) estimates that there were 1,40,594 new cases of Hansen's disease detected in the world in 2021 and India is responsible for 75,394 (53.62%) of these new cases [1].The clinical signs of Hansen disease are quite broad and diversified, and they may be mistaken for a number of disorders that are not connected to one another. It is possible for patients to present with anything from a little skin lesion to a severe condition that causes major deformities and impairments [2]. The immunological condition of the patient is connected to the histological features that occur in Hansen's illness [3]. Tuberculoid (TT), borderline tuberculoid (BT), mid- borderline (BB), borderline lepromatous (BL), and lepromatous (LL) are the five groups that make up the histological categorization of Ridley and Jopling (1966) suggested representing the immunological spectrum[4]. In further studies of

Hansen's disease, the researchers established clinical and bacteriological data for each group, along with immunological and histological findings [5]. The classification of Hansen's disease based on the clinical criteria has also been given the same nomenclature, which has been embraced by clinicians. TheWHO divided leprosy into multibacillary and paucibacillary types in its 6th technical report in 1988. This was done to simplify the establishment of an appropriate method of treatment and frequent follow-up with patients in order to minimise unfavourable sequelae [6]. Clinical factors such as anaesthesia or hypoesthesia in skin lesions, thickening of peripheral nerves, and the presence of acid-fast bacilli (AFB) in slit skin smears or tissue biopsies have been used to diagnose Hansen's illness.

The present study was conducted due to scarcity of Hansen's disease related histopathological data in central India and to evaluate histopathological alterations that occur throughout the range of Hansen's disease.

MATERIAL AND METHODS

The current research was a cross-sectional observational study, carried out in dermatology outpatient department at a tertiary care centre from June 2021- May 2022for one year duration. All newly diagnosed instances of Hansen's illness that had a clinical suspicion associated with them were included in the research. After receiving the Institutional ethics committee approval and written informed consent of the patient, a comprehensive clinical history and examination was done. A total of 35 clinically suspected untreated individuals were included in the study, independent of their age, gender, socioeconomic background, or employment. Cases that had previously been identified and those who were under treatment were not considered. The clinical diagnosis was done based on clinical signs and symptoms. In the clinical evaluation of skin lesions, aspects such as the number, size, location, margins, symmetry, dryness, loss of hair and sensation, and the existence of neurological involvement were taken into consideration. The skin biopsy sample was obtained from the most active portion of the lesion and was then sent for histopathological examination in department of pathology in 10% formalin solution. Patients with Hansen's disease were categorised by the Ridley-Jopling (RJ Scale) into the following subtypes: tuberculoid (TT), borderline tuberculoid (BT), mid-borderline (BB), borderline lepromatous (BL), and lepromatous (LL) in both clinical and histopathological diagnosis. Histopathological evaluation included epidermal and dermal changes with predominant dermal inflammatory infiltrates. The data was recorded and compiled on Microsoft Excel sheet and subjected to descriptive statistical analysis.

RESULTS

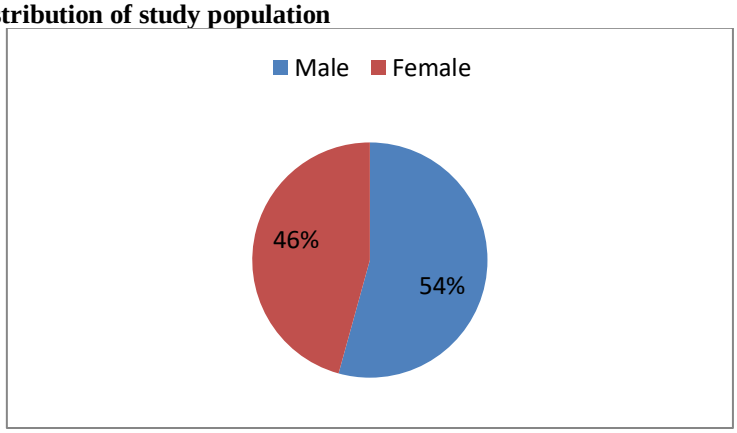
A total of 35 patients were studied with age group ranging between 20 to 79 years. The majority of cases were encountered between 20-29 years (40%) of age group followed by 30-39 years in 20% cases. On the other hand, the least affected age- group noticed was 70-79 years in 5.7% cases(Table1).

Table 1: Age distribution of study population

Age distribution	Male	Female	Total (%)
20-29	6	8	14 (40%)
30-39	3	4	7 (20%)
40-49	3	0	3 (8.57%)
50-59	2	2	4 (11.42%)
60-69	3	2	5 (14.28%)
70-79	2	0	2 (5.71%)
Total	19	16	35

Out of 35 patients in our study, 19 were males and 16 were females with male to female ratio being 1.88:1. (Figure 1)

Figure 1. Gender distribution of study population



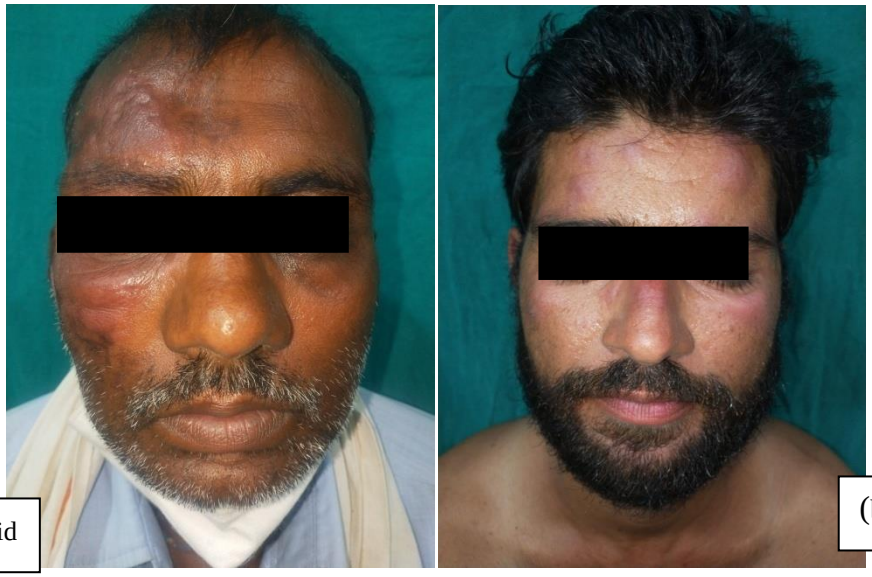
As per the individual type of Hansen's disease is concerned, borderline lepromatous was the most dominant type (48.57%) followed by borderline tuberculoid (25.71%)in the present research. (Table 2) (Fig. 2a & Fig. 2b)

Table 2: Types of Hansen's disease encountered in study population

Hansen's disease Types	Number	%
Borderline Lepromatous	17	48.57
Borderline Tuberculoid	9	25.71
Lepromatous Leprosy	3	8.57
Tuberculoid Leprosy	2	5.71
Lepra Reaction	2	5.71
Histoid Leprosy	2	5.71

Figure 2: Clinicaland respective histopathological images of Hansen's disease cases in our study

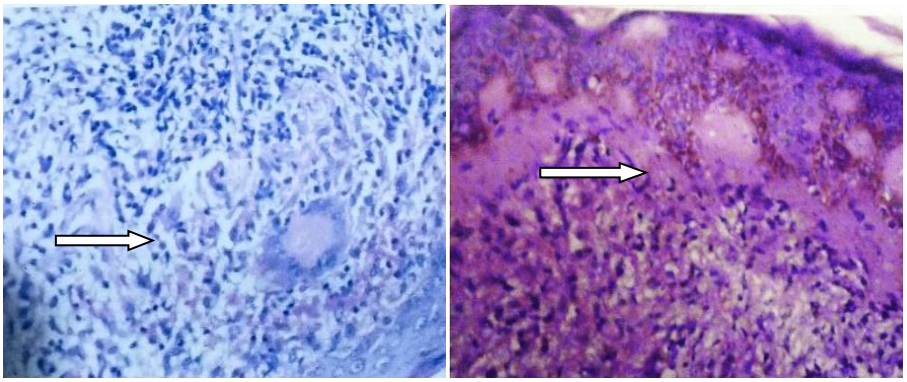
Fig.2a & Fig. 2b



(a) Borderline tuberculoid

(b) Borderline lepromatous

Fig.2c & Fig.2d



c) BT leprosy histopathology showingepitheloid granuloma with langhans giant cells surrounded by lymphocytes.

d) BL leprosy histopathology showing foamy histiocytes and Grenz zone.

On histopathological assessment of various types of Hansen's disease, the common epidermal changes observed were atrophy and flattened rete ridges (60% each) and these were found predominantly in borderline lepromatous type(42.86%).Ulceration/ erosions and unremarkable changes were detected in 5.71% cases each in borderline tuberculoid and tuberculoid leprosy equally. (Table 3)

Table 3: Epidermal changes

Epidermal Changes	Tuberculoid Leprosy	Borderline Tuberculoid	Borderline Lepromatous	Lepromatous Leprosy	Lepra Reaction	Histoid Leprosy	Total
Atrophy	0	6(17.14%)	15(42.86%)	0	0	0	21(60%)
Flattened Rete Ridges	0	6(17.14%)	15(42.86%)	0	0	0	21(60%)
Ulceration/ Erosion	0	2(5.71%)	0	0	0	0	2(5.71%)
Unremarkable	2(5.71%)	0	0	0	0	0	2(5.71%)

The commonest dermal changes in various types of Hansen's disease observed in our study were peri-appendageal lympho-histiocytes(45.71%) and were found most frequently in borderline lepromatous (28.57%) followed by equal proportion in borderline tuberculoid, lepromatous leprosy and lepra reactions in 5.71% cases each. The common inflammatory infiltrates were foamy histiocytes (51.43%), found frequently in borderline lepromatous Hansen in 34.29% cases. Perineural lympho-histiocytes and grenz zone were the next common finding in the dermis in 40% cases each and found in borderline lepromatous pole in 40% and 31.43% cases respectively. (Table 4) (Fig. 3c & Fig. 3d)

Table 4: Dermal changes

Dermal Changes	Tuberculoid leprosy	Borderline Tuberculoid	Borderline Lepromatous	Lepromatous Leprosy	Lepra Reaction	Histoid Leprosy	Total
Epitheloid Granuloma	2(5.71%)	11(31.43%)	0	0	0	0	13(37.14%)
Giant Cells	2(5.71%)	8(22.86%)	0	0	0	0	10(28.57%)
Periappendageal Lymphocytes	2(5.71%)	7(20%)	5(14.29%)	0	0	0	14(40%)
Perivascular Lymphocytes	2(5.71%)	6(17.14%)	0	0	2(5.71%)	0	10(28.57%)
Perineural Lymphocytes	2(5.71%)	5(14.29%)	0	0	0	0	7(20%)
Periappendageal Lymphohistiocytes	0	2(5.71%)	10(28.57%)	2(5.71%)	2(5.71%)	0	**16(45.71%)**
Perivascular Lymphohistiocytes	0	4(11.43%)	1(2.86%)	0	1(2.86%)	1(2.86%)	7(20%)
Perineural Lymphohistiocytes	0	0	14(40%)	0	0	0	14(40%)
Macrophages	0	0	12(34.29%)	2(5.71%)	2(5.71%)	2(5.71%)	**18(51.43%)**
Grenz Zone	0	0	11(31.43%)	3(8.57%)	0	0	14(40%)

DISCUSSION

Hansen's disease is an old illness that has been affecting humans for a very long time. The causative agent of Hansen's disease, Mycobacterium leprae causesa persistent granulomatous infection, that progresses slowly and mostly affects the skin and peripheral nerves in the body. [7]Depending on the immunological state of the host, Hansen's disease may manifest itself in a variety of various clinicopathological manifestations.It mostly affects the skin and the peripheral nerves, but it may also damage reticuloendothelial system, eyes,bone, joints, muscles, adrenals, and testicles. It has a wide variety of clinical symptoms, many of which are linked to immunological responses of the host. The condition may progressively worsen over a duration time and result in irreversible damage to the skin, nerves, limbs and eyes.

In the present study, third decade was the age group that was impacted most often in 40% cases. Guha et al [8], Kaur S et al [9], Sehgal et al [10], and Murthy et al [11] all produced observations that were in agreement with this theory.

Clinically and histopathologically, the most prevalent diagnosis in present study was borderline lepromatous (48.57%). There was a 100% correlation in instances with clinically confirmed histoid leprosy (2/35) and lepra reaction (2/35) cases.In previous research conducted by Semwal S et al, there was a link found between the clinical and histopathological findings in 62.9% of the patients (73/116) with BT as histological subtype seen in 40 out of 116 cases (34.48%) and BT and BL had clinico-histopathological correlation in 44.8% and 47.3%, respectively. [12]

Clinically, Nandwani R.R. and colleagues found that 46 percent of patients (n = 23) fell into the borderline range with borderline tuberculoid morphologic type as the most common one, occurring in 32% (n = 16) of the cases.[13]Likewise in previous studies conducted by Kumar et al [14], Bal A et al [15] and Manandhar U et al [16], the commonest type of Hansen's disease

being diagnosed in their study was borderline tuberculoid type.

Atrophy and flattening of the rete ridges (60% each) were the epidermal changes that were seen most often in our study. The researchers Suri SK et al [17] and Banushree CS et al [18]observed atrophy in 66.7% and 29.9% in their respective studies. These alterations are often detected in lepromatous leprosy spectrum, but they were also seen in borderline tuberculoid Hansen in our current investigation.

The most common dermal change observed in borderline tuberculoid was epitheloidgranuloma (31.43%), which was also present in the study done by Banushree CS et alin 44.85% cases[18]. The most prominent finding in present study in borderline lepromatous leprosy was perineural lymphohistiocytes (40%) and Grenz zone (8.57%) in lepromatous leprosy. Similar observations were found in study done by SuriSKet al.[17]

The level of clinicopathological agreement for lepromatous leprosytype was found to be the highest (97.1%). There was the relatively less amount of agreement found for tuberculoid leprosy (88.4%) as well as borderline tuberculoid (86.5%) cases.Because of the clinical presentation of some of the cases, TT was reclassified as BT on the basis of the histopathology, and vice versa. This change in the composition of one group is rationalized by the fact that clinical and histopathological characteristics of TT and BT were highly similar to one another.

On the other hand, classifying TT and BT according to their histopathological manifestations is essential because doing so alerts the treating clinician to the possibility of a type 1 reaction, which was found to be prevalent among patients of BT in a treatment study carried out by Atram MA et al.[19]

Histopathology examination is considered to be the gold standard for diagnosing leprosy since it also provides information on the nature of the host response. Biopsy is an intrusive operation that can only be performed in specialist institutes. In order to solve this problem, a technique known as fine needle aspiration cytology (FNAC) of Hansen's disease lesions has arisen as a method that is risk-free, easy to use, quick, and causes less stress than other diagnostic methods [7].

Since leprosy may appear in such a wide variety of ways, it can be challenging for even the most seasoned dermatologists to make a correct clinical diagnosis of early leprosy lesions.In leprosy, clinico-histopathological correlation is essential for both monitoring the patient's response to therapy and determining whether or not the patient has had a relapse or reactivation of the illness. While there has been a significant reduction in the number of leprosy patients since the deployment of MDT for leprosy, we have not yet reached our objective of eradicating leprosy. It is a well-established fact that dormant bacilli may continue to reside in the nerves of borderline or ambiguous patients for years after therapy has been finished. We will not be able to realize our dream of ridding our nation of the scourge of leprosy until all proven cases of Hansen's disease are subjected to regular follow-up after treatment and are scrupulously screened for bacillary load prior to being labelled as disease free. If these limitations are fulfilled then only, we will be able to achieve this goal.[9]

CONCLUSION

We concluded that the detailed histopathological evaluation of Hansen’s disease spectrum marksdecisive role to identify stages of disease activity and ongoing shifts in various forms and to formulate the first line management.Even for expert dermatologists, the clinical diagnosis of early leprosy lesions may be challenging due to the fact that patients might appear in a variety of clinicopathological forms depending on the health of the host immune system. In order to correctly diagnose and classify leprosy, it is necessary to establish a link between the disease's clinical, histological, and bacteriological aspects.

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