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Leprosy in the 21st Century - An Evaluation of Clinical Spectrum and Histopathological Correlation of Leprosy in Tertiary Care Hospital in Karnataka

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Abstract: ***Background: Leprosy (Hansen's disease), a communicable disease still continue to be a social stigma and leading cause of permanent physical disability. It is classified into 5 groups based on Ridley Hopping classification. However a great variation has been observed in interpretation of histopathological examination of skin biopsies and clinical presentation of disease. Objectives: To correlate clinical diagnosis with histopathological diagnosis of Leprosy patients in Tertiary Care Hospital. Materials and Methods: This study was conducted from January 2020 to November 2021 in Tertiary Care Hospital on 50 untreated clinically suspected case of Leprosy classified as per Ridley Jopling classification. Skin biopsies were taken from active lesion in all patients and were stained with H&E stain and Fire feraco stain for identification of M. leprae, Slit smears were done to study bacillary index. Statistical Analysis: Descriptive analysis was done in form of percentage or proportion. Results: In this study 50 cases of Leprosy diagnosed as per Ridley Jopling clinical classification were evaluated histopathologically, most of the cases were seen in young adult males and between 20 - 30 years, majority of cases presented with erythematous lesion (26 cases, 52%) and 16 cases (32%) presented with hypopigmented lesion. Multiple skin lesions and multiple nerve involvement were commonly seen in lepromatous spectrum. BT Hansen was the most common type (19 cases, 38%) clinically and histopathologically. Overall correlation seen in 42 cases. Conclusion: As clinical diagnosis of early Leprosy lesions are difficult due to lack of cardinal signs hence biopsy should be done in all cases in order to improve classification and treatment.***

Keywords: Hansen's Disease, Borderline Tuberculoid Leprosy, Fite Feraco Stain, Ridley Jopling

1. Introduction

Leprosy presents in a variety of clinico - pathological forms depending on the immune status of the host and is a significant public health issue in developing nations, including India [1]. Mycobacterium leprae, which causes leprosy, is a chronic granulomatous inflammation that frequently affects the skin, nerves, muscles, eyes, bones, testicles, and internal organs. Clinical manifestations can range from an insignificant skin lesion to a serious illness that results in significant disabilities and deformities [2].

Leprosy prevalence in India as a whole has decreased from 5.27/10000 in 2000 to 0.67/10000 in 2018. Leprosy remains a public health challenge despite all medical science advancements [3]. India accounts for 60% of all newly reported cases worldwide each year, necessitating sustained efforts to lower the numbers [4]. In April 2016, WHO unveiled a five - year plan titled "Global leprosy strategy 2016 - 2020" with the slogan "Accelerating towards a leprosy - free world" [5].

Based on immunological characteristics, Ridley and Jopling divided leprosy into a total of five types in 1960: Tuberculoid (TT), Borderline Tuberculoid (BT), Mid Borderline (BB), Borderline Lepromatous (BL), and Lepromatous Leprosy (LL) [6]. It is further divided based on the Bacteriological Index (BI), which expresses the number of acid - fast bacilli in the dermis on a logarithmic scale [7]. Based on skin lesions and/or nerve trunk involvement, WHO recommended classifying leprosy into Paucibacillary (PB) and Multibacillary (MB) in 1982 (PB leprosy 5 lesions; MB leprosy >5 lesions) [8].

Diagnosis of leprosy is based on clinical examination, demonstration of acid fast bacilli in skin smears by Fite - faraco stain and histopathological examination [9].

Leprosy has a wide range of clinical manifestations, making clinical diagnosis challenging at times. Skin biopsies' histopathological analysis is an invaluable tool for confirming diagnoses, precisely classifying them, prescribing appropriate treatments, and monitoring disease progression and remission in patients receiving care. Leprosy clinico - pathological correlation thus assumes greater significance [10]. The goal of this study was to use Ridley - Jopling classification to estimate the degree of agreement between clinical and histopathological diagnosis in leprosy cases and to classify leprosy skin biopsies into various subtypes based on histopathological examination.

Objectives:

To correlate clinical diagnosis with histopathological diagnosis of Leprosy patients in Tertiary Care Hospital.

2. Materials and Methods

This study was conducted from January 2020 to November 2021 in Tertiary Care Hospital on 50 untreated clinically suspected case of Leprosy classified as per Ridley Jopling classification. Skin biopsies were taken from active lesion in all patients and were stained with H&E stain and Fire feraco stain for identification of M. leprae, Slit smears were done to study bacillary index.

Inclusion criteria: Newly diagnosed leprosy patients with hypopigmented patches with loss of sensation were included in the study.

Exclusion criteria: Patient who had taken antileprosy treatment in past, patient who was on anti - leprosy treatment and inadequate biopsy sample were excluded from the study.

Biopsies which lacked the full depth of dermis along with a portion of subcutaneous fat were considered as inadequate. Detailed clinical history like age, sex and clinical diagnosis was noted. Skin biopsies were performed by the Dermatologist and were sent to the Department of Pathology in 10% formalin. After adequate fixation, the biopsies were submitted for routine processing, followed by paraffin embedding and sectioning. All sections were stained with H&E and Fite - faraco stain to demonstrate acid fast bacilli. The cases were classified according to Ridley Jopling classification [6]. The histopathological slides, Fite - faraco slides and BI were reviewed.

3. Statistical Analysis

The data was collected and entered into Microsoft excel spread sheet and percentages were calculated.

4. Results

The present study included 50 skin biopsies were clinically diagnosed as leprosy. Age group of patients ranged from 11 years to 76 years. Majority of patients 23 (46%) were in the age group of 21 to 40 years followed by 14 (28%) in 41 to 60 years [Table/Fig - 1].

Age group in years	Number of cases	Percentage %
Below 20	4	8
21 - 40	23	46
41 - 60	14	28
61 - 76	9	18
Total	50	100

There were 30 (60%) male patients and 20 (40%) female patients, with male to female ratio (M: F) of 1.5: 1. Most of the patients presented with hypopigmented patch i. e 26 (52%) cases followed by erythematous macule i. e 16 (32%), papule and nodule. Clinically, maximum 23 (46%) cases were diagnosed as BT leprosy followed by Lepromatous leprosy 12 cases (24%), BL 8 (16%), TT leprosy 4 (8%), BB leprosy 2 (4%), and 1 (2%) cases of histoid leprosy.

On histopathological examination, the most common type was BT leprosy in 19 cases followed by Lepromatous leprosy in 8 cases, BL in 3 cases, BL leprosy in 4 cases and TT leprosy in 3 and Histoid leprosy in 1cases (table 2)

Clinical Diagnosis	Histopathological diagnosis								Others
	TT	BT	BB	BL	LL	HISTOID	IL	ENL	
TT (4)	3	1							
BT (23)	3	19							1
BB (2)			1				1		
BL (8)			3	4					1
LL (12)				2	8			1	1
HISTOID (1)						1			
IL (0)									
TOTAL (50)	6	20	4	6	8	1	1	1	3

On histopathological examination, one case showed features of indeterminate leprosy and erythema nodosumleprosum which were clinically diagnosed as Mid borderline and LL.

Overall concordance of histopathological diagnosis with clinical diagnosis was seen in 36 cases (72%). The clinico - histopathological concordance was highest in BT leprosy.

In our study, 8 cases were not diagnosed as leprosy histopathologically. So Fite - faraco staining was done in 8 cases. Out of 8 cases, 5 (10%) were found positive for Fite - faraco stain. No acid fast bacilli could be demonstrated in cases of TT leprosy and BB leprosy. All histologically diagnosed cases of BL leprosy, LL and histoid leprosy showed positivity for lepra bacilli.

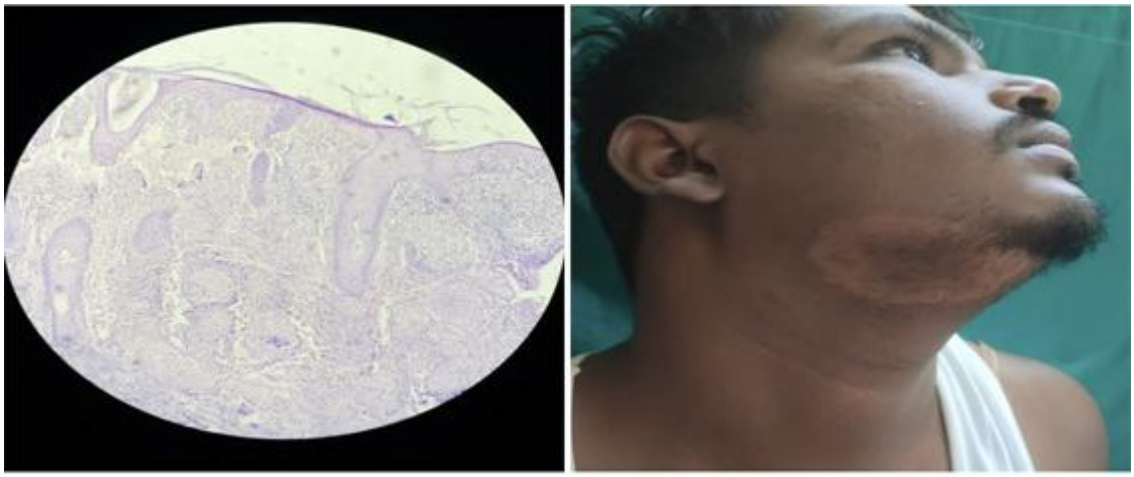

Figure 1: Case of Tuberculoid Leprosy with well defined hypopigmented patch present over neck (right side), TT Leprosy showing epithelioid cell granuloma eroding the basal layer of epidermis (left)

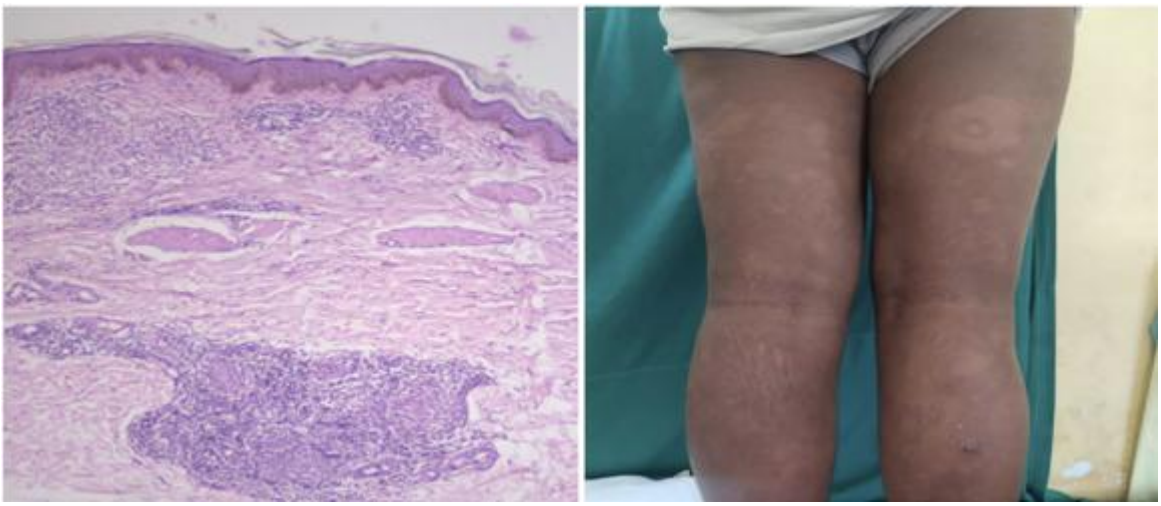

Figure 2: Case of Borderline Tuberculoid Leprosy with multiple well defined hypopigmented patches present over lower limb (right), BT leprosy Showing granuloma of epithelioid cells and lymphocytes in dermis

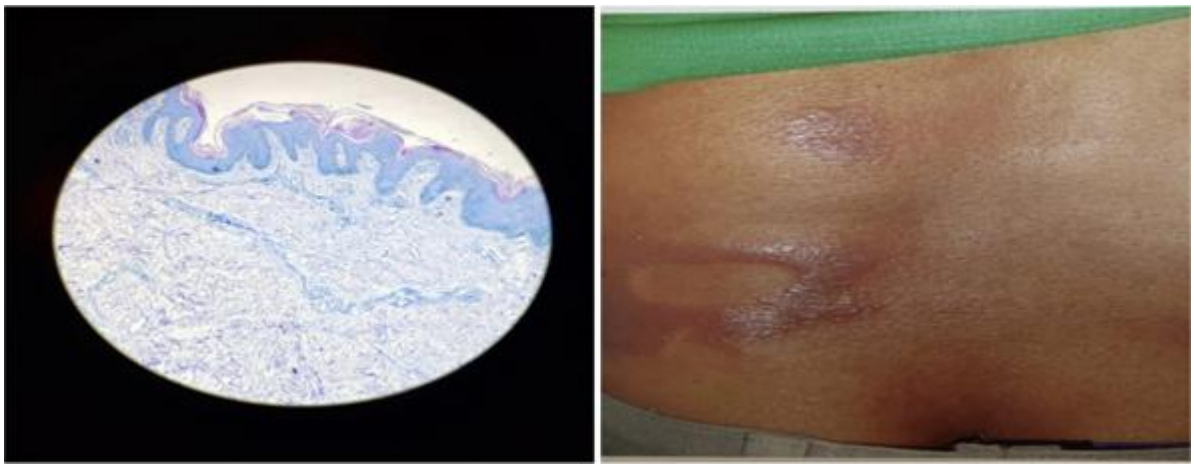

Figure 3: Case of Mid borderline Leprosy with well defined annular erythematous plaque with central clearing appearing as swiss cheese appearance (right), Mixed granuloma composed of immature epithelioid cells and bacteria laden macrophages (left).

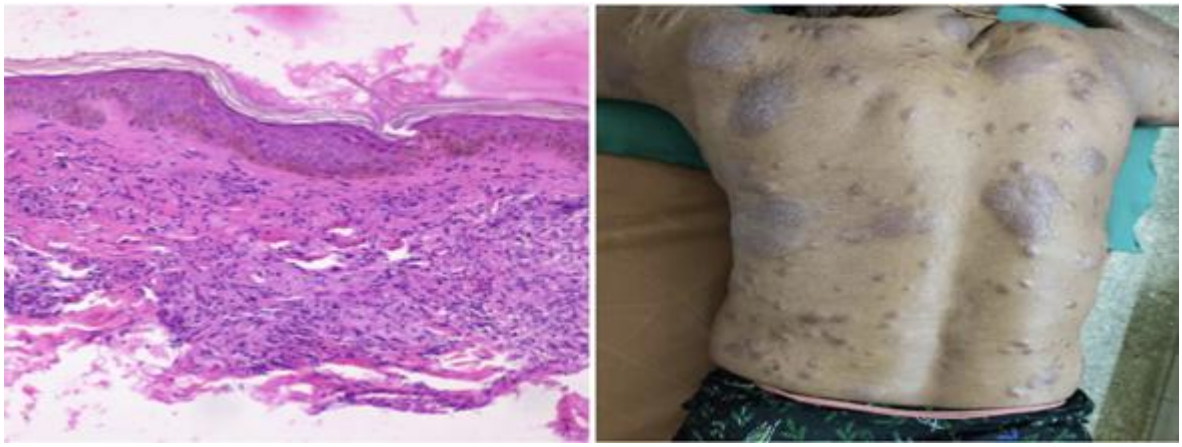

Figure 4: Case of Borderline Lepromatous Leprosy with multiple assymetrical erythematous plaque present over trunk (right), Epidermis is atrophic, clear Grenz zone with slight foamy cytoplasm (left)

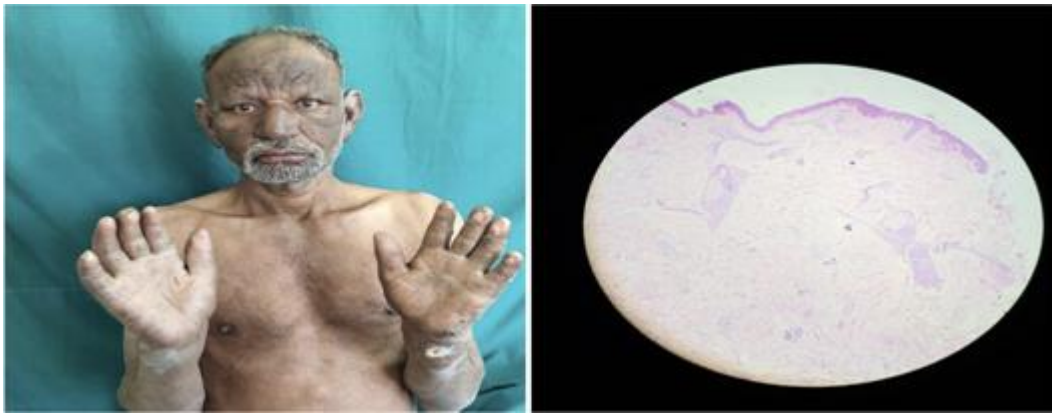

Figure 5: Case of Lepromatous Leprosy with diffuse infiltration of face, bilateral supraciliarmadarosis with trophic ulcers present over tips of fingers and left forearm (right), LL leprosy Showing Grenz zone with foamy macrophages in dermis (left).

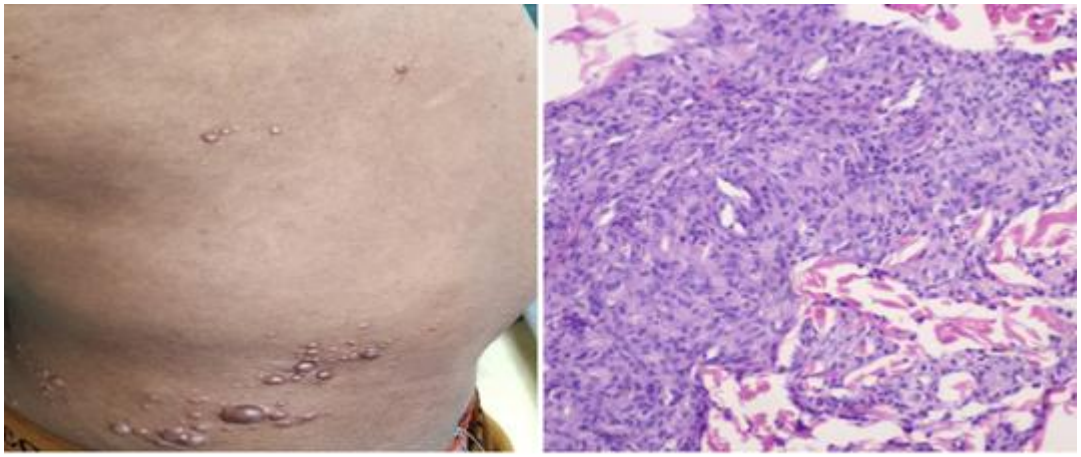

Figure 6: Case of Histoid leprosy (right), Histoid leprosy Showing interlacing bands of spindle cells (left)

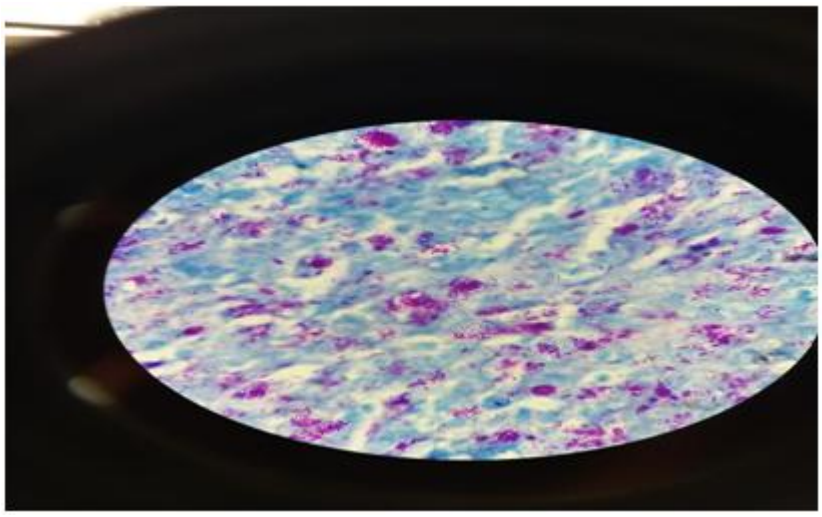

Figure 7: Fire Feraco stain showing Acid fast bacilli arranged in clump

5. Discussion

Leprosy is one of the oldest diseases known to man. It is a chronic contagious disease with various clinical presentations, which can mimic many diseases other than leprosy. A definitive diagnosis of leprosy cases cannot be reached based on clinical examination alone; thus the diagnostic accuracy is enhanced through the histopathological examination [6]. So, histopathological examination continues to be an important tool in accurate diagnosis and classification of leprosy and still remains the gold standard. During the study period of 18 months 50 skin biopsies were clinically diagnosed as leprosy.

In present study majority of cases were male (60%) and the male to female ratio was (1.5: 1). These findings were correlated with the findings of other studies [11 - 13]. The possible cause of male predominance of leprosy is considered to be environmental, more chances of contact, urbanisation and industrialisation. Leprosy can be seen in any age. In present study maximum cases were in 21 - 40 years of age group. Majority of the studies showed maximum cases in the same age group [12, 14]. In our study, least number of cases (8%) were reported below the age of 20 years. This may be due to longer incubation period of lepra bacilli [15]. The eldest case in our study was a 72 - year - old while a 11 - year - old girl was the youngest case. Most of the patients presented with hypopigmented patch (52%) and the remaining with erythematous macule (32%) and papule. Similar studies were seen in some other studies also [13, 14, 16]. Vahini G et al., observed 56% cases of hypopigmented plaque with loss of sensation [17]

In the present study, the majority of the patients were found to be in the borderline spectrum of leprosy. Similar findings were seen by Shivamurthy V et al., and Banushree CS et al., [13, 18]. In our study clinically and histopathologically, the most common diagnosis was BT leprosy which is in concordance with Tiwati M et al., Shivamurthy V et al., and Bal A et al., [12, 13, 19]. In a recent study of Semwal S et al., Vahini G and Hazarika D et al., also reported the maximum cases of BT leprosy [11, 17, 20].

Histopathologically, in TT leprosy well formed epitheloid cell granuloma with a rim of lymphocytes distributed throughtout the dermis and enroaching the basal layer of the epidermis were seen. In BT leprosy, granulomas have a fewer number of lymphocytes and more giant cells and epidermal erosion will not be seen. Erosion into the epidermis with absence of grenz zone when present is a useful feature in differentiating TT leprosy and BT leprosy. In BL leprosy, the lymphocytes are more prominent and there is a tendency for some activation of macrophages to form poorly to moderately defined granulomas. Perineural fibroblast proliferation forming an ‘onion skin’ is typical. Foamy cells are not prominent and LL diffuse sheets of foamy histiocytes with grenz zone [21]

Indeterminate leprosy is not included in Ridley Jopling classification system due to lack of distinguishing features. It is considered as early form of leprosy which consists of a skin lesion with slightly less sensitivity to touch. It may resolve or progress further to one of the five forms of leprosy within the Ridley Jopling system. In present study no cases were confirmed histologically. Early detection and diagnosis of indeterminate leprosy is due to increased awareness of the people about leprosy. In indeterminate leprosy, there is mild lymphocytic infiltration around neurovascular bundles, sweat glands and erector pili muscle. No formed epitheloid cell granulomas are observed [22a].

Only one cases (2%) was clinically and histopathologically diagnosed as histoid leprosy; . Semwal S et al., and Arunagirinathan M et al., were observed complete agreement of clinical and histological diagnosis of histoid leprosy [11, 22]. In our study clinico - histopathology concordance was observed in 72% of cases. The similar results reported by. various other studies [11, 16, 18, 23 - 27].

Author [refrence]	Year of study	Place of study	Clinico - histopathology concordence (%)
Mathur MC et al., [23]	2011	Nepal	80.4%
Giridhar M et al., [16]	2012	Amritsar	60.23%
Mohan N and Mishra N, [24]	2013	Uttar Pradesh	56.5%
Kumar A et al., [25]	2014	Rajasthan	62.9%
Rizvi AA et al., [26]	2015	Maharashtra	70%
Banushree CS et al., [18]	2016	Puducherry	79.44%
Semwal S et al., [11]	2018	Bhopal	62%
Ramesh A and Sampath V, [27]	2019	Chennai	61.22%
Present study	2020	Davanagere	72%

Maximum clinico - pathological concordence was seen in BT leprosy (82.6%). Similar observations were noted by Mathur MC et al., (80.4%) and Mohan N et al., (56.54%) [23, 24].

In 1982, World Health Organisation (WHO) classified leprosy as MB and PB on the basis of BI. Indeterminate leprosy, TT leprosy and BT leprosy cases of leprosy were classified as PB and BB leprosy, BL and LL cases of leprosy were classified as MB [28]. When BI value two or more at any site indicated therapy for MB leprosy and BI value less than two indicated therapy for PB leprosy. The cell mediated immune response and bacterial load is determined by BI. Thus, BI is supportive parameter for the diagnosis and treatment of leprosy patients.

In our study, Fite - faraco stain was positive in all cases of BL leprosy, LL and histoid leprosy. Similar findings were seen in other studies [13, 17, 18]. Despite specific histopathological findings in different forms, overlapping features are seen in different types of leprosy.

Thus, selection of the site for biopsy play an important role in histopathological diagnosis since clinically dissimilar lesions biopsied from the same patient can show different types of histopathology [29]. Hence, it is necessary to correlate clinical, histopathological features along with BI appears to be more useful for accurate typing of leprosy [17].

6. Limitation

Proper biopsy technique could have contributed to accurate histopathological diagnosis and due to social stigma many patients specially females do not come to hospital because of this actual disease burden remain under reported.

7. Conclusion

There can be significant degree of overlapping clinical features as well as histopathological findings among different types of leprosy. So, concordence of clinical and histopathological features as well as BI should be considered for accurate typing of leprosy. Same is the key to achieve elimination of leprosy cases in the community.

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