Original Article

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Finding Correlation in Clinical and Pathological Diagnosis in Reemerging Context of Leprosy in India: A Tertiary Care Center Experience

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ABSTRACT

Background: Leprosy was supposed to be eliminated by WHO from the world by the end of the year 2000. However, it still affects the major population in India. It is well realized that even after elimination target has been achieved, new leprosy cases will keep coming for at least some years due to continuation of some level of disease transmission or manifestation of disease by subclinical cases. Hence there is the need to review this disease with proper understanding.

Objective: To determine the current leprosy profile and its relation between clinical and pathological diagnosis, at our centre catering the population of Western Uttar Pradesh.

Methods and Material: It's a retrospective study and was carried out on skin biopsy samples sent for histopathological diagnosis in clinical suspicion of leprosy at Jawaharlal Nehru Medical College and Hospital, Aligarh, from June 2015 to November 2017. Tissue Sections were stained with Haematoxylin and Eosin stain for morphological studies, and modified fite stain to identify acid fast bacilli.

Results: Out of 325 clinically suspected leprosy cases, we diagnosed leprosy in 282 cases with 86.7% parity. Most commonly affected age group was between 16 -30 years (110 cases). Tuberculoid leprosy was the most common histological subtype (69/282, 24.4%) followed by lepromatous leprosy (58/282, 20.56%), borderline tuberculoid (53/282, 18.7%), borderline lepromatous (42/282, 14.8%), indeterminate leprosy (34/282, 12%) and mid borderline leprosy (22/282, 7.8%). Additionally, histioid type of leprosy was diagnosed histologically in 1.4% (4/282) of the cases.

Conclusions: Identification of suspicious skin patch as leprosy with prompt histological diagnosis especially in population of below 30 years is required for timely intervention and eradication. Both clinician and pathologist should have a focused approach especially in diagnosing indeterminate leprosy.

Keywords: *Correlation Study, Leprosy, Reemerging Context*

Introduction

Leprosy is a chronic infectious disease caused by Mycobacterium leprae (also known as Hansen's bacillus), which can affect all ages and both sexes. Leprosy is transmitted by close and prolonged contact between a susceptible person and a bacillus-infected patient through inhalation of the bacilli present in nasal secretion. The nasal mucosa is considered to be the main route of transmission [1,2]. However, transmission can occur by skin erosions [2]. Other routes, such as blood, insect bites, vertical transmission and breast milk are also involved in transmission [3]. It is assumed that asymptomatic, infected individuals, may have a transitional period of nasal release of lepra bacilli [4,5].

The pathogenesis of this disease is multiplex and depends upon host-bacterial immunological interplay. Hence it will follow the immunological spectrum ranging from tuberculoid leprosy (TT) to lepromatous leprosy (LL) based on clinical, immunological, microbiological and histopathological criteria as defined by Ridley & Jopling (1962,1966)[6,7]. The borderline form falls between TT and LL and is further divided into borderline-tuberculoid leprosy (BT), borderline-lepromatous leprosy (BL), according to the greater proximity to one of the poles, and borderline-borderline (BB) at the middle. Leprosy has a continuum spectrum, and patients may move in either direction according to host response and treatment.

The introduction of the multidrug therapy (MDT) by WHO in 1981, markedly changes the leprosy epidemiology (16). The reduction in treatment duration, affected the prevalence, from over 5 million cases in the 1980s to 208,641 new cases reported worldwide in 2019 [8,9,10]. With the global reduction of disease prevalence, WHO established the global goal of leprosy elimination in 1991 with the target of less than one person affected per 10,000 inhabitants [11]. With this prevalence rate, it was believed that there would be a reduction in leprosy transmission and natural

disappearance of the disease. By the end of 2018, 1,84,212 new cases were reported globally and the prevalence rate stands at 0.2/10,000. In India, the prevalence rate is still high 0.57/10,000 population [12].

In India, in 1993, the National Leprosy Elimination Programme (NLEP) was initiated with the goal of decreasing the prevalence rate of leprosy below 1 case/10,000 population. India has achieved elimination of leprosy as a public health problem in December 2005 by recording a prevalence rate of 0.95/10,000 population [13], further declined to 0.57 /10,000 population by the end of 2018 [12]. It is a general assumption presently that this disease has been eradicated from our country, however the scenario is different as reported form different studies. There are reports that the numbers of leprosy cases presenting to skin specialists in teaching and non teaching hospitals are increasing due to discontinuation of peripheral surveillance activities [14].

Considering the Indian scenario, a total of 1,35,485 new cases were detected during the year 2016-17, which gives Annual New Case Detection Rate (ANCDR) of 10.17 per 100,000 population, as against 1,27,334 cases in 2015-16 [22]. However, the present data indicating the scenario, far from satisfactory. Aligarh represents 0.24% of the population of India, as per the 2011 census, with a sex ratio of 862 females per thousand males [15]. Being an urban area, it lead to many challenges for health services management, including social, cultural and economic inequalities and unawareness or inability of vulnerable population to access services. Industrialization and migrant population has further added new cases to our national leprosy data.

To tackle these problems, leprosy services have been integrated with the general health system. But health system is facing certain flaws with the implications. Sometimes, the primary health centre (PHC) medical officers missed or wrongly diagnosed the leprosy cases [16]. This happens because of lack of effective proper training and variety in disease presentations. Hansen's disease is a great mimic and even the experienced leprologist confuses at times. Strengthening and proper channelizing of referral networks is important for effective integrated leprosy control services. It is well realized that even after elimination target has been achieved, new leprosy cases will keep coming for at least some years due to continuation of some level of disease transmission or manifestation of disease by subclinical cases [17]. Although most of the times the clinical diagnosis is well matched with that of pathological diagnosis, sometimes there is discrepancies between the two.

The purpose of this study was to evaluate the agreement between clinical and pathological diagnosis of leprosy in the current situation of continuously emerging new cases of leprosy. This will provide an insight into diagnostic discrepancies and challenges and will help in standardizing the diagnostic resources.

There is a need to review the epidemiology and to find out the relation between clinical and pathological diagnosis of this disease, which still seems to be a problem in our country. Knowing the current status of leprosy will help in making appropriate plans and review our strategies in eliminating this disease.

Material and Methods

It is a retrospective data analysis carried out on skin biopsy samples sent for histopathological diagnosis in clinical suspicion of leprosy at Jawaharlal Nehru Medical College and Hospital, Aligarh in a period from June 2015 to November 2017. The biopsies were fixed in 10% buffered formalin. The skin biopsies were processed and embedded in paraffin and sectioned with 5 µm thickness. Tissue Sections were stained with Haematoxylin and Eosin stain (H &E) to study morphological features, and modified fite stain to identify acid fast bacilli (AFB). AFB was graded and interpreted according to Ridley scale. A standardized set of definitions were used for biopsy assessments in terms of histological features, possible diagnosis and reactions associated with them and recorded. The data was analyzed according to age, gender, clinical and histological features.

Results

A total of 325 skin biopsy samples were sent from skin OPD to our department for histopathological diagnosis with the clinical suspicion of leprosy over a period of 30 months. Out of these 325 samples, we have found leprosy in 282 cases which accounts for percentage parity of 86.7. Out of these 282 positive cases, 190 were males and 92 were females with male: female ratio of 2.1:1. Most of the cases fall in the age group of between 16 -30 years (110 cases) followed by age group of 31-45 years (84 cases) (Table I).

Table 1: Leprosy incidence among different age group.

Age groups (in years)	No of leprosy cases (Total = 282)
0-15	17
16-30	110
31-45	84
46-60	57
>60	14

Tuberculoid leprosy was the most common histological subtype (69/282, 24.4%) followed by lepromatous (58/282, 20.56%), borderline tuberculoid (53/282, 18.7%),

borderline lepromatous (42/282, 14.8%), indeterminate leprosy (34/282, 12%) and mid borderline leprosy (22/282, 7.8%). Additionally, histioid type of leprosy was recorded in 1.4% (4/282) of histologically diagnosed cases (Table II). Histopathology and AFB staining pattern of different spectral subtypes are elicited from Fig 1 to Fig 7.

Table 2: No of cases segregated by histopathological patterns and their corresponding bacteriological index

Serial Number	HPE diagnosis	Number of cases Total 282	Bacteriologi-callndex
1	TT	69	0
2	BT	53	0 to 1+
3	BB	22	2+ to 3+
4	BL	42	2+ to 5+
5	LL	58	5+ to 6+
6	IL	34	0 to 1+
7	Histoid	04	6+

TT=Tuberculoid leprosy, BT=Borderline Tuberculoid, BB=Borderline Borderline,

BL=Borderline Lepromatous, LL=Lepromatous Leprosy ,IL=Indeterminate Leprosy

Disparity with the clinical diagnosis was mostly encountered with the clinical diagnosis of indeterminate leprosy (out of 25, 16 has no leprosy) which accounts parity of only 36%. Whereas, histoid subtype showed the 100% parity (4/4) between clinical and histological diagnosis. Percentage parity observed in other subtypes :- Lepromatous leprosy 87.03% (47/54), borderline tuberculoid 73.84% (48/65), borderline lepromatous 71.05% (27/38), Tuberculoid leprosy 62.3% (66/106) and borderline 60.60% (20/33) (Graph 1).

Bacteriological index ranges for different subtypes are shown in Table II.

Discussion

In our study of 325 clinically suspicion cases, 282 were histologically confirmed. Most of the diagnosed patients were of age below 30 years accounting 45% of the cases, which reflects the increased burden of the disease in early age group. Kaur et al.,2017, reported that most of the leprosy cases had age between 16-45 years in their study[18] . Singh et al.,2017, observed the age group of leprosy patients, ranged from 10 to 72 years with a mean age of 25.8 years with maximum patients[19] . Whereas, Vishwanathan.,2018, found the age group of 41-50 years

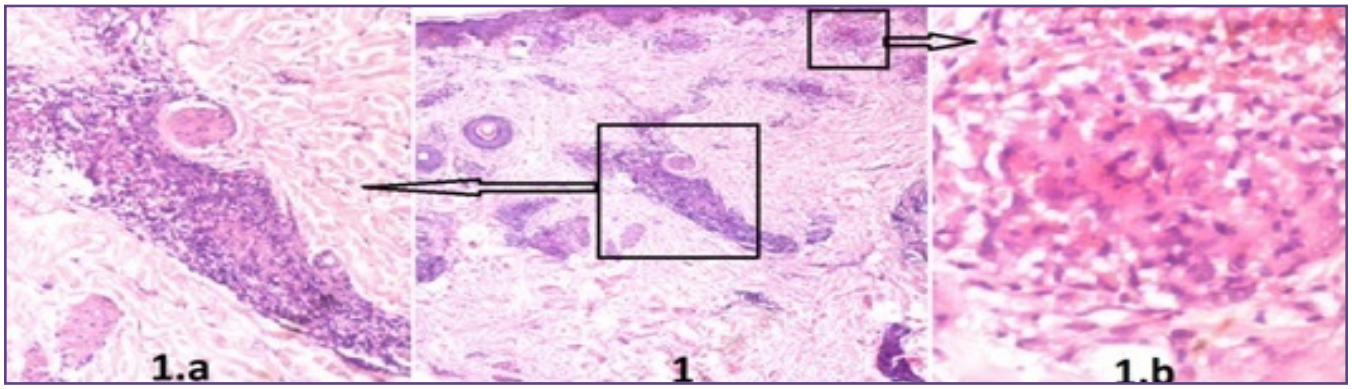


Fig. 1: Tuberculoid leprosy (TT) (Acid fast bacilli –negative) 1.a Peril neural Inflammation 1.b Epithelioid cell granuloma.

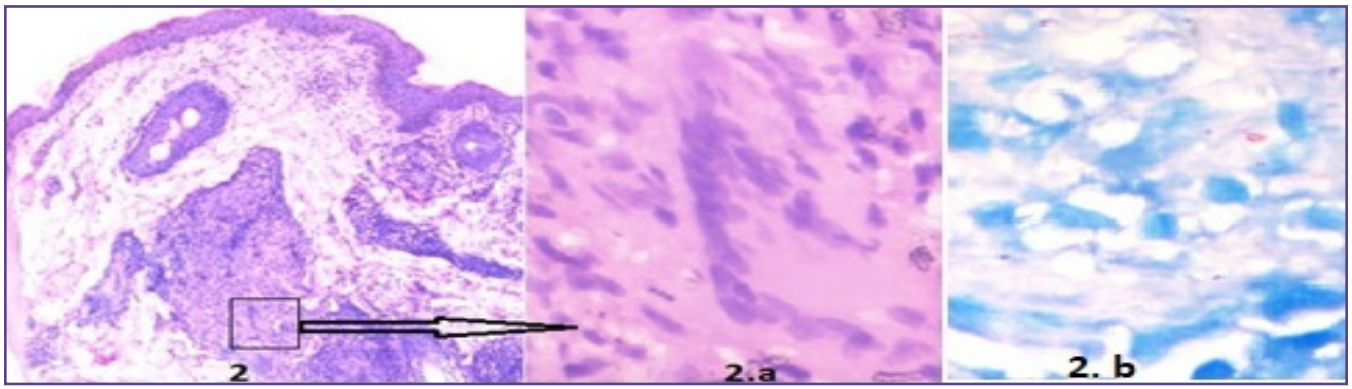


Fig. 2: Borderline tuberculoid (BT), 2.a Epithelioid cell granuloma (40X), 2.b AFB stain in BT (40X).

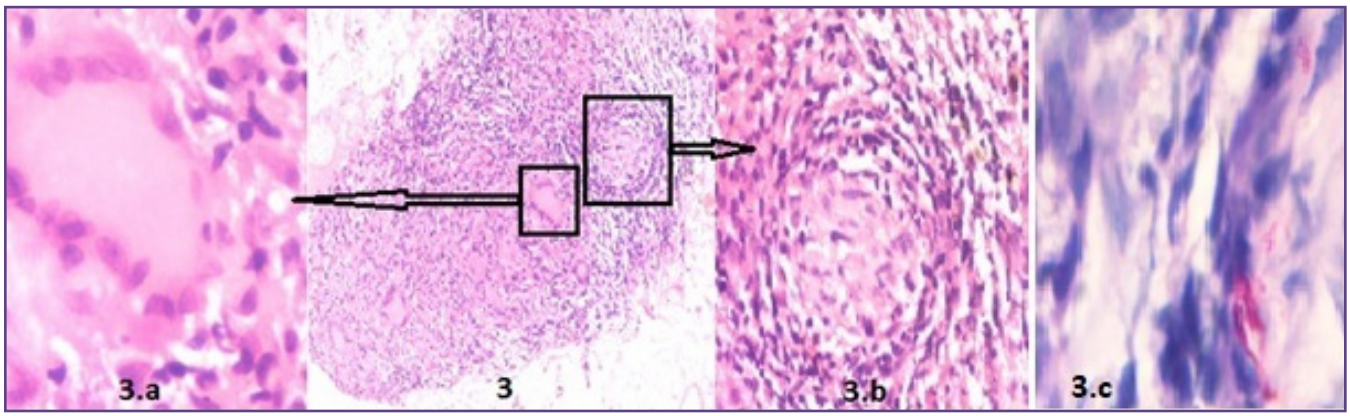


Fig. 3: Mid Borderline (BB) H&E (4X), 3.a Epithelioid cell granuloma and langhans giant cell(40X), 3.b Foamy macrophages (10X), 3.c AFB Stain in BB (100X, oil immersion).

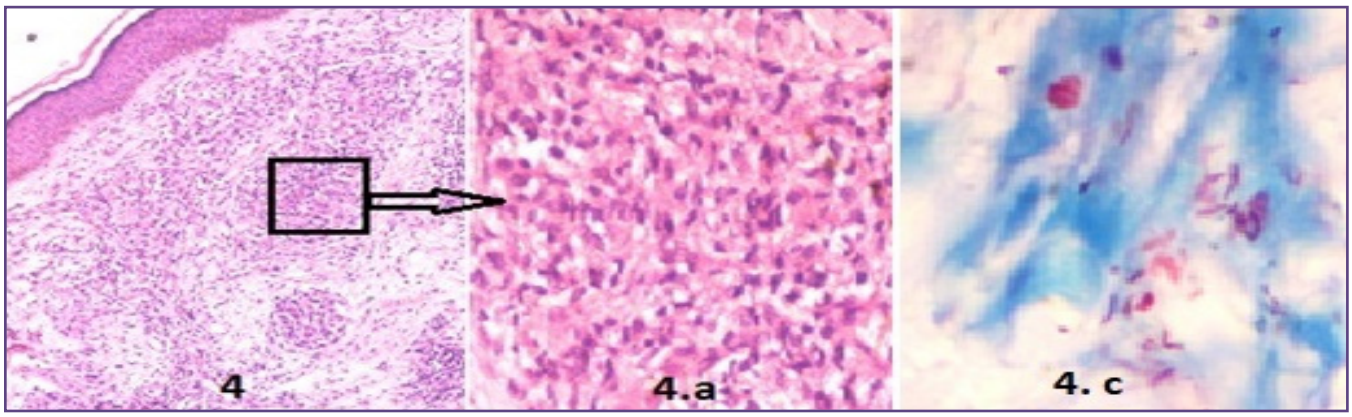


Fig. 4: Borderline lepromatous (BL), H & E (4X), 4.a foamy macrophages (40X), 4.b AFB Stain in BL (100X, Oil Immersion).

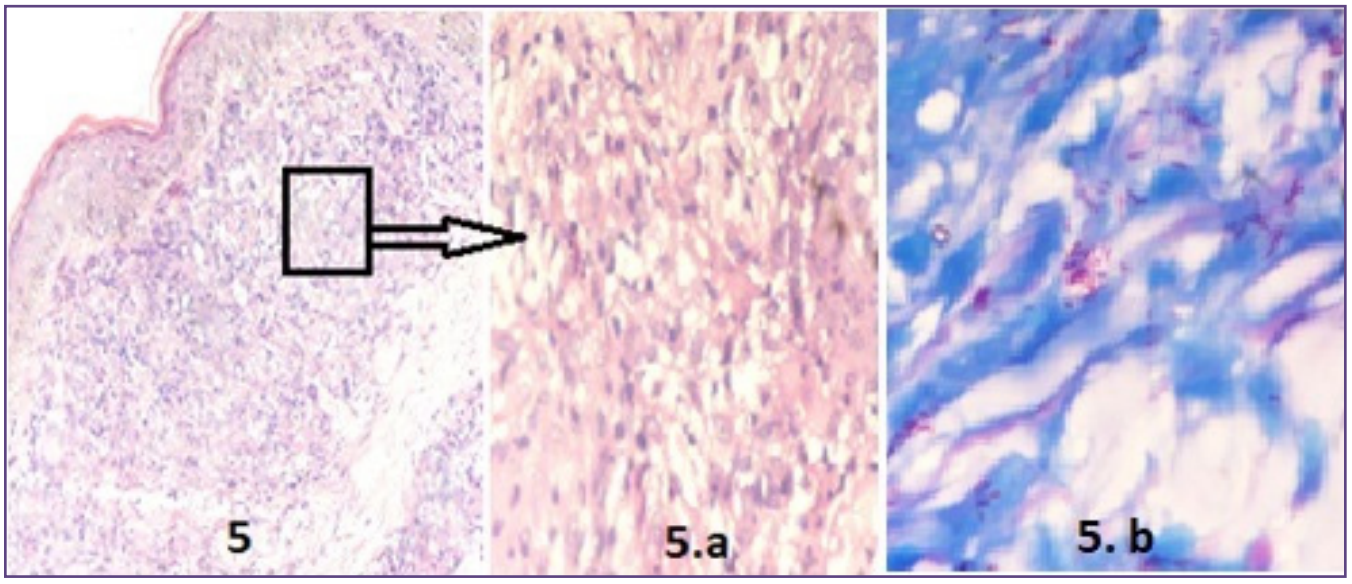


Fig. 5: Lepromatous leprosy (LL), H & E (4X), 5.a foamy macrophages (40X), 5.b AFB stain in LL (100X, Oil Immersion).

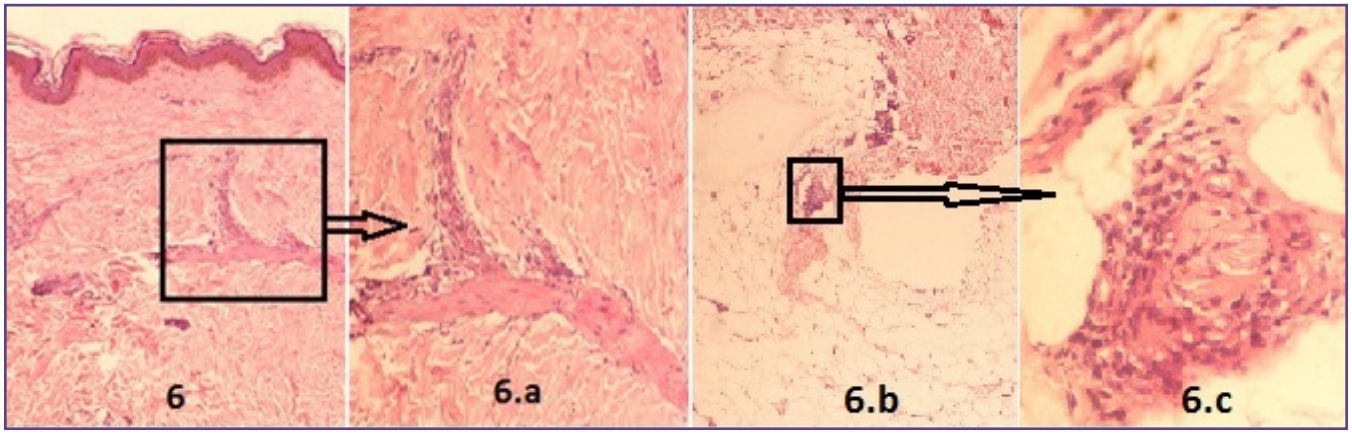


Fig. 6: Indeterminate Leprosy (IL),H & E (4X), AFB –Negative, 6.a Periappendiceal infiltrates (10X). Fig 6.b Inflammation in deep dermis and subcutaneous fat (4X), 6.c Peri neural chronic inflammation (40X).

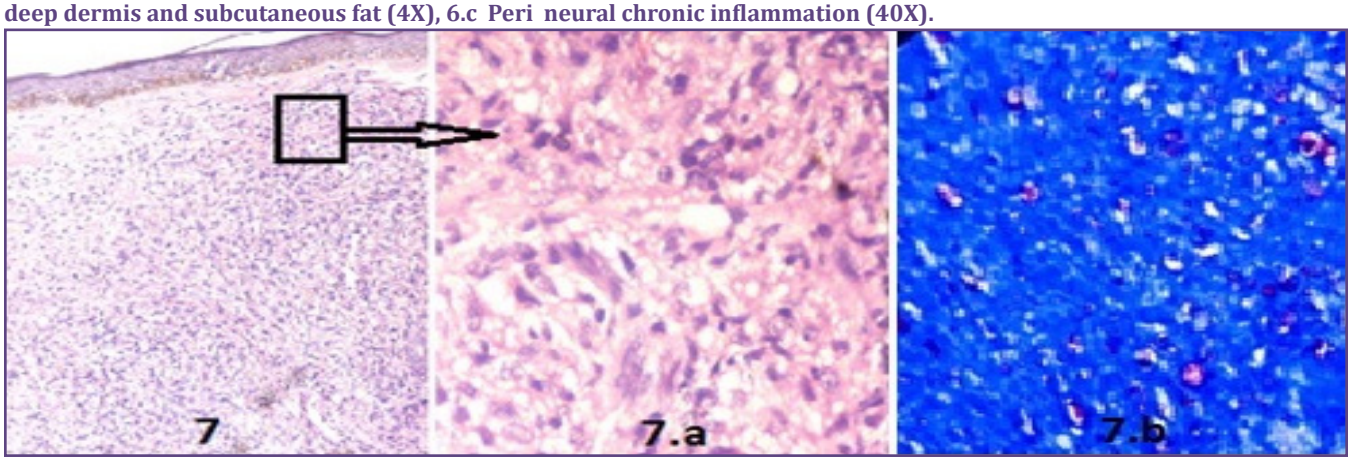
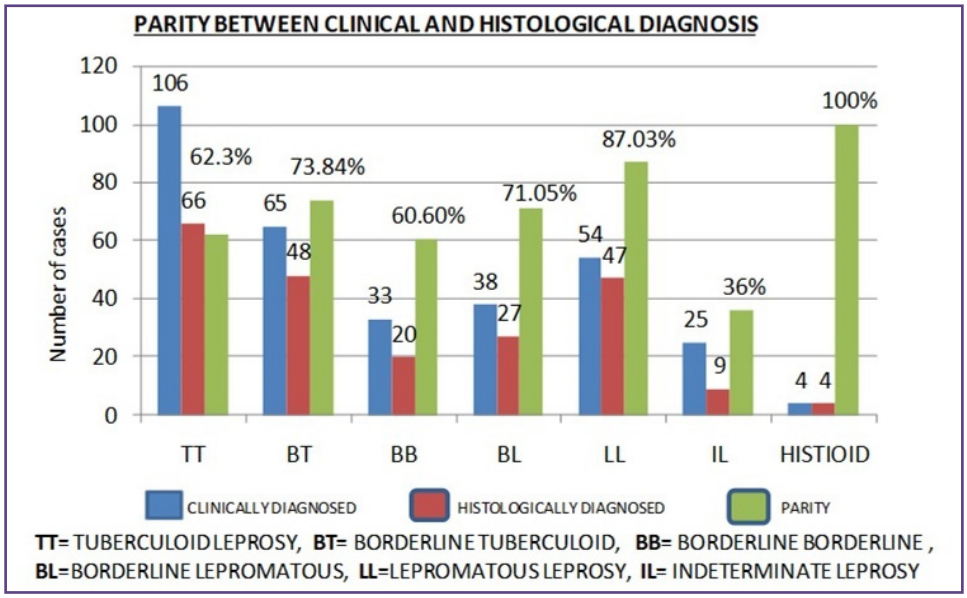


Fig. 7: Histoid leprosy (HL), H & E (4X), 7.a foamy & spindly macrophages giving appearance of sarcoma (40X), 7.b AFB stain in HL demonstrating globi (40X).



Bacteriological index ranges for different subtypes are shown in Table II.

were mostly affected[20] . In our study, 5% cases belongs to >60 year age group. Wide distribution of the disease in every age group pointing that leprosy continues to be transmitted in the community.

The higher male to female ratio (2.1:1) in our series can be explained by increased chances of contact in males, and lack of social perceptive towards women health care. Vishwanathan., 2018,also showed the male to female ratio of 2.84:1 in his study[20] . This observation was similar to those of Gokhale et al., 2018, who did a five-year retrospective study (2012-2016) of leprosy trend in thane district, Maharashtra and reported that the percentage of female patients has ranged between 28% - 45% [21]. However,

Singh et al., 2017 showed higher male to female ratio of 4:1.5 (13). As mostly males migrate to cities for employment, this could be an explanation for higher proportion of males in our study. Other authors as well reported that the disease prevalence may be affected by demography [10,22] .

Tuberculoid leprosy was the most common subtype encountered both clinically and histologically in our study. Similar observation was found in Shrestha et al., 2017 with clinical and histopathological diagnosis of tuberculoid, 44% and 38%, respectively [23] . However, Borderline tuberculoid was the most common clinical as well as histological diagnosis in studies- by Kini et al.,2017[24]. Histoid leprosy was the least common type clinico-histopathologically in present study.

Overall clinico-pathological concordance of diagnosing the leprosy broadly in our study was 86.7% which is in approximation of 92.4% reported by Kini et al., 2017[24]

In present study, Indeterminate leprosy had maximum disparity of 64% between clinical and histological diagnosis, followed by borderline borderline (disparity = 39.40%), tuberculoid leprosy (disparity=37.7%), borderline leprosy (disparity=28.95%),borderline tuberculoid (disparity=26.16%) and lepromatous leprosy (disparity=12.97%). However, histoid subtype had 0% disparity in our study. Still, a sharp eye should be kept for correct diagnosis of each subtype by every means.

Semwal et al.,2018, documented 100% disparity in indeterminate and borderline borderline leprosy and 0% disparity in tuberculoid and histoid leprosy cases in their study [25] . Shrestha et al.,2017 showed better correlation between clinical and histological diagnosis in indeterminate leprosy (100% parity) as well as in histoid leprosy (100% parity) [23] . So, findings of both these studies, agreed with our observation of 100% parity in histoid leprosy cases. However, in the present study, high percentage of agreement in histoid leprosy could be due to low sample size. Mathur et al, Moorthy et al, Bhatia et al and Nadkarni et al documented maximum correlation in lepromatous leprosy whereas Kar et al and Kalla et al observed maximum correlation in tuberculoid leprosy group [26-31] .

There was no complete correlation seen in borderline lepromatous, mid-borderline, and borderline tuberculoid diagnosed clinically in our study. Bhatia et al and Kalla et al found minimum correlation in mid-borderline leprosy [28,31] .

Correlation between clinical and histopathological diagnosis has been the focus over the last few years. Biopsies have been emphasized in all leprosy cases to correlate its results with those of the clinical diagnoses and its implication to improve classification as well as prognosis of patient. Confirmation of the leprosy diagnosis for determining the disease prevalence in a given population and the correct clinical classification of patients and related risks are important motives for performing the histopathological examination.

In the absence of confirmatory investigations, clinical suspicion with such disparity lead to inappropriate treatment and decrease cure rate, which further increase the disease burden in the society.

This was a retrospective data analysis based on records available in department, hence chances of bias in clinicopathological correlation cannot be totally ruled out. We could include only those cases presented to our own centre which happens to be tertiary care referral centre. More complicated cases could be assumed, were being recorded. It could be clarified by Community-based surveys on the population of Aligarh district. Additionally, our centre registered a higher proportion of migrant workers, who reside in Delhi for short periods.

Conclusion

Identification of suspicious skin patch as leprosy with prompt histological diagnosis especially in population of below 30 years is required for timely intervention and eradication. Both clinician and pathologist should have a focused approach especially in diagnosing indeterminate leprosy.

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