

ORIGINAL RESEARCH

Clinico-histopathological features and bacillary index in leprosy at a tertiary care hospital in Uttar Pradesh

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Received: 29 November, 2023

Accepted: 8 December, 2023

ABSTRACT

Introduction: Leprosy is a slowly progressive, infectious granulomatous disease caused by acid fast rod shaped bacillus *Mycobacterium Leprae*. Early diagnosis and prompt treatment can lessen the disease effects and render the patient non-infectious. correlating the clinical and histopathological findings with the bacteriological index (BI) obtained by SSSE (slit-skin smear examination) may be helpful in diagnosing, isolating, and successfully monitoring the treatment particularly in developing countries. **Aim:** This study aimed to analyze the correlation of clinical and histopathological findings with the BI in different types of leprosy at our institution. **Materials and Methods:** Data from all untreated patients, among both genders, voluntarily reporting to out-patient department and clinically fulfilling the WHO (world health organization) leprosy case definition and undergoing SSSE and skin biopsy for histopathological confirmation was included in this study. **Results:** Maximum number of cases were recorded in the third decade of life (27%). Childhood leprosy was observed in 8% of cases. There was marked male predominance (72%) PB was the most frequent clinical type (61%) correlating 100% with BI of 0 on SSSE. The most common clinical presentation was that of single or multiple well-demarcated hypopigmented plaques with hypoesthesia (61%) and the most common histopathological diagnoses was BT (49%) followed by LL (24%). The overall correlation of the histopathological diagnosis and clinical diagnosis was 80%, which was a statistically significant correlation ($P < 0.05$). **Conclusion:** In presence of ambiguous clinical features, confirmation of leprosy can be problematic and therefore correlation of clinical features and histopathological diagnosis with BI seems more helpful in typing the leprosy and can guide physicians to provide better patient care and management. All suspected patients should therefore undergo a skin biopsy for histopathological examination in order to rule in leprosy

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INTRODUCTION

Leprosy is a slowly progressive, infectious granulomatous disease caused by acid fast rod shaped bacillus *Mycobacterium Leprae*, discovered in 1873 by a Norwegian scientist Gerhard-Henrik Armauer Hansen [1]. The bacteria are transmitted via droplets from the nose and mouth during close and/or frequent contact with untreated cases [1]. Leprosy has affected humanity for over 4000 year [2], It may cause serious cosmetic disfigurement, progressive and permanent disabilities if not diagnosed and treated early [3].

In order to achieve zero transmission of leprosy by 2027, the Government of India launched National Strategic Plan (NSP) & Roadmap for Leprosy (2023-27) on 30th January, 2023,. However with various interventions introduced under NLEP (national leprosy eradication program) in the last few years,

number of new leprosy cases detected have significantly declined from 1,25,785 in 2014-15 to 75,394 in 2021-22, accounting for 53.6% of global new leprosy cases. State wise NLEP data for financial year 2022-23 (up to Jan'2023) reveals Chhattisgarh with highest prevalence rate of 2.3/10000 population while Tripura, Meghalaya, Lakshadweep reported zero prevalence [4]. This data indicates that although the burden of leprosy in India has greatly diminished but the disease is far from being eliminated to a "zero level" which necessitates our persistent need to study its biological behavior and patterns of presentation better in order to eradicate it [4].

The registered global prevalence of leprosy (number of cases on treatment at the end of 2021) is reported as 133 802 with a prevalence rate of 16.9 per million population. Of the 143 countries Brazil, India and

Indonesia continue to report more than 10 000 new cases each. Brazil, India and Indonesia accounted for 74.5% of the new leprosy cases detected worldwide in 2021. India accounts for more than 55% cases globally indicating active transmission. The highest number of new G2D (grade 2 disability)cases have been reported by India (1863), followed by Brazil (1737) and Indonesia (678). Even more disturbing is the fact that 51 countries reported relapse in 3201 patients even after completion of MDT(multidrug therapy), with the most in Brazil (1212), followed by India (510) [3,5,6].

Clinically Leprosy is diagnosed on the basis of presence of following cardinal signs: (i) hypopigmented or erythematous hypoesthetic patch on skin, (ii) thickened and/or tender peripheral or cutaneous nerve supplying the affected area, and (iii) acid fast bacilli (AFB) in the skin smear. However the two primary signs of leprosy are cutaneous lesions and peripheral nerve involvement. Anesthesia, physical disability, psychological disorders, economic and social marginalization are all fall outs of nerve degeneration in leprosy [3]. The clinical and immunological presentation of leprosy is diverse, can overlap with a variety of unrelated diseases and vary from an insignificant skin lesion to extensive impairment and deformities [7]. It can also involve muscles, eyes, bones, and other internal organs. Nodules and lumps, particularly on the cheeks and ears, loss of digits, claw hands, plantar ulcers, foot drop, claw toes, nose depression, and other deformities are indications of advanced disease [8]. Depending upon the immune status of the patient and response to treatment, the spectrum of leprosy is a continuum and can manifest itself in two polar forms, namely tuberculoid and lepromatous leprosy [8]. In between the two polar types, borderline forms of leprosy occur [8]. The term borderline is used to denote patterns that share some features of both tuberculoid and lepromatous leprosy [2]. There is also a very early type of the disease known as indeterminate leprosy, which manifests as microscopic hypopigmented macules in the skin with no loss of sensation. It may wane off if the cell mediated immunity improves or may progress further if left untreated [2].

Slit-Skin Smear Examination (SSSE) is a simple, cost effective highly reproducible diagnostic test for leprosy [9] performed to : 1) confirm the diagnosis, 2) classify types of leprosy, 3) determine treatment response and assess prognosis of disease, and 4) follow-up . Due to risk of HIV transmission, the number of sites for sample collection have now been reduced to four [10] . Currently, the most common sites for biopsy are 1) lobe of the right ear, 2) forehead, 3) chin, and 4) left gluteal region in the men and left upper thigh in the women [10] . The concentration of bacilli in smears is known as the bacterial or bacteriological index (BI) and includes living and dead bacilli. The standard enumeration of

leprosy bacilli in lesions follows Ridley's logarithmic scale [11] which is based on the number of bacilli for the purpose of oil immersion and applies to both skin biopsies and slit skin smears . At least 100 immersion oil smears are checked before reporting BI slides. The sensitivity of detection of AFB by histologic means remains poor, because about 1,000 bacilli per cubic centimeter of tissue must be present in order to detect one bacillus in a section [11].

Histopathological examination of skin biopsies remains the gold standard in establishing a definitive diagnosis of leprosy, determining its subtypes, assessing treatment response, prognosis and for exclusion of other mimickers [11-13]. The standard histopathological classification of leprosy follows that of "Ridley and Jopling" [11] with categories defined, along the spectrum as follows:

- TT (Tuberculoid)
- BT (Borderline Tuberculoid)
- BB (Borderline Borderline)
- BL (Borderline Lepromatous)
- LL (Lepromatous)
- Histoid leprosy

In presence of ambiguous cardinal features, confirmation of leprosy can be problematic [2]. Integration of histopathological findings with those of clinical, microbiological findings is very important in disease management particularly in early detection and difficult to diagnose cases. Early diagnosis and prompt treatment can lessen the disease effects and render the patient non-infectious.

Therefore, correlating the clinical and histopathological findings with the BI obtained by SSSE may be helpful in diagnosing, isolating, and successfully monitoring the treatment particularly in developing countries.

AIM OF THE STUDY

This study aimed to analyze the correlation of clinical and histopathological features with the BI in different types of leprosy at our institution.

MATERIALS AND METHODS

Study Design and Setting: The present study is a retrospective descriptive cross-sectional study conducted using the digital and manual registered records of patients attending the outpatient department (OPD) of Leprosy Clinic at a tertiary care center in Northern India between Oct 2019-OCT 2023. The study was carried out in conformity with the Helsinki Declaration, the terms of local legislation and was approved by the institutional ethics and research committees.

Selection of patients: Inclusion criteria: Data from all untreated patients, among both genders, voluntarily reporting to OPD and clinically fulfilling the WHO (world health organization) leprosy case definition [14] and undergoing SSSE and skin biopsy for histopathological confirmation was included in this study

Exclusion criteria: Patients with bleeding disorders, HIV or malignancy were excluded from this study. Patients whose biopsies were suboptimal for making a confirmatory diagnosis and refused re-biopsy were also excluded from the study

Sample size calculation: Sample size was calculated using formula $n = Z^2 P(1-P) / d^2$, where n is the sample size, Z corresponds to level of confidence, P is expected prevalence and d is precision (corresponding to effect size). A sample size of 107 was calculated based on previous study by Swagatika Agrawal et al. [12].

Study material: The study material consisted of socio-demographic and clinical data of patients, SSSE and skin biopsies from representative lesions of patients clinically diagnosed with leprosy prior to the onset of MDT

Study Procedures: After approval by the Institutional Ethics and Research Committees patient data was included in the study. During the post Covid-19 period of study, history of exposure was also taken and vaccination status were verified using unique identification numbers.

SSSE for AFB was performed using the Ziehl-Neelsen technique and the BI was determined according to the Ridley's logarithmic and BI. The slit-skin smears were sent to the Department of Microbiology and data was collected from HIS (Hospital Information System) and counter checked physically from the archives of Microbiology Department. Viable bacilli were considered as those that appear as uniformly red solid-stained rods having a length five times greater than the breadth with rounded, straight or pointed ends. The dead or broken bacilli were considered as those that stain irregularly and appear granular or fragmented [15]. In the present study BI was applied on SSSE.

Skin punch biopsies of full dermal thickness measuring at least 4mm from untreated cases of leprosy were performed in the Department of Dermatology and reported in the histopathology section of the Department of Pathology. The biopsy was preferably taken from the advancing border of an active lesion. After adequate fixation in 10% neutral buffered formalin, the biopsies are submitted for tissue processing, followed by paraffin embedding and finally sections of 3-5µ thickness were stained with hematoxylin and eosin (H & E) stain. All biopsy specimens were examined for: - a) Epidermal atrophy, epithelioid granulomas, number and distribution of lymphocytes, histiocytes (including foamy histiocytes). b) Infiltration of nerves, blood vessels and adnexa. c) Grenz zone. Special stain Fite-Faraco (FF) was performed on all biopsies with enough material. M. leprae was identified as a nonmotile, red rod shaped, shorter granular shaped AFB.

No specialized laboratory or electrophysiological tests were conducted for cranial nerve involvement. As a routine, fifth (trigeminal) and seventh (facial) cranial

nerves were tested clinically for sensory and motor functions in the Leprosy clinic.

Method of Data Collection: The mode of case detection was categorized as passive method which meant that the leprosy cases were referred by physicians or patients reporting voluntarily.

Following data was collected :1. socio-demographic variables, 2. detailed history particularly previous treatment history and exposure to COVID-19 including history of vaccination ,3. disease severity status with pattern and distribution of lesions including the predominant lesion, 4. size consistency sensation in peripheral nerves of upper and lower limbs, 5.location and type of lepra reaction and disabilities, 6.SSSE including ZN stain , 7.skin biopsy including FF stain. Data was retrieved from the physical registers and digital archives of Leprosy clinic ,pathology and microbiology department and HIS .Digital data was collected using appropriate WHO ICD-10(International classification of diseases) [16] codes indicating the parameters such as the personal identity (medical record number, age, gender, date of visit, previous treatment history), lesional topography, presence or absence of disabilities/deformities ,date of biopsy, clinical diagnosis , microbiological and histopathological diagnosis .

REFERENCE STANDARDS AND CRITERIA USED

WHO case definition [14] : A new case is defined as one who had not been diagnosed earlier and had no history of treatment for leprosy . The WHO case definition of leprosy is Mycobacterium leprae infection in an individual who has not completed a course of treatment and has 1 or more of the following:

- definite loss of sensation in a pale (hypopigmented) or reddish skin patch;
- a thickened or enlarged peripheral nerve, with loss of sensation and/or weakness of the muscles supplied by that nerve;
- the presence of AFB in a slit-skin smear.

CLASSIFICATION FOR CLINICAL DIAGNOSIS OF LEPROSY

Using Ridley Jopling classification [11] and as per the criteria laid down under NLEP [4] patients were further categorized either as multibacillary (MB) or paucibacillary (PB).

Patients were classified as PB if he/she had equal to or less than 5 patches or lesions on the skin with or without one to two thickened main cutaneous nerves [17].

Patients were classified as MB if he/she had equal to or more than 6 patches or lesions on the skin and/or infiltrations of more than two thickened nerves with or without papules or nodules [17]

MICROBIOLOGICAL CLASSIFICATION

Paucibacillary (PB): includes all smear-negative cases.

Multibacillary (MB): includes all smear-positive cases.

CRITERIA FOR BI USED FOR DIAGNOSIS OF LEPROSY

BI was performed on SSS and was assigned using Ridley's logarithmic measurement ^[11], which is based on the number of bacilli for the purpose of oil immersion.

- 6+ more than 1000 bacilli in an average field
- 5+ 100 to 1000 bacilli in an average field
- 4+ 10 to 100 bacilli in an average field
- 3+ 1 to 10 bacilli in an average field
- 2+ 1 to 10 bacilli in 10 fields
- 1+ 1 to 10 bacilli in 100 fields
- No bacilli in 100 fields (oil immersion)

CRITERIA FOR HISTOPATHOLOGICAL DIAGNOSIS OF LEPROSY

On histopathological examination leprosy was categorized according to Ridley Jopling classification into Tuberculoid (TT), Borderline Tuberculoid (BT), mid-borderline (BB), Borderline Lepromatous (BL), Lepromatous (LL), Histoid Hansens (HH) ^[11].

TT Leprosy was diagnosed when there were large epithelioid cells arranged in compact granulomas along with neurovascular bundles, with dense peripheral lymphocytic accumulation absence of Langhans giant cells, absence or lymphocytic erosion of dermal nerves and absence of AFB.

BT Leprosy was diagnosed when there were lymphocytes along superficial vascular plexuses or granulomas with peripheral lymphocytes with infiltration of sweat glands and erector pili muscles, variable number of medium sized Langhans giant cells with obvious nerve erosion and/or obliteration and presence of AFB (BI ranging from 0 to 2).

BB Leprosy was diagnosed when epithelioid cells were randomly and uniformly distributed without forming distinct granulomas, scanty lymphocytes, absence of Langhans giant cells, dermal edema and presence of AFB (BI ranging from 3-4).

BL Leprosy was diagnosed when epithelioid cells formed poorly to moderately defined granulomas, with prominent lymphocytes, peri-neural fibroblast proliferation, forming an "onion skin" appearance and presence of AFB (BI ranging from 4 to 5).

LL was diagnosed when there was extensive cellular infiltrate separated from the flattened epidermis by a narrow grenz zone of normal collagen, a mild-to-moderate, superficial and deep, perivascular and periadnexal infiltrate of foamy histiocytes with destruction of cutaneous appendages and extension into the subcutaneous fat, absence of lymphocytes and presence of packed (cigar/globi) AFB (BI ranging from 5-6).

HL was diagnosed when spindle-shaped macrophages oriented in a storiform pattern formed dermal nodules with stretching of overlying epidermis and presence of clump like sheaves of wheat AFB (BI of 6).

Clinical diagnosis of leprosy cases was correlated with the results of histopathologic examination of their respective biopsies. Cases which revealed non specific histopathological features or showed features of reactional leprosy were excluded from clinic-histopathological correlation.

CRITERIA FOR LEPRO REACTIONS

Leprosy reactions were assessed as Type 1 (T1R) or Type 2 reaction (T2R). T1R was diagnosed if the patient had redness and swelling of existing lesions, nerve thickenings, and edema in the hands, feet or face. T2R or erythema nodosum leprosum was diagnosed when multiple small, tender, evanescent nodules with or without ulcerations associated with fever, asthenia, nerve thickening and pain, myalgia and lymphadenitis were developed ^[3].

CLASSIFICATION FOR DISABILITY

- Disability in leprosy were defined by the WHO ^[18] grading system:
- Grade-0 (G0D): absence of disability (no anesthesia) with no visible damage or deformity on eyes, hands, or feet
- Grade-1 (G1D): loss of protective sensibility on eyes, hands, and feet;
- Grade-2 (G2D): presence of deformities or visible damage to the eyes, hands, or feet.

DATA MANAGEMENT AND STATISTICAL ANALYSIS

The data was entered against variables and processed in MS Excel, rechecked manually to delete duplications and analyzed according to age, gender, lesional topography, date of biopsy, clinical, microbiological (SSSE data) and histopathological diagnosis, type of leprosy, presence or absence of disabilities/lepra reactions, Covid exposure. Further statistical analysis was processed using commercial software SPSS version 29 (Statistical Package for Social Science, IBM SPSS Statistics, Version 23.0. Armonk, NY: IBM Corp). Continuous variables were represented using mean and median values, whereas categorical variables were expressed using frequencies and percentages. The means were rounded off to nearest decimal. The Mann-Whitney test for independent samples was employed to compare. The chi-squared χ^2 test was used to compare proportions for categorical variables, which were reported as counts between different clinical and histopathological categories. Pearson's Chi-square test was calculated as follows: Where X^2 is Pearson's cumulative test statistic, O_i is an observed frequency, E_i is an expected frequency, asserted by the null hypothesis, and n is the number of cells in the table.

When the data was sparse, Fisher's exact test was utilized. Linear regression analysis was performed using data regarding independent variables to measure the strength of associations if any. Categorical data were summarized as in proportions and percentage (%) while discrete as mean \pm SD. A p-value <0.05 was considered statistically significant.

RESULTS

The present study identified 107 patients who had both SSSE and skin biopsy for a clinical diagnosis of leprosy between Oct 2019-Oct 2023. There was a consistent rise in the total number of leprosy cases during the post Covid-19 period. No patients were identified during the year 2020 due to hospital being designated only for Covid-19 management. The study shows a marked male predominance in cases diagnosed as leprosy (77 cases; 72%) with male to female ratio of 2.5:1. PB was the most frequent clinical type (65; 61%) (Table 1, 2). Maximum number of cases were recorded in the 3rd decade of life (29; 27%), followed by 4th (23; 21%) and 5th decades (22; 20%). Childhood leprosy was observed in 8% of cases. It was interesting to note a case of 7 year old female with histoid leprosy who has co-existent protein energy malnutrition and growth retardation.

At initial presentation to the leprosy clinic the most common immune reaction noted was T1R (66; 62%) characterized by redness and swelling of skin lesions associated with involved nerve trunks (Pie Chart 1). A spike in T1R was noted in the post Covid-19 period, particularly in patients who had received both doses of Covid-19 vaccination. The most common site involved was the upper-limb (forearm) (49; 46%), followed by the lower limb (21; 20%) (Figure 1a, 2a), upper back (20; 19%), the shoulder and face (11; 10% each) (Figure 3a, 4a). The most common clinical presentation was that of single or multiple well-demarcated hypopigmented plaques with hypoesthesia (66; 61%) followed by raised erythematous nodular lesions (41; 38%) (Figure 1a, 2a). Overall, the most common presentation for any type of leprosy was hypoesthesia. G1D (76; 71%) was consistently more common than G2D (31; 29%) (Figure 5a, b, Pie Chart 2). The most common deformities affected the hands (66; 61%) followed by trophic ulcers in feet (41; 38%). All cases with G1D clinically correlated with PB and BI 0 while G2D correlated with MB exhibiting a BI ranging between 4+ to 6+. No cases with G0D were identified. Glove and stocking sensory impairment was noted among 80 (75%) patients. Clinically the most common nerve involved in the upper limb was the ulnar nerve (35; 33%) followed by radial nerve (7; 6%) and median nerve (6; 5%). The common nerves involved in the lower limbs were the common peroneal (31; 29%), posterior tibial nerve and sural nerve (9; 8% each).

The most common histopathological type in all age groups was BT (52; 49%) (Pie Chart 3) which correlated with clinical presentation of well-defined hypopigmented plaques with hypoesthesia. Microscopic examination of BT revealed granulomas with variable Langhans giant cells and peripheral lymphocytes involving neurovascular bundles, sweat glands and erector pili muscles (Figure 1b). On FF stain AFB were scanty (BI ranging from 1 to 2+). TT leprosy showed large well formed epithelioid cell granulomas along the neurovascular bundles, with dense peripheral lymphocytes. Langhans giant cells were present. AFB were absent (Figure 2b). BL leprosy showed prominent lymphocytes with occasional epithelioid cells forming poorly defined granulomas with foci of perineural fibroblastic proliferation, forming an "onion skin" and involving adnexal structures (Figure 3b). AFB on FF stain for BL were scanty (BI of 3 to 4+). LL showed prominent grenz zone with poorly formed nodules of foamy histiocytes (Figure 4b) and frequent AFB arranged as globi (BI ranging from 4 to 5+). HL leprosy showed nodules of spindle-shaped histiocytes oriented exhibiting storiform pattern. AFB were frequent (BI of 6+).

On clinico-histopathological correlation the most common clinical presentation in BB was hypoesthesia, hypopigmentation with anesthesia in BT and TT, erythematous lesion in BL, hypoesthesia in LL and nodule or nerve thickness in histoid. Highest level of clinic-histopathological concordance was seen in HL (100%) followed by LL (93.33%). Concordance was more towards lepromatous pole than tuberculoid pole. Among 15 (14%) clinically diagnosed ENL (erythema nodosum leprosum) cases, 8 (53%) were of TT type, 1 (7%) was of BL type.

Regarding the overall patients' BI (Ridley scale) on SSSE Table 3, 61% had score 0, 18% had score 5+, 21% had score 6+ (Figure 6a) and only 9% had score 4+. There were no SSSE amounting to BI of score 1+ to 3+.

FF staining to identify AFB was done in cases with sufficient biopsy material. It was positive in 85 (75%) of cases. It was interesting to note a variable morphology of the mycobacterium leprae in our study on FF stain which was that of red rod shaped organisms with knobbed, beaded heads and predilection for adnexal structures particularly adnexal ducts, hair shafts and sebaceous glands (Figure 6 b, c). BI on SSSE correlated well with the histological type of leprosy. Rare bacilli were noted in cases of TT leprosy, whereas all cases of LL and HL showed presence of AFB. An interesting observation was that BI on SSSE correlated well with that of FF-stained sections in LL. FF stain was more helpful towards the TT pole of leprosy.

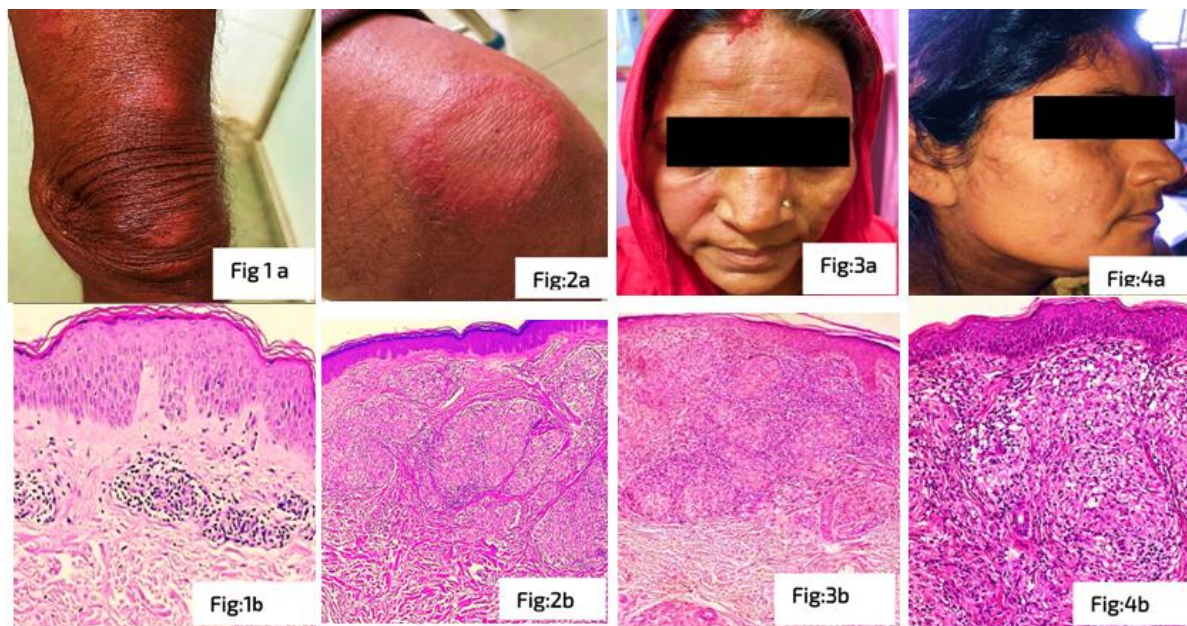


Figure 1 a :Borderline Tuberculoid Leprosy; Photograph with consent showing two hypopigmented hairless plaques around the knee.

Figure 1b: Borderline Tuberculoid Leprosy; ; H & E stained section at 20x showing an acellular grenz zone and dense lymphocytes around superficial neurovascular bundles

Figure 2 a :Tuberculoid Leprosy ; Photograph with consent showing large anesthetic skin patch on the knee appearing as an erythematous plaques with raised margins and a flat hypopigmented center.

Figure 2 b: Tuberculoid Leprosy ; H & E stained section at 20x showing infiltration of papillary dermis with non-caseating epithelioid granulomas predominantly centered around small cutaneous nerves and surrounded by lymphocytes

Figure 3 a :Borderline Lepromatous Leprosy ; Photograph with consent of a 55 year old female with skin-colored firm plaques and papules involving many parts of the body in a non-symmetrical fashion. The face had the most striking features in the form of general leonine waxy appearance

Figure 3 b: Borderline Lepromatous Leprosy ; ; H & E stained section at 20x showing infiltration of dermis with non-caseating epithelioid granulomas involving adnexal structures below and surrounded by heavy lymphocytes

Figure 4a: Lepromatous leprosy ; Photograph with consent of a 52 year old female involving the face in the form of multiple symmetrical infiltrated papules and plaques over the face

Figure 4 b: Lepromatous leprosy ; ; H & E stained section at 20x showing a grenz zone of sparing in the papillary dermis with poorly formed nodules of foamy histiocytes devoid of lymphocytes. The histiocytes are exhibiting vacuolated foamy cytoplasm with a grayish-blue tinge (on H&E due to clusters of leprosy bacilli)



Figure 5 a: Photograph with consent showing G1D “claw hand” affecting both hands

Figure 5 b: Photograph with consent showing G2D “trophic ulcer” affecting sole of left big toe

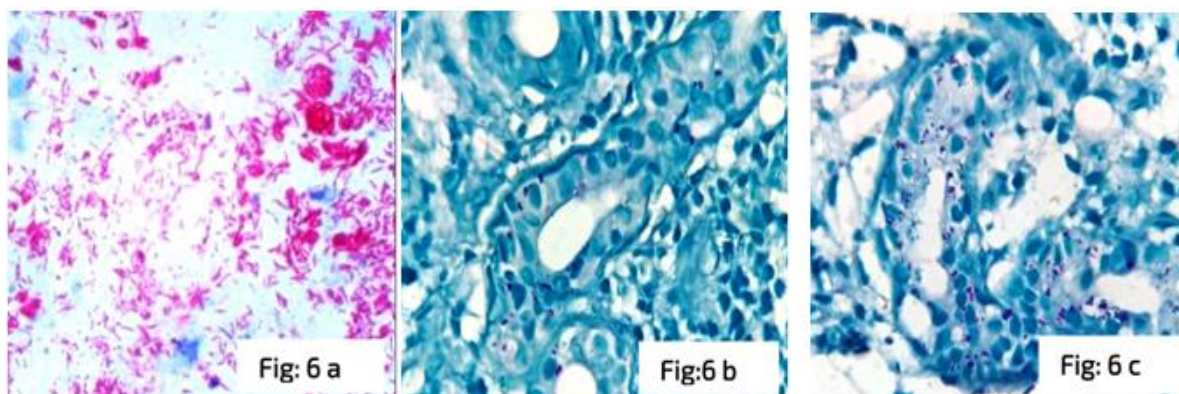


Figure 6 a: ZN stained section showing clumps of AFB ,BI 6+

Figure 6 b: FF Stain at Oil Immersion showing cropped field of BI 4+

Figure 6 c: FF Stain at Oil Immersion showing cropped field of BI 5+

Globo of eosinophilic lepra bacilli with knobbed, beaded heads involving adnexal ducts

TABLE I: YEARWISE GENDER DISTRIBUTION AND CLINICAL CLASSIFICATION (n=107)

Year	New Cases	Gender Distribution		Clinical Classification	
		M	F	PB	MB
2019	24 (22%)	20 (83%)	4 (16%)	11 (46%)	13 (54%)
2020	-	-	-	-	-
2021	38 (36%)	25 (66%)	13 (34%)	22 (58%)	16 (42%)
2022	32 (30%)	23 (72%)	9 (28%)	22 (69%)	10 (31%)
2023	13 (12%)	9 (69%)	4 (31%)	10 (77%)	3 (2%)
Total	107	77 (72%)	30 (30%)	65 (61%)	42 (39%)

*2020 Hospital designated as COVID Management Hospital Only

TABLE 2: AGE WISE PATIENT CHARACTERISTICS AND HISTOPATHOLOGICAL CORRELATION (N=107)

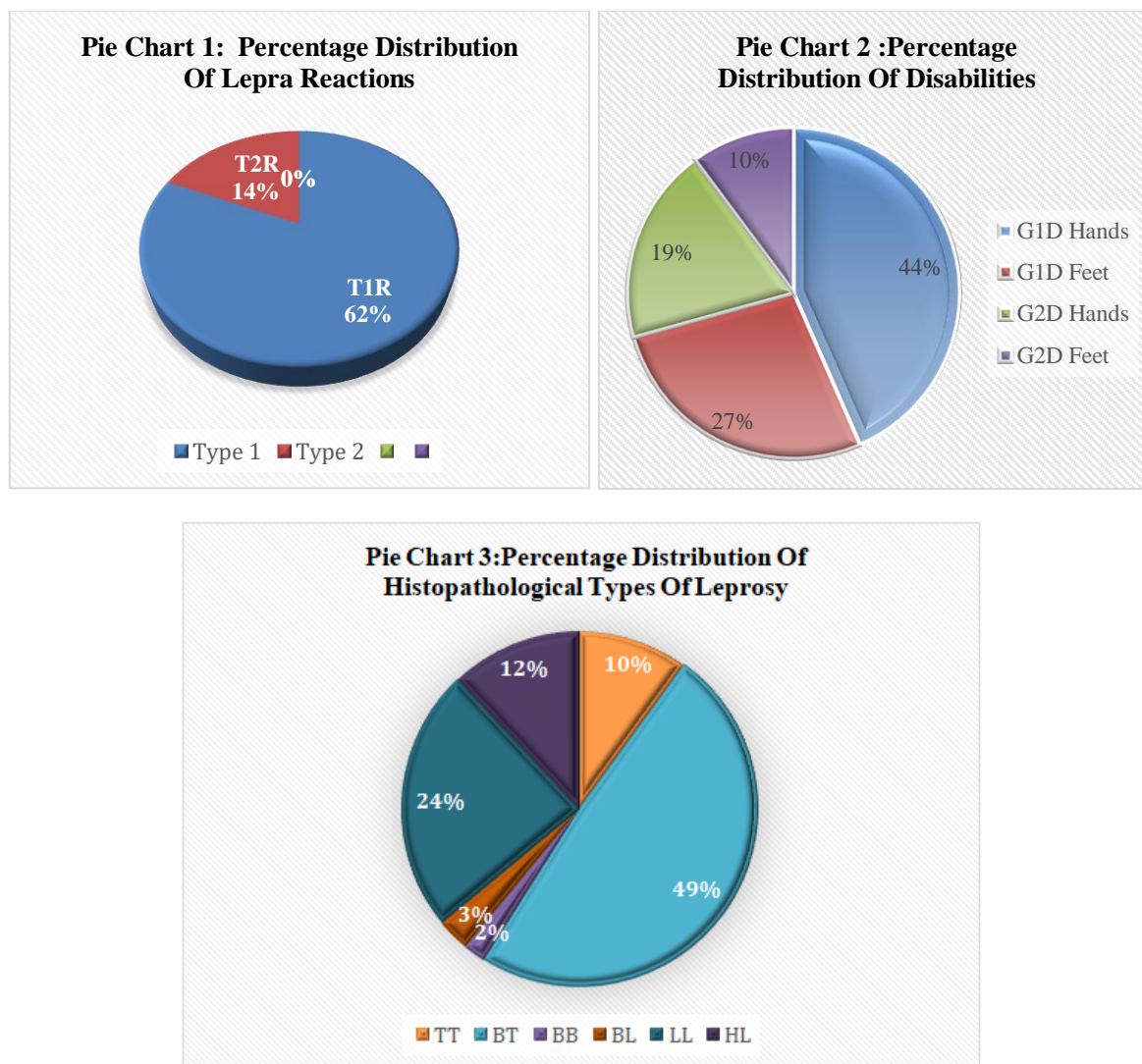
Age group	N=	M	F	Most Predominant Lesion	Histopathological Classification					
					TT	BT	BB	BL	LL	HH
1-10	6	5	1	Well demarcated, hypoesthetic Hypopigmented patches	2	3	-	-	-	1
11-20	8	5	3	Well demarcated, hypoesthetic Hypopigmented patches	-	4	1	1	1	1
21-30	29	18	11	Hypoesthetic, hypopigmented patches and raised erythematous lesions	3	20	-	-	5	1
31-40	23	18	5	Hypoesthetic, hypopigmented patches and raised ill defined erythematous lesions	2	15	-	-	5	1
41-50	22	15	7	Raised ill defined erythematous lesions	3	10	1	1	4	3
51-60	8	6	2	Raised ill defined erythematous lesions and nodular lesions	1	-	-	-	5	2
61-70	8	8	-	Nodular lesions	-	-	-	1	4	3
71-80	3	2	1	Nodular lesions	-	-	-	-	2	1
Total	107	77	30		11	52	2	3	26	13

TABLE 3: YEAR WISE MICROBILIGICAL AND HISTOPATHOLOGICAL CORRELATION(N=107)

Year	Microbiological Classification					Histopathological Classification					
	B 0	B1+ to B 3+	B4+	B5+	B6+	TT	BT	BB	BL	LL	HL
2019	11 (46%)	-	-	7 (29%)	6 (25%)	3 (13%)	8 (33%)	-	2 (8%)	8 (3%)	3 (13%)
2020	-	-	-	-	-	-	-	-	-	-	-
2021	22	-	1	6	9	5	16	1	-	10	6

	(58%)		(3%)	(16%)	(24%)	(13%)	(42%)	(3%)		(26%)	(16%)
2022	22 (69%)	-	-	6 (19%)	4 (13%)	2 (6%)	21 (66%)	1 (3%)	-	5 (16%)	3 (9%)
2023	10 (77%)	-	-	-	3 (23%)	1 (8%)	7 (54%)	--	1 (8%)	3 (23%)	1 (8%)
Total N=107	65 (61%)	-	1 (9%)	19 (18%)	22 (21%)	11 (10%)	52 (49%)	2 (2%)	3 (3%)	26 (24%)	13 (12%)

*2020 Hospital designated as Covid Management Hospital Only



DISCUSSION

In general in the present study a post COVID-19 surge in PB was noted which could be partly explained by the long duration of lock down, lack of access to healthcare for disease detection and variation in individual immune status post COVID 19 infection and vaccination.

AGE AND GENDER DISTRIBUTION

In the present study, the majority of patients were in the 3rd decade of life (29;27%), followed by 4th (23; 21%) and 5th decades (22;20%). The mean age was 35 years. These findings are comparable with those of Mahajan R et al. [19], B.n.R et al. [20], Roy Prerona et al. [21], and Menghani B et al. [22], who found that the

most common age group affected was 21-30 years of age followed by 31-40 age group.

The study shows a marked male predominance in cases diagnosed as leprosy (77 cases;72%) with male to female ratio of 5:2 in the study population. This finding is comparable with those of Mahajan R et al [19], B.n. R et al. [20], Roy Prerona et al. [21], Menghani B et al. [22] and Semwal S et al. [23] who also reported leprosy more commonly in men as compared to the women.

FREQUENT CLINICAL SITE AND TYPE OF LESIONS

The most common site involved was the upper limb (forearm) (49;46%), followed by the lower limb

(21;20%), upper back (20;19%), the shoulder and face (11;10% each). This result is comparable with the findings of Shrestha et al. [24] and Naik SM [13]. Shrestha et al. [24] reported the most common lesions in the upper extremities (15 ;30%) followed by the lesions in all the body (13 ;26%). Similar results were reported by Semwal S et al. [23] who reported the most common primary sites of involvement as upper extremities (35%) followed by face (30%), trunk (15%), lower extremities (12%), head and neck (6%), and back (2%).

In the present study the most common clinical presentation was that of single or multiple well-demarcated hypopigmented plaques with hypoesthesia (66;61%) followed by raised erythematous nodular lesions (41;38%) which is consistent with the studies of Swagatika Agrawal et al. [12], Kumar U et al [25], Yadav Neha et al. [26]. Tekwani D et al. [27] reported 91 (67.40%) cases with hypo pigmented lesion and 44 (32.60%) cases with erythematous lesions.

CLINICAL TYPE OF LEPROSY AND BI

In the present study, PB was the most frequent clinical type (65;61%) correlating 100% with BI of 0 on SSSE. The rest were MB (42 ;39%) correlating with BI of 5+(19;18%) to BI 6+(22;21%) on SSSE. These results are comparable with Tekwani D et al. [27] who reported PB (69.72%) more common than MB patients (30.37%). Naik SM et al. [13] reported MB slightly more common than PB (55 ;55% and 45; 45% respectively). However, Mushtaq S et al. [28] and Gupta R et al. [29] reported MB leprosy as the most common form among 627 patients (84.4%) from Jammu region and 80.17% cases from Bihar respectively. This variation could partly be explained firstly ;by the frequency of internal migration of population from neighboring states to UP and hence our study population is not representative of the region .Secondly by the fact that the classification system of assigning PB and MB purely based on number and pattern of clinically evident lesions has been criticized for misclassifying MB patients as PB, with negative repercussions given that treatment for the PB form is only 6 months—compared to 12 for MB [17]. In the present study this discrepancy was avoided by assigning the type based on clinical number and pattern of lesions as well as on BI on SSSE. The BI in the MB patients was comparable with BI in the studies of Naik SM et al. [13] (50%), Tiwari M et al.(66.2%) [30], and Kakkad K et al. (50%) [31]. Interestingly a study by Kumaran SM et al. [32] suggests that BI within a granuloma may be a better indicator of the true bacillary load in leprosy as compared to BI within SSSE material. It is crucial to management, especially in tertiary care facilities, to avoid "under-treating" so-called PB cases—which in fact might benefit from MB regimens.

HISTOPATHOLOGICAL TYPE OF LEPROSY

In the present study, the most common histopathological type in all age groups was BT (52; 49%) which is consistent with the observations reported in the studies of Naik SM et al. (52%) [13], Tekwani D et al. (57.77%) [27], Swagatika A et al.(41%) [12], Jindal R et al. (49.5%) [33] and A Kamale et al. (15,33.3%) [34].

The second most common histopathological diagnosis in the current study was LL (26, 24%) which is comparable to that of Naik SM et al. (20%) [13], Jindal R et al. (21.3%) [33], Nadia et al. (21.2%) [35], Kumar U et al. (21.7%) [25], Arif T et al. (28.2%) [36], Gupta R et al. (21%) [29]. On the other hand only 5.18% and 9.5% of LL cases were identified in the studies conducted by Tekwani D et al. [27] and Kadam Y et al. [37], respectively.

Histoid leprosy was detected in 12% of the cases in the present study which is twice higher than other contemporary studies in the northern region such as Gupta R et al. 18 (3.87%) [29], Mushtaq S et al. (27; 3.6%) [28], Jindal R et al. (5 ;2.4%) [33], Gupta N et al. (28 ;2.98%) [38]. This discordance could be partly explained by the doubling of cases immediately post Covid-19 pandemic in the present study attributable to the depressed immune status of the study population post exposure. A reassessment of its real versus transitory spike after a window period of total disease remission would require further study.

CORRELATION OF HISTOPATHOLOGICAL DIAGNOSIS AND BI ON SSSE

In the present study, there was 75% correlation between the histopathological diagnosis and BI on SSSE. The highest correlation was seen in the BT (100%), LL (100%), histoid disease (100%), and followed by BL (44.2%) BB (20%) and TT patients (0%). Similar results were reported by Naik SM et al. [13] with a correlation of 63% between BI on SSSE and histopathological diagnosis which was 100% in BL,LL ,BT followed by BT (44.2%) and TT(0%). Ramesh A et al. [39] reported 100% correlation in LL followed by BT (80%) and Semwal S et al. [23] reported that the correlation was 100% in HL,LL and BL. Premalatha P et al. [40] reported 100% correlation between SSSE and histopathological diagnosis in BL and HL ,very good for LL (88.8%) and poor for TT (0%). Slight variation in patterns of correlation could be partly explained by the fact that the specificity of SSSE is almost 100% as it directly demonstrates the presence of AFB but the sensitivity is low and varies from 10-50%.

CLINICO-HISTOPATHOLOGICAL CORRELATION

The overall correlation of the histopathological diagnosis and clinical diagnosis was 80%, which was a statistically significant correlation ($P < 0.05$). In the present study the highest level of clinic histopathological concordance was seen in HL

(100%) followed by LL (93.33%). Our results are consistent with those of Naik SM et al. (80%)^[13], Tekwani D et al. (72.59%)^[27], Tekwani D et al.^[27] reported 100% correlation in HL followed by TT (83.33%), BT (79.76%), BL (54.16%), LL (50%) and BB (25%). Yadav Neha et al.^[26] reported 100% clinico-histopathological correlation in IL and TT followed by 60 % in BL . A slightly lower clinico-histopathological correlation was reported by Semwal S et al.^[23] 62.9% .On the other hand Sindhushree N et al.^[41] reported lower clinic histopathological correlation of 33.7% which could be partly explained by interobserver interpretative variability both in the clinical and histopathological side.

SUMMARY

In the current study, following observations were made:

1. Maximum number of cases were recorded in the third decade of life (29;27%), followed by 4th (23; 21%) and 5th decades (22;20%). Childhood leprosy was observed in 8% of cases.
2. Marked male predominance was noted (77 cases;72%) with male to female ratio of 2.5:1
3. PB was the most frequent clinical type (65;61%) correlating 100% with BI of 0 on SSSE.
4. Most common site involved was the upper-limb (forearm) (49;46%), followed by the lower limb (21;20%), upper back (20;19%), the shoulder and face (11;10% each).
5. The most common clinical presentation was that of single or multiple well-demarcated hypopigmented plaques with hypoaesthesia (66;61%) followed by raised erythematous nodular lesions (41;38%).
6. The most common histopathological diagnoses was BT (52;49%) followed by LL (26;24%), HL (13;12%), TT (11;10%), BL (3;3%) and BB (2;2%).
7. BI on SSSE was B0 in 65(61%), B4+ in 1(9%), B5+ in 19(18%) and B6+ in 22 (21%).
8. The overall correlation of histopathological diagnosis and BI on SSSE was 75% with the highest correlation seen in the BT (100%), LL (100%), histoid disease (100%), and followed by BL (44.2%) BB (20%) and TT patients (0%). Lepra bacilli with knobbed, beaded heads with predilection for adnexal structures were noted.
9. The overall correlation of the histopathological diagnosis and clinical diagnosis was 80%, which was a statistically significant correlation ($P < 0.05$).

LIMITATIONS

The major limitation of the present study is its retrospective nature. The fact that partial data retrieval was performed using physical record registers as opposed to complete digital format acquired through HIS may have introduced some degree of information

bias. All data starting from patient profile, disease severity status, treatment given till reporting new cases to the national leprosy register should be digitalized with network connectivity among medical institutions and national health services through nodal centers with open access to medical researchers. Also the WHO criteria of assigning PB and MB has its inherent limitation as it is purely based on number and pattern of clinically evident lesions and has thus been criticized for misclassifying, over or under-diagnosing MB patients as PB, which might have happened in the present study too.

CONCLUSION

The study shows that although new case detection in this area of otherwise low prevalence is stable the burden of leprosy infection in the community has not changed significantly. The disease continues to be a significant cause of disabilities in this region of the country despite "zero level" elimination strategy of the NLEP. Urban immigration could partly be implicated in the regional variation of disease status. However, data from a single institution is not reflective of real time national burden of infection and multicenter and large population-based studies are required to eliminate information bias. Finally diagnosing leprosy in resource-limited settings is a challenge. Histopathological examination is the gold standard for accurate diagnosis and typing of leprosy. It should be done in all leprosy cases along with SSSE for the proper and early diagnosis and treatment of leprosy in order to limit disfiguring disabilities. This study also concludes that correlation of clinical and histopathological features along with BI is more useful for accurate typing of leprosy than considering any of the single parameter alone so that early and appropriate treatment could be started. In presence of ambiguous clinical features, confirmation of leprosy can be problematic and therefore correlation of clinical features and histopathological diagnosis with BI seems more helpful in typing the leprosy and can guide physicians to provide better patient care and management.

To achieve complete eradication from this disease, newer strategies like vigorous implementation of programs aimed at elimination, effective vaccine development and drug-resistance testing should be implemented along with open access, sharing and consolidation of state and national level patient related data between all stakeholders for research purposes.

DISCLOSURES

Conflict of Interests: The authors declare that neither this research nor the article has any form of conflict of interest including financial interest or commercial association with any of the subject matter or products mentioned in this article.

Ethical Clearance: The procedures followed in the present study were approved by and are in accordance with the ethical standards of the CIMS & Hospital's

ethical committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2000.

Funding: This is a non-funded research paper

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