Indian J Lepr 2021, 93 : 143-156

http://www.ijl.org.in

Original Article

A Single Centre Cross-Sectional Study of Clinicopathological Correlation in Leprosy: Discordance and Spectral Shift

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Received : 27.07.2020 Accepted : 27.12.2020

Classifying a case of Leprosy is very important from the point of view of management, prognosis and complications. Among the various methods, the Ridley-Jopling (R-J) classification is most widely used. However, there are discrepancies between the clinical diagnosis and histopathological diagnosis across the spectrum, necessitating correlation for accurate diagnosis and management. This study aimed to correlate the clinical and histopathological diagnosis of Hansen's disease and study its effect on the classification. Seventy-nine non-reactional cases of leprosy were subjected to clinical and histopathological examination and classified separately according to R&J classification and WHO classification. On confirmation, the diagnoses were correlated, concordance and discordance noted and analysed. A perfect correlation was found in total of 48.1% patients, maximum in TT (66.7%) followed by BL (65%). Major mismatch was seen in 31.7% of cases. A statistically significant correlation of the Fite Faraco positivity for Acid-fast bacilli was found with the histopathological diagnosis than with the clinical. The higher 51.9% discordance in the clinical and histopathological classification points towards the possibility of a spectral shift having occurred in the Indian population (from paucibacillary to multibacillary), which may be responsible for the resurgence of cases and pushing us back in time with regards to the elimination of Leprosy and failure of the existing control programs. Hence clinicopathological correlation should be mandatory in every case.

Keywords : Correlation, Discordance, Mismatch, Classification, Leprosy

Introduction

Leprosy is also known as Hansen's disease, is the oldest known disease to mankind. In January 2006, leprosy was declared to be eliminated from India (Announcement 2006). However, due to the increased new case detection rate from high endemic pockets in 2016-17, the situation in the country has regressed, and the national health policy - 2017 has announced leprosy (re) elimination at the national level (Rao & Suneetha 2018, National Health Policy 2017).

Leprosy is remarkable due to the enormously

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wide variation in the way the disease presents itself. Ridley and Jopling (R-J) were the first to suggest a subdivision of leprosy on an immunological basis into the following types: Early indeterminate (IND), Tuberculoid (TT), Borderline tuberculoid (BT), Borderline (BB), Borderline lepromatous (BL) and Lepromatous (LL). Later they further developed this idea and correlated clinical and bacteriological findings in each group with respective immunological and histological findings (Ridley & Jopling 1966). Indian Association of Leprologists (IAL) later came out with a better consensus classification which also gives due emphasis to neuritic leprosy important in Indian patients (IAL 1982).

Histopathological examination of skin and nerve biopsies and demonstration of lepra bacilli in skin smears are the only laboratory means of confirming the diagnosis of leprosy. Each form of leprosy is accompanied by a specific histopathological picture. At the tuberculoid hemisphere, cell-mediated immunity prevails, and epithelioid granulomas with scarce or no bacilli predominate. At the lepromatous hemisphere, a specific inflammation represented by lepromatous granulomas containing modified macrophages called lepra cells or virchowcytes is seen. In borderline leprosy, both types of granulomas may coexist, not infrequently with modified epithelioid or lepra cells (Abulafia & Vignale 1999). IND is an early and transitory stage of leprosy found in persons whose immunological status is yet to be determined, and it may progress to one or the other determinate forms of the disease.

Earlier studies have found a discrepancy in the clinical and histopathological diagnosis (Modlin & Rea 1998, Jerti & Desai 1982). The correlation was better at the stable poles (LL and TT) than the borderline disease (BT, BB, BL). The correlation was least in IND.

This study was done to correlate the clinical and histopathological diagnosis of leprosy and compare the clinical and histopathological correlation with previous reports with respect to shift in the spectrum of disease. We have also tried to emphasize the increasing importance of clinicopathological correlation (CPC) in evaluating this shift.

An important point to be considered is inter-observer variation, both clinically and histopathologically (Moorthy et al 2001). Though the histological features of leprosy have been well defined, the diagnostic criteria for borderline leprosy are overlapping, hence increasing chances of inter-observer variability. Thus there is a need to standardise these features.

Materials and Methods

The study is a single centre descriptive observational cross-sectional study conducted in the department of dermatology in a tertiary care public hospital in Mumbai. The study population included 79 new cases of leprosy with a confirmed diagnosis on clinical features and biopsy; those that attended OPD/ IPD from June 2016 to May 2017 and consented to biopsy. Cases with reactions were excluded. The study was carried out after obtaining the requisite ethics committee permission and the written consent from the study population.

The most infiltrated skin lesion was biopsied. In each of the patients, a 5 mm punch biopsy specimen from the active lesion was collected, processed as per standard procedure, subjected to haematoxylin and eosin (H&E) stain as well as Fite Faraco (FF) stain. Cases in which histopathology did not conclude the diagnosis of leprosy were excluded. The clinical & histopathological features were recorded to diagnose the different spectrums of Hansen's disease based on criteria laid down by R&J classification as summarised in

Table 1 and 2 (Kar 2016A, Kar 2016B). They were also classified into paucibacillary (PB) and multibacillary (MB) according to the WHO 1988 classification summarised in Table 3 (WHO Expert Committee on leprosy 1988) for better understanding. Fite-Faraco stained slide was examined for the bacillary index (BI).

In 1998, the WHO's Expert Committee on Leprosy determined that treatment could be started before smear tests were done to make it a more practical and safer approach.

Pure neuritic leprosy was considered separately. IAL defined these cases as those having nerve involvement without skin lesions. As a rule, no classical leprosy skin lesions/patches are present, however, skin along the distribution of the affected nerve is usually hypo-anaesthetic or anaesthetic. The NLEP (2009) further classified these cases into paucibacillary and multibacillary: Single nerve involvement as PB and more than one nerve involvement as MB. According to R&J, Pure neuritic leprosy needed to be classified within the TT-LL spectrum in a similar manner and on the same criteria on the basis of histopathology of the affected nerve.

The clinical and histopathological diagnosis were correlated. Wherever the diagnosis did not match, the lower of the two spectrums (towards

Table 1 : Clinical aspects of Ridley-Jopling Classification of Leprosy (Kar 2016A)

Observation or test	Type of leprosy				
	TT	**BT**	**BB**	**BL**	**LL**
Number of lesions	Single usually (up to 3)	Few (up to 10)	Several (10-30)	Many, asymmetrical (>30)	Innumerable symmetrical
Size of lesions	Variable, usually large	Variable, some are large	Variable	Small, some can be large	Small
Surface of lesions	Very dry, scaly, turgid	Dry, scaly, bright and infiltrated	Slightly shiny	Shiny	Shiny
Sensation in lesions (not face)	Absent	Markedly diminished	Moderately diminished	Slightly diminished	Not affected or minimally affected
Hair growth in lesions	Absent	Markedly diminished	Moderately diminished	Slightly diminished	Not affected
AFB in lesions	Nil	Nil or scanty	Moderate numbers	Many	Plenty (plus globi)
AFB in nasal scraping or in nose blows	Nil	Nil	Nil	Usually nil	Very many (plus globi)
Lepromin test	Strongly positive (+++)	Weakly positive (+ or ++)	Negative / weakly positive	Negative	Negative

lepromatous) was kept as the final diagnosis. Major mismatch was defined as a shift from the PB (IND, TT, BT) to MB group (BB, BL, LL) and vice versa, whereas minor mismatch was defined as a shift within the respective group. This correlation was compared with other previous studies based on the data collected.

Statistical analysis: The quantitative data was represented as their mean +/- SD. Categorical and nominal data were expressed in percentage. Categorical data were analysed by using the chi-square test. The significance threshold of p-value was set at <0.05. All analysis was carried out by using SPSS software version 21.

Results

Demographic profile of 79 showed that in our study, the age ranged from 7 years to 86 years with average age of 35.76 years. The proportion of childhood leprosy (<15 yrs of age) was 8.9 %. Most cases fall in age group 15-29 years and only 5 cases (6.3%) were aged 60 years or above. There were 67 (84.8%) males and 12 (15.2%) females with a M:F ratio of 5.6: 1. Duration of disease symptoms is presented in Table 4.

Table 2 : Histology of various types of leprosy according to RJ (Kar 2016B)

Parameter	IND	TT	BT	BB	BL	LL
Granuloma	Absent	Epitheloid cells	Epitheloid cells	Mixed cellular	Macrophages	Macrophages
T-lymphocytes	++++	++++	+++	++	++	+
Epitheloid cells	Absent	++++	+++	++	+	Absent
Giant cells	Absent	+++	++++	Absent	Absent	Absent
Macrophage	Absent	Absent	+	++	+++	++++
BI	Negative	Negative	1+	2-3+	3-4+	5-6+
Nerves	Only lymphocytes	Destroyed	Damaged	Identifiable	Preserved for long	Late destruction
Reactions	Absent	T1R	T1R	T1R	T1R/ENL	ENL

Table 3 : WHO classification 1988 (WHO Expert Committee on leprosy 1988)

Paucibacillary leprosy: It includes only smear negative cases belonging to:
1. Indeterminate (IND), tuberculoid (TT) and borderline tuberculoid(BT) cases as classified under Ridley-Jopling classification, and
2. Indeterminate (I) and tuberculoid (T) cases under Madrid classification
Multibacillary leprosy: Includes all
1. Mid borderline (BB), borderline lepromatous (BL) and lepromatous (LL) under Ridley- Jopling classification, and
2. Borderline (B) and Lepromatous (L) under the Madrid classification
3. Any other smear positive case

Table 4 : Duration of disease symptoms

Duration	Frequency	Percent
< / = 1 week	2	2.5
1 week - 1 month	6	7.6
1-6 months	32	40.5
6-24 months	30	38
>24 months	9	11.4
Total	79	100.0

Table 5 : Clinical morphology of lesions

Primary lesion	Frequency	Percent
Hypopigmented macule	57	72.2
Papule	12	15.2
Plaque	30	38
Annular plaque	22	27.8
Nodule	2	2.5
Ulcer	4	5
Ichthyotic skin	31	39.2
Diffuse shiny skin infiltration	6	7.6
Area of numbness without patch	16	20.3
Multiple vague nonanaethetic patches	14	17.7
Muscular weakness without skin lesions	8	10.1
Ocular disability	3	3.8
Epistaxis	7	8.9
Earlobe infiltration	8	10.1
Madarosis	9	11.4

The total duration of disease symptoms ranged from 3 days to 5 years. Most patients (43.2%) came for treatment with disease duration of 1-6 months and 9 cases (7.2%) were having disease for more than 2 years.

Only 5 patients (6.3%) had family history of leprosy. Only 1 patient out of these 5 was a child.

Clinical features

Types of lesions: Clinical morphology of lesions is summarised in Table 5.

Hypopigmented macules and ichthyotic skin were among the commoner skin lesions seen amongst our sample, followed by plaques and papules. Nodules and ulcers were seen less commonly. Patchy sensory loss without hypopigmentation was seen in 20.3% of cases, and vague non anaesthetic patches were seen in 17.7% cases. Ocular disability, madarosis and earlobe infiltration were less common.

Nerve involvement: Type of nerve involvement in

Table 6 : Nerves involvement in the patients included in the study

Nerve thickening	Frequency	Percent
Ulnar	50	63.3
Common peroneal nerve	40	50.6
Radial cutaneous nerve	35	44.3
Inferior orbital nerve	12	15.2
Supraclavicular nerve	12	15.2
Posterior tibial nerve	10	12.7
Sural	5	6.3
Anterior tibial nerve	6	7.6
Greater auricular nerve	2	2.5
Supraorbital nerve	1	1.3
Radial nerve	3	3.8

Table 7 : Clinical and histopathological diagnosis as per Ridley-Jopling classification

Spectrum of Clinical diagnosis			Spectrum of Histopathological diagnosis		
	Total patients	Percent		Total patients	Percent
IND	3	3.8	IND	6	7.6
TT	3	3.8	TT	6	7.6
BT	39	49.4	BT	24	30.4
BB	0	00.0	BB	0	00.0
BL	20	25.3	BL	38	48.1
LL	12	15.2	LL	5	6.3
Pure neuritic*	2	2.5			
Total	79	100.0	Total	79	100.0

*These two cases showed granulomas suggestive of BT and BL in the hypoesthetic skin

Table 8 : Clinical and histopathological diagnosis according to WHO classification 1988

	CLINICALLY			HISTOPATHOLOGICALLY	
	Frequency	Percent		Frequency	Percent
Paucibacillary (IND+TT+BT+PN)	47	59.5	Paucibacillary (IND+TT+BT)	36	45.6
Multibacillary (BB+BL+LL)	32	40.5	Multibacillary (BB+BL+LL)	43	54.4
Total	79	100		79	100

these 79 cases is summarised in Table 6.

The Ulnar nerve (63.3%) was the most commonly affected peripheral nerve, followed by the common peroneal nerve (50.6%) and the radial cutaneous nerve (44.3). The remaining nerves were found in less than 20 % of the cases. The sensory function of the nerve was affected in a good percentage of patients (79.7%), whereas motor damage was seen only in 26.6 %

Diagnosis

Comparison of clinical and histopathological diagnosis is presented in Table 7. Clinically, out of the 79 cases, BT was found to be the most commonly seen in 49.4 % of the cases followed by BL (25.3 %); LL was seen in 15.2% whereas only a handful of indeterminate (3.8%), TT (3.8%) and pure neuritic (2.5%) cases were seen. We did not encounter a single case of non-reactional BB leprosy (Table 7). Both the cases of pure neuritic leprosy had single nerve affection with no skin lesion. Thus, according to WHO 1988 classification (Table 8) the total number of PB patients (IND+TT+BT+Pure neuritic) were 47 (59.5%), and MB (BB+BL+LL) were 32 (40.5%).

On histopathological examination, BL Hansen's (48.1%) was the most common, followed by BT (30.4%), TT (7.6%) and IND (7.6%). LL pole was seen only in 6.3% of the cases (Table 3). In the two cases of pure neuritic leprosy, a biopsy from the anaesthetic patch revealed findings suggestive of BT Hansen's in one and BL Hansen's in the other, so nerve biopsy was unwarranted in them. Thus 45.6 % of patients were classified into PB leprosy and 54.4% into MB leprosy on the basis of histopathology.

Correlation of Fite Faraco (FF) positivity with clinical and histopathological diagnosis : Acid fast bacilli were seen in the specimens of skin biopsy in 9 (75%) LL cases, 12 (60%) BL cases, 16 (41%) of BT and 1 (33.3%) of IND. (Table 9). We found a statistically significant correlation of the FF positivity for AFB with the histopathological diagnosis than with the clinical, being positive in 5 (100%) LL cases, 29 (76.3%) BL cases, 3 (12.5%) BT and 1 (16.7%) TT case. (P-value-0.0001) (Table 9).

Table 9 : Correlation of Fite Faraco positivity with clinical and histopathological diagnosis

Clinical diagnosis	Total patients	Fite-Faraco positivity (no. of patients)	Histopathological diagnosis	Total patients	Fite-Faraco positivity (no. of patients)
IND	3	1* (33.3%)	IND	6	0 (00.0%)
TT	3	0 (00.0%)	TT	6	1 (16.7%)
BT	39	16† (41%)	BT	24	3 (12.5%)
BL	20	11 (55%)	BL	38	29 (76.3%)
LL	12	9 (75%)	LL	5	5 (100%)
Pure neuritic	2	0 (00.0%)			
Total	79	37 (46.8%)	Total	79	37 (46.8%)
Chi square-9.51, p value-0.09.			Chi square-37 p value-0.0001		

*this case was BL histopathologically

†twelve out of these 16 were BL histopathologically

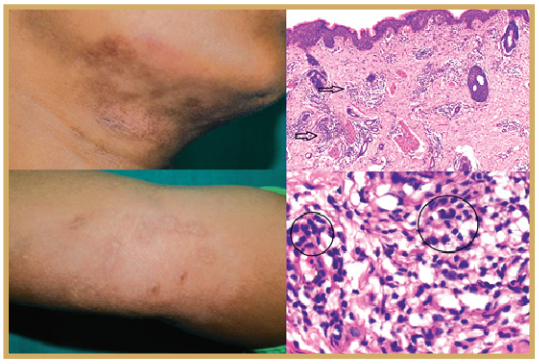

Fig. 1 : Two hypoesthetic patches without nerve thickening; clinically diagnosed as BT. Mixed macrophage and lymphocyte granuloma (black arrows) with abundant plasma cells (black circles) on histopathology (Hematoxylin and eosin, 50X, 200X) consistent with BL. FINAL DIAGNOSIS after Clinicopathological correlation (CPC): BL

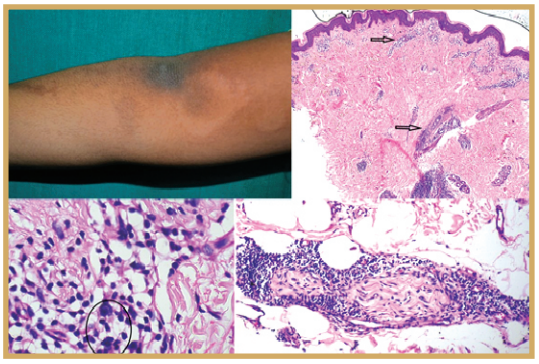

Fig. 2 : Two hypoesthetic plaques without peripheral nerve thickening; was clinically diagnosed as BT. Histopathology (Hematoxylin and eosin, 50X, 100X, 200X) revealed elongated lymphohistiocytic granulomas (black arrows) with mast cells, plasma cells; infiltration and partial destruction of nerve substance consistent with BL. FINAL DIAGNOSIS after CPC: BL

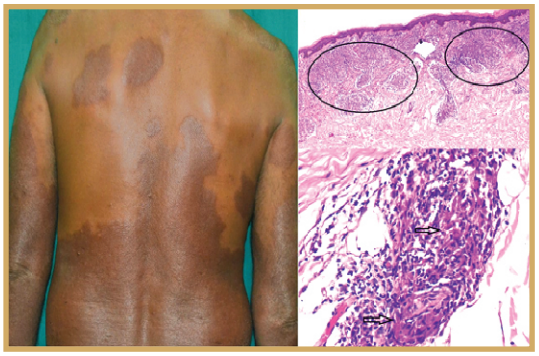

Fig. 3 : Multiple hypoesthetic plaques symmetrically distributed all over body, bilateral asymmetric nerve thickening; clinically diagnosed as BL. Histopathology (Hematoxylin and eosin, 50X, 100X showed multiple nodular tuberculoid granulomas (black circle) involving the neurovascular bundle (black arrow) suggestive of BT. FINAL DIAGNOSIS after CPC: BL

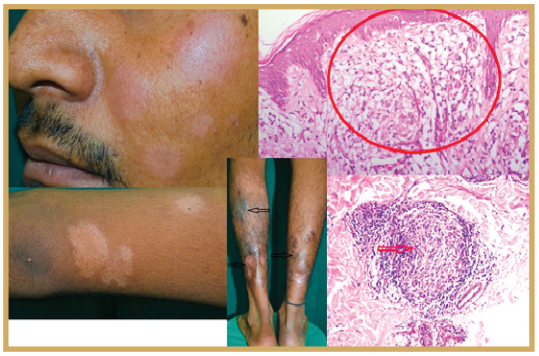

Fig. 4 : Multiple plaques (black arrows) with variable sensations all over body, multiple nerve thickening suggestive of BL leprosy. Histopathology (Hematoxylin and eosin, 100X, 200X) showed multiple sarcoidal and tuberculoid granulomas with loss of grenz zone (red circle) in the with complete destruction of nerve (red arrow) suggestive of TT leprosy. FINAL DIAGNOSIS after CPC: BL

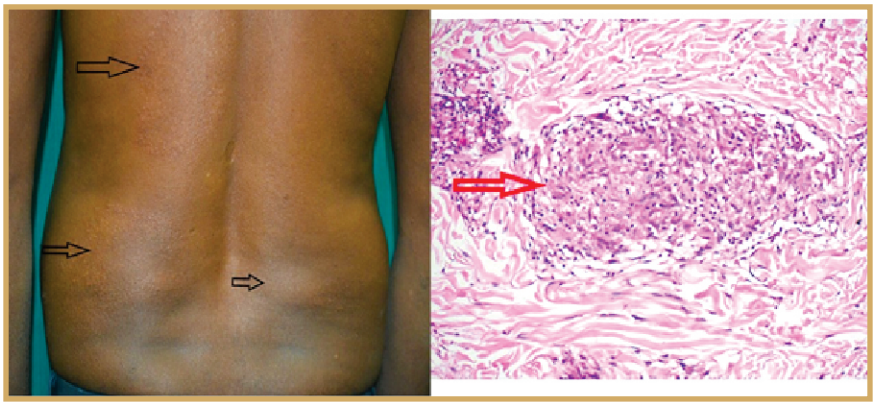

Fig. 5 : Multiple hypopigmented normoesthetic patches, annular plaques (black arrows) and infiltrated papules distributed symmetrically over the body without evident thickening of the nerves. Clinical diagnosis was LL. Histopathology (Hematoxylin and eosin, 200X) showed mature epitheloid granulomas in the mid dermis (red arrows) suggestive of BT leprosy. FINAL DIAGNOSIS after CPC: LL

Table 10 : Clinicopathological correlation of the R-J classification

Clinical diagnosis	Histopathological diagnosis					Total
	Indeterminate (% within clinical diagnosis)	TT (% within clinical diagnosis)	BT (% within clinical diagnosis)	BL (% within clinical diagnosis)	LL (% within clinical diagnosis)	
Indeterminate	1 (33.3%)	1 (33.3%)	0 (00.0%)	1 (33.33%)	0 (00.0%)	3 (100%)
TT	1 (33.3%)	2 (66.7%)	0 (00.0%)	0 (00.0%)	0 (00.0%)	3 (100%)
BT	4 (10.3%)	2 (5.1%)	17 (43.6%)	16 (41%)	0 (00.0%)	39 (100%)
BL	0 (0%)	1 (5%)	5 (25%)	13 (65%)	1 (5%)	20 (100%)
LL	0 (0%)	0 (0%)	1 (8.3%)	7 (58.3%)	4 (33.3%)	12 (100%)
Pure neuritic	0 (0%)	0 (0%)	1 (50%)	1 (50%)	0 (0%)	2 (100%)
Total	6 (7.6%)	6 (7.6%)	24 (30.4%)	38 (48.1%)	5 (6.3%)	79 (100%)

Chi square -43.7, P value- 0.002

Clinical and histopathological correlation : A perfect correlation was found in total of 48.1% of patients, maximum correlation (66.7%) was found in TT, followed by 65 % in BL leprosy, 43.6% in BT and 33.3 % correlation was found in IND and LL leprosy (Table 10). Interesting cases are depicted in Figs. 1-5.

Clubbing these cases together in PB and MB leprosy according to the WHO classification, out of the 47 PB cases, 29 (61.7%) were consistent with PB leprosy, and amongst the 32 MB leprosy, 25 (78.1%) were consistent with MB leprosy.

A minor mismatch does not hold value on the field level as the duration of MDT does not change.

Table 11 : Final diagnosis after clinico-pathological correlation

Spectrum	Frequency	Percent
IND	1	1.3
TT	4	5.1
BT	24	30.4
BB	0	00.0
BL	37	46.8
LL	13	16.4

Table 12 : Comparison of clinicopathological correlation in previous studies with the current study

Author(s)	Study Year	No. of Biopsy(n)	Correlation%	Discordance%
Ridley and Jopling (1966)	1966	82	68.30	31.70
Sehgal et al(1997)	1977	95	36.8	63.2
Giridhar et al (2012)	1982	100	60.2	39.8
Bhatia et al (1993)	1993	1272	69	31
Nadkarni & Rege (1999)	1999	2640	81.8	18.2
Singh et al (2003)	2003	104	58.6	41.4
Mathur et al (2011)	2011	156	80.4	19.6
Bijjaragi et al (2012)	2012	171	57.3	42.7
Shivaswamy et al (2012)	2012	182	74.7	25.3
Thakkar & Sangita (2014)	2014	30	60	40
Bomnakanti et al (2016)	2014	75	56	44
Tiwari et al (2015)	2015	53	54	46
Pokhrel et al (2016)	2016	21	71.4	28.6
Rodrigues Junior et al (2016)	2016	49	46.9	53.1
Our study	2017	79	48.1	51.9

Major mismatch likely to cause significant impact on the leprosy control programs were seen in 25 (31.6%) patients, a majority in BT spectrum (41%), 30% in BL, 33.3% in IND, 8.3% in LL and 50% (1 case out of 2) in pure neuritic leprosy.

After clinical and histopathological correlation, the final diagnosis included 37(46.8%) patients of BL, 24 (30.4%) of BT, 13(16.4%) of LL, 4(5.1%) of TT and 1 (1.3%) of IND (Table 11). The final diagnosis correlated with the clinical diagnosis in 57 (72.2%) patients as well as with the histopathological diagnosis in 57(72.2%) patients (equal correlation).

Discussion

Ridley and Jopling classified the various spectrums of leprosy based on immunological properties, and it is this classification that is being used for research purposes. It includes two

immunologically stable forms of leprosy (TT) and (LL) and an early indeterminate stage. In between the two polar forms of leprosy, exists a wide stretch of borderline leprosy (BT, BB, BL) always unstable due to continuing attempts by the immune cells to contain the bacilli.

Thirty eight (48.1%) of the 79 non-reactional cases showed perfect clinical and histopathological correlation. Various earlier studies showed clinicopathological concordance from 36.8% to 81.8% (Table 12).

Maximum correlation was found in polar tuberculoid pole (66.7%), followed by BL (65%), BT (43.6%), LL (33.3%) and IND (33.3%) leprosy. Bhatia et al (1993) reported 91% correlation for LL, 77% for BT, 50% for TT, 43% for BL, 36% for IND and 26% for B. Few earlier studies have found higher correlation across the spectrum. In the study done by Shivaswamy et al (2012) maximum correlation was seen in LL (84.2%) followed by BL (73.3%), BT (64.1%), TT (56%), BB (50%) and IND (50%). A correlation of 95.2% in LL, 89.7% in BT, 73.2% in TT, 72.4% in BL and 64.7% in BB was observed by Mathur et al **(**2011). Nadkarni & Rege (1999) showed 98% correlation in LL, 97% in TT, 95% in BT, 89% in BB and 87% in LL.

Clinicopathological correlation among the paucibacillary and multibacillary groups : Tuberculoid leprosy (TT) and BT are similar to a large extent both clinically as well as histologically. With patients presenting with few lesions, differentiating TT from BT becomes difficult as both these present as a well-defined lesion(s) with partial or complete loss of sensation with or without a thickened nerve. Histopathologically, both will show well-defined granulomas with lymphocytic infiltration with the difference in the shape of granulomas and degree of infiltration. Since both TT and BT are considered PB, LL and BL are considered MB for treatment purposes, differentiating TT from BT or BL from LL is, perhaps, therapeutically irrelevant. Thus clubbing (IND+TT+BT) together and (BB+BL+LL) together, we noted a better clinicopathological correlation. The overall concordance was 61.7% for the PB group and 78.1% for the MB group.

A shift towards the lepromatous end of the spectrum was seen in 22.8% of the cases and towards the tuberculoid spectrum in 8.9% of the patients. The former includes few cases of single lesion single nerve disease. This figure of 22.8% MB cases being misclassified as PB if not subjected to histopathology and being undertreated is likely to have a powerful impact on the persistence of leprosy in the population, its increased transmission, drug resistance and relapses in the apparently treated population, while 8.9 % patients are at risk of overtreatment.

Borderline group (BT and BL) : Cases in the borderline group are in continuously changing immunological spectrum and have shown greater clinicopathological discordance compared to polar TT and LL in earlier studies (Bomnakanti et al 2016). Out of the total 59 cases of borderline leprosy (BT, BL), clinicopathological correlation was found in 30 (50.8 %) cases. Forty one percent of the BT patients were classified as BL, and 25% of the BL patients were classified as BT. This could be due to the dynamic nature of the patients' immunity in the borderline spectrum, which is also reflected in the different histology obtained from different sites in these patients (Ganapati & Desikan 1974). Thus, combining BT+BL together, we could achieve a higher clinicopathological concordance of 75.9%.

Mid borderline (BB) : Like study of Lobo et al (2014), our study did not find a single case of BB leprosy both clinically as well as histopathologically. Mid borderline leprosy is immunologically the least stable, and a variety of clinical lesions of different morphology may be found in the same patient explaining the deficiency of this

spectrum in our study. Also, the histopathology findings may vary in different lesions in the same patient highlighting the need to relate the histological features with the clinical characteristics presented by the particular morphological lesion subjected to biopsy in order to achieve a better correlation of clinical with the histological changes (Sharma et al 2008).

Lepromatous leprosy (LL) : LL was found to have the lowest correlation of 33.3% only. This is in contrast to earlier studies that have reported a correlation of 84-98% in LL cases (Bhatia et al 1993, Nadkarni & Rege 1999, Mathur et al 2011, Shivaswamy et al 2012). In our study 7 of the 8 mismatched cases were classified as BL, 5 of which had clinical evidence of having downgraded towards the LL pole but was not reflected histologically. One, however, was classified as BT.

Indeterminate leprosy (IND) : There were 6(7.5%) cases of IND leprosy diagnosed histopathologically, the clinical diagnosis of 1 being IND, 4 BT and 1 TT. Nerve involvement was a consistent feature of all these cases. Indeterminate leprosy is evolution wise a pre-granulomatous stage of leprosy preceded by only lymphocytic infiltration. Definitive diagnosis of IND leprosy presently depends upon the demonstration of nerve lesion(s) (Liu et al 1982). It cannot be classified within the TT to LL spectrum due to lack of distinguishing features, and this happens more often histologically than clinically. Nadkarni & Rege (1999) also diagnosed a sizeable proportion (15.9%) of the cases as IND histopathologically, who were clinically classified as cases of TT, BT, BB or BL leprosy. Sharma et al (2008) also observed a good proportion (20%) diagnosed as IND on histopathology as against 6.48% cases clinically. In the present study, we found indeterminate histopathology in TT-BT cases only.

Clinical and histopathological correlation with Fite Faraco positivity : Detection of Acid fast bacilli (AFB) from tissue biopsy with Fite-Faraco technique takes lower cost and is a simpler method than PCR. The sensitivity detection of AFB remains poor because it requires about 1000 bacilli per cubic centimetre of tissues to present in order to detect 1 AFB in a section. Routine acid fast stain is also not sensitive due to the variability in its ability to decolorize AFB using acid alcohol (Sandhika et al 2016). In our study, we found a sensitivity of 46.8 % of the Fite Faraco staining overall spectrums of leprosy. The BI < 2 in the PB (IND+TT+BT) and > 2 in the MB (BL+LL). The sensitivity for the clinical BL and LL cases was 55% and 75%, respectively, while for Histopathological BL and LL cases, it was 76.3% and 100%, respectively. This better correlation of the FF stain with the histopathological diagnosis was found to be statistically significant, thus reinforcing the clinicopathological discordance described in our study.

After clinical and histopathological correlation, the final diagnosis included 46.8% patients of BL, 30.4% of BT, 16.5% of LL, 5.1% of TT and 1.3% of IND. It shows that a large number of patients with a high bacillary load are infective in the community. These could be responsible for the increase in the disease load in the country. The proportion of patients with BT, TT and IND have lessened in comparison. Pure TT has become obsolete. When only clinical diagnosis is relied on, BT is more common when actually many of these cases may be BL Leprosy. We found 22.8% of such cases may be treated inadequately. Targeting this gap in management would probably help reduce the risk of transmission, relapses, drug resistance and strengthen our Leprosy control program. Thus, studies on clinicopathological correlation should be done to better understand the changing spectrum of disease and for documentation. Our current knowledge has to be updated in view of new observations and changes in

technology as a part of continuing research.

The final diagnosis correlated with the clinical diagnosis in 57 (72.2%) patients as well as with the histopathological diagnosis in 57 (72.2%) patients (equal correlation). This clearly shows considering any one of these as Gold standard may be wrong and that they are complementary rather than mutually exclusive. Thus we recommend histopathological examination of the most infiltrated lesion in all cases of leprosy followed by clinicopathological correlation. This will help unveil the exact position of the case in the ever changing spectrum of the disease. The more advanced finding (the one towards the lepromatous pole) should be given greater significance, and cases classified and treated accordingly. Our current knowledge should also be improvised, and case definitions are re-established with set protocols for classification purpose. Major and minor criteria would add more objectivity to the clinical classification. It would be worthwhile to narrow down the histopathological classification only to pauci-bacillary and multibacillary, stable and unstable, which will be acceptable to the clinician for management purpose as well as simplify the exercise of classification, thus reducing the learning curve. The treatment criteria may also need modification to re-reach the stage of elimination of the disease from the country. Significance of various interpretations made in our analysis has to be established by properly conducted prospective studies taking into consideration the current WHO classification and treatment strategy (WHO 2018) which is also accepted by our National Leprosy Eradication Programme.

Acknowledgements

Authors acknowledge the support of Dr Nerges Mistry, Director; Dr Vanjana P. Shetty, Emeritus Senior Scientist and Mr Ramchandra Chile, Asst. Technician, The Foundation of Medical Research, Mumbai, for their valuable support in the Fite Faraco staining for this project

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How to cite this article : Chadha AA, Dongre A, Khopkar US (2021). A Single Centre Cross-Sectional Study of Clinicopathological Correlation in Leprosy: Discordance and Spectral Shift. *Indian J Lepr.* **93**: 143-156.