Exploring the Spectrum: A Clinico-Histopathological Insight into Suspected Leprosy Cases at a Tertiary Care Hospital

R. Mahra[1], V. Sanklecha[2], B. N Hiwale[3], Gayathri[4]

[1]MBBS, MD, Junior Resident, Department of Pathology

[2]MBBS, MD, Associate Professor, Department of Pathology

[3]MBBS, MD, Professor and Head, Department of Pathology

[4]MBBS, MD, Junior Resident, Department of Pathology
Corresponding Author Email: *gayathrisukumaran0[at]gmail.com*

Abstract: *The histopathological study of leprosy is crucial for understanding the disease, its types, and its varied manifestations and complications, as clinical diagnosis alone is often insufficient. This study aimed to evaluate suspected cases of leprosy at a tertiary care hospital, classifying them and observing associated morphological changes. Conducted at JJ Hospital, Mumbai, over ten months, the study analyzed 80 skin biopsies from suspected leprosy patients. The findings included a higher prevalence in males 78.75, with the most common age group being 21-40 years. Borderline Tuberculoid Leprosy was the most frequently diagnosed type. Histopathological examination proved vital in confirming the exact subtype of leprosy, thereby facilitating accurate therapy.*

Keywords: Leprosy, Histopathological Correlation, Clinical Diagnosis, Skin Biopsy, Leprosy Subtypes

1. Introduction

Leprosy is a chronic infectious disease caused by bacteria Mycobacterium leprae. It mainly affects the cooler parts of the body such as the skin, peripheral nerves, mucosa of the upper respiratory tract, and eyes, but it can also involve muscles, bones, testis, and internal organs [1]. Leprosy is an important public health problem mainly in the developing countries of the world. Control of leprosy is based on identifying the causative organism and destroying or attacking it [2]. Currently India is running one of the largest leprosy eradication programme in the world, but despite this 120,000 to 130,000 new cases of leprosy are reported every year in India. This accounts for 58.8% of the global total new cases [3]. Leprosy has low pathogenicity and 95% of people who contract Mycobacterium leprae do not develop the disease [4]. Spread is thought to occur through cough or contact with fluid from the nose of the person infected with leprosy [5]. Genetic functions and immunity of the person plays an important role in determining how much chances a person has for catching the disease [4,6]. The clinical manifestation of Leprosy is very varied and diverse, it can mimic a variety of unrelated diseases. The presentation can vary from an insignificant skin lesion to extensive diseases causing profound disability or deformity [7]. Since it is sometimes impossible to determine the exact type of leprosy based on clinical observations, the histopathological study of leprosy is crucial for understanding the disease, its types, varied manifestations, and complications. For the correct treatment and management, early and accurate diagnosis is very important. So, clinical and histopathological correlation becomes extremely important in patients care and management. This study was undertaken to know the histopathological features of leprosy in skin biopsies, to categorize them into various types based on histopathological features and to correlate with clinical features wherever possible.

2. Material & Methods

This prospective observational study was conducted in Department of Pathology in JJ hospital Mumbai over a period of 10 months from December 2021 to September 2022 after institutional ethics clearance (IEC/732/2022). All patients sample coming to the Department of Pathology within this defined study period, suspected clinically with leprosy were included in this study. We were able to enroll 80 patients in this study. Demographic data collection including age, gender, socio-economic status was noted. Clinical examination was done for the patients. Provisional diagnosis of the patients and gross examination findings were noted down. Clinical data is obtained from hospital records and skin biopsies received in the department. Gross examination carried out on arrival in the department, routinely processed, 3-5 microns thick sections made from paraffin embedded blocks and stained with H and E and Fite Faraco stain. The various parameters assessed in the study included: Demographic details (age, gender), clinical examination findings, histopathological findings in different types of leprosy, Fite Faraco stain findings, incidence of different types of leprosy according to histopathological classification noted in the study, relationship between clinical and histopathological diagnosis and clinicopathological agreement noted in study.

Statistical Analysis: After data collection, data entry was done in a Microsoft Excel sheet with the help of statistical software IBMSPSS22. Quantitative data was presented with the help of Mean and Standard deviation, wherever applicable. Descriptive statistics were used to note down the

distribution of patients based on age, clinical findings histopathological findings etc. Association between various histomorphological parameters evaluated. Comparison of age between various subgroups of patients was done using unpaired t test.

3. Result

In the present study patients are ranged from 7 years to 80 years. Maximum patients belong to 21-40 years age group, and minimum patients belongs to 61-80 years age group.

Table 1: Age wise distribution of data

Age	Frequency	Percentage
0-20	16	20
21-40	38	48
41-60	16	20
61-80	10	13
Total	80	

The study shows 63 (78.75%) patients were males and 17 (21.25%) were females. Male to female ratio was 3.7:1.

Table 2: Sex wise distribution of data

Gender				
	Frequency	Percent	Min	Max
ale	63	78.75	13	78
Female	17	21.25	7	80
Total	80	100		

In our study, most common clinical feature in Indeterminate Leprosy(IL) is presence of hypopigmented lesion seen in all 3 (100%) cases, in Tuberculoid Leprosy(TT) are anesthesia and presence of thickened nerve seen in all 14 (100%) cases, in Borderline Tuberculoid(BT) is anesthesia seen in 24 out of 25 i.e. (96%) cases, in Borderline Leprosy(BL) are anesthesia and hypopigmented lesions seen in 10 (8%) cases out of 12 cases, in Lepromatous Leprosy(LL) anesthesia is seen in all 11 (100%) cases, and in Histoid Leprosy(HL) hypopigmented lesions, erythematous lesions, anesthesia and nodules are seen in both the cases of HL (100%).

Table 3: Clinical signs and symptoms in different types of leprosy

Clinical signs and symptoms	Different types of Leprosy					
	IL	TT	BT	BL	LL	HL
Hypopigmented lesions	3 (100%)	12 (85.7%)	19 (76%)	10(83.3%)	9 (81.8%)	2 (100%)
Erythematous lesions	0	4 (28.5%)	13 (52%)	6 (50%)	4 (36.3%)	2 (100%)
Combinations	0	2 (14.2%)	6 (24%)	1(8.3%)	0	0
Anesthesia	1(33.3%)	14 (100%)	24 (96%)	10(83.3%)	11(100%)	2 (100%)
Nodules	0	0	2 (8%)	0	3 (27.2%)	2 (100%)
Trophic ulcer	0	0	2 (8%)	2(16.6%)	1 (9.09%)	0
Thickened nerve	0	14 (100%)	21(84%)	8(66.6%)	8 (72.7%)	1 (50%)

In the present study, according to clinical diagnosis, out of 80 patients, highest number of cases are of BT 24 (30%), followed by BL 12(15%), TT 9(11.25%), ENL 8(10%) and LL 7(8.75%). 3(3.75%) cases of BL with ENL, 2(2.5%) cases of BL in Type 1 lepra reaction, 2(2.5%) cases of HL, 2(2.5%) cases of LL with ENL, 1(1.25%) case each of Type 1 lepra reaction, LL to rule out HL, IL, BT in Type 1 reaction, BT with ENL, BB/BT, BB, BB progressing to BL, TL/BT, LL/HL and Leprosy/leishmania/sarcoidosis.
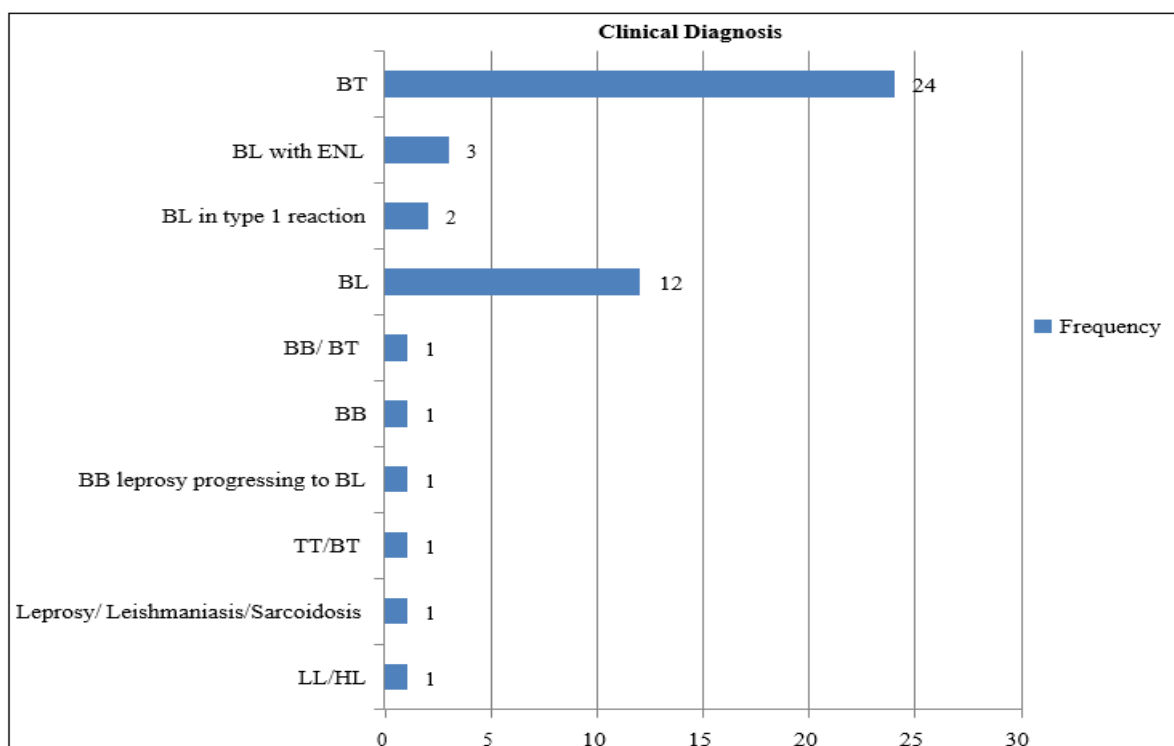

Figure 1: Clinical diagnosis

Maximum number of cases according to histopathological diagnosis are of BT 25(31.25%) cases, followed by TT 14(17.5%) cases, BL 12(15%) cases, LL 11(13.75%) cases. ENL is noted in 9(11.25%) cases, out of 9, 7 cases are ENL with LL background and 2 cases are ENL with BL background. Type 1 lepra reaction in 4 (5%) cases, out of these 4, 1 case is of Type 1 lepra reaction in BT, 2 cases are Type 1 lepra reaction in BL and 1 case of Type 1 lepra reaction which was clinically diagnosed as ENL. IL in 3(3.75%) cases, histoid leprosy in 2(2.50%) cases and no case of BB is noted in the present study.
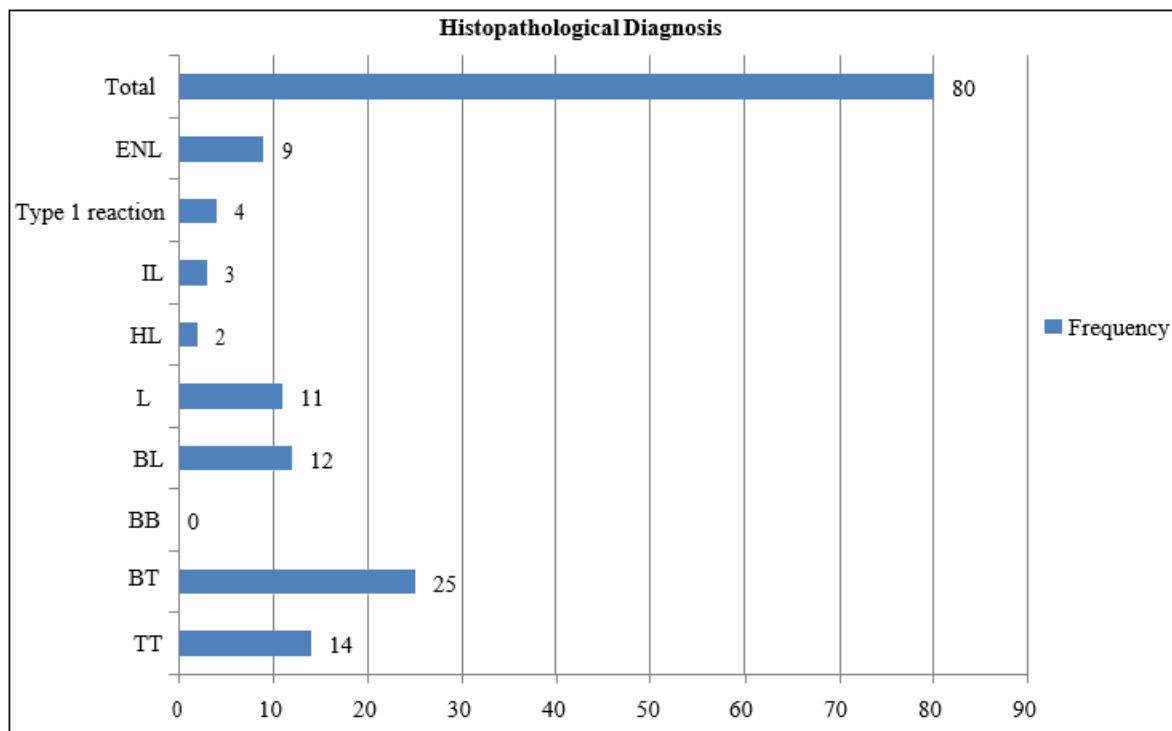

Figure 2: Histopathological diagnosis

Total 14 cases are diagnosed on histopathological examination of skin biopsy as TT, out of them well formed epithelioid granuloma, lymphocytic infiltrate, perineural inflammatory infiltrate and nerve edema is seen in all the 14 (100%) cases. Perivascular inflammatory infiltrate is seen in 9(64.2%) cases and Langhans Giant cells are seen in 8(57.1%) of the cases.

Out of 25 cases of BT, histomorphological feature of ill/poorly formed epithelioid granuloma, lymphocytic infiltrate, perineural, periadnexal inflammatory infiltration and nerve edema is seen in all 25(100%) cases.

The most common histomorphological feature noted in BL (12 cases) is presence of foamy macrophages, granuloma formation and presence of sparse lymphocytes seen in all 12(100%) cases. Grenz zone is seen in 4(33.3%) cases.

Out of 11 cases of LL, presence of epidermal atrophy, grenz zone, foamy macrophages and periadnexal inflammatory infiltrates, are seen in all the 11 (100%) cases of LL. Macrophage granuloma is seen in 4(36.3%) cases and sparse lymphocytes seen in 3(27.2%) cases.

Total 3 cases are diagnosed as features suggestive of IL on histopathological examination and clinical follow up is advised. The most common histomorphological features seen in all 3(100%) cases are subepidermal inflammatory infiltrates, lymphocytes, perineural, perivascular and periadnexal inflammatory infiltration.

Total 2 cases of HL are diagnosed on histopathological examination. The most common histomorphological features seen in both (100%) cases are presence of epidermal atrophy, grenz zone, spindle cell and foamy macrophages. Sparse lymphocytic infiltrate is seen in one (50%) of the case.

Total 4 cases of Type 1 lepra reaction are diagnosed on histopathological examination of skin biopsies. All 4(100%) cases show dermal edema, presence of granuloma and intragranuloma edema. Out of 9 cases of ENL, histomorphological features of macrophage granuloma, neutrophils, foamy macrophages, periadnexal, perineural and perivascular inflammatory infiltrates are the most common and seen in all 9 (100%) cases, followed by lobular panniculitis and lymphocytes seen in 8 (88.8%) cases.
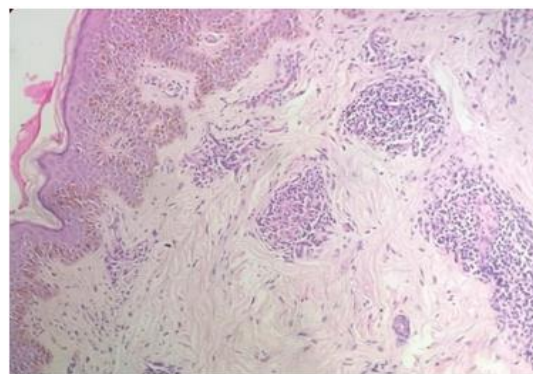

Figure 3: Tuberculoid leprosy: Epithelioid cells and lymphocytesinfiltrating enlarged, edematous nerve (H&E
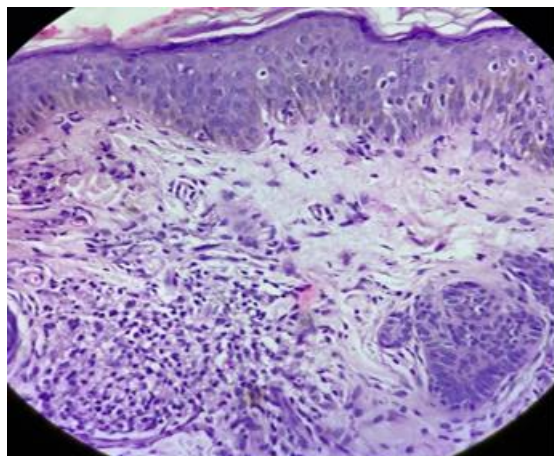
stained section 40x)

Figure 4: Borderline Lepromatous leprosy: Macrophage granuloma with lymphocytes (H&E stained section 40x)
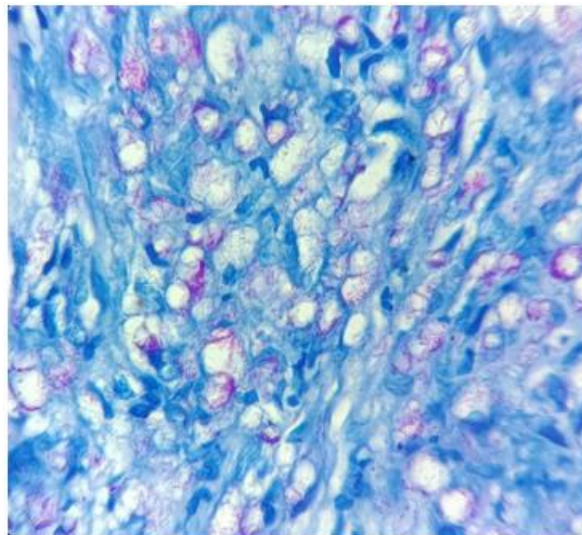

Figure 5: Histoid Leprosy: Spindle cell proliferation of macrophage in a storiform pattern. (H&E stained section 40x).

Figure 6: Histoid Leprosy: Fite Faraco stain positive M. leprae in the spindle shaped macrophages

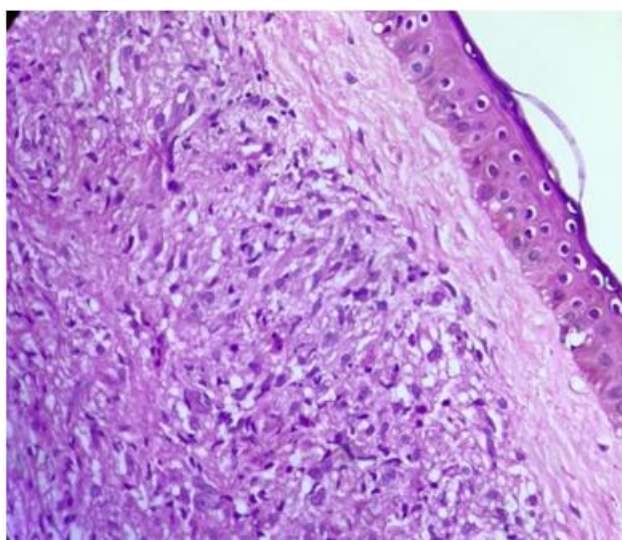In this study, it is observed that the overall concordance between clinical and histopathological diagnosis is 78.75 %. Maximum concordance is seen in TT (100%) and in one case of IL on clinical and histopathological examination (100%), however since Fite Faraco came out to be negative, histopathological diagnosis is given as suggestive of IL and clinical follow up is advised, followed by LL (85.71%), followed by BT (83.33%), followed by BL and Type 1 reaction (75%) each, followed by HL (66.66%), followed by ENL (64.2%). It is minimum in BB (0%). 4 cases are of doubtful clinical diagnosis. 1 case of LL/HL on clinical diagnosis is diagnosed as BL on histopathological examination. 1 case of leprosy / leishmaniasis /sarcoidosis on clinical diagnosis is diagnosed as BT on histopathological examination, 1 case of TT/BT clinically is diagnosed as BT on histopathological examination, another case of BB/BT on clinical diagnosis came out to be suggestive of IL on histopathological diagnosis.

Table 4: Correlation of clinical and Histopathological classification in leprosy

Type	Clinical diagnosis	Histopathological Diagnosis										Percentage of parity
		TT	BT	BB	BL	LL	IL	Type 1 reaction	ENL	HL	No evidence of leprosy	
TT	9	9	0	0	0	0	0	0	0	0	0	100
BT	24	3	20	0	0	0	1	0	0	0	0	83.33
BB	2	1	0	0	1	0	0	0	0	0	0	0
BL	12	1	0	0	9	2	0	0	0	0	0	75
LL	7	0	0	0	1	6	0	0	0	0	0	85.71
IL	1	0	0	0	0	0	1	0	0	0	0	100
Type 1reaction	4	0	1	0	0	0	0	3	0	0	0	75
ENL	14	0	2	0	0	2	0	1	9	0	0	64.2
HL	3	0	0	0	0	1	0	0	0	2	0	66.66
Caseswith doubtful clinical diagnosis	4											
	LL/HL (1)	0	0	0	1	0	0	0	0	0	0	
	Leprosy/ Leishmaniasis /Sarcoidosis (1)	0	1	0	0	0	0	0	0	0	0	
	TT/BT (1)	0	1	0	0	0	0	0	0	0	0	
	BB/BT (1)	0	0	0	0	0	1	0	0	0	0	
Total	80	14	25	0	12	11	3	4	9	2	0	78.75

4. Discussion

The clinicopathological manifestations of leprosy are a consequence of immunopathology and host response. In our study, maximum number of patients belonged to the age group of 21-40 years (48%). In the similar study done by Singh et al, 48 % of patients belonged to age group 21-40 years. We documented 78.5% of patients are males and 21.25% are females. Similarly, Singh et al found the disease in 69% of males [8]. According to IAL textbook of leprosy, an ill-defined hypopigmented lesion, flat without any surface changes may be IL, thick, elevated margin of a lesion with or without granularity is suggestive of TT/BT. Punched out lesion is suggestive of BB. Erythematous, firm nodules are seen in BL/LL. Glistening, well-defined nodules are suggestive of HL. The degree of sensory loss may be variable in different lesions (IL +/-, TT and BT ++, LL +/- or normal). A patient in reaction may not be able to appreciate lesional sensory loss and neuritis is found to be much more common in Type 1 lepra reaction than in ENL [9]. The clinical findings in the present study are in concordance with the findings mentioned in the IAL textbook of leprosy. In the similar study, conducted by Archana et al in the year 2020, maximum cases (50%) belong to BT, which is in concordance with our study [10]. Similarly, in the study conducted by Sikha et al between 2015-2018, maximum patients belong to BT (52%), which is in concordance with our study [11]. In the present study, BT being the most common type of leprosy on histopathological diagnosis correlates with the study conducted by Sikha et al, maximum number of cases belong to BT (35%), followed by TT (30%), followed by BL (3%) cases [11]. Similar study conducted by Neha et al in 2019, the most common histopathological feature in TT was well formed epithelioid cell granuloma seen in (100%) cases followed by lymphocytic infiltrate in (80%) cases, in BT it was presence of lymphocytic infiltrates in (87.5 %) cases, followed by ill formed epithelioid cell granuloma in (62.5%) cases. This is in concordance with the present study [12]. In another study conducted by Munton et al in 2022, the most common histopathological feature in BL was presence of perineural lymphocytic infiltrates seen in (100%) cases, peri appendageal infiltrates seen in (85.7%) cases, Virchow cells seen in (78.5%) and epidermal atrophy seen in (71.4%) cases, in LL was presence of Grenz zone and Virchow cells seen in (100%) cases, plasma cells seen in (90%) cases, epidermal atrophy seen in (80%) cases, this is similar to our present study [13]. Also, in the study conducted by Neha et al in 2019, the most common histopathological feature in IL was presence of scant lymphocytic infiltrates in (85.7 %) cases, followed by perivascular lymphocytic infiltrates in (66.6%) cases, which is in concordance with the present study [12]. In a study conducted by Suri SK et al in 2014, the most common histopathological feature in HL was presence of epidermal atrophy, Grenz zone and foamy macrophages (100%) cases, similar to the present study findings [14].

It is observed that the overall concordance between clinical and histopathological diagnosis is 78.75 % in our study, which is similar to the studies conducted by Bhanushree CS et al (79.44%) and Mathur et al (80.4%). The results in the present study are similar to the study conducted by Semwal et al in 2018, where maximum correlation was in TT, HL (100%) each, followed by BL (47.3%), followed by BT (44.8%), followed by LL (27.2%). Minimum correlation was in BB (0%) [16,17].

5. Conclusion

In conclusion it can be said that, many a times leprosy poses a significant problem in clinical diagnosis. Histopathological examination of the lesions confirms the exact subtype of the disease and facilitates the institution of accurate mode of therapy. So, correlation of clinical and histopathological features is necessary for accurate typing of leprosy than clinical diagnosis alone. Thus, histopathology remains the gold standard for the diagnosis of all clinically suspected cases of Leprosy.

References

[1] Park K, Park K. Epidemiology of communicable diseases. Park's textbook of preventive and social medicine. 2011 Feb; 22: p215-225

[2] Ganapathy R, Revankar CR (1994). Leprosy Controle. In: Valia RG, Valia AR, editors Textbook And Atlas of Dermatology, Bombay Bhalani Publishing House; p.1427-1437

[3] Sengupta U. Elimination of leprosy in India: An analysis. Indian J Dermatol Venereol Leprol 2018;84:131-136

[4] Guidelines for the diagnosis, treatment and prevention of leprosy. New Delhi: World Health Organization, Regional Office for South-East Asia; 2017. Licence: CC BY-NC-SA 3.0 IGO.

[5] Hansen's Disease Transmission.cdc.gov.April 29,2013.

[6] Montoya D, Modlin RL. Learning from leprosy: insight into the human innate immune response. Adv Immunol. 2010; 105: 1-24. doi: 10.1016/S0065-2776(10)05001-7. PMID: 20510728.

[7] Shantaram B, Yawalkar SJ. Leprosy–Differential Diagnosis. Text book and atlas of dermatology. 1994; 1: 1385.

[8] Singh S, Sinha AK, Banerjee BG, Jaswal N. Participation level of the leprosy patients in society. Indian J Lepr. 2009 Oct-Dec;81(4):181-7. PMID: 20704073.

[9] Kar HK, Kumar B. IAL textbook of leprosy. India: Jaypee. 2010:152-66. p214-223.

[10] Dr. Archana, Dr. Hilda Fernandez et al (2020). Clinico-Histopathological correlation in Hansen's disease: A retrospective study; International Journal of Clinical and Diagnostic Pathology,3(3): 168-172.

[11] Shikha Ghanghoria,Arvind Ghanghoria ,Sonal Meshram, "Clinico-Histopathological Correlation in Leprosy: At M.Y. Hospital Indore," *SSRG International Journal of Medical Science*, vol. 6, no. 7, pp. 14-19, 2019. *Crossref,* https://doi.org/10.14445/23939117/IJMS-V6I7P103

[12] Yadav N, Kumar B, Joshi U, Kumar M, Agarwal S. Histomorphological Study of Leprosy with Clinical Correlation in Kumaon Region. ijmsci [Internet]. 2019 Dec. 13 [cited 2024 Jul. 21];6(12):4657-63.

[13] Jidnyasa K. Munot, Mukund Shivaji Unde, Sadhana Khaparde, Babaji Shinde et al (2022). Histomorphological Features of Leprosy: A Retrospective Study of 60 cases at a Tertiary Care Hospital; IJPCR;14(9);690-695.

[14] Suri SK, Iyer RR, Patel DU, Bandil S, Baxi S et al (2014). Histopathology and clinico- histopathological correlation in Hansen's disease. J Res Med Den Sci 2014;2(1):37-44.

[15] Poonam Tulshiram, Ashish kumar gupta, Nighat Hussain, Satyaki Ganguly et al (2021).

[16] Clinico-histopathological correlation in Leprosy lesions: Study in a tertiary care Institute in Chhattisgarh; Annals of Pathology and Laboratory Medicine, Vol 8, Issue 10, October.

[17] Banushree Cs, Bhat R V, Udayashankar C, Clinicopathological correlation of Hansen's disease: a retrospective study of skin biopsies. *Indian J Pathol Oncol* 2016;3(3):491-495

[18] Mathur MC, Ghimire RB, Shrestha P, Kedia SK. Clinicohistopathological correlation in leprosy. Kathmandu Univ Med J (KUMJ). 2011 Oct-Dec;9(36):248-51. doi: 10.3126/kumj.v9i4.6338. PMID: 22710532.