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A Clinico-Pathological Study and Bacteriological Study of Leprosy Cases in a Tertiary Care Hospital

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ABSTRACT
Leprosy is a chronic infectious disease caused by Mycobacterium leprae, affecting the skin, peripheral nerves and mucosal surfaces. Accurate diagnosis and classification of leprosy are crucial for effective management and prevention of transmission. This study aims to evaluate the correlation between clinical and histopathological findings in leprosy cases at a tertiary care hospital. A total of 53 leprosy cases were analyzed for clinical presentation and histopathological findings. The bacteriological index was assessed and the concordance between clinical and histopathological diagnoses was calculated. Acid-fast bacilli (AFB) positivity and the bacteriological index were used to evaluate bacterial load in different leprosy types. The overall concordance rate between clinical and histopathological diagnoses was 66%. Tuberculoid leprosy (TT) showed a 100% concordance rate, while borderline tuberculoid (BT) had an 81.8% concordance. Borderline lepromatous (BL) and lepromatous leprosy (LL) had concordance rates of 80% and 55.6%, respectively. Indeterminate leprosy (IL) also had a concordance rate of 55.6%. The bacteriological index varied, with LL showing the highest bacterial load. AFB positivity was observed in 54.7% of cases, with lepromatous forms showing the highest rates. Histopathological confirmation is essential for accurately diagnosing leprosy, particularly in cases with ambiguous clinical features. While concordance is generally high for tuberculoid and lepromatous forms, intermediate and indeterminate forms present diagnostic challenges. These findings underscore the need for comprehensive diagnostic strategies to improve leprosy management.

INTRODUCTION

Leprosy, also known as Hansen's disease, is a chronic infectious disease caused by Mycobacterium leprae. It primarily affects the skin, peripheral nerves, mucosal surfaces of the upper respiratory tract and the eyes[1]. Despite significant advances in its control and treatment, leprosy remains a public health concern in many developing countries, including India. Early diagnosis and appropriate treatment are crucial in preventing long-term complications and reducing transmission. Leprosy presents a broad spectrum of clinical manifestations, which are categorized based on the Ridley-Jopling classification system into tuberculoid, borderline and lepromatous types. Each form exhibits distinct clinical, immunological and pathological features that influence treatment response and prognosis[2].

Clinico-pathological and bacteriological studies play a pivotal role in understanding the disease's varied presentations and in optimizing management strategies. Histopathological examination of skin biopsies remains a cornerstone in diagnosing and classifying leprosy[3]. It provides critical insights into the host's immune response and the bacillary load, which are key determinants of disease progression and treatment outcomes. Bacteriological studies, including slit-skin smears and molecular diagnostic techniques, further complement histopathology by confirming the presence of M. leprae and assessing bacterial load[4].

Several studies have explored the clinico-pathological correlation in leprosy. For instance, Moorthy *et al.* (2001) conducted a comprehensive analysis of skin biopsies from leprosy patients, highlighting the correlation between clinical presentation and histopathological findings[5]. Sharma and Singh (2022) focused on the bacteriological aspects, emphasizing the role of molecular diagnostics in leprosy detection[6]. Despite these efforts, significant research gaps persist, particularly in understanding the immunological underpinnings of leprosy's diverse clinical manifestations and the factors influencing treatment resistance.

While much progress has been made in leprosy research, there remains a gap in comprehensive studies that integrate clinical, pathological and bacteriological data to provide a holistic understanding of the disease. The relationship between histopathological changes and the patient's immune status, especially in the context of multidrug therapy, is not fully elucidated[7]. Furthermore, the role of emerging molecular techniques in routine diagnosis and monitoring of leprosy cases warrants further exploration. Additionally, there is a need to assess the impact of socio-economic and environmental factors on the disease's epidemiology and management outcomes.

This study aims to bridge these gaps by conducting a detailed clinico-pathological and bacteriological analysis of leprosy cases in a tertiary care hospital. The primary objectives are to evaluate the correlation between clinical presentation and histopathological findings, assess the utility of bacteriological studies in diagnosis and monitoring and identify factors influencing treatment response. Through this study, we hope to enhance our understanding of leprosy's complex pathogenesis and improve strategies for its management and control.

MATERIALS AND METHODS

Study Design: This study was designed as both retrospective and prospective, focusing on skin biopsies suspected of leprosy collected over the period from January 2022-June 2024.

Sample Collection: A total of 244 skin biopsies of various skin lesions were received in the Department of Pathology at MAMS, Bachupally, from the Dermatology Department. Out of these, 53 cases were clinically suspected of leprosy.

Processing and Staining: The 53 skin punch biopsies that were clinically suspected of leprosy underwent the following procedures:

1. **Paraffin Embedding:** The biopsies were processed using routine paraffin embedding techniques.
2. **Sectioning:** Sections of 2-4µm thickness were cut with proper orientation of the tissue.
3. **Staining:**
4. **Hematoxylin and Eosin (H and E) Staining:** Routine H and E staining was performed on the sections to observe general histopathological features.
5. **Fite-Faraco Method:** This special staining technique was used to identify acid-fast bacilli (AFB) in the tissue sections.

Inclusion Criteria:

- All clinically suspected cases of leprosy, irrespective of age and gender, were considered for the study.

Exclusion Criteria:

- Cases with inadequate biopsy material were excluded from the study.

Statistical Analysis: The histopathological and bacteriological data obtained from the stained sections were analyzed to correlate clinical features with

pathological findings. The presence of AFB and the spectrum of histopathological changes were documented and classified according to standard criteria.

RESULTS AND DISCUSSIONS

The table 1 presents the age-wise distribution of leprosy lesions in a cohort of patients from a tertiary care hospital. The data shows that leprosy lesions are predominantly observed in adults, with no cases reported in individuals aged 1-20 years. The highest number of cases, 15, is observed in the 21-30 year age group, indicating that young adults are most affected by the disease. This is closely followed by the 31-40 and 41-50 year age groups, each with 13 cases, suggesting that middle-aged adults are also significantly impacted. The 51-60 year age group shows a slight decrease in cases, with 11 reported instances, while only a single case is noted in the 61-70 year age group. This distribution suggests a decline in the number of new leprosy cases as age increases beyond 60 years, highlighting a potential age-related pattern in the prevalence of leprosy lesions within this population. These findings may reflect the demographic characteristics of the region or specific risk factors associated with leprosy in different age groups.

Fig. 1 shows the distribution of leprosy cases by gender, revealing a significant difference in the number of cases between males and females. Among the 53 total cases observed in the study, males account for the majority, with 37 cases. This suggests a higher prevalence or detection rate of leprosy in males compared to females, who represent 16 cases. The male-to-female ratio is approximately 2.3:1, indicating that men are more than twice as likely to be diagnosed with leprosy as women in this cohort. This disparity may be attributed to various factors, including differences in exposure to risk factors, health-seeking behavior, or biological susceptibility. Understanding the reasons behind this gender disparity is crucial for developing targeted interventions and improving leprosy control measures within the community.

Table 2 presents the clinical presentation of leprosy cases categorized by type, highlighting the presence of hypopigmented patches and erythematous lesions (including plaques, nodules and macules). Tuberculoid leprosy (TT) shows 2 cases with hypopigmented patches and none with erythematous lesions. Borderline tuberculoid (BT) has 11 cases with hypopigmented patches and 2 with erythematous lesions. Borderline borderline (BB) includes 2 cases with hypopigmented patches. Borderline lepromatous (BL) exhibits 3 cases with hypopigmented patches and 7 with erythematous lesions. Lepromatous leprosy (LL) shows 2 cases with hypopigmented patches and 18 with erythematous lesions, indicating severe skin involvement and high bacterial load. Indeterminate leprosy (IL) includes 7 cases with hypopigmented patches and 2 with erythematous lesions. Overall, 27 cases present with hypopigmented patches and 26 with erythematous lesions, reflecting the diverse clinical manifestations of leprosy, with LL showing the most severe form.

Table 3 summarizes the histopathological results of leprosy cases, displaying both the number of cases and their respective percentages for each type. Tuberculoid leprosy (TT) accounts for 2 cases, representing 3.8% of the total. Borderline tuberculoid leprosy (BT) comprises 11 cases, making up 20.8%. No cases were identified as borderline leprosy (BB). Borderline lepromatous leprosy (BL) includes 5 cases, corresponding to 9.4%. Lepromatous leprosy (LL) is the most prevalent type, with 18 cases, constituting 34.0% of the total, indicating its predominance in the studied population. Indeterminate leprosy (IL) is seen in 9 cases, accounting for 17.0%. Additionally, 8 cases (15.1%) tested negative for acid-fast bacilli (AFB), suggesting an absence of detectable bacteria in these samples. These histopathological findings provide a comprehensive overview of the distribution and severity of leprosy types within the cohort, highlighting the variation in immune response and bacterial load among different forms of the disease.

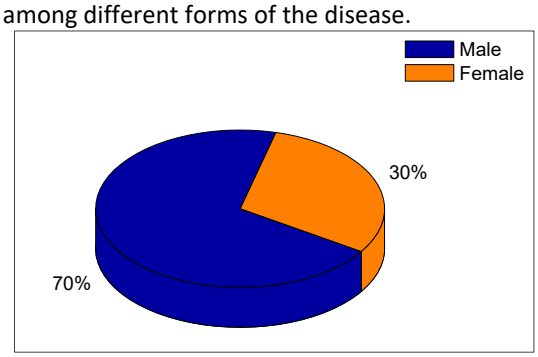

Fig. 1: Sex Distribution of Leprosy Cases

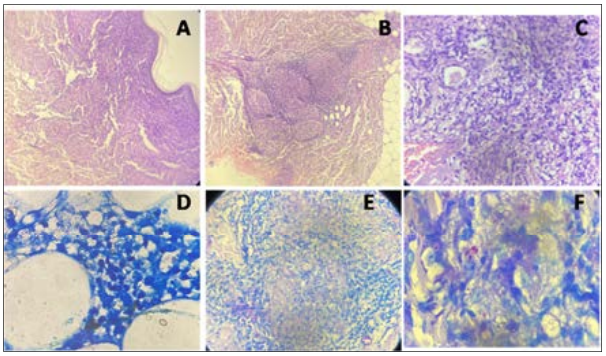

Fig. 2: Histopathological and Bacteriological Features in Various Types of Leprosy

Table1: Age-Wise Distribution of Leprosy Lesions

Age Group (years)	Number of Cases
1-10	0
11-20	0
21-30	15
31-40	13
41-50	13
51-60	11
61-70	1

Table 2: Clinical presentation of different types of leprosy cases

Clinical diagnosis	Hypopigmented patch	Erythematous/ Plaque/ Nodule/ Macule
TT (Tuberculoid Leprosy)	2	0
BT (Borderline Tuberculoid Leprosy)	11	2
BB (Borderline Leprosy)	2	0
BL (Borderline Lepromatous Leprosy)	3	7
LL (Lepromatous Leprosy)	2	18
IL (Indeterminate Leprosy)	7	2
Total	27	26

Table 3: Histopathology Results with Percentages

Histopathological Type	Number of Cases	Percentage (%)
TT (Tuberculoid Leprosy)	2	3.8%
BT (Borderline Tuberculoid Leprosy)	11	20.8%
BB (Borderline Leprosy)	0	0%
BL (Borderline Lepromatous Leprosy)	5	9.4%
LL (Lepromatous Leprosy)	18	34.0%
IL (Indeterminate Leprosy)	9	17.0%
Negative for AFB (Acid-Fast Bacilli)	8	15.1%

Table 4: Showing Clinical and Histopathological Distribution of Leprosy Cases

Type of Leprosy	Clinical No. of Cases	Clinical %age	Histopathological No. of Cases	Histopathological %age
TT (Tuberculoid Leprosy)	2	3.8%	2	7.5%
BT (Borderline Tuberculoid Leprosy)	13	20.8%	11	28.3%
BB (Borderline Leprosy)	2	0%	0	3.8%
BL (Borderline Lepromatous Leprosy)	10	9.4%	5	15.1%
LL (Lepromatous Leprosy)	20	34.0%	18	22.6%
IL (Indeterminate Leprosy)	6	17.0%	9	13.2%
Non specific dermatitis with Negative for AFB (Acid-Fast Bacilli)	0	15.1%	8	9.4%
Total	53	100%	53	100%

Table 5: Showing Positivity of AFB in Different Types of Leprosy

Type of Leprosy	Positive No. of Cases	Positive %age	Negative No. of Cases	Negative %age	Total No. of Cases
TT (Tuberculoid Leprosy)	0	0%	2	100%	2
BT (Borderline Tuberculoid Leprosy)	4	36.4%	7	63.6%	11
BB (Borderline Leprosy)	0	0%	0	0%	0
BL (Borderline Lepromatous Leprosy)	5	100%	0	0%	5
LL (Lepromatous Leprosy)	18	100%	0	0%	18
IL (Indeterminate Leprosy)	2	22.2%	7	77.8%	9
Negative for AFB (Acid-Fast Bacilli)	0	0%	8	100%	8
Total	29	54.7%	24	45.3%	53

Table 6: Showing Bacteriological Index in Various Types of Leprosy

Type of Leprosy	0	1+	2+	3+	4+	5+	6+
TT (Tuberculoid Leprosy)	2 (100%)	-	-	-	-	-	-
BT (Borderline Tuberculoid Leprosy)	7 (63.6%)	2 (18.2%)	2 (18.2%)	-	-	-	-
BB (Borderline Leprosy)	-	-	-	-	-	-	-
BL (Borderline Lepromatous Leprosy)	-	-	-	1 (20%)	3 (60%)	1 (20%)	-
LL (Lepromatous Leprosy)	-	-	-	-	2 (11.1%)	5 (27.8%)	11 (61%)
IL (Indeterminate Leprosy)	7 (77.8%)	1 (11.1%)	1 (11.1%)	-	-	-	-

Table 7: Correlation Between Clinical and Histopathological Findings

Type of Leprosy	Clinical No. of Cases	Histopathological No. of Cases	Correlated Cases	Concordance Rate (%)
TT (Tuberculoid Leprosy)	2	2	2	100%
BT (Borderline Tuberculoid Leprosy)	13	11	11	81.8%
BB (Borderline Leprosy)	2	0	0	-
BL (Borderline Lepromatous Leprosy)	10	5	5	80%
LL (Lepromatous Leprosy)	20	18	18	55.6%
IL (Indeterminate Leprosy)	6	9	6	55.6%
Negative for AFB (Acid-Fast Bacilli)	0	8	0	62.5%
Total	53	53	35	66%

Table 4 shows the clinical and histopathological distribution of leprosy cases, highlighting differences between clinical diagnosis and tissue analysis. Tuberculoid leprosy (TT) shows 2 cases clinically (3.8%) and histopathologically (7.5%). Borderline tuberculoid (BT) has 13 clinical cases (20.8%) but 11 histopathological cases (28.3%). Borderline leprosy (BB) is clinically reported in 2 cases (0%) with none

confirmed histopathologically, suggesting diagnostic overlap. Borderline lepromatous leprosy (BL) includes 10 clinical cases (9.4%) and 5 histopathological cases (15.1%). Lepromatous leprosy (LL) has 20 clinical cases (34.0%) and 18 histopathological cases (22.6%), showing close alignment. Indeterminate leprosy (IL) is noted in 6 clinical cases (17.0%) and 9 histopathological cases (13.2%). Non-specific dermatitis with negative AFB shows no clinical cases but 8 histopathological cases (9.4%), indicating discrepancies. This table emphasizes the importance of histopathological confirmation to accurately diagnose leprosy types and address discrepancies in clinical assessments.

A) This image shows the histopathological features typical of histioid leprosy, characterized by the presence of spindle-shaped histiocytes.

B) This image shows multiple granulomas in a leprosy lesion, typically seen in tuberculoid leprosy.

C) A high-magnification view showing foamy histiocytes surrounding adnexal structures, often seen in lepromatous leprosy.

D) This image highlights the presence of acid-fast bacilli (AFB) in a borderline lepromatous leprosy case, stained using a specific method to visualize the bacteria.

E) An image showing a tuberculoid leprosy case with no detectable acid-fast bacilli, indicating a low bacterial load typical of this form.

F) This image shows globi, which are clusters of leprosy bacilli, within histioid tissue, a feature of histioid leprosy.

Table 5 illustrates the acid-fast bacilli (AFB) positivity in different types of leprosy, highlighting the variation in bacterial presence across clinical types. In tuberculoid leprosy (TT), both cases (100%) are negative for AFB, reflecting the low bacterial load typical of this form. Borderline tuberculoid leprosy (BT) shows 4 positive cases (36.4%) and 7 negative cases (63.6%), indicating a moderate bacterial presence. There are no cases of borderline leprosy (BB). Borderline lepromatous leprosy (BL) and lepromatous leprosy (LL) exhibit 100% AFB positivity, with 5 and 18 cases respectively, consistent with their high bacterial load. Indeterminate leprosy (IL) has 2 positive cases (22.2%) and 7 negative cases (77.8%). Additionally, 8 cases are negative for AFB, indicating no detectable bacteria. Overall, 29 out of 53 cases (54.7%) are AFB positive, and 24 cases (45.3%) are negative, underscoring the variability in bacterial presence across leprosy types and the importance of AFB testing in confirming diagnosis and assessing disease severity.

Table 6 explains the bacteriological index (BI) in various leprosy types, indicating the density of acid-fast bacilli. Tuberculoid leprosy (TT) shows 100% of cases with a BI of 0, indicating no detectable bacteria. In borderline tuberculoid leprosy (BT), 63.6% have a BI of 0, while 18.2% have BIs of 1+ and 2+, suggesting a low to moderate bacterial presence. Borderline lepromatous leprosy (BL) has higher bacterial loads, with 60% of cases showing a BI of 4+. Lepromatous leprosy (LL) exhibits the highest bacterial load, with 61.1% of cases having a BI of 6+. Indeterminate leprosy (IL) primarily shows a BI of 0 (77.8%), indicating low bacillary density. This table demonstrates the correlation between BI and leprosy type, with lepromatous forms having the highest bacillary presence.

Table 7 shows the correlation between clinical and histopathological findings for different types of leprosy, emphasizing the concordance rate between the two diagnostic methods. For tuberculoid leprosy (TT), all 2 cases have a perfect concordance rate of 100%, indicating complete agreement between clinical and histopathological diagnoses. Borderline tuberculoid leprosy (BT) has a concordance rate of 81.8%, with 11 out of 13 clinical cases confirmed histopathologically. Borderline leprosy (BB) has no histopathological cases or concordance, suggesting misclassification. Borderline lepromatous leprosy (BL) shows an 80% concordance rate, with 5 out of 10 clinical cases confirmed. Lepromatous leprosy (LL) and indeterminate leprosy (IL) both have a concordance rate of 55.6%, indicating moderate agreement. Cases negative for acid-fast bacilli (AFB) show a 62.5% concordance rate. Overall, 35 out of 53 cases (66%) show agreement between clinical and histopathological findings, highlighting the importance of combining both diagnostic approaches for accurate leprosy classification.

The correlation between clinical and histopathological findings in leprosy is crucial for accurate diagnosis and effective management. This study revealed a 66% overall concordance rate between clinical and histopathological diagnoses across various types of leprosy. This aligns with findings from previous research, although variations in concordance rates have been reported due to differences in study populations, diagnostic criteria, and methodologies.

In this study, tuberculoid leprosy showed a perfect concordance rate of 100%, consistent with earlier studies such as Bongiorno *et al.,* which also reported high concordance rates due to the distinct clinical and histopathological features of TT[8]. These results suggest that TT can be reliably diagnosed clinically and histopathologically due to its strong immune response and well-defined lesions.

The concordance rate for borderline tuberculoid leprosy was 81.8%. Similar studies have reported varying rates of concordance. For example, Bhatia *et al.* found a concordance rate of around 70% due to the overlap of clinical features with other borderline forms[9]. This indicates that while there is significant

agreement, some clinical cases may be misclassified without histopathological confirmation.

The concordance rate for borderline lepromatous leprosy in this study was 80%, which is slightly higher than the rates reported by previous studies such as Salodkar and Kalla, which found rates closer to 75%[10]. This high concordance rate can be attributed to the characteristic clinical features of BL, such as diffuse skin lesions and moderate bacterial load, which are often confirmed histopathologically.

The study found a concordance rate of 55.6% for lepromatous leprosy, which is somewhat lower than those reported in other studies, such as Chavarkar and Suiam which found rates of approximately 70%[11]. The lower concordance in this study might be due to the broad spectrum of clinical presentations in LL and the potential for misdiagnosis without histopathological confirmation.

Indeterminate leprosy also had a concordance rate of 55.6%. Studies like those conducted by Kumar *et al.* have reported similar challenges in diagnosing IL due to its early-stage presentation, which often lacks definitive clinical and histopathological characteristics[12]. This highlights the need for careful evaluation and follow-up to accurately diagnose and manage IL.

Cases negative for AFB showed a concordance rate of 62.5%. This finding underscores the difficulty in diagnosing leprosy when clinical signs are subtle, and histopathological findings are nonspecific. Previous studies, such as those by Maymone *et al.,* emphasize the importance of combining clinical evaluation with advanced diagnostic techniques to improve accuracy[13].

CONCLUSION

The findings of this study shows the significance of histopathological confirmation in diagnosing leprosy, especially in cases with ambiguous clinical presentations. While concordance rates are generally high for tuberculoid and lepromatous forms, the intermediate and indeterminate forms pose diagnostic challenges that require a multidisciplinary approach. Moreover, indeterminate and borderline lepromatous leprosy necessitate further follow-up to monitor the disease's progression. These results align with previous research, highlighting the essential role of comprehensive diagnostic strategies in the effective management of leprosy.

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