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A study to compare clinical spectrum, bacteriological index in slit skin smear and histopathology in Hansen's disease

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ABSTRACT:

Background: Leprosy (Hansen's disease) remains a significant global health issue, especially in India, which, along with Brazil and Indonesia, reports 80.2% of new cases. Despite India achieving the elimination target in 2002, the annual new case detection rate is still concerning. This study investigates newly diagnosed Hansen's disease patients by examining their clinical profiles, slit skin smears, and histopathological features, aiming to correlate clinical manifestations with these diagnostic methods across different disease types.

Methods: In this cross-sectional study, 50 newly diagnosed Hansen's disease patients were included with written consent. Data, including epidemiological details and medical history, were collected via structured questionnaires. Patients underwent dermatological and systemic examinations, classified by Modified Ridley Jopling Classification. Laboratory investigations, including slit skin smear staining and skin biopsies, were performed.

Results: Most subjects were males (68%), predominantly aged 31-45 years (58%). Plaques (44%) and loss of sensation (38%) were common presentations. The ulnar nerve was most affected (78%), and lepra reactions occurred in 24%. Lepromatous leprosy was the most prevalent clinical diagnosis (34%). Slit skin smears showed 38% with 5+ acid fast bacilli, and histopathology confirmed lepromatous leprosy in 38%. Clinical and histopathological findings had statistically significant correlations, validating clinical diagnoses.

Conclusion: Hansen's disease primarily affects young adult males, presenting mainly with plaques and loss of sensation. Ulnar nerve involvement and lepra reactions were notable. Clinical diagnosis of lepromatous leprosy, supported by slit skin smear examinations, showed significant correlation. Discrepancies in histopathology highlight the need for cautious interpretation, emphasizing the importance of clinical examination.

KEYWORDS: Clinical Spectrum, Bacteriological Index, Slit Skin Smear, Histopathology, Hansen's Disease

I. INTRODUCTION

Leprosy, or Hansen's disease (HD), is an ancient affliction caused by Mycobacterium leprae, posing significant global health challenges, especially in India, Brazil, and Indonesia, which account for 80.2% of new cases. The worldwide prevalence is 0.25 per 10,000 people, with India alone contributing 59.8% of new cases (Boyle B et al., 2013; Narang T et al., 2022). HD primarily affects the skin and peripheral nerves but can impact multiple organs, leading to severe deformities and disabilities. The disease also inflicts profound social and psychological scars due to persistent stigma and isolation (Sermrittirong S and Van Brakel WH, 2014).

Effective classification systems, such as the Ridley Jopling and WHO classifications, are essential for understanding and managing HD (Jopling WH and Mc Dougall AC, 1996). Despite India's success in meeting the National Health Policy 2002 target of less than one case per 10,000 population by 2005, the annual new case detection rate (ANCDR) remains concerning, highlighting gaps in current control measures (NLEP annual report, 2007).

A comprehensive diagnostic approach is imperative, combining clinical assessments, slit skin smear examinations, and histopathological tests to ensure accurate diagnosis and prevent underdiagnosis of multi-bacillary patients. Moving forward, a multi-faceted strategy is needed to tackle HD. This includes refining diagnostic techniques, enhancing public awareness to reduce stigma, and intensifying research for better treatments. Global collaboration is crucial for

sharing knowledge, resources, and experiences (Vollset M, 2013; Luker V and Buckingham J, 2017).

By integrating medical expertise with socio-cultural understanding, we can aim to eradicate both the physical manifestations of Hansen's disease and the social prejudices associated with it. A holistic and inclusive approach is essential to ultimately eliminate Hansen's disease from public health concerns. Thus the study included patients newly diagnosed with Hansen's disease by studying their clinical profile, slit skin smear, and histopathological features, to establish correlations between the clinical manifestations and slit skin smear / histopathological findings across various types of Hansen's disease.

II. METHODOLOGY

The cross-sectional study included 50 newly diagnosed Hansen's disease patients of all ages and genders from the Dermatology, Venereology, and Leprology department. Written informed consent was obtained. Exclusions were patients already on anti-leprosy drugs, those with pure neuritic leprosy, or those who refused consent.

Data was collected via a structured questionnaire covering epidemiological details and comprehensive medical history. Patients were classified using the Modified Ridley Jopling Classification. Laboratory examinations included slit skin smears (SSS) and skin biopsies. SSS involved staining four sites (two from lesions, two from ear lobes) using the Ziehl Neelsen method, with a minimum of 100 oil immersion fields examined for low bacterial index (BI) slides and 25 fields for higher BI slides. The BI was calculated by averaging scores from the sampled sites. A skin biopsy from the most active lesion was stained with Hematoxylin and Eosin and the Fite method to examine granuloma type, character, and presence of acid-fast bacilli (AFB).

Data collection was standardized through a detailed proforma, ensuring systematic and cohesive documentation of epidemiological features, clinical presentations, dermatological and systemic examinations, and laboratory findings.

The details compiled from the selected cases were documented in Microsoft Excel. Descriptive statistics, such as means and standard deviations, were used to represent continuous data, while categorical data was expressed in frequencies and proportions. Statistical analysis was carried out using R-Software, employing appropriate tests of significance based on the nature of the data. A p-value below 0.05 was considered statistically significant, with adherence to all relevant rules of statistical tests.

III. OBSERVATIONS AND RESULTS

The study included 68% males (34) and 32% females (16). Most participants were aged 31-45 years (58%), with similar proportions among males (58.8%) and females (56.3%). Participants aged 46-60 years made up 20%, and those 16-30 years comprised 10%. Only 2 males were under 15 years old, and 4 participants were over 60. Family history of leprosy was reported by 6% (3 individuals), all under 20 years old, with no significant gender differences. (Table 1)

The study found plaques as the most common clinical presentation (44%), followed by loss of sensation (38%), macules and patches (32%), and papules and nodules (18%). Other manifestations, like sudden appearance and trophic ulcer, were evident in 8% of cases each. Deformities were observed in 6% of individuals, with no significant gender differences. (Figure 1)

The skin lesions were categorized and analyzed in the study. The most common types were multiple plaques (24%), single plaque (20%), multiple patches (18%), and single patch (14%). Regarding lesion numbers, 54% had more than five lesions, 28% had 2-5 lesions, and 18% had only one lesion. Most lesions had well-defined margins (56%) and normal surfaces (50%), followed by dry surfaces (24%) and dry, scaly surfaces (20%). Shiny lesions were rare (6%). Overall, lesion types, numbers, margins, and surfaces showed similar patterns between male and female participants in the study, with no significant difference between genders. (Table 2)

In the study, nerve involvement was assessed in all patients. The ulnar nerve was predominantly affected (78%), followed by the radial cutaneous nerve (54%), greater auricular nerve (40%), and common peroneal nerve (32%). Lesser involvement was seen in the anterior tibial nerve (22%) and posterior tibial nerve (20%). Comparing genders, a statistically significant difference was found only in ulnar nerve involvement ($p = 0.011$), more common in males. (Figure 2)

Most subjects (76%) in the study did not develop lepra reactions. Among those who did, type 2 reactions were most common, affecting 18% of cases, with 9 individuals affected (6 males, 3 females). Type 1 reactions were observed in 6% of cases, with 2 males and 1 female affected. No significant gender difference was found in the occurrence of lepra reactions, suggesting similar rates in both genders. (Figure 3)

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In the study, clinical diagnosis relied on cardinal signs, with subjects categorized using the Modified Ridley Jopling Classification. Most were diagnosed with lepromatous leprosy (34%), consistent across genders. Borderline tuberculoid leprosy (22%) followed, with similar distributions by gender. Slit skin smear examination showed varying AFB counts, but no significant gender differences were found. Histopathological examination confirmed diagnoses, with lepromatous leprosy (38%) most prevalent, consistent across genders. Other diagnoses included borderline tuberculoid leprosy (24%), tuberculoid leprosy (18%), borderline lepromatous leprosy (14%), and histoid type (4%). Despite differences in diagnosis sequence, gender distributions were similar. (Table 3)

The study correlated clinical diagnoses with slit skin smear findings. Tuberculoid leprosy was diagnosed in cases lacking AFB (100%), while mid borderline leprosy was identified in those with 2+ AFB (100%). Borderline lepromatous leprosy was diagnosed in cases with 4+ AFB (100%). Borderline tuberculoid leprosy predominated in cases with 1+ AFB (91.7%). Lepromatous leprosy was common in cases with 5+ or 6+ AFB. These findings validated clinical diagnoses in most cases, with statistical significance ($p < 0.001$). (Table 4)

The study also assessed the correlation between clinical diagnoses and histopathological findings in leprosy cases. Clinical diagnosis accuracy was highest for tuberculoid and histoid types (100.0%), but decreased for borderline tuberculoid (91.7%) and lepromatous (89.5%) types. Accuracy dropped notably for mid borderline (50.0%) and borderline lepromatous (77.8%) types. Misdiagnoses occurred, notably in mid borderline and borderline lepromatous cases. However, a significant association ($p < 0.001$) between findings supports clinical diagnosis validity in most cases. (Table 5)

Table 1: Gender wise distribution of characteristics of study subjects

Subjects (N=50)		Gender				Total (N=50)	
		Male (N=34)		Female (N=16)			
		N	%	N	%	N	%
Age group	<15 years	2	5.9%	0	0.0%	2	4.0%
	16-30 years	3	8.8%	2	12.5%	5	10.0%
	31-45 years	20	58.8%	9	56.3%	29	58.0%
	46-60 years	6	17.6%	4	25.0%	10	20.0%
	>60 years	3	8.8%	1	6.3%	4	8.0%
Family history	Yes	2	5.9%	1	6.3%	3	6.0%
	No	32	94.1%	15	93.8%	47	94.0%

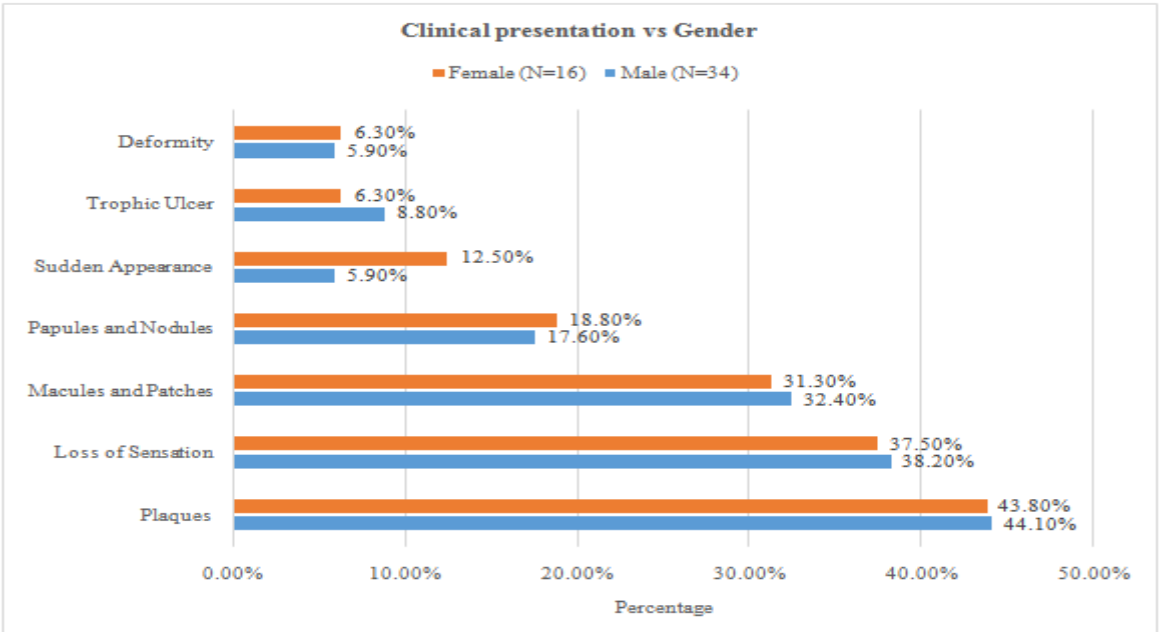

Figure 1: Gender wise distribution of clinical presentation

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Table 2: Gender wise distribution of characteristics of lesions

Subjects (N=50)		Gender				Total (N=50)	
		Male (N=34)		Female (N=16)			
		N	%	N	%	N	%
Type	Single patch	5	14.7%	2	12.5%	7	14.0%
	Multiple patches	6	17.6%	3	18.8%	9	18.0%
	Single plaque	7	20.6%	3	18.8%	10	20.0%
	Multiple plaques	8	23.5%	4	25.0%	12	24.0%
	Multiple lesions	8	23.5%	4	25.0%	12	24.0%
Number	Single lesion	7	20.6%	2	12.5%	9	18.0%
	2 to 5 lesions	9	26.5%	5	31.3%	14	28.0%
	>5 lesions	18	52.9%	9	56.3%	27	54.0%
Margin	Well defined	19	55.9%	9	56.3%	28	56.0%
	Well to Ill defined	4	11.8%	4	25.0%	8	16.0%
	Ill defined	11	32.4%	3	18.8%	14	28.0%
Surface	Normal	18	52.9%	7	43.8%	25	50.0%
	Dry	8	23.5%	4	25.0%	12	24.0%
	Dry and Scaly	6	17.6%	4	25.0%	10	20.0%
	Shiny	2	5.9%	1	6.3%	3	6.0%

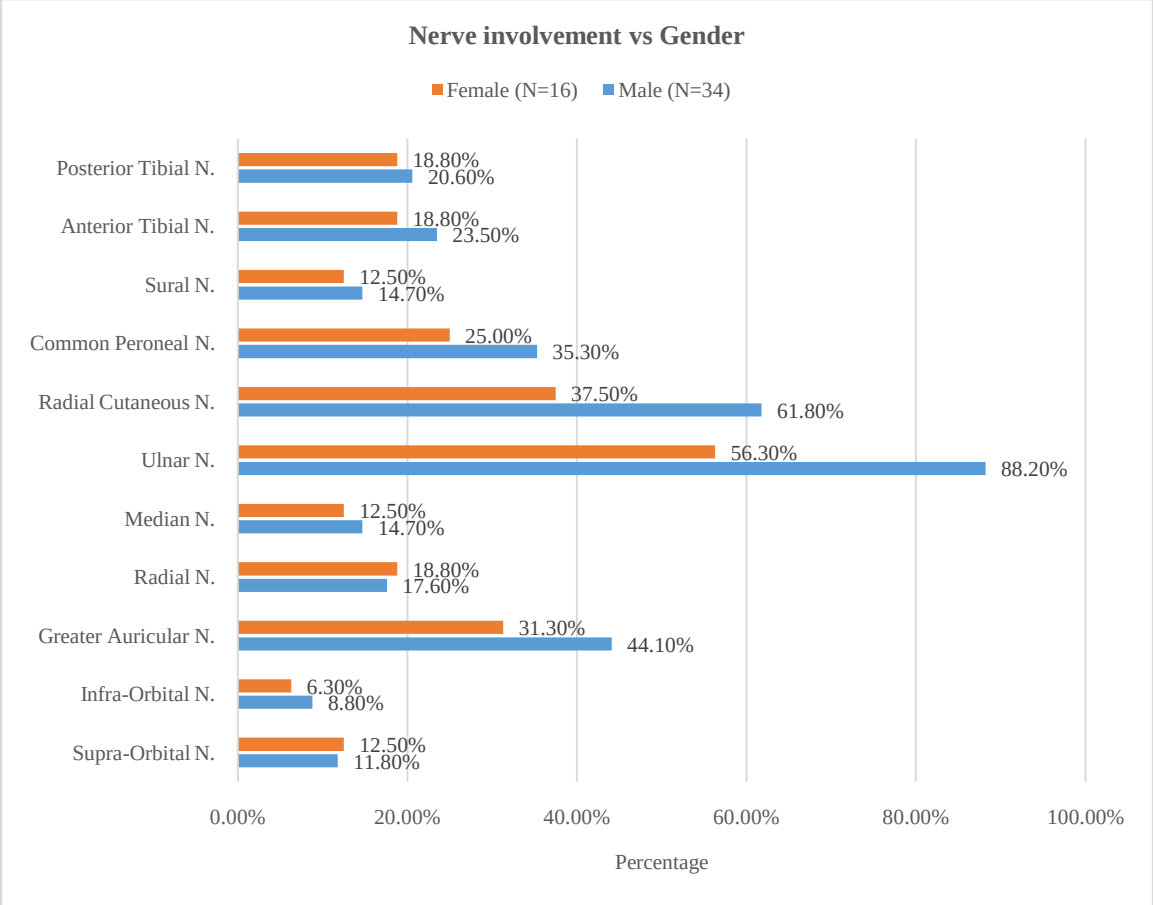

Figure 2: Gender wise distribution of nerve involvement

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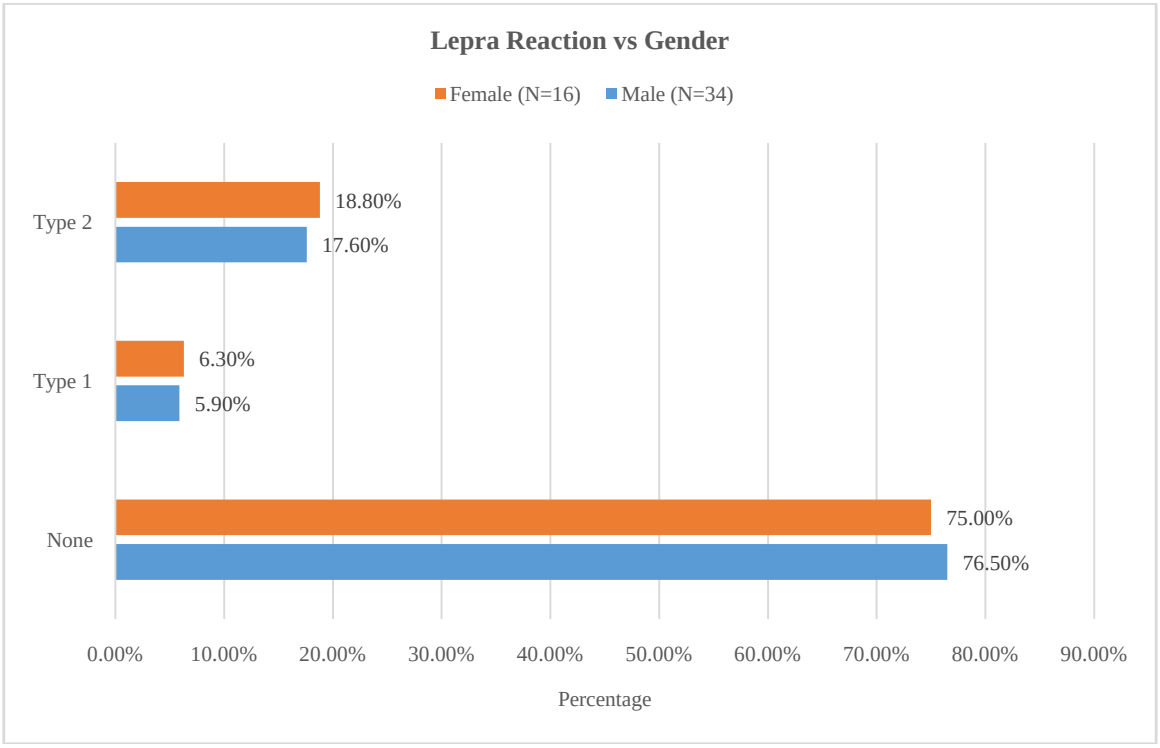

Figure 3: Gender wise distribution of lepra reactions

Table 3: Gender wise distribution of clinical diagnosis

Subjects (N=50)		Gender				Total (N=50)	
		Male (N=34)		Female (N=16)			
		N	%	N	%	N	%
Clinical diagnosis	TT	6	17.6%	3	18.8%	9	18.0%
	BT	8	23.5%	3	18.8%	11	22.0%
	BB	1	2.9%	1	6.3%	2	4.0%
	BL	6	17.6%	3	18.8%	9	18.0%
	LL	11	32.4%	6	37.5%	17	34.0%
	HL	2	5.9%	0	0.0%	2	4.0%
SSS findings	0	6	17.6%	3	18.8%	9	18.0%
	1+	8	23.5%	4	25.0%	12	24.0%
	2+	1	2.9%	0	0.0%	1	2.0%
	3+	0	0.0%	0	0.0%	0	0.0%
	4+	3	8.8%	1	6.3%	4	8.0%
	5+	12	35.3%	7	43.8%	19	38.0%
	6+	4	11.8%	1	6.3%	5	10.0%
HPE features	TT	6	17.6%	3	18.8%	9	18.0%
	BT	8	23.5%	4	25.0%	12	24.0%
	BB	1	2.9%	0	0.0%	1	2.0%
	BL	5	14.7%	2	12.5%	7	14.0%
	LL	12	35.3%	7	43.8%	19	38.0%
	HL	2	5.9%	0	0.0%	2	4.0%

Table 4: Correlation between the clinical profile and slit skin smear findings

Subjects (N=50)		Slit Skin Smear													
		0		1+		2+		3+		4+		5+		6+	
		N	%	N	%	N	%	N	%	N	%	N	%	N	%
Clinical	TT	9	100.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%

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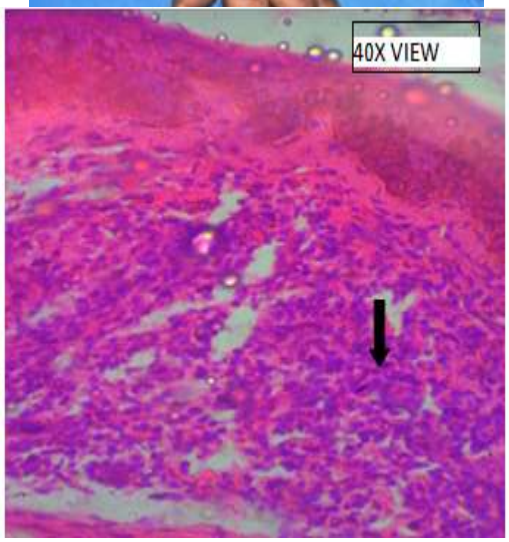
Diagnosis	**BT**	0	0.0%	11	91.7%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
	BB	0	0.0%	1	8.3%	1	100.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
	BL	0	0.0%	0	0.0%	0	0.0%	0	0.0%	4	100.0%	4	21.1%	1	20.0%
	LL	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	14	73.7%	3	60.0%
	HT	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	5.3%	1	20.0%

Table 5: Correlation between the clinical profile and HPE features

Subjects (N=50)		**HPE Features**											
		TT		**BT**		**BB**		**BL**		**LL**		**HT**	
		N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Clinical Diagnosis	**TT**	9	100.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
	BT	0	0.0%	11	91.7%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
	BB	0	0.0%	1	8.3%	1	100.0%	0	0.0%	0	0.0%	0	0.0%
	BL	0	0.0%	0	0.0%	0	0.0%	7	100.0%	2	10.5%	0	0.0%
	LL	0	0.0%	0	0.0%	0	0.0%	0	0.0%	17	89.5%	0	0.0%
	HT	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	2	100.0%

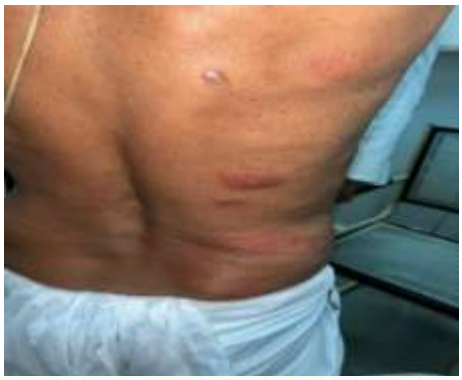
PICTURES &HISTOPATHOLOGICAL FINDINGS

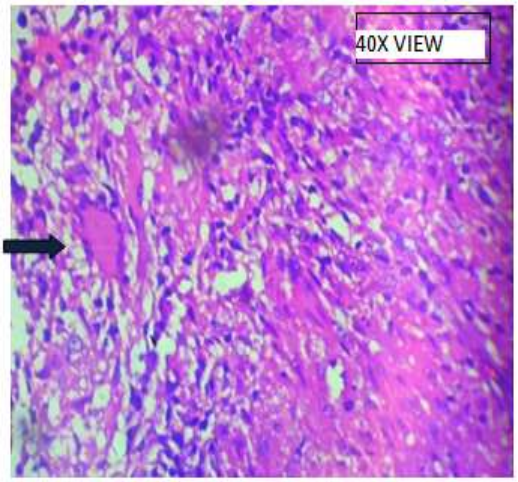
TUBERCULOID LEPROSY



H & E section showing well defined granulomas high up in dermis and also surrounding the neurovascular structures with absent Grenz zone

BORDERLINE TUBERCULOID LEPROSY





H & E section showing multiple poorly organized granulomas, composed of epitheloid cells, few scattered Langhan's giant cells and few lymphocytes follow the neurovascular bundles and periappendageal infiltrates

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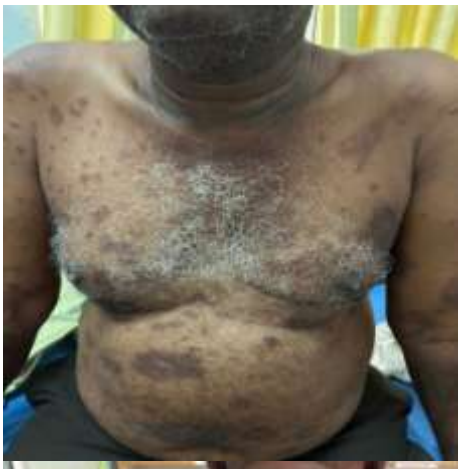
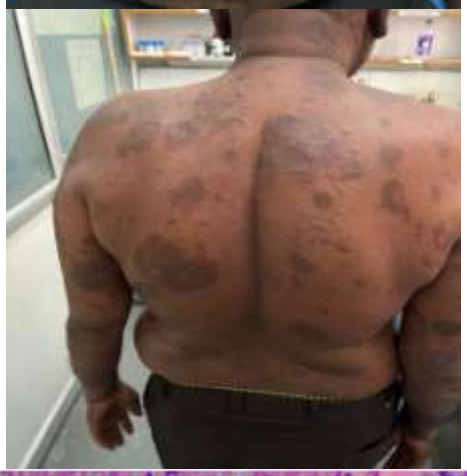
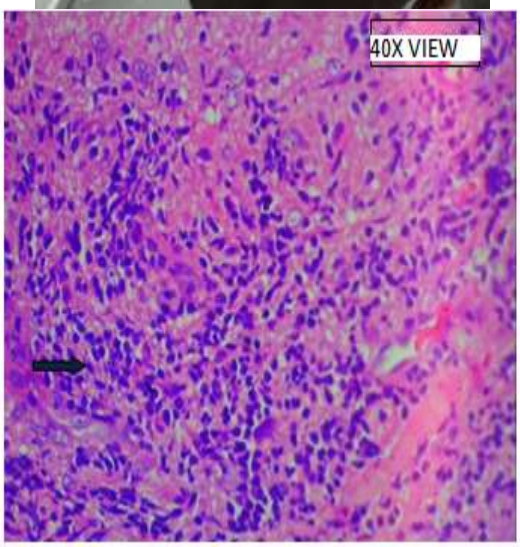
BORDERLINE BORDERLINE LEPROSY

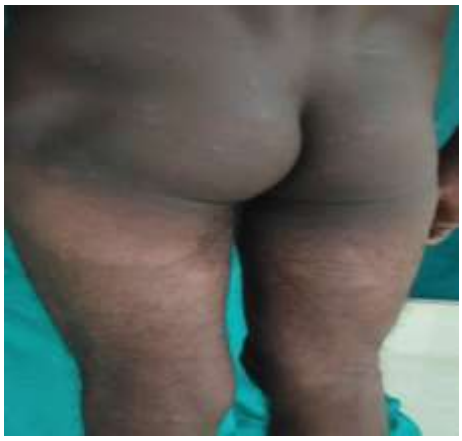


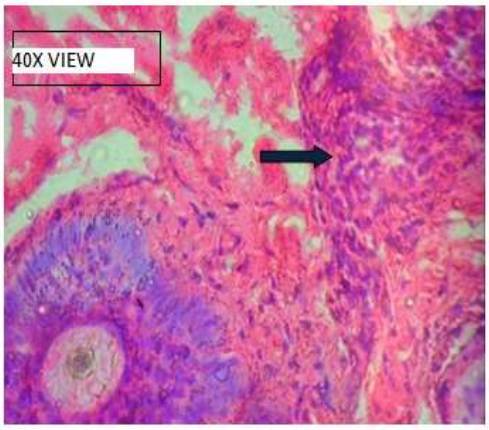




H & E section showing macrophages are uniformly activated to epitheloid cells but not focalized into distinct granulomas and lymphocytes are scanty

BORDERLINE LEPROMATOUS LEPROSY





H & E section showing multiple granulomas composed of lymphocytes and histiocytes with less prominent foamy cells and numerous fite positive AFB

LEPROMATOUS LEPROSY

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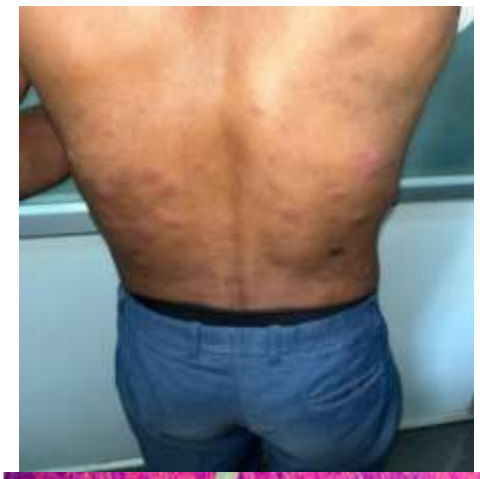
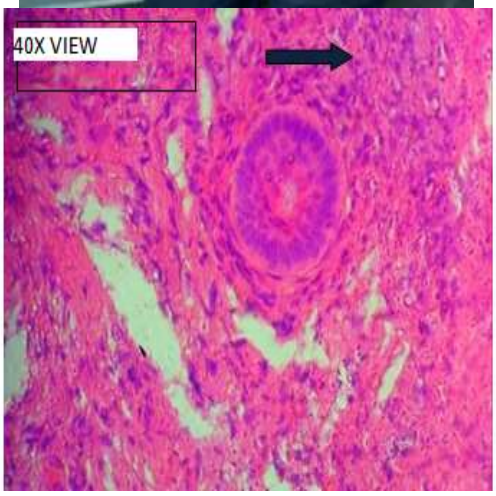
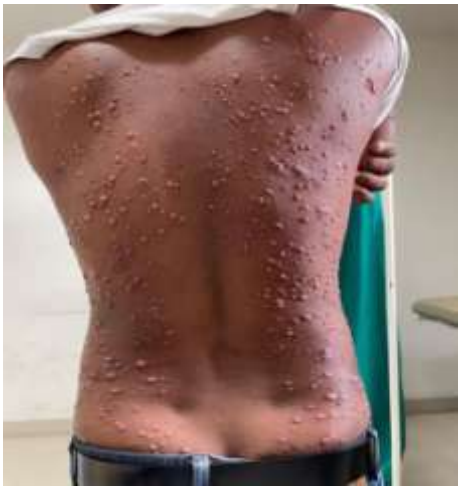
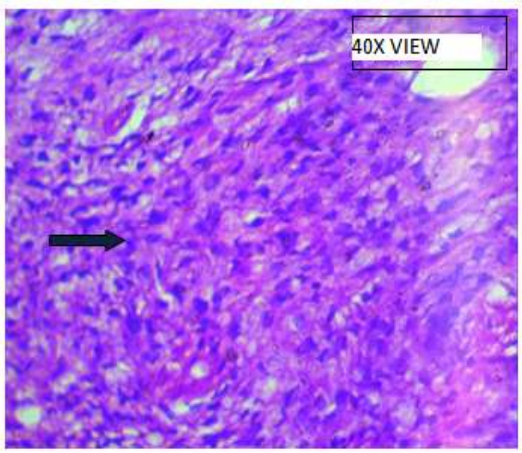




H & E section showing pandermal aggregates of foamy macrophages and scattered lymphocytes extending from superficial to deep dermis with neumerous fite positive AFB

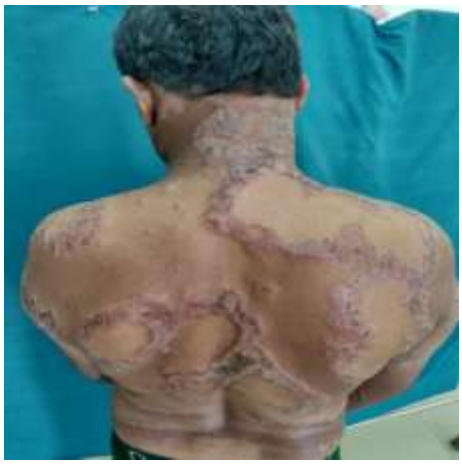
HISTIOID LEPROSY





H & E section showing abundant spindle shaped foamy histiocytes and lymphocytes with numerous fite positive AFB

TYPE 1 LEPRA REACTION



TYPE 2 LEPRA REACTION

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IV. DISCUSSION

Leprosy, or Hansen's disease, caused by Mycobacterium leprae, affects skin, nerves, mucous membranes, and various organs. Despite medical advancements, leprosy remains a global health concern. Precise diagnosis is vital for surveillance and management. However, in rural areas, limited access to specialists and diagnostic tools delays diagnosis and treatment, perpetuating transmission. Key tools like slit skin smear and histopathology aid accurate diagnosis. Research on the clinical-histopathological-bacteriological index relationship is lacking, crucial for understanding and treating leprosy effectively.

In the cross-sectional study, 50 newly diagnosed Hansen's disease patients were included from the Dermatology, Venereology, and Leprology department. Their informed consent was obtained. Data, including epidemiological details and medical history, was collected through a structured questionnaire covering demographics, symptoms, medical, family, and personal history.

The NLEP report for 2016-2017 indicated that females constituted 39.17% of newly detected leprosy cases in India, with a male to female ratio of 1.55:1. Consistently, the study found a predominant male population (68.0%), aligning with ratios from previous research such as Singh A et al., 2013 (1.50:1), Patel C and Nishal A, 2019 (3.28:1), Sinha R et al., 2023 (1.83:1), and Bhagyesh S et al., 2023 (1.42:1). This trend reflects documented patterns. Increased female leprosy awareness could be attributed to NLEP efforts, improved education, and heightened social awareness, indicating positive effects on early detection, treatment, and prevention efforts.

The study revealed that the most affected age group by leprosy was between 31 to 45 years, constituting 58.0% of the population, with only 4.0% below 15 years and 8.0% above 60 years. This mirrors previous research findings, indicating a predominance of leprosy among adults. Previous studies also reported similar mean ages; Singh A et al., 2013 (36.38 years), Hazarika N et al., 2021 (33.90 years), Naik SM et al., 2022 (36.50 years), and Mufti ST, 2023 (35.00 years). The data highlights the disease's impact on the economically active population, crucial for productivity, emphasizing the necessity of addressing leprosy in this demographic for both public health and economic stability.

The predominant clinical presentations in the study were plaques (44.0%) followed by loss of sensation (38.0%), with deformities being the least common (6.0%). These findings align with prior research by Gangwar D et al (2017), Patel C and Nishal A (2019), Bhagyesh S et al (2023), and Premalatha P et al (2016). They collectively indicate a pattern where hypopigmented patches and loss of sensation are common in leprosy patients, emphasizing early detection to prevent complications like deformities.

In the study, most patients (54.0%) presented with over five skin lesions, indicating widespread disease distribution. A significant proportion (56.0%) had well-defined lesion margins, and half (50.0%) displayed lesions with normal surface texture, highlighting clinical variability in leprosy presentation. Nerve involvement was universal, with the ulnar nerve most commonly affected (78.0%), followed by the radial cutaneous nerve (54.0%) and the greater auricular nerve (40.0%). Infraorbital nerve involvement was least common (8.0%). These insights into clinical characteristics and nerve involvement aid early diagnosis and targeted management to prevent further nerve damage and disabilities.

In the study, lepra reactions occurred in a minority (24.0%) of patients, with 18.0% experiencing type 2 reactions and 6.0% type 1 reactions. This variability in immune responses underscores the complex immunopathogenesis of leprosy. Slit skin smear examinations revealed diverse bacterial loads, with 38.0% showing high bacterial counts (5+), 24.0% indicating lower counts (1+), and 18.0% negative. These patterns mirrored previous studies by Singh A et al (2013), Atram MA et al (2020), and Hazarika N et al (2021). Discrepancies with other studies like Sinha R et al (2023), Bhagyesh S et al (2023), and Mufti ST (2023) may stem from population or methodological differences. Nonetheless, consistent findings across studies validate slit skin smear examination for assessing bacterial load in leprosy.

The study diagnosed leprosy patients using clinical exams with confirmation by histopathology and classification according to the Modified Ridley Jopling Scale. Lepromatous leprosy was most common (38.0%), followed by tuberculoid (24.0%), and least commonly mid-borderline (14.0%). This distribution differed from previous studies such as Patel C and Nishal A (2019), Atram MA et al (2020), Naik SM et al (2022), Sinha R et al (2023), potentially due to regional variations, patient demographics, or diagnostic methods. These findings highlight the need for standardized approaches to leprosy diagnosis and classification for improved global comparisons.

The study analysed the correlation between clinical diagnoses and histopathological examination (HPE) findings. Clinical diagnosis accuracy was high for tuberculoid leprosy and histoid type (100.0%). However, it slightly decreased for borderline tuberculoid and lepromatous leprosy (91.7% and 89.5%, respectively), and further dropped for mid-borderline and borderline lepromatous leprosy (50.0% and 77.8%, respectively). These results emphasize the importance of integrating clinical and histopathological assessments for accurate leprosy diagnosis and classification, highlighting the complexities involved and the need for comprehensive diagnostic protocols and ongoing healthcare professional training.

V. CONCLUSION

The study identified male predominance among 31 to 45-year-olds in Hansen's disease, with common presentations like plaques and sensory loss. The ulnar nerve is frequently involved, with notable lepra reactions. Skin lesions typically manifest as well-defined plaques with normal surface texture. Initial diagnoses rely on clinical examination, with lepromatous leprosy most prevalent, followed by borderline tuberculoid leprosy. Slit skin smear examinations support these diagnoses, revealing acid-fast bacilli. Histopathological confirmation generally aligns with clinical diagnoses, albeit with discrepancies, emphasizing the need for careful interpretation and ongoing efforts to enhance diagnostic accuracy and refine patient care.

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