Original Article

Histopathological Insights into Hypopigmentary Skin Lesions

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Abstract

Background: Skin is our body's largest organ and serves functions including protection, immunity, metabolism, sensation, and maintenance of physiological balance. It can be affected by a wide range of conditions, including infectious, inflammatory, and autoimmune disorders. While a detailed clinical history and examination provide valuable diagnostic clues, these are often insufficient alone, necessitating histopathological evaluation aided by special stains and immunohistochemistry. **Material and Methods:** This retrospective study was conducted in the Department of Pathology, SIMS, Hapur, UP, from January 2024 to December 2024. During this period 150 skin biopsies were received, out of which 50 were diagnosed as hypopigmented lesions and were included in the study. **Results:** Among the 50 cases of hypopigmented skin lesions, six distinct histopathological patterns were identified, with leprosy and its variants comprising the majority. **Conclusion:** A comprehensive clinical examination combined with a detailed history can lead to a correct diagnosis in many instances; however, histopathological examination is often indispensable, particularly when clinical findings are inconclusive.

Keywords: Hypopigmented lesions, skin, dermatopathology, Leprosy.

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Introduction

Hypopigmented cutaneous disorders are one of the most frequently encountered skin conditions in clinical practice. These disorders may arise from various pigmentary disturbances involving the number or function of melanocytes.[1,2]

The underlying etiologies include infections, inflammatory disorders, autoimmune diseases and other systematic disorders. Such varied etiologies make histological diagnosis particularly important as treatment for these disorders need to be specific. Accurate histopathological diagnosis is essential not only for therapeutic decisions but also for determining prognosis, particularly in potentially serious or infectious conditions such as leprosy.[3] Social stigma associated with such disorders contribute to psychological stress particularly in dark-skinned people.[4]

Histopathological examination of skin biopsies plays a crucial role in differentiating between various conditions. Key parameters assessed include the presence or absence of melanocytes, the type and pattern of inflammatory infiltrate, epidermal atrophy and dermal changes. Histopathology is particularly valuable when clinical features are equivocal.[5,6]

Common causes of hypopigmented skin lesions include pityriasis alba, pityriasis versicolor, vitiligo, leprosy, nevus depigmentosum, lichen sclerosis et atrophicus, discoid lupus erythematosus, parapsoriasis, post inflammatory hypopigmentation, pityriasis lichenoides chronica, lichen striatus.[7]

This study aims to analyse the reported cases with respect to age and gender distribution, anatomical pattern of lesion involvement, and the types of lesions observed, along with their defining histopathological features used for diagnosis.

Materials and Methods

This was a retrospective hospital based observational study conducted on archived skin biopsies received between January 2024 to December 2024 in the Department of Pathology, SIMS, Hapur, U.P.

During this study period a total of 150 skin biopsies were received from the outpatient department of dermatology. Out of which 50 were identified as hypopigmented lesions and were included in this study. Cases with generalised hypomelanosis and depigmented lesions were excluded from the study. Biopsies that were insufficient or showed autolysis were also excluded.

Data was collected from the histopathology requisition forms which included age, gender, clinical history, examination findings and a list of differentials.

Methodology: All specimens were fixed in 10% neutral buffered formalin and subjected to routine histological processing. Tissues were dehydrated in graded alcohol, cleared in xylene, and embedded in paraffin to prepare formalin-fixed, paraffin-

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embedded (FFPE) tissue blocks. Serial sections of 3–5 µm thickness were cut and stained with routine hematoxylin and eosin (H&E) stain for microscopic examination. In selected cases, special stains were used when indicated. Fite-Faraco stain was used in cases suspected of Hansen's disease to demonstrate Mycobacterium leprae, and Periodic Acid-Schiff (PAS) stain was used in a few cases to highlight fungal elements or basement membrane changes. Fite-Faraco stain was performed on 31 cases, with 13 yielding positive results, while Periodic Acid-Schiff (PAS) stain was used in 6 cases, of which 2 showed thickened basement membrane.

Microscopic examination was conducted to assess the pattern and type of inflammatory infiltrate, epidermal changes, pigmentary alteration, presence of granulomas, and other disease-specific histological features. Final diagnoses were made based on histopathological findings, with clinicopathological correlation where necessary. The collected data were organized and represented in the form of tables and charts, and descriptive statistics were used to express categorical variables such as age distribution, lesion types, anatomical sites involved, and histological diagnoses as frequencies and percentages.

Results

Out of 150 skin biopsies received during the study period, 50 cases were histologically diagnosed as hypopigmented skin lesions and were included in the study. The age and sex distribution is shown in [Table 1]. The most affected age groups were 21-30 and 11–20 years, comprising of 12 (24%) and 11 (22%) patients each, followed by the 31–40 years group (10 patients, 20%). Males (68%) were more frequently affected than females (32%), with a male-to-female ratio of approximately 2.1:1.

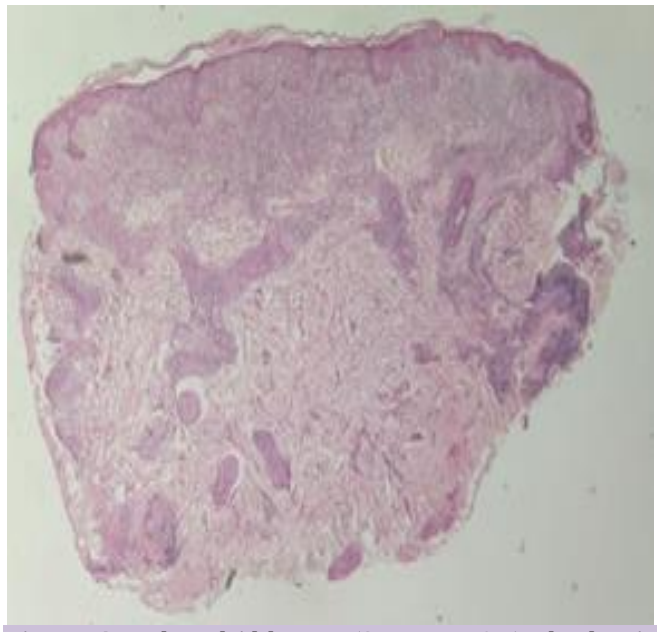

Figure 1A: Tuberculoid leprosy (Scanner, H&E) The dermis exhibits epithelioid cell granulomas comprising of lymphocytes, histiocytes and foamy macrophages. Granulomas are seen surrounding the nerve bundles as well as adnexal structures.

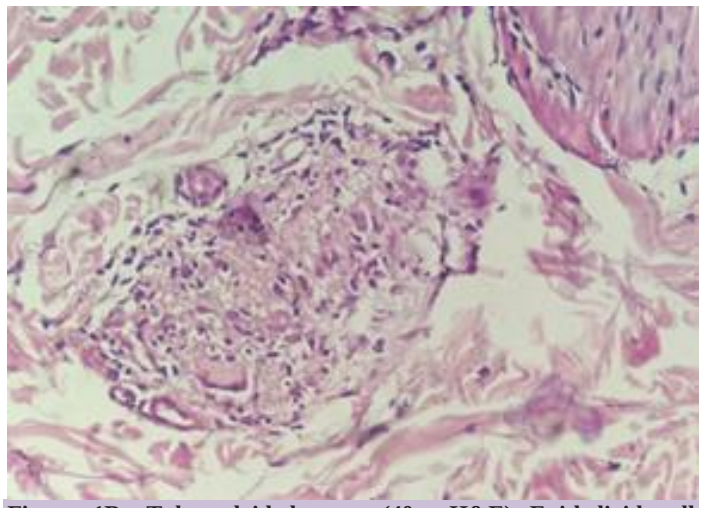

Figure 1B: Tuberculoid leprosy (40x, H&E) Epithelioid cell granulomas within the dermis are accompanied by occasional langhans type of giant cells.

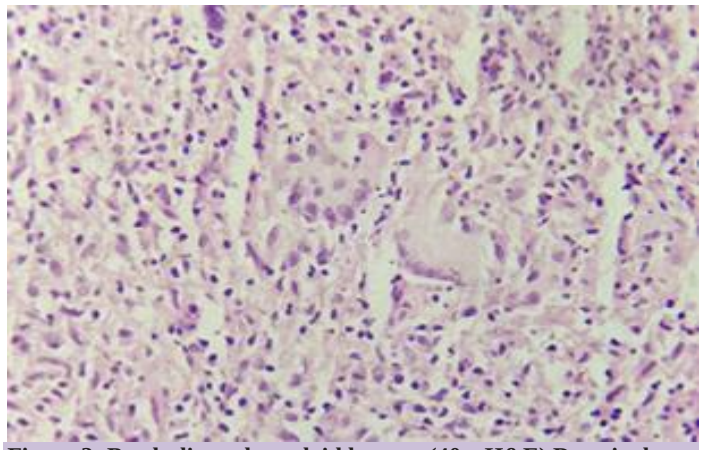

Figure 2: Borderline tuberculoid leprosy (40x, H&E) Dermis shows well-formed epithelioid cell granulomas circumscribed by a peripheral cuff of lymphocytes, with the presence of langhans type of giant cells.

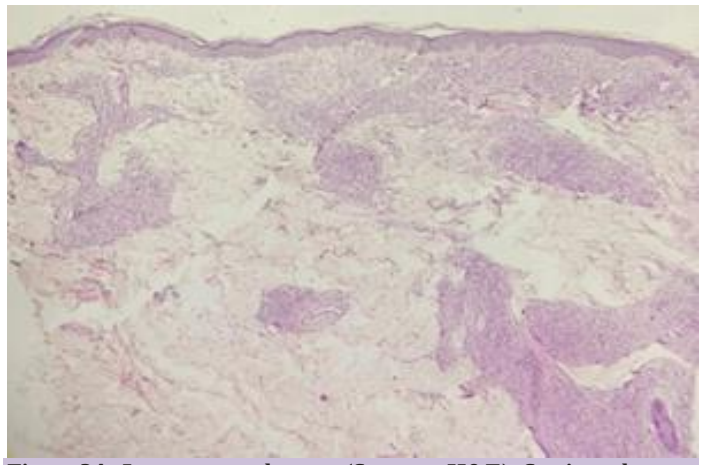

Figure 3A: Lepromatous leprosy (Scanner, H&E): Sections show an atrophied epidermis with a clear grenz zone. Dermis is extensively infiltrated by sheets and poorly defined collection of epithelioid histiocytes and numerous foamy macrophages. Perivascular and periappendageal infiltrate is also seen.

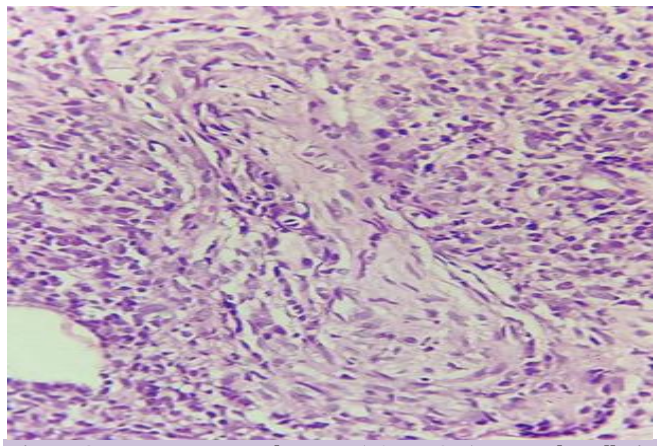

Figure 3B: Lepromatous leprosy (40x, H&E) Nerve bundle is seen infiltrated by Inflammatory cells with involvement of perineural sheath.

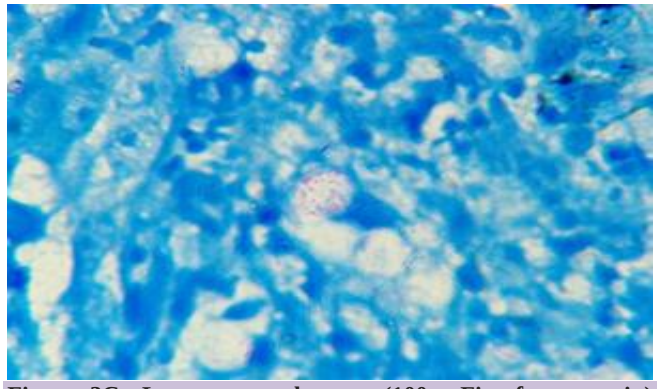

Figure 3C: Lepromatous leprosy (100x, Fite faraco stain) Numerous acid fast bacilli morphologically consistent with Mycobacterium leprae, were identified as slender, red-pink rod shaped bacilli predominantly located within macrophages often arranged in parallel bundles (globi).

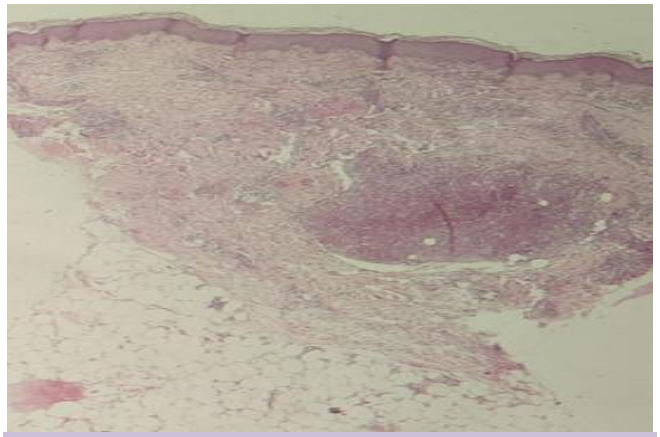

Figure 4A: Type 2 Lepra reaction (Erythema nodosum leprosum) (scanner, H&E) Sections show atrophic epidermis with an ill-defined grenz zone. The dermis shows chronic inflammatory cell infiltrate comprising of macrophages, epithelioid histiocytes, lymphocytes and admixed neutrophils. The infiltrate involves the perivascular and perineural region and adnexal structures. Other features include leukocytoclastia, dermal edema, folliculotropism and mixed inflammatory cell infiltrate extending into subcutaneous fat consistent with panniculitis.

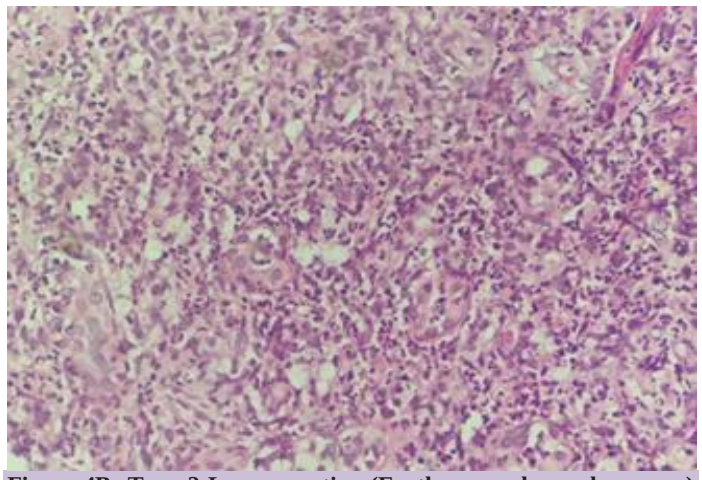

Figure 4B: Type 2 Lepra reaction (Erythema nodosum leprosum) (40x, H&E) Mixed inflammatory cell infiltrate is seen in the dermis.

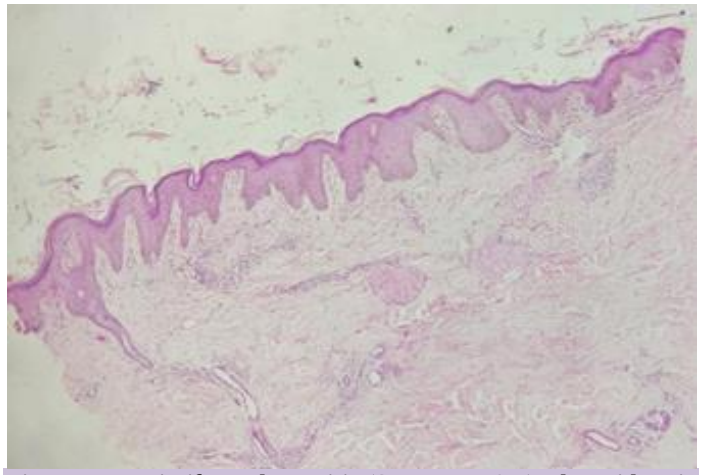

Figure 5: Psoriasiform dermatitis (Scanner, H&E) The epidermis shows irregular, slender, elongated and club shaped rete ridges with hyperkeratosis and acanthosis. The periappendageal region show mild chronic inflammatory cell infiltrate and focal dermal fibrosis.

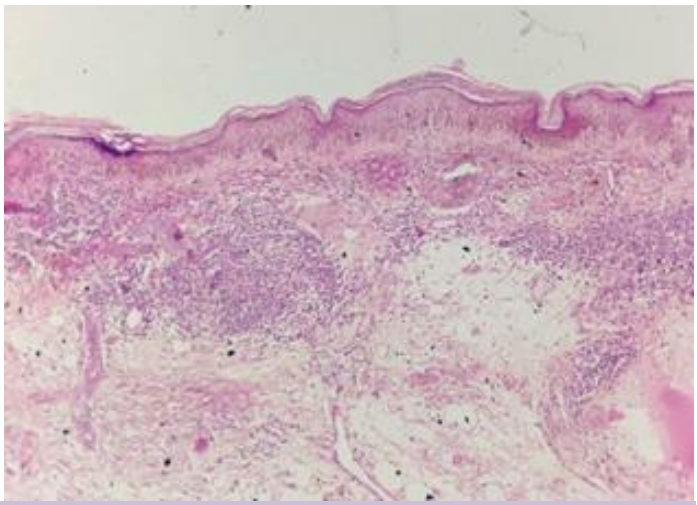

Figure 6: Discoid lupus erythematosus (10x, H&E) The epidermis exhibits hyperkeratosis, parakeratosis with marked thickening of basement membrane. Superficial dermis shows deposition of mucinous material. The deeper dermis shows lymphoplasmacytic infiltrate along with focal area of edema.

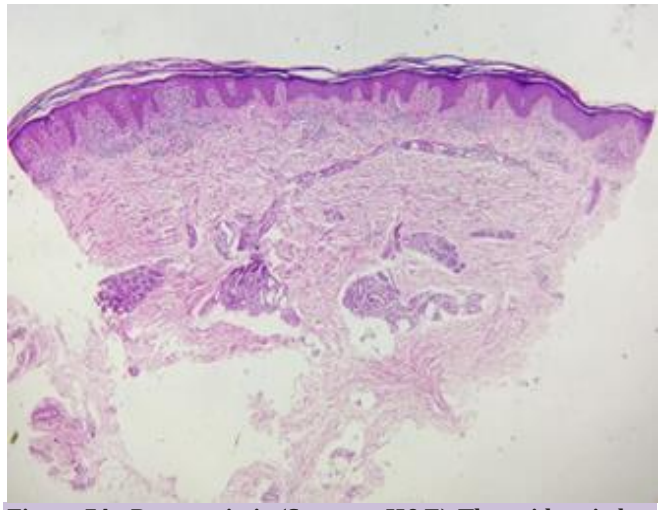

Figure 7A: Parapsoriasis (Scanner, H&E) The epidermis has variable sized rete ridges. Superficial dermis shows lymphocytic infiltrates.

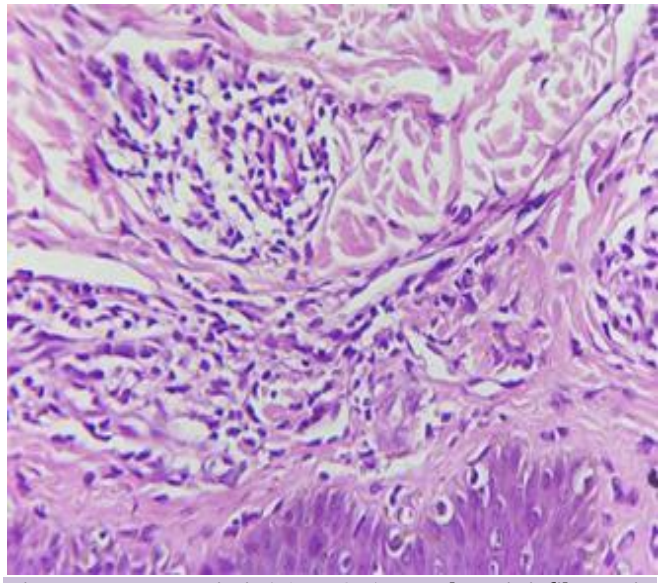

Figure 7B: Parapsoriasis (40x, H&E) Lymphocytic infiltrates in superficial dermis.

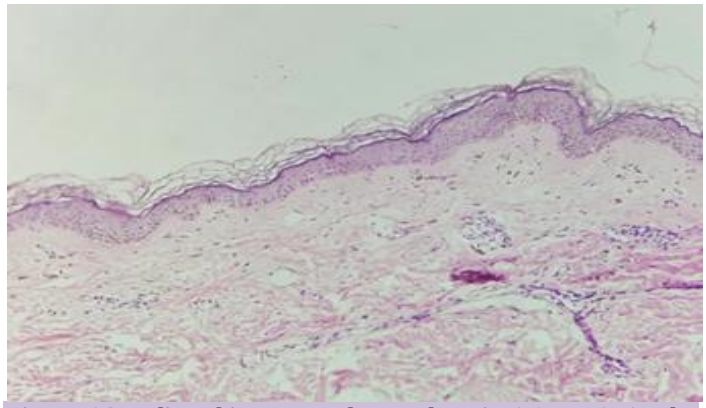

Figure 8A: Idiopathic guttate hypomelanosis (10x, H&E) The epidermis shows hyperkeratosis with keratin arranged in a basket weave pattern and focal epidermal atrophy. Focal loss of melanin pigment is noted in the basal layer.

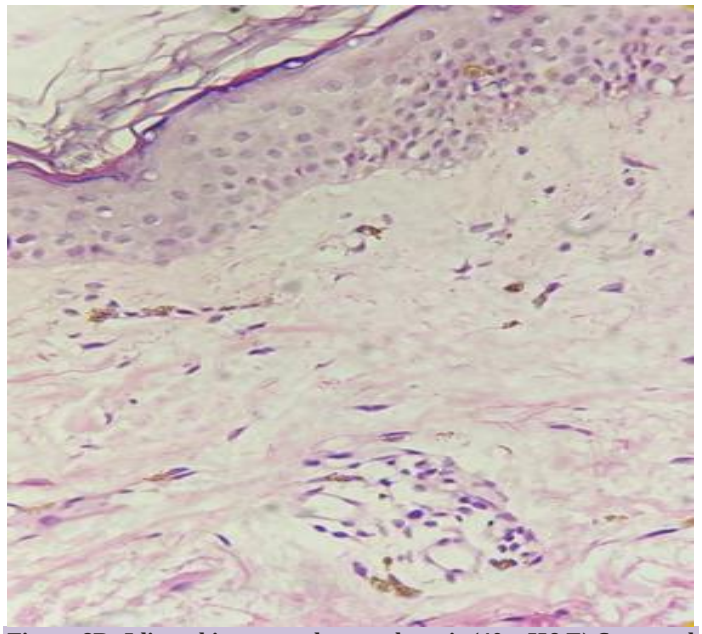

Figure 8B: Idiopathic guttate hypomelanosis (40x, H&E) Scattered melanophages within the epidermis consistent with pigment incontinence.

Table 1: Age and sex distribution of patients.

Age Group (Years)	Male	Female	Total	Percentage
0-10	-	-	-	0%
11-20	6	5	11	22%
21-30	5	7	12	24%
31-40	10	-	10	20%
41-50	3	2	5	10%
51-60	5	2	7	14%
61-70	3	-	3	6%
71-80	2	-	2	4%
Total :	34 (68%)	16 (32%)	50	100%

Table 2: Frequency of the common sites involved.

No.	Site	Incidence	Percentage
1	Head and neck	4 (tongue, scalp, cheek)	7.02%
2	Chest	-	0%
3	Back	15	26.32%
4	Upper limbs	23	40.35%
5	Lower limbs	10	17.54%

6	Abdomen	1	1.75%
7	Genitalia	-	0%
8	Unspecified	4	7.02%
	Total :	57	100%

The upper limbs were the most frequently affected site (40.5%), followed by the back (26.32%) and lower limbs (17.54%). Lesions involving the head and neck region were noted in 7.02% of cases which included the tongue, scalp, and cheek. In four cases (7.02%) the site of lesion was not specified in the history forms and was classified as 'unspecified'. Some patients presented with lesions at multiple anatomical sites, accounting for a total of 57 site entries across the 50 cases.

Table 3: Frequency of the diagnoses.

No.	Diagnosis	Incidence	Percentage
1	Leprosy	37	74%
2	Discoid Lupus Erythematosus	3	6%
3	Idiopathic guttate hypomelanosis	1	2%
4	Parapsoriasis	2	4%
5	Chronic non-specific dermatitis	1	2%
6	Psoriasiform lesion	6	12%
	Total	50	100%

As shown in [Table 3], leprosy was the most common diagnosis, observed in 37 cases (74%). Other diagnoses included, discoid lupus erythematosus (6%), idiopathic guttate hypomelanosis (2%), parapsoriasis (4%), chronic non-specific dermatitis (2%), and psoriasiform lesion (12%).

Table 4: Site-wise distribution of lesions in hypopigmentary diseases.

Site	Leprosy	Discoid lupus erythematosus	Idiopathic guttate hypomelanosis	Parapsoriasis	Chronic non-specific dermatitis	Psoriasiform lesion
Head and neck	1	3				
Chest						
Back	13		1			1
Upper limbs	19			2	1	1
Lower limbs	6					4
Abdomen				1		
Genitalia						
Unspecified	4					

[Table 4] shows site-wise distribution of lesions in various diagnoses. Majority of lesions in leprosy were found on limbs (58%) and the back (30%). All three cases of discoid lupus erythematosus involved the head and neck region (scalp and cheeks). Idiopathic guttate hypomelanosis presented as hypopigmented flat spots on the back. Parapsoriasis had lesions on upper limbs as well as abdomen. In chronic non-specific dermatitis case the lesions were on upper limb. Lower limbs were more affected in psoriasiform lesion.

Table 5: Distribution of types of lesion in leprosy.

S.No.	Type of lesion	Incidence with percentage
1	Tuberculoid Leprosy	3 (08.11%)
2	Borderline Tuberculoid leprosy	4 (10.81%)
3	Mid-borderline	8 (21.62%)
4	Borderline Lepromatous	1 (02.70%)
5	Lepromatous leprosy	7 (18.92%)
6	Indeterminate Leprosy	6 (16.22%)
7	Leprosy	4 (10.81%)
8	Lepra reaction (Type 2)	3 (08.11%)
9	Leprosy with treatment associated changes	1 (02.70%)
	Total :	37

Among the 37 cases of leprosy, the distribution of lesion types is shown in Table 5. The most frequent forms included mid-borderline leprosy (8 cases, 21.62%), lepromatous leprosy (7 cases, 18.92%), and indeterminate leprosy (6 cases, 16.22%). Other types included borderline tuberculoid leprosy, tuberculoid leprosy and reactional states. 4 cases were reported as leprosy without further classification, while 1 case was reported as leprosy with treatment-related changes.

Discussion

In the present study, leprosy constituted the majority of hypopigmented skin lesions (74%), reaffirming its status as a leading cause of such presentations in endemic regions. This finding is consistent with previous studies, including those by

Kumar et al. (2019),[8] and Sarkar et al (2017),[9] which similarly documented leprosy as the predominant etiology among hypopigmented dermatoses. The histopathological hallmark of leprosy—granulomatous inflammation with nerve involvement—proved to be a reliable diagnostic feature, supporting earlier observations by Job CK.[10] Importantly, these results underscore the continuing diagnostic value of skin biopsy in differentiating leprosy from other hypopigmented disorders, particularly in early or atypical cases where clinical findings may be inconclusive.

Psoriasiform lesions in this series often resembled pityriasis alba or early vitiligo due to their hypopigmented presentation. However, histopathological features—such as regular acanthosis, Munro's microabscesses, and parakeratosis—helped in confirming psoriasis. These findings are in agreement with Chandrashekar et al. (2018),[11] who also documented diagnostic challenges in early hypopigmented psoriasis, particularly in individuals with skin of color.

DLE, a chronic autoimmune dermatosis, presented with hypopigmented plaques that clinically overlapped with vitiligo. In the present study histopathological features included interface dermatitis, thickened basement membrane, follicular plugging, and periadnexal inflammation, consistent with observations by Mehta et al. (2016).[12] Although direct immunofluorescence was not available in all cases, routine H&E stains proved useful, as supported in earlier studies evaluating discoid lupus erythematosus (DLE).

Idiopathic guttate hypomelanosis (IGH) predominantly affects older individuals and is often misdiagnosed as early vitiligo or post-inflammatory hypopigmentation. Histological analysis revealed features such as epidermal thinning and reduced basal pigmentation, correlating with the findings of Bhat et al. (2015),[13] who emphasized the benign nature of IGH but stressed the importance of histological confirmation in atypical cases.

Lepra reactions—particularly Type 1 (reversal) and Type 2 (erythema nodosum leprosum)—posed diagnostic challenges due to overlapping inflammatory features. The histological findings in type 1 reaction were edema and intensified granulomatous inflammation while type 2 reactions demonstrated neutrophilic vasculitis. These were comparable to the descriptions by Ridley and Jopling and further supported by Rao et al. (2013).[14,15]

Compared to previous studies, we observed a relatively higher proportion of psoriasiform dermatitis and DLE, possibly reflecting a potential referral bias or demographic variation. Similar variability was noted by Ahmed et al. (2020),[16] who reported differing frequencies of DLE and pityriasis lichenoides depending on the study population.

A key strength of present study is the clinicopathological correlation across a wide spectrum of hypopigmented lesions, underscoring the limitations of clinical diagnosis alone. As emphasized by Patel et al. (2020),[17] histopathological assessment remains indispensable, especially in early or ambiguous presentations.

However, the present study had certain limitations, including unavailability of advanced modalities such as immunohistochemistry or PCR-based assays, particularly for atypical leprosy or early mycosis fungoides cases. Despite this, findings of this study support the role of early biopsy and routine histology in distinguishing infectious, autoimmune, and idiopathic causes of hypopigmented skin lesions.

Conclusion

Hypopigmented skin lesions comprise a diagnostically diverse group of conditions. The present study findings reaffirm the diagnostic value of clinicopathological correlation in hypopigmented lesions, particularly in settings where advanced modalities are not readily available. Early skin biopsy and microscopic assessment are particularly valuable in resource-limited settings allowing prompt and appropriate treatment. Findings of this study are largely consistent with published data from leprosy-endemic regions. However, regional variations in lesion spectrum highlight the importance of considering local disease prevalence while evaluating hypopigmented lesions. Further studies integrating molecular and immunological tools may refine the diagnostic approach, particularly in resource-limited environments.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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