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Original Research Article

# A Clinicopathological Study of Hypopigmentary Disorders of Skin

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**Abstract**

**Background:** Skin can be divided into two separate but interdependent layers the epidermis and the dermis. They are composed of varying type of cells with distinct functions like mechanical, photo protection, immunosurveilance, nutrient metabolism and repair. The intention of this study is to correlate the histopathological findings with clinical findings of hypopigmented disorders of skin to arrive at an accurate diagnosis.

**Material and Methods:** Present study was conducted at Department of Pathology associated with Department of Dermatology, NMCH, Patna, Bihar from October 2018 to March 2020. During the period of 18 months of study a total of 106 biopsies of skin, were received. Of these, 53 biopsies were hypopigmented lesions. This formed almost 50% of the skin biopsies received.

**Results:** Of the 53 cases, included in the study 35 were male and 18 were female. The maximum percentage of patients was between the age group of 40 to 60 years. The different types of clinical diagnosis observed in this study were totally 11. They were pityriasis versicolor, Hansen's disease, vitiligo, LSA, Lichen striatus, IGH, PLC, parapsoriasis, Woronoff ring of psoriasis, DLE and PMLE. The HPE evaluation was done for all cases and special stains and IHC were done for relevant cases. Clinicopathological correlation was observed in 86.7% of cases. Of which pityriasis versicolor showed 83.3%, Lichen striatus showed 50%, PLC showed 66.6% correlation and parapsoriasis showed 33.3%correlation.

**Conclusion:** Systematic approach of clinical, histopathological examination and Immunohistochemistry will provide an accurate diagnosis of hypopigmented disorders and thereby reducing the patient distress.

**Keywords:** Hypopigmented lesions, pityriasis versicolor, parapsoriasis, histopathological



## Background

Skin color is a vital and visible sociocultural feature of an individual. The human skin color depends upon the black-brown eumelanin and yellow-red pheomelanin [1]. Other significant contributors include the DNA, urocanic acid, and amino acids [2]. Altered skin pigmentation can result from increased or decreased melanin, abnormal melanin distribution, decreased hemoglobin, or deposition of exogenous substances. Hypopigmentation refers to any form of decreased pigmentation whereas

depigmentation describes the total loss of pigmentation, resulting in a whitish appearance. Hypopigmentation and depigmentation have been referenced in many ancient religious texts as a curse. Hypopigmentary disorders in darker skin individuals like Indians can be distressing to the patients and the family. These disorders cover a wide range of pathologies including infections, inflammatory disorders, autoimmune diseases, lymphoproliferative disorders, and sclerosing diseases. Histological diagnosis is very important because treatment and prognosis for these diseases are varied and specific.

These hypopigmentary disorders could be classified based on their etiology (congenital or acquired), age of onset (childhood or adulthood) and extent of lesions (localized or generalized). Further differentiation could be made on the basis of clinical findings, degree of pigment loss, and sites of involvement. The intention of this study is to correlate the histopathological findings with clinical findings of hypopigmented disorders of skin to arrive at an accurate diagnosis [2].

## Material and Methods

This prospective study was done at Department of Pathology, Nalanda Medical College and Hospital, Patna, Bihar from October 2018 to March 2020 (18 months). Collected samples were processed and reported in Department of pathology in NMCH.

### Inclusion Criteria

- The study included patients of pediatric as well as adult age group presenting with one or more hypopigmented lesions.
- Both scaly and non-scaly presentations were included.

### Exclusion Criteria

- Cases of chemical leukoderma and leukoderma secondary to topical applications were excluded.
- Cases with lesions only over the face and/or mucosa (due to increased vascularity)
- Cases with generalised hypomelonosis were also excluded from the study.

A total of 53 Patients attending the dermatology outpatient department with hypopigmented skin lesions were included for this study. After getting the consent, skin biopsy was taken for all the patients using punch biopsy of size 3.5mm. Classical, hypopigmented lesion was selected for biopsy. After anaesthetizing the area a biopsy was taken using a disposable punch. With minimal handling the taken biopsy was transferred to a 10% NBF (neutral buffered formalin) container with proper labeling.

The tissue was processed in the following sequence for obtaining paraffin embedded tissue sections; fixation by 10% NBF, dehydration by using ascending grades of alcohol of 50%, 70% and absolute alcohol, clearing by xylene and wax was infiltrated and finally the tissue was embedded in wax with proper orientation. Sections of 6 micron thickness were taken and stained with haemtoxylin and eosin stain. Special stains like PAS (per iodic acid schiff) were done for identifying fungus and fite faraco stain was done for identifying acid fast bacilli. Immunohistochemistry (IHC) was done for 11 cases selecting one case from each diagnosis using HMB 45 marker.

HMB 45 is a monoclonal antibody obtained from an extract of malignant melanoma which identifies oncofetal glycoconjuagte associated with immature melanosomes and probably related to the tyrosinase enzymatic system.

### Statistical Analysis

The collected data were analysed with IBM.SPSS statistics software 23.0 Version. To describe about the data descriptive statistics frequency analysis, percentage analysis were used for continuous variables.

## Results

Of these, 53 biopsies were hypopigmented lesions. This formed almost 50% of the skin biopsies received.

**Table 1: Frequency of the hypopigmented disorders**

| S. No. | Diagnosis | Incidence | Percentage |
|---|---|---|---|
| 1 | Pityriasis versicolor | 12 | 22.6% |
| 2 | Hansen's disease | 10 | 18.9% |
| 3 | Vitiligo | 7 | 13.2% |
| 4 | Lichen sclerosus et Atrophicus | 5 | 9.4% |
| 5 | Idiopathic guttate hypomelonosis | 4 | 7.5% |
| 6 | Lichen striatus | 4 | 7.5% |
| 7 | Pityriasis Lichenoides chronica | 3 | 5.7% |
| 8 | Parapsoriasis | 3 | 5.7% |
| 9 | Woronoff ring in Psoriasis | 3 | 5.7% |
| 10 | Discoid Lupus Erythematosus | 1 | 1.9% |
| 11 | Polymorphous Light Eruptions | 1 | 1.9% |
| Total | | 53 | 100 |

Pityriasis versicolor was the most common disorder showing 12 cases (22.6%), followed by Hansen's disease which were 10 cases (18.9%) and Discoid Lupus Erythematosus, Polymorphous Light Eruptions were the least observed, one case each (1.9%).

**Table 2: Distribution of lesions based on histopathological examination**

| S. No. | Diagnosis | Incidence (no: of cases) | Percentage |
|---|---|---|---|
| 1 | Pityriasis versicolor | 10 | 18.9% |
| 2 | Hansen's disease | 10 | 18.9% |
| 3 | Vitiligo | 7 | 13.2% |
| 4 | Lichen sclerosus et Atrophicus | 5 | 9.4% |
| 5 | Idiopathic guttate hypomelonosis | 4 | 7.5% |
| 6 | Lichen striatus | 2 | 3.8% |
| 7 | Pityriasis Lichenoides chronica | 2 | 3.8% |
| 8 | Parapsoriasis | 2 | 3.8% |
| 9 | Woronoff ring in Psoriasis | 3 | 5.7% |
| 10 | Discoid Lupus Erythematosus | 1 | 1.9% |
| 11 | Polymorphous Light Eruptions | 1 | 1.9% |
| 12 | Chronic nonspecific dermatitis | 6 | 11.2% |
| Total | | 53 | 100 |

In Histopathological examination also pityriasis versicolor and Hansen's were the most commonly diagnosed constituting about 18.9% and Discoid lupus erythematosus and polymorphous light eruptions were the least observed (1.9%).

The predominant age group involved was 41-60 years. About 16 cases were observed in this age group. The least age of

distribution observed was 61-80 years. 10 cases were seen in this age group. The patients under 20 years of age were 15 (28.3%). The pediatric cases seen were three in number.

Out of the total 53 study cases, 35 were male (66%) and 18 were female (34%) as shown in the chart 4. The age wise sex distribution was studied and the results were, sex distribution was equal among both sexes in the age group of 60 and above of 5 caseseach. Among the cases below 20 years of age there was male predominance. Of the15 cases below 20 years of age, 13 were male and 2 were female.

Of the 53 cases, the most common site involved was extremities followed by trunk. The Pityriasis versicolor and Hansen's showed multiple sites of involvement. Two cases were found to be seen on the extremities and chest in Pityriasis versicolor and one case of Hansen's was found to involve both the extremity and abdomen.

**Table 3: Frequency of the common sites involved**

| S. No. | Site | Incidence | Percentage |
|---|---|---|---|
| 1 | Chest and back | 14 | 26.4% |
| 2 | Extremities | 30 | 56.7% |
| 3 | Genitals | 5 | 9.4% |
| 4 | Abdomen | 4 | 7.5% |
| | Total | 53 | 100% |

The lesions were classified based on the size and shape of the lesions. Patch forms the most common type of lesion among the 53 hypopigmented lesions. Few lesions had 71 multiple forms of presentations. Two cases of Pityriasis versicolor showed both macules and patches in the same patient. The vitiligo lesions studied also were in multiple forms like macules and patches.

**Table 4: Distribution of the clinical presentation of the hypopigmentedlesions based on size and shape**

| S. No. | Site | Incidence | Percentage |
|---|---|---|---|
| 1 | Macule | 8 | 15.1% |
| 2 | Papule | 16 | 30.2% |
| 3 | Patch | 17 | 32% |
| 4 | Ring | 3 | 5.7% |
| 5 | linear | 4 | 7.5% |
| 6 | Combination | 5 | 9.5% |
| | Total | 53 | 100% |

The lesions were classified based on the surface of the lesions into scaly and non-scaly lesions.

**Table 5: Classification of the lesions based on the surface**

| Disease with scaly lesions | Diseases with non-scaly lesions |
|---|---|
| Pityriasis versicolor | Hansen's |
| Pityriasis lichenoides chronica | Vitiligo |
| Psoriasis | Idiopathic guttate hypomelonosis |
| Polymorphous light eruptions | Lichen sclerosis et atrophicus |
| Lichen striatus | Discoid Lupus Eryphematosus |
| Parapsoriasis | |

**Table 6: Distribution of the lesion based on the surface**

| Type of lesion | Incidence | Percentage |
|---|---|---|
| Scaly lesion | 16 | 30.1% |
| Non scaly | 37 | 69.8% |

Among the hypopigmented lesions the non-scaly lesions formed the majority of about 69.8% and the scaly lesions contributed to 30.1%.

**Table 7: Distribution of types of lesion in leprosy**

| S. No. | Type of lesion | Incidence |
|---|---|---|
| 1 | Early indeterminate type | 2 |
| 2 | Tuberculoid leprosy | 2 |
| 3 | Mid Borderline leprosy | 2 |
| 4 | Borderline lepromatous leprosy | 1 |
| 5 | Lepromatous leprosy | 2 |
| 6 | Lepra reaction | 1 |
| | Total | 10 |

**Table 8: Clinicopathological correlation**

| S. No | Diagnosis | Clinical diagnosis incidence | Clinicopathological correlation | Percentage |
|---|---|---|---|---|
| 1 | Pityriasis versicolor | 12 | 10 | 83.3 |
| 2 | Hansen's disease | 10 | 10 | 100 |
| 3 | Vitiligo | 7 | 7 | 100 |
| 4 | Lichen sclerosus | 5 | 5 | 100 |
| 5 | Idiopathic guttate hypomelonosis | 4 | 4 | 100 |
| 6 | Lichen striatus | 4 | 2 | 50 |
| 7 | Pityriasis lichenoides chronica | 3 | 2 | 66.6 |
| 8 | Parapsoriasis | 3 | 1 | 33.3 |
| 9 | Woronoff ring in psoriasis | 3 | 3 | 100 |
| 10 | Discoid Lupus erythematosus | 1 | 1 | 100 |
| 11 | Polymorphous Light eruptions | 1 | 1 | 100 |
| | Total | 53 | 46 | 86.7 |

Clinicopathological correlation of all the hypo pigmented lesions, which was 86.7%. Of this Pityriasis versicolor showed 83% correlation, PLC showed 66.6% correlation, lichen striatus had 50% correlation and 33.3% correlation in parapsoriasis and 100% correlation in other diagnosis. The clinically diafgnosed parapsoriatic cases showed non specific findings in histopathology in 2 cases and the diagnosis was excluded by IHC, as there was normal immunoreactivity with HMB45 when compared with normal skin.

## Discussion

Acquired hypopigmentary disorders encompass a significant group of disorders that affect Indians. The incidence of hypopigmented lesions among the skin biopsies received was 50% in this study as compared to Yalla ASD *et al* Study [3] where the incidence was 27.3%.

The relative incidence of the various hypopigmented lesions were compared with other similar studies and were found to be concordant. Pityriasis versicolor was the most common disorder and the relative incidence of the hypopigmented lesions studied compared to Deepadarshan K *et al* [4] study.

The etiology of these disorders ranges from infections, autoimmune processes, sclerosing diseases to lymphoproliferative disorders. In this study, hypopigmentary disorders due to infections have contributed to 37.7%, autoimmune disorder contributed to 30.1%, sclerosing diseases for about 9.4%, post inflammatory conditions include 5.6%, and genetic disorder contributed 1.9%. Histological diagnosis is essential as treatment differs for these disorders.

Among these disorders pityriasis versicolor and Hansen were more common in men which were in concordance with the study of Ghosh SK *et al* [5]. The predominant age group affected was 41-60 years (32.1%) in this study, which differed from the study of Deepadarshan K *et al* that showed 21-30 years as the most common age group involved 27 and Yalla ASD *et al* study showed predominant age group distribution between 30 to 40 years.

In the present study, pityriasis versicolor was the most common disorder which was concordant with previous studies. Usually pityriasis versicolor is observed in more physically active younger individuals. This study also proved the fact. Of the 10 cases, 6 were male and 4 were female. Histopathological examination (HPE) of these lesions showed one case with hyperplasic epidermal change, two cases with acanthosis and all the cases showed mild lymphocytic infiltration in the dermis, similar to the study of Abdulwahab S *et al*. [6].

Second most common was Hansen's disease. Among the 10 cases, 6 were male and 4 were female. HPE of these lesions revealed epidermal atrophy (80%) in all the cases except two cases, whereas epidermal atrophy was 60% in K SS *et al* study [7]. All the cases showed periadnexal lymphocytic infiltration, and (50%) of the cases showed granulomas in the dermis. The clinicopathological picture is determined by the equilibrium between the agent and the host resistance. Skin has different pathophysiological subunits which cause some local modulation of the central host response as a result of which there are different grades of resistance and hence different clinicopathological responses in different areas. As Pandya A *et al* [8] concluded in their study, that histopathological examination should be carried out in all cases of leprosy to arrive at a definite diagnosis of leprosy and to classify the type of the disease. The different subtypes in Pandya A *et al* study are compared with this study.

Study on histopathological changes in lesions of vitiligo by Nagaral GV *et al* [9] showed acanthosis, and mild perivascular lymphocytic infiltration in all cases, whereas our study showed the following changes; 57% showed acanthosis and spongiosis, 43% showed keratinocyte degeneration, and all the 7 cases showed lymphocytic infiltration in the dermis (lymphocytic infiltration in papillary dermis in 2 cases, periadnexal lymphocytic infiltration in remaining 5 cases.

The IHC of vitiligo lesion revealed absence of melanocytes confirming with Benzekri L *et al* [10] study where he stated the depigmentation of vitiligo results in a progressive and chronic melanocyte loss with rare melanocytes occasionally remaining in the epidermis or the hair follicle reservoirs. Destruction by immune

infiltrates in close contact with melanocytes within microvesicles and/or detachment of melanocytes followed by their transepidermal elimination should be regarded as possible mechanisms of chronic loss of pigment cells. In this study the lesions were all macules and patches with ill-defined borders with absence of melanocytes in HPE. Benzekri L *et al* in his other study [11] stated that hypomelanotic poorly defined border lesions correlated with active lesion and amelanotic sharply demarcated border lesions correlated with stable lesions. So the lesions studied in the present study were active lesions.

Lichen Sclerosis et Atrophicus had female preponderance in Dalal V *et al* study [12] but in this study male preponderance was observed. All the cases showed epidermal atrophy (except one case) and collegenization, lymphocytic infiltration in dermis which was concordant with Rambhia K *et al* study [13]. One study by Velazquez *et al* states lichen sclerosus associated with penile carcinoma showed a low grade squamous intraepithelial lesion suggesting LSA may be a precancerous lesion particularly those not associated with human papilloma virus. So, early and prompt diagnosis of LSA is mandatory.

In the current study, all the cases of Idiopathic Guttate Hypomelonosis showed epidermal atrophy, focal loss of melanocytes and loss of rete pegs without any dermal changes. These findings were concordant with Joshi R *et al* study [14] and differed with Shin MK *et al* study [15] which documented elastic changes in papillary dermis.

The HPE findings of the lichen striatus were spongiosis, exocytosis of lymphocytes and focal parakeratosis and superficial perivascular lymphocytic infiltrate in the dermis. Lichenoid eruptions represent a heterogeneous group of conditions. The spectrum of clinical diseases which is related to the lichenoid tissue reaction is wider. Most of the components of the lichenoid spectrum like lichen planus, lichen nitidus exhibit basal cell damage and a band-like lymphocytic infiltrate that hugs the dermo epidermal junction however, there are subtle differences that define the particular variant like lichen striatus where, focal band like lymphocytic infiltration seen. In the present study two cases showed focal band like lymphocytic infiltration in the upper dermis which were concordant with clinical diagnosis of lichen striatus. Other two cases did not show the findings and diagnosed as chronic non specific dermatitis. So the clinicopathological correlation was only in 505 cases. Zhang Y *et al* [16] in his study stated parakeratotic finding in 57% of cases wherein Maheswari GR *et al* study [17] parakeratotic finding was 80%. In this study there was no parakeratosis but other diagnostic findings were observed.

Of the 3 cases of pityriasis lichenoides chronica and 3 parapsoriasis cases seen clinically, 2 cases of PLC were concordant histologically and one case was diagnosed as parapsoriasis. Of the 3 cases of parapsoriasis only one correlated histologically and other 2 were diagnosed as chronic non specific dermatitis. Both the diseases are clonal T cell disorders and were found to be associated with cutaneous T cell lymphoma. A comparative clinicopathological study on pityriasis lichenoides chronica and parapsoriasis was conducted by Benmaman O *et al* [18], the findings were, SPP was clinically characterized by scaly oval plaques on the trunk and proximal aspect of extremities. Spongiosis was the salient histopathological feature, with absence of fibrosis or melanophages. PLC presented with a scaly papular eruption over the trunk and extremities and histologically was characterized by an interface dermatitis Nair P *et al* [19] in his study of pityriasis

lichenoides clinically observed hypopigmented macules in all the 39 cases. Subsequent HPE revealed hyperkeratosis, atrophy, parakeratosis, acanthosis, exocytosis spongiosis, basal cell vacoualtion and perivascular infiltrate in the dermis. In this study on hypopigmented pityriasis lichenoides chronic similar histological findings were observed in 2 cases.

El-Dourouti *et al* [20] in his 7 year study of 34 hypopigmented disorders concluded that the hypopigmented parapsoriasis was a new variant of the parapsoriasis family and showed histological features of small plaque parapsoriasis. In this study also, 3 cases of new variant of hypopigmented parapsoriasis was observed clinically and one case correlated histologically.

In the current study, 3 cases of psoriatic patients showed hypopigmentation around the treated plaques. HPE of these hypopigmented lesions were consistent with psoriasis. Clinically, the hypopigmentation around the treated psoriatic plaques in this study was similar to Penneys NS *et al* study [21].

In this study, only one case of discoid lupus erythematous (DLE) was observed. HPE of the lesion showed vacuolar degeneration of keratinocytes, basement membrane thickening, loss of melanocytes, lymphocytic infiltration in dermo-epidermal junction and interstial mucin deposition. Karumbaih *et al* [22] in his study of 9 cases of DLE observed perivascular and periappendageal lymphocytic infiltration in the dermis, in addition to the above findings.

Eby chacko *et al* study [23] showed the incidence of hypopigmented polymorphous light eruption (PMLE) cases as 43%. In this study also one case of hypopigmented PMLE was observed which showed spongiosis, perivascular and periappendageal lymphocytic infiltration in dermis in HPE. These diagnostic changes of PMLE have also been documented in Prasad *et al* study [24]. This hypopigmentation may be a post inflammatory lesion

Chug *et al* [25] had conducted clinico-pathological correlation study of acquired hypopigmentary disorders in 50 patients. The overall clinico-pathological correlation in their study was 80%. In this study, there was 86.7% correlation in 53 cases.

The principles of immunohistochemical analysis were first conceptualized by Coons *et al* [26]. Generally, Immunohistochemistry is done for confirming the hypopigmented disorders in cases with diagnostic dilemmas. But, here it was done to classify the hypopigmented disorders as melanopenic or melanocytopenic in addition to confirming the diagnosis. The melanocytopenic disorders were devoid of melanocytes and the current study showed vitiligo and DLE to be melanocytopenic. Seleit l *et al* [27] and Franca AFE da C *et al* [28] showed vitiligo and DLE were melanocytopenic with HMB 45 marker in their studies respectively. When there is a dilemma between vitiligo and other close differentials like pityriasis versicolor, LSA, pityriasis alba this marker can be used. The melanopenic disorders show normal number of melanocytes but with hypomelanisation, and this finding helps in differentiating the depigmented lesions from others. HMB45 study showed reduced immunoreactivity in melanopenic cases and nonimmunoreactivity in melanocytopenic cases.

## Conclusion

Therefore clinical diagnosis of hypopigmented disorders alone is never specific and cannot be used as a single diagnostic tool for confirmation. Histopathological examination helps in arriving at a specific etiology and good clinicopathological correlation. Furthermore, Immunohistochemistry helps in differentiating between melanopenic or

melanocytopenic and in confirming diagnosis. Hence, a systematic approach of clinical, histopathological examination and Immunohistochemistry will provide an accurate diagnosis of hypopigmented disorders and thereby reducing the patient distress.

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