



## FROM CLINIC TO MICROSCOPE: BRIDGING THE GAP IN HYPERPIGMENTATION DIAGNOSIS-A RETROSPECTIVE OBSERVATIONAL STUDY AT A TERTIARY CARE CENTRE IN CENTRAL INDIA.

### Pathology

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### ABSTRACT

Pigmentary skin lesions are a cosmetic as well as a diagnostic concern. Hyperpigmentary skin lesions have a significant overlap in their clinical presentation because of their varying underlying etiologies. Thus, a detailed histopathological examination becomes essential for an accurate diagnosis of these lesions to establish a targeted and effective treatment. A 1year retrospective observational study was conducted in the Department of Pathology in a tertiary care institute in central India. Punch biopsies of hyperpigmentary skin lesions of patients from all ages and both genders were studied and subjected to routine histopathological processing and staining. Special stains and IHC was done wherever required. Out of 168 cases studied, maximum number of lesions were observed in 5thdecade with slight female predominance. The most common site of involvement was lower limb (50,29.7%). Majority cases were non neoplastic (137, 81.5%) followed by benign 29 (17.26%) and malignant 2 (1.1%) lesions. Lichen planus and its variants 25 (14.88%) was the most common lesion followed by prurigo nodularis 19 (11.30%), ashly dermatosis 12 (7.14%), seborrheic keratosis 11(6.54 %). A positive correlation was seen in 95.9% cases and negative correlation in 4.10% cases. A variety of hyperpigmented skin lesions have significant overlap in clinical presentation. Histopathological examination becomes imperative especially in neoplastic malignant cases which can be mistaken for benign non neoplastic conditions clinically. Thus, it emphasizes the utility of histopathology in diagnosing hyperpigmentary lesions with clinicopathological correlation for accurate diagnosis and effective management and patient care.

### KEYWORDS

Histopathology, Skin, Hyperpigmentation, Lichen planus

#### INTRODUCTION:

Acquired pigmentary disorders are found all over the world, but can be particularly distressing in patients with skin of color. These hyperpigmentary disorders have a significant overlap in their clinical presentations because of varying etiologies including inflammatory, infective, neoplastic; making their precise diagnosis and effective management a priority both for the patients and clinicians. In present study we describe and discuss the utility of histopathology in the diagnostic work of hyperpigmentary lesions. The differential diagnosis of these lesions can be narrowed down by careful clinical examination and studying subtle histomorphological parameters for an accurate diagnosis.[1]

#### MATERIALS AND METHODS:

Present study was a 1year retrospective observational study in a tertiary care hospital. Total 168 patients having hyperpigmented skin lesions were selected. After informed consent, punch biopsies of skin lesions were taken, fixed in formalin and sent for histopathology accompanied by all clinical details. Histopathological examination with routine staining H&E was done. Special stains and IHC were done whenever required. Final diagnosis was noted with the consensus of 2 pathologists.

**Inclusion Criteria:** Skin biopsies of all patients presenting with hyperpigmented skin lesions.

**Exclusion Criteria:** Inadequate and inconclusive biopsies.

#### RESULT:

In a period of 1 year, total 168 patients were studied, 83(49.40%) were males, 85(50.59%) were females. Majority patients presenting with hyperpigmented skin lesions (40, 23.80%) belonged to the age group of 41-50 years of age. Age range was 3-82 years. [Table 1]

Most common site involved in non-neoplastic cases was lower limb (48, 28.5%). Majority of the benign and malignant lesions were found on head & face (9, 5.3%) and chest & abdomen (1,0.5%) respectively.

Amongst the total cases, 137 (81.5%) cases were non neoplastic, 29 (17.26%) cases were benign, 2 (1.1%) cases were malignant [Table 2]. Lichen Planus and its variants (25, 14.88%) was the overall most common lesion, followed by prurigo nodularis (19,11.33%), ashly

dermatosis (12,7.14%), seborrheic keratosis (11,6.54%). A detailed histomorphology of epidermis and dermis of all the lesions were studied [Table 3 and 4]. Out of 25 cases of lichen planus and its variants, 19 (76%) cases showed hyperkeratosis, 25 (100%) cases showed band like lymphocytic inflammatory infiltrate and basal cell degeneration [Figure 1]. Out of 19 cases of prurigo nodularis, 17 (90%) cases showed hyperkeratosis, 16 (87%) cases showed acanthosis, 17 (90%) cases showed pseudoepitheliomatous change, 16 (84%) cases showed parakeratosis and 12 (63.1%) cases showed blunting of rete ridges in the epidermis and all 19 (100%) cases characteristically showed increased vertically oriented collagen bundles in the dermis. 12 cases of ashly dermatosis were reported, 11 (91.6%) cases showed hyperkeratosis and hypergranulosis, 10 (83.33%) cases showed basal cell vacuolar degeneration in epidermis and 12 (100%) showed characteristic pigment incontinence in dermis. Present study revealed 6 cases of DLE, 6 (100%) cases showed hyperkeratosis in epidermis with focal parakeratosis 1(16.6%), mild exocytosis of lymphocytic inflammatory infiltrate (6, 100%) at dermoepidermal junction [DEJ] and dense perivascular, periadnexal mononuclear inflammatory infiltrate (6, 100%) in dermis. Present study reported 11 cases of psoriasis with hyperkeratosis (7, 63.63%), parakeratosis (9,81.81%) and all (11,100%) cases showed hypergranulosis, acanthosis, munro's micro abscess in stratum corneum and elongation of rete ridges. In the dermis 11 (100%) cases showed perivascular inflammatory infiltrate and 7 (63.63%) cases showed periadnexal inflammatory infiltrate and pigment incontinence. 9 (81.81%) cases showed neutrophilic inflammatory infiltrate.

Current study reported 2 infective cases. A 17 year old male, clinically presented with multiple, intensely itchy skin-coloured macules on trunk on histopathology revealed epidermis with hyperkeratosis and numerous fungal hyphae and spores in the stratum corneum. Special stains PAS was performed which showed magenta pink coloured spores and hyphae in the stratum corneum, diagnosis of pityriasis versicolor was confirmed [Figure 2]. Another case, 52year old, seropositive male, clinically misdiagnosed as epidermoid cyst. On histopathology revealed diffuse lymphoplasmacytic inflammatory infiltrate and a single multinucleated giant cell. Special stain AFB confirmed presence of acid-fast bacilli suggestive of tuberculosis.

Our study reported 2 cases of cutaneous amyloidosis presented with a hyperpigmented plaque on lower limb. Histopathology showed

hyperkeratosis, hypergranulosis and a acellular, amorphous, eosinophilic material just beneath the papillary dermis which on special stain with Congo Red revealed a salmon pink colour.[Figure 3] Amongst the neoplastic (benign) cases, most common lesion was seborrheic keratosis (11, 6.5%). On histological examination, all 11 (100%) cases showed hyperkeratosis and acanthosis, 5 (45.45%) cases showed parakeratosis, 6 (54.5%) cases showed papillomatosis with pseudohorn cyst formation.

A 13year old, female child, presented with well-defined hyperpigmented cystic lesion. Clinically diagnosed as pilar cyst. On histology dermis showed nests, trabeculae and cords of proliferating nevi cells with underlying periadnexal inflammatory infiltrate. IHC on tumour cells with S100 was positive. Diagnosis of congenital melanocytic nevus was given [Figure 4].

A 74year old male, presented with hyperpigmented plaque over foot. Epidermis showed hyperkeratosis, acanthosis and numerous epidermotropic lymphocytes. IHC for CD4, CD3 was positive and CD8 negative proving clonal nature of T lymphocytes. A diagnosis of mycosis fungoides was confirmed.

A 30year old female, presented with single solid asymptomatic hyperpigmented nodule right upper chest for 1-1.5 years clinically misdiagnosed as Epidermoid cyst. On histology epidermis and dermis showed tumour composed of nests of basaloid cells arranged in fronds like pattern surrounded by classical papillary mesenchymal bodies and keratin horns at places. Final diagnosis of trichoepithelioma was given.

A 45year old female, presented with hyperpigmented asymptomatic swelling over upper back for 7-8 months Clinical misdiagnosed as sebaceous cyst or epidermoid cyst. Histopathology revealed a tumour with proliferating bland spindle shaped cells arranged in storiform pattern. A diagnosis of cutaneous dermatofibroma was given.

Present study reported two malignant cases, 1 case of basal cell carcinoma (1.1%), 1 case of carcinoma en crurae, cutaneous metastasis of intraductal carcinoma breast (1.1%).

Positive clinicopathological correlation was noted in 161 (95.9%) cases. The overall disparity was seen in total 7 (4.1%) cases. 2 cases of seborrheic keratosis were clinically over-diagnosed as basal cell carcinoma and squamous cell carcinoma. 3 cases each of tuberculosis, trichoepithelioma, cutaneous dermatofibroma were clinically misdiagnosed as epidermoid cyst. 1 case of congenital melanocytic nevus was clinically misdiagnosed as pilar cyst. 1 case of pseudoepitheliomatous hyperplasia was clinically misdiagnosed as fibroma.

**Table 1 : Age And Gender Wise Distribution Of Patients Presenting With Hyperpigmented Skin Lesions.**

Age Range	Cases (n=168)	Male (n=83)	female (n=85)
0-10	4(2.38%)	1 (1.20%)	3 (3.52%)
11-20	26(15.47%)	11(13.25%)	15 (17.64%)
21-30	(11.30%)	9 (10.85%)	10 (11.76%)
31-40	(19.64%)	15 (18.07%)	18 (21.17%)
41-50	(23.80%)	23 (27.71%)	18 (21.17%)
51-60	(10.11%)	10 (12.04%)	7 (0.83%)
61-70	(10.71%)	8 (9.63%)	10 (11.76%)
>71	(14.70%)	6 (7.22%)	4 (4.70%)
<b>TOTAL</b>	<b>168 (100%)</b>	<b>83 (49.40%)</b>	<b>85 (50.59%)</b>

**Table 2. Distribution Of Hyperpigmented Skin Lesions**

Sr No.	NON NEOPLASTIC CASES (N=137,81.5%)	Number
1	Lichen Planus and its variants	25 (14.88%)
2	Prurigo Nodularis	19 (11.31%)
3	Ashy dermatosis	12 (7.14%)
4	Psoriasis	10 (5.95%)
5	Fixed drug reactions	9 (5.36%)
6	Spongiotic Dermatitis	9 (5.36%)
7	Discoid Lupus Erythematosus[DLE]	6 (3.57%)
8	Polymorphous light eruption [PLE]	5 (2.98%)
9	Pityriasis Rosea	5 (2.98%)
10	Reactive perforating collagenosis	4 (2.38%)

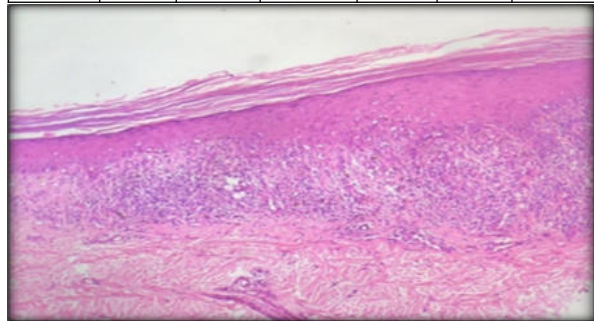
11	Amyloidosis	4 (2.38%)
12	Erythroderma	2 (1.19%)
13	Pityriasis versicolor	2 (1.19%)
14	Seborrheic melanosis	2 (1.19%)
15	Acrokeratosis veruciformis	1 (0.60%)
16	Acquired digital fibrokeratoma	1(0.60%)
17	Discoid eczema	1(0.60%)
18	Acute eczema	1(0.60%)
19	Frictional melanosis	1(0.60%)
20	Heriditary palmoplantar keratoderma	1(0.60%)
21	Lupus comedonicus	1(0.60%)
22	Post inflammatory hyperpigmentation	1(0.60%)
23	Pseudoepitheliomatous hyperplasia	1(0.60%)
24	Rheils melanosis	1(0.60%)
25	Small vessel vasculitis	1(0.60%)
26	Scleroderma	1(0.60%)
27	Tinea incognito	1(0.60%)
28	Melasma	1(0.60%)
<b>Sr no.</b>	<b>Neoplastic- benign cases (29, 17.26%)</b>	<b>Number, %</b>
1	Seborrheic keratosis	11(6.55%)
2	Verrucous vulgaris	10 (5.95%)
3	Beckers nevus	1(0.60%)
4	Congenital melanocytic nevus	1(0.60%)
5	Mycosis fungoides	1(0.60%)
6	Benign Fibrous histiocytoma	1(0.60%)
7	Bowenoid papulosis	1(0.60%)
8	Collagen nevus	1(0.60%)
9	Nevus linear lentiginous	1(0.60%)
10	Trichoepithelioma	1(0.60%)
<b>Sr no.</b>	<b>Neoplastic- malignant cases</b>	<b>Number</b>
1	Basal cell carcinoma	1(0.60%)
2	Carcinoma en crurae	1(0.60%)

**Table 3. Histopathological Features In Epidermis Of Different Hyperpigmentary Skin Lesions**

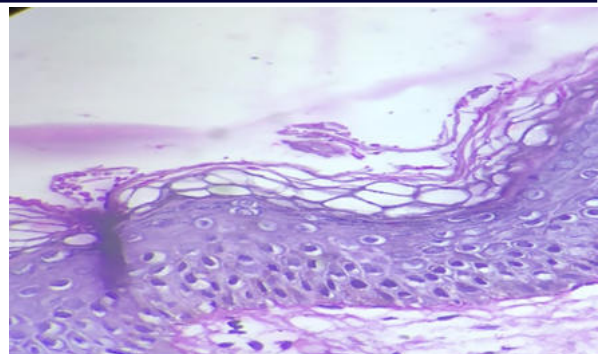
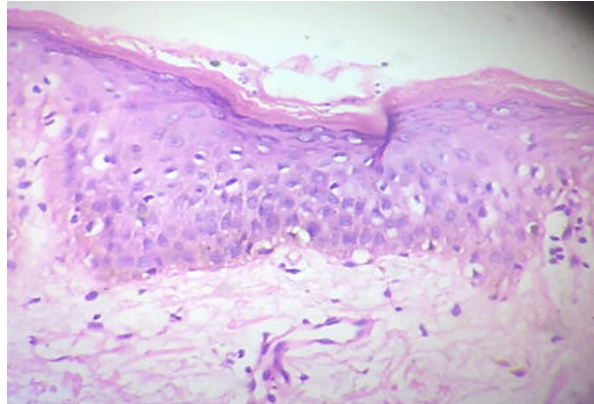
	Lichen Planus N=25	Prurigo Nodularis N=19	Ashy dermatosis N=12	Seborrh eic Keratosis N=11	Discoid Lupus Erythematous N=6	Polymorphous Light Eruption N=5
Hyperkeratosis	19 (76%)	17 (90%)	11 (91.6%)	11 (100%)	6 (100%)	3 (60%)
Parakeratosis	3 (12 %)	16 (84%)	-	5 (45.45%)	1 (16.6%)	
Hypergranulosis	8 (32%)	-	11 (91.66%)	-	-	
Acanthosis	7 (28%)	16 (87%)	-	11 (100%)	2 (33.3%)	3 (60%)
Spongiosis	2 (8%)	2 (10.5%)	-	-	-	4 (80%)
Atrophy	-	-	-	-	4 (66.6%)	-
Pseudoepitheliomatous hyperplasia	-	17 (90%)	-	-	-	-
Rete ridges	Saw toothing 8(32%)	Blunting 12 (63.1%)	-	Papillomatosis 6 (54.5%)	-	-
Basal cell degeneration	25 (100%)	-	10 (83.33%)	3 (27.27%)	3 (50%)	2 (40%)
Civatte bodies	6 (24%)	-	-	-	3 (50%)	-

**Table 4: Histopathological Features In Dermis Of Different Hyperpigmentary Skin Lesions**

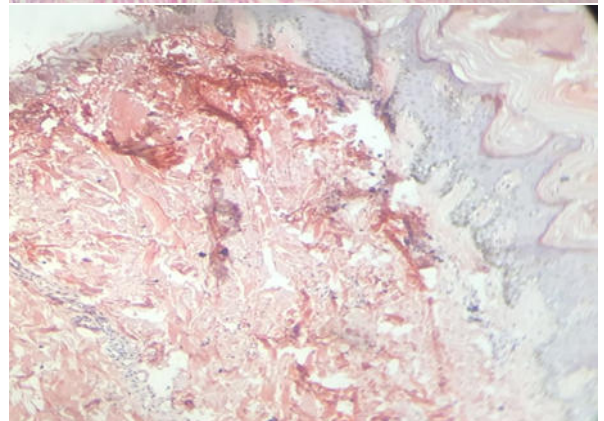
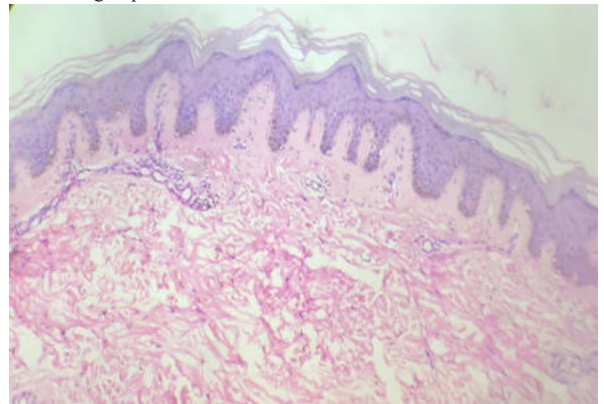
	Lichen Planus N=25	Prurigo Nodularis N=19	Ashy dermatitis N=12	Seborrheic Keratosis N=11	Discoid Lupus Erythematosus N=6	Polymorphous Light Eruption N=5
Edema	-	-	-	1 (9%)	3 (50%)	4 (80%)
Band like inflammatory infiltrate	25 (100%)	-	-	-	-	-
Increased Collagen bundles	-	19 (100%)	-	-	-	-
Lymphocytic inflammatory infiltrate	25 (100%)	-	4 (33.33%)	2 (18.1%)	6 (100%)	4 (80%)
Neutrophilic inflammatory infiltrate	-	-	-	-	-	-
Eosinophils	-	-	-	-	-	-
Histiocytes	-	-	-	-	-	-
Perivascular inflammatory infiltrate	23 (92%)	19 (100%)	11 (91.6%)	4 (36.35%)	6 (100%)	5 (100%)
Periadnexal inflammatory infiltrate	-	-	-	-	6 (100%)	1 (20%)
Pigment incontinence	20 (80%)	7 (28%)	12 (100%)	3 (27.27%)	1 (16.66%)	-



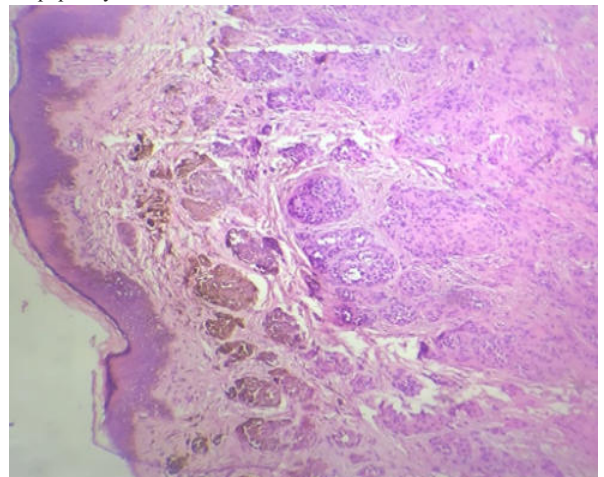
**Figure 1:** Lichen Planus. H&E, 10X: Epidermis shows hyperkeratosis, hypergranulosis with band like lymphocytic inflammatory infiltrate.

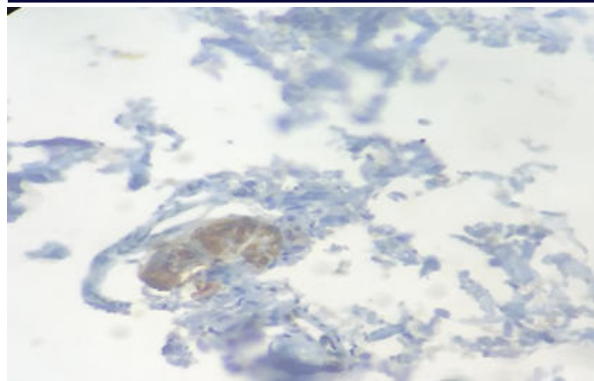


**Figure 2:** Pityriasis versicolor. H&E,40x: Epidermis shows hyperkeratosis with fungal spores and hyphae in stratum corneum with increased basal cell layer pigmentation. : Special stain PAS, 40x: shows fungal spores in stratum corneum.



**Figure 3:** cutaneous amyloidosis. H &E,10x: Epidermis shows eosinophilic, amorphous material in the papillary dermis. Special stain- congo red 40x: shows a “salmon-pink” colour amyloid deposit in the papillary dermis.





**Figure 4:** Congenital Melanocytic nevi. H&E,10x: Dermis shows nests, trabeculae and cords of proliferating nevi cells. Dermis shows periadnexal inflammatory infiltrate. IHC, S100: Nests of tumor cells showing S100 positivity.

#### DISCUSSION:

Hyperpigmented skin lesions comprise a large component of most histopathologists' workload, and there is a wide spectrum of histological appearances thus it carries great importance from dermatopathologist point of view. The histopathology-based treatment principles may be helpful for establishing a standardized treatment algorithm for hyperpigmented skin lesions. In diagnostic evaluation of hyperpigmentary lesions further characterization by studying morphology, pattern, distribution with clinical correlation of these lesions is helpful to make an accurate diagnosis.[2]

Present study was a retrospective observational institutional study of total 168 skin biopsies of patients presenting with hyperpigmented skin lesions. We reported a higher sample size compared to all other studies done by Shilpa et al (102)[3], Sneha et al (100)[4], Rajendra prasad et al (88)[5] Siresh et al (80)[6], Swarnim et al (65)[7], Vidya et al (56)[8], Saha et al (52)[9], Rashmi et al (26)[10], as our institute is a Government hospital catering to large number of patients from central India.

A slight female predominance was seen in the present study with 85 female patients (50.59%) and Female:Male ratio (1.02), Sneha et al (53%) [4], Vidya et al (58%) [8], Smitha et al (55%) [11] also showed female predominance.

Over-all the most common age group affected in our study was 41-50 years of age. Shilpa et al (45-65 years), [3] Siresh et al (41-50 years) [6] Anand et al (41-50 years) [12], Ahmed et al (41-50 years) [13] reported similar results.

The commonest site of involvement in non-neoplastic lesions was lower limb affecting 48 (28.57%) cases. Studies done by Shilpa et al (37.14%) [3], Rajendra prasad et al (20, 66.67%) [5] and Anand et al [12] also found lower extremity region to be the commonest site of involvement for non-neoplastic lesions.

Amongst neoplastic cases, head, face, chest and abdomen was the most commonly affected site in present study. Studies done by Shilpa et al (64.17%) [3], Ahmed et al (73.33%) [13], Suvernakar et al (63.64%) [14] reported similar findings.

In present study, the commonest non neoplastic lesion was lichen planus and its variants. Studies done by Shilpa et al (25.71%),[3], Sneha et al (24%) [4], Rajendra prasad et al (47%) [5], Siresh et al (44.12%), [6] Smitha et al (26%) [11] Parvathi et al (20 %) [15] also found lichen planus as the commonest non neoplastic lesion.

The commonest benign lesion in present study was seborrheic keratosis (11.6.5%). Siresh et al [6], Parvathi et al [15] also found seborrheic keratosis as the commonest benign neoplasm with (39.13%), (4.98%) cases respectively. Rajendra prasad et al (40%) [5], reported seborrheic keratosis as the 2<sup>nd</sup> most common benign lesion.

This study reported 2 malignant cases, 1 case each of basal cell carcinoma and cutaneous metastasis of intraductal carcinoma breast. Rajendra prasad et al (70%) [5], Siresh et al (69.56%)[6], Parvathi et al (17.5%)[15] also reported basal cell carcinoma as most common malignant lesion.

In present study, 7 cases (4.10%) showed discordance and 161 cases (95.9%) showed concordance between clinical and histopathological diagnosis. The results were comparable to a study done by Gore et al [2] who also reported a lower discordance in 2% cases and high concordance in 98% cases. In contrast, studies done by Sneha et al [4], Rajendra prasad et al [5], saha et al [9], Rashmi et al [10], Smitha et al [11], Parvathi et al [15], Sushan S J [16] et al reported a lower positive concordance of 90%, 85%, 84%, 44%,95%,81%,78.9%. A high positive concordance in present study attributed to a thorough clinical evaluation and multiple differential diagnoses raised by the clinicians at the time of patient presentation.

#### CONCLUSION:

Hyperpigmentary skin lesions range from inflammatory to malignant entities, recognising these lesions at the earliest not only helps in establishing the diagnosis but also plays an important role in prognosis. Present study, Lichen planus as the most common lesion overall and seborrheic keratosis and basal cell carcinoma were the most common benign and malignant lesions respectively. This study highlights the value of histopathology in evaluating hyperpigmentary disorders that afflicts so many of Indians seeking medical assistance. A specific diagnosis of hyperpigmentary skin lesions is possible based on histopathological findings and its interpretation in the context of clinical presentation. Thus early detection, diagnosis and treatment of hyperpigmented skin lesions is crucial to decrease functional and cosmetic morbidity.

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