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Original Article

Study on the Histomorphological Spectrum of Non-neoplastic Skin Disorders at A tertiary care Centre

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ABSTRACT

Background: Rudolph Virchow emphasized the delicacy of internal viscera, and the skin, the body's largest organ, serves as their protective interface.. Along with preventing mechanical injury and excessive fluid loss, skin provides sensory perception and supports endocrine activity through vitamin D synthesis. Many non-neoplastic dermatoses share overlapping morphologies (macules, papules, plaques, nodules, pustules, and pigmentary changes), so clinically distinct entities may appear similar. Histopathology remains the gold standard for confirmatory diagnosis and for meaningful clinicopathological correlation. **Objective:** To describe the histopathological spectrum of clinically suspected non-neoplastic skin disorders and to assess clinicopathological concordance. **Methods:** This observational study was conducted at NRI Institute of Medical Sciences, Sangivalasa, Visakhapatnam, Andhra Pradesh, India, from April 2020 to October 2022. Consecutive patients with clinically suspected non-neoplastic skin disorders were included (n = 100). A representative 4-mm punch biopsy was obtained from each case, followed by routine fixation and tissue processing. Sections were stained with hematoxylin and eosin and examined microscopically. Final histopathological diagnoses were assigned, grouped into standard non-neoplastic categories, and compared with provisional clinical diagnoses to determine concordance. **Results:** Of 100 biopsied non-neoplastic dermatoses, non-infectious erythematous papulosquamous disorders were most frequent(42%). Infectious lesions comprised 17% (including Hansen's disease), followed by inflammatory disorders of skin adnexae(9%), pigment disorders(8%), connective tissue disorders(7%), vascular disorders(5%), and cutaneous drug toxicities(4%). Vesiculobullous disorders, vesiculopustular disorders, and genodermatoses each accounted for 3%. Non-infectious granulomatous disorders(1%) and degenerative/perforating diseases(1%) were least common. Overall, clinicopathological concordance was 72%(72/100). **Conclusion:** Non-neoplastic dermatoses often share similar clinical appearances, increasing the risk of misdiagnosis and inappropriate therapy. Histopathology with clinicopathological correlation improves diagnostic precision and guides lesion-specific management, helping to minimize both under and overtreatment.

Keywords*: Papulosquamous; vesiculobullous; Hansen's disease; punch biopsy; non-neoplastic dermatoses; histopathology; clinicopathological correlation.*

INTRODUCTION

Rudolph Virchow, the father of cellular pathology, emphasized that the internal viscera are delicate and highly sophisticated structures. The skin, being the largest organ of the human body, serves as a vital protective covering for these organs. It acts as an effective barrier against mechanical injury, chemical insults, microbial invasion, and excessive fluid loss. In addition, the skin plays an essential role in sensory perception, thermoregulation, immune surveillance, and endocrine function through vitamin D synthesis. Owing to these diverse and complex functions, the skin reflects both local and systemic pathological processes, making it an important indicator of overall health [1,3].

A wide spectrum of disorders affects the skin, ranging from transient inflammatory conditions and infectious diseases to chronic immune-mediated disorders and malignancies. Many of these conditions arise due to disturbances in the normal homeostasis of epidermal and dermal cells, which may result from genetic predisposition, infections, immune dysregulation, environmental factors, or adverse drug reactions [1]. In India, skin diseases constitute one of the most common health problems encountered in clinical practice. Despite their high prevalence, many dermatological conditions are often underestimated or neglected, largely because they are perceived as non–life-threatening. However, these disorders can significantly impair quality of life, cause psychosocial distress, and in some cases signal underlying systemic disease [4].

Clinically, skin diseases tend to present with a limited number of morphological patterns, such as hyperpigmentation, hypopigmentation, macules, papules, plaques, nodules, pustules, vesicles, and bullae. Although careful clinical examination provides valuable diagnostic clues, considerable overlap exists in the clinical appearance of different dermatoses. Conversely, the same disease entity may show varied morphology at different stages or in different individuals. This overlap often leads to diagnostic ambiguity when clinical evaluation alone is relied upon [2,4].

Histopathological examination of skin biopsy specimens plays a pivotal role in resolving these diagnostic challenges. Many clinically similar skin disorders demonstrate distinct histomorphological features on microscopic examination, allowing precise classification and confirmation of diagnosis. Skin biopsy, therefore, remains the gold standard for diagnosing a wide range of non-neoplastic skin lesions [2,3]. Accurate histopathological diagnosis is essential because treatment protocols and prognostic outcomes vary significantly among different dermatoses. Several studies have highlighted the importance of clinicopathological correlation in reducing diagnostic errors and ensuring appropriate patient management [5,10].

In this context, systematic evaluation of the histomorphological spectrum of non-neoplastic skin disorders, along with assessment of clinicopathological concordance, is of considerable importance. Such studies not only enhance diagnostic accuracy but also contribute to better therapeutic decision-making and improved patient outcomes, particularly in a tertiary care setting where a wide variety of skin diseases are encountered .

MATERIALS AND METHODS

Place of study, study design, and study period

The present observational study was conducted at the NRI Institute of Medical Sciences, Sangivalasa, Visakhapatnam, Andhra Pradesh. Skin biopsies were obtained using a 1 mm punch from patients with clinically suspected non-neoplastic skin disorders. The study was carried out over a period of two and a half years, from April 2020 to October 2022.

Sample size

During the study period, a total of 500 skin biopsy specimens, including both neoplastic and non-neoplastic lesions, were received. Among these, 100 cases diagnosed clinically as non-neoplastic skin disorders and fulfilling the inclusion and exclusion criteria were selected for detailed histopathological evaluation.

Study population

The study population comprised patients of all age groups and both sexes presenting with clinically suspected non-neoplastic skin lesions and referred for skin biopsy.

Inclusion criteria

All patients of either sex with clinically suspected non-neoplastic skin disorders were included in the study. Only cases with adequate skin biopsy material and complete clinical details were considered. Informed written consent was obtained from all patients prior to biopsy.

Exclusion criteria

Cases of neoplastic skin lesions were excluded from the study. Inadequate or poorly preserved skin biopsy specimens and oral mucosal biopsies were also excluded.

Method of specimen collection
Skin biopsies were obtained using a 1 mm punch biopsy technique from representative sites of the lesions, selected in consultation with the treating dermatologist. Biopsy specimens were immediately fixed in 10% neutral buffered formalin and transported to the pathology laboratory for further processing.

Histopathological processing and examination
The fixed biopsy specimens were processed routinely, embedded in paraffin, and sectioned at 3–5 µm thickness. Sections were stained with hematoxylin and eosin for histopathological examination. Special stains were employed whenever required to aid in diagnosis.

Data collection and analysis
Clinical details, including age, sex, site of lesion, duration, and provisional clinical diagnosis, were recorded. Histopathological findings were documented and lesions were categorized into appropriate non-neoplastic groups. Clinicopathological correlation was performed by comparing clinical and histopathological diagnoses. Data were analyzed using descriptive statistics and results were expressed as frequencies and percentages.

Ethical considerations
The study was conducted after obtaining approval from the Institutional Ethics Committee. Patient confidentiality was maintained throughout the study, and all procedures were performed in accordance with ethical standards.

RESULTS
The present study comprised of 100cases of non-neoplastic skin disorders, which satisfied the inclusion criteria and were studied.

Age wise distribution
The present study showed a distribution of skin lesion in the age group of 13 to 78 years. The youngest age of presentation is 13 years where as the older age being 78years. The maximum distribution of lesions seen in age group of 21-30years (39%) followed by 41-50years (18%). The mean age of presentation was 36.7 years.

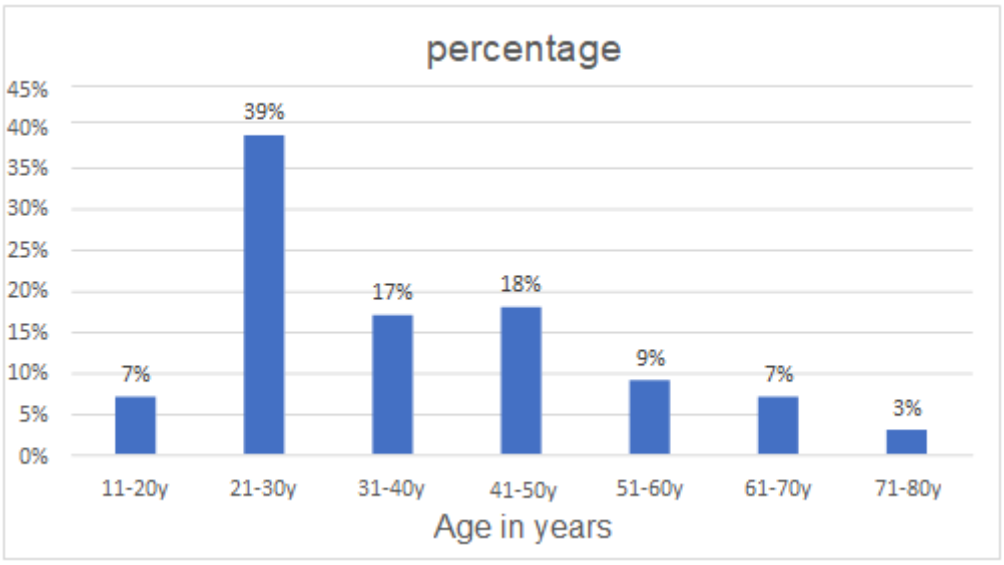

Figure1: Distribution of lesions in relation to age

Sex wise distribution of lesions
Out of 100cases, 52cases (52%) of male and 48 cases (48%) of female were seen. The M:F ratio is 1.08:1 which shows slight male preponderance

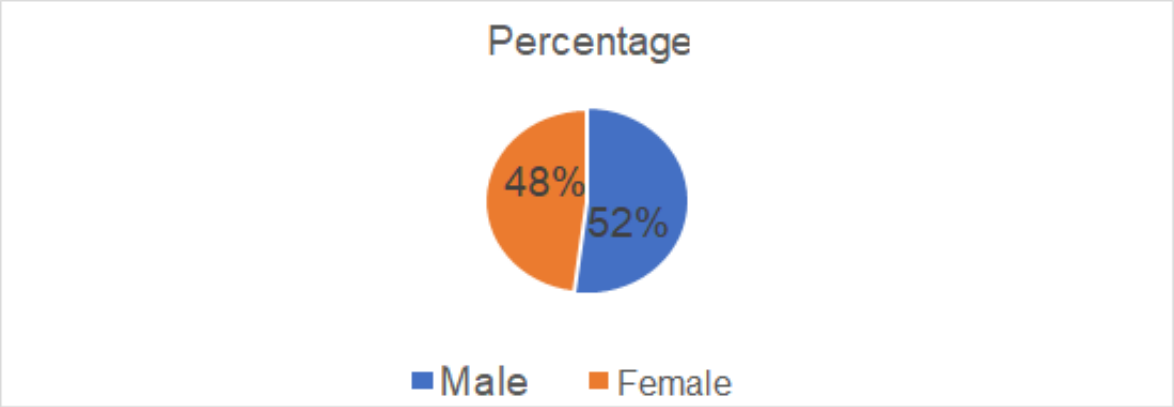

Figure2: Distribution of lesions in relation to sex

Distribution of lesion in relation to site

In this study, lesions are included according to the site at which the lesion present predominantly. Those are divided as head & neck, extremities, axilla, trunk, abdomen and miscellaneous which include lesions present all over body with equal proportion, penile, vaginal skin and nail bed.

Most of the lesions present on extremities (56%) followed by head & neck region (16%) in our study.

Table1: Distribution of lesions in relation to site(n=100)

Site on which lesion present	**Percentage of lesion**
Extremities	56%
Head and neck region	16%
Trunk	13%
Abdomen	4%
Axilla	4%
Other sites	7%
Total	100%

Histopathological distribution of skin lesions in present study

Majority of the lesions in this study are non-infectious erythematous, papulosquamous lesions (42%) followed by infectious lesions (17%).

Table 2: Histopathological distribution of skin lesions in the study (n=100)

No	Name of Lesion	No. of cases	Percentage (%)
1	Non infectious erythematous Papulosquamous disorders	42	42%
2	Infectious lesions	17	17%
3	Inflammatory diseases of hair follicles, sweat glands and nails	9	9%
4	Connective tissue disorders	7	7%
5	Vascular diseases	5	5%
6	Cutaneous drug toxicities	4	4%
7	Vesiculobullous and vesiculopustular disorders	3	3%
8	Genodermatoses	3	3%
9	Pigment disorders	8	8%
10	Noninfectious granulomatous disorders	1	1%
11	Degenerative and perforating diseases	1	1%
	Total	100%	100%

Correlation between clinical and histopathological diagnosis

In this study, out of 42 cases of non-infectious erythematous papulosquamous disorders, 30(71.43%) cases are correlated and 12(28.74%) are uncorrelated (Table 3).

Table3: Clinical and Histopathological correlation of Non-infectious erythematous papulosquamous lesions

S. No	Name of lesion	Total	Correlated	Uncorrelated
1	Psoriasis	12	10(83.33%)	2(16.66%)
2	Lichen planus	10	7(70%)	3(30%)
3	Pityriasis roseae	3	1(33.33%)	2(66.67%)
4	Pityriasis Lichenoides et varioliformis acuta	3	3(100%)	-
5	Pityriasis rubra pilaris	2	2(100%)	-
6	Prurigo nodularis	2	2(100%)	-
7	Pityriasis Lichenoidchronica	2	1(50%)	1(50%)
8	Asteatotic Eczema	1	1(100%)	-
9	Erythematous granuloma annulare	1	1(100%)	-
10	Erythematous annulare centrifugum	1	1(100%)	-
11	Seborrheic dermatitis	1	1(100%)	-
12	Pityriasoriform dermatoses	1	-	1(100%)
13	Parapsoriasis	1	-	1(100%)
14	Classic lichenoid dermatitis	1	-	1(100%)
15	Interface reaction of lichenoid pattern	1	-	1(100%)
	Total	**42**	**30(71.43%)**	**12(28.47%)**

In present study, all 3(100%) cases of vesiculobullous and vesiculopustular disorder are correlated. 2 cases are Bullous phemphigoid and 1case is Pemphigus Vulgaris. In infectious cutaneous diseases, out of 17 cases, 14(82.35%) cases are correlated, 3(17.64%) cases are uncorrelated (Table4) where as in pigment cutaneous disorders, a total of 8 cases, 5(62.5%) are correlated, 3(37.5%) are uncorrelated. Vitiligo (2), Becker's melanosis(1) and idiopathic guttate hypomelanosis (1) are completely correlated, whereas intradermal nevus(1), Ashy dermatitis(1) are uncorrelated. Pigmented contact dermatitis (2), 1 case correlated with clinical diagnosis other 1 was not correlated. In cutaneous connective diseases, out of 7 cases,5 (71.42%) cases of Morphea are correlatedand 2 cases(28.57%), 1 is morphea and another is Atrophoderma.

Table 4: Clinical and Histopathological correlation of infectious cutaneous lesions.

S. No	Name of lesion	Total	Correlated	Uncorrelated
1	Hansen's disease	8	8(100%)	-
2	Warts	5	3(60%)	2(40%)
3	Molluscum contagiosum	1	1(100%)	-
4	Tinea incognito	1	1(100%)	-
5	Onycholysis	1	1(100%)	-
6	Tinea versicolor	1	-	1(100%)
	Total	**17**	**14(82.35%)**	**3(17.64%)**

In our study 9 cases of inflammatory lesions of skin adnexae are seen. Of these 9, 5 (55.56%) cases are correlated and 4(44.44%) cases are not correlated (Table 5). Out of 5 cases of vascular diseases, 4 cases(80%) are correlated and 1 case(20%) of Lymphocytic vasculitis was uncorrelated. Among 4 cases of cutaneous drug toxicities 3 cases(75%), 2 are Erythema multiforme and 1 case of Lichenoid drug eruption were correlated and 1(25%) of Leucoderma was uncorrelated. All the cases of Genodermatoses (3), Degenerating and Perforating disorders(1) and Non-infectious granulomatous disorders(1) are correlated.

Table 5: Clinical and Histopathological correlation of infectious cutaneous lesions.

S. No	Name of lesion	Total	Correlated	Uncorrelated
1	Alopecia	3	3(100%)	-
2	Steatocystoma multiplex	1	-	1(100%)
3	Pilar cyst	1	-	1(100%)
4	Hidradenitis suppurativa	1	-	1(100%)
5	Trichilemmal cyst	1	-	1(100%)
6	Fox Fordyce disease	1	1(100%)	-
7	Acne vulgaris	1	1(100%)	-
	Total	**9**	**5(55.56%)**	**4(44.44%)**

Table 6: Correlation between clinic histopathological diagnosis

S.n o	Name of lesion	No. of cases correlated	No. of cases not correlated	P value
1	Non-infectious Papulosquamous erythematous lesions	30 (71.43%)	12 (28.57%)	<0.00001 Chisquare-1150 Degreeoffreedom-14
2	Noninfectious vesiculobullous& vesiculopustular disorders	3(100%)	0	NA
3	Infectious disorders	14 (82.35%)	3(17.64%)	<0.000001 Chisquare-465.8 Degreeoffreedom-5
4	Inflammatory diseases of skin adnexae	5(55.56%)	4(44.44%)	NA
5	Connective tissue Disorders	5(71.43%)	2(28.57%)	NA
6	Vascular diseases	4(80%)	1(20%)	NA
7	Cutaneous Drug Toxicities	3(75%)	1(25%)	NA
8	Genodermatoses	3(100%)	0	NA
9	Pigment Disorders	5(62.5%)	3(37.5%)	NA
10	Degenerating & proliferating disorders	0	1(100%)	NA
11	Non-infectious granulomatous Disorders	0	1(100%)	NA
	Total	**72(72%)**	**28(28%)**	**<0.00001 Chisquare-503.7 Degreeoffreedom-10**

DISCUSSION

Variable number of dermatological disorders are present now a days. The pattern of skin diseases depends on geographical & environmental factors [2]. Each clinical presentation is common to many histopathological pictures and so histopathology was required for their confirmation. As treatment and prognosis varies for different lesions, histopathology helpful for proper diagnosis and better treatment [23].

In present study 100 cases were analysed whereas 92cases by Veldurthy VS et al[9],112 cases by Singh et al[12] and 80 cases by Rajsekhar et al[11].

Table 6: Total number of cases included in different studies

Studies	No. of cases
Present study	100
Veldurthy VS et al	92
Singh et al	112
Rajsekhar et al	80

Age

In the present study, the highest proportion of cases was observed in the 21–30-year age group, accounting for 39% of patients. This finding is comparable to observations reported by Veldurthy VS et al. and Bajaj P et al. [5], who also noted a predominance in younger adults. In contrast, studies by Gupta P et al. [13] and Rajsekhar et al. reported a higher frequency of cases in the 31–40-year age group. The mean age at presentation in the current study was 36.7 years, which closely corresponds with the mean age reported by Sherpa P et al. [15] (36 years) in a study conducted in Nepal.

Sex

A slight male predominance was noted in the present study, a trend that is consistent with findings from studies by Chalise et al[23]. and Vijayasankar S et al. [25]. The male-to-female ratio in the current study was 1.08:1, which is comparable to ratios reported by Sherpa P et al. (1.02:1) and Vijayasankar et al. (1.32:1), indicating a relatively balanced sex distribution with marginal male preponderance.

Site of lesion

The extremities were the most commonly involved site in the present study, accounting for 56% of cases, followed by the head and neck region (16%). These findings are in agreement with those reported by Chalise et al., who observed extremities as the predominant site (48.8%), followed by head and neck involvement (29.3%). This distribution highlights the predilection of non-neoplastic skin disorders for exposed and trauma-prone areas of the body.

Non-infectious erythematous papulosquamous disorder:

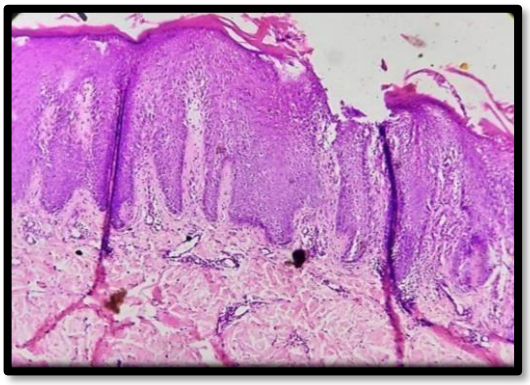

Fig 3: Psoriasis: Epidermis with parakeratosis, acanthosis and elongated rete ridges and papillary dermis with perivascular lymphocytic infiltration (H&E- 10x)

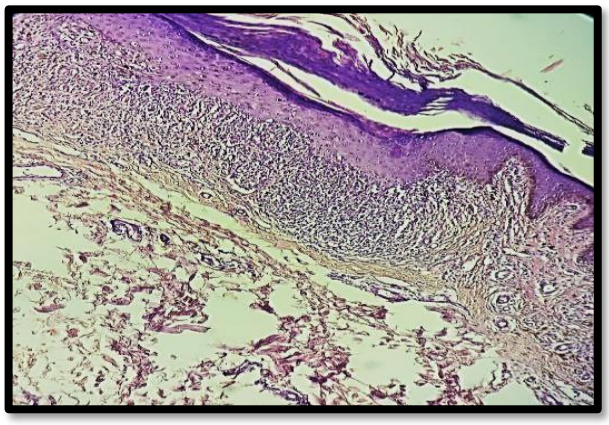

Fig 4 : Lichen Planus: shows dense band like infiltration of inflammatory cells predominantly consists of lymphocytes in papillary dermis extend to epidermis(H&E- 10X)

In present study out of 42 cases of Non infectious erythematous papulosquamous disorders, Psoriasis (28.57%)(Fig3) is highest which is similar to studies conducted by Chabbi K et al[6] (42%) and and Agarwal S et al (60%)[8]. The most common age of presentation for psoriasis in our study 3rd decade whereas Chabbi et al and Kumari et al[24] studies show in 5th decade and 3rd decade respectively.

In our study lichen planus is the 2nd most common Non infectious erythematous papulosquamous disorder which shows23.80% similar to studies conducted by Chabbi et al and Agarwal et al. In contrast to present study, lichen planus(Fig 4) is most common in studies conducted by Chandrika VLK et al[7] (64%), Patel B et al[16].

Vesiculobullous and Vesiculopustular disorder:

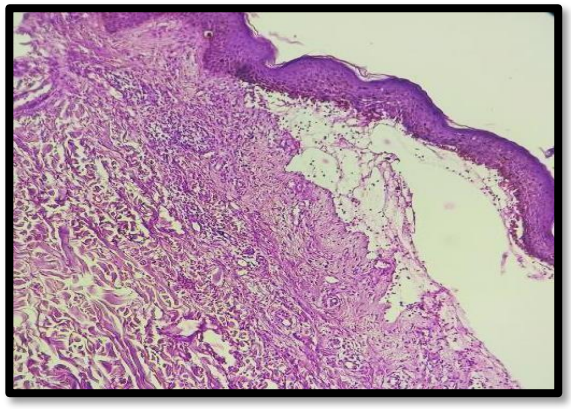

Fig 5: Bullous pemphigoid: Histomorphological photomicrograph shows subepidermal blister with inflammatory infiltrate in dermis (H&E-10x)

In present study, among vesiculobullous and vesiculopustular disorders, bullous pemphigoid(Fig 5) (66.67%) is most common followed by pemphigus vulgaris (Fig 6) (33.33%).In contrast to this study, studies conducted by Vijay Sankar S et al and Anupama Raj et al[26] showed pemphigus vulgaris was highest followed by bullous pemphigus.

In the study conducted by Gupta I et al[10] showed dermatitis(39.90%)followed by pemphigus vulgaris(37.1%) and Sherpa P et al showed spongiotic dermatitis(36%) followed by lichen simplex chronicus (12%).

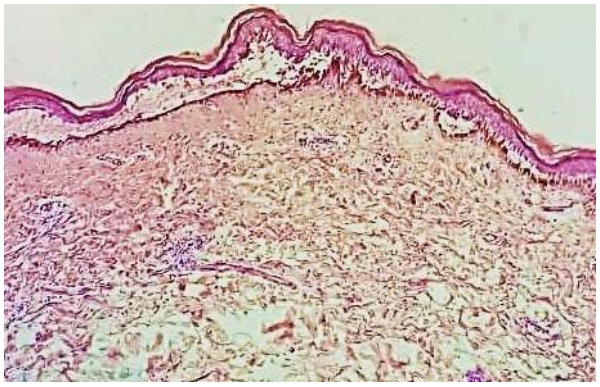

Fig 6: Pemphigus Vulgaris: Histomorphological photomicrograph shows suprabasal blister with acantholysis (H&E-10x)

Infectious cutaneous disorders:

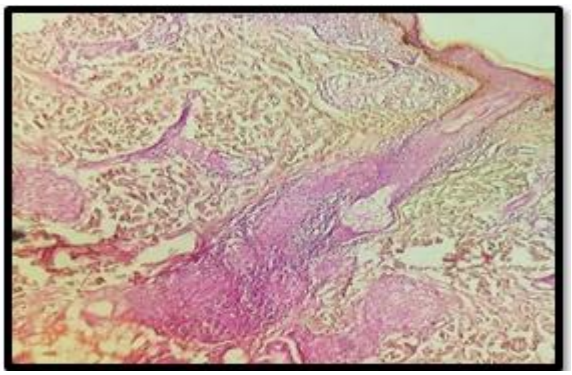

Fig 7: Hansen's disease : Histomorphological photomicrograph shows tuberculoid Leprosy with perineural and periadnexal granulomas (H&E-10x)

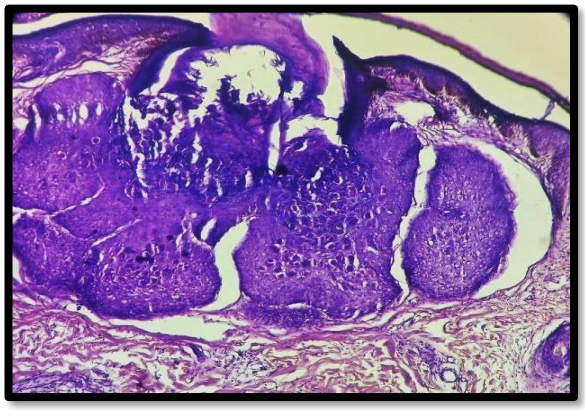

Fig 8: Molluscum contagiosum : Histomorphological photomicrograph shows Molluscum bodies in epidermis(H&E-10x)

In our study in all infectious disorders, leprosy (Fig 7) (47.05%) similar to studies conducted by Vijay Sankar S et al(25.84%), Chandra kanta et al [17](40.9%). Agarwal D et al[18] also show leprosy as commonest disease among infectious skin lesions.

In contrast to this study, previously conducted some studies in Pakistan show more tuberculous lesions and in Nepal

shows dermatophytosis as more common. Adhikari et al[23] show fungal infection (35.3%) as highest incidence. 2nd most common infectious disorder in our study was warts(verruca) (29.41%) which is similar to study conducted by Chalise et al (27.27%). Whereas Vijay Sankar S et al, Agarwal D et al showed tuberculosis as 2nd common lesion in their studies.

Inflammatory skin adnexal lesions:

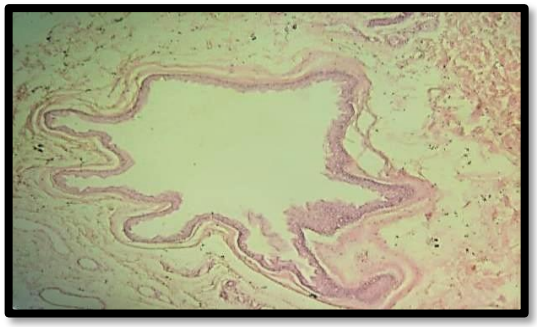

Fig 9: Steatocystomamultiplex : Histomorphological photomicrograph shows cyst wall with numerous infoldings (H&E- 10x)

In present study among skin adnexal lesions Alopecia (33.34%) was the commonest followed by remaining all cases with equal preponderance. Adhikari et al study showed scarring alopecia (59.1%) followed by rosacea (27.3%).

In the study conducted by Mamatha et al[27] showed Alopecia areata (75%) is commonest followed by hidradenitis suppurativa (25%) and by Gupta I et al has identified two cases each of Rosacea and acute folliculitis with fungal infection. In our study Rosacea even single case was not identified.

Pigment disorders of skin:

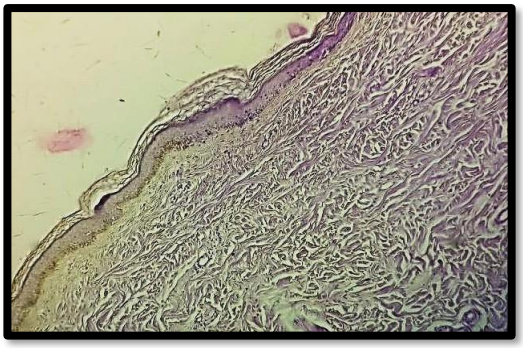

Fig 10: Idiopathic guttate hypomelanosis : Histomorphological photomicrograph shows Epidermis with orthokeratosis and basal layer with melanotic and hypomelanotic areas (H&E-10x)

In this study, vitiligo and pigmented contact dermatitis are commonest in all pigment disorders of skin. 2cases(25%) of each were seen. In Chandrakantha et al study post inflammatory pigmentation (66.67%) was common whereas study conducted by Gupta P et al showed Nevus (77.78%) is most common followed by Ashy dermatosis. In our study 1case each of ashy dermatosis and intradermal nevus were seen.

Cutaneous connective tissue disorders:

In cutaneous connective tissue disorders in our study, Morphea (85.72%) is most common followed by scleroderma(7.14%) and atrophoderma(7.14%) which is similar to studies conducted by Gupta I et al (40%) and sherpa P et al study(40%). Adhikari et al shows lichen sclerosus et atrophicus (40%) followed by Morphea (36%).Discoid lupus erythematosus, keloid, hypertrophic lupus erythematosus and Lichen sclerosus et atrophicus were not seen in our present study.

Cutaneous Vascular disorders:

In our study 3cases of genodermatoses which include actinic porokeratoses, dyschromatosis universalis hereditaris and keratoderma (33.33%) each were reported. Sherpa P et al study show 4 cases which include urticaria pigmentosa, Darier's disease, Hailey hailey, Netherton disease with equal proportion each with 25%.In study conducted by Gupta I et al show porokeratosis (50%) was more common followed by Acrokeratosis of hopf and Darriers disease each 25% were seen.

Cutaneous drug toxicities:
In the present study, cutaneous drug toxicities accounted for 4% (4 cases) of all non-neoplastic skin disorders. Among these, erythema multiforme was the most frequently encountered lesion, constituting 50% of cases, followed by lichenoid drug eruption and leukoderma, each accounting for 25%. A comparable proportion of cutaneous drug reactions (4.4%) was reported by Sherpa P et al., although the spectrum of lesions differed. In their study, acute generalized exanthematous pustulosis was the most common presentation (33.2%), followed by cutaneous drug reaction and drug-induced dermatitis, while exanthematous and morbilliform drug reactions were observed in equal proportions (16.7% each). In contrast, Veldurthy et al. reported a lower incidence of cutaneous drug toxicities, with only two cases (2.17%) documented in their series.

Degenerative diseases and perforating diseases:
One interesting and rare case of degenerative and perforating disorder, kyrle's disease was seen in our study.
Kyrle's disease is a rarely seen disorder with eruption of large number of papules which coalesce to form plaque. It shows a follicular or extrafollicular cornified plug with focal parakeratosis embedded in an epidermal invagination, basophilic degenerated material identified throughout the plug, with absence collagen and elastin, abnormal vacuolated and/or dyskeratotic keratinization of the epithelial cells. This dyskeratotic keratinization extends upto the basal cell zone. It also shows irregular epithelial hyperplasia and an inflammatory component that is typically granulomatous with small foci of suppuration[3].

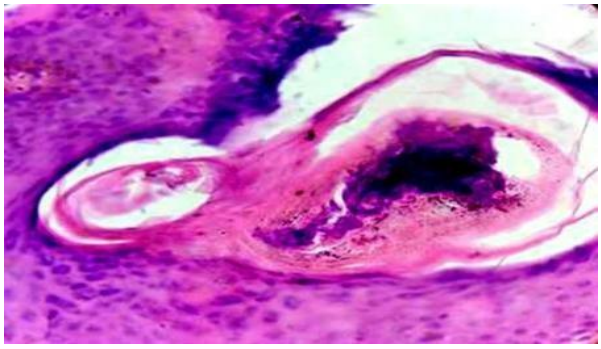

Fig 11: Kyrle's disease : Histomorphological photomicrograph show crater formation in epidemis with Keratin plug and basophilic degeneration (H&E-40x)

Correlation of clinical and histological diagnosis of all cases of present study:
In present study clinical and histological diagnosis corelated with 72% of cases and 28% are not correlated. This is similar to study conducted by Goyal N et al[19] was 63% were correlated and 21.4% not correlated and 15.6% were inconclusive.

In terms of clinicopathologic consistency, Bisht M et al[25] found about 51.67% of cases showed complete clinicopathologic consistency and 23.33% of them were partial clinicopathologic correlation. While 25% cases had histopathologic diagnosis inconsistent with the clinical diagnosis.

In their study done by Nageen S et al[21] show 80.6% of cases are clinically and histopathologically correlated. In their study done by AI-Saif FM et al[22] in Saudi has also similar correlation of 76% of lesions.

CONCLUSION
Histomorphological examination remains the gold standard for the accurate diagnosis of non-neoplastic skin disorders. Owing to the considerable overlap in clinical presentation among various dermatoses, reliance on clinical assessment alone may result in diagnostic errors. Histopathology provides definitive structural details that aid in distinguishing clinically similar conditions. In the present study, clinicopathological concordance was observed in 72% of cases, underscoring the value of histological evaluation in routine dermatological practice. Accurate histopathological correlation not only confirms the clinical diagnosis but also plays a crucial role in guiding appropriate therapy. This approach helps to prevent both under-treatment and overtreatment, thereby improving patient management and clinical outcomes

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