PATTERNS OF HISTOMORPHOLOGICAL VARIANTS OF SKIN DISEASES IN A RURAL TERTIARY CARE CENTRE
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Abstract
Background: Skin biopsy is a common procedure in Dermatology practice. The usual intent of skin biopsy is to further characterize the nature of a skin growth or eruption and assist in diagnosis by allowing histopathological evaluation of a tissue sample. Although histopathology remains the gold standard for most dermatologic diagnoses, it must be recognized that not all lesions are amenable to definitive specific histological diagnosis¹.

Material & Methods: The present study is undertaken in the department of Pathology, Index Medical College Hospital and Research Center, Indore (M.P). This was a cross sectional observational study which included skin biopsy specimen from 122 cases reported for histopathological evaluation attending Skin & VD OPD of the institute from June 2018 to Feb 2020. On the basis of histopathological features these skin disorders were classified in different groups as per Lever’s classification².

Results: out of 116 cases included in the study, maximum cases belonged to group III (n=43) followed by group V (n=38), group IV (n=11), group I (n=7), group II (n=7), group VI (n=7) and group VII (n=3). Overall most common disease observed was Psoriasis followed by Leprosy. Highest number of cases were found in age group 41-50 years (n=25) and clinicopathological correlation was seen in 79.09% cases.

Conclusion: The skin biopsy and subsequent histopathological examination has been proved as gold standard for identifying a specific dermatoses and appropriate management, being most cost effective tool.

Keywords: Skin, Histopathology, Psoriasis, Leprosy

Introduction
Skin disorders are one of the most common health problems in India with a wide spectrum ranging from nonspecific dermatoses and inflammatory diseases to neoplastic changes in various components of skin. Interpretation of skin biopsy must require a substantial clinicopathological correlation¹.

The histological diagnosis is used as gold standard by the clinicians to manage patients. The most accurate diagnosis is the one that most closely correlates with the clinical features & helps in planning the most appropriate clinical intervention, it is very well known that not all lesions are amenable to definitive specific histological diagnosis.

Much work on skin disorders has been done by investigators outside India. On the contrary less number of studies have been done in our country especially central India in the field of dermatopathology. Hence this work has been undertaken, covering patients in and around Indore, to study the spectrum of various skin disorders that affect our population.

Materials and Methods
The present study was undertaken in the department of Pathology, Index Medical College Hospital and Research Center, Indore (M.P). The study is cross sectional, observational and prospective in nature, from June 2018 to Feb 2020, which included skin biopsy specimen from 122 cases reported by histopathological evaluation attending Skin & VD OPD of the institute.

Out of these 122 cases, 06 biopsies were normal and showed no histopathological changes, which were excluded and sample size of 116 skin biopsy specimen was taken for our study.

Inclusion Criteria: all skin biopsies received in histopathology section were included in the study.

Exclusion Criteria: Inadequate skin biopsies and inconclusive biopsies or biopsies showing normal histology were excluded from the study.

All the cases in the study were analysed by collecting the clinical information with histomorphological features.

Results
The present study was a prospective study in which we included all the skin biopsies received in department of Pathology at Index Medical College, Hospital & Research Center, Indore during June 2018 to Feb 2020. We studied 116 cases out of total 122 biopsies received. Six biopsies were excluded which were either inadequate or showed normal features. Sixty four cases were female while 52 were males and majority of the cases belonged to middle age group between 31-50 years (n=46).
We have grouped the lesion into 8 groups based on their site, pattern of involvement and histological features, as per criteria of Lever’s Histopathology of Skin. Group I: Disorders of Epidermis and Stratum Corneum; Group II: Localized superficial epidermal or melanocytic proliferations; Group III: Disorders of the superficial cutaneous reactive unit; Group IV: Acantholytic, vesicular & pustular disorders; Group V: Perivascular, diffuse & granulomatous infiltrates of the reticular dermis; Group VI: Tumors & cysts of the dermis and subcutis; Group VII: Inflammatory disorders of skin appendages; Group VIII: Disorders of the subcutis.

Table 1: Distribution of skin diseases in various categories

<table>
<thead>
<tr>
<th>Group</th>
<th>Disease</th>
<th>Number (%)</th>
<th>Group</th>
<th>Disease</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>Hypertrophic scar</td>
<td>1 (0.86%)</td>
<td>Group V</td>
<td>Leprosy</td>
<td>27 (23.27%)</td>
</tr>
<tr>
<td>(n=7, 6.03%)</td>
<td>Keratin cyst</td>
<td>1 (0.86%)</td>
<td>(n=38, 32.75%)</td>
<td>Granulomatous lesion</td>
<td>4 (3.44%)</td>
</tr>
<tr>
<td></td>
<td>Becker melanosis</td>
<td>1 (0.86%)</td>
<td></td>
<td>Calcinosis cutis</td>
<td>2 (1.72%)</td>
</tr>
<tr>
<td></td>
<td>Ichthyosis vulgaris</td>
<td>2 (1.72%)</td>
<td></td>
<td>scleroderma</td>
<td>2 (1.72%)</td>
</tr>
<tr>
<td></td>
<td>Erythema dyschromicum perstans</td>
<td>1 (0.86%)</td>
<td></td>
<td>keloid</td>
<td>1 (0.86%)</td>
</tr>
<tr>
<td>Group II</td>
<td>Seborrhic keratosis</td>
<td>2 (1.72%)</td>
<td></td>
<td>Granuloma annulare</td>
<td>1 (0.86%)</td>
</tr>
<tr>
<td>(n=7, 6.03%)</td>
<td>Verruca vulgaris</td>
<td>3 (2.58%)</td>
<td></td>
<td>Cutaneous vasculitides</td>
<td>1 (0.86%)</td>
</tr>
<tr>
<td></td>
<td>Simple papillomatous hyperplasia</td>
<td>2 (1.72%)</td>
<td>Group VI</td>
<td>Squamous cell carcinoma</td>
<td>1 (0.86%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(n=7, 6.03%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group III</td>
<td>psoriasis</td>
<td>28 (24.13%)</td>
<td></td>
<td>Sebaceous cyst</td>
<td>3 (2.58%)</td>
</tr>
<tr>
<td>(n=43, 37.06%)</td>
<td></td>
<td></td>
<td></td>
<td>Metastatic deposits</td>
<td>1 (0.86%)</td>
</tr>
<tr>
<td></td>
<td>Lichen planus</td>
<td>6 (5.17%)</td>
<td></td>
<td>Capillary hemangioma</td>
<td>1 (0.86%)</td>
</tr>
<tr>
<td></td>
<td>Lichen simplex chronicus</td>
<td>5 (4.31%)</td>
<td></td>
<td>Urticaria pigmentosa</td>
<td>1 (0.86%)</td>
</tr>
<tr>
<td></td>
<td>Lichen sclerosis et atrophicus</td>
<td>1 (0.86%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lichenoid dermatitis</td>
<td>1 (0.86%)</td>
<td>Group VII</td>
<td>Toxic epidermal necrolysis</td>
<td>1 (0.86%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(n=3, 2.5%)</td>
<td>Discoid lupus erythematosus</td>
<td>1 (0.86%)</td>
</tr>
<tr>
<td></td>
<td>Pityriasis lichenoides chronicus</td>
<td>1 (0.86%)</td>
<td></td>
<td>trichoepithelioma</td>
<td>1 (0.86%)</td>
</tr>
<tr>
<td></td>
<td>Mycosis fungoides</td>
<td>1 (0.86%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group IV</td>
<td>Pemphigus vulgaris</td>
<td>5 (4.31%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=11, 9.48%)</td>
<td>Bullous pemphigoid</td>
<td>3 (2.58%)</td>
<td></td>
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<tr>
<td></td>
<td>Erythema multiforme</td>
<td>1 (0.86%)</td>
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<td></td>
<td></td>
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<tr>
<td></td>
<td>Pallegra</td>
<td>1 (0.86%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dermal bullous lesion</td>
<td>1 (0.86%)</td>
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</tbody>
</table>

In this study we divided skin diseases in eight categories according to Lever’s classification and observed distribution of various diseases accordingly. Table 1 shows distribution of skin diseases in various categories. The categorization of the skin disease was done on the basis of the location in the skin and subcutis. We found that maximum cases belonged to Group III disorders i.e. disorders of the superficial cutaneous reactive unit (37.06%) which includes Psoriasis, Lichen Planus, Mycosis Fungoides, Lichen Simplex Chronicus, Lichen Sclerosis et atrophicus and Pityriasis Lichenoides Chronicus followed by Group V disorders i.e. Perivascular, diffuse, and granulomatous infiltrates of the reticular dermis (32.75%) including majority of cases of Leprosy along with Granulomatous Lesion, Scleroderma, Calcinosis Cutis, Granuloma Annulare, Keloid and Cutaneous Vasculitides. Least number of cases were seen in group VII i.e. inflammatory disorders of skin appendages including single...
case each of TEN, DLE and Trichoepithelioma. Group I (disorders of Epidermis & superficial stratum corneum) and group II (localized superficial epidermal or melanocytic proliferations) were found to have equal distribution each comprising 6.03% of total cases. In our study Group I included Ichthyosis Vulgaris, Hypertrophic scar, Keratin cyst, Becker melanosis and Erythema Dyschromicum Perstans whereas Group II comprised of Seborrheic Keratosis, Verruca Vulgaris and Simple Papillomatous Hyperplasia. Group IV (diseases with acantholytic, vesicular and pustular morphology) constituted 9.48% of total biopsies with cases diagnosed as Pemphigus Vulgaris (4.31%), Bullous Pemphigoid (2.58%), Erythema Multiforme (0.86%) and Pallegra (0.86%) whereas Group VI comprised of 6.03% cases including sebaceous cyst (2.58%), SCC (0.86%), Metastatic deposits (0.86%), Capillary Hemangioma (0.86%) and Urticaria Pigmentosa (0.86%). During analysis of these groups in our small study, it is well brought out that Psoriasis (24.13%), Leprosy (23.27%) and Pemphigus Vulgaris (4.31%) were predominant lesions in this geographical area being covered by our institute.

Figure 2: Psoriasis, H&E

Figure 3: Lepromatous Leprosy, H&E

Figure 4: Lichen Planus, H&E
Skin lesions are heterogeneous, common in all ages and have varied clinical and histomorphological picture. Clinically different lesions may show specific histological patterns, therefore histopathology is considered the gold standard in dermatological diagnosis. However, there exist few limitations; therefore, the correlation of histopathological features and clinical findings must be done to arrive at a possible diagnosis.

In this prospective study, we included 116 skin biopsy specimen. All paraffin sections were stained with H&E to analyze the pattern of skin lesions & to evaluate distribution of skin diseases according to age, gender and category in the background of clinical findings. Ziehl Neelsen stain reactivity and other histochemical stained sections examined along with clinicohistopathological correlation wherever needed.

In the present study, out of 116 cases, maximum number of cases belonged to 41-50 years age group (n=25; 21.55%) with slight male preponderance, followed by 21-30 years (n=22; 18.96%). Least number of cases belonged to 0-10 years age group (n=4; 3.44%). It was only the age group 21-30 years which showed females preponderance with male to female ratio (1:2.6). This is contrary to study conducted by Narang et al. Symvoulakis et al. revealed over all female preponderance with male to female ratio 1:1.2 which is contrary to our study showing male to female ratio 1.2:1.

In this study we encountered maximum cases in group III and group V. In group V, leprosy was seen in 23.27% (N=27) and nonlepromatous tuberculoid granuloma were 3.44% (n=4). This study revealed group V disorders i.e. disorders showing perivascular, diffuse & granulomatous infiltrates of the reticular dermis, constituting 32.75% of total biopsies, out of which Leprosy was diagnosed most commonly (n=27, 23.27%) among group cases. Other cases included granulomatous lesions (3.44%), granuloma annulare (0.86%), scleroderma (1.72%) and calcinosis cutis (1.72%). This completely disagrees with the findings in the study by Das S et al, in which leprosy accounted for 5.64% of the total cases. This is also found higher in comparison to Narang et al which showed leprosy comprising only 17.55% of total cases.

The vesiculobullous dermatoses is included in Group IV, which showed maximum of Pemphigus Vulgaris (n=5; 4.31%). Most characteristic findings observed in these cases were prominent acanthosis with tombstone
appearance of superficial layers. It has been reported higher in females by Deepti et al\textsuperscript{6} & S R Arya et al\textsuperscript{7}.

Our findings also differ from study by Vandana et al\textsuperscript{4} where group VI i.e. Tumors and cysts of dermis and subcutis (34.16%), were most commonly observed with sebaceous cyst (13%) contributing maximum number of cases. Probably theses are studied from those parts of country where such lesions are very common. The study from Vandana et al\textsuperscript{4} has included the surgical excisions of skin lesions whereas we included only pure dermatological cases.

Group III disorders ie. disorders of the superficial cutaneous unit, disorders constituted 37.06% of total cases which happens to be the most common group in our study, out of which majority of the cases were reported as Psoriasis (n=28; 25.13%) followed Lichen Planus (n=6; 5.17%). This is quite high as compared to findings of Rao et al\textsuperscript{2} in which Psoriasis & other papulosquamous disorders constituted 2.43% of the cases. Other than Psoriasis in our study Lichen Simplex Chronicus, Pityriasis Lichenoides Chronicus, Lichen Sclerosis et atrophicus, Lichenoid dermatitis and mycosis fungoides were also observed in group III. These findings also differ from Vandana et al\textsuperscript{4} where Group III diseases were seen in only 7.61% cases.

In group I diseases (disorders limited to epidermis & stratum corneum) in our study, only 2 were diagnosed as Ichthyosis vulgaris (1.72%) followed equally by Becker melanosis, Keratin cyst, Hypertrophied scar & Erythema dyschromicum perstans (0.86%) each, whereas in Narang et al\textsuperscript{5} study group I comprised only 2 cases (1.14%) of total cases with Corn and Vitiligo one each.

In group II diseases i.e. disorders showing localized superficial epidermal or melanocytic proliferations, Verruca Vulgaris was most common (n=3, 2.58%) along with simple papillomatous lesion and Seborrhic Keratosis (n=2, 1.72%) each. This is quite low as compared to findings of Das K K et al\textsuperscript{9} in which Verruca Vulgaris or Wart (41.44%) was the commonest disorder due to viral infections. however Sandhya et al\textsuperscript{8} showed squamous papilloma to be the most common lesion in Group II followed by basal cell carcinoma and verruca vulgaris. Shweta et al\textsuperscript{11} also showed relatively higher cases of Verruca Vulgaris (10.8%) as compared to our findings.

Among group IV disorders ie. acantholytic, vesicular & pustular disorders,Which constituted 9.48% of total biopsies in this study, Pemphigus Vulgaris was the most common (n=5, 4.31%) , followed by Bullous Pemphigoid (n=3, 2.58%). Other cases included Erythema Multiforme, Dermal bullous lesion and Pellagra. This differs from the findings of Das K K et al\textsuperscript{9} in which Vescicobullous disorders constituted 0.68% of the cases with Pemphigus Vulgaris constituting 40.83% of the cases, followed by Dermatitis Herpetiformis (36.22%) & Bullous Pemphigoid (15.91%). However our observation is in concordance with Mamatha K et al\textsuperscript{12} study which also showed Pemphigus Vulgaris comprising 4.19% of cases.

Therefore based on the analysis of cases, our study clearly emphasizes that three most common skin diseases in cohort of our patients are infective (Leprosy; 23.27%), papuloaquamous (Psoriasis; 24.13%) and vesiculobullous (Pemphigus Vulgaris; 4.31%). Although Psoriasis was commonest but other studies have reported lower percentage amongst papulosquamous group.

Ziehl Neelsen stain was performed on 28 biopsies out of which 16 (57.14%) biopsies came out to be negative for acid fast bacilli while 12 (42.85%) biopsies demonstrated presence of acid fast bacilli. This varies widely as compared to Narang et al\textsuperscript{5} in which only 4.87% biopsies were found to be positive for acid fast bacilli whereas 95.12% were negative for the same.

We also attempted to correlate the clinical diagnosis with histomorphological features in 110 cases provided with the same. We found histomorphological resemblance to clinical diagnosis in 79.09% cases whereas in 21.81% clinico-histopathological correlation was not established. This observation is high as compared to Vandana et al\textsuperscript{4} where correlation was seen in 68.02% cases. Skin diseases often put Pathologist in difficult situation and have been a challenge to reach the most accurate diagnosis. Clinical information, knowledge of skin microanatomy and histomorphological features of various dermatoses with systematic approach are essential to narrow down the differential diagnostic; thereby achieving the most accurate and appropriate diagnosis.

The variations in the present study as compared to studies carried out elsewhere in the past could be due to difference in the geographical distribution of the several etiological factors responsible for causation of these conditions.

Conclusion

It is very obvious that in our country the Leprosy is still a menace to manage cases and a very potent eradication programme needs to be implemented to make country leprosy free. the skin diseases are very common, however very much neglected by the patients as well as health workers. It is very clear that skin is most accessible organ for clinical examination as well as diagnosis. The skin biopsy and subsequent histopathological examination has been proved as gold standard for identifying a specific dermatoses and appropriate management, being most cost effective tool.

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