Original Research Article

Histomorphological analysis and clinical correlation of neoplastic and non neoplastic skin lesions: a study in a tertiary care centre of Western Uttar Pradesh, India

Mithila Bisht*, Anjana Arya, B. C. Choudhry

Department of Pathology, Rohilkhand Medical College and Hospital, Bareilly, Uttar Pradesh, India

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*Correspondence:
Dr. Mithila Bisht,
E-mail: dr.mithila@gmail.com

ABSTRACT

Background: Clinical examination may suffice in making diagnosis of most dermatologic disorders but histopathological examination is often required to confirm the diagnosis and further categorize the lesions. Authors carried out this study to analyse the demographic and histomorphological characteristics of skin lesions, to determine the frequency of various dermatological disorders in the region and to evaluate the agreement between clinical and histopathological diagnosis.

Methods: Punch biopsies of skin lesions received in histopathology section, were included in the study. Cases over a period of six months were analysed. Clinical details were recorded and histopathological analysis done. Special stains were applied wherever required.

Results: Of the 120 cases studied, maximum cases fell in the category of 31-40 years, with male predominance. Authors observed wide variety of non-neoplastic and neoplastic lesions. Infectious diseases were the most common of all pathologies. Leprosy was the most common histopathological diagnosis. Complete clinicopathologic correlation was seen in 51.67% of cases while partial correlation was noted in 23.33% making a total of 75%. 25% histopathological diagnosis were inconsistent with the clinical diagnosis.

Conclusions: Histopathology is a gold standard investigation and plays a very important role in confirmation of clinical diagnosis of various skin lesions. Punch biopsy is a relatively easy outpatient procedure to perform.

Keywords: Histopathology, Punch biopsy, Skin lesions

INTRODUCTION

Skin is the largest organ of the body. It is a complex organ which plays many vital functions including defence via various immune mechanisms. It exerts multiple vital protective functions against environmental aggressions, rendered possible due to an elaborate structure, associating various tissues of ectodermal and mesodermal origin, arranged in three layers, including (from top to bottom) the epidermis (and its appendages), the dermis, and the hypodermis.1 Besides having an aesthetic role, skin acts as a line of defence in our immune system, provides protection against ultraviolet radiations and helps in sensory perception.

Many diseases affect the skin viz. neoplastic, non-neoplastic lesions. Neoplastic lesions include the inflammatory, benign and malignant lesions of the epidermis and dermis. The non neoplastic lesions encompass a wide variety of lesions like Genodermatoses, Non-infectious erythematos and papulosquamous lesions, Vascular disorders, Non-infectious vesicobullous and vesicopustular diseases, Connective tissue diseases, Infectious diseases.
Inflammatory diseases of skin adnexa, Non-infectious granuloma, Cutaneous Toxicities of Drugs, Degenerative Diseases and Perforating Disorders, Inflammatory Diseases of subcutaneous fat, Histiocytosis, Pigmentary disorders etc.¹ Due to varied and diverse presentations of the dermatoses, during the early 19th century dermatology evolved as a separate branch.² Many skin diseases can be diagnosed in no time, by their unique clinical signs and symptoms but in many cases additional investigations become mandatory for the diagnosis. Skin biopsy followed by histopathology remains the gold standard for the diagnoses of plethora of lesions encountered in skin opd.³ A dermatologist makes a differential diagnosis based on the clinical signs and symptoms and skin biopsy is done, to be sent for histopathology. Skin biopsy is a relatively easy, convenient and most commonly practiced method in which a tissue piece is taken from an affected area by various methods like punch biopsy, shave biopsy, excision biopsy, wedge biopsy and sent to histopathology lab in 10% Neutral Buffered Formalin.

Punch biopsy is most widely used and relatively easy method where, a piece of lesional tissue is punched out using a disposable or sterilisable punch available in varying sizes. Non-facial lesions recommend a 4-mm punch; and a punch of 5 mm or more is needed in granulomatous and atypical lesions.⁴ It is advisable not to take biopsies less than 3 mm as vital features may be missed in such small biopsies. The punch biopsy site heals by secondary intention. In a biopsy, a fully developed lesion gives a better result than early or involuting lesion.⁵

In conditions like dermatitis herpetiformis, a shave biopsy is preferred as it provides a larger surface area. A biopsy with perilesional area is often ideal but it’s not feasible in mucosal lesions. In lesions requiring direct fluorescence studies (e.g. Cutaneous LE, Dermatomyositis, vasculitides, LP), biopsy should be taken from lesional area.¹ Histopathology has an added advantage that it can be supplemented with immunohistochemistry especially in case of tumors and special stains can be applied, wherever needed e.g. Ziehl Nelsen stain for acid fast bacilli, Fite faraco stain for lepra bacilli and Periodic Acid Schiff(PAS) stain and silver stains for demonstrating fungal elements.⁴

Histopathological diagnosis, which gives the definite diagnosis of the lesion, helps to assess the clinicopathologic consistency of various groups of lesions and to comprehend the entire dermatologic disease spectrum. In the present era, dermatopathology has become an indispensable tool for a clinical dermatologist to confirm a clinical diagnosis. Moreover tissue specimen sent for histopathology can be used to perform ancillary tests, special stain, immunohistochemistry and immunofluorescence. Prevalence and incidence of skin diseases shows regional variation. Disease distribution patterns vary from one country to another and various regions within.

**METHODS**

Present study is a prospective study which was done from February 2019 onwards over a period of 6 months in the histopathology section of Department of Pathology, Rohilkhand Medical College and Hospital, Bareilly after taking approval from institutional ethics committee. All the well preserved skin punch biopsies received in the department of pathology of our hospital were included in the study. A total of 120 cases were included in the study. The punch biopsies received in 10% neutral buffered formalin were subjected to routine processing using automated tissue processor. After dehydration, clearing and impregnation, paraffin wax sections with the embedded skin biopsy were cut in microtome and 4 micron thickness sections were taken on glass slides. Staining with routine Haematoxylin and Eosin stain was done. Special stains like Ziehl Nielsen stain (for Acid Fast Bacilli), Fite faraco stain for lepra bacilli and Periodic Acid Schiff(PAS) stain were applied wherever necessary as per the standard protocols.⁴

Histopathological diagnosis was made by two independent pathologists was made and microscopic findings were correlated with the clinical diagnosis. Based on the histopathological diagnosis, the cases were divided into 15 broad groups, namely Genodermatoses, non-infectious erythematous, papular and squamous diseases, vascular diseases, vesicobullous and pustular diseases, connective tissue diseases, inflammatory diseases of adnexal structures, infectious diseases, tumors and cysts of skin, histiocytosis, pigmentary disorders, degenerative and perforating disorders(perforating folliculitis), non-infectious granuloma, inflammatory diseases of subcutaneous fat, pigmentary disorders.³ A category of nonspecific dermatoses was given to the cases in which nonspecific histopathologic findings were reported. Other demographic data including age, sex along with site of lesion, type of lesion, duration of symptoms, provisional clinical diagnosis was recorded and analysed. The histopathological diagnosis given was matched with the single or multiple provisional clinical diagnoses made by the dermatologist and clinicopathologic consistency was evaluated. Cases were divided as being clinicopathologically consistent where the provisional diagnosis/diagnoses matched with the histopathologic diagnosis, clinicopathologically inconsistent where it did not match. Cases were labelled as partially consistent, where a specific variety of a dermatologic lesion was missed in the clinical diagnosis or authors found some another pathologic lesion in addition to the provisional clinical diagnosis. Statistical analysis was done using R studio.

**RESULTS**

A total of 120 cases were studied in the present study. Microscopic and clinical findings were observed, correlated and results were tabulated. Histopathological diagnoses were further divided into 15 broad groups.
The age and sex distribution of the 120 cases is given in Table no.1. Maximum number of cases (%) belonged to the age group of 31-40 years age group followed by 21-30 years as depicted in Table 1. The age range recorded in our study was between 4 years to 80 years. Males were predominant in our study with a M:F ratio of 1.45:1. Amongst the various groups, authors observed that female cases were seen more in cutaneous toxicity of drugs, tumors and cysts of skin and vascular lesions.

With regards to duration of illness in the various cases received, in 24 cases the patients came with a history of <1 month, 27 cases had a history of >12 months (1 year), maximum cases i.e.47 (39.16%) cases presented with a history of 1 to 6 months and 22 presented with a history of 6 to 12 months.

Out of the 120 lesions, 61 showed localized presentation while 59 had generalized involvement (maximum cases of generalized lesions being that of leprosy i.e.23).

The clinical presentation of lesions was that of plaques (36 cases), macules (21 cases), papules (21 cases), nodules (9 cases), localized swelling (9 cases), bullae and vesicles (8 cases), sensory loss (6 cases), thickened skin (4 cases), ulcerated lesions (4 cases) localized pigmented lesion (1 case) and verrucous lesion (1 case).

Sensory loss was clinical feature seen in leprosy cases and in a case of systemic sclerosis, while swelling was clinically seen in most tumors and cysts of skin and in a lesion of rhinophyma. Thickened skin was a feature of morphea cases.

### Table 1: Age and sex distribution.

| Age group (Years) | Sex | Total | Percentage of age group (%) |
|-------------------|-----|-------|-----------------------------|
|                   | Female | Male |                             |
| <10               | 1     | 3     | 4                           | 3.33 |
| 11-20             | 13    | 10    | 23                          | 19.16 |
| 21-30             | 12    | 17    | 29                          | 24.17 |
| 31-40             | 19    | 15    | 34                          | 28.34 |
| 41-50             | 1     | 9     | 10                          | 8.34  |
| 51-60             | 2     | 11    | 13                          | 10.83 |
| 61-70             | 1     | 4     | 5                           | 4.16  |
| >70               | 0     | 2     | 2                           | 1.67  |
| Total             | 49    | 71    | 120                         | 100   |
| Percentage of sex | 40.8% | 59.2% |                             |

### Table 2: Histopathological findings and disease groups.

| Group                                           | Total cases in group (%) | Histopathological diagnosis                      | No. of cases | % of Histopathological diagnosis |
|-------------------------------------------------|--------------------------|--------------------------------------------------|--------------|----------------------------------|
| Infectious diseases                             | 49 (40.83%)              | Leprosy                                          | 43           | 35.83                            |
|                                                 |                          | Lupus vulgaris                                   | 4            | 3.33                             |
|                                                 |                          | Mycetoma                                         | 1            | 0.83                             |
|                                                 |                          | Tuberculosis verruca cutis                       | 1            | 0.83                             |
| Non infectious erythematous, papular and squamous diseases | 14 (11.66%)              | Lichen planus pigmentosus                        | 5            | 4.16                             |
|                                                 |                          | Lichen planus                                    | 4            | 3.33                             |
|                                                 |                          | Lichen piloipilaris                              | 1            | 0.83                             |
|                                                 |                          | Lichen nitidus                                   | 1            | 0.83                             |
|                                                 |                          | Psoriasiform dermatitis                          | 1            | 0.83                             |
|                                                 |                          | Pustular psoriasis                               | 2            | 1.66                             |
| Connective tissue diseases                      | 13 (10.83)               | Morpha                                           | 9            | 7.5                              |
|                                                 |                          | Keloid                                           | 1            | 0.83                             |
|                                                 |                          | Hypertrophic lupus erythematosus                 | 1            | 0.83                             |
|                                                 |                          | Discoid lupus erythematosus                      | 1            | 0.83                             |
|                                                 |                          | Systemic sclerosis                               | 1            | 0.83                             |
| Tumors and cysts of skin                       | 12 (10%)                 | Angiolipoma                                      | 1            | 0.83                             |
|                                                 |                          | Basal cell adenoma                               | 1            | 0.83                             |
|                                                 |                          | Basal cell carcinoma                             | 1            | 0.83                             |
| Type of leprosy                               | No. of cases | No. of cases positive for fite faraco stain |
|----------------------------------------------|--------------|--------------------------------------------|
| Tuberculoid leprosy                          | 4            | 0                                          |
| Borderline tuberculoid leprosy               | 2            | 0                                          |
| Borderline borderline leprosy                | 6            | 2                                          |
| Borderline lepromatous leprosy               | 6            | 4                                          |
| Lepromatous leprosy                          | 4            | 4                                          |
| Indeterminate leprosy                        | 12           | 6                                          |
| Erythema nodosum leprosum                    | 8            | 8                                          |
| Histiod leprosy                              | 1            | 1                                          |
| Lupus vulgaris                               | 4            | 0                                          |
| Tuberculous verruca cutis                    | 1            | 0                                          |
| Mycetoma                                     | 1            | NA                                         |
| Total                                        | 49           | 25                                         |

Table 2 reveals the distribution of cases based on the histopathological diagnosis and their distribution according to various disease groups.
Table 4: Clinicopathologic consistency in various disease groups.

| Groups                                           | Consistent | Partially consistent | Non consistent |
|--------------------------------------------------|------------|----------------------|----------------|
| Histiocytoses                                     | 1          | 0                    | 0              |
| Connective tissue diseases                        | 11         | 0                    | 2              |
| Cutaneous toxicities of drugs                     | 2          | 0                    | 1              |
| Degenerative diseases and perforating disorders   | 0          | 0                    | 1              |
| Genodermatoses                                    | 4          | 0                    | 0              |
| Infectious diseases                               | 19         | 26                   | 4              |
| Inflammatory diseases of skin adnexa              | 1          | 0                    | 2              |
| Inflammatory diseases of subcutaneous fat         | 0          | 0                    | 1              |
| Non infectious erythematous, papular and squamous diseases | 11         | 1                    | 2              |
| Non infectious granuloma                          | 1          | 0                    | 0              |
| Non infectious vesicobullous and vesicopustular diseases | 5         | 0                    | 0              |
| Pigmentary disorders                              | 1          | 0                    | 0              |
| Tumors and cysts of skin                          | 5          | 1                    | 6              |
| Vascular diseases                                 | 1          | 0                    | 4              |
| Non specific dermatoses                           | 0          | 0                    | 7              |
| Grand total                                       | 62         | 28                   | 30             |
| Percentage consistency (%)                        | 51.67%     | 23.33%               | 25%            |

Figure 1: H&E stained sections (a) Pustular psoriasis (Non infectious erythematous and papulosquamous diseases), munromicroabscess (b) Hailey Hailey disease (Genodermatoses), dilapidated brick wall appearance, (c) Keratosis pilaris, (Inflammatory diseases of skin adnexa) plugged hair follicle with orthokeratin (d) Leucocytoclastic vasculitis (Vascular diseases), perivascular neutrophilic infiltrates and leucocytoclasia (karyorrhexis) in insat.

Out of 120 cases, definite diagnosis was given in 113 cases while in 7 cases, non-specific histologic findings were described (Non-specific dermatoses).

The frequency of various diagnosis shows a wide variety of neoplastic and non-neoplastic lesions. Authors observed 47 varieties of lesions in our experience (Figure 1-5) which authors further divided into 15 broad groups as depicted in Table 2.

Figure 2: H&E stained sections (a)Pemphigus vulgaris (Non infectious Vesicobullous disorder), intraepidermal blister in suprabasal plane, (b) Morphea(Connective tissue disorder), absence of adnexa and presence of fibrosis and collagen, (c) Congenital melanocytic nevus (Pigmentary lesions), groups of nevus cells (Pigment laden melanoma cells in insat), (d) Lichen nitidus (Non infectious erythematous and papulosquamous diseases), dense infiltrate of lymphocytes, histiocytes in dermal papillae.
Most common cases were those of infectious diseases (40.83%), in which leprosy was the most common disease with 43 cases in all (35.8%), followed by non-infectious erythematous, papular and squamous diseases (12.4%) included 11 cases of lichen planus and its variants, 2 cases of pustular psoriasis and a case of psoriasiform dermatitis. Third most common group of disease in our study was connective tissue disorder, in which predominantly morphea was seen (9 cases) and other cases were of hypertrophic lupus erythematosus, discoid lupus erythematosus, systemic scleroderma and keloid with 1 case of each. Least common cases belonged to the groups of Histiocytosis (Xanthelasma), Pigmentary disorders (Congenital melanocytic nevus), degenerative and perforating disorders (Perforating folliculitis), non-infectious granuloma (Granuloma annulare), inflammatory diseases of subcutaneous fat (Panniculitis) with a single case in each category.

In this study, maximum cases on histopathological spectrum belonged to the infectious diseases group (40.83% of all cases), the distribution of which is given in Table 3 and Figure 4. Maximum number of cases were of leprosy (87.7% of all infectious diseases) followed by lupus vulgaris, tuberculoid verruca cutis and mycetoma. Fite faraco stain was done in all the cases and 51% cases showed positivity. Bacillary indices were highest in cases of erythema nodosum leprosum, lepromatous leprosy and Histioid leprosy. Authors divided the cases based on Ridley Jopling classification. Amongst the leprosy cases, indeterminate leprosy was the most common specific diagnosis followed by Erythema Nodosum leprosum (ENL). Tuberculoid (TT) leprosy was the least common.

With regard to the consistency with the diagnosis between dermatologist and dermatopathologist, it was observed that out of 120 cases, about 51.67% of cases showed complete clinicopathologic consistency (Table 4). 23.33% of the cases showed partial clinicopathologic correlation. Most of these cases belonged to leprosy where there was discrepancy in the specific diagnosis in the spectrum of leprosy lesions (tuberculoid to lepromatous). One case is worth mentioning (Figure 5), where a provisional diagnosis of trichoepithelioma was given, histopathological findings aided in identifying additional finding of granulomatous pathology in the same lesion. In another case, a diagnosis of lichen planus pigmentosus was given clinically diagnosed as erosive lichen planus. In about 25% of the cases, the clinical
diagnosis was inconsistent with the histopathological cases. So overall 75% of cases were either consistent or partially consistent.

**DISCUSSION**

Spectrum of dermatological lesions in our country is influenced by a variety of factors like climatic conditions, availability of clinics or health care facility, socio economic status, literacy status and cultural factors.

The age and sex distribution of the 120 cases revealed that maximum number of cases (28.34%) belonged to the age group of 31-40 years age group followed by 21-30 years (24.17%). The youngest patient in our study was 4 years old and the eldest, 80 years old, both being males. This is similar to studies by Rohit et al where also, the most common age groups were 30-39 years (26.67%) and 20-29 years (23.33%), another study by Kumar et al, with most common age groups 21-30 years (22%) and 31-40 years (19.8%). Study by Reddy et al, with maximum cases in 31 to 40 years age group (23.75%), and a study by Bajaj et al, with most common age group being 21-30 years followed by 31-40 years. A contrasting result is seen in a cross sectional study by Grover et al, with maximum cases in 11-20 age group. Also, males were predominant in this study with a M:F ratio of 1.45:1. The findings are similar to studies by Bajaj et al (1.29:1), Rohit et al (1.72:1), Kumar et al (1.56:1), D Costa et al (1.38:1).

In this study maximum clinical lesions presented as plaque like lesions, similar to finding by study of Bajaj et al. In this study, with respect to duration of illnesses, 39.16% of cases presented with a duration of 1-6 months in agreement with the study of Vaghela et al where also, most cases (44%) presented within 0-6 months.

In this study authors observed that maximum number of cases i.e. 49 (40.83%) cases in the infectious diseases group out of which leprosy cases comprised the most number of cases (35.83%, 43 cases). Second most common group was that of non-infectious erythematous, papulosquamous diseases (11.66%, 14 cases), maximum cases being those of lichen planus and its variants. Third most common group was connective tissue disorders (10.83%; 13 cases) with morphea (7.5%; 9 cases) being the predominant lesion. Likewise, Rohit et al in a study in Jaipur also found infectious diseases as the most common group in their study comprising 38.33% of all cases followed by non-infectious erythematous papular and squamous diseases (25%) and third most common were the connective tissue disorders.

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Infectious disorders have comprised 23% to 64% of skin dermatoses among Indian population in various studies. In a study by Kumar et al in Ahmedabad, leprosy was the most common histopathological diagnosis (30.6% of cases) followed by vesicobullous disorders comprising 12.5% of the cases. Vesicobullous lesions were less common in our study with 5 (4.16%) reported cases. Leprosy was also the most common lesion in studies by Bajaj et al, Narang et al, D Costa et al (study in pediatric population) and Rohit et al. In another study also conducted in western UP over a 4 year period by Grover et al, inflammatory diseases (Bullous lesions and Psoriasis) was the most common group (73.47% cases) while infectious diseases was the second most common group (22.99% cases), leprosy being the most common.

In this study, leprosy comprised 87.7% of the infectious lesions, this percentage was 78.26% in study by Rohit et al.

In a study of non neoplastic skin lesions by Vaghela et al in Gujarat, most common lesion was observed to be inflammatory disease of the dermis and epidermis (51%), while infectious diseases of skin (25%) was the second most common. Bharambhe et al, carried out a study of non-infectious erythematous and papulosquamous lesions, where lichenoid lesions (46.57%) and psoriasis (19.88%) were the most common diagnosis on histopathology, this is in coherence with the distribution of papulosquamous lesions in this study.

In contrast, another study on the non-infectious erythematous papulosquamous lesions, by Reddy et al, most common histopathological diagnosis was Psoriasis (42.5%) followed by Lichen planus. Similar findings were observed by Rohit et al, where psoriasis was commoner lesion than lichenoid lesions amongst the category of papulosquamous lesions.

In terms of clinicopathologic consistency, authors found about 51.67% of cases showed complete clinicopathologic consistency and 23.33% of the cases showed partial clinicopathologic correlation, while 25% cases had histopathologic diagnosis inconsistent with the clinical diagnosis. So, overall, 75% cases had either consistent or partially consistent correlation with the clinical diagnosis. This is similar to a study by Bajaj et al where they found clinicopathologic consistency to be 75.34%. In all the skin lesions and 84.8% for the non neoplastic lesions. Aslan et al reported 76.8% cases having positive histopathologic correlation.

This is in confirmation with this study. In a study conducted in Indore by Sarang et al clinicohistopathological correlation was seen in 43.98% cases which is lesser as compared to this study.
CONCLUSION

Present study, to our best knowledge is second study of its kind in western UP region which tried to explore and characterize the various dermatological lesions encountered in skin opd. It included 120 punch biopsies and histopathological studies revealed a wide spectrum of dermatological lesions of about 47 varieties which is representative of the spectrum of lesions seen in this region. 51.67% of the diagnosis were consistent with the clinical diagnosis, while, 25% cases were inconsistent with the clinical diagnoses. This emphasizes the role histopathology plays in coming to a definite diagnosis in various skin lesions. Maximum number of cases was in the age group 20-40 years, with males predominating. Maximum number of cases were from the broad group of infectious diseases, leprosy being the most common infectious disease, which is similar to other similar Indian studies. There is a need of adequate measures for control and prevention of this disease which is endemic in Uttar Pradesh. Histopathology of skin biopsy is an essential and gold standard method for diagnosing various neoplastic and non neoplastic skin lesions. Punch biopsy is a relatively easy method of taking skin biopsy samples. Routine histopathological examination is very useful in making the diagnosis and it can also be supplemented with other ancillary tests like special stains, immunohistochemistry, immunofluorescence to increase the diagnostic efficacy in well equipped centers. Authors can conclude that dermatopathology is an emerging branch of histopathology and has immense diagnostic potential.

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