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Histomorphological Study of Non Neoplastic Skin Lesions: A Retrospective Approach

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ABSTRACT

Introduction: Non-neoplastic skin disorders encompass a wide spectrum of pathological processes which show age, sex and geographical variation in distribution. Histopathological examination continues to play an invaluable role in diagnosis and management of non neoplastic skin disorders. The present study aims to analyse the histomorphological spectrum of non-neoplastic skin lesions received in a tertiary care hospital, to study their age and sex distribution and to classify the lesions into categories that predict clinically important attributes.

Material and Methods: The current study is an observational retrospective study conducted in Department of Pathology in a Tertiary Care Hospital in South Gujrat. 205 skin specimen of non neoplastic skin lesions received over a period of one year (February 2019 to January 2020) were studied.

Results: Among 205 cases of non neoplastic skin lesions, male predominance was seen. 21-30 years and 31-40 years were the most common age group. Infectious disorders were the most common category (73 cases) followed by non-neoplastic cutaneous cysts (72 cases). Epidermoid cyst was the common skin lesion closely followed by Leprosy. Borderline Tuberculous was the most frequent subtype of leprosy. Leprosy was most common in 21-30 years age group. Most common vesicobullous disease was Spongiotic Dermatitis followed by *Pemphigus Vulgaris*. Psoriaform and lichenoid dermatitis showed equal incidence.

Conclusion: Heterogeneity in the clinical presentation of skin diseases makes histopathological examination a gold standard technique for final diagnosis. Cutaneous cysts and infectious formed the bulk of cases. Leprosy was the most common non cystic non neoplastic skin lesion of our study.

Key Words: *Pemphigus Vulgaris*, Epidermoid cysts, Borderline Tuberculoid leprosy

INTRODUCTION

Despite advancement in molecular techniques in diagnosis and prognosis, morphology still remains the basis of diagnosis for most neoplasms and many inflammatory dermatoses.[1]

Non-neoplastic skin disorders encompass a wide spectrum of pathologic processes ranging from autoimmune to infectious to diseases of unknown etiology. In contrast to neoplastic lesions, the histopathology of inflammatory skin diseases frequently does not exhibit a one-to-one correlation with a single diagnosis and requires correlation with the Clinical presentation for a definitive diagnosis. In some cases, a specific histologic diagnosis is not required by the dermatologist while few others, accurate histological diagnoses plays the critical role of role in determining the course of treatment.[2]

The pattern of skin diseases shows variation from country to country and even region to region within a country due to different ecological factors, genetics, hygienic standards and social customs.[3] Majority of skin lesions presenting in skin outpatient department can be diagnosed on the basis of clinical history and presentation. Only in lesions where clinical find-

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ings are insufficient to reach a conclusion biopsy is sent to assist in diagnosis. The aim of the dermatopathologist should be to provide the submitting physician with a clinically relevant differential diagnosis (in the standard language of clinical dermatology) based on a description of the microscopic pathology, and, when possible, a specific diagnosis. [4] Commonly used skin biopsy techniques are punch biopsy, superficial and deep shave biopsy, deep incisional biopsy, complete excision, and curettage. [1]

As the understanding of inflammatory skin disorders is incomplete and continues to evolve, it becomes obvious that no single uniform classification of disease has been or is likely to be perfect for all uses. Instead, as many disorders as possible are classified by presumed etiology, and the rest are classified based on their most distinctive features.[4] Our study aimed at describing the histopathological profile of non-neoplastic dermatological disorders in a Tertiary Care Institute in Gujrat.

AIMS AND OBJECTIVES

Our study aims

- To study the histomorphological spectrum of non-neoplastic skin lesions received at a tertiary care institute
- To study the age and sex distribution
- To classify the lesions into major categories that predict clinically important attributes such as prognosis or response to therapy and determine the incidence of each subcategory.

MATERIAL AND METHODS

STUDY DESIGN- Observational study (retrospective)

Study Location- Study was conducted in department in a tertiary care hospital in South Gujrat

Study duration- 1 year (1st February 2019 to 30th January 2020)

Sample size –205

Inclusion criteria-

- All biopsies that showed definite signs of any specific non neoplastic pathology were included.

Exclusion criteria-

- All skin biopsies that didn't showed definite signs of any specific pathology or inadequate were excluded.
- All skin biopsy specimen showing neoplastic etiology

The present study is an observational retrospective study undertaken in Department of Pathology in a tertiary care hospital in South Gujrat. The study included a total of 205 biopsy specimens of skin(punch biopsy, excision biopsy and shave biopsy) received in histopathological section over a period of one year from February 2019 to January 2020 in which a conclusive diagnosis of non neoplastic skin lesion was made. The specimens were fixed in 10% Neutral Buffered Formalin. Specimens measuring 3 mm or less were submitted in toto, those measuring 4–6 mm were cut through the center and both halves submitted while those measuring 7 mm or more were cut in 2–3 mm slices and then submitted for processing. Tissue processing was done as per standard procedure and paraffin embedded blocks were made. Tissue sections of 5 µ thick were cut using rotary microtome and stained by Haematoxylin and Eosin followed by microscopic examination. Special stains such as Ziehl Neelsen stain, Wade Fite stain, PAS (Periodic Acid Schiff) and Masson Trichrome were performed whenever required. Detailed patient history, clinical examination findings were noted from the histopathological requisition form sent alongside the specimen

RESULTS

A total of 205 cases were included in this study. Out of these, 152 cases were male patients while 53 were female patients. Male: Female ratio was 2.8:1. Patients' age ranged from 3 years to 85 years. Most cases belonged to 31-40 years and 21-30 years age groups with 54 cases(26.3%) each.(Table I)

Histopathological examination results revealed a wide spectrum of skin lesions despite similar clinical presentation in different patients (Table II). As no single classification can perfectly encompass all lesions of skin so an attempt was made to classify the non neoplastic disorders on the basis of etiology, location in skin and pattern of inflammation. The cases were classified into Genodermatoses, Non-infectious erythematous papular and squamous diseases, infectious disorders, Vesicobullous disorders, connective tissue disorders, vasculitis, pigment disorders, deposition disorders, disorders pertaining to skin appendages(hair and nail) , photosensitivity disorders and Cutaneous cysts.(Table III)(Figure I)

Category wise, Infectious disorders of skin constituted maximum number of cases with 73 cases (35.65%) followed by Cutaneous cysts (72 cases; 35.1%) and distantly followed by Vesicobullous disorders (11 cases;8.2%).Non infectious erythematous papular and squamous diseases comprised 17 cases (7.8%).), disorders pertaining to skin appendages 6 cases(2.9%), pigment disorders 4 cases (1.9%), and connective tissue disorder 9 cases (3.9%) and Deposition disorders 4 cases Uncommon categories were Photodermatosis (2 cases) and Vasculitis (1case) and Genodermatoses(1case). Epidermoid cysts with 64 cases (31.2%) was the most common skin lesion closely followed by Lepromatous cases (60 cases; 29.2%).

Infectious Disorders

Among 73 infectious skin lesions, bacterial etiology was found in 65 cases followed by viral etiology in 8 cases. Among bacterial diseases, 61 cases were of Hansen's disease 2 while 4 cases were of Tuberculosis.

Among 61 cases of Hansen's Disease, most common was Borderline Tuberculoid leprosy (Figure II) with 15 cases (24.5%) followed by Tuberculoid Leprosy (14 cases;22.9%) and Lepromatous Leprosy (11 cases; 29.5%). Borderline Lepromatous lesions and Midborderline lepromatous lesion were 6 cases (9.8%) each. 4 cases (6.5%)of Indeterminate and 3 cases of Histoid Leprosy (4.9%) (Figure III) were also reported. Among Lepromatous Reactions, 2 cases of Type II Leprosy reaction Erythema Nodosum Leprosum were reported. (Figure IV) 21-30 years age group was the most common age group seen in 32.7% cases followed by 31-40 years. Males were more commonly affected than females(M:F=4.0:1).

There were 4 cases of cutaneous tuberculosis comprising of 2 cases of Lupus Vulgaris and 1 case each of Scrofuloderma and Tuberculous Verrucosa Cutis. All 8 cases of cutaneous viral infections were of Verrucosa Vulgaris.

Cutaneous Cysts

Out of 72 cases of cutaneous cysts, 64 cases were epidermoid cyst and 8 cases were of Trichilemmal cyst. Epidermoid cyst were most commonly seen in 21-30 Years (11 cases; 35%) and 70% cases belonged to 11-40 years age group. Male preponderance was seen (M:F= 1.6:1)

Vesicobullous diseases

Among the 17 cases of Vesico-Bullous Diseases, most cases were Intra-Epidermal Blisters (15 cases; 88.2%) while Sub-Epidermal blisters constituted only 2 cases(11.7%). Sub classifying Intraepidermal blisters on basis of location of blister, there were 2 cases of Corneal/Sub-corneal blisters, 7 cases of spinous Layer blister and 5 cases of Supra basilar blisters. Spinous layer blister comprised cases of Hailey-Hailey disease, Transient Acanthotic diseases and Spongiotic Dermatitis

Most common vesico-bullous disease was Spongiotic Dermatitis(5 cases) followed by Pemphigus Vulgaris (4 cases). (Table IV)

Non-Infectious Inflammation of Epidermis and Dermis

"Papulosquamous" disorders is defined clinically and is rather a heterogeneousgroup in terms of pathogenesis. In a histologic classification, most of these conditions fall into the general category of diseases of the superficial cutaneous reactive unit. These disorders are characterized by superficial predominantly lymphocytic inflammation, with variable effects on the other structures of the superficial integument—the epidermis, the vessels of the superficial capillary-venular plexus, and the papillary dermis and includes basic patterns of perivascular, lichenoid, and psoriasiform dermatitis.[1]

In our study, 7 cases of Psoriasiform Dermatitis, 7 cases of Lichenoid Dermatitis and 2 cases of Perivascular inflammatory dermatoses were seen.

Psoriasiform Dermatitis was seen in Psoriasis Vulgaris (2 cases)(Figure V), Parapsoriasis (2 cases) and Prurigo Nodularis (3 cases). Among cases of Interface Dermatitis, Lichenoid Interface Dermatitis was seen in Lichen Planus (3 cases), Pityriasis Lichenoid (2 cases) and *Pityriasis Lichenoides et Varioliformis Acuta* (PLEVA) (2 cases). Perivascular Dermatitis was seen in urticaria and *Pityriasis Rosea*.

Connective tissue disorders of skin comprised of 5 cases of Discus Lupus Erythematosus, 3 cases of Morphea and one case of Solar Elastosis were seen. Non-neoplastic Pigment disorders included 3 cases of Ashy Dermatosis, one case of Melasma. Deposition disorders included one case each of Non Granulomatous Inflammatory Tattoo Reaction, Ochronosis and Calcinosis Cutis.

DISCUSSION

In the present study, 205 skin biopsies of non neoplastic lesions with conclusive opinion were received over a period of one year were analysed. Age groups 31-40 yrs and 21-30 years showed equal predominance. 21-30 years age was the most common age group affected in Veldurthy[5], Kumar et al.[6] while 31-40 years was the most common age group affected in studies done by Gupta et al.[7]

Male predominance was observed in this study (M: F=2.8:1). This is consistent with most studies like Kumar et al.[8], Veldurthy[5]. This can be explained on the basis that epidermoid cysts(64 cases) and Hansen's disease (61 cases) formed the bulk of the cases and both had shown male predominance. As most patients visiting government hospital belong to lower socio-economic group hence illiteracy, occupation and social inhibition may be responsible for less reporting of cases in females in India.

Infectious disorders were the most common categories in our study followed by Non-Neoplastic cutaneous cysts. Epidermoid cyst was the most common non neoplastic skin lesion with 64 cases (31.2%) closely followed by Hansen's disease (60 cases; 29%). Hansen's Disease was the most common lesion in studies done by Mittal et al.[9], Kumar et al.[8] and Yalla et al.[10]. Non infectious erythematous papulosquamous lesions was the most common category in studies done by Gupta et al.[7] and Gulia et al.[3] On the other hand non infectious and vesicobullous Disease was

the most common category in studies done by Adhikari et al.[6] due to large number of spongiotic Dermatitis cases. As most studies on histomorphological spectrum of skin lesions are done on punch biopsy hence epidermoid cyst has not been included in many studies. It is however one of the most common lesion of skin seen. If epidermoid cyst is excluded, Leprosy with 61 cases (48.7%) will be the most common non neoplastic skin lesion of this study.

Leprosy was the most common infection in our study (84% cases). This is consistent with most studies like George et al.[11] , Yalla et al.[10], Mittal et al.[9], Kumar et al.[8] and Agarwal et al.[12].

India continues to account for 60% of new cases reported globally each year.[13] Skin biopsy is of vital importance in Hansen's disease for not only diagnosis but also for correct histological classification, bacillary index and follow up of treatment response and disease activity. It is also helpful in differentiating relapse from reversal reaction and to categorise lepromatous reaction into type 1 and 2. In our study, among cases of Hansen disease, most common lesions were Borderline Tuberculoid leprosy with 23.3% cases followed by Tuberculoid Leprosy. Borderline Tuberculoid Leprosy was the most common form of leprosy reported in George et al.[11] and Mamatha et al.[14] and Roy et al.[15] while Tuberculoid Leprosy was the most common lepromatous lesion in Yalla et al.[10] and Agarwal et al.[12](Table V)

Diagnosis of Leprosy can be made on the basis of clinical findings and skin biopsy is indicated if the diagnosis is in doubt, as in indeterminate leprosy and when other granulomatous disorders like lupus vulgaris or sarcoidosis cannot be ruled out. Indeterminate, polar Tuberculoid (TT) and Borderline Tuberculoid (TT) patients are included in the Paucibacillary group. The Multibacillary group includes Midborderline(BB), Borderline Leprosy(BL), polar Lepromatous Leprosy(LL).[16] Since Multibacillary Leprosy forms can easily be diagnosed clinically therefore lesser skin biopsies from these lesions are sent to histopathology for confirmation. Hence BT and TT forms the bulk of the cases received in histopathology department. Borderline Tuberculoid Leprosy is the most common form of leprosy in India. Mid-borderline (BB) group is unstable and very prone to reactions, and may upgrade to BT or downgrade to BL. Ridley indicated that the BB group is very uncommon because "it is unstable". For these reasons some authors have not included this borderline group in their classification.[16]

Leprosy was more commonly seen in males than females. This consistent with Veena et al.[17], Vasikar et al.[18] Male predominance may be because of many factors such as industrialization, urbanization and more opportunities for contact in males, social customs and taboos may account for the smaller number of females reporting for treatment to the hospital.

Vesico-bullous diseases constituted 5.8% cases of all cases and 8.2% of all non neoplastic non cystic diseases. Intra-epidermal blisters with 85% cases comprised most of the vesicobullous cases as compared to sub-epidermal blisters (15%) which is consistent with literature. Most common vesico bullous disease in our study is spongiotic dermatitis 5 cases; 29.4%) was the most common vesicobullous disease closely followed by Pemphigus Vulgaris (4 cases; 23.5%). This is consistent with studies done by Gupta et al.[7] and Adhikari et al.[6]. Pemphigus Vulgaris was the most common vesicobullous lesion in studies done by Mamatha et al.[14], Narang et al.[19], Kumar et al.[8]

While clinical findings like age, location and distribution of blister, gross blister characteristics, arrangement of blisters, associated inflammatory background and medical history can help in assessing a blister and forming a differential diagnosis, biopsy is essential to form definite diagnosis.[4] Histopathological examination is required for assessing the blister separation plane the mechanism(s) of blister formation and the character of the inflammatory infiltrate.[1]

In our study, lichenoid interface dermatitis and psoriaform dermatitis show equal predominance with 7 cases each. Psoriasis Vulgaris was the most common case of psoriaform dermatitis and Lichen Planus most common form of Interface (Lichenoid) Dermatitis.

Lichen planus was the most common non infectious erythematous papulosquamous disease followed by Psoriasis in studies done by George et al.[11], Chavan et al.[20], Barman et al.[21] and D costa et al.[22] Psoriasis was more common than lichen planus in studies done by Adhikari et al.[6], Yalla et al.[10] and Agarwal et al.[12]

Connective disorder constituted 3.6% cases, pigment disorders constituted 1.9%, adnexal disorders constituted while genodermatoses and Vasculitis constituted less than 1%. In studies done by Adhikari et al.[6], connective tissue disorder, pigment disorders, non-neoplastic disorders of adnexal structures constituted 2.4%, 0.7%, 1% while, genodermatoses and vasculitis comprised 2.1% and 1% respectively. In Studies done by Gupta et al.[7], connective tissue disorder, pigment disorders, non-neoplastic disorders of adnexal structures comprised 7.32%, 0.4%, 0.98%, 0.98%, 1.95%. Other studies have shown similar distribution.

It is to be noted that no classification is perfect and overlapping can be seen in several categories. For example Discus Lupus Erythematosis has been included in connective tissue disorders in our study but it is also a type of interface dermatitis (Vacuolar Degeneration). Similarly Darier's Disease has been included in intra epidermal vesico-bullous disease in our study but it is also a type of Genodermatoses and included in that category by studies done by Gupta et al.[7]

CONCLUSION

Despite advancement in molecular techniques in diagnosis and prognosis, morphology still remains the basis of diagnosis for most neoplasms and many inflammatory dermatoses. Our study included 205 cases of non neoplastic skin biopsy specimen and has documented the histopathological profile of skin lesions at our tertiary care center with a fairly high presence of infectious disorders and cutaneous cysts. Maximum biopsies received were in the age range of 21-30 years and 31-40 years. Males were predominantly affected. Most common non neoplastic skin lesion in our study was epidermoid cyst followed by Hansen's disease. Borderline Tuberculous was the most common subtypes of leprosy. Most common vesicobullous disease was Spongiotic Dermatitis followed by Pemphigus Vulgaris. The heterogeneity in the clinical presentation of skin diseases makes histopathological examination a gold standard technique for final diagnosis and clinicopathological correlation.

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Authors' Contribution

Author's Name	Conceiving and designing analysis	Collection of Data	Contributed data or analysis tools	Wrote the paper
Dr.Arpita Nishal	+	+	+	+
Dr.Himani Bajaj	+	+	+	+
Dr.Rasik Hathila	+		+	+
Dr.Mubin Patel	+		+	
Dr.Pinal Shah	+		+	
Dr. Archana Patel	+		+	
Dr. Rishikesh Balvalli		+		+

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Table I: Age Distribution of Non-Neoplastic Skin Specimen

AGE RANGE	NUMBER OF CASES	PERCENTAGE
0-10	7	3.4
11-20	27	13.1
21-30	**54**	**26.3**
31-40	**54**	**26.3**
41-50	33	16
51-60	18	8.7
61-70	2	1
71-80	5	2.4
81-90	2	1

Age groups 31-40 yrs and 21-30 years showed equal predominance

Table II: Spectrum of Skin Diseases Based on Histopathology

Name of Disease	Number of cases
Leprosy	61
Tuberculous verrucosa cutis	1
Scrofuloderma	1
Lupus Vulgaris	2
Wart	8
Epidermoid Cyst	64
Trichilemmal Cyst	8
Pemphigus Foliaceous	2
Spongiotic Dermatitis	6
Grover's disease(Transient Acantholytic Disorder)	1
Hailey-Hailey Disease	1
Darier's Disease	1
Pemphigus Vulgaris	4
Dermatitis Herpetiformis	2
Pityriasis Rosea	2
Papular Urticaria	1
Lichen Planus	3
Pityriasis LichenoidesChronica	2
Pityriasis Lichenoid et VarioliformisAcuta(PLEVA)	2
Psoriasis Vulgaris	3
Parapsoriasis	2
Prurigo simplex	3
Discus Lupus Erythematosis	5

Table II: *(Continued)*

Name of Disease	Number of cases
Morphea	3
Solar Elastosis	1
Pseudopilade of Brocq	1
Frontal fibrosing Alopecia	1
Keratosis Pilaris	1
Atrophoderma Vermiculata	1
Perforating Folliculitis	1
Nail psoriasis	1
Ashy Dermatosis	3

Epidermoid cyst was the most common non neoplastic cutaneous lesion followed by Hansen's disease.

Table III: Classification of Non Neoplastic Skin Lesions

Disease Category	Skin disease- Biopsy report			Number of cases	Percentage
Non-infectious erythematous papular and squamous diseases	Lichenoid Dermatitis-Lichen Planus, Pityriasis Lichenoid Chronica, *Pityriasis Lichenoid et Varioloformis* Psoriaform Dermatitis-Psoriasis vulgaris, Parapsoriasis Prurigo simplex Perivascular Dermatitis- Urticaria, Pityriasis Rosea			17	7.8%
Vesico-bullous disorders	Pemphigus Foliaceous Dermatitis Herpetiformis Darier's Disease Hailey-Hailey Disease Pemphigus Vulgaris Grover's disease(Transient Acantholytic Disorder) Spongiotic Dermatitis			17	8.2%
Infectious diseases	Bacterial	Leprosy	61	73	35.6
		Cutaneous Tuberculosis	4		
	Viral	Verrucae Vulgaris	8		
Connective tissue disorders	Discus Lupus Erythematosis Morphea Solar elastosis			9	3.6%
Vascular diseases				1	0.48%
Pigment disorders	Ashy Dermatosis Melasma			4	1.9
Deposition disorder	Ochronosis Calcinosis Cutis Tattoo reaction			3	1.4
Genodermatoses	Atrophoderma Vermiculata			1	0.48%
Photosensitivity reaction	Polymorphous light reaction			2	0.97%
Disorders pertaining to skin appendages	Hair	5		6	2.9%
	Nail	1			
Cutaneous cyst	Epidermoid Cyst	64		72	35.1
	Trichilemmal Cyst	8			
Total				205	100%

Infectious disorders were the most common categories in our study followed by Non-Neoplastic cutaneous cysts

Table IV: Distribution of Vesicobullous Disorders

TYPE OF BLISTER	LEVEL OF SPLIT	DISEASE	Number of cases	Total cases
Intra-Epidermal Lesion	Corneal	Pemphigus Foliaceous	2	15
	Spinous	Hailey-Hailey Disease	1	
		Transient Acantholytic Disorders	1	
		Spongiotic Dermatitis	5	
	Supra-Basal	Darier's Disease	1	
		Pemphigus Vulgaris	4	
Sub-Epidermal	Dermatitis Herpetiformis			2
Total				17

Intra-epidermal vesicobullous lesions showed predominance. Most common vesico-bullous disease was Spongiotic Dermatitis followed by Pemphigus Vulgaris

Table V: Comparative Study of Spectrum of Hansen's Disease

	Present study	George et al.[11]	Mamatha et al.[14]	Yalla et al.[10]	Agarwal et al.[12]	Vasikar et al.[18]
Indeterminate type	6.6%	2.6%	3.2%	22%	8.7	10.4
Lepromatous	18.0%	22%	27.4%	6%	26.0	11.9
Borderline lepromatous	10%	10.3%	11%	9%.	8.7	20.8
Mid-Borderline	10%	7.8%	4%	--	--	--
Borderline Tuberculoid	**24.5%**	**44%**	**42%**	13.6	17.4	35
Tuberculoid Leprosy	22.9%	11.7%	5.4%	**22%**	**30.43**	13
Histiod	4.9%	1.3%	4.4%		8.9	--
Erythema nodosum leprosum	3.27%			9%		

Most common lesion was Borderline Tuberculoid leprosy in our study among the cases of Hansen's disease

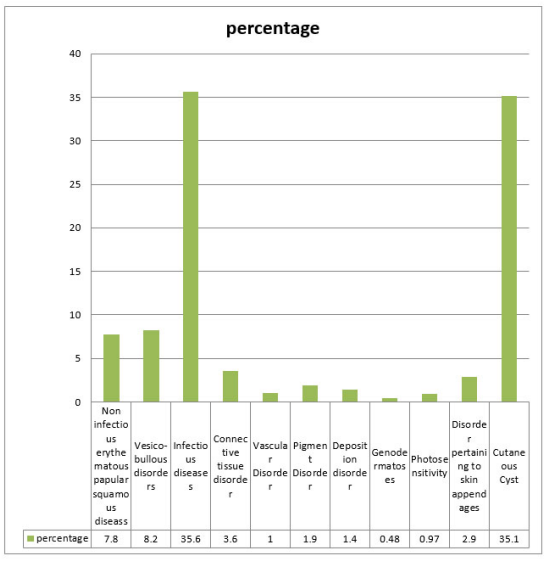

Figure I : Classification of Non-Neoplastic Skin Disorders.

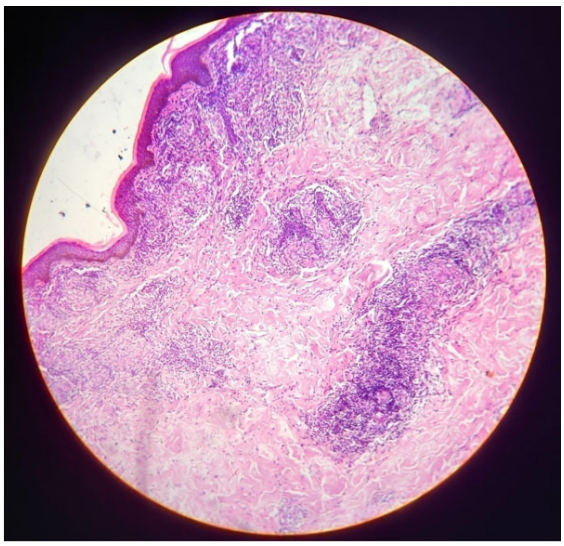

Figure II Photomicrograph of Tuberculoid Leprosy (H&E Stain 10X). Dermis showing well formed granulomas.

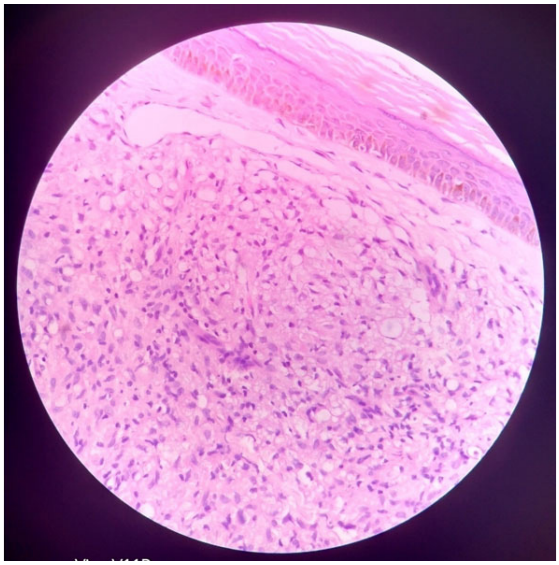

Figure III: Photomicrograph of Histiod Leprosy (H&E stain 40X).

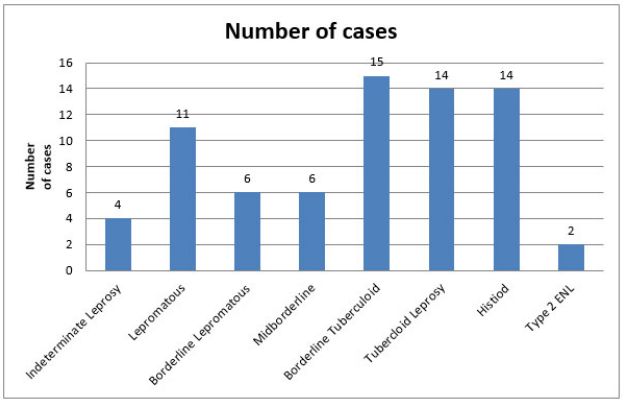

Figure V: Distribution Histological Subtypes of Leprosy.

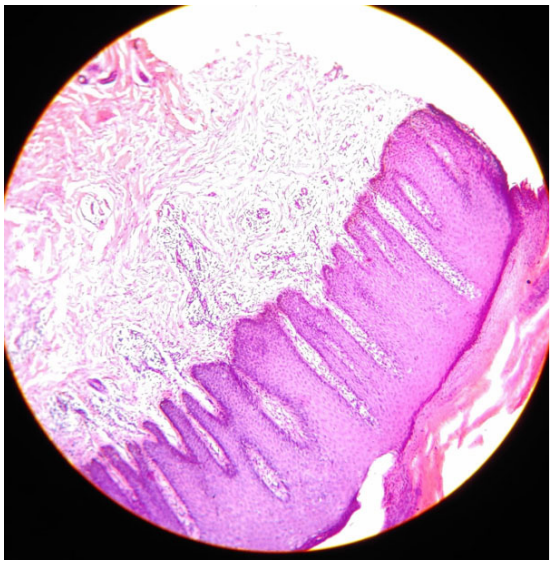

Figure IV: Photomicrograph of Psoriasis Vulgaris (H&E Stain 10X).

Skin biopsy shows hyperkeratosis with parakeratosis, regular acanthosis with elongated rete ridges, thinning of suprapapillary ridges.