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Original Article

Histopathological Study of Spectrum of Vesiculobullous Lesions of the Skin at Tertiary Care Hospital and its Clinical Correlations

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ABSTRACT

Context/Background: VESICULOBULLOUS DISEASES – one of the most primary morphological patterns of skin reaction to various external and internal pathological stimuli leading to vesiculobullous eruptions over body. Though some of vesiculobullous lesions are characteristic in their appearance and distribution, clinically many a times definitive diagnosis cannot be made by physical examination alone. – Histopathological Examination is one of the most valuable means of diagnosis. Diagnostic accuracy is obtained by correlating the clinical and histological findings.

Aims/Objectives:

- To study Histopathology of vesiculobullous disorder of skin by light microscopy and its clinical correlations.
- To correlate Histopathological findings with clinicalfindings.

Methodology: Histopathological study of skin of 50 cases during the period of 12 months was carried out on skin biopsies that were sent in 10 % formalin in histopathology section. It was kept for 24 hours in 10% formalin for proper fixation, subsequent dehydration, clearing, embedding in paraffin wax were carried out. Blocks were made, sections of 3 micrometer thickness were cut and stained with Haris Hematoxylin & Eosin stain and histopathological examination done.

Results: The commonest lesion was pemphigus vulgaris (9 cases-18%) followed by bullous pemphigoid (8 cases- 16%).

Conclusions: Punch biopsy is simple, inexpensive and safe out patient procedure with minimal discomfort to the patient and no scarring. Clinical examination along with histopathological examination of skin both together forms an important technique ensures timely diagnosis guide treatment decisions, reduce morbidity and improve patient outcomes in vesiculobullous disease.

Keywords: *Vesiculobullous disorders, histopathological study, skin biopsies, pemphigus vulgaris.*

INTRODUCTION

Vesiculobullous skin lesions (VBLs) represent a diverse group of dermatological disorders with a wide range of clinical and pathological manifestations. These lesions may arise from various underlying causes, including infectious, inflammatory, drug-induced, genetic, and autoimmune conditions. Accurate diagnosis is crucial for effective management and minimizing associated morbidity and mortality. (1)

Though some of the VBLs have a characteristic clinical presentation, many times it may not be possible to make a definite diagnosis on physical examination alone. Therefore, a histopathological examination is essential for arriving at a diagnosis and classification. (2)

Vesiculobullous diseases are the manifestations of skin response to various external and internal stimuli and it is one of the most important primary morphological patterns of skin reaction Blisters including, both vesicles and bullae which are

cavities filled with fluid present either in or underneath the epidermis. Cavities which are less than 0.5 cm in diameterare called vesicles and those which are greater than 0.5 cm in diameter are called bullae. [3]

In various disorders blisters occur at different levels within the skin. Based on site they are classified as suprabasal, intraepidermal. subcorneal and subepidermal. [4]

Objectives:

- To study Histopathology of vesiculobullous disorder of skin by light microscopy and its clinical correlations.
- To correlate Histopathological findings with clinicalfindings.

METHODOLOGY:

A histopathological study of vesiculobullous lesions of skin of 50 cases was carried out on skin biopsies received from Department of Skin, SMIMER Hospital, Surat, Gujarat over the period of one year in department of Pathology.

For the present study, all the cases presenting with vesiculobullous lesions in outpatient or inpatient department during the study period and underwent skin biopsy for histopathology were included in the study.

Inclusion criteria:

All skin biopsies from the cases with vesiculobullous disorders and suspected cases of vesiculobullous disorders irrespective of age, sex and associated diseases will be taken.

Exclusion criteria:

Biopsies of painful conditions like herpes simplex, herpes zoster, varicella etc will not be taken.
Poorly preserved skin biopsies.

- A detailed clinical history and general and local examination with particular reference to the mode of onset, characteristic and distribution pattern of the lesion was done. Under local anaesthesia, skin biopsies were taken using punch biopsy needle of 3-5 mm.
- Preserved in 10 % buffered formalin solution.
- Kept for 24 hours for proper fixation.
- Tissue processing is done.

Blocks are made and sections of 3 um thickness are cut and stainedwith Hematoxylin and eosin stain. (Harris's hematoxylin) and slides are examined by light microscopy.

RESULTS:

Age distribution:

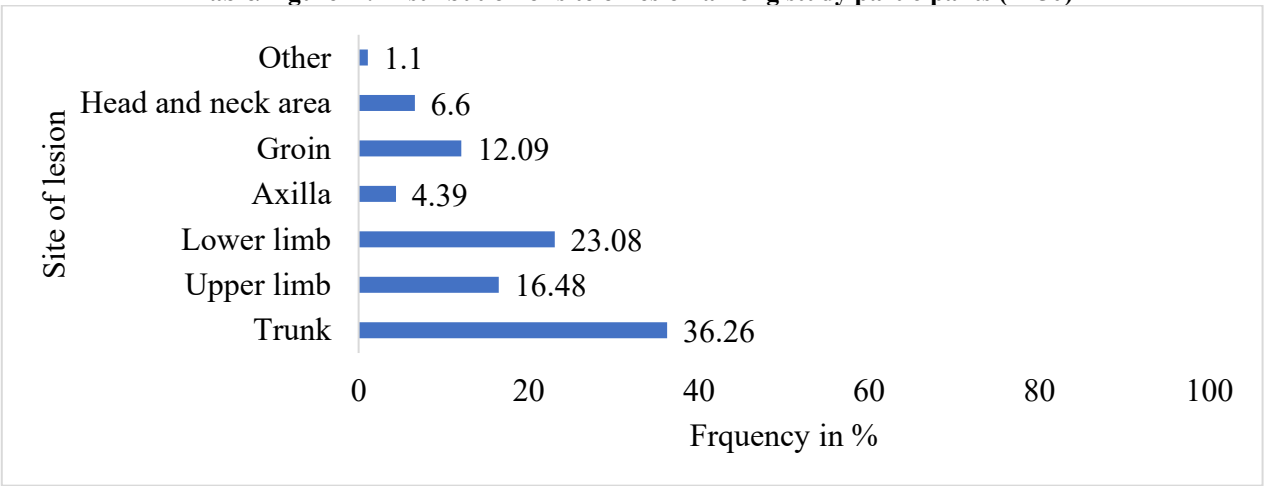
In our study, the maximum number of patients were in the age group of 41-50 years (26%), followed by 51 to 60 years (16%). The youngest patient in the study was a male child of 6 years and oldest patient was a male of 90 years, thus reveals a broad age range.

Sex distribution:

The dataset comprises a total of 50 participants, with a nearly balanced distribution between males and females. Among them, 27 (54%) are male, while 23 (46%) are female.

Site:

Table/Figure 1 : Distribution of site of lesion among study participants (n=50)



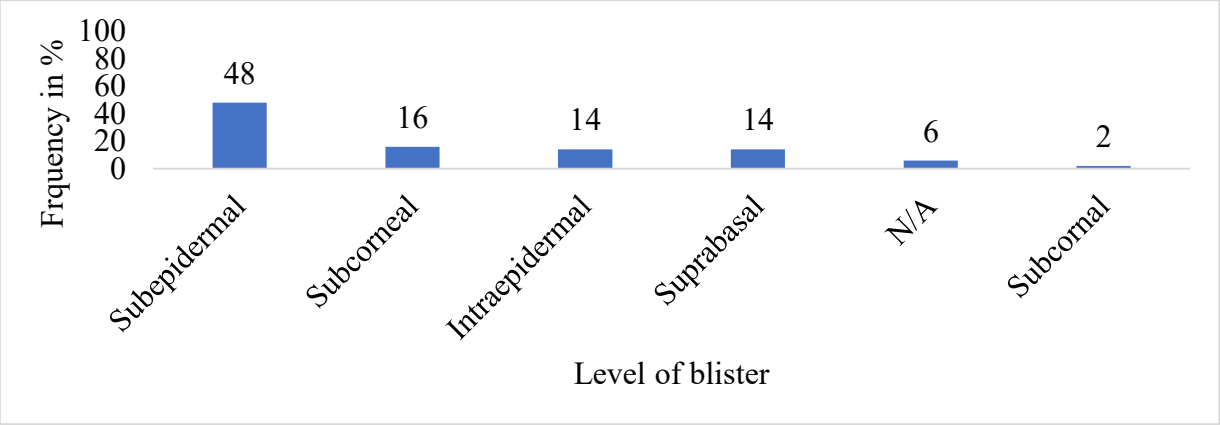
Among the 50 study participants, the most common site of lesion was the trunk, accounting for 36.26% (33 cases) of the total. The lower limb was the second most affected site, observed in 23.08% (21 cases), followed by the upper limb-16.48% (15 cases). Lesions in the groin region were noted in 12.09% (11 cases), while the head and neck area accounted for 6.6% (6 cases). Axillary involvement was seen in 4.39% (4 cases), and only one case (1.1%) was categorized under "other" sites. (Table/Figure 1)

Histopathology:

The assessment approached in our study were as follows:

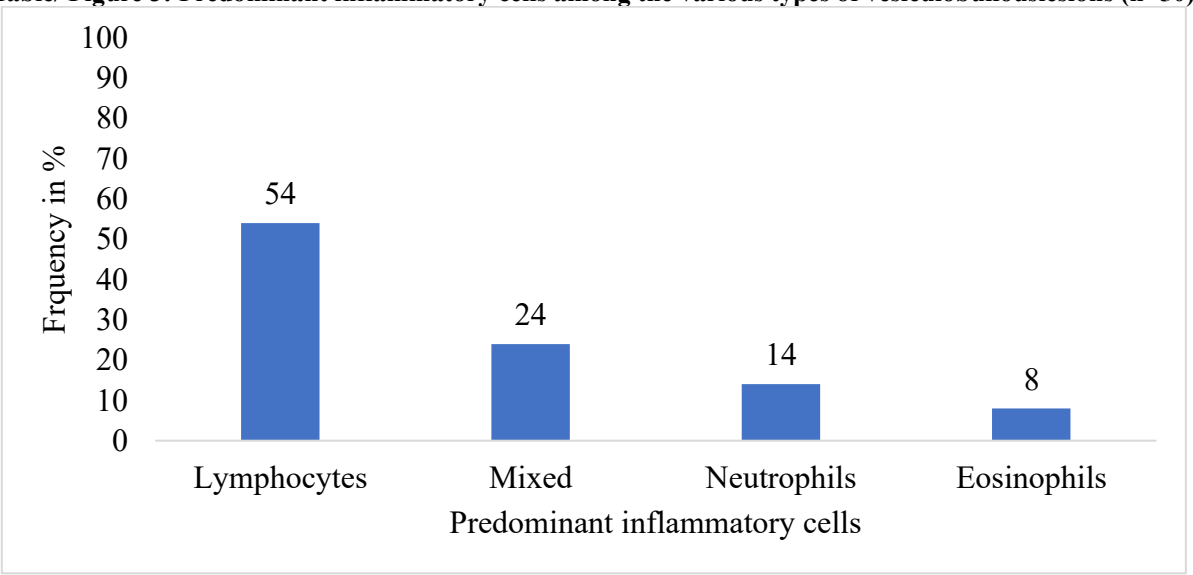
1. 1.Blister separation plane.
2. Character of inflammation.

Table/Figure 2: Level of blister formation among study participants (n=50)



A few cases of pemphigus vulgaris had suprabasal bullae due to extension of lesion. It could be explained due to the re-epithelisation of the blister. Level of blister formation was as shown in (Table/figure 2)

Table/ Figure 3: Predominant inflammatory cells among the various types of vesiculobullouslesions (n=50)



In the present study among the various types of vesiculobullous lesions, the lesions showing lymphocytic infiltrate (54%- 27 cases) were the most common followed by mixed inflammatory cell infiltrate (24%- 12 cases), lesion showing neutrophils (14%- 7 cases) and eosinophils (8%- 4 cases) in descending order. (Table/figure 3)

Histopathological diagnosis profile:

Table/ Figure 4: Histopathological diagnosis among study participants (n=50)

Histopathological diagnosis	Frequency	Percent
Bullous Pemphigoid	8	16
Dermatitis	1	2
Descriptive	2	4
Discoid Lupus erythematosus	2	4
Drug induced blisters	3	6

Epidermolysis bullosa dystrophicans	1	2
Erythema multiforme	3	6
Hailey Hailey Disease	1	2
Linear IgA Dermatosis	3	6
Pemphigus Foliaceous	5	10
Pemphigus Vulgaris	9	18
Pustular psoriasis	3	6
Subacute spongiotic dermatitis	1	2
Subcutaneous Lupus Erythematosis	3	6
Toxic Epidermal Necrolysis	2	4
Vesiculobullous disease	3	6
Total	50	100

The present study highlight a diverse range of dermatological conditions. Pemphigus Vulgaris is the most common diagnosis, accounting for 18% (9 cases), followed closely by Bullous Pemphigoid at 16% (8 cases). Drug reactions (10%), Pemphigus Foliaceous (10%), and Vesiculobullous disease (12%) also represent a notable proportion of cases, reflecting the complexity of blistering and inflammatory skin conditions.Other diagnoses, such as Discoid Lupus Erythematosus (4%), Linear IgA Dermatosis (4%), Steven Johnson Syndrome (4%), and Subcutaneous Lupus Erythematosus (6%), further highlight the diversity of autoimmune and drug-induced dermatological disorders. Less frequently occurring conditions include Epidermolysis Bullosa Dystrophicans, Hailey Hailey Disease, Phytophoto Dermatitis, Subacute Spongiotic Dermatitis, Subcorneal Pustular Dermatosis, Subepidermal Blister Disease, and Toxic Epidermal Necrolysis, each contributing 2% (1 case). The term descriptive is given to those cases where definite feature of a particular lesion could not be found. There were 2 such cases.(Table/Figure 4)

Discrepancies between clinical and histopathological diagnosis:

Table/ Figure 5:Discrepancies between clinical and histopathological diagnosis:

Clinical diagnosis	**Histopathological diagnosis**	**cases**
Steven Johnson syndrome	**Erythema Multiforme**	**2**
Drug reaction	**Toxic epidermal necrolysis**	**1**
Vesiculobullous disease	**Pustular psoriasis**	**3**
Vesiculobullous disease	**Discoid lupus erythematosus**	**1**
Vesiculobullous disease	**Descriptive**	**2**
Total		**9**

Out of 6 broadly classified clinically as vesiculobullous lesions 2 were given descriptive, 3 cases were of pustular psoriasis and 1 as discoid lupus erythematosus. 2 cases of clinically diagnosed as steven johnson syndrome were given as erythema multiforme and 1 case of drug reaction was given as toxic epidermal necrolysis.

DISCUSSION:

The mean age of participants in our study was 47.12 years, with an age range of 6 to 90 years. This is comparable to a study by **Gupta et al**.[2], who reported a mean age in the fourth and fifth decades, indicating that vesiculobullous disorders are most prevalent in middle-aged adults.

Comparison of Gender Distribution Across Studies

Study / Author	Male (%)	Female (%)	Remarks
Present Study	54%	46%	Male preponderance
Gupta et al.[2]	Near equal	Near equal	Near-equal gender ratio
Patel et al.[4]	60%	40%	Male predominance
V. SaiAbhisheket al.[5]	39.5%	60.4%	Female predominance
Ali et al.[6]	45.3%	54.7%	Female predominance
Jachaket al.[7]	49.3%	50.6%	Near-equal gender ratio

In our study, males constituted 54% of the sample and 46% of females showing Male preponderance which is opposite to studies by V. SaiAbhishek.[5], Ali et al.[6]showing female preponderence. And similar to studies by Patel et al.[4] showing male preponderance and some studies like Gupta et al.[2]and Jachaket al.[7]showing near equal gender ratio. Male predominance can be attributed to more occupational exposure of males at work. and in some studies female predominance are due to autoimmunity/immune mediated under the influence of sex hormones.

Distribution of Histopathological Diagnoses

	Diagnosis	Frequency & Percentage in Present Study	Percentage in Siddiqui et al[1]	Percentage in Gupta et al. Study[2]	Percentage in V.SaiAbhisheket al.[5]	Percentage in Ali et al.[6]	Percentage inJachak et al[7]
1	Pemphigus Vulgaris (PV)	9(18%)	50%	32.25%	18.75%	27.3%	44.57%
2	Bullous Pemphigoid (BP)	9(16%)	7%	17.2%	16.66%	31.3%	24.09%
3	Pemphigus Foliaceous	5(10%)	24%	4.3%	35.41%	4.7%	14.45%

Pemphigus Vulgaris (PV) and Bullous Pemphigoid (BP) were the most common histopathological diagnoses, accounting for 18% and 16%, respectively. This similar pattern were found inGupta et al.'s study[2]. and Jachak et al[7].

In contrast, Ali et al.[6] observedBullous Pemphigoid (BP) as the predominant lesion, comprising 31.3% followed by Pemphigus Vulgaris (PV) with 27.3%. Siddiqui et al[1] documented 50% cases of Pemphigus Vulgaris (PV) and 24% cases of Pemphigus Foliaceous (PF). SaiAbhisheket al.[5] reported 35.41% cases of Pemphigus Foliaceous (PF) and 18.75% of Pemphigus Vulgaris (PV).

These variations may be attributed to genetic predisposition, environmental factors and geographic distribution differences.

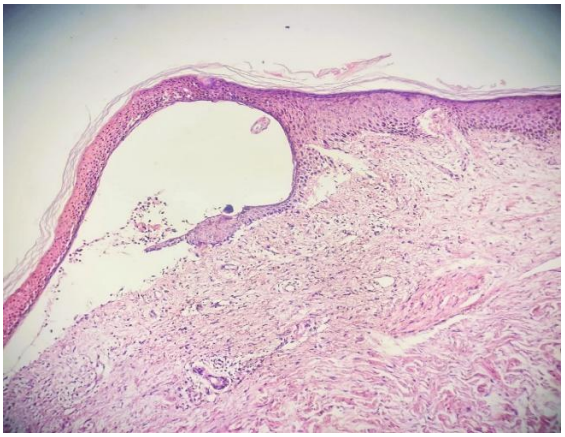
Comparative Analysis of Histopathological Blister Levels in Vesiculobullous Disorders

Study / Source	Condition	Predominant Level of Blister	Percentage / Key Observation
Present study	Bullous Pemphigoid (BP)	Subepidermal	Majority of cases
	Pemphigus Vulgaris (PV)	Suprabasal	Majority of cases
Siddiqui et al[1]	Bullous Pemphigoid (BP)	Subepidermal	All cases
	Pemphigus Vulgaris (PV)	Suprabasal	All cases
Gupta et al. [2]	Bullous Pemphigoid (BP)	Subepidermal	93.75%
	Pemphigus Vulgaris (PV)	Suprabasal	Present in all cases
Sheetal et al[3]	Bullous Pemphigoid (BP)	Subepidermal	All cases
	Pemphigus Vulgaris (PV)	Suprabasal	All cases
V. SaiAbhisheket al.[5]	Bullous Pemphigoid (BP)	Subepidermal	All cases
	Pemphigus Vulgaris (PV)	Suprabasal	88.8%
	Pemphigus Foliaceous(PF)	Subcorneal	88.23%
Ali et al.[6]	Bullous Pemphigoid (BP)	Subepidermal	All cases
	Pemphigus Vulgaris (PV)	Suprabasal	All cases

In the present study, subepidermal blisters were most common (48%), followed by subcorneal blisters (16%) followed by Suprabasal blisters were noted in 16% of cases. Majority cases of Pemphigus Vulgaris(PV) exhibit suprabasal bullous formation, while all cases of Bullous Pemphigoid demonstrated subepidermal bullous formation, same findings were reported by Gupta et al.[2] with BP predominantly showing subepidermal blistering (93.75%) and PV exhibiting suprabasal blisters in all cases, Sheetal et al[3], V. Sai Abhishek et al.[5] and Ali et al.[6].

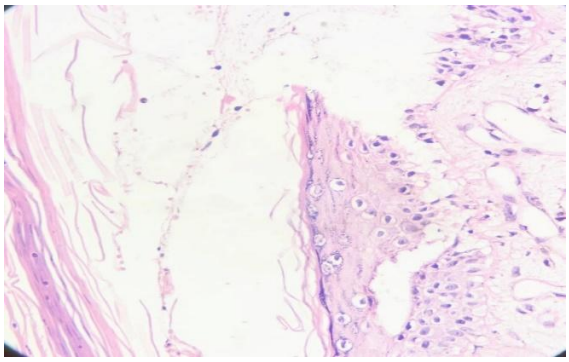
The predominance of autoimmune blistering diseases highlights their significance in dermatopathology, while the observed histopathological patterns provide valuable insights for improving diagnostic accuracy and patient management. Future research focusing on immunofluorescence and molecular studies may further enhance our understanding of these conditions and facilitate the development of targeted therapies.

Bullous pemphigoid- Tense bullae



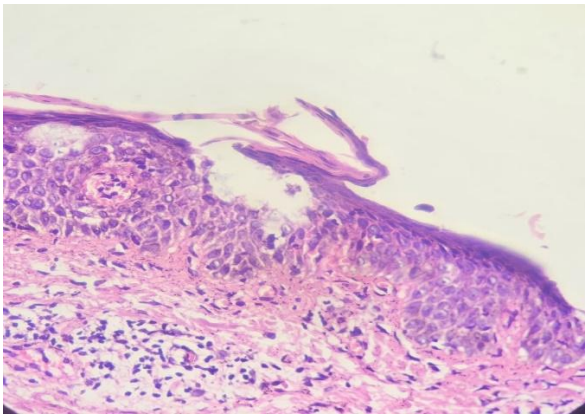
Bullous pemphigoid- Subepidermal blister formation with inflammatory cell infiltrates(10x)

Pemphigus Vulgaris- Fluid filled bullae

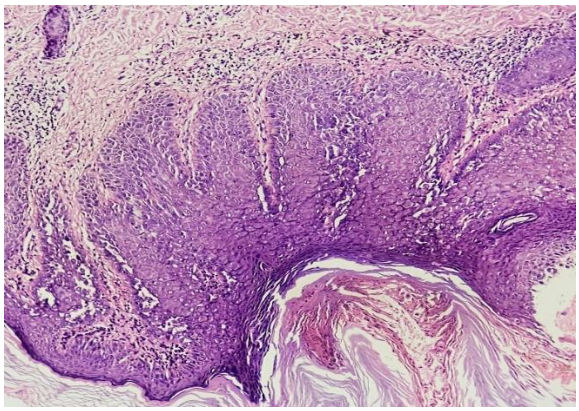


Pemphigus Vulgaris- Intra epidermal acantholytic blister has a suprabasal cleavage plan. Also showing spongiosis. (40x)

Pemphigus foliaceous



Pemphigus foliaceous- Subcorneal blister formation (10x)



Hailey Hailey disease-full-thickness acantholysis of the epidermis known as the dilapidated brick wall appearance (10x)

CONCLUSION:

This study successfully highlighted the critical role of histopathological examination in the diagnosis and classification of vesiculobullous skin disorders. Clinical features alone, though informative, were insufficient for definitive diagnosis, and histopathology proved indispensable in confirming disease subtype and guiding management.

The majority of vesiculobullous lesions displayed clear diagnostic patterns under light microscopy, supporting the value of biopsy as a standard diagnostic tool in dermatology. The clinical correlation revealed strong alignment between histological findings and patient presentation, particularly for common lesions like vesicles and bullae. The study also demonstrated the heterogeneity of vesiculobullous disorders, both in clinical morphology and histological architecture, reinforcing the need for a meticulous, combined diagnostic approach.

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