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## Histomorphological Spectrum of Vesiculobullous Lesions of Skin: A Retrospective Study in a Tertiary Care Centre

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### ABSTRACT

Dermatological lesions are universally encountered, with their prevalence and characteristics varying across countries, regions and populations. Among these, vesiculobullous lesions represent one of the most commonly encountered clinical challenges. This retrospective observational study was conducted over two years, from December 2022 to December 2024, at Konaseema Institute of Medical Sciences and RF, Amalapuram, India. A total of 56 biopsies diagnosed as non-infective vesiculobullous lesions were studied. Maximum patients were between the 5th and 7th decade of life with the male-female ratio being close to 1.08 (52% were males and 48% were females). Of the 56 non-infective vesiculobullous lesions, 46.4% cases were bullous pemphigoid, 37.5% were pemphigus vulgaris and Dermatitis herpetiformis, pemphigus foliaceus and Darier disease were 3.57% each Bullous pemphigoid was the most prevalent entity, followed by pemphigus vulgaris, dermatitis herpetiformis, pemphigus foliaceus and Darier disease.

## INTRODUCTION

The skin, as the body's largest organ, serves as the primary protective barrier, covering the entire external surface and providing a crucial first-line defense against environmental factors<sup>[1]</sup>. Skin diseases encompass a wide range of conditions, including non-specific, non-infectious and infectious disorders, as well as various benign and malignant lesions. Dermatological lesions are universally encountered, with their prevalence and characteristics varying across countries, regions and populations. These variations are influenced by factors such as age, sex, systemic comorbidities, socioeconomic conditions, literacy levels, racial characteristics and cultural practices. The prevalence of skin diseases has been reported to range between 6.3% and 11.16%<sup>[2]</sup>. Among these, vesiculobullous lesions represent one of the most commonly encountered clinical challenges<sup>[3]</sup>. A vesiculobullous lesion of the skin refers to a group of dermatological disorders characterized by diverse clinicopathological features<sup>[4]</sup>. These lesions include vesicles and bullae, which are fluid-filled cavities that form within or beneath the epidermis. Vesicles are defined as being <0.5 cm in diameter, while bullae are larger, exceeding 0.5 cm in diameter. Such lesions can present in various dermatoses, encompassing inflammatory, infectious, autoimmune, drug-induced and genetic conditions<sup>[5]</sup>. Bullous diseases display considerable variability, with some forms being potentially life-threatening. Certain bullous lesions may lead to significant sequella, necessitating early diagnosis and intervention to minimize associated morbidity and mortality<sup>[6]</sup>. Diagnosing blistering skin diseases typically requires a punch biopsy or the saucerized removal of an intact bulla when feasible<sup>[7]</sup>. A punch biopsy is a straightforward, cost-effective and safe outpatient procedure that causes minimal discomfort to the patient. Histopathological examination of biopsy specimens provides definitive diagnostic features in most primary cases of vesiculobullous skin lesions<sup>[8]</sup>.

## MATERIALS AND METHODS

This retrospective observational study was conducted over two years, from December 2022 to December 2024, at Konaseema Institute of Medical Sciences and RF, Amalapuram, India. A total of 498 skin punch biopsies were analyzed from patients with clinical suspicion of vesicobullous lesions. The specimens were fixed in 10% formal saline, followed by dehydration, clearing and embedding in paraffin wax. Paraffin blocks were prepared and 3 µm-thick sections were cut and stained using Harris' hematoxylin and eosin staining technique. This study abides by the guidelines laid by the declaration of Helsinki. The data were collected into excel sheets and statistical analysis was done using Microsoft Excel 2013.

## RESULTS AND DISCUSSIONS

56 skin biopsies were received during the study period with diagnosis pertaining to non-infective vesiculobullous lesions of the skin. Maximum patients were between the 5<sup>th</sup> and 7<sup>th</sup> decade of life with the male-female ratio being close to 1.08 (52% were males and 48% were females). Of the 56 non-infective vesiculobullous lesions, 46.4% cases were bullous pemphigoid, 37.5% were pemphigus vulgaris and Dermatitis herpetiformis, pemphigus foliaceus and Darier disease were 3.57% each. The detailed list is depicted in (Table 1). 30 cases (53.57%) were subepidermal, 23 cases (41.07%) and 3 cases (5.3%) were sub-corneal. The table showing the plane of separation in relation to the type of lesion is shown in (Table 3).

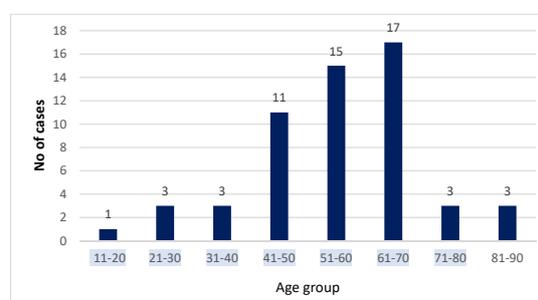


Fig. 1: Age Distribution of Vesiculobullous Lesions

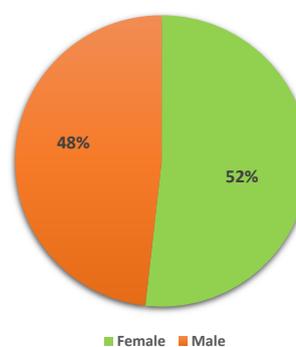


Fig. 2: No. of Cases

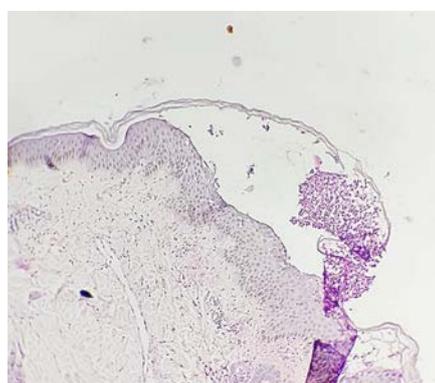


Fig. 3: Showing 10x Magnification Histopathological Section of Sub Corneal Bullae Pemphigus Foliceous

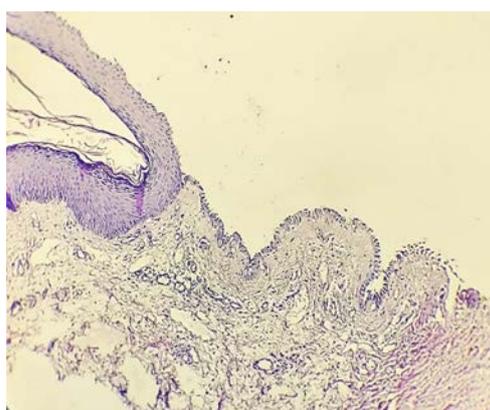


Fig. 4: Showing 10x Magnification Histopathological Section of Supra Basal Bullae, Pemphigus Vulgaris

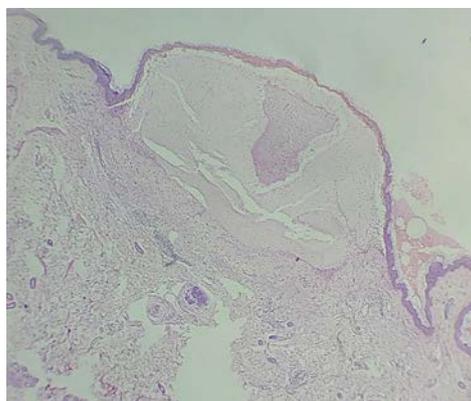


Fig. 5: Showing 10x Magnification Histopathological Section of Sub Epithelial Bullae, Bullous Pemphigoid

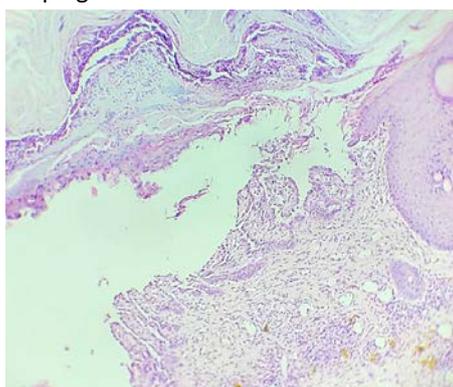


Fig. 6: Showing 10x Magnification Histopathological Section of Supra Basal Acantholysis, Darier Disease

Histological type	No of cases	%
Bullous pemphigoid	26	46.43*
Pemphigus vulgaris	21	37.50
Dermatitis herpetiformis	02	3.57
Pemphigus foliaceus	02	3.57
Linear IgA disease	01	1.79
Darier disease	02	3.57
Bullous fixed drug eruption	01	1.79
Pemphigus erythematosus	01	1.79
Total	56	100

Plane of separation	No of cases	%
Sub epidermal	30	53.57
Supra basal	23	41.07
Sub corneal	3	5.36
	56	100.00

Type of lesion	Plane of separation		
	Sub epidermal	Suprabasal	Sub corneal
Bullous pemphigoid	26	0	0
Pemphigus vulgaris	0	21	0
Dermatitis herpetiformis	2	0	0
Pemphigus foliaceus	0	0	2
Linear IgA disease	1	0	0
Darier disease	0	2	0
Bullous fixed drug eruption	1	0	0
Pemphigus erythematosus	0	0	1
%	53.57%	41.07%	5.36%

This study analyzed 498 biopsies received over the study period, identifying 11.24% (56 cases) as non-infectious vesiculobullous lesions of the skin. The demographic and histopathological findings from this cohort provide significant insights into the epidemiology and pathology of these conditions. The age distribution showed that the majority of patients were in their 5<sup>th</sup>-7<sup>th</sup> decades of life, highlighting the predilection of non-infective vesiculobullous lesions for older populations<sup>[9]</sup>. This is particularly evident in conditions such as bullous pemphigoid, which constituted 46.4% of cases, consistent with its known association with advancing age<sup>[10]</sup>. The male-to-female ratio of 1.08, with 52% males and 48% females, indicates a near-equal gender distribution, aligning with global trends reported for these disorders<sup>[11]</sup>. 44.7 percent of the patients were older than 50 years old, and 54.7 percent of the patients were female in a study conducted by Ali<sup>[12]</sup>. Pemphigus vulgaris accounted for 37.5% of cases, reaffirming its prominence as a common autoimmune vesiculobullous disorder, particularly in regions such as India, where genetic predisposition and environmental factors may play contributory roles<sup>[11]</sup>. The relatively lower prevalence of dermatitis herpetiformis, pemphigus foliaceus and Darier disease, each constituting 3.57% of cases, reflects the rarity of these conditions, emphasizing the need for histopathological evaluation to differentiate them from more common entities<sup>[12]</sup>. The histopathological analysis of these lesions revealed valuable diagnostic patterns. Subepidermal blistering, observed in 53.57% of cases, was predominantly associated with bullous pemphigoid, whereas intra epidermal blistering, accounting for 41.07% of cases, was commonly seen in pemphigus vulgaris. Sub corneal blistering, present in 5.3% of cases, was indicative of rarer conditions such as pemphigus foliaceus. These findings underscore the importance of recognizing the plane of separation as a crucial diagnostic marker for differentiating between vesiculobullous disorders. In their study, Khalili *et al*, observed Pemphigus vulgaris (29.5%) and bullous pemphigoid (21.6%) were the most frequent illnesses<sup>[13]</sup>. About 55 instances of vesiculobullous diseases in terms of prevalence, 49.09% were affected by pemphigus vulgaris, whereas

12.72% were affected by bullous pemphigoid in a study by Pratibha<sup>[14]</sup>. In various other studies including the present study, Bullous pemphigoid was the most common lesion<sup>[15,12]</sup>. The most prevalent process implicated in the study by Pavani *et al* was the breakdown of the epidermal foundation membrane, which led to the creation of subepidermal bullae (56%). 25% of cases result in intra epidermal bullae due to acantholysis<sup>[16]</sup>. While this study provides a robust histopathological perspective, it is important to acknowledge certain limitations. The absence of direct immunofluorescence (DIF) testing limits the ability to confirm autoimmune pathogenesis definitively, particularly in atypical cases. Future studies incorporating DIF or serological testing could enhance diagnostic accuracy and expand the understanding of these lesions' immunological underpinnings.

### CONCLUSION

The vesiculobullous illnesses are a diverse category of skin conditions that can show in a variety of ways. The outpatient treatment known as a punch biopsy of the skin is easy, cheap, safe and causes the patient very little discomfort. Bullous pemphigoid was the most prevalent entity, followed by pemphigus vulgaris, according to our study that compared the relative frequencies of several vesiculobullous skin diseases. Due to the diagnostic utility of histopathology in the majority of our patients, our study also highlighted the diagnostic utility of skin punch biopsy. When looking for a potential diagnosis in histology, the amount of bulla development is considered the most relevant characteristic. While the DIF might be helpful in some circumstances, it isn't always required.

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