

Original Research Article

CLINICO-HISTOPATHOLOGICAL SPECTRUM OF VESICULOBULLOUS SKIN LESIONS: A HOSPITAL-BASED CROSS-SECTIONAL STUDY

Nupur Tiwari¹, Suman Nayak², Surabhi M³

¹Assistant professor, Department of Pathology, Raniganj Institute of Medical Science, Raniganj, India.

²Assistant Professor, Department of Pathology, IQ City Medical College and Hospital, Durgapur, India.

³Senior Resident, Department of Pathology, Farookh Academy of Medical Education, Mysore-Madikeri Road, Near Ilavala, Hunsur Taluk, Mysore District, Karnataka, India.

Received : 28/03/2026
Received in revised form : 14/05/2026
Accepted : 01/06/2026

Corresponding Author:

Dr. Suman Nayak,
Assistant Professor, Department of Pathology, IQ City medical college and Hospital, Durgapur, India.
Email: docsumannayak@gmail.com

DOI: 10.70034/ijmedph.2026.2.539

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2026; 16 (2); 3257-3262

ABSTRACT

Background: Vesiculobullous skin lesions comprise a heterogeneous group of disorders characterized by the formation of vesicles and bullae due to diverse etiologies including autoimmune, infectious, inflammatory, and genetic causes. Accurate diagnosis is often challenging due to overlapping clinical features, making histopathological evaluation essential. The objective is to study the clinico-histopathological spectrum of vesiculobullous skin lesions and to evaluate the correlation between clinical and histopathological findings.

Materials and Methods: This hospital-based cross-sectional study was conducted on 100 patients presenting with vesiculobullous lesions at a tertiary care center over a period of two years. Detailed clinical evaluation was performed, followed by skin biopsy for histopathological examination using hematoxylin and eosin staining. Data were analyzed using descriptive statistics and chi-square test, with a p-value <0.05 considered statistically significant.

Results: The mean age of patients was 51.17±14.76 years, with a predominance of females (59%). The majority of cases belonged to the 51-60 years age group. Intraepidermal lesions (62%) were more common than subepidermal lesions (38%) (p=0.016). Pemphigus vulgaris was the most frequent histopathological diagnosis (45%), followed by bullous pemphigoid (29%). A significant clinico-histopathological correlation was observed in 92% of cases (p<0.001). A small proportion of cases (6%) remained inconclusive.

Conclusion: Vesiculobullous lesions show a wide clinico-histopathological spectrum, with autoimmune disorders being the most common. Histopathological examination, along with clinical correlation, plays a crucial role in accurate diagnosis and management of these conditions.

Keywords: Vesiculobullous lesions. Pemphigus vulgaris. Histopathology.

INTRODUCTION

Vesiculobullous skin lesions constitute a diverse group of dermatological disorders characterized by the presence of fluid-filled cavities within or beneath the epidermis. Vesicles are defined as small blisters less than 0.5 cm in diameter, whereas bullae are larger lesions exceeding 0.5 cm. These lesions can arise at different levels of the skin, ranging from intraepidermal to subepidermal layers, depending on the underlying pathology. The etiological spectrum is broad and includes autoimmune, infectious, inflammatory, genetic, and drug-induced conditions,

each exhibiting distinct clinical and histopathological characteristics.^[1]

Clinically, vesiculobullous lesions present with varied morphology such as tense or flaccid blisters, erosions, crusting, and mucosal involvement. Autoimmune disorders like pemphigus vulgaris and bullous pemphigoid are among the most significant causes, wherein antibodies target adhesion molecules within the skin, leading to acantholysis or dermoepidermal separation. In contrast, inherited conditions such as epidermolysis bullosa arise due to structural defects in skin proteins, while infections

like herpes simplex and varicella produce vesicles through cytopathic viral effects.^[2]

Histopathological examination plays a pivotal role in diagnosing these lesions. It provides valuable insights into the level of blister formation, nature of inflammatory infiltrate, and associated epidermal and dermal changes. However, the interpretation can be challenging, especially in older lesions where secondary changes may obscure the primary pathology. Therefore, correlation between clinical findings and histopathological features is essential for accurate diagnosis and classification.^[3]

Advances in diagnostic techniques such as direct immunofluorescence (DIF) have significantly improved the understanding and identification of autoimmune vesiculobullous disorders. DIF helps detect tissue-bound antibodies and complements, thereby aiding in differentiating between various immunobullous diseases and predicting disease activity or relapse. Despite these advancements, histopathology remains the cornerstone of diagnosis, particularly in resource-limited settings.^[4]

Aim: To study the clinico-histopathological spectrum of vesiculobullous skin lesions.

Objectives

1. To evaluate the clinical presentation and demographic distribution of vesiculobullous skin lesions.
2. To analyze the histopathological patterns of various vesiculobullous disorders.
3. To correlate clinical findings with histopathological diagnosis for accurate disease classification.

MATERIALS AND METHODS

Source of Data: The data were collected from patients presenting with vesiculobullous skin lesions attending the Dermatology Outpatient Department of the tertiary care hospital. All clinically suspected cases were referred for histopathological examination.

Study Design: The present study was a hospital-based cross-sectional observational study.

Study Location: The study was conducted in the Department of Pathology in collaboration with the Department of Dermatology at a tertiary care hospital.

Study Duration: The study was carried out over a period of 2 years.

Sample Size: A total of 100 patients with clinically diagnosed vesiculobullous lesions were included in the study.

Inclusion Criteria

- Patients presenting with vesiculobullous skin lesions.
- Patients of all age groups and both sexes.
- Patients who provided informed consent for participation in the study.

Exclusion Criteria

- Patients who refused to give consent.

- Patients with inadequate or poorly preserved biopsy samples.
- Patients already on treatment that could alter histopathological findings.

Procedure and Methodology: All patients were evaluated clinically with detailed history taking including age, sex, duration of disease, symptoms, drug history, and associated systemic illnesses. A thorough dermatological examination was performed to assess the morphology, distribution, and type of lesions.

Skin biopsies were obtained under aseptic conditions using punch biopsy technique from representative lesions. In selected cases, perilesional skin was also biopsied for better diagnostic accuracy. Clinical details were recorded in a predesigned proforma.

Sample Processing: Biopsy specimens were fixed in 10% buffered formalin and processed routinely. Paraffin-embedded sections were prepared and stained with Hematoxylin and Eosin (H&E). Special stains and direct immunofluorescence (where required) were performed to confirm the diagnosis.

Statistical Methods: Data were entered into Microsoft Excel and analyzed using appropriate statistical software. Descriptive statistics such as mean, standard deviation, frequency, and percentage were calculated. Chi-square test was applied to assess the association between clinical and histopathological findings. A p-value <0.05 was considered statistically significant.

Data Collection: Data were collected using a structured proforma including demographic details, clinical features, laboratory findings, and histopathological diagnosis. All observations were systematically recorded and analyzed to establish clinico-histopathological correlation.

RESULTS

The present study included 100 patients with vesiculobullous skin lesions, with a mean age of 51.17±14.76 years (95% CI: 48.24-54.10), indicating a predominance of middle-aged and elderly individuals. Females constituted a higher proportion (59.0%) compared to males (41.0%); however, this difference was not statistically significant ($\chi^2=3.24$, $p=0.072$). Intraepidermal lesions were more common, accounting for 62.0% of cases, compared to 38.0% subepidermal lesions, and this difference was statistically significant ($\chi^2=5.76$, $p=0.016$), suggesting a higher prevalence of intraepidermal pathology in the study population. A strong clinico-histopathological correlation was observed in 92.0% of cases (95% CI: 85.0-96.1), which was highly statistically significant ($\chi^2=70.56$, $p<0.001$), highlighting the diagnostic reliability of combined clinical and histopathological assessment. Only 2.0% of cases were diagnosed purely on histology, while 6.0% remained inconclusive, reflecting the occasional diagnostic challenges in vesiculobullous disorders.

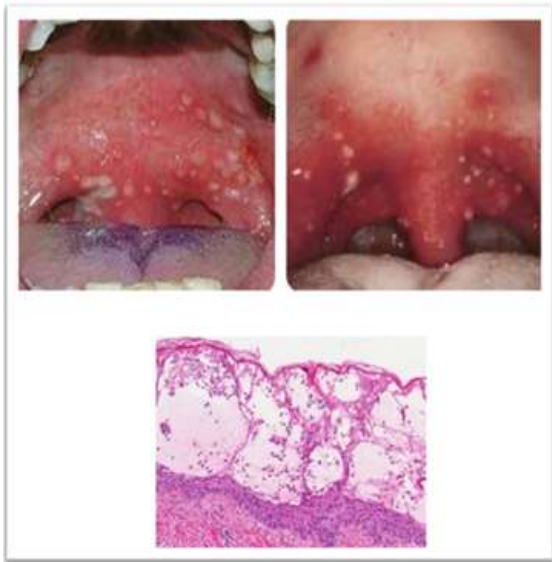


Figure 1: Herpangina



Figure 2: Pemphigus



Figure 3: Epidermolysis bullosa

Table 1: Overall clinico-histopathological spectrum of vesiculobullous skin lesions

Variable	n (%) / Mean±SD	95% CI	Test value	p-value
Age	51.17±14.76 years	48.24-54.10		
Male	41 (41.0%)	31.8-50.8	$\chi^2=3.24$	0.072
Female	59 (59.0%)	49.2-68.2		
Intraepidermal lesions	62 (62.0%)	52.2-70.9	$\chi^2=5.76$	0.016
Subepidermal lesions	38 (38.0%)	29.1-47.8		
Clinical-histopathological correlation present	92 (92.0%)	85.0-96.1	$\chi^2=70.56$	<0.001
Diagnosis purely on histology	2 (2.0%)	0.5-7.0		
Histology inconclusive	6 (6.0%)	2.8-12.5		

Table 2: Clinical presentation and demographic distribution of vesiculobullous skin lesions

Variable	n (%) / Mean±SD	95% CI	Test value	p-value
Age	51.17±14.76 years	48.24-54.10		
1-20 years	6 (6.0%)	2.8-12.5	$\chi^2=30.30$	<0.001
21-30 years	8 (8.0%)	4.1-15.0		
31-40 years	15 (15.0%)	9.3-23.3		
41-50 years	21 (21.0%)	14.2-30.0		
51-60 years	33 (33.0%)	24.6-42.7		
>60 years	17 (17.0%)	10.9-25.5		
Male	41 (41.0%)	31.8-50.8	$\chi^2=3.24$	0.072
Female	59 (59.0%)	49.2-68.2		
Upper extremity involvement	28 (28.0%)	20.1-37.5	$\chi^2=35.64$	<0.001
Lower extremity involvement	23 (23.0%)	15.8-32.2		
Trunk/abdomen involvement	17 (17.0%)	10.9-25.5		
Neck involvement	15 (15.0%)	9.3-23.3		
Face involvement	8 (8.0%)	4.1-15.0		
Scalp involvement	6 (6.0%)	2.8-12.5		
Ear involvement	3 (3.0%)	1.0-8.5		

The age distribution of patients showed that the majority belonged to the 51-60 years age group (33.0%), followed by 41-50 years (21.0%) and >60 years (17.0%), while younger age groups constituted a smaller proportion. This distribution was statistically significant ($\chi^2=30.30$, $p<0.001$), indicating a higher burden of disease in older age groups. The mean age was 51.17±14.76 years (95% CI: 48.24-54.10). Females (59.0%) outnumbered males (41.0%), although the difference was not

statistically significant ($p=0.072$). Regarding anatomical distribution, the upper extremities were most commonly involved (28.0%), followed by lower extremities (23.0%) and trunk/abdomen (17.0%). Other sites included neck (15.0%), face (8.0%), scalp (6.0%), and ear (3.0%). The variation in site distribution was statistically significant ($\chi^2=35.64$, $p<0.001$), suggesting that vesiculobullous lesions have a predilection for certain anatomical regions, particularly the extremities.

Table 3: Histopathological patterns of vesiculobullous disorders

Histopathological diagnosis	n (%)	95% CI	Test value	p-value
Pemphigus vulgaris	45 (45.0%)	35.6-54.8	$\chi^2=137.08$	<0.001
Bullous pemphigoid	29 (29.0%)	21.0-38.5		

Pemphigus vegetans	5 (5.0%)	2.1-11.2		
Pemphigus erythematosis	5 (5.0%)	2.1-11.2		
Dermatitis herpetiformis	5 (5.0%)	2.1-11.2		
Pemphigus foliaceus	2 (2.0%)	0.5-7.0		
Linear IgA bullous dermatosis	2 (2.0%)	0.5-7.0		
Oral pemphigus	1 (1.0%)	0.2-5.5		
IgA pemphigus	1 (1.0%)	0.2-5.5		
Chronic bullous dermatosis of childhood	1 (1.0%)	0.2-5.5		
Epidermolysis bullosa acquisita	1 (1.0%)	0.2-5.5		
Histology inconclusive	3 (3.0%)	1.0-8.5		

Histopathological analysis revealed that pemphigus vulgaris was the most common diagnosis, accounting for 45.0% of cases (95% CI: 35.6-54.8), followed by bullous pemphigoid (29.0%). Other less common conditions included pemphigus vegetans, pemphigus erythematosis, and dermatitis herpetiformis, each contributing 5.0% of cases. Rare entities such as pemphigus foliaceus and linear IgA bullous dermatosis accounted for 2.0% each, while oral

pemphigus, IgA pemphigus, chronic bullous dermatosis of childhood, and epidermolysis bullosa acquisita were observed in 1.0% of cases each. Histopathology was inconclusive in 3.0% of cases. The distribution of histopathological diagnoses was highly statistically significant ($\chi^2=137.08$, $p<0.001$), indicating a clear predominance of autoimmune blistering disorders, particularly pemphigus vulgaris, in the study population.

Table 4: Correlation of clinical findings with histopathological diagnosis

Clinical-histopathological correlation	n (%)	95% CI	Test value	p-value
Clinical diagnosis correlated with histopathology	92 (92.0%)	85.0-96.1	$\chi^2=70.56$	<0.001
Diagnosis made purely on histology	2 (2.0%)	0.5-7.0		
Histopathology inconclusive/difficult	6 (6.0%)	2.8-12.5		
Total	100 (100.0%)			

A high level of agreement between clinical and histopathological diagnosis was observed, with 92.0% of cases showing positive correlation (95% CI: 85.0-96.1), which was statistically highly significant ($\chi^2=70.56$, $p<0.001$). Only 2.0% of cases required diagnosis based solely on histopathology, while 6.0% of cases were inconclusive or diagnostically challenging. These findings underscore the importance of clinico-histopathological correlation in accurately diagnosing vesiculobullous skin lesions and highlight that histopathology serves as a valuable adjunct, particularly in atypical or ambiguous cases.

DISCUSSION

In the present study, the mean age of patients was 51.17 ± 14.76 years, with the maximum proportion belonging to the 51-60 years age group (33.0%), followed by 41-50 years (21.0%). This finding is comparable with Dharani et al. (2022),^[4] who also observed that vesiculobullous disorders were common in middle-aged and older adults, particularly in the 41-60 years age range. Kumar et al,^[2] (2020) reported a relatively younger age predominance, with more than half of cases occurring in the third and fourth decades, suggesting that age distribution may vary according to geographic and referral patterns. In the present study, females were more commonly affected (59.0%) than males (41.0%), though the difference was not statistically significant. This female predominance was similar to Dharani et al. (2022),^[4] who reported female preponderance, whereas Khursheed et al,^[5] (2022) observed a male predominance in their study.

In the present study, intraepidermal vesiculobullous lesions constituted 62.0% of cases, while subepidermal lesions accounted for 38.0%, showing a statistically significant predominance of intraepidermal disorders ($p=0.016$). Similar findings were reported by Ali et al. (2021),^[6] where intraepidermal lesions were more frequent than subepidermal lesions. This supports the observation that pemphigus group disorders form a major burden among autoimmune vesiculobullous diseases. Ali et al (2021),^[6] also found pemphigus vulgaris to be the commonest diagnosis, followed by bullous pemphigoid and other blistering disorders.

Regarding clinical distribution, upper extremities were the most commonly involved site (28.0%), followed by lower extremities (23.0%), trunk/abdomen (17.0%), and neck (15.0%), with statistically significant site variation ($p<0.001$). This pattern indicates that exposed and friction-prone areas were frequently affected. The present findings are broadly consistent with Gupta et al. (2022),^[3] who observed that the skin was the most common site of involvement in vesiculobullous disorders, although certain conditions such as pemphigus vulgaris and severe mucocutaneous disorders showed additional mucosal involvement.

Histopathologically, pemphigus vulgaris was the most common diagnosis in the present study, accounting for 45.0% of cases, followed by bullous pemphigoid (29.0%). This distribution was highly significant ($p<0.001$). These findings are in agreement with Suresh et al. (2024),^[7] who reported pemphigus vulgaris as the leading diagnosis, and Gupta et al. (2022),^[3] who found pemphigus vulgaris to be the most frequent lesion followed by bullous pemphigoid. Similarly, Kumar et al,^[2] (2020)

observed that the pemphigus group constituted the majority of vesiculobullous lesions, confirming the predominance of autoimmune intraepidermal blistering disorders.

In the present study, less common histological diagnoses included pemphigus vegetans (5.0%), pemphigus erythematosus (5.0%), dermatitis herpetiformis (5.0%), pemphigus foliaceus (2.0%), linear IgA bullous dermatosis (2.0%), oral pemphigus (1.0%), IgA pemphigus (1.0%), chronic bullous dermatosis of childhood (1.0%), and epidermolysis bullosa acquisita (1.0%). Comparable rare lesions were also documented by Narkhede et al. (2021),^[9] who reported a similar spectrum of less common vesiculobullous disorders. These findings indicate that although pemphigus vulgaris and bullous pemphigoid are dominant, vesiculobullous lesions represent a broad histopathological spectrum requiring careful microscopic evaluation.

Clinical-histopathological correlation was present in 92.0% of cases in the present study, while 2.0% were diagnosed purely on histology and 6.0% remained inconclusive. This strong correlation was highly significant ($p < 0.001$), emphasizing the diagnostic value of combining clinical examination with histopathological assessment. Ndukwe et al. (2022),^[10] similarly concluded that accurate diagnosis requires both clinical and histological evaluation. Parvez et al,^[11] (2023) also emphasized that histopathology plays a crucial role in confirming diagnosis and guiding management, especially in ambiguous cases. Furthermore, Khursheed et al^[1] (2022) highlighted the importance of clinicopathological correlation in improving diagnostic accuracy in vesiculobullous lesions.

The present study showed that vesiculobullous skin lesions were more common in middle-aged to elderly females, with a predominance of intraepidermal lesions. Pemphigus vulgaris was the most frequent histopathological diagnosis, followed by bullous pemphigoid. These findings are consistent with several previous studies, including Italiya et al. (2022),^[12] and Kaul et al (2023),^[8] which reported a similar predominance of autoimmune blistering disorders in histopathological analyses. The high clinical-histopathological agreement further confirms that integrated clinico-pathological evaluation remains the cornerstone for accurate diagnosis and classification of vesiculobullous disorders.

CONCLUSION

The present hospital-based cross-sectional study on the clinico-histopathological spectrum of vesiculobullous skin lesions highlights that these disorders predominantly affect middle-aged and elderly individuals, with a slight female predominance. Intraepidermal lesions were found to be more common than subepidermal lesions, indicating a higher prevalence of pemphigus group

disorders in the study population. Among the various histopathological diagnoses, pemphigus vulgaris emerged as the most frequent entity, followed by bullous pemphigoid, confirming the predominance of autoimmune blistering diseases.

A high degree of clinico-histopathological correlation (92%) was observed, emphasizing the importance of integrating clinical findings with histopathological examination for accurate diagnosis. However, a small proportion of cases remained inconclusive or required histopathological confirmation alone, indicating the diagnostic challenges posed by overlapping clinical features.

Overall, the study reinforces that histopathological examination remains the cornerstone in the diagnosis and classification of vesiculobullous skin lesions. Early and accurate diagnosis through combined clinical and histopathological assessment is essential for appropriate management and improved patient outcomes.

Limitations of the study

1. The study was conducted at a single tertiary care center, which may limit the generalizability of the findings.
2. The sample size of 100 cases, though adequate, may not fully represent the entire spectrum of vesiculobullous disorders.
3. Direct immunofluorescence (DIF) was not performed in all cases, which could have improved diagnostic accuracy.
4. Some cases showed inconclusive histopathological findings due to lesion age or secondary changes.
5. Lack of long-term follow-up limited assessment of disease progression and treatment response.
6. Selection bias may be present as only hospital-attending patients were included.
7. Rare vesiculobullous disorders were underrepresented due to their low incidence.
8. Clinical data relied partly on patient history, which may introduce recall bias.
9. Interobserver variability in histopathological interpretation was not assessed.
10. Molecular and immunological diagnostic methods were not utilized due to resource constraints.

REFERENCES

1. Khursheed S, Shah H, Ijaz A, Mehmood M, Tanvir N, Sharif S. Histopathological spectrum and role of clinicopathological correlation in the diagnosis of vesiculobullous lesions. *J Ayub Med Coll Abbottabad*. 2022 Jul 1;34(3 Suppl 1):635-9.
2. Kumar A, Shreya AS, Baig MA. Study of vesiculobullous lesions of the skin clinical and histopathology correlation. *IP J Diagn Pathol Oncol*. 2020;3(3):214-8.
3. Gupta S, Varma AV, Sharda B, Malukani K, Malpani G, Sahu H. Histopathological finding of vesiculobullous lesions of skin in relation to their clinical presentation: Prospective study from a tertiary care center. *MGM Journal of Medical Sciences*. 2022 Oct 1;9(4):448-58.
4. Dharani DK. Histopathological study of vesiculobullous skin lesions-a prospective study in a tertiary care hospital. *European Journal of Molecular & Clinical Medicine*.;9(04):2022.

5. Khursheed S, Shah H, Ijaz A, Mehmood M, Tanvir N, Sharif S. Histopathological spectrum and role of clinicopathological correlation in vesiculobullous lesions-a tertiary care hospital experience. *Journal of Ayub Medical College Abbottabad*. 2022 Jun 24;34(3 (SUPPL 1)).
6. Ali J, Islam S, Ali SM, Yaqeen SR, Aslam A, ul ain Khan Q, Malik UA, Irfan M, Naqvi H, Hashmi AA, ALI SM. Morphological spectrum of vesiculobullous skin lesions: An institutional perspective. *Cureus*. 2021 May 30;13(5).
7. Suresh M, Padma M, Parvatala A, Sreelekhy A, Vijayasree M. Clinicopathological Study Of Cutaneous Vesiculobullous Lesions-A Three Year Study In A Teaching Hospital From South India. *European Journal of Cardiovascular Medicine*. 2024 Jul 1;14(3).
8. Kaul U, Chawla AA, Sahu S, Dhar R. Spectrum of non-neoplastic skin diseases: a histopathology-based clinicopathological correlation study. *MGM Journal of Medical Sciences*. 2023 Oct 1;10(4):660-6.
9. Narkhede ND, Nikham B, Jamale V, Hussain A, Kale M. Evaluation of dermoscopic patterns of vesiculobullous disorders. *Indian journal of dermatology*. 2021 Jul 1;66(4):445.
10. Ndukwe CO, Ndukwe CC, Uzoigwe JC, Eni AO, Nnamani CS, Nwokoro OC, Chiemeka ME. Histopathological spectrum of skin lesions in the elderly: Experience from a tertiary hospital in Southeast Nigeria. *Journal of Applied Sciences and Clinical Practice*. 2022 Jan 1;3(1):14-9.
11. Parvez M, Uddin R, Mahmud S. Histomorphological study of skin lesions in a specialized tertiary care hospital: a descriptive study. *Glob Acad J Med Sci*. 2023;5.
12. Italiya SW, Purohit AS, Gohel AR, Prajapati HI. Histopathological study of non-neoplastic lesions of skin. *Asian J Pharm Clin Res*. 2022 Sep 7;15(9):180-4.