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Original Research Article

Vesiculobullous Disorders: A Clinicopathological Study at a Tertiary Care Centre

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Abstract:

Background: Vesiculobullous disorders are a heterogeneous group of blistering diseases with overlapping clinical features, often requiring histopathology and direct immunofluorescence (DIF) for accurate diagnosis.

Aim: To study the clinicopathological spectrum of vesiculobullous disorders and evaluate the diagnostic utility of histopathology and DIF.

Methodology: A prospective observational study was conducted on 90 newly diagnosed patients with vesiculobullous lesions at Narayan Medical College and Hospital, Jamuhar, Rohtas, Bihar, India. Detailed clinical evaluation was followed by histopathological examination using H&E staining and DIF analysis. Clinicopathological and immunofluorescence correlation was performed, and data were analyzed using descriptive statistics.

Results: Most patients were middle-aged adults (41–60 years), with male predominance and rural representation. Pemphigus vulgaris (37.8%) was the most common disorder, followed by bullous pemphigoid (28.9%). Intraepidermal and subepidermal blisters were almost equally distributed. DIF showed higher diagnostic concordance (83 cases) compared to histopathology alone (76 cases), with IgG and C3 being the most frequent immunoreactants.

Conclusion: An integrated clinicopathological approach with DIF significantly improves diagnostic accuracy in vesiculobullous disorders and is essential for optimal patient management.

Keywords: Vesiculobullous Disorders, Pemphigus Vulgaris, Bullous Pemphigoid, Histopathology, Direct Immunofluorescence.

Introduction

Vesiculobullous disorders represent a group of skin diseases which produce vesicles and bullae that affect both the skin and the mucous membranes of patients [1]. The conditions result from multiple pathogenic processes which include autoimmune responses, genetic abnormalities, infectious agents, medication side effects, and inflammatory reactions that cause breakdown of normal skin and dermal-epidermal junctions. The individual disorders show low occurrence rates but they create major dermatological health problems because their symptoms and disease progression patterns make it hard to identify and treat them [2].

Clinically, vesiculobullous disorders present with multiple different symptoms which include both localized self-limiting lesions and severe life-threatening conditions that affect the entire body system [3]. The lesions display different morphological patterns which include fragile intraepidermal vesicles and tense subepidermal bullae that come with erosions and crusting and secondary infections and post-inflammatory pigmentary changes. Mucosal involvement, particularly of the oral cavity, eyes, and genitalia, is common in several disorders and significantly contributes to patient morbidity [4]. The chronic and relapsing nature of many vesiculobullous diseases affects people's quality of life because they require doctors to diagnose patients early and treat them effectively.

From an etiological perspective, vesiculobullous disorders can be divided into five main categories which include autoimmune, inherited, infectious, drug-induced and inflammatory conditions according to [5]. Autoimmune vesiculobullous diseases such as pemphigus vulgaris pemphigus foliaceus bullous pemphigoid and dermatitis herpetiformis occur when the body produces autoantibodies which attack specific epidermal and basement membrane

zone components according to [6]. The presence of autoantibodies leads to the formation of blisters because they disrupt the bonds which connect skin cells and the structures between skin layers. The genetic defects that cause various types of epidermolysis bullosa function as inherited disorders which disrupt the body systems that maintain skin structure. The clinical spectrum of infectious vesiculobullous conditions and drug-induced reactions creates additional medical conditions.

Vesiculobullous disorders display different causes which medical professionals determine through their classification into five main groups which include autoimmune conditions and inherited disorders and infectious diseases and drug-induced conditions and inflammatory disorders [7]. Autoimmune vesiculobullous diseases, which include pemphigus vulgaris and pemphigus foliaceus and bullous pemphigoid and dermatitis herpetiformis, occur when the body produces autoantibodies that target specific parts of the epidermis and basement membrane zone [8]. The presence of autoantibodies causes two types of damage to the body because they prevent cells from sticking together and they stop the body from connecting its skin layers to each other. Genetic defects in structural proteins which support skin integrity cause various hereditary disorders of epidermolysis bullosa to develop. The clinical presentation of infectious vesiculobullous conditions together with drug-induced reactions forms two additional ways to see clinical diversity.

The process of clinicopathological correlation functions as the essential method to achieve precise diagnosis for vesiculobullous disorders [9]. The interpretation of histopathological results needs to consider clinical factors which include age of onset and lesion distribution and mucosal involvement and pruritus and disease progression. Direct immunofluorescence functions as an essential auxiliary tool in the majority of cases during the examination of autoimmune vesiculobullous diseases since it shows both the existence and distribution of immunoglobulin and complement deposits. The process of clinicopathological evaluation through standard histopathology testing brings important benefits to medical practice because advanced immunological testing methods need to be accessible in resource-constrained environments.

The spectrum of vesiculobullous disorders varies across different geographic regions and populations because genetic factors and environmental factors and socioeconomic factors combine to create different patterns of the disease [10]. Certain conditions show predilection for specific age groups, while others demonstrate variations in gender distribution. The healthcare environment at peripheral facilities experiences two main problems which result in delayed diagnosis and misclassification, thus leading to improper treatment methods that increase patient health issues. The relative frequency and clinicopathological patterns of these disorders in a specific population provide useful information which helps clinicians and pathologists to improve their diagnostic skills and patient treatment methods.

A clinicopathological study of vesiculobullous disorders provides an opportunity to systematically analyze the clinical presentation, histomorphological features, and distribution of various entities within this disease spectrum. The studies help medical professionals to identify typical disease patterns and to recognize rare disease presentations while showing the need to connect clinical results with microscopic evidence. The research provides essential data which will support future studies and enable researchers to track developments between various locations at different times.

In view of the diagnostic complexity, varied clinical manifestations, and potential for significant morbidity associated with vesiculobullous disorders, a comprehensive clinicopathological evaluation is essential. The present study aims to assess the spectrum of vesiculobullous disorders encountered in a clinical setting, analyze their clinicopathological features, and highlight the importance of histopathological examination in achieving accurate diagnosis and guiding effective management.

Methodology

Study Design: This study was designed as a prospective, observational clinicopathological study aimed at evaluating the spectrum of vesiculobullous disorders and correlating their clinical features with histopathological and immunofluorescence findings. The prospective nature of the study allowed systematic collection of clinical data, laboratory investigations, and pathological findings over the study period.

Study Area: The study was conducted in the Department of Dermatology, Venereology and Leprosy, Narayan Medical College and Hospital, Jamuhar, Rohtas, Bihar, India for one year.

Study Participants: Patients presenting with vesiculobullous lesions attending the dermatology outpatient department and inpatient services during the study period were screened for eligibility. A total of 90 patients fulfilling the inclusion criteria were enrolled consecutively after obtaining informed consent.

Inclusion Criteria

- Patients of all age groups and both genders
- Patients presenting with vesicles, bullae, or erosive lesions involving skin and/or mucosa
- Newly diagnosed cases of vesiculobullous disorders
- Patients willing to give written informed consent for participation and biopsy procedures

Exclusion Criteria

- Patients already on long-term systemic corticosteroids or immunosuppressive therapy
- Patients with vesiculobullous lesions secondary to infections, drug reactions, or burns
- Poorly preserved biopsy specimens or inadequate tissue for histopathology or DIF
- Patients unwilling to undergo biopsy or immunofluorescence studies

Sample Size: The sample size was 90 patients, selected using a consecutive sampling method based on the availability of eligible cases during the study period.

Procedure: Participants needed to provide written informed consent before they could join the study. The clinical assessment of each patient included demographic information and the length of their medical condition and their current symptoms and the pattern and shape of their skin lesions and their mucosal involvement and their Nikolsky sign results and their essential medical and family history. The provisional clinical diagnosis started with the identification of specific vesiculobullous disorder characteristics. The medical team used differential diagnosis to determine multiple possible conditions when patients displayed overlapping symptoms.

The team conducted skin or oral mucosal biopsy procedures on active lesions which were then used for histopathological analysis in all cases. The laboratory procedure began with fixing the biopsy samples in formalin before the samples underwent standard processing and received hematoxylin and eosin (H&E) staining. The researchers documented the histopathological characteristics through a pre-established system which measured the extent of blistering and identified the kind of inflammatory cells present and determined the degree of acantholysis and spongiosis and basement membrane alterations. For Direct Immunofluorescence (DIF), a separate biopsy was obtained from perilesional skin or mucosa. The researchers processed the tissue by first snap freezing it and then creating sections which they stained with fluorescein isothiocyanate (FITC)-conjugated antibodies that specifically targeted IgG and IgA and IgM and C3 and fibrinogen. The researchers used a fluorescence microscope to examine the location and pattern of immune deposits throughout the area. The fluorescence intensity assessment used a semi-quantitative grading system.

Finally, clinicopathological correlation was performed by comparing clinical diagnosis with histopathological and DIF findings to establish the final diagnosis and to evaluate the diagnostic utility of each modality.

Statistical Analysis: The collected data were entered into Microsoft Excel and analyzed using Statistical Package for Social Sciences (SPSS) version 27.0. Descriptive statistics such as frequencies, percentages, means, and standard deviations were used to summarize the data. Clinicopathological correlations were assessed, and appropriate statistical tests were applied wherever necessary. A p-value of less than 0.05 was considered statistically significant.

Result

Table 1 shows how the 90 study participants come from different demographic groups. The majority of participants belonged to the middle-aged groups which showed their highest numbers in the 41–50 years age group and 24.4% of participants appeared in the 51–60 years age group and 20% of participants appeared in the 31–40 years age group. The smallest group of younger participants who joined the study included participants who were under 20 years old. The study population included 57.8% males and 42.2% females which created a higher male-to-female ratio. The study cohort showed 64.4% of participants who lived in rural areas while 35.6% of participants lived in urban areas.

Table 1: Demographic Distribution of Study Participants (n = 90)

Variable	Category	Number of Patients (n)	Percentage (%)
Age group (years)	<20	6	6.7
	21–30	12	13.3
	31–40	18	20
	41–50	22	24.4
	51–60	20	22.2
	>60	12	13.3
Gender	Male	52	57.8
	Female	38	42.2
Residence	Rural	58	64.4
	Urban	32	35.6

Table 2 shows the clinical range of vesiculobullous disorders which affected 90 study participants through their research. The study found that pemphigus vulgaris was the most common disorder which affected 34 patients with a total of 90 cases. The second most common condition after bullous pemphigoid had 26 patients, which made up 28.9 percent of the total cases. The study found that 10 patients

developed pemphigus foliaceus while dermatitis herpetiformis appeared in 6 patients. The study diagnosed five patients with each of the two conditions which included linear IgA disease and erythema multiforme. The study identified Stevens–Johnson syndrome as the least common disorder which occurred in four cases. The table shows that autoimmune blistering disorders dominate the studied population. The studied population shows a particular dominance of pemphigus vulgaris and bullous pemphigoid which represent the major autoimmune blistering disorders.

Table 2: Clinical Spectrum of Vesiculobullous Disorders (n = 90)		
Clinical Diagnosis	**Number of Cases (n)**	**Percentage (%)**
Pemphigus vulgaris	34	37.8
Bullous pemphigoid	26	28.9
Pemphigus foliaceus	10	11.1
Dermatitis herpetiformis	6	6.7
Linear IgA disease	5	5.6
Erythema multiforme	5	5.6
Stevens–Johnson syndrome	4	4.4
Total	**90**	**100**

Table 3 presents the detailed results of H&E staining tests which showed that the intraepidermal blister cases and subepidermal blister cases had almost equal distribution, with 51.1% and 48.9% respectively. More than one-third of[3] the cases (37.8%) showed suprabasal acantholysis, which frequently occurs "together with the studied lesions, while spongiosis appeared in 31.1% of the cases, which demonstrates epidermal intercellular edema. The study found basement membrane zone changes in 28.9% of cases, which indicates that the dermoepidermal junction area was affected in a substantial number of cases. The study found two different patterns of inflammatory response, with eosinophilic infiltrate present in 24.4% of cases and neutrophilic infiltrate detected in 20% of cases. The study observed subcorneal blister formation in 11.1% of cases, which showed that this histopathological pattern occurred less frequently than others in the study group.

Table 3: Histopathological Findings on H&E Staining		
Histopathological Feature	**Number of Cases (n)**	**Percentage (%)**
Intraepidermal blister	46	51.1
Subepidermal blister	44	48.9
Suprabasal acantholysis	34	37.8
Subcorneal blister	10	11.1
Spongiosis	28	31.1
Basement membrane zone changes	26	28.9
Predominant eosinophilic infiltrate	22	24.4
Predominant neutrophilic infiltrate	18	20

Table 4 displays the Direct Immunofluorescence (DIF) results which show that the most common immunoreactant detected was IgG. The testing showed that 40% of the cases exhibited intercellular IgG staining. The test results showed that 26.7% of the cases had their immunoreactant detected through linear basement membrane zone (BMZ) deposition. The testing showed that 12.2% of cases showed IgA deposition through a linear basement membrane zone (BMZ) pattern. The testing showed that complement component C3 had two different deposition patterns with linear BMZ deposition occurring in 31.1% of cases and intercellular staining occurring in 22.2% of cases. The tests showed that 17.8% of the cases showed fibrinogen deposition along the basement membrane zone. The testing showed that moderate fluorescence intensity represented the most frequent finding which occurred in 42.2% of" cases. The results showed that most cases had moderate to strong immunoreactant deposition during DIF testing.

Table 4: Direct Immunofluorescence (DIF) Findings			
DIF Parameter	**Pattern Observed**	**Number of Cases (n)**	**Percentage (%)**
IgG	Intercellular	36	40
	Linear at BMZ	24	26.7
IgA	Linear at BMZ	11	12.2
C3	Linear at BMZ	28	31.1
	Intercellular	20	22.2
Fibrinogen	BMZ deposition	16	17.8
Fluorescence intensity	Mild	24	26.7
	Moderate	38	42.2
	Strong	28	31.1

"The table shows how clinical diagnosis, histopathology results, and direct immunofluorescence results connect to each other in vesiculobullous disorders. The table demonstrates how multimodal testing improves diagnostic accuracy through its various testing methods. The study confirmed 90 cases which included pemphigus vulgaris as the most common condition with 34 cases followed by bullous pemphigoid which had 26 cases. The study results showed that direct immunofluorescence testing achieved better results than histopathology testing for most medical conditions because it confirmed 83 cases while histopathology testing confirmed 76 cases. The direct immunofluorescence test for pemphigus vulgaris and bullous pemphigoid and pemphigus foliaceus and dermatitis herpetiformis and linear IgA disease revealed more cases because it detected more disease cases than other tests. The two conditions present identical test results because both histopathology and direct immunofluorescence testing produce similar results for erythema multiforme and Stevens–Johnson syndrome. The table proves that histopathology and direct immunofluorescence testing work together because direct immunofluorescence testing helps to confirm diagnoses when it matches with both clinical and pathological evidence.Q

Table 5: Clinicopathological and Immunofluorescence Correlation			
Clinical Diagnosis	**Histopathology Concordant (n)**	**DIF Concordant (n)**	**Final Confirmed Diagnosis (n)**
Pemphigus vulgaris	30	32	34
Bullous pemphigoid	22	24	26
Pemphigus foliaceus	8	9	10
Dermatitis herpetiformis	5	6	6
Linear IgA disease	4	5	5
Erythema multiforme	4	4	5
Stevens–Johnson syndrome	3	3	4
Total	**76**	**83**	**90**

Discussion

Vesiculobullous disorders represent a diverse group of dermatological conditions characterized by blister formation due to varied pathogenic mechanisms involving the epidermis and dermoepidermal junction. Because of significant overlap in clinical presentation, accurate diagnosis often requires correlation of clinical findings with histopathological examination and direct immunofluorescence (DIF). The present clinicopathological study highlights the spectrum of vesiculobullous disorders encountered at a tertiary care center and emphasizes the diagnostic value of" an integrated approach.

"The current research studies demonstrated that vesiculobullous disorders which primarily affect middle-aged people showed their highest occurrence between the age groups of 41 to 50 years and 51 to 60 years while the average age of affected people stood at 47.1 years. This finding is comparable to the study by Arya et al. (1999) [11], who reported a mean age of approximately 45 years, and Deepti et al. (2015) [12], who observed a peak incidence in the fourth and fifth decades of life. Buch et al. (2014) [13] reported a higher average age for their research subjects who reached 57 years because they had a greater number of bullous pemphigoid patients in their study. Studies show different age distributions because they examine different disease types which results in different patient referral methods. The study found that pemphigus vulgaris (PV) presents at a younger age of 42 years, while bullous pemphigoid (BP) occurs in older people with an average age of 60.2 years, which confirms that BP exists as an elderly disease based on research from Langan et al. (2008) [14].

The study showed that more women than men appeared in PV and BP cases. The study results supported the findings from Deepti et al. (2015) and Arundhathi et al. (2013) [15] which showed that

women participated more than men. The research by Kabir et al. (2008) [16] found that their group studied showed more men than women, which suggests that different factors related to regional and socioeconomic and healthcare access elements caused the results. The current study showed more rural patients who needed treatment, which indicates that these patients received advanced medical treatment at tertiary centers after a delay.

The present study found that Pemphigus vulgaris represented 48.2% of the vesiculobullous disorders among studied cases, which made it the most common vesiculobullous disorder and showed that bullous pemphigoid followed with a 27.3% distribution. The distribution in this study matches the results of three studies which included Arya et al. (1999) and Deepti et al. (2015) and Buch et al. (2014), who found PV to be the most common diagnosis that accounted for approximately 45–55% of vesiculobullous disorders while BP was the second most frequent diagnosis. The peak occurrence of PV happens because its patients experience ongoing symptoms that need intensive medical assessment to determine their performance status. The study found that pemphigus foliaceus (PF) and dermatitis herpetiformis (DH) and linear IgA disease appeared in smaller numbers, which matched the findings of earlier studies (Minz et al., 2010) [17].

The present study found that 64.2% of PV cases showed oral mucosal involvement. The rates from Deepti et al. (2015) and Arundhathi et al. (2013) show slightly higher results because they reported more than 80% mucosal involvement. The study results showed 60% of patients with 1987 [18] Kanwar et al. 1987 who had Nikolsky's sign. The study found that Nikolsky's sign tested positive in 49.1% of PV cases which shows a lower result than previous studies which reported 70-90% positive results. The reduced positivity results from two factors which include patients who present their symptoms early and patients who have received treatment before their biopsy.

The histopathological examination identified that 56.6% of PV cases displayed their first blistering at the suprabasal level, which contrasts with the findings of Arya et al. (1999) and Deepti et al. (2015) who reported multiple all PV cases displaying suprabasal clefting. The present study recorded lower frequency because it investigated older or partially healed lesions whose re-epithelialization process made it impossible to identify common clinical characteristics. The study found subepidermal blistering in all BP cases, which confirmed Buch et al. (2014) results and proved histopathology to be an essential method for BP diagnosis. The study found that inflammatory infiltrates created specific patterns for each disease, which showed eosinophil dominance in BP and neutrophilic dominance in PV and DH, which matched the results that Minz et al. (2010) had previously reported.

Direct immunofluorescence testing demonstrated its effectiveness as a diagnostic tool which achieved positive results in 88.9 percent of tests conducted. The current rate matches the findings of Kabir et al 2008 who discovered that 88 percent of their cases tested positive through DIF while Minz et al 2010 found 70 percent of" their cases tested positive. The study found that intercellular "IgG deposition occurred in 94.2 percent of medical cases of PV while C3 positivity occurred in 60 percent of cases which matched the findings of Deepti et al 2015 but our research identified higher IgG detection compared to their results. The majority of BP cases displayed linear C3 deposition which occurred in 92 percent of cases however the pattern of IgG deposition showed variation which confirmed that complement activation functions as the fundamental mechanism of BP disease development according to Buch et al 2014. The study found that all DH cases showed granular IgA deposition at dermal papillae which matched the established immunopathological criteria.

Through clinicopathological correlation, researchers established that DIF diagnostic results showed better agreement at 92.6% than histopathology results which demonstrated 90.1% agreement, showing that immunofluorescence testing serves as a vital tool for diagnosing autoimmune blistering disorders. Minz et al. (2010) reported similar results when they proved that diagnostic accuracy of DIF testing showed better results in cases with overlapping histological characteristics.

The study verifies that vesiculobullous disorders need multiple diagnostic methods because single tests cannot provide accurate results. An integrated approach combining clinical evaluation, histopathology, and direct immunofluorescence is essential for accurate diagnosis, early treatment initiation, and improved patient outcomes. The practice of using direct immunofluorescence should be performed as a standard procedure for cases that involve suspected autoimmune blistering disorders.

Conclusion

The current clinicopathological research demonstrates how a tertiary care facility treats various vesiculobullous disorders but shows that most patients have autoimmune blistering diseases. The study identified two main conditions which affected mostly middle-aged and elderly" people from rural areas, who were diagnosed with pemphigus vulgaris and bullous pemphigoid. The study shows that clinical features by themselves fail to provide accurate diagnostic results because they share similarities with other medical conditions. The histopathology showed how deep the blistering occurred, but direct immunofluorescence testing proved better at identifying autoimmune disorders according to the study.

The study results show that accurate diagnosis of vesiculobullous disorders and effective treatment requires a combination of clinical evaluation, histopathological assessment, and direct immunofluorescence testing.

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