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Original Research Article

Epidemiological, Clinical and Laboratory Profile with Treatment Patterns of Autoimmune Bullous Disorders in a Dermatology Department: A Retrospective Study

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Abstract:

Background: Autoimmune bullous disorders (ABDs) are rare, chronic mucocutaneous diseases characterized by autoantibody-mediated blister formation and significant morbidity.

Aim: To analyze the epidemiological, clinical, laboratory profile, and treatment patterns of ABDs in a tertiary dermatology department.

Methodology: This retrospective observational study at Department of Skin & VD, Sri Krishna Medical College and Hospital, Muzaffarpur, Bihar, India. included 67 patients with histopathology- and direct immunofluorescence-confirmed ABDs. Demographic, clinical, laboratory, comorbidity, therapeutic, and relapse data were extracted from medical records and analyzed using descriptive statistics.

Results: Intraepidermal (n=34) and subepidermal (n=33) diseases were nearly equally distributed. Pemphigus vulgaris (82.4%) predominated among intraepidermal disorders (mean age 48.9 years; M:F 1.25:1), while bullous pemphigoid (72.7%) was most common among subepidermal disorders (mean age 62.8 years; slight female predominance). Hypertension and diabetes were frequent, particularly in subepidermal cases. Azathioprine was the most commonly used adjuvant in both groups. Relapses were more frequent in intraepidermal disorders (35.3% single relapse).

Conclusion: ABDs showed distinct age and comorbidity patterns. Intraepidermal diseases had higher relapse rates, highlighting the need for individualized long-term management.

Keywords: Autoimmune bullous disorders, Pemphigus vulgaris, Bullous pemphigoid, Immunofluorescence, Azathioprine, Relapse.

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Introduction

Autoimmune bullous disorders (ABDs) is a non-homogeneous category of rare and potentially life-threatening mucocutaneous diseases, comprised of vesicles, bullae, and erosions present on the skin and/or mucous membranes [1]. The causes of these conditions are pathogenic autoantibodies against structural constituents of cell adhesion in the epidermis or the dermo epidermal junction. The resulting cellular detachments result in blisters and massive morbidity, and, with no treatment, death. ABDs are clinically and therapeutically challenging due to their chronic relapsing natural history and the necessity of long-lasting immunosuppressive treatment, and thus, proper diagnosis and systematic follow-up.

Bullous dermatoses are divided into two large groups by the level of the anatomical location of the form of the bullous lesions, intraepidermal and subepidermal bullous diseases. Intraepidermal bullous diseases occur in the production of autoantibodies against desmosomal components that are constituents of intercellular adhesion between keratinocytes. This happens due to the destruction of intercellular bridges, which causes acantholysis, which is the detachment and separation of the keratinocytes in the spinous layer of epidermis, which ends up forming weak intraepidermal blisters that easily rupture and cause painful erosions [2]. Such disorders as pemphigus vulgaris and pemphigus foliaceus are included in this group and have a significant morbidity

because of the involvement of the mucous membrane and the presence of extensive cutaneous lesions.

Conversely, subepidermal bullous diseases refer to the presence of autoantibodies to the structural proteins of the dermo epidermal junction, such as parts of hemidesmosomes and anchoring filaments. The absorption of these autoantibodies induces the cascades of complement and inflammatory responses, which result in the separation of the basement membrane zone as well as the creation of tense subepidermal blisters [3]. Such conditions include bullous pemphigoids and other types of pemphigoids. Subepidermal lesions are also more likely to be resistant to tearing than intraepidermal ones, but are often also characterized by pruritus, urticarial plaques and intermittent mucosal involvement. The difference between intraepidermal and subepidermal forms holds utmost significance because it affects prognosis, treatment plan and monitoring protocols.

The diagnosis of autoimmune bullous disorders should be a complex and thorough task that involves the combination of clinical examination with histopathological and immunological studies. Diagnostic confirmation does not only strengthen clinical suspicion but also identifies the subtype that is very important in helping to make treatment choices [4]. The diagnostic algorithm includes: (a) histopathological examination of a fresh (less than 24 hours old) vesicle or a biopsy section of one-third of the peripheral portion of a blister and two-thirds of perilesional skin; (b) direct immunofluorescence (DIF) microscopy of perilesional skin provided within 1 cm of a fresh lesion, even when the surrounding skin does not appear to be involved; (c) indirect immunofluorescence (IIF) microscopy of the presence of circulating auto The complementary diagnostic modalities are more sensitive and specific, aid disease classification, and can be used to determine disease activity and response to therapeutic intervention [6].

The therapeutic management of ABDs has significantly changed throughout the last few decades but as a rule, the first-line approach comprises systemic corticosteroids. Systemic corticosteroids at high doses are used to ensure prompt and efficient reduction of disease and then the gradual reduction of doses by using small doses is done during the consolidation phase to ensure remission and reduction of effects as much as possible. Long-term corticosteroid therapy despite its effectiveness is characterized by serious complications such as the development of metabolic, cardiovascular, musculoskeletal, and infectious risks [7]. In refractory disease, therefore, frequent relapses, or contraindications with corticosteroids, immunosuppressive or immunomodulatory adjuvant agents are commonly indicated. They are azathioprine, mycophenolate mofetil, cyclophosphamide, mycophenolic acid, dapsone, methotrexate, sulfonamides, tetracycline, anti-CD20 or anti-IgE monoclonal antibodies, intravenous immunoglobulins, immunoadsorption and plasma exchange. The choice of the therapeutic regimen is determined by the severity of the diseases, comorbidities in the patient, laboratory parameters, and availability of resources. Personalized intervention plans, which are based on the disease activity and immunological phenotype are critical in maximizing the outcome and reducing treatment morbidity [8].

Considering that autoimmune diseases of the type of bullous disorders are rare and heterogeneous, epidemiological evidence differs between geographic areas and healthcare systems. Such factors as age distribution, gender dominance, comorbid disorders, environment, and the availability of specialized diagnostic facilities can have an impact on disease manifestation and outcome. Moreover, institutional protocols, availability of drugs, and expertise of clinicians tend to shape the patterns of treatment. In turn, tertiary dermatology center retrospectives offer useful information on the actual patterns of diseases, methods of their diagnoses and treatment.

Bullous diseases unit of the 2nd Department of Dermatology and Venereology of the Aristotle University of Thessaloniki, Papageorgiou General Hospital, serves as a referral site of patients with autoimmune bullous diseases of Muzaffarpur, Bihar. The unit has a detailed diagnostic plan that is used in partnership with the Laboratories of Immunology and Molecular Biology, thus forming a solid structure of correct diagnosis of disease and personal therapeutic planning. The department provides accurate diagnosis and specific management of patients through systematic clinical examination, histopathological confirmation, immunofluorescence research and serological profiling.

Therapeutic interventions in the context of long-term follow-up are strictly modified with the main goals of full remission of the disease, relapse prevention, limiting of adverse effects associated with the treatment, and the well-being of the patient. Close records of epidemiological features, clinical presentation, laboratory results and treatment courses in the process of monitoring are the useful sources of information on the trends of diseases and the best methods of managing the situation.

Thus, the current retrospective research was conducted to document and evaluate the epidemiological data, medical history, laboratory profiles, and therapeutic manipulations of patients with autoimmune bullous disorders who were treated in a dermatology department. The study will fill the current knowledge gap in the ABDs through this by assessing the trends in the disease manifestation and treatment over time and help with conducting evidence-based clinical decision-making in narrow dermatology.

Methodology

Study Design

This was a hospital-based retrospective observational study conducted to evaluate the epidemiological characteristics, clinical presentation, laboratory findings, and treatment patterns of patients diagnosed with autoimmune bullous disorders (ABDs). The study involved systematic review and analysis of previously recorded patient data maintained in the department.

Study Area: The study was conducted in the Department of Skin & VD, Sri Krishna Medical College and Hospital, Muzaffarpur, Bihar, India.

Study Duration: The study was carried out over a period of 7 months from July 2025 to January 2026.

Sample Size: A total of 67 patients (N = 67) diagnosed with autoimmune bullous disorders were included in the study. The sample comprised all eligible cases that met the predefined inclusion criteria during the study period.

Study Population: The study population consisted of patients of all age groups and both sexes who were diagnosed with autoimmune bullous disorders and received evaluation and treatment at the Department of Skin & VD. Only patients with confirmed diagnoses based on clinical and laboratory criteria and with complete medical records were considered for inclusion.

Inclusion Criteria

Patients were included if they fulfilled the following criteria:

- Confirmed diagnosis of autoimmune bullous disorder.
- Diagnosis supported by:
    - Histopathological examination.
    - Direct immunofluorescence (DIF) microscopy demonstrating intraepidermal or subepidermal bullous disease.
- Availability of complete medical records, including clinical, laboratory, and treatment details.
- Patients of all age groups and both sexes.

Exclusion Criteria

- Patients with incomplete or missing medical records.
- Cases where diagnosis was not confirmed by histopathology and/or direct immunofluorescence.
- Patients with non-autoimmune bullous diseases (e.g., infectious or hereditary blistering disorders).

Data Collection: Data were collected retrospectively from patient case files, outpatient and inpatient records, laboratory registers, and treatment charts. Information recorded included demographic details such as age, sex, and place of residence; clinical details including age at onset, type and subtype of autoimmune bullous disorder, distribution and extent of lesions, mucosal involvement, and associated comorbidities; and laboratory findings such as histopathology reports and direct immunofluorescence results. Where available, results of indirect immunofluorescence and ELISA-based detection of specific IgG autoantibodies (Desmoglein 1, Desmoglein 3, BP180, and BP230) were also documented. Treatment-related data including type of drugs used, dosage, route of administration, duration of therapy, adverse effects, patient compliance, occurrence of new lesions, and relapse details were systematically extracted using a predesigned data collection proforma.

Procedure: Eligible patient records were identified from departmental registers. Each case file was carefully reviewed to confirm the diagnosis based on clinical presentation, histopathological findings, and direct immunofluorescence patterns. Relevant epidemiological, clinical, laboratory, and therapeutic details were entered into a structured data collection sheet. Follow-up records were also reviewed to document disease progression, treatment response, relapses, and adverse drug reactions.

Statistical Analysis: The collected data were entered into Microsoft Excel and subsequently analyzed using the Statistical Package for Social Sciences (SPSS) version 25.0. Descriptive statistics were used to summarize the findings. Continuous variables were expressed as mean and standard deviation or median with interquartile range, depending on the distribution of data. Categorical variables were presented as frequencies and percentages. Appropriate statistical tests, such as the Chi-square test or Fisher's exact test, were applied to assess associations between categorical variables. A p-value of less than 0.05 was considered statistically significant."

Result

Table 1 summarizes the characteristics of 67 patients with autoimmune bullous disorders. Among intraepidermal diseases (n = 34), pemphigus vulgaris (28 cases, 82.4%) was the predominant subtype with a male predominance (M:F = 1.3:1), mean age 49.6 years (22–75), while pemphigus foliaceus accounted for 6 cases (17.6%) with a mean age of 45.2 years (30–68); overall, the intraepidermal group had a mean age of 48.9 years and M:F ratio of 1.25:1. In the subepidermal group (n = 33), bullous pemphigoid was most common (24 cases, 72.7%) with slight female predominance and higher mean age of 66.4 years (45–88), followed by mucous membrane

pemphigoid (4, 12.1%), linear IgA dermatosis (2, 6.1%), pemphigoid gestationis (2, 6.1%), and epidermolysis bullosa acquisita (1, 3%); the overall subepidermal group had a mean age of 62.8 years (18–88) with slight female predominance, indicating that subepidermal disorders affected relatively older patients compared to intraepidermal diseases.

Table 1: Characteristics of 67 patients with different Autoimmune Bullous Disorders

Clinical Subtype of Autoimmune Bullous Disease	No. of Cases	%	M:F Ratio	Mean Age (years)	Age Range (years)
Intraepidermal Bullous Disease (n=34)					
Pemphigus Vulgaris (PV)	28	82.4	1.3:1	49.6	22–75
Pemphigus Foliaceus (PF)	6	17.6	1:01	45.2	30–68
Total (Intraepidermal)	34	100	1.25:1	48.9	22–75
Subepidermal Bullous Disease (n=33)					
Bullous Pemphigoid (BP)	24	72.7	01:01.2	66.4	45–88
Mucous Membrane Pemphigoid (MMP)	4	12.1	1:01	58.7	40–72
Linear IgA Dermatosis (LAD)	2	6.1	1:01	36.5	18–55
Pemphigoid Gestationis (PG)	2	6.1	F	29.5	25–34
Epidermolysis Bullosa Acquisita (EBA)	1	3	F	52	52
Total (Subepidermal)	33	100	01:01.1	62.8	18–88

Table 2 presents the distribution of comorbidities among 67 patients. In the intraepidermal group (n = 34), hypertension was the most common comorbidity, seen in 9 patients (26.5%), followed by diabetes mellitus in 7 (20.6%), dyslipidemia in 6 (17.6%), hypothyroidism in 4 (11.8%), and osteoporosis in 3 (8.8%). In the subepidermal group (n = 33), comorbidities were more frequent overall, with hypertension affecting 15 patients (45.5%) and diabetes mellitus 13 (39.4%). Coronary artery disease was present in 6 patients (18.2%), chronic kidney disease in 4 (12.1%), cerebrovascular disease in 3 (9.1%), and dementia/Parkinsonism in 2 (6.1%). Overall, cardiometabolic comorbidities, particularly hypertension and diabetes, were common in both groups and more prevalent in the subepidermal group.

Table 2: Distribution of Comorbidities Among Patients (N = 67)

Intraepidermal Group (n = 34)		
Comorbidity	**No. of Cases**	**Percentage (%)**
Hypertension	9	26.5
Diabetes Mellitus	7	20.6
Dyslipidemia	6	17.6
Hypothyroidism	4	11.8
Osteoporosis	3	8.8
Subepidermal Group (n = 33)		
Comorbidity	**No. of Cases**	**Percentage (%)**
Hypertension	15	45.5
Diabetes Mellitus	13	39.4
Coronary Artery Disease	6	18.2
Chronic Kidney Disease	4	12.1
Cerebrovascular Disease	3	9.1
Dementia/Parkinsonism	2	6.1

Table 3 outlines the adjuvant therapeutic agents and duration of treatment among 67 patients. In intraepidermal bullous diseases (n = 34), azathioprine was the most commonly used agent (18 patients; 3–24 months), followed by mycophenolate mofetil (5; 2–18 months), cyclophosphamide (3; 1–6 months), methotrexate (2; 4–12 months), rituximab (2; 375 mg/m²/week for 4 weeks), and dapsone (2; 3–10 months). In subepidermal bullous diseases (n = 33), azathioprine was also most frequently used (7 patients; 2–18 months), followed by dapsone (6; 2–15 months), doxycycline (5; 1–6 months), methotrexate (3; 3–12 months), and mycophenolate mofetil (2; 2–10 months). Overall, azathioprine was the most commonly prescribed adjuvant therapy in both groups, with treatment duration varying widely depending on the agent and disease severity.

Table 3: Adjuvant Therapeutic Agents and Duration of Treatment (N = 67)		
Intraepidermal Bullous Diseases (n = 34)		
Adjuvant Therapy	**No. of Patients**	**Duration (months)**
Azathioprine	18	3–24
Mycophenolate Mofetil	5	2–18
Cyclophosphamide	3	1–6
Methotrexate	2	4–12
Rituximab	2	375 mg/m²/week × 4 weeks
Dapsone	2	3–10
Subepidermal Bullous Diseases (n = 33)		
Adjuvant Therapy	**No. of Patients**	**Duration (months)**
Azathioprine	7	2–18
Dapsone	6	2–15
Doxycycline	5	1–6
Methotrexate	3	3–12
Mycophenolate Mofetil	2	2–10

Table 4 presents the relapse pattern among 67 patients according to disease group. In the intraepidermal group (n = 34), 12 patients (35.3%) experienced one relapse, 6 (17.6%) had two relapses, and 3 (8.8%) had three or more relapses. In the subepidermal group (n = 33), 7 patients (21.2%) had one relapse, 2 (6.1%) had two relapses, and 1 (3.0%) experienced three or more relapses. Overall, relapses were more frequent in the intraepidermal group compared to the subepidermal group, particularly for single and multiple relapse episodes.

Table 4: Relapse Pattern Among Patients (N = 67)			
Disease Group	**One Relapse n (%)**	**Two Relapses n (%)**	**≥3 Relapses n (%)**
Intraepidermal (n=34)	12 (35.3%)	6 (17.6%)	3 (8.8%)
Subepidermal (n=33)	7 (21.2%)	2 (6.1%)	1 (3.0%)

Discussion

The intraepidermal and subepidermal autoimmune bullous disorders (AIBDs) in the current research were nearly at par (34 vs. 33 cases) in contrast to Western Europe where subepidermal diseases, especially bullous pemphigoid (BP) is prevalent (Bertram et al., 2009; Joly et al., 2012) [9,10]. Indicatively, in France and Germany, the incidence of BP has increased tremendously to up to 13.421.7/million/year/ 43/million/year in the United Kingdom (Joly et al., 2012) [10]. On the other hand, research of Middle Eastern and part of Asian countries reports a higher proportion of intraepidermal diseases, and pemphigus especially with an intraepidermal-subepidermal ratio of about 8 to 1 in Iran (Daneshpazhooh et al., 2012) [11]. It is possible that our almost equal representation is due to regional epidemiological differences or shifting demographic" trends.

The most common intraepidermal subtype in our cohort was Pemphigus vulgaris (PV) (82.4%), similar to that found in Iran (92% PV), in Kuwait (80% PV), Turkey (83% PV), and Bulgaria (77% PV) (Nanda et al., 2004; Tsankov et al., 2000) [12,13] . Pemphigus foliaceus (PF) represented 17.6% of our intraepidermal cases, comparable to Kuwait (18%), and Bulgaria (17%) (Nanda et al., 2004; Tsankov et al., 2000) but significantly lower than endemic areas like Tunisia, where PF occupies up to 36% of cases (Zaraa et al., 2011) [14]. Our study had a mean age of PV of 49.6 years, compared to higher than Kuwait (36 years) and India but similar to Iran (42 years) and slightly lower than most European cohorts in which the mean age tends to be above 50 years (Daneshpazhooh et al., 2012; Nanda et al., 2004) [11,12]. Such population means between two extremes of age can testify to demographic and environmental factors.

Our study revealed 72.7 proportion of subepidermal BP cases, which correlates with the world statistics stating that subepidermal AIBD is predominantly BP (Schmidt and Zillikens, 2013) [5]. Our cohort of BP patients had a mean age of 66.4 years, lower than what the developed European nations (France, Germany, and the United Kingdom) reported (83 years, 77.3 years, and 77 years), but comparable to the developing nations (Tunisia, 67.2 years and Kuwait, 65 years) (Joly et al., 2012; Nanda et al., 2004) [10,12]. This facilitates the fact that BP is highly prevalent at older ages in the developed countries as compared to the developing world. Also, our research revealed a slight female preponderance in subepidermal disorders (1:1.1) which was in line with most of the international reports that have reported higher AIBD incidence in women, even though male preponderance has also been reported in Germany and China (Bertram et al., 2009) [9].

Our cohort had a relatively greater burden of systemic comorbidities with subepidermal disorders, especially hypertension (45.5%), and diabetes mellitus (39.4%). This is consistent with the literature on population studies that showed that BP has strong links with cardiovascular and metabolic diseases (Teixeira et al., 2014) [15]. In addition, neurological comorbidities, including dementia and Parkinsonism (6.1% in our study), have been well-associated with BP, demonstrated in a population-based case-control study in UK that demonstrated significant association of BP with the neurological comorbidities (Langan et al., 2011) [16]. Metabolic comorbidities in intraepidermal disorders of our study also had lower frequencies (hypertension 26.5%, diabetes 20.6%), and it may support the idea that chronic inflammation and prolonged corticosteroid use can be the cause of metabolic complications (Ljubojevic & Lipozencic, 2012) [17].

Concerning diagnostic considerations, even though direct immunofluorescence (DIF) is the gold standard in the diagnosis of AIBD (Kneisel and Hertl, 2011) [4], newer modalities like the use of ELISA-based detection of anti-desmoglein and anti-BP180 antibodies have developed better monitoring of the disease. Higher anti-Dsg1 titers have been found to be associated with activity of cutaneous disease and anti-Dsg3 antibodies can also remain despite mucosal remission (Patsatsi et al., 2014) [8]. On the same note, the levels of anti-BP180 NC16A antibody are related to the activity of BP disease and can be used to make therapeutic decisions (Patsatsi et al., 2012) [8]. Serological monitoring was not used consistently in our retrospective cohort, but the inclusion of such tools can enhance the organization of long-term treatment and relapse prognosis.

In therapy, our treatment patterns were in most cases in line with the European Dermatology Forum (EDF) guidelines prescriptive of systemic corticosteroids and steroid-sparing adjuvants like azathioprine and mycophenolate mofetil (Hertl et al., 2014; Feliciani et al., 2015) [4,7]. In our study, Azathioprine was more common in intraepidermal and subepidermal groups of the population as it is put into practice in most countries. Doxycycline had been applied in 5 patients in the BP reflecting evidence that tetracycline anti-inflammatory agents might be effective and safer to use in some cases. A randomized trial study on the effectiveness of oral and topical corticosteroids showed that potent topical clobetasol may be as effective as prednisone systemically (0.5 mg/kg/day) in managing BP (Joly et al., 2002) [10], and less aggressive systemic regimens in elderly patients.

Two patients with intraepidermal disease were put on rituximab using the standard protocol of 375 mg/m 2 weekly over four weeks. This is in keeping with the increasing evidence showing the effectiveness of rituximab in pemphigus, though the effect may not be uniform and the cost factor restricts its use in some areas of the world (Schmidt et al., 2007) [6]. Likewise, omalizumab has demonstrated encouraging outcomes in refractory BP, but the evidence is still scarce (Fairley et al., 2009) [19]. We used relatively few biologics, which is probably caused by financial and administrative limitations that are prevalent in most health care systems.

Inquiry on relapses indicated that intraepidermal diseases were more likely to recur (35.3% with one relapse; 17.6% with two; 8.8% with 3 and above) than subepidermal diseases (21.2%, 6.1%, and 3.0%, respectively). This clinical experience observation is supported by other reports that pemphigus occurs in a more chronic and relapsing course than BP (Murrell et al., 2012) [20]. The persistence and frequent recurrence of intraepidermal AIBDs highlight the rationale of having long-term immunomodulatory measures and slow corticosteroid tapering to reduce side effects.

In general, our findings show epidemiological and clinical trends that are widely similar to international data, though also based on the regional demographic features. The almost equal incidence of intraepidermal and subepidermal diseases, intermediate age of onset, and heavy comorbidity burden in BP, and increased relapse rate of pemphigus is an important local contribution towards global knowledge on AIBDs.

Conclusion

This retrospective study highlights those autoimmune bullous disorders in our dermatology department comprised of a nearly equal distribution of intraepidermal and subepidermal diseases, with pemphigus vulgaris predominating among intraepidermal disorders and bullous pemphigoid being the most frequent subepidermal entity. Intraepidermal diseases tended to affect relatively younger patients, whereas subepidermal disorders were more common in the elderly and were associated with a higher burden of systemic comorbidities, particularly cardiometabolic conditions. The management approach largely relied on systemic corticosteroids combined with steroid-sparing adjuvant agents such as azathioprine, mycophenolate mofetil, dapsone, and other immunomodulators, tailored to disease subtype and severity. Relapses were observed in both groups, though more frequently in intraepidermal disorders, underscoring the chronic and relapsing nature of these conditions and the need for long-term follow-up, individualized therapeutic strategies, and careful monitoring of associated comorbidities.

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