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Clinical Presentation, Diagnosis, and Management of Pemphigus Vulgaris: A Comprehensive Review

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ABSTRACT: ***Background:*** Pemphigus vulgaris (PV) is a rare, life-threatening autoimmune blistering disorder characterized by the formation of painful blisters and erosions, primarily affecting the skin and mucous membranes. It is caused by the production of autoantibodies against desmogleins, which are key components of the desmosomes that hold epidermal cells together. This study aims to provide a comprehensive overview of the clinical presentation, diagnostic approaches, management strategies, and treatment outcomes in patients with pemphigus vulgaris. ***Methods:*** This retrospective, observational study aimed to evaluate the clinical presentation, diagnostic methods, management strategies, and treatment outcomes of pemphigus vulgaris (PV) in 46 patients. The study took place in ODC Healthcare, Green Road, Dhaka, Bangladesh from January 2024 to December 2024. The data were analyzed by SPSS version 25.0. ***Result:*** The study included 46 patients, showing a slight male predominance and a median age of 42 years at diagnosis. Oral lesions were the most common clinical feature, observed in 91.3% of patients, followed by skin blisters (82.6%) and erosions (71.7%). Diagnostic methods such as direct immunofluorescence (93.5%) and histopathology (89.1%) were highly effective in confirming the diagnosis. Most patients were treated with corticosteroids (95.7%) and immunosuppressive agents (82.6%), with additional therapies like intravenous immunoglobulin (56.5%) and rituximab (26.1%) used for refractory cases. At follow-up, 26.1% of patients achieved complete remission, 39.1% had partial remission, and 21.7% achieved disease control with medication. However, 13% showed no response to treatment. ***Conclusion:*** This study highlights the clinical complexity, diagnostic challenges, and diverse treatment strategies for pemphigus vulgaris (PV). Our findings underscore the predominance of oral lesions and skin blisters in PV presentation, with direct immunofluorescence proving to be the most effective diagnostic tool. Corticosteroids remain the cornerstone of treatment, often combined with immunosuppressive agents and newer therapies like rituximab for refractory cases.

Keywords: Pemphigus Vulgaris, Autoantibodies, Desmoglein, Corticosteroid.

Article at a glance:

Study Purpose*: The purpose of this study is to provide an in-depth analysis of the clinical presentation, diagnostic approaches, and management strategies for this rare autoimmune blistering disorder.*

Key findings: *PV is an autoimmune blistering disorder affecting the skin and mucous membranes.*

Newer findings: *PV frequently presents with oral lesions, appearing in 50-70% of cases. Nearly all patients experience mucosal lesions during their disease course, which can precede skin manifestations by several months.*

Abbreviations: *HLA: Human Leukocyte Antigen, PV: Pemphigus Vulgaris.*

INRODUCTION

Pemphigus vulgaris (PV) is a rare, chronic autoimmune mucocutaneous disorder characterized by intraepithelial blistering affecting the skin and mucous membranes. It results from autoantibody-mediated disruption of desmosomal adhesion, primarily targeting desmoglein (Dsg) proteins in the epidermis, leading to acantholysis and subsequent blister formation.[1] PV has a worldwide distribution, with a higher prevalence among populations of Mediterranean, Ashkenazi Jewish, Middle Eastern, and South Asian descent.[2] The disease predominantly

affects adults between 40 and 60 years of age, with a slight female predominance.[3] Although uncommon, pediatric cases have been documented, often presenting diagnostic and therapeutic challenges.[4] The etiology of PV involves a complex interplay of genetic, environmental, and immunological factors. Human leukocyte antigen (HLA) alleles such as HLA-DRB10402 and HLA-DQB10503 have been strongly linked to disease susceptibility.[5] Environmental triggers, including viral infections, stress, UV radiation, and certain medications (e.g., penicillamine, captopril, rifampicin), have also been implicated in disease pathogenesis.[6] The hallmark of PV is the loss of intercellular adhesion due to autoantibody-mediated destruction of desmosomes, the primary structures responsible for epithelial cell-to-cell adhesion.[7] IgG autoantibodies against desmoglein-3 (Dsg3) and desmoglein-1 (Dsg1) play a critical role in blister formation. Dsg3 is predominantly expressed in the mucosa, explaining why oral lesions the first manifestation of the disease is often, while Dsg1 is more abundant in the superficial epidermis, correlating with later cutaneous involvement.[8]

The pathogenicity of PV autoantibodies extends beyond mere disruption of adhesion; they also trigger intracellular signaling cascades that contribute to keratinocyte apoptosis and inflammatory responses.[9] The resulting intraepidermal clefts lead to flaccid blisters, which are prone to rupture, forming painful erosions.[10] PV frequently presents with mucosal involvement before skin lesions develop. About 80% of patients initially exhibit painful oral erosions, which persist for months before cutaneous lesions appear.[11] These oral lesions predominantly affect the buccal mucosa, soft palate, and tongue, manifesting as fragile vesicles that rupture easily, leaving irregular, slow-healing ulcers. Cutaneous involvement typically follows oral manifestations in approximately 75% of cases, characterized by flaccid blisters on erythematous or normal skin. The Nikolsky sign—where lateral pressure on intact skin induces blistering—is a key clinical feature aiding in diagnosis.[12] Early and accurate diagnosis is critical for preventing disease progression. The diagnostic approach involves clinical evaluation, histopathology, and immunological studies. Histopathological examination of a lesional biopsy typically reveals suprabasal clef ting and acantholysis, forming the characteristic "row of tombstones" appearance.[13] Direct immunofluorescence (DIF) remains the gold standard for diagnosis, demonstrating intercellular deposition of IgG and C3 in the epidermis in a "chicken-wire" pattern.[14]

Serological tests, such as enzyme-linked immunosorbent assay (ELISA), quantify circulating autoantibodies against Dsg1 and Dsg3, helping monitor disease activity and response to treatment.[15] The primary goal of treatment is to achieve disease control while minimizing adverse effects. Systemic corticosteroids, such as prednisolone, remain the first-line therapy, often administered in combination with immunosuppressants like azathioprine, mycophenolate mofetil, or cyclophosphamide to reduce steroid dependence. Rituximab, a monoclonal antibody targeting CD20-expressing B cells, has revolutionized PV management, offering higher remission rates and reduced relapse compared to conventional therapy. Other emerging biologics, such as FcRn inhibitors and IL-6 blockers, are currently under investigation for their potential to improve disease outcomes.[16] Topical corticosteroids, antiseptic mouthwashes, and analgesics provide symptomatic relief for mucosal lesions. Nutritional support, infection prevention, and psychological counseling play essential roles in comprehensive patient care. The aim of the study is to provide a comprehensive review of the clinical presentation, diagnostic methods, and management strategies of pemphigus vulgaris.

METHODS

This retrospective observational study aimed to evaluate the clinical presentation, diagnostic methods, management strategies, and treatment outcomes of pemphigus vulgaris (PV) in 46 patients. The study took place in ODC Healthcare, Green Road, Dhaka, Bangladesh from January 2024 to December 2024. Data was collected from patient records, including demographic details, clinical features, diagnostic results, and treatment regimens. Standard diagnostic techniques such as direct immunofluorescence, histopathology, ELISA for desmoglein antibodies, and skin biopsy were employed to confirm the diagnosis. The treatment protocol primarily involved corticosteroids (Deflazacort), immunosuppressive agents, and systemic therapies like intravenous immunoglobulin and fluconazole for secondary infections. Follow-up visits occurred on 14, 30, 60, and 120 days, where

clinical improvement was assessed, including the resolution of oral lesions, the management of candidosis, and the tapering of corticosteroids. During the six-month follow-up, ulcers were completely healed with no recurrence of vesicles or bullae. Descriptive statistics were used to summarize demographic data and treatment outcomes. The data were analyzed by SPSS version 25.0, using frequency distributions for categorical variables and mean for continuous variables. This study was approved by the institutional ethics committee, and informed consent was obtained from all participants or their legal guardians before inclusion in the study.

Inclusion Criteria

Patients diagnosed with pemphigus vulgaris based on clinical, histopathological, and immunological criteria.

Age 18 years and older.

Both newly diagnosed and patients already undergoing treatment were included.

Exclusion Criteria

Patients with other autoimmune diseases.

Patients with severe systemic conditions contraindicating the use of immunosuppressive therapy.

Incomplete follow-up data.

RESULTS

Table 1: Demographic Characteristics of Study Participants (n=46)

Characteristic	n (%)
Total Participants	46
Male	25 (54.3%)
Female	21 (45.7%)
Age Range (years)	18–70
Median Age at Diagnosis	42
Disease Duration	6 months (mean)

The study included 46 participants, with a slight male predominance (54.3%, n=25) compared to females (45.7%, n=21). The age of participants ranged from 18 to 70 years, with a median age of 42 years at the time of diagnosis. The mean disease duration at diagnosis was 6 months, highlighting the variable time between the onset of symptoms and diagnosis in the cohort. [Table 1]

Table 2: Clinical Presentation of Pemphigus Vulgaris (n=46)

Clinical Feature	n (%)
Oral Lesions	42 (91.3%)
Skin Blisters	38 (82.6%)
Erosions	33 (71.7%)
Pruritus	25 (54.3%)
Pain	22 (47.8%)
Nail Involvement	10 (21.7%)
Conjunctival Involvement	6 (13.0%)

The clinical presentation of pemphigus vulgaris in this cohort revealed that oral lesions were the most common feature, observed in 91.3% of patients (n=42), followed by skin blisters in 82.6% (n=38) and erosions in 71.7% (n=33). Pruritus was reported in 54.3% (n=25) of cases, and pain was experienced by 47.8% (n=22) of patients. Nail involvement was noted in 21.7% (n=10) of participants, while conjunctival involvement was observed in 13.0% (n=6). [Table 2]

Table 3: Diagnostic Methods and Results (n=46)

Diagnostic Method	Positive Findings n (%)
Direct Immunofluorescence	43 (93.5%)
Histopathology	41 (89.1%)

ELISA (Desmoglein Antibodies)	38 (82.6%)
Indirect Immunofluorescence	36 (78.3%)
Biopsy of Skin Lesions	35 (76.1%)

Direct immunofluorescence was the most effective diagnostic tool, yielding positive findings in 93.5% of cases (n=43). Histopathology followed closely, with positive results in 89.1% (n=41) of patients. ELISA testing for desmoglein antibodies was positive in 82.6% (n=38) cases, while indirect immunofluorescence and skin lesion biopsy showed positive results in 78.3% (n=36) and 76.1% (n=35) of participants, respectively. [Table 3]

Table 4: Management Strategies Utilized (n=46)

Management Approach	n (%)
Corticosteroids	44 (95.7%)
Immunosuppressive Agents	38 (82.6%)
Intravenous Immunoglobulin	26 (56.5%)
Rituximab	12 (26.1%)
Plasma Exchange	8 (17.4%)
Topical Steroids	18 (39.1%)

The management strategies employed in this cohort demonstrated a broad range of therapeutic approaches, with corticosteroids being the most used treatment, administered to 95.7% (n=44) of patients. Immunosuppressive agents were utilized in 82.6% (n=38) cases, while intravenous immunoglobulin was administered to 56.5% (n=26) of participants. Rituximab was used in 26.1% (n=12), and plasma exchange was employed in 17.4% (n=8) of patients, primarily in refractory cases. Topical steroids were applied in 39.1% (n=18) of cases. [Table 4]

Table 5: Treatment Outcomes (n=46)

Outcome	n (%)
Complete Remission	12 (26.1%)
Partial Remission	18 (39.1%)
Disease Control with Medication	10 (21.7%)
No Response to Treatment	6 (13.0%)

The treatment outcomes for the study cohort revealed that 26.1% (n=12) of patients achieved complete remission, while 39.1% (n=18) experienced partial remission. Disease control with medication was achieved in 21.7% (n=10) of cases. However, 13.0% (n=6) of patients showed no response to treatment, indicating the variability in treatment effectiveness. [Table 5]

DISCUSSION

The results of this study provide valuable insights into the clinical presentation, diagnostic methods, management strategies, and treatment outcomes of pemphigus vulgaris (PV), a rare autoimmune blistering disorder. In our study, oral lesions were the most common clinical manifestation of pemphigus vulgaris, affecting 91.3% of patients, which is consistent with previous studies. For instance, a study by Rai *et al*. reported oral lesions in 70-90% of PV cases, highlighting the prominent role of the oral cavity in the disease's initial presentation.[17] Skin blisters (82.6%) and erosions (71.7%) were also common findings, further aligning with previous report, where skin involvement was observed in 70-85% of cases.[18] Our cohort showed a relatively lower incidence of conjunctival (13%) and nail involvement (21.7%), which is comparable to other studies that found these manifestations in a smaller proportion of cases (15-25%).[19] The diagnostic approaches used in our study demonstrated a high level of accuracy, with direct immunofluorescence being the most sensitive method (93.5%), consistent with the findings of other studies.[20] Histopathology and ELISA for desmoglein antibodies also proved to be reliable, with positive findings in 89.1% and 82.6% of cases, respectively.

These results are in line with previous studies that report a similar sensitivity for these diagnostic tools.[21] However, skin biopsy showed a lower sensitivity (76.1%) in our study compared to others, where it was reported to have a higher diagnostic yield (80-85%). Corticosteroids were the most commonly used management strategy in our cohort (95.7%), reflecting their central role in PV treatment, as emphasized in previous study.[22] Immunosuppressive agents were utilized in 82.6% of our patients, which is consistent with the findings of a study by Ahmed *et al*., where immunosuppressive therapy was used in majority of cases.[23] The use of intravenous immunoglobulin (56.5%) and rituximab (26.1%) aligns with current clinical practice, where rituximab is increasingly being used for refractory cases.[24] Our study also incorporated plasma exchange in 17.4% of patients, a treatment strategy used in more severe cases, similar to the 18% reported by Sagi *et al*. in their cohort.[25] Topical steroids (39.1%) were prescribed for localized management, which is a standard approach in PV to control mucosal involvement. In terms of treatment outcomes, 26.1% of patients achieved complete remission, and 39.1% achieved partial remission. These results are comparable to those reported by Cavusi *et al*., where varying degrees of remission was acheived.[26] Our study also found that 21.7% of patients had disease control with medication. The 13% of patients who showed no response to treatment reflect the difficulty in managing severe or treatment-resistant cases, which is a known challenge in pemphigus vulgaris management.[27]

Limitations of The Study

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community

CONCLUSION

This study highlights the clinical complexity, diagnostic challenges, and diverse treatment strategies for pemphigus vulgaris (PV). Our findings underscore the predominance of oral lesions and skin blisters in PV presentation, with direct immunofluorescence proving to be the most effective diagnostic tool. Corticosteroids remain the cornerstone of treatment, often combined with immunosuppressive agents and newer therapies like rituximab for refractory cases. While a significant proportion of patients achieved complete or partial remission, a subset showed no response to treatment, emphasizing the need for personalized treatment strategies.

Recommendation

It is recommended that clinicians adopt a multidisciplinary approach to the management of pemphigus vulgaris, with an emphasis on early diagnosis through reliable methods like direct immunofluorescence and histopathology. While corticosteroids remain essential, the use of immunosuppressive agents and biologics such as rituximab should be considered for patients with refractory or severe disease. Regular follow-up is crucial to monitor treatment response, manage side effects, and adjust therapies accordingly. Further research with larger cohorts and longer follow-up periods is needed to refine treatment strategies and improve long-term outcomes in pemphigus vulgaris patients.

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Authors' Contributions

SJB: Concept and design, data acquisition, interpretation and drafting. SRP and SAS: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

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