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Prevalence of Immunobullous Disorder in a Tertiary Medial Care Hospital in South Rural District in South India

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ABTRACT

Background: Autoimmune bullous diseases are extremely uncommon skin conditions. These disorders are difficult to diagnose because of their rarity and variability in symptoms, thus a prompt and precise diagnosis is critical for developing an effective treatment strategy.

Material and Methods: Sixty patients were enrolled in the study who attended OPD in The of Department of Dermatology; Venereology & Leprosy, Shri Sathya Sai Medical College and Research Institute, Nellikuppam, Tamil Nadu, India. This study was done between the time frame of April 2022 to March 2023.

Results: Bullous illnesses have a wide range of diagnostic specificity based on clinical symptoms. The clinical presentation of the numerous bullous disorders shares many similarities. Bullous pemphigoid and dermatitis herpetiformes are two conditions that linear IgA dermatosis can look like. When in its non-bullous prodromal stage or when presenting atypically, bullous pemphigoid can seem a lot like other skin conditions.

Conclusion: This study found that people between the ages of 51 and 60 had the highest prevalence of autoimmune bullous diseases. The majority of people with an autoimmune bullous illness had pemphigus vulgaris. Women were disproportionately affected by the

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 08, 2023

pemphigus group of diseases. Subepidermal diseases disproportionately affected males.

Keywords: Immunoblot disease, diagnostics, direct immunofluorescence

INTRODUCTION

Autoimmune bullous illnesses are uncommon skin conditions that can affect anyone. These disorders are difficult to diagnose because of their rarity and polymorphic appearance; therefore, it is crucial to arrive at an accurate diagnosis as soon as possible so that appropriate therapy may be planned. The autoimmune reaction against the structural proteins of skin mediating cell to cell and matrix adhesion causes the blistering disorders [1, 2].

Vesicles are described as fluid-filled cavities developed in or below the epidermis and smaller than 0.5 cm in diameter. A bulla is a fluid-filled lesion with a diameter bigger than 0.5 cm. The fluid is made up of a combination of tissue fluid, plasma, and a number of different cell types both inflammatory and noninflammatory. There is a wide range of dermatoses that can manifest as blisters [3, 4].

Unna's seminal work in dermatopathology provides a foundation for both contemporary dermatology and immunofluorescence research in the field of skin immunopathology. In his histology research, Lever distinguished between pemphigoid and pemphigus. Immunofluorescence research conducted by Ernst Beutner and colleagues established an autoimmune basis for pemphigus and pemphigoid. Autoimmune bullous illnesses are categorized by the molecular target of autoantibodies, as determined by diagnostic assays like ELISA, and by the deposition of immunoreactants like IgG, IgM, IgA, and C3 over intercellular gaps or over the dermoepidermal interface [5, 6].

The autoantibody direct immunofluorescence (DIF) test aids in the identification of immunobullous illnesses and the classification of histologically similar ailments that vary in therapy and prognosis. Connective tissue disorders, vasculitis, lichen planus, amyloidosis, and psoriasis are just few of the many diseases for which DIF can be used as an adjunct to histology in making a diagnosis. DIF is also useful for gauging the efficacy of treatment and anticipating recurrence. When it comes to detecting the immunological activity of the disease, direct immunofluorescence is more sensitive than indirect immunofluorescence in patients in clinical remission [7, 8].

It was anticipated that by studying the demographic pattern and predicting the clinic pathological association and utility of DIF in a tertiary care center, we could better understand the immunobullous illnesses that present with such a wide range of clinical presentation [9]. The study's primary purpose was to examine the prevalence of immunobullous illnesses as a

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 08, 2023

whole. The goal of this study is to evaluate the diagnostic value of direct immunofluorescence for immunobullous illnesses in terms of speed, consistency, and precision. The goal of this study is to identify any clinicopathological correlations in immunobullous illnesses.

Materials and Methods

Sixty patients were enrolled in the study who attended OPD in The of Department of Dermatology; Venereology & Leprosy, Shri Sathya Sai Medical College and Research Institute, Nellikuppam, Tamil Nadu, India. This study was done between the time frame of April 2022 to March 2023.

InclusionCriteria

- Male and Female patients who are diagnosed with immunobullous disease
- Patients above 18 years of age
- Patients who are ready to consent to participitate in the study

ExclusionCriteria

- Pregnant and nursing mothers
- Patients who refuse to consent to the study.
- Patient below 18 years of age

Clinical examination was done for the presence of bullae, vesicles, and erosions of the skin and mucosa visiting the Outpatient department of Dermatology. Each patient's name, age, sex, address, contact number, op number and inpatient number, occupation, presenting complaints with duration, presence of other associated symptoms, treatment history, presenting comorbid illness, treatment history of any drug intake for other conditions, family history of similar complaints, and sexual history were recorded. A thorough clinical examination was performed, including a review of systems and vital signs, and was documented using the provided proforma.

RESULTS

Sixty patients were enrolled in the study. The median age was 52.41 (range, -14 to 80) years old.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 08, 2023

Table1: Agewisedistribution

Sr. No.	Agegroup	Frequency
1.	18-30years	7
2.	31-40years	8
3.	41-50years	10
4.	51-60years	20
5.	61-70years	10
6.	>70years	5
	Total	60

Those between the ages of 51 and 60 had severe clinical signs. The youngest patient to present to the hospital was 20 years old. At the time of their initial medical evaluation, the oldest patient was 80 years old.

Table2: General condition of patients

Sr. No.	Generalcondition	Frequency
1.	Stable	51
2.	Unstable	9
	Total	60

Durationofillness:

The duration of the symptoms at the time of presentation was typically between one and three months.

Table3:Duration of illness

Sr. no.	Duration	Frequency
1.	<=1 month	10
2.	1–3months	20
3.	3–6months	14
4.	6–12months	12
5.	>1year	04

Co-morbidities

Type 2 Diabetes mellitus and systemic hypertension were the most often observed co-

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 08, 2023

morbidities.

Table4:Comorbidities

Sr. No.	Comorbidities	Frequency	Percentage
1.	Type II DM	18	30%
2.	Systemic hypertension	10	16.6%
3.	Systemic hypertension/Type II DM	10	16.6%
4.	Systemic lupus erythematosus	3	5%
5.	Late latent syphilis	1	1.66%
6.	Dyslipidema	1	1.66%
7.	No association	17	28.3%
	Total	60	

Morphology of skinlesions

Erosion-filled bullae were the most prevalent form of presentation.

Table5:Vesicles

Sr. no.	**Vesicles**	**Frequency**	**%**
1.	Present	40	66.66
2.	Absent	20	33.33
	Total	60	100.0

Distribution of cutaneous lesions:

The trunk was the most common site involved, followed by the arms and legs.

Table6:Trunk

Sr. no.	Trunk	Frequency	%
1.	Yes	57	95.7
2.	No	3	4.3
	Total	60	100.0

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 08, 2023

Table7:Upper and lowerlimbs

Sr. no.	Limbs	Frequency	%
1.	Yes	54	91.4
2.	No	6	8.6
	Total	60	100.0

Mucosal involvement

About 44.3% of individuals had erosions that affected their oral mucosa. In 12% of patients, the genital mucosa was affected. Oral erosions were present in 28 Pemphigus vulgaris patients. Oral erosions were found in 2 of the patients with Bullous SLE. Oral erosions were observed in 1 patient with bullous pemphigoid.

Table8:Mucosalinvolvement

Sr. no.	Mucosa	Frequency	%
1.	Present	27	45
2.	Absent	33	55
	Total	60	100.0

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 08, 2023

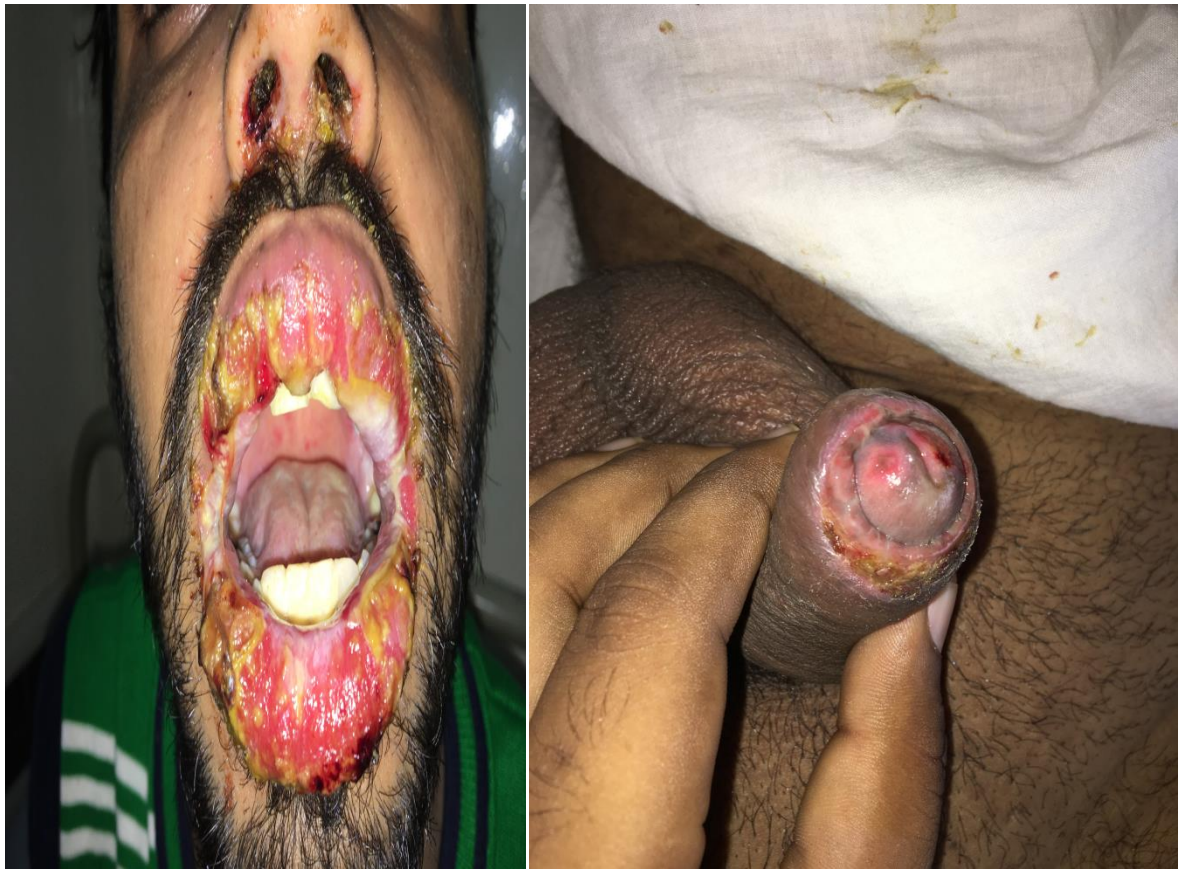
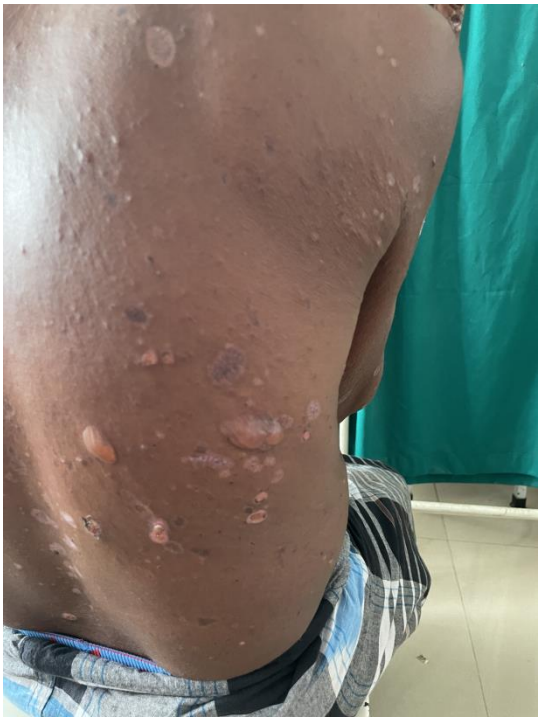


FIG 1 & 2

ORAL AND GENITAL ULCER IN PATIENT WITH PEMPHIGUS VULGARIS

Clinical signs might have a wide range of specificity for diagnosing bullous disorders. The clinical presentation of the numerous bullous disorders shares many similarities. Bullous pemphigoid and dermatitis herpetiformes are two conditions that linear IgA dermatosis can look like. At its nonbullous prodromal stage or in atypical presentations, bullous pemphigoid can be difficult to distinguish from other dermatoses, such as localized or generalized drug reactions, contact and allergic dermatitis, prurigo, urticaria, urticarial vasculitis, arthropod reactions, scabies, ecthyma, and pityriasis lichenoides. An IgA pemphigus attack can look like pemphigus foliaceus, pemphigus herpetiformis, or sub corneal pustular dermatosis. Staining with histopathological and immunofluorescence methods aids in making a definitive diagnosis.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 08, 2023



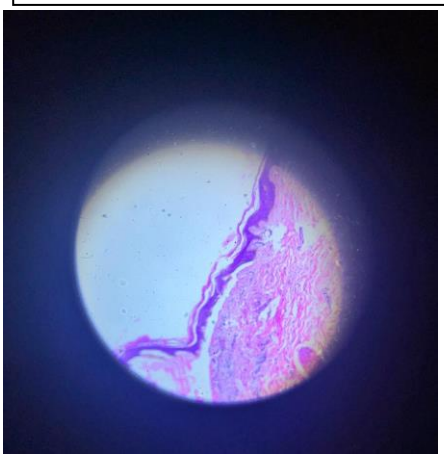


Figure 4: Sub epidermal blister with superficial perivascular mixed inflammatory infiltrate with eosinophils in dermis and blister cavity. Eosinophils are also seen lining up along the dermoepidermal junction extending into epidermis.

FIG 3

BULLOUS PEMPHIGOID CASE PRESENTING WITH MULTIPLE TENSE VESICLES AND BULLA OVER TRUNK

DISCUSSION

The immune system's reaction against the epidermis or the basement membrane zone causes immunobullous diseases. Current practice in the diagnosis of autoimmune bullous illnesses involves a mix of clinical, histological, immunological, and molecular data. DIF is useful for identifying immunoglobulins and complement proteins inside a biopsy specimen.A total of 60 participants joined the trial. In our analysis, the median age of presentation was 52.41 (range, 14–80) years old. For men, the average age of onset was 51.97. For women, the average age of onset was 52.88. Consistent with the findings of Basu et al. and Khannan et al., the average age of onset for intraepidermal bullous diseases was 49.61 years. Both the study by De et al. and the study by Tham SN et al. found that 55.93 was the most common age of onset for subepidermal bullous diseases [10-12].

Males were overrepresented among those diagnosed with the autoimmune bullous illnesses we looked at. Like the studies of Basu et al. and Khannan et al., we found that females were disproportionately afflicted by intraepidermal bullous diseases. Both De et al. and Tham SN et al. found that males were more likely than females to experience subepidermal bullous

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 08, 2023

diseases. The average duration of symptoms before to presentation was between one and three months. This mirrored the findings of Jindal et al. In terms of cutaneous lesions, bulla with erosions was the most prevalent presentation, followed by erosions alone. Consistent with the findings of Basu et al., the most common cutaneous lesion in the intraepidermal group of diseases was flaccid bulla with widespread erosions. Tense bulla with erosions was the most prevalent cutaneous lesion in the subepidermal group of diseases, correlating with previous research by De et al. In contrast to the study conducted by De et al., which found systemic hypertension to be the most prevalent concomitant ailment before diabetes mellitus, we found the opposite to be true [12-14].

Lesions were more typically found on the trunk, then the limbs. In a study conducted by Khannan et al., it was shown that the trunk was implicated in 52% of cases, with the limbs accounting for 48%. Forty-four percent of patients exhibited oral lesions, suggesting mucosal involvement. Eighty-two percent of people with pemphigus vulgaris also had mouth lesions. Twelve percent of patients with the pemphigus group of illnesses experienced genital erosions. One person with bullous pemphigoid had oral lesions. De et al. found that 40% of bullous pemphigoid patients had mucosal lesions. In 25% of cases, the nail was affected. Onycholysis was the second most prevalent diagnosis after subungual hyperkeratosis. Gopal et al. found that 72.5% of patients had nail involvement; paronychia and onychorhexis were the most common findings [13-15].

Patients with a positive direct Nikolsky sign made up 48.57 percent of the sample. The Nikolsky sign was positive in 79.4 percent of patients, which is quite close to the 72 percent of patients who showed it in a research by Basu et al. Four patients with a pemphigus-related disease did not have a positive indirect Nikolsky sign. In 5 patients with pemphigus group illnesses, the direct Nikolsky sign was negative. This may have been the result of remission or earlier therapy. Thirty-one patients had a positive Tzanck test for acantholytic cells. Thirty-one patients with pemphigus-related diseases tested positive for Tzanck. Tzanck test positivity was found in 88.24% of patients in the study by Basu et al. Tzanck test results were negative for 8 patients with Pemphigus group diseases [14-16].

Twelve percent of patients had an equivocal diagnosis. Pemphigus vulgaris and bullous pemphigoid were both possible diagnoses in four of the cases. Tzanck test for acantholysis was inconclusive in all four cases since the patients exhibited both flaccid and few tight blisters. Two cases showed a positive Nikolsky sign, while the other two showed a negative one. Bullous pemphigoid/linear IgA disease was identified in three patients. One patient presented with a string of pearls lesion in one place and bullous pemphigoid-like tense blisters

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 08, 2023

with a few erosions in another. In cases 2 and 3, the patients had a negative medication history and lesions that resembled both linear IgA illness and bullous pemphigoid. These prodromal symptoms included itching and urticarial lesions [15-17].

Pemphigus vulgaris and pemphigus were both difficult to distinguish in two cases. These individuals exhibited a wide variety of skin lesions, including vegetative ones on the scalp and chest, as well as flaccid bulla and erosions elsewhere. The buccal mucosa was unaffected in one patient, while very mild erosions were present in the other. Both patients showed a positive Nikolsky sign and Tzanck test. Pemphigus vulgaris had traditional characteristics such a suprabasal split, acantholytic cells in the bulla cavity, and a "row of tombstones" look. Pemphigus foliaceus displayed the characteristic subcorneal detachment. Pemphigus erythematosus is characterized by interface dermatitis and subcorneal separation. Subepidermal bullae with inflammatory infiltration rich in eosinophils and lymphocytes are characteristic of bullous pemphigoid [16-18].

The clinical diagnosis of four patients was initially ambiguous, but they were later determined to exhibit characteristics consistent with bullous pemphigoid. Pemphigus vulgaris was present in two cases with an equivocal clinical diagnosis due to the presence of suprabasal splits with acantholytic cells. Subcorneal split was found in one patient whose clinical diagnosis of pemphigus vulgaris or pemphigus foliaceus was ambiguous. Two of the three pemphigus foliaceus cases tested positive for DIF. In both cases, IgG was found deposited in the upper epidermal layers' intercellular space in a characteristic "fishnet" pattern. One patient's C3 deposition took the form of a fishnet pattern in the intercellular region. DIF reveals Ig Gand C3 accumulation in the upper epidermal layers of ICS in pemphigus foliaceus. This research is useful for telling pemphigus foliaceus apart from pemphigus vulgaris [19-21].

In a study of 27 people with bullous pemphigoid, all of them tested positive for DIF. Twenty-six patients had C3 deposited in a linear fashion along the dermo-epidermal junction. IgG was shown to be deposited in a linear fashion along the dermo-epidermal interface in 21 individuals. Deposition of IgA in a linear fashion at the dermoepidermal junction in a single patient. Linear pattern IgG and C3 staining was seen in 68% of participants in the study by Buch A C et al. Bullous pemphigoid, cicatricial pemphigoid, and pemphigoid gestationis belong to the pemphigoid group of disorders, which are characterized by the presence of C3 deposits with greater intensity than IgG along the dermoepidermal junction [22, 23]. They occur in smooth, delicate, and linear patterns. The diagnosis of subepidermal bullous illnesses can be made with greater sensitivity using the salt split technique of skin. Two of the three patients with bullous systemic lupus erythematosus had a positive DIF from lesional skin. All

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 08, 2023

of them had been diagnosed with SLE before and were now receiving treatment. In both instances, the IgG and C3 were deposited in a linear fashion along the dermo-epidermal interface. Serological evidence of systemic lupus erythematosus is used to distinguish bullous SLE from epidermolysis bullosa acquisita. DIF/indirect immunofluorescence in these bullous lesions beneath the epidermis. When comparing IF on salt split skin to standard DIF, the former produces a higher rate of positive [22-25].

CONCLUSION

The most prevalent age range for autoimmune bullous diseases was 51-60 years. The most prevalent form of autoimmune bullous disease was pemphigus vulgaris. Males disproportionately suffered from the subepidermal group of diseases. Immunobullous diseases were most frequently linked to the development of type 2 diabetes mellitus. Direct immunofluorescence testing was able to provide results in just two days, making it a more time-efficient method of diagnosis. Sixty patients had positive direct immunofluorescence. Fifty-two of these patients tested positive for IgG. Most immunoreactants in the pemphigus group of diseases were deposited in a fishnet pattern along intercellular gaps. One patient with bullous systemic lupus erythematosus had multiple immunoreactant deposition. Together, DIF testing plus clinical/histopathological results were accurate in diagnosing 95.71 percent of patients.

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Conflict of interest

None

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