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FREQUENCY OF CLINICOPATHOLOGICAL SPECTRUM OF IMMUNOBULLOUS DISORDERS

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Abstract

Introduction: Autoimmune vesiculobullous disorders are rare diseases that are characterized by blisters over skin and oral erosions. An accurate diagnosis is achieved by clinical examination, pathological correlation, and immunofluorescence.

Objective: To determine the frequency of clinicopathological spectrum of immunobullous disorders presenting to a tertiary care setup.

Methodology: This cross-sectional study conducted at the Department of Dermatology, Civil Hospital, Karachi, spanned six months from February 28, 2018, to August 28, 2018. The subjects comprised all patients meeting the inclusion criteria who visited the department during this period. Following ethical approval and obtaining informed written consent, the patients underwent a comprehensive evaluation, including a brief history and thorough cutaneous and systemic examinations. The study aimed to delineate the clinicopathological spectrum of immunobullous disorders.

Results: A total of 55 patients with immunobullous disease were included. 19 patients (34.5%) were males & 36 patients (65.5%) were females with the mean age was 44.04±13.620 years. Clinicopathological variants of immunobullous disorders was Subepidermal in 26 (47.3%) & Intraepidermal in 29 (52.7%).

Conclusion: Thorough clinical examination, aided by histopathology was helpful in arriving at a diagnosis of these vesiculobullous disorders in resource-poor center like ours where the gold standard immunofluorescence studies are not available.

Key Words: Autoimmuno bullous disorders, Bullous pemphigoid, Pemphigus

Introduction

Immunobullous diseases are a diverse group of disorders characterized by formation of autoantibodies directed against various antigens present in the skin, leading to blister formation (1).

These illnesses are classified as intraepidermal or subepidermal immunobullous disorders based on the location of the antigen (2). The cleavage plane formed by the split secondary to autoantibodies acting on local skin antigens is used to categorize immunobullous diseases (3). Clinically, it may show up as erosions or bullae development that damage the mucous membranes and the skin (4). The clinical presentation, histological analysis, and immunofluorescence confirmation evidence all contribute in the diagnosis (5). Only in highly developed research laboratory are more sophisticated methods like immunoblotting and immunoelectron microscopy accessible, which may help clarify the diagnosis by accurately identifying the antigen-antibody complexes (6).

A decade-long investigation conducted in the Indian population between 2005 and 2015 demonstrated that, among 45 cases analyzed, 71% were diagnosed with pemphigus, 22.22% with bullous pemphigoid, 4.44% with childhood chronic bullous dermatosis, and 2.2% with bullous systemic lupus erythematosus, highlighting a limited exploration of immunobullous disorders (2). Bullous pemphigoid (11.6%) and pemphigus vulgaris (81.2%) were determined to be the two most frequent autoimmune bullous disorders in the Iranian population, according to another research (7). Another 13-year research conducted in Iran from 1999 to 2012 found that pemphigus vulgaris, with 131/168 cases (78%) and bullous pemphigoid, with 21/168 cases (12.5%), was the most common autoimmune bullous illness. The prevalence of immunobullous disease varies geographically. According to an Iranian research, 70–80% of instances of immunobullous diseases are caused by pemphigus vulgaris (8). The range of average prevalence is 0.5-3.1 per 100,000 people (9,10).

The study's objective is to ascertain the clinical and histopathological spectrum of different autoimmune bullous disorders in our nation because no prior research of a similar nature has been conducted in Pakistan; nevertheless, the frequencies of the clinicopathological spectrum have been assessed in other nations in the region. Research performed in the Western population indicates that female patients in the older age group had a higher prevalence of pemphigus vulgaris (11). However, a rise in incidence has been seen in younger patients in our area. My research will assist in assessing how these autoimmune bullous disorders vary from the western population in terms of demographic characteristics.

Objective: To determine the frequency of clinicopathological spectrum of immunobullous disorders presenting to a tertiary care setup

Methodology

Study Design

This cross-sectional study was conducted in the Department of Dermatology at Civil Hospital, Karachi. The research spanned a duration of six months, commencing on February 28, 2018, and concluding on August 28, 2018. The sampling technique employed was non-probability consecutive sampling, aiming to select participants based on their consecutive presentation to the healthcare facility rather than through a random sampling method. This approach facilitated the sequential inclusion of patients with immunobullous disorders, contributing to the comprehensive examination of cases within the specified time frame.

Sample Size

The sample size for this study was determined using the WHO sample size calculator, referencing a prior investigation conducted in India, which reported a prevalence of 71% for pemphigus vulgaris (3). Consequently, the calculated sample size was established at 55, with a margin of error set at 12%.

Inclusion Criteria

The inclusion criteria for participant selection in this study was defined as follows: individuals exhibiting clinical manifestations of immunobullous disease with confirmatory histological findings were eligible. The age range for inclusion was set between 10 and 65 years, encompassing both

genders. Patients presently suffering from malignancy were included, provided they met other criteria and provided informed consent for participation.

Exclusion Criteria
Excluded were those with a prior immunobullous disorder diagnosis and individuals with blistering diseases lacking confirmation as autoimmune bullous disorders on histopathology.

Data Collection
After explaining goals of the study and taking informed consent, patients with clinical presentation of blistering disorders were interviewed and thorough clinical examintion was performed. Skin biopsy was done and sent for histopathology. After confirmation through histopathology, data was entered in a predesigned Performa. Both inpatient and outpatient department patients were interviewed as per protocol. Thorough history and complete cutaneous and systemic examination was performed with data being enclosed in a Performa. Information including demographics, nature and extent of disease and histopathological findings were documented.

Data Analysis
Data was analyzed through SPSS version 17. Frequency and percentages was computed for gender, age group, tense vs. flaccid blisters, type of intraepidermal or subepidermal disorder, type of inflammatory infiltrate and mucosal involvement. Mean and standard deviation was calculated for age, duration of disease and treatment. Stratification was done for age, gender, duration, tense vs flaccid blister, type of immunobullous disorder, mucosal involvement and type of inflammatory infiltrate through Chi Square Test. P value ≤ 0.05 was taken as significant.

Results
This study enrolled 55 patients diagnosed with immunobullous disease, with an average age of 44.04 ± 13.620 years. Males constituted 34.5% (19 patients), while females accounted for 65.5% (36 patients) of the study population with observed variables including tense blisters in 25 patients (45.5%) and flaccid blisters in 30 patients (54.5%). The average duration of symptoms in the study cohort was 11.35 ± 6.007 months, with 16 patients (29.1%) experiencing symptoms for less than 6 months, and 39 patients (70.9%) reporting symptoms persisting for more than 6 months (Table 1).

Table 1: Clinical Profile of Patients with Immunobullous Disease

Characteristics	**Frequency (n=55)**	**Percentage**
Average Age	44.04 ± 13.620	
Gender Distribution		
Male	19	34.5
Female	36	65.5
Blister Types		
Tense Blister	25	45.5
Flacid Blister	30	54.5
Duration of Symptoms		
< 6 months	16	29.1
> 6 months	39	70.9
Mean Duration of Symptoms	11.35 ± 6.007	

The occurrence of a family history of the disease was noted in 3 patients (5.45%), itching was reported by 24 patients (43.6%), and a present history of malignancy was documented in 3 patients (5.45%), as depicted in figure 1. Additionally, Joint pain was reported by 3 patients (5.45%), alopecia in 3 patients (5.45%), oral ulcers in 27 patients (49.1%), diarrhea or gluten intolerance in 7 patients (12.7%), and weight loss in 23 patients (41.8%). Among female patients, 2 experienced pregnancies. Nail involvement was observed in 29 patients, with disease exacerbation by trauma noted in 9 patients

and exacerbation by sunlight in 21 patients as shown in figure 2.

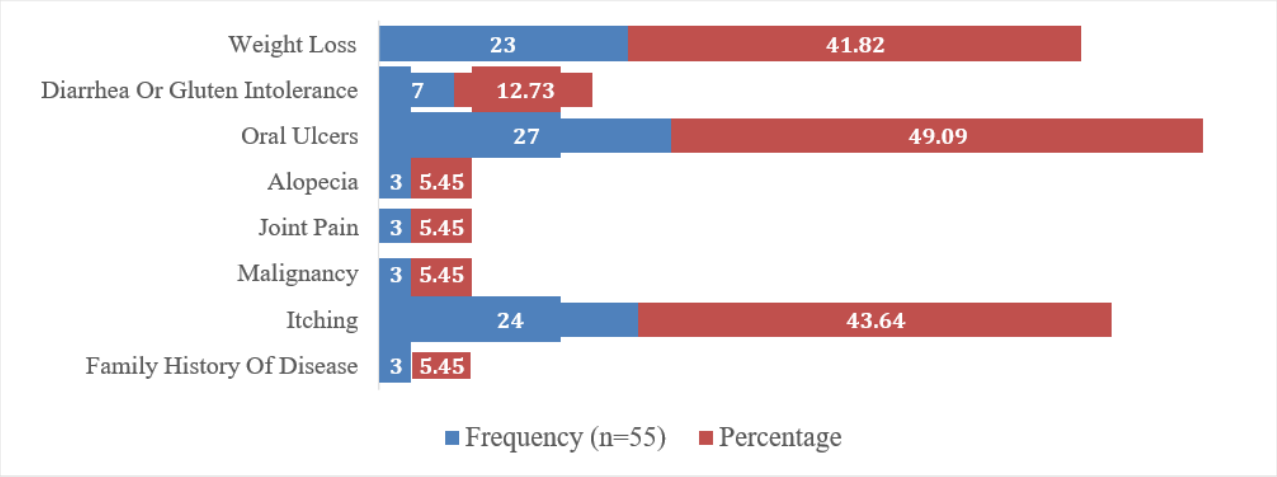

Figure 1: Clinical Features and Comorbidities in Patients with Immunobullous Disease

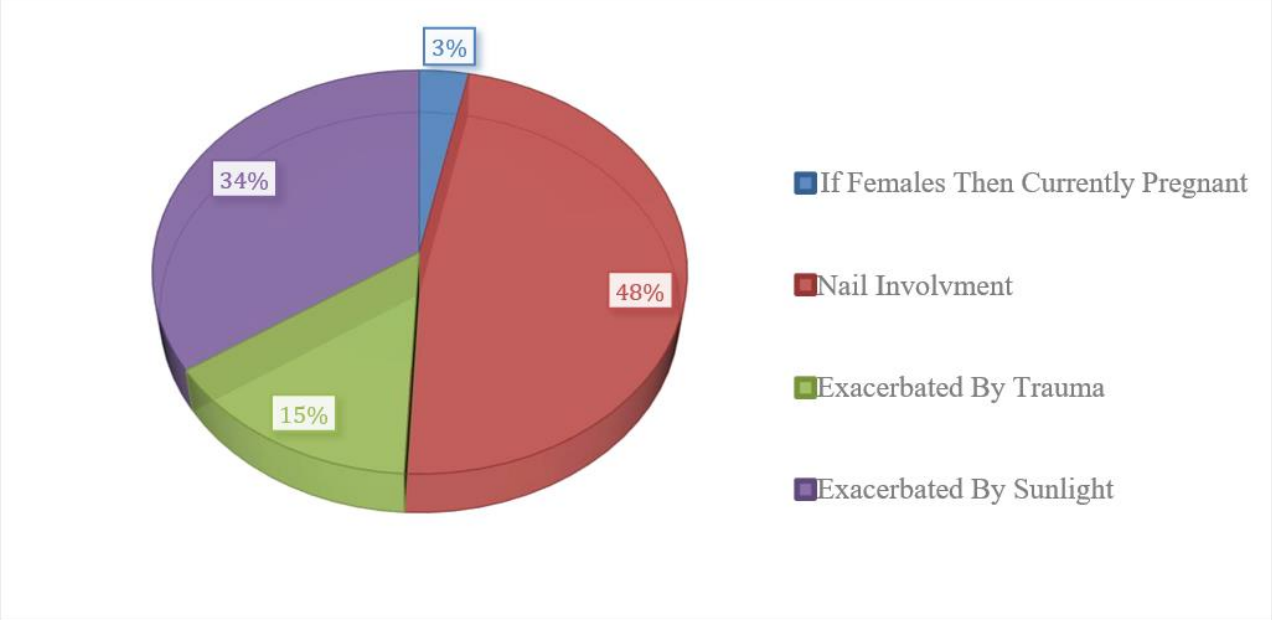

Figure 2: Demographic and Clinical Characteristics of Patients with Immunobullous Disorders

During examination, Nikolsky sign was present in 29 patients (52.72%), Bullae spreading sign in 25 patients (45.5%), blister characteristics were confluent in 28 patients (50.9%) and discrete in 27 patients (49.1%), and mucosal involvement was noted in 22 patients (40%). Nail changes were Paronychia in 17(30.9%), Subungual hematoma in 18(32.7%) & Nail dystrophies in 20(36.4%), Ocular involvement was present in 12 (21.8%) & Predominant involvement of body area was Flexures in 49(89.1%) while extensors in 6(10.9%) , as shown in table 2.

Table 2: Clinical Features and Manifestations in Patients with Immunobullous Disease

Variables	**Frequency (N=55)**	**Percentage**
Nikolsky Sign	29	52.72
Bullae Spreading Sign	25	45.5
Characteristic Of Blister		
Confluent	28	50.9
Discrete	27	49.1
Mucosal Involvement	22	40.0
Nail Changes		

Paronychia	17	30.9
Subungual Hematoma	18	32.7
Nail Dystrophies	20	36.4
Ocular Involvement	12	21.8
Predominant Involvement of Body Area		
Flexures	49	89.1
Extensors	6	10.9

The histopathological analysis of blisters revealed a subepidermal origin in 26 cases (47.3%) and an intraepidermal origin in 29 cases (52.7%). The inflammatory infiltrate exhibited eosinophils in 11 cases (20%), neutrophils in 25 cases (45.5%), lymphocytes in 8 cases (14.5%), and a mixed pattern in 11 cases (20%). In terms of clinicopathological variants of immunobullous disorders, subepidermal manifestations were observed in 26 cases (47.3%), while intraepidermal manifestations were noted in 29 cases (52.7%). Among the intraepidermal immunobullous disorders, Pemphigus vulgaris accounted for 26 cases (47.2%), and Paraneoplastic pemphigus for
3 cases (5.4%). Meanwhile, among the subepidermal immunobullous disorders, Bullous pemphigoid was identified in 11 cases (20%), Mucous membrane pemphigoid in 3 cases (5.5%), Linear IgA disease in 2 cases (3.6%), Pemphigoid gestationis in 1 case (1.8%), Epidermolysis bullosa acquisita in 4 cases (7.3%), Bullous systemic lupus erythematosus in 3 cases (5.5%), and dermatitis herpetiformis in 2 cases (3.6%) as shown in Table 3

Table 3: Clinicopathological Spectrum of Immunobullous Disorders

Variables		**Frequency N=(55)**	**Percentage (%)**
Histopathology of Blister			
Subepidermal		26	47.3
Intraepidermal		29	52.7
Inflammatory Infiltrate			
Mixed		11	20
Esinophils		11	20
Neutrophils		25	45.5
Lymphocytes		8	14.5
Clinicopathological Spectrum of Immunobullous Disorders			
Intraepiderma l	Pemphigus Vulgaris	26	47.2
	Paraneoplastic Pemphigus	3	5.4
Subepidermal	Bullous Pemphigoid	11	20.0
	Mucous Membrane Pemphigoid	3	5.5
	Linear IgA Disease	2	3.6
	Pemphigoid Gestationis	1	1.8
	Epidermolysis Bullosa Acquisita	4	7.3
	Bullous Systemic Lupus Erythematosus	3	5.5
	Dermatitis Herpetiformis	2	3.6

In Table 4, a comparative analysis of age and gender distribution in intraepidermal and subepidermal immunobullous disorders reveals no significant age difference but a significant gender disparity, with more females in the intraepidermal group. The presentation and duration of symptoms show no significant differences. Table 5 explores the relationship between clinical symptoms and immunobullous disorders, indicating no significant associations with family history, itching, malignancy history, joint pain, alopecia, oral ulcers, diarrhea, or weight loss. However, a significant link is found between immunobullous disorders and trauma exacerbation, predominantly in the intraepidermal group, and a near-significant association with sunlight exacerbation, mainly in the subepidermal group. Chi-square tests were employed, and significance was considered at a p-value ≤ 0.05.

Table 4: Comparison of Age and Gender in Intraepidermal and Subepidermal Immunobullous Disorders

Age Years	Clinicopathological Spectrum of Immunobullous Disorders		N,%	P-Value
	Intraepidermal	Subepidermal		
10-40	13(23.63%)	12(21.81%)	25(45.45%)	0.583
41-65	16(29.09%)	14(25.45%)	30(54.54%)	
Total	29(52.72%)	26(47.27%)	55(100%)	
Gender	Clinicopathological Spectrum of Immunobullous Disorders		N,%	P-Value
	Intraepidermal	Subepidermal		
Male	10(18.18%)	9(16.36%)	19(34.54%)	0.001
Female	19(34.54%)	17(30.90%)	36(65.45%)	
Total	29(52.72%)	26(47.27%)	55(100%)	
Presentation	Clinicopathological Spectrum of Immunobullous Disorders		Total	P-Value
	Intraepidermal	Subepidermal		
Tense Blister	0(%)	25(44.45%)	25(44.45%)	0.964
Flacid Blister	29(%)	1(1.81%)	30(54.54%)	
Total	29(52.72%)	26(47.27%)	55(100%)	
Duration Of Symptoms	Clinicopathological Spectrum of Immunobullous Disorders		Total	P-Value
	Intraepidermal	Subepidermal		
≤6 Months	8(14.54%)	8(14.54%)	16(29.09%)	0.610
>6 Months	21(38.18%)	18(32.72%)	39(70.9%)	
Total	29(52.72%)	26(47.27%)	55(100%)	
Chi Square test was applied, P-value ≤ 0.05 considered as significant, Not Significant at 0.05 level				

Table 5: Relationship between Clinical Symptoms and Immunobullous Disorders

Variables	Immunobullous Disorders	N,%	P-Value
Family History of Disease			
Present	Intraepidermal: 0 (0%)	3 (5.45%)	
	Subepidermal: 3 (5.45%)		0.060
Absent	Intraepidermal: 29 (52.72%)	52 (94.54%)	
	Subepidermal: 23 (41.81%)		
Itching			
Present	Intraepidermal: 10 (18.18%)	24 (43.63%)	
	Subepidermal: 14 (25.45%)		0.195
Absent	Intraepidermal: 19 (34.54%)	31 (65.36%)	
	Subepidermal: 12 (21.81%)		
Present History of Malignancy			
Present	Intraepidermal: 3 (5.45%)	3 (5.45%)	
	Subepidermal: 0 (0%)		0.092
Absent	Intraepidermal: 26 (47.27%)	52 (94.54%)	
	Subepidermal: 26 (47.27%)		
Joint Pain			
Present	Intraepidermal: 0 (0%)	3 (5.45%)	
	Subepidermal: 3 (5.45%)		0.060
Absent	Intraepidermal: 29 (52.72%)	52 (94.54%)	
	Subepidermal: 23 (41.81%)		
Alopecia			
Present	Intraepidermal: 0 (0%)	3 (5.45%)	
	Subepidermal: 3 (5.45%)		0.060
Absent	Intraepidermal: 29 (52.72%)	52 (94.54%)	
	Subepidermal: 23 (41.81%)		
Oral Ulcers			
Present	Intraepidermal: 21 (38.18%)	27 (49.09%)	
	Subepidermal: 6 (10.90%)		0.493

Absent	Intraepidermal: 8 (14.54%)	28 (50.90%)	
	Subepidermal: 20 (36.36%)		
Diarrhea or Gluten Intolerance			
Present	Intraepidermal: 2 (3.63%)	7 (12.7%)	0.185
	Subepidermal: 5 (9.09%)		
Absent	Intraepidermal: 27 (49.09%)	48 (87.27%)	
	Subepidermal: 21 (38.18%)		
Weight Loss			
Present	Intraepidermal: 7 (12.72%)	23 (41.81%)	0.371
	Subepidermal: 16 (29.09%)		
Absent	Intraepidermal: 22 (40%)	32 (58.18%)	
	Subepidermal: 10 (18.1%)		

Chi Square test was applied, P-value ≤ 0.05 considered as significant, Not Significant at 0.05level

Tables 6, 7 and 8, present comprehensive associations and correlations in immunobullous disorders. Table 6 explores the link between pregnancy, nail involvement, and exacerbating factors, revealing no significant associations with pregnancy but significant correlations with trauma exacerbation. In Table 7, clinical signs such as Nikolsky and Bullae Spreading signs show strong associations with intraepidermal disorders and subepidermal disorders respectively, while nail changes, ocular involvement, and body area predominance demonstrate significant correlations. Additionally, Table 8 analyzes the distribution of inflammatory infiltrates, indicating no significant differences between intraepidermal and subepidermal disorders. Chi-square tests were employed, with significance considered at a p-value ≤ 0.05.

Table 6: Association of Pregnancy and Nail Involvement with Immunobullous Disorders

Feature	**Immunobullous Disorders**	**N,%**	**P-Value**
If Females Then Currently Pregnant			
Yes	Intraepidermal: 0 (0%)	2 (3.63%)	0.205
	Subepidermal: 2 (3.63%)		
No	Intraepidermal: 29 (52.72%)	43 (78.18%)	
	Subepidermal: 24 (43.63%)		
Nail Involvement			
Present	Intraepidermal: 17 (30.90%)	29 (52.72%)	0.125
	Subepidermal: 12 (21.81%)		
Absent	Intraepidermal: 12 (21.81%)	26 (47.27%)	
	Subepidermal: 14 (25.45%)		
Exacerbated By Trauma			
Yes	Intraepidermal: 5 (9.09%)	9 (16.36%)	0.025
	Subepidermal: 4 (7.27%)		
No	Intraepidermal: 24 (43.63%)	46 (86.63%)	
	Subepidermal: 22 (40%)		
Exacerbated By Sunlight			
Yes	Intraepidermal: 10 (18.18%)	21 (38.18%)	0.080
	Subepidermal: 11 (20%)		
No	Intraepidermal: 19 (34.54%)	34 (61.8%)	
	Subepidermal: 15 (27.27%)		
Chi Square test was applied, P-value ≤ 0.05 considered as significant, Not Significant at 0.05 level			

Table 7: Correlation of Clinical Signs with Immunobullous Disorders

Feature	Immunobullous Disorders	N,%	P-Value
If Females Then Currently Pregnant			
Yes	Intraepidermal: 0 (0%)	2 (3.63%)	0.205
	Subepidermal: 2 (3.63%)		
No	Intraepidermal: 29 (52.72%)	43 (78.18%)	
	Subepidermal: 24 (43.63%)		
Nail Involvement			
Present	Intraepidermal: 17 (30.90%)	29 (52.72%)	0.125
	Subepidermal: 12 (21.81%)		
Absent	Intraepidermal: 12 (21.81%)	26 (47.27%)	
	Subepidermal: 14 (25.45%)		
Exacerbated By Trauma			
Yes	Intraepidermal: 5 (9.09%)	9 (16.36%)	0.025
	Subepidermal: 4 (7.27%)		
No	Intraepidermal: 24 (43.63%)	46 (86.63%)	
	Subepidermal: 22 (40%)		
Exacerbated By Sunlight			
Yes	Intraepidermal: 10 (18.18%)	21 (38.18%)	0.080
	Subepidermal: 11 (20%)		
No	Intraepidermal: 19 (34.54%)	34 (61.8%)	
	Subepidermal: 15 (27.27%)		
Nikolsky Sign			
Present	Intraepidermal: 29 (52.72%)	29 (52.72%)	0.000
	Subepidermal: 0 (0%)		
Absent	Intraepidermal: 0 (0%)	26 (47.27%)	
	Subepidermal: 26 (47.27%)		
Bullae Spreading Sign			
Present	Intraepidermal: 0 (43.63%)	25 (45.45%)	0.000
	Subepidermal: 26 (1.81%)		
Absent	Intraepidermal: 29 (9.09%)	30 (54.54%)	
	Subepidermal: 0 (45.45%)		
Characteristic of Blister			
Confluent	Intraepidermal: 19 (34.54%)	28 (50.90%)	0.309
	Subepidermal: 9 (16.36%)		
Discrete	Intraepidermal: 10 (18.18%)	27 (49.09%)	
	Subepidermal: 17 (30.90%)		
Mucosal Involvement			
Present	Intraepidermal: 12 (21.81%)	22 (40%)	0.300
	Subepidermal: 10 (18.18%)		
Absent	Intraepidermal: 17 (30.90%)	33 (60%)	
	Subepidermal: 16 (29.09%)		
Nail Changes			
Paronychia	Intraepidermal: 7 (12.72%)	17 (30.90%)	0.159
	Subepidermal: 10 (18.18%)		
Subungual Hematoma	Intraepidermal: 10 (18.18%)	18 (32.72%)	
	Subepidermal: 8 (14.54%)		
Nail Dystrophies	Intraepidermal: 12 (21.81%)	20 (36.36%)	
	Subepidermal: 8 (14.54%)		
Ocular Involvement			
Present	Intraepidermal: 4 (7.27%)	12 (21.81%)	0.205
	Subepidermal: 8 (14.54%)		
Absent	Intraepidermal: 25 (44.45%)	43 (78.18%)	

	Subepidermal: 18 (32.72%)		
Predominant Involvement of Body Area			
Flexures	Intraepidermal: 26 (47.27%)	49 (89.09%)	0.019
	Subepidermal: 23 (41.81%)		
Extensors	Intraepidermal: 3 (5.45%)	6 (10.90%)	
	Subepidermal: 3 (5.45%)		
Chi Square test was applied, P-value ≤ 0.05 considered as significant, Not Significant at 0.05 level			

Table 8: Distribution of Inflammatory Infiltrate in Intraepidermal and Subepidermal Immunobullous Disorders

Inflammatory Infiltrate	Intraepidermal	Subepidermal	Total	P- Valu e
Mixed	11(20%)	0(0%)	11(20%)	0.807
Esinophils	0(0%)	11(20%)	11(20%)	
Neutrophils	10(18.18%)	15(27.27%)	25(45.45%)	
Lymphocytes	8(14.54%)	0(0%)	8(14.54%)	
Absent	0(%)	0(0%)	0(0%)	
Chi Square test was applied, P-value ≤ 0.05 considered as significant, Not Significant at 0.05 level				

Discussion

Autoimmune vesiculobullous disorders are characterized by antibody mediated destruction of structures essential for maintaining the integrity of skin leading to blisters and erosions over skin and mucosa (12). The keratinocytes of the epidermis are tightly bound together by desmosomes and intercellular substances. Beneath the epidermis lies the basement membrane zone, a special area of cell extracellular matrix adhesion (13). Antibodies may target against many of the component in these locations e.g. desmoglein-III and desmoglein-I antigens of pemphigus vulgaris and pemphigus foliaceus respectively or bullous pemphigoid antigen (14). Deposition of antibody can be demonstrated at the level of blister formation or at the site adjacent to blisters (15).

They are categorized intraepidermal and subepidermal blistering disorders. Intraepidermal disorders include pemphigus vulgaris, pemphigus foliaceus and paraneoplastic pemphigus. Subepidermal disorders include bullous pemphigoid, cicatricial pemphigoid, linear immunoglobulin A dermatosis, lichen planus pemphigoides, dermatitis herpetiformis, epidermolysis bullosa acquisita, and bullous SLE (16). Thorough clinical examination aided by light microscopy and immunofluorescence would help us to make a definitive diagnosis of these bullous disorders (17). Although immunofluorescence is considered as the gold standard, in resource poor settings where this facility could not be availed even in private laboratory, diagnosis is based on the clinical and light microscopic findings only (18).

In our present study, Clinicopathological variants of immunobullous disorders was Subepidermal in 26 (47.3%) & Intraepidermal in 29 (52.7%), Variants of intraepidermal immunobullous disorders were Pemphigus vulgaris in 26 (47.2%) & Paraneoplastic pemphigus in 3 (5.4%), while Variants of Subepidermal immunobullous disorders were Bullous pemphigoid in 11 (20%), Mucous membrane pemphigoid in 3 (5.5%), Linear IgA disease in 2 (3.6%), Pemphigoid gestationis in 1 (1.8%), Epidermolysis bullosa acquisita in 4 (7.3%), Bullous systemic lupus erythematosus in 3 (5.5%) & dermatitis herpetiformis in 2 (3.6%), as aligned to previous studies (19-21). Predominant age group for pemphigus was noted in the range 41-60 which was comparable with other studies (22,23). Pemphigus and all other blistering disorders showed a higher incidence in females (62.14%) which was contradictory to earlier studies (24,25).

In our study Bullous pemphigoid was the predominant subepidermal disorder noted, which is similar and is comparable with other study (26). In bullous pemphigoid the sub-epidermal bullae contain small to moderate number of eosinophils and neutrophils. Korossy (2010) showed that deposition of C3 was present in all (100%) of 11 cases, they studied (27). Predominant age group of bullous pemphigoid was between 41 and 70, with majority of patients presenting in the age group of 51-60. This was contradictory to earlier studies (28,29).

Diagnosis of blistering diseases can often have made on the basis of clinical features but in some cases it may be possible to produce only differential diagnosis (30). More than 50% of clinical diagnoses show concordance with final diagnosis in present study. Direct immunofluorescence study has definitive role in distinguishing immune mediated blistering diseases from others. Some immunopathological patterns are disease specific, such as fishnet pattern of epidermal intercellular deposits are specific for pemphigus (31). The lesions with basement membrane zone depositions may be sometimes inconclusive and deposits along the epidermal-dermal junction can be found in many diseases, such as lupus erythematosus, epidermolysis bullosa acquisita and porphyria (32). Direct and indirect immunofluorescence tests with split-skin studies enable the typing and localization of immunoglobulin deposits, which can be used in special situations (33). Direct immunofluorescence technique, combined with routine histology, is a useful method in distinguishing most of the bullous diseases, if not all. Indirect immunofluorescence test is helpful commonly in pemphigus cases, frequently in bullous pemphigoid and occasionally in linear IgA dermatosis (34). Indirect immunofluorescence test can be utilized as an alternative or preliminary test in these cases when direct immunofluorescence test could not be done as some patient may refuse biopsy and can be utilized also for the patients staying in remote area from where sera can be easily collected and transported (35). By Tzanck smears accurate diagnosis can be made in pemphigus group of diseases where acantholytic cells and/or typical Tzanck like cells are present (36). No acantholytic cells with predominant eosinophils indicate a case of bullous pemphigoid. But in most of cases with subepidermal blisters the smear findings are nonspecific. Before a definitive diagnosis to be made it requires clinical correlation with the disease. This is particularly helpful in differentiating the other various bullous diseases from pemphigus (37). All cases of pemphigus vulgaris (100%) showed suprabasal bulla and acantholytic cells on histopathology and all pemphigus foliaceus case showed subcorneal bulla which was comparable with studies (38,39)

Conclusion

In conclusion, our study sheds light on the clinicopathological spectrum of immunobullous disorders in a resource-constrained setting, emphasizing the pivotal role of thorough clinical examination and histopathology for accurate diagnosis. Despite the absence of gold-standard immunofluorescence studies, our findings underscore the significance of basic diagnostic tools in elucidating the diverse manifestations of these rare diseases. The predominance of intraepidermal disorders, notably Pemphigus vulgaris, aligns with global trends, while variations in demographic patterns underscore the importance of regional epidemiological studies. This research contributes valuable insights into the diagnostic challenges and patterns of immunobullous disorders, fostering a foundation for further investigations in our population.

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