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VESICULOBULLOUS LESIONS: A JOURNEY THROUGH HISTOPATHOLOGY IN TERTIARY CARE CENTRE.

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KEYWORDS
vesiculobullous lesions,pemphigus vulgaris,pemphigus foliaceous,dermatoses

Introduction: Vesiculobullous disorders represent a heterogeneous group of dermatoses with protean manifestations usually associated with fluid filled skin lesions. They usually occur as a part of the spectrum of various infectious, drug-induced, genetic, inflammatory and autoimmune disorders. Distinguishing between different diseases can be challenging, as they may share similar appearances, making clinical diagnosis difficult. Histopathology serves as a crucial tool in resolving diagnostic uncertainties, acting as a bridge towards accurate identification.
Aim and Objectives: To establish clinical and histopathological correlation in diagnosing disease. To study definitive diagnosis in diseases with overlapping presentation
Material and Method: In the present study evaluation of vesiculobullous lesions were studied over the period of 2 years (July 2022- July 2024). A total number of 58 skin biopsies were received in histopathology section in department of pathology were studied.
Results: In Vesiculobullous group of disorders, there were 33(56.8%) cases of Pemphigus Vulgaris,Pemphigus foliaceous 12 (20.6%),Bullous pemphigoid 11(18.9%),Darriers disease1 (1.72%),pemphogoid Gestationis 1 (1.72%).there was female preponderance, age group affected was in range of 25 to 65 years.
Conclusion: Correct diagnosis plays an important role in treatment and counselling about type, duration and prognosis of disease, maintaining remission and avoidance of aggravating or causative factors.

INTRODUCTION

Skin is the largest organ of the body, having varied presentation of various disorders. Vesiculobullous disorders, are disorders in which primary lesion is vesicle/bulla on skin or mucous membrane or both. Dermatological conditions can manifest with diverse clinical presentations, sometimes deviating significantly from the typical characteristics. Distinguishing between different diseases can be challenging, as they may share similar appearances, making clinical diagnosis difficult. Histopathology serves as a crucial tool in

resolving diagnostic uncertainties, acting as a bridge towards accurate identification. Histopathological examination helps for definitive diagnosis and classification of disease

Vesiculobullous disorder is an autoimmune disease which is rare with an incidence of 0.5 to 3.2 cases/100,000 population.(1) It is a dermatological disorder in which the autoantibodies are directed against antigens present in epidermis or dermoepidermal junction.(2,3) Vesiculobullous diseases are the manifestations of skin response to various external and internal stimuli and it is one of the most important primary morphological patterns of skin reaction Blisters include both vesicles and bullae which are cavities filled with fluid present either in or underneath the epidermis. Cavities which are less than 0.5 cm in diameter are called vesicles and those which are greater than 0.5 cm in diameter are called bullae.(4) Vesiculobullous disorders can involve mucosal surface of oral cavity, conjunctiva, nasopharynx, oesophagus, urethra, vulva, cervix, scalp, chest, face and upper back. Lesions may also involve the flexor surfaces of the arms and legs, abdomen, axillae and groin.(5) A comprehensive understanding of the clinical presentation and pathogenesis of these diseases is key to diagnosis.

Autoimmune bullous disorders are classified into various groups based on clinical, histomorphological and immunological criteria. They are divided into intraepidermal and subepidermal based on the location of the bulla. Among intraepidermal bullous disorders, pemphigus vulgaris (PV) is most common accounting for around 70%. It is a disease of middle age.(6)

A genetic predisposition to develop pemphigus has been documented, which, in the presence of certain environmental triggers, results in acantholysis. Narbutt et al. evaluated the polymorphisms in genes encoding co-stimulatory receptors – cytotoxic T-lymphocyte antigen 4 (CTLA4) and inducible T-cell co-stimulator (ICOS) – on T cells and concluded that the expression and function of these genes is significantly altered in PV and pemphigus foliaceus (PF).(3) In PV, autoantibodies are primarily directed against desmosomal cadherins, desmoglein (Dsg) 3 and Dsg 1, whereas PF patients only have antibodies against Dsg 1. Mao et al. identified autoantibodies to Desmoglein 3 as of pathologic importance in PV. (4)

AIMS AND OBJECTIVES

- To establish clinical and histopathological correlation in diagnosing disease
- To study definitive diagnosis in diseases with overlapping presentation

Materials and methods

- In the present study, histopathological evaluation of vesiculobullous lesions were studied over the period of 2 years (July 2022- July 2024)
- A total number of 58skin biopsies were received in histopathology section in department of pathology

Inclusion criteria: All skin biopsies from the cases with vesiculobullous disorders irrespective of age, sex and associated diseases.

Exclusion criteria: Mechanical, thermal, suction and chemical blisters, Drug induced blisters and blisters due to congenital causes, Blisters due to irritant contact dermatitis and eczematous dermatitis, Bullous lesions secondary to infection.

RESULT

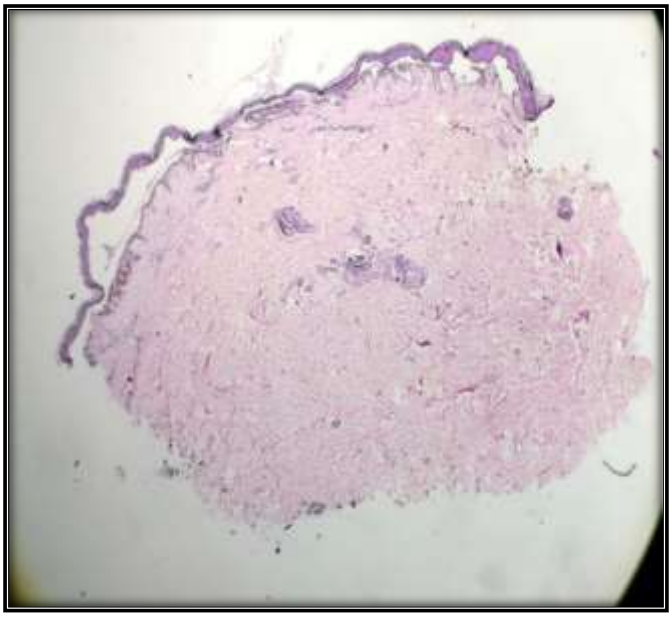
Table 1: Showing distribution of various vesiculobullous disorders.

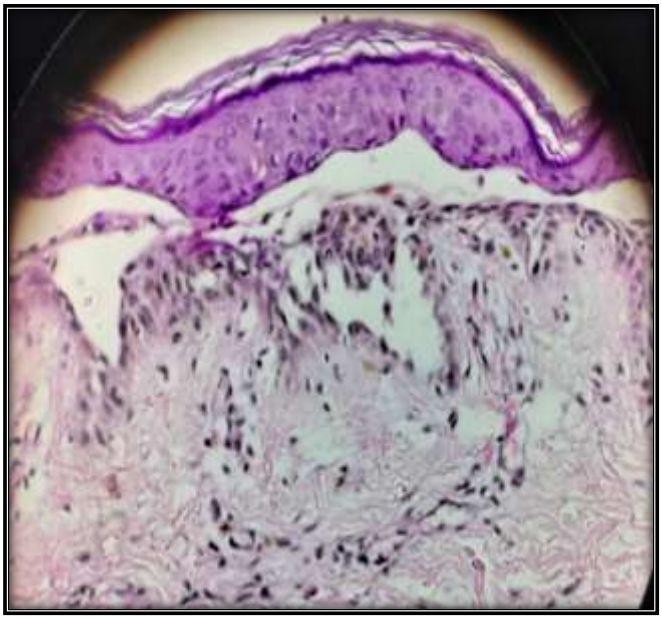
Lesion	No. of Cases	Percentage
Pemphigus Vulgaris	33	56.8%
Pemphigus foliaceus	12	20.6%
Bullous Pemphigoid	11	18.9%
Darier's disease	01	1.72%
Pemphigoid gestationis	01	1.72%
Total	58	100%

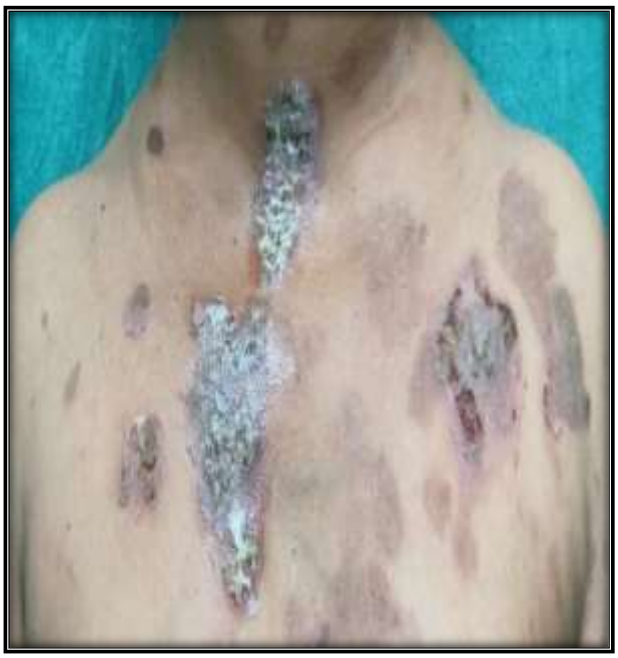
Table 2: Showing the Range and Mean Age of Presentation.

Lesion	Range of age	Mean Age
Pemphigus Vulgaris	30-60 yrs	39 yrs
Pemphigus foliaceus	25 -75 yrs	45 yrs
Bullous Pemphigoid	40 -75 yrs	62 yrs
Darier's disease	50 yrs	50 yrs
Pemphigoid gestation	27 yrs	27 yrs

Pemphigus vulgaris







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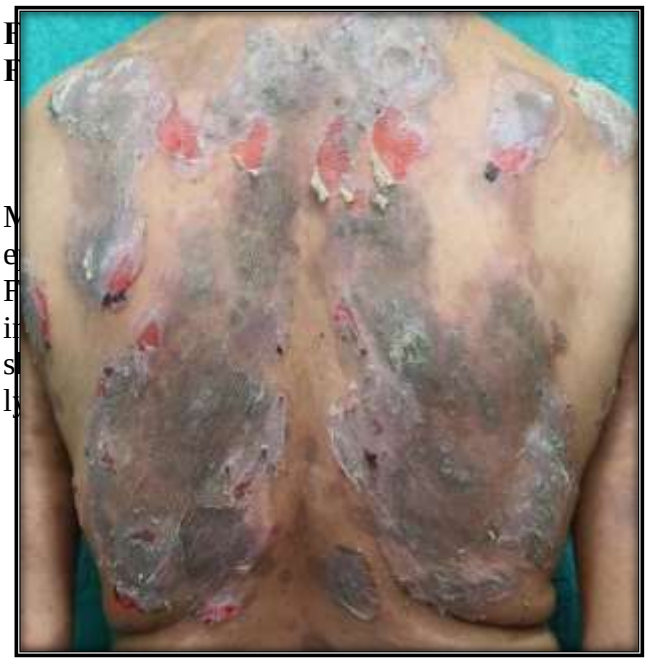
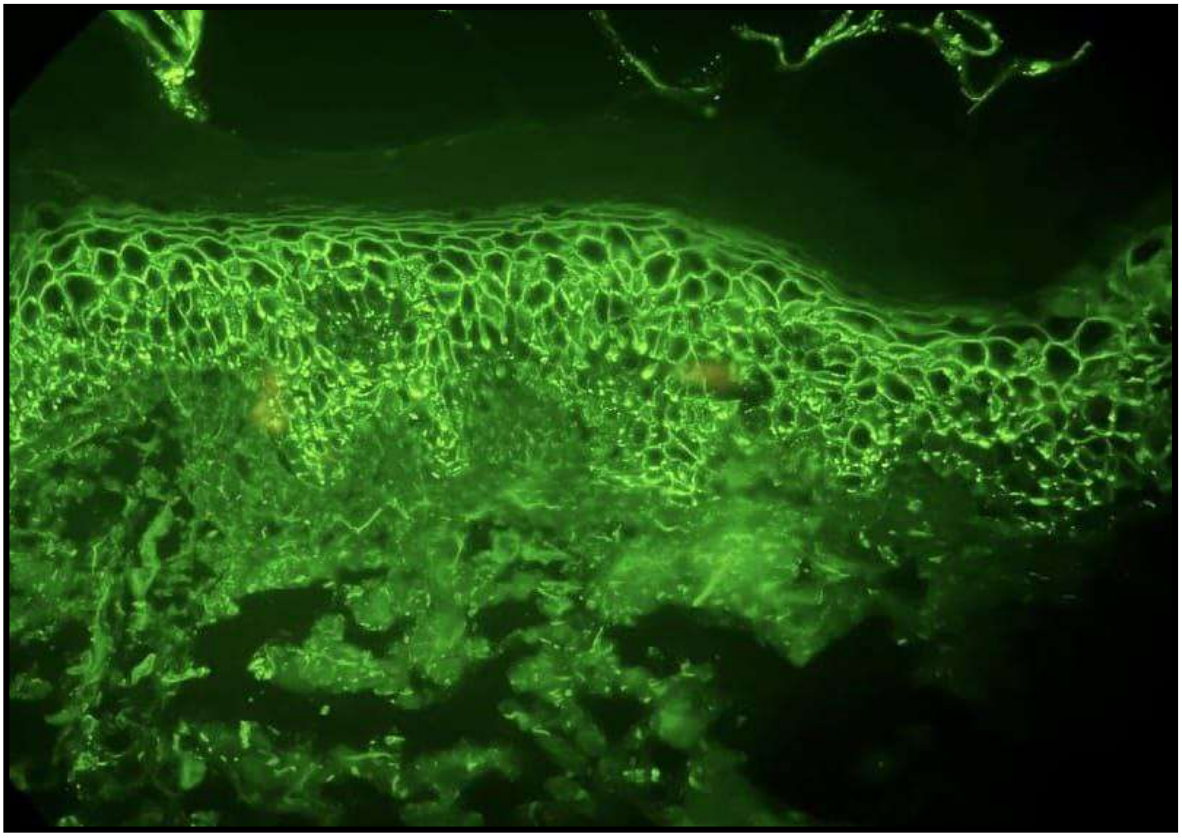


Direct immunofluorescence test image showing full thickness fish net appearance



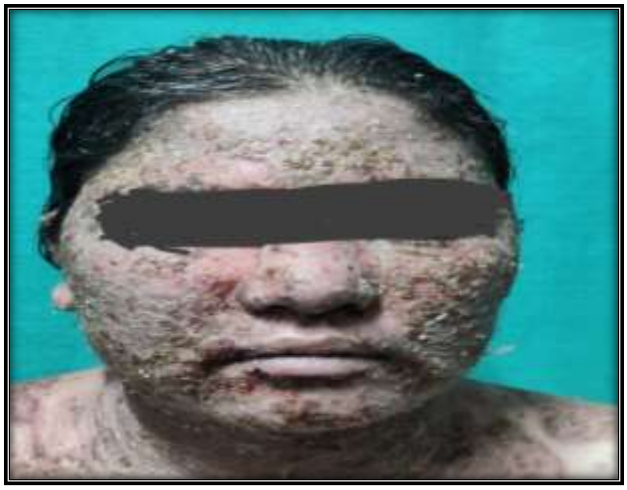


Image1

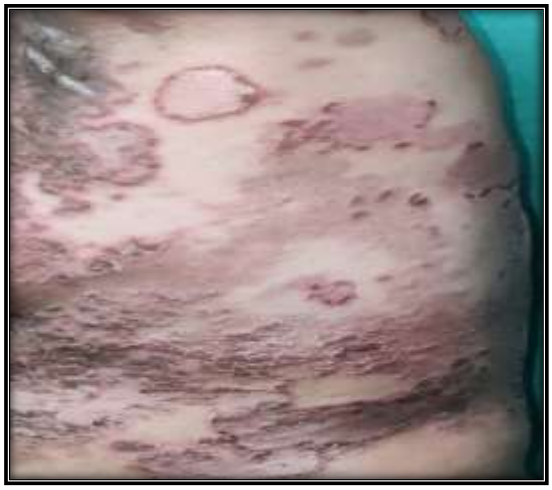


Image2

Image 1 and 2 On examination lesions on face, chest, abdomen and back shows flaccid bullae with crusting and scaling.

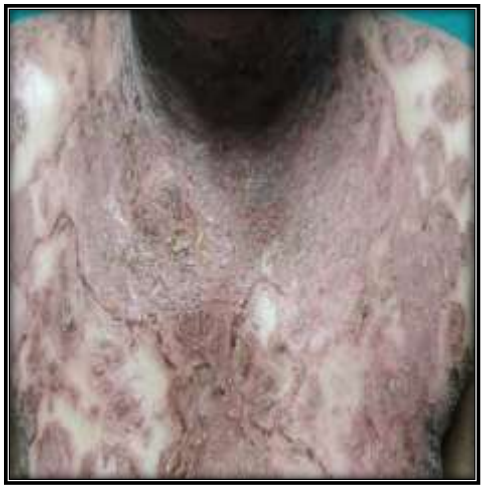


Image3

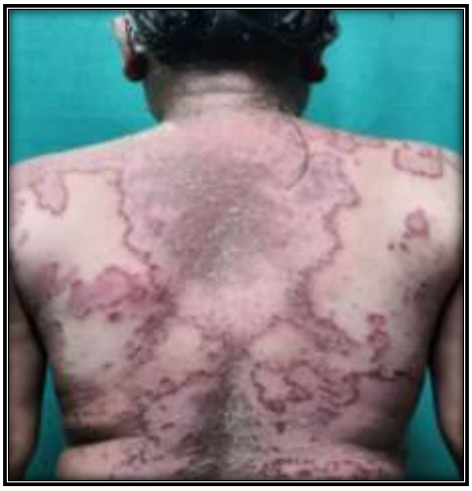
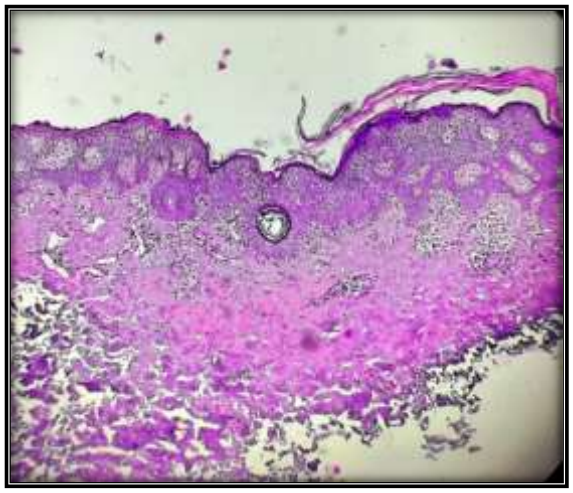


Image4

- On examination lesions on face, chest, abdomen and back shows flaccid bullae with crusting and scaling.
- Image 3 and 4 showing lesion in geographic pattern.



Foliaceus

Fig.3 H&E 10X View of Pemphigus Foliaceus

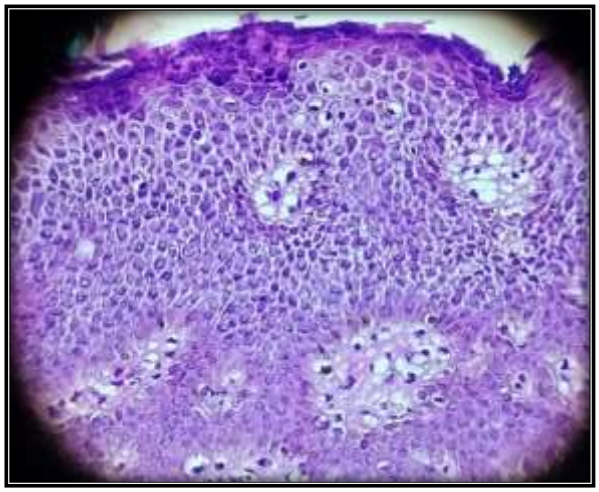
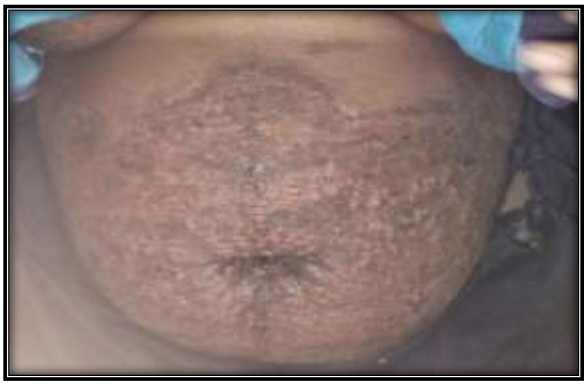
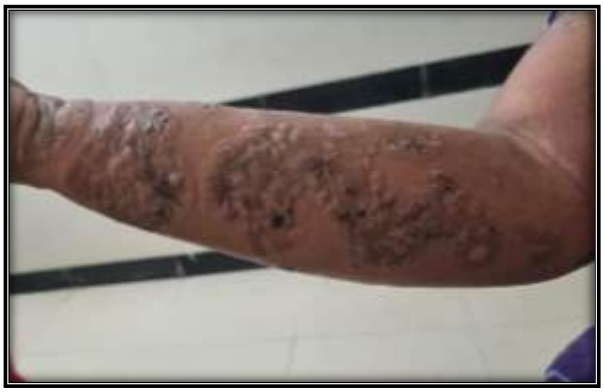


Fig.4 H&E 40X View of Pemphigus Foliaceus

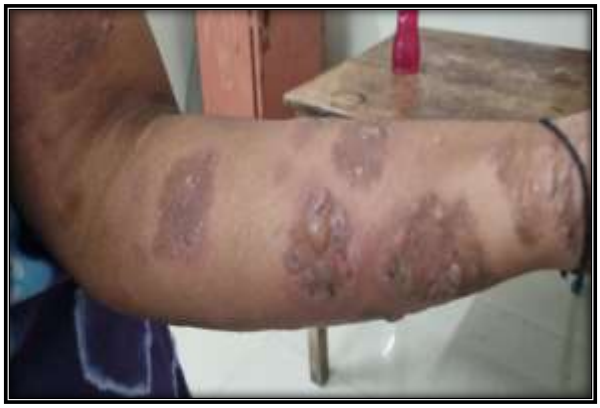
M/E shows keratinized stratified squamous epithelium showing only acontholytic suprabasal layer with with tomstone appearance and focally increased pigmentation. Acantholysis is seen deep down in the hair follicle. Papillary dermis show perivascular inflammatory infiltatres of lymphocyte and plasma cells.

Pemphigoid gestationis





On examination multiple grouped vesicles in anular forms around hyperpigmented plaques over Upper limb and trunk.



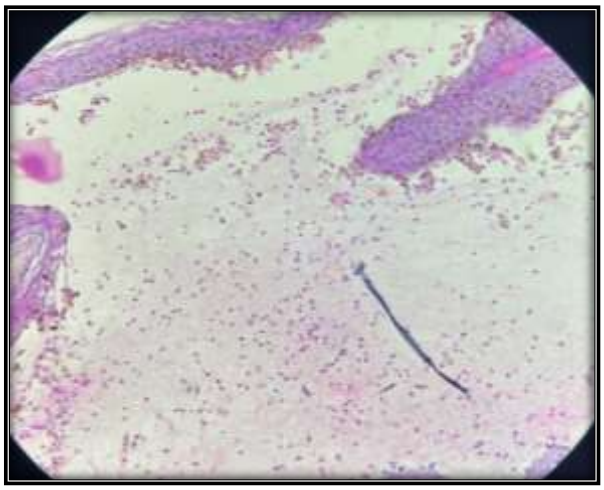


Fig.5 H & E 10X Pemphigus Gestationis

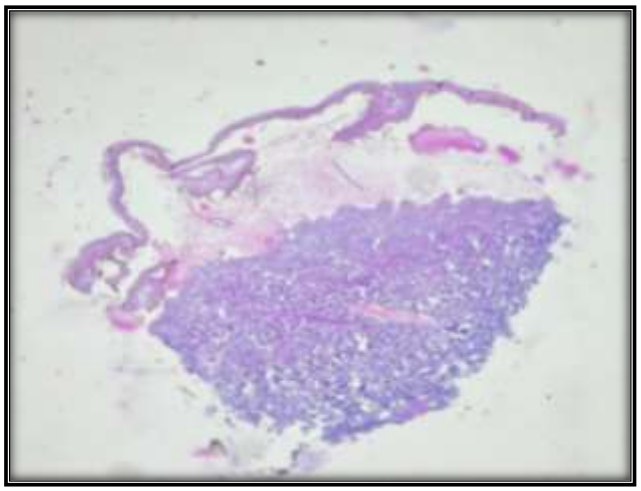
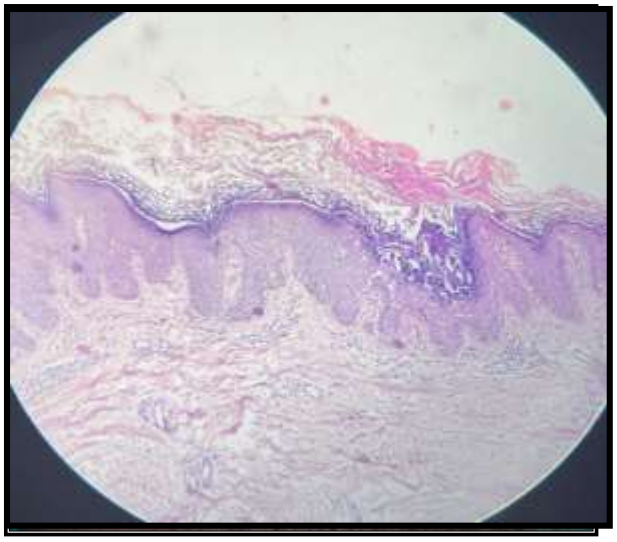
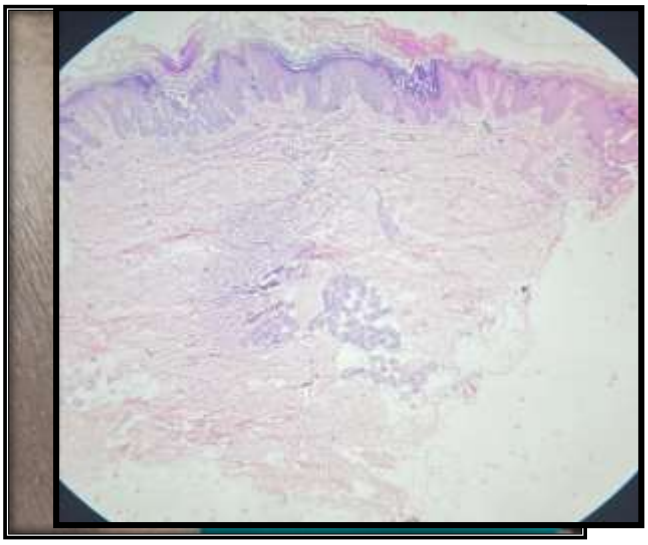


Fig.6 H & E 40X Pemphigus Gestationis

M/E shows keratinized stratified squamous epithelium underneath shows separation of dermoepidermal junction filled with protinacious fluid with eosinophills and few lymphocytes. Dermis shows periadnexal inflammatory infiltrates of eosinophills and lymphocytes.

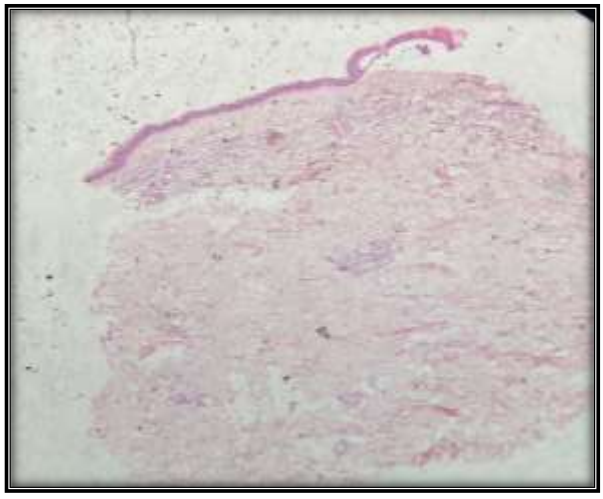
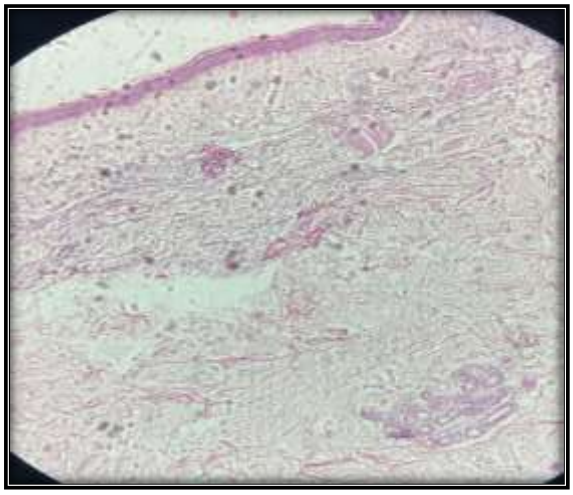
Bullous pemphigoid

On examination bullae consist of tense blisters that usually fail to rupture, as their roof consist of intact epidermis.

Fig.7 H&E 10X Bullous Pemphigoid **Fig.8 H&E 40X Bullous Pemphigoid**

M/E shows keratinized stratified squamous epithelium underneath shows focal subepidermal separation. Dermoepidermal junction shows vacuolar degeneration along with fibrin deposition. Papillary and superficial dermis show dilated, congested blood vessels with sparse inflammatory infiltrate of eosinophil, lymphocyte and polymorphs.

Darrier's Disease

Fig.9 H&E 10X View of Darriers disease **Fig.10 H&E 40X View of Darriers disease**

M/E shows hyperkeratotic, parakeratotic pappilomatous stratified squamous epithelium with prominent granular layer. Focally suprabasal clefting noted. Dermis shows perivascular chronic inflammatory infiltrates of lymphocytes predominantly with histiocytes.

Discussion

Vesiculobullous disorders present clinically with various cutaneous manifestations based on the severity of the lesion. [3] The disorders range from benign conditions like suction blisters to life threatening conditions with systemic involvement like toxic epidermal necrolysis (TEN). Also, few vesiculobullous disorders like the autoimmune group which includes pemphigus group of disorders present with near similar clinical features. Hence the diagnosis of vesiculobullous disorders can be challenging to the dermatologist. Early and accurate diagnosis of disease is essential to prevent morbidity and mortality which is highlighted by this study.

- Among the vesiculobullous lesions in the pemphigus group, pemphigus vulgaris is the commonest variety with 33 cases out of 58 (56.8%) which was similar to study conducted by, Shafi M et al.[2] The most common age at presentation is 4th decade with female preponderance compared with western literature where it shows equal sex predilection.[3,4,5] All patients may not present clinically with classical morphological features. In such conditions where clinical diagnosis is difficult, biopsy from the lesion helps in arriving at a diagnosis. In cases where histopathological findings are not typical, DIF helps to diagnose the disease which shows typical pattern of immune deposition at the appropriate site. In some cases DIF can be negative, which may be due to stage of the disease or prior treatment received.[3,6] Pemphigus vulgaris has a higher incidence in Indian, Southeast European, and Middle Eastern populations.[7] This is in agreement with the study by Khannan et al (53%),Deepti et al(34%) and Buch et al (27%)all of which showed pemphigus vulgaris to be the commonest entity among all vesiculobullous disease.[8,9,10] Pemphigus Vulgaris was the commonest disorder among the pemphigus group in all four studies. On histopathology,suprabasal cleft was seen in all 100% comparable to studies conducted by Khannan et al[8] and Selvaraj et al[7] described 100% cases of PV showing suprabasalbulla.All the cases of PF showed subcorneal bulla 100% as shown by Khannan et al. Early diagnosis with help of morphological data can prevent morbidity and mortality and may improve the quality of life of the patient in vesiculobullous group of disorders. Pemphigus foliaceus consisted of 12 cases accounting for 20.6% of all case with female preponderance in present study. It is important to differentiate between pemphigus foliaceus and pemphigus vulgaris, since pemphigus foliaceus has a relatively benign course as compared to pemphigus vulgaris [11,12,13]. Arya et al [14] and L. Jubojevics et al [15] reported acantholysis and suprabasal blister to be the feature of pemphigus vulgaris and subcorneal blister in the pemphigus foliaceus. This observations were similar to our present study.
- Bullous pemphigoid shows clinical similarity to pemphigus (hence its name) but the blisters are sub-epidermal, not intraepidermal [16]
- It is most common in people over the age of 50 years, with male preponderance.
- A rare case of pemphigoid gestationis was encountered which is self limiting, subepidermal bullous disease

CONCLUSION

- ❖ Although the primary vesiculobullous lesions of skin are seen in a small group of people, but morbidity and mortality caused is substantial.
- ❖ Our study also underscored the diagnostic value of skin punch biopsy and histopathology.
- ❖ The direct immunofluorescence test is useful adjunctive tool but not essential in every cases.

CONFLICT OF INTEREST: None.
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