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A Study of Clinical & Immunpathological Correlation of Anti-Desmoglein Antibodies in Pemphigus Group of Disorders

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***Abstract**: **Introduction:** Pemphigus group of disorders are classified by antibody mediated bullous lesions affecting skin and mucosa. Accurate diagnosis of these disorders requires clinico pathological correlation along with ELISA and DIF study.*
***Aims and objectives:** To correlate the clinical and immunopathological findings as well as diagnostic significance of desmogleins(ELISA) in Pemphigus group of disorders.*
***Patients and methods:** A total of 25 Pts with Pemphigus group of disorders diagnosed over a period of one year at Department of DVL, GGH were analysed retrospectively . Detailed clinical examination , HPE examination, ELISA(desmogleins) and immunofluorescence study were done in all cases.*
***Results:** In our study Pemphigus vulgaris was predominant type with 21 cases followed by 3 cases of pemphigus foliaceous and single case of pemphigus erythematosus. Mean age of presentation was 3rd and 5thdecade.Majority of patients 15(60%) had both cutaneous and mucosal involvement. Tzanck smear was positive for acantholytic cells in 20 cases. HPE showed 100% positive correlation. ELISA showed anti desmoglein antibodies 100% in all patients as well as DIF was also positive in all cases in our study.*
***Conclusion:** DIF and anti desmoglein antibodies were equally sensitive in establishing the diagnosis of Pemphigus group, where as ELISA is quantitatively important in both diagnostic and prognostic value for Pemphigus group of disorders.*
***Keywords:** Pemphigus vulgaris, Pemphigus foliaceous, Pemphigus erythematosus, Direct and Indirect Immunofluorescence*

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I. Introduction

Pemphigus is an immunobullous disorder where antibodies (Abs) are directed against desmogleins (Dsgs) belonging to epidermal cadherin family and is classified into Pemphigus vulgaris and Pemphigus foliaceous with subtypes.

Auto-antibodies in Pemphigus are detected by DIF & IIF where cell staining pattern is almost identical with PV & PF. Immunofluorescence is a histochemical staining technique used for demonstrating the presence of antibodies bound to antigens in tissue or circulating body fluids. These techniques are essential to supplement clinical findings, histopathology in diagnosis of immunobullous disorders .

Indirect IF/ ELISA is a simple and effective tool for quantitative estimation of antibody levels. Harman et al used ELISA to measure serial Anti-Dsg1 & Dsg3 antibody levels and correlated them with severity of oral and skin lesions in PV & PF. Hereby we conducted this study to correlate clinical and immunopathological findings in Pemphigus group as well as to evaluate diagnostic significance of ELISA.

II. Aims and objectives

To correlate the clinical and immunopathological findings as well as diagnostic significance of desmogleins (ELISA) in Pemphigus group of disorders.

III. Patients & methods

A total of 25 Pts with pemphigus group of disorders diagnosed over a period of one year at Department of DVL, GGH were analysed retrospectively. A detailed history and thorough clinical examination was carried out in all cases. Tzanck smear was done by scrapping the wall of the deroofed bulla which was stained with Giemsa and observed under light microscope. HPE was done by taking skin or mucosal biopsy of a representative lesion which was stained with H&E and observed under light microscope. For DIF, skin or mucosal biopsy was taken from perilesional tissue.10 ml of blood was collected and sent for ELISA.

IV. Results

A total of 25 cases of Pemphigus was studied. Of these 21 cases(84%) belonged to P.vulgaris(P.V) , 3 cases (12%) were P.foliaceus(P.F) and 1 case (4%) was P.erythematosus(P.E).

Table no 1: Percentage of Pemphigus group in the present study

Type	No .of cases	Percentage
PV	21	84
PF	3	12
PE	1	4
Total	25	100

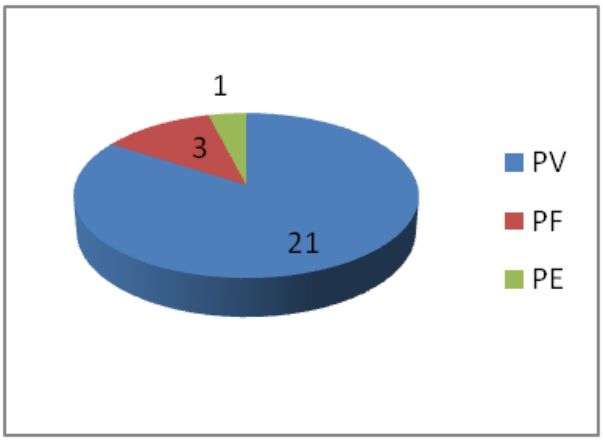
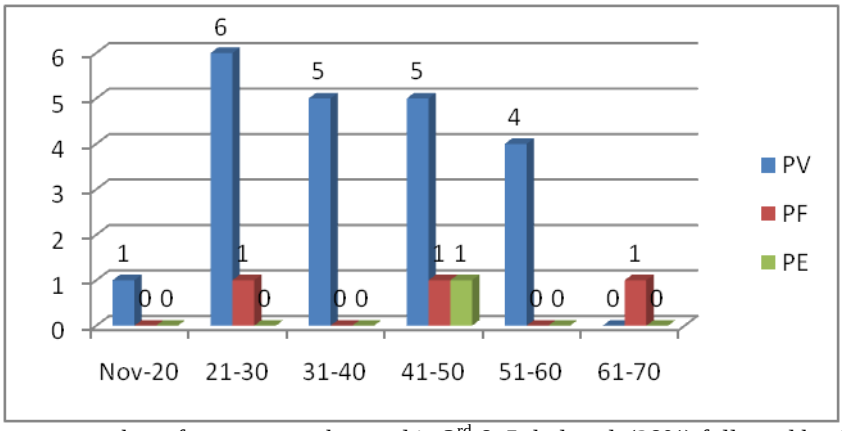


Table no 2: Age distribution in Pemphigus group

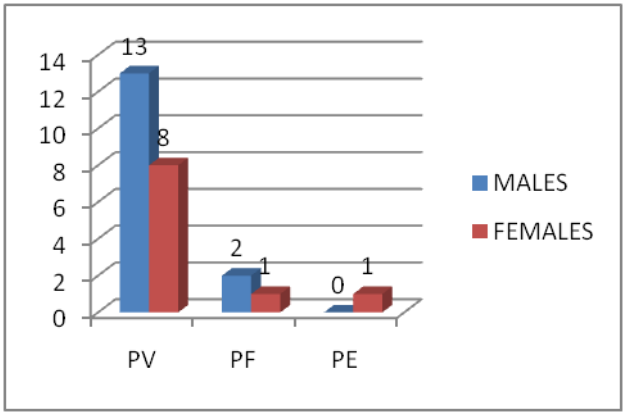
Age in years	**PV(n=21)**	**PF(n=3)**	**PE(n=1)**	Percentage
11-20	1	0	0	4
21-30	6	1	0	28
31-40	5	0	0	20
41-50	5	1	1	28
51-60	4	0	0	16
61-70	0	1	0	4



Out of 25 patients most number of cases were observed in 3rd & 5 th decade(28%) followed by 1st and 6th decade(4%).

Table no 3: Sex distribution in Pemphigus group

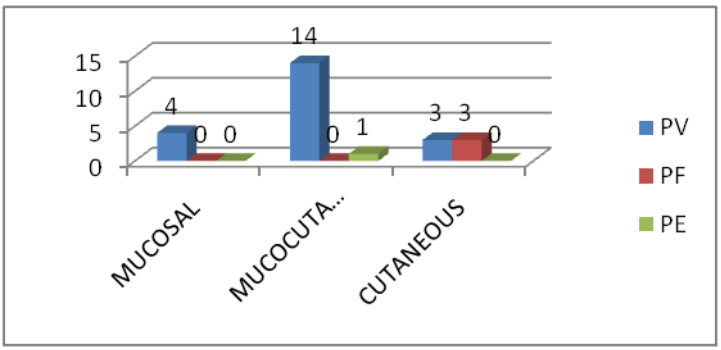
Type	Male	%	Female	%
PV	13	52	8	32
PF	2	8	1	4
PE	0	0	1	4
Total	15	60	10	40



Out of 25 cases, there was a slight male preponderance.

Table no 4: Site of involvement

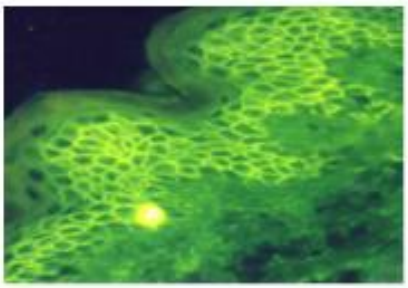
Predominant				%
Site of involvement	PV	PF	PE	
Mucosal	4	0	0	16
Mucocutaneous	14	0	1	60
Cutaneous	3	3	0	24
Total	21	3	1	100



Out of 21 pts of PV 4 cases (16%) had mucosal involvement , 14 cases(60%) had mucocutaneous involvement where as 3 cases(24%)had only cutaneous involvement. In PF group all 3 cases had skin lesions without mucosal involvement, where as single case of PE presented with mucocutaneous involvement.

Tzank smear was positive for acantholytic cells in 20 cases out of total 25 cases.HPE of PV in most cases (18) showed suprabasal blisters followed by intra epidermal (2 cases) and sub corneal blister(1 case) with acantholytic cells and inflammatory infiltrate. PF patients on HPE showed subcorneal bullae in 2 cases and 1 case showed hyperkeratosis, irregular acanthosis with local parakeratosis with small foci of neutrophils with no bullae. 1 case of PE showed subcorneal bullae with few acantholytic cells

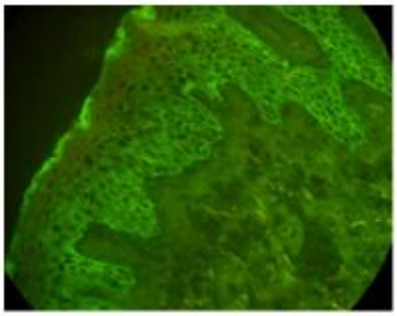
DIF of all 21 cases of PV showed intercellular deposits of IgG and C3.



FISH NET PATTERN of staining throughout the epidermis in Pemphigus vulgaris.

DIF showed intercellular deposits of IgG and C3c which could not distinguish between PV and PF. One case of PE showed intercellular deposits of IgG and C3c in the intercellular area and along the basement membrane zone.

Intercellular deposits of IgG and C3c more towards the upper layers in Pemphigus foliaceous



In this study of 21 cases of PV 4 cases had predominant mucosal involvement and Dsg3 positive, 14 patients had mucocutaneous involvement but only 13 were positive for both and 1 patient had Dsg1 positive. 3 patients with predominant cutaneous involvement had only Dsg1 positive. In PF ELISA showed Dsg 1(cutaneous involvement) positive in all 3 cases. In PE Dsg1 & 3 were positive along with ANA positivity.

Table no 5: ELISA RESULTS IN PEMPHIGUS GROUP

Type	No.	Dsg1	Dsg3
PV	21	17	17
PF	4	4	1
Total	25	21	18

Cut off positive index value of anti-Dsg 1&3 was 20 U/ml.
For Dsg1 ELISA, 4 of 4 (100%) PF patients and 17 of 21 (80.9%) PV patients and for Dsg3 ELISA, 17 of 21 (80.9%) PV patients and 1 of 4(25%) PF patients exceeded the cut off value.

V. Discussion

With dsg1&3 being target antibodies, hence estimation of antibody titres of dsg1&3 and their correlation with clinical, HPE & DIF is useful for longterm management and follow up.

Pemphigus vulgaris is divided into mucocutaneous, mucosal and cutaneous subtypes based on clinical involvement, HPE, DIF and IIF findings. DIF shows similar fishnet pattern in all subtypes of Pemphigus vulgaris. IIF by ELISA method is useful in Pemphigus vulgaris subtypes.

Out of 25 patients included in the study, majority belonged to PV, 21(84%) patients with equal sex distribution and majority of patients were within 21-50 years age group which were consistent with observations of Handa et al, Fernandez et al.

Cytological examination revealed acantholytic cells in 18 of 21 patients of Pemphigus vulgaris and 2 of 4 patients of Pemphigus foliaceous. Histopathology showed Suprabasal acantholysis in 18 of 21 patients of Pemphigus vulgaris and Subcorneal blister in 3 of 4 patients of Pemphigus foliaceous. DIF showed intercellular deposition of IgG and C3c in all patients of Pemphigus vulgaris, Pemphigus foliaceous and also along basement membrane zone in a patient of Pemphigus erythematosus.

Anti Dsg antibody titres were done in all(25) patients. Anti Dsg 1 antibodies were found in 4 patients of PV with cutaneous involvement. Anti Dsg 3 antibodies were found in 4 patients of PV with mucosal involvement . Anti Dsg 1& 3 antibodies were found in 13 patients of PV with mucocutaneous involvement and also in 1 patient of PE. Anti Dsg 1 antibodies were positive in 3 patients PF.

All the patients in the study group showed 100% correlation with clinical phenotype, histopathology, DIF and ELISA findings which is in accordance with studies conducted by Amagai M et al.

DIF and anti Dsg antibodies were 100% positive in all cases of Pemphigus which shows that both the methods are equally sensitive in establishing the diagnosis of Pemphigus group. However DIF cannot distinguish between the clinical subtypes of Pemphigus, on the other hand anti Dsg antibody profile gives an idea of the clinical subtype of Pemphigus and the predominant site of involvement in Pemphigus vulgaris. In addition ELISA is less invasive, less time consuming and can be used as an important diagnostic adjunct in the initial diagnosis of Pemphigus.

As the method used for the detection of anti dsg antibodies is a semiquantiative assay titres could not be correlated with disease activity in this study. However an observation of high titres in patients with clinically severe disease was made (as per the available assay range 5-150 U/ml).

Our findings suggest that at any given period, the level of the antibodies correlate with disease severity. However, this may not be true for a small proportion of patients. A detailed prospective study for evaluating the ELISA levels of a given patient for prolonged periods would be helpful in actual correlation with the disease severity and changes that may occur in the spectrum of the disease.

VI. Conclusion

Desmoglein ELISA is a rapid, specific and sensitive method in the accurate diagnosis of Pemphigus group when correlated with clinical and immunopathological findings. This can be used for long term management of patients and to monitor the response to treatment.

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