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## **A Clinico pathological study on Pemphigus vulgaris with cytological and histopathological correlation and with possible confirmation with immunofluorescence**

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### **Abstract**

Pemphigus vulgaris (PV) is a potentially fatal, chronic autoimmune, vesiculobullous intraepithelial disease characterized by flaccid blisters and erosions of the skin and mucous membranes and histologically by acantholysis. It is mediated by circulating desmoglein-reactive autoantibodies directed against keratinocyte cell surfaces. Pemphigus vulgaris commonly occur in middle aged and elderly between the ages 40 to 60 years and effects men and women equally. Pemphigus vegetans is a clinical variant involves the large skin folds with vegetating lesions. Oral lesions are relatively non-specific and is difficult to diagnose. With early accurate diagnosis with cytological diagnosis, histopathological correlation and confirmation by using immunofluorescence techniques disease treatment, prognosis and outcome will be better.

**Keywords:** Pemphigus vulgaris, Vesiculobullous lesions, acantholysis, keratinocyte

### **Introduction**

**Aims and Objectives:** The main objective is early accurate diagnosis and treatment of all vesiculobullous lesions of pemphigus vulgaris helps to control the disease, prevent relapses, avoid adverse events associated with the prolonged use of steroids and immunosuppressive agents and also to reduce the hematological and gastrointestinal cancer risk.

Early detection is essential for giving timely treatment, to improve prognosis, to prevent disease wide spread dissemination and also to reduce the cancer risk.

### **Material and Methods**

It was a 3-year study between 2010 to 2013 in Mamata medical college Khammam. We have received 39 patients with vesiculobullous skin oral mucosal lesions out of total no of 1575 patients who have visited the Dermatology outpatient department between the years 2010 to 2013. Patients were sent for cytological evaluation first by using Tzanck smears. Tzanck smears were prepared from the floor of the blisters in these patients by derroofing the bullae, scraping done from the base of the lesion and the smears prepared on clean glass slides and then allowed them for air dry at room temperature finally smears were fixed with preservatives. Immunofluorescence staining was done with anti-human IgG. Skin biopsy was also done and samples were sent for histopathological evaluation by using Hematoxylin and Eosin stain.

### **Results**

In the study period of 3 years a total of 1575 cases were seen in the dermatology department. Among the 1575 cases 45 cases were blistering diseases and out of 49 cases, 39 cases were diagnosed as vesiculo bullous lesions. Out of 39 patients diagnosed with vesiculo bullous lesions 13 cases were diagnosed as Pemphigus vulgaris.

### **Cytology findings on Tzanck smear**

Cytosmear showed Tzanck (acantholytic) cells with a high nuclear–cytoplasmic ratio with hyperchromatic nuclei and a very smooth nuclear outline.

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**Histopathology findings**

Acantholysis and bulla formation in the suprabasal layer of epidermis. The roof of the bulla formed by stratum and floor by the basal cells which remains attached to the dermis. These basal cells are giving the appearance of row of tomb stones. Histologically, there is presence of intraepithelial blister, rounded acantholytic, and Tzanck cells [2, 4, 7], demonstrating degenerative changes, including round, swollen hyperchromatic nuclei with a clear perinuclear halo

in the cytoplasm [8], which was also evident in our study.

**Immunofluorescence test results:** IgG antibodies were found against the cell surface of keratinocytes demonstrated by Indirect immunofluorescence test done on patient's sera and also by Direct immunofluorescence test done on patient's skin lesions 8 cases having pemphigus vulgaris showed bright green fluorescence on the membrane of acantholytic cell.

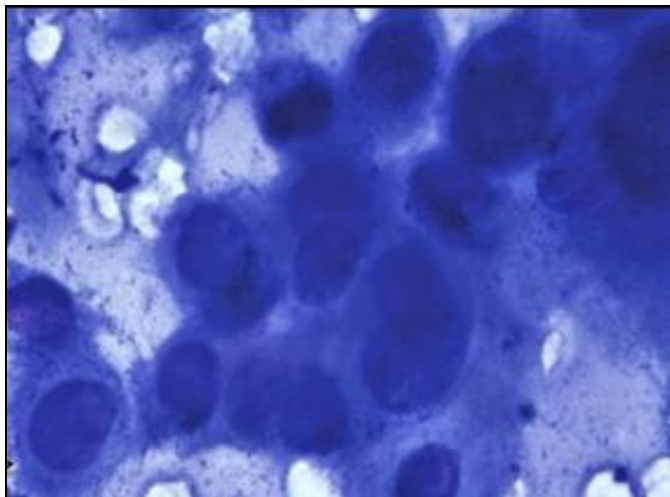


Fig 1: Leishman 100X



Fig 2: 40x

**Histopathology Smears**

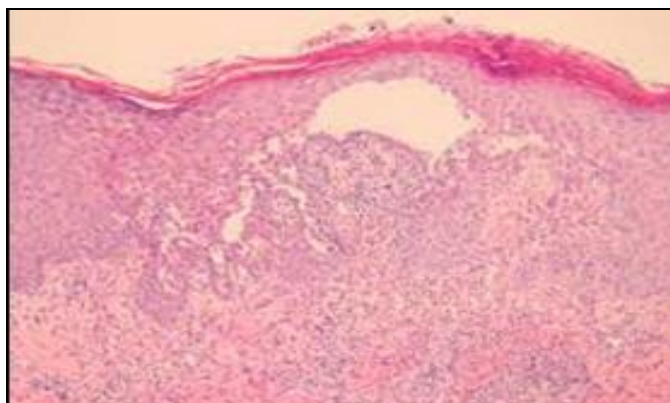


Fig 3: 10x H&E 3

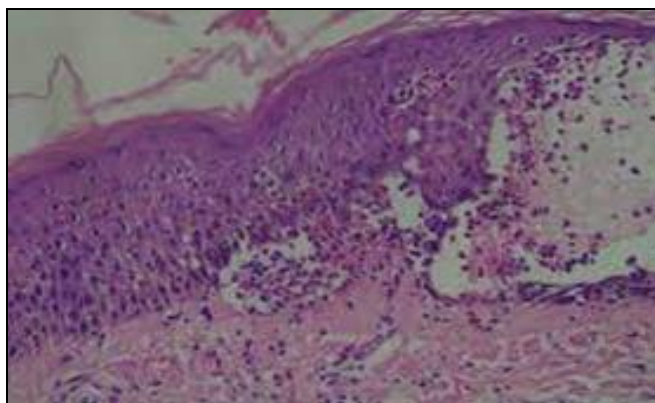


Fig 4: 40X H&E

**Immunofluorescence study: Anti-IgG antibodies against the cell surface of keratinocytes with intercellular and intra epithelial deposits shown in dark apple green color.**

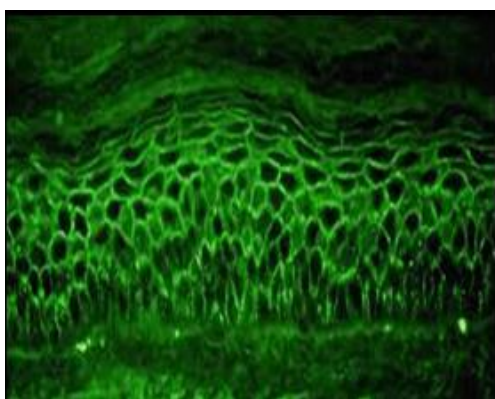


Fig 5: Indirect IF

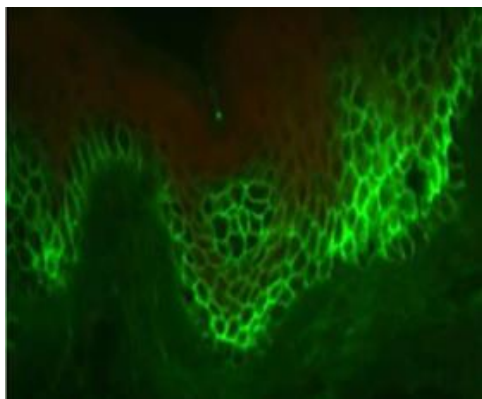


Fig 6: Indirect IF

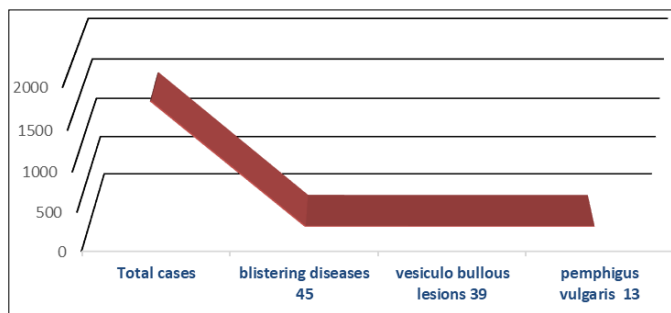


Fig 7: Total no of cases 1575

Male patients 19 and female patients were 20. Among the 39 patients 7 patients were presented with other autoimmune disease association. The clinical disease history was lasting from 1 month to 4 months.

**Age wise distribution:** 18 cases seen between the ages of 51 to 60 year and 13 cases were between 40 to 50 years. 5 cases were seen between 30 to 39 years. 1 case between 10 to 19 and 2 cases between 0 to 9.

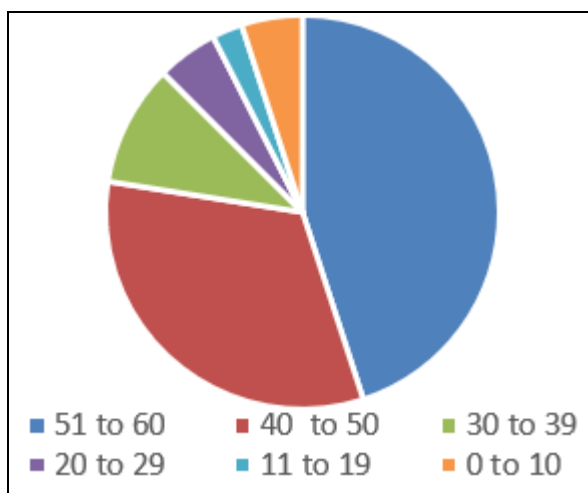


Fig 8: Show the 18 cases between the ages of 51 to 60 year and 13 cases were between 40 to 50 years

**Introduction**

Pemphigus is derived from the Greek word *pemphix* meaning blister or bubble [8]. The antigens involved in PV are desmogleins 1 (Dsg1) and 3 (Dsg3), which are 160 and 130 kDa transmembrane glycoproteins, respectively; they are an integral part of the desmosomes of the cadherin family, responsible for the intercellular adhesion of the squamous stratified epithelium. The basic pathophysiology of pemphigus is the inhibition of the adhesive function of desmogleins by autoantibodies, which leads to the formation of blisters [9]. The following are possible explanations for the association between pemphigus and esophageal and laryngeal neoplasms: involvement of the mucous membranes of these organs in cases of PV, since they express desmoglein 3, the main PV antigen; and persistent inflammation, inducing mutations, resistance to apoptosis, and angiogenesis. These diseases are more common in Jewish and Mediterranean descent are more prone to get these vesiculobullous autoimmune blistering diseases. The onset of these diseases is more common in adult hood. It affects men and women equally [10]. The blisters may heal

without causing scarring, but some areas may show pigmentation and lasts for several months. In majority of PV patients, the oral lesions are followed by the development of skin lesions. If oral PV is recognized early, progression of the disease to skin involvement can be prevented. Early oral lesions of PV are difficult to diagnose and diagnostic delay of more than 6 months is common as they are nonspecific, presenting as ulcerations or superficial erosions, and they rarely present with the intact bullae formation. Tzanck test also Tzanck smear, is scraping of an ulcer base to look for Tzanck cells. According to Coscia-Porrazzi *et al.*, acantholytic/Tzanck cells were recognized in 37 out of 40 PV patients and stated that cytomorphologic studies are useful to screen the cases suspected to be oral PV [11]. Tzanck test offers the advantage of being a simple, fast, and inexpensive diagnostic test but it requires certain amount of skill and experience for accurate interpretation [4]. The technique of this test is simple that can be performed with minimal patient discomfort or cost. Tzanck smear requires expertise [8] in preparing the slide, in interpreting cytology and false negatives may occur in early or late disease. Individuals with autoimmune diseases tend to develop autoimmune comorbidities. In cohort studies, PV has been associated with systemic lupus erythematosus, rheumatoid arthritis, autoimmune thyroiditis, type 1 diabetes, and myasthenia gravis [11]. It is also important to assess the mental health of PV patients, since higher rates of depression were observed in all age groups, including children, as well as Parkinson's disease [12]. The influence of genetic and immunological factors on PV onset is well established. However, environmental factors (such as drugs, diet, and viruses, among others) may induce or impact the disease [13]. Surprisingly, a recent systematic review concluded that smoking is a possible protective factor for PV, although other studies with different methodologies have failed to replicate this result [13]. The relationship between hematological neoplasias and paraneoplastic pemphigus is indisputable, there is still a lack of evidence to prove the association with PV [14]. An uncontrolled study demonstrated that the frequency of non-Hodgkin's lymphoma and leukemias in PV cases was 50% higher than expected [15]. A recent German study suggested that the prevalence of hematological neoplasias is twice as high in patients with PV when compared with controls. The association with chronic leukemia remained significant even after adjustment for PV immunosuppressive therapy [16]. Case-control studies have demonstrated an association between PV and oropharyngeal, gastrointestinal, and lung neoplasms. Before the advent of corticosteroids and immunosuppressants, the two-year mortality rate of PV was 50%. Currently, the mortality rate is approximately 10%. The main cause of death in PV patients is septicemia.

**Conclusion**

In our study group 39 patients were selected among a total of 1575 patients who have clinical, and immunopathological features of vesiculobullous lesions. Out of 39 patients 13 were diagnosed with pemphigus vulgaris on cytology and histopathological evaluation and the results were confirmed with immunofluorescence test by identifying anti-IgG antibodies and the bright green fluorescence on the membrane of acantholytic cells [1]. Pemphigus vulgaris is a serious and sometimes life-threatening disease early

diagnosis is very important when it is localized to skin or limited to oral cavity and a close follow-up is essential. Careful assessment and correlation of the clinical appearance, histological features, and immunofluorescence findings should be done.

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**Conflicts of interest:** There are no conflicts of interest

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