

Oral mucosal lesions in patients with pemphigus and pemphigoid skin diseases: a cross sectional study from southern India

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Abstract

Objective: To assess the prevalence of oral mucosal lesions in patients with pemphigus and pemphigoid diseases from Southern India. **Design and Methods:** A cross-sectional hospital based study was conducted from August 2010 to July 2011. Patients with confirmed pemphigus and pemphigoid skin disease were selected and informed to participate in the study. Oral examination of all participants were done to document site and type of oral manifestation and diagnostic procedures such as histopathological and Immunofluorescence methods were performed to confirm the diagnosis. Demographic details such as age, gender and occupation were also documented. The results of the study were analyzed by SPSS software version 19.0 (Armonk, NY) and presented as descriptive statistics. **Results:** Sixty percent of the patients exhibited oral mucosal manifestations. A higher female (86.66%) predilection of autoimmune blistering disease was observed in the study. A slightly higher number of pemphigoid patients (53.33%, 16 out of 30) were reported than pemphigus (46.66%, 14 out of 30 cases). The most common subtypes of pemphigus is Pemphigus vulgaris 71% (10 out of 14) among pemphigus, and bullous pemphigoid 87.5% (14 out of 16) among pemphigoid. Buccal mucosa (92.85%) is the most common site in pemphigus patients, where as hard palate (12.5%) is mostly commonly reported site in pemphigoid patients. Initial involvement of oral tissue in disease process was observed in 78.57% of pemphigus, and 12.5% of pemphigoid patients. **Conclusion:** Oral mucosal lesions are more frequently associated in pemphigus patients. Oral mucosal lesions are the initial site of disease process in pemphigus patients. The significance of diagnosis of oral lesions at earlier stage of disease, specifically pemphigus may help in early intervention of disease and help to reduce the morbidity and mortality state. The study emphasizes multidisciplinary approach in diagnosis and management of both pemphigus and pemphigoid.

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Introduction

Mucocutaneous are a group of disorders primarily observed in dermatology practice. Oral mucosal manifestations may be an initial presentation, most important clinical symptom, or often times it is the only sign of such disease process. In most instances, the mucocutaneous disorders are known to affect the skin and mucus membranes, with severe clinical manifestations affecting the oral mucosal membranes. The oral presentations of such mucocutaneous are primarily as fluid filled blister such as vesicle, bullae, erosive or ulcerative

conditions.¹ Early identification of oral manifestation and correlation with dermatological condition may help in diagnosis, treatment planning and prognosis.

Pemphigus is one of the few potentially fatal autoimmune diseases affecting predominantly skin and oral mucosa. It is an autoimmune disease characterized by the clinical presentation of fluid filled blisters, and raw eroded surfaces when the blister burst open. The disease had been considered to be associated with the autoantibodies (IgG) and complement factor (C3) against the desmosome structure at the intercel-

lular components of epithelium and epidermis. The autoimmune process that destructs the intercellular proteins such as desmosomes is histologically termed as acantholysis. The acantholysis of epithelial or epidermal cells are responsible for the resultant cleft formation above the basal layer. Epithelial or epidermal blisters or bullous presentation are the hallmark of this disease, however erosions or ulcers over the mucosal membranes and skin or epidermis are also classical clinical presentation of this disease process.² The most commonly oral sites are palate, labial mucosa, buccal mucosa, ventral surface of tongue, and gin-

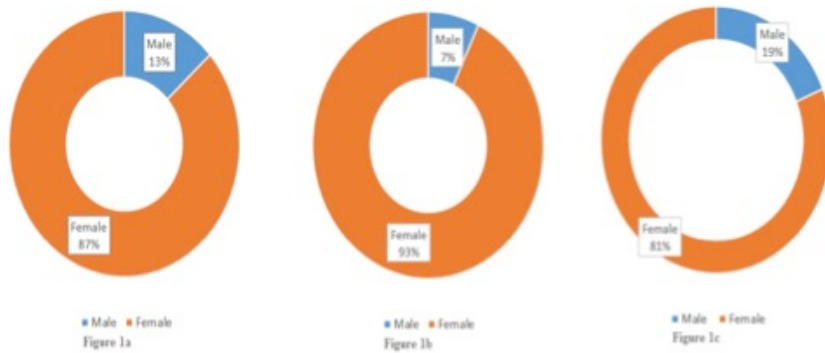


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Figure 1: Distribution of study population according to gender



gival. Pemphigus includes three primary clinically recognizable subsets such as pemphigus vulgaris, pemphigus foliaceus, and paraneoplastic pemphigus.³ Histologically the lesion is identified based on the supra basal or intra epithelial cleft formation, with acantholytic or tzanck cells. Clinical and histopathological findings are usually confirmed by direct or indirect Immunofluorescence methods.¹ Pemphigoid is an autoimmune disease characterized by the vesiculo-bullous manifestations over skin and mucosal surfaces. The two distinct clinical forms of this disease includes bullous and cicatricial pemphigoid.⁴ The disease process is known to be mediated by autoantibodies directed against components of basement membrane zone. The disease is clinically recognized as bullous lesions, which may rupture to produce ulcers. The healing is usually accompanied by scarring in cicatricial type of pemphigoid, and not in bullous forms. Histologically the lesion is identified based on the sub-basal cleft formation. Clinical and histopathological findings are usually confirmed by direct or indirect

Immunofluorescence methods.^{1,5} The main aim of the present study is to assess the prevalence of oral mucosal lesions in patients with pemphigus and pemphigoid diseases from Southern India.

Methods

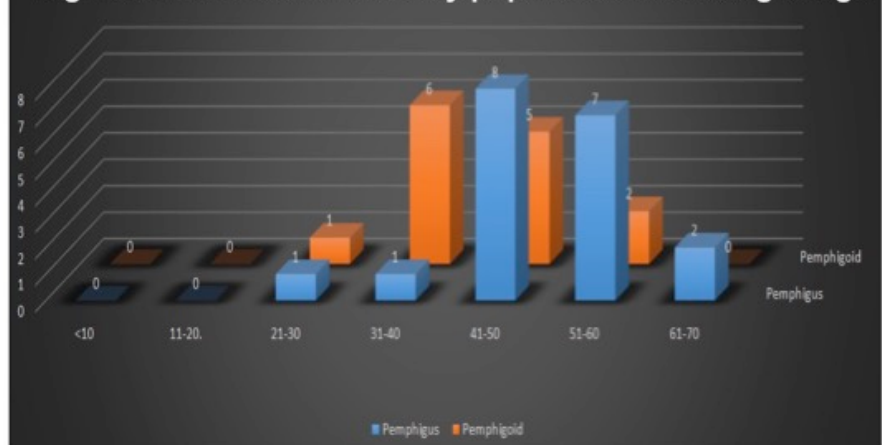
The study was approved by ethics committee/institutional review board of the SIBAR Institute of Dental Sciences, Guntur. The study obtained verbal consent from all participants involved; also ethics committee/institutional review board of the SIBAR Institute of Dental Sciences approval was received on the consent form. The present study has been conducted

in full accordance with the World Medical Association Declaration of Helsinki.

Sampling, inclusion and exclusion criteria

The study was conducted at the Dermatology department at Government General Hospital, Guntur, Andhra Pradesh, India from the period August 2010, to July 2011. All the patients with pemphigus or pemphigoid disease were invited to participate in the present study. The participants who provided the consent for clinical evaluation, and histopathological diagnostic procedures were included in the study. The confidentiality of the patients' clinical, histological, and photographic details was maintained. The study was conducted by a qualified dental surgeon, and institutional ethics approval was received. During the clinical examination, patients' socio-demographic details such as age, gender, occupation, marital status, residential address, and other oral hygiene habits, primary site of disease manifestations, disease symptoms, and other under-

Figure 2: Distribution of study population according to age



lying medical conditions (if any) were obtained. The patients' conditions such as pemphigus and pemphigoid were diagnosed by consultant dermatologist of the hospital, and dental surgeon performed oral examination and biopsy procedure for histological and Immunofluorescence exami-

paraffin wax. The microtomed tissue sections were stained with hematoxylin and eosin (H and E) and examined using bright field microscope. To evaluate the presence of autoantigens in the oral tissue sections, an Immunofluorescence procedure was conducted for the part of biopsied speci-

using 1,4-Diazabicyclooctance DABCO solution. The preparations were examined using fluorescent microscope.

Clinical and histopathological data were documented in the prescribed forms. Data on clinical and histopathological details were documented in Microsoft 2007 Excel spreadsheets, followed by tabulations of various parameters. The descriptive statistical analysis using SPSS software version 19.0 (Armonk, NY) was done for presentation of study results.

Results

Age, gender and occupation demographics of the study participants

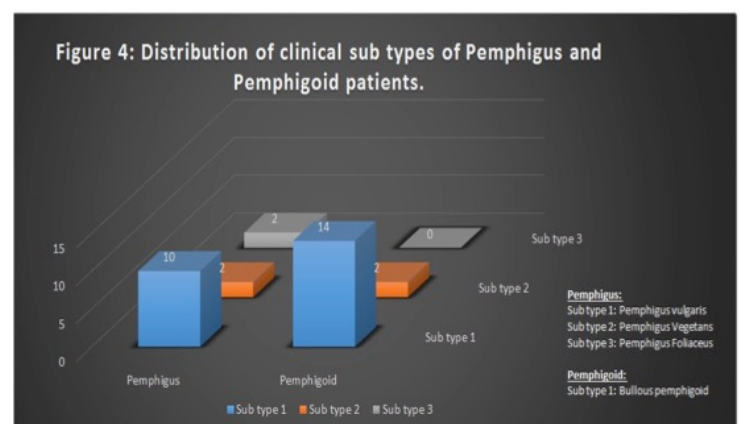
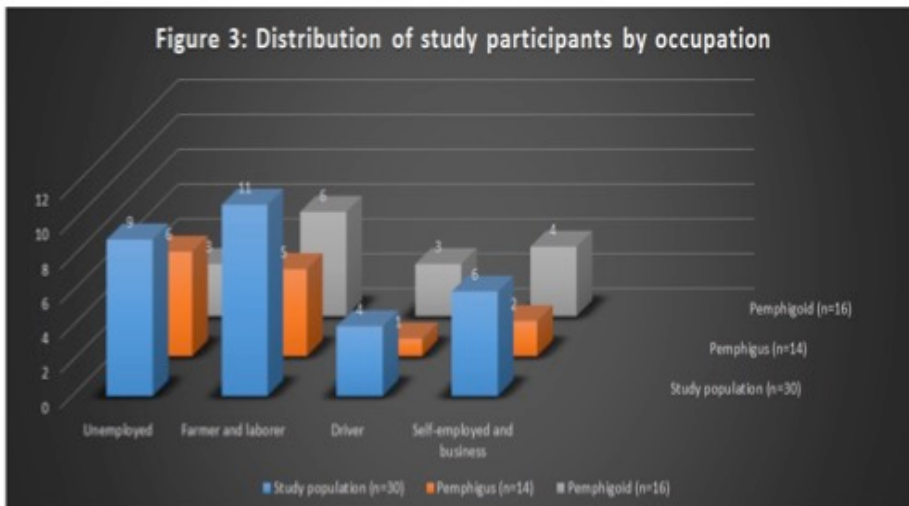
A total of 30 patients were examined and consisted of male 4 (13.33%) and female 26 (86.66%) with pemphigus or pemphigoid had participated in the present study during the period of August 2011 to July 2012 (Figure 1a). In pemphigus, 1 male (7.14%) and 13 female (92.85%) patients were observed (Figure 1b). Whereas in Pemphigoid, 3 male (18.75%) and 13 female (81.25%) were reported (Figure 1c). Female predilection was observed in both pemphigus and Pemphigoid. The patients in

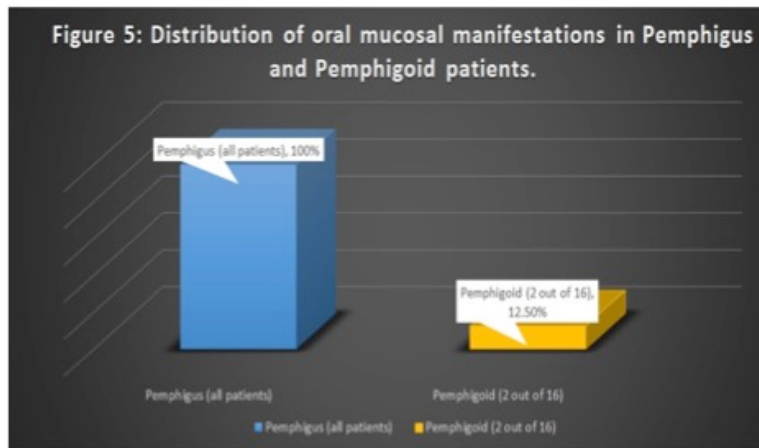
nation. Examining dental surgeon performed excisional biopsy on all the study participants. Tissue was anesthetized using Lignocaine HCL 2% and biopsy procedure was done using scalpel blade no. 15. The details of the clinical presentation of skin and oral mucosa were recorded in the Microsoft Excel data sheet for software analysis. The final histopathological diagnosis of the oral biopsies was given by an expert oral and maxillofacial pathologist at SIBAR Institute of Dental Sciences, Guntur, Andhra Pradesh, India.

Histopathological examination (Hematoxylin and eosin stain; and Immunofluorescence)

Oral tissue biopsies were taken from the lesional areas. The tissue was fixed in formalin solution and eventually embedded in

men. The tissues for Immunofluorescence procedure were stored in Michel's medium. Immunofluorescence methods for detection of auto-antibodies in the tissue sections were performed with thin (less than 6 micrometer) cryostat sections. The sections were washed with 0.1M Phosphate buffered saline with three changes over a period of thirty minutes. Excess of the solution were drained and covered with diluted conjugate and allowed to react for thirty minutes at room temperature. Then sections were mounted by





the total study ranged between 21-70 years. The mean age of the Pemphigus patients were 42 years, and pemphigoid was 48 years. (Figure 2) Analysis of the participants occupation showed farmers were 11(36.6%), unemployed 9(30%), drivers 4(13.33%) and self employed or business 6(20%). (Figure 3).

Prevalence of clinical sub types and oral mucosal involvement in pemphigus and pemphigoid

The analysis of the clinical subtypes of pemphigus and pemphigus in the study population revealed that, pemphigus vulgaris 10(71.42%), Pemphigus vegetans 2 (14.28%), and Pemphigus foliaceus 2(14.28%); and Bullous pemphigoid 14(87.5%), and Cicatricial pemphigoid 2(12.5%) was observed. (Figure 4) A total of 53.33% (16 out of 30) patients showed oral mucosal manifestations. Higher prevalence of oral mucosal lesions were observed in Pemphigus 14(100%), and in pemphigoid 2(12.5%) (Figure 5)

Initial site involvement of skin versus oral mucosa in pemphigus and pemphigoid

site of manifestation of diseases. A higher frequency of oral mucosa as a initial site of manifestation was observed in pemphigus patients 11(78.57%); and pemphigoid 1(6.25%) (Figure 6)

Oral mucosal site geography in pemphigus and pemphigoid

Buccal mucosa was the most common site for pemphigus 13(92.85%), and hard palate was most common site among patients with pemphigoid 2 (12.5%). Most of the patients had presented the oral lesions with more than one site. (Figure 7)

Immunofluorescence characterization in pemphigus and Pemphigoid

In pemphigus, direct Immunofluorescence method demonstrated the presence of IgG and C3 components. All the patients (100%) showed the positivity for IgG autoantibody, and 8 out of 13 (61.53%) patients showed

A total of 60% (18 out of 30) patients has skin as a initial site of manifestation, and 40% (12 out of 30) as oral mucosa as a initial

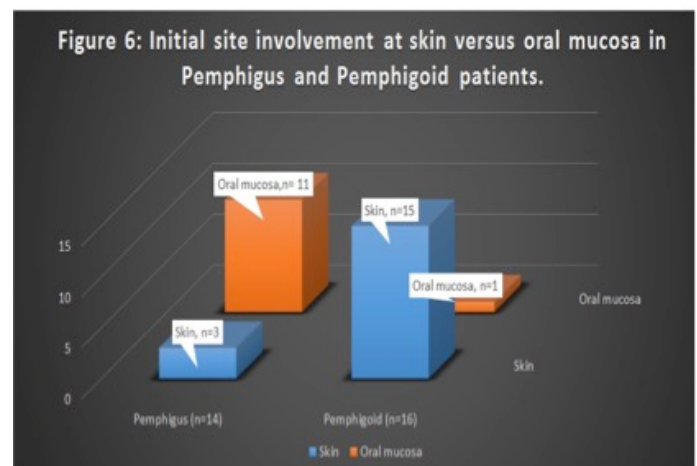
C3 component positivity. Whereas in Pemphigoid, direct immunofluorescent method demonstrated the positivity for IgG and C3 components in basement membrane zones of two oral tissue specimens. (Figure 8)

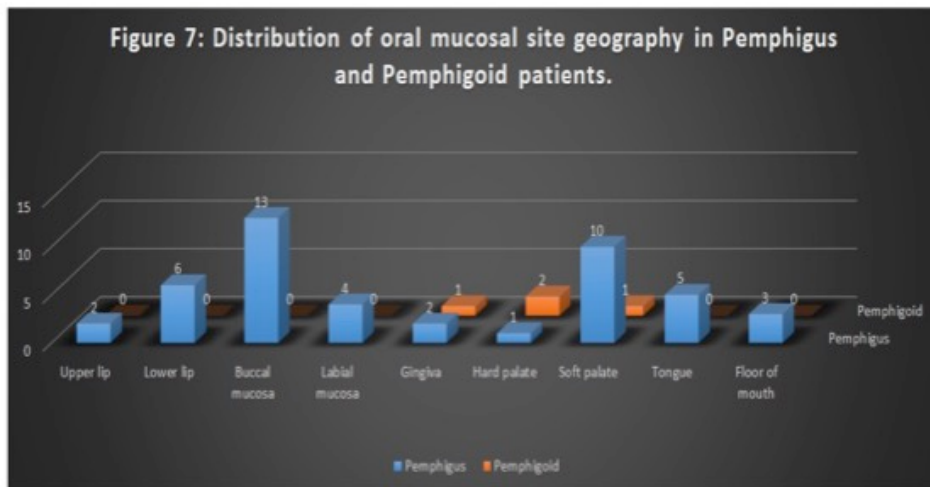
Mortality in pemphigus and pemphigoid

Mortality rate of the pemphigus in the present study is 14.28% (2 out of 14), a patient with pemphigus foliaceus and another patient with pemphigus vegetans. No death observed in pemphigoid patients during study period.

Discussion

Pemphigus and pemphigoid are considered to be a predominantly a dermatological condition. Oral manifestations of these diseases provides a great chance to dental surgeons to identify the disease at earlier stage, and help in early intervention and eventually for a better prognosis.⁶ The present study showed a higher prevalence of pemphigus and pemphigoid in females. Similar report was published in a study from Mexico.⁷ The present study





showed a higher prevalence among farmers and laborers, and our results were consistent with previously published study from Kerala population of India.⁸ The peak age of pemphigus and pemphigoid disease in the present study has fall between the 31-40 years, with the mean age of 42 years for pemphigus and 48 years for pemphigoid. Ajith Kumar et al., in their study reported that incidence of pemphigus is higher in the age group between 40-50 years from Thrissur district of Kerala, India.⁹

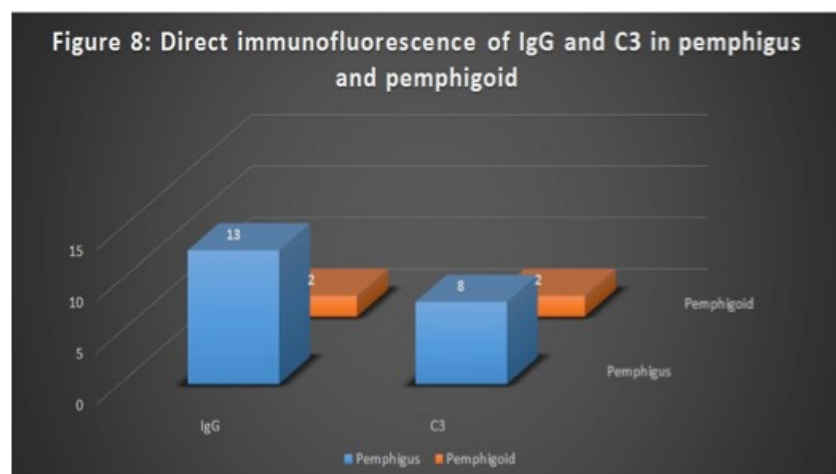
The prevalence of pemphigus in the present study is 46.66%, with higher prevalence of pemphigus vulgaris (71.42%) among the various clinical subtypes of pemphigus, which is followed by Pemphigus vegetans (14.28%) and Pemphigus foliaceus (14.28%). However, the present study had not reported any paraneoplastic pemphigus. Mortality rate of the pemphigus in the present study is considered to be 14.28% (2 out of 13), a patient with pemphigus foliaceus and another patient with pemphigus vegetans had died due to the severity of the disease. Lan-

gan et al in 2008, mentioned that mortality rate of pemphigus may range as 4.8% and 54%.¹⁰ Oral mucosal manifestation (fluid filled blisters or bullous, erosions) was observed in all the patients, and most prevalent oral site was buccal mucosa (92.85%), which is followed by Soft palate (71.42%), lower lip (42.85%), tongue (35.71%), labial mucosa (28.57%), floor of mouth (21.42%), upper lip (14.28%), gingival (14.28%), and hard palate (7.14%). 78.57% (11 out of 14) patients had reported that, oral mucosal manifestation as a primary site of disease process. In the published reports of Thorakkal Shamim et al., revealed that pemphigus vulgaris is the

most common subtype, with the primary site of oral mucosa in 53.52% of cases. The most commonly affected site was buccal mucosa, followed by palate, lips, tongue, floor of mouth and gingival.¹¹

The histopathological examination of the pemphigus tissue was characterized by the presence of acantholytic epithelial cells with resultant cleft formation within the oral epithelium. Direct Immunofluorescence method demonstrated the presence of IgG and C3 components. All the patients (100%) showed the positivity for IgG autoantibody, and 8 out of 13 (61.53%) patients showed C3 component positivity. Anuradha et al., in 2011 stated that direct Immunofluorescence of pemphigus showed deposition of IgG was observed in 80% and 14% of cases showed C3 positivity.¹²

The frequency of pemphigoid in the present study is 53.33%, with higher prevalence of bullous pemphigoid 87.5% among the clinical subtypes of pemphigoid. The study results suggested a



female predilection in pemphigoid disease. Fadia et al in 2011, suggested that pemphigoid is more common in females of fifth or sixth decade of life. Majority of the patients (6 out of 16, 37.5%) fall between age group of 31-40 years.¹³ The median age of pemphigoid disease in the present study is 48 years. Oral mucosal manifestation (fluid filled blisters or bullous) in pemphigoid in the present study is 12.50% (2 out of 16 patients) which is considered to be relatively low, and only one patient (6.25%) had reported oral mucosa as an initial site of disease manifestation. The most commonly affected site in oral cavity is hard palate (12.5%), which is followed by gingiva (6.25%), and soft palate (6.25%). Sunil dogra et al in 2003, reported that palate and gingival as most common area for pemphigoid disease.¹⁴ The histopathological examination of pemphigoid tissue was characterized by the presence of sub basilar cleft formation in the oral biopsied specimens. Direct immunofluorescent method demonstrated the positivity for IgG and C3 components in basement membrane zones of two oral tissue specimens. Stephen et al in 2001, stated the direct Immunofluorescence of pemphigoid tissues shows a linear deposition of IgG and C3 at basement membrane zone.¹⁵

Conclusion

Identification of oral manifestations in pemphigus and pemphigoid are important in both dental and dermatology practice. Early detection of oral lesions in dental

practice, and referral to expert dermatologist may help in early intervention. The collaborative approach will eventually alter the prognosis, and provides a scope to reduce morbidity and/or mortality rate.

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