

## ORIGINAL ARTICLE

## ORAL WHITE LESIONS - HISTOMORHOLOGICAL ASSESSMENT AND ASSOCIATED RISK FACTORS

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**Background:** Oral white lesions constitute a major clinical problem in Pakistan and South Asian countries. The study was done with the objective to analyse oral white lesions histologically and clinically, and evaluate association between various risk factors in different ages, gender, ethnic groups, sites and sizes of the lesion. **Methods:** A total of 80 patients presenting with oral white lesions were included in this cross-sectional study conducted at Department of Histopathology, Armed Forces Institute of Pathology (AFIP), Rawalpindi. The biopsy sample was fixed in 10% formalin and after standardized processing, slides were prepared, stained by Hematoxylin and Eosin, with special stains when required. The histo-pathological diagnosis of lesion was recorded. Mean and standard deviation were calculated for quantitative variable. Frequency and percentages were calculated for qualitative variables. **Results:** Out of total 80 patients 43 were females and 37 males. The mean age of cases was 47.92 years. Majority of the patients were between 30–39 years. Buccal mucosa was affected in majority of the cases (55%), followed by lateral border of tongue 17.5% and lip mucosa (8.8%). No risk factor had been observed in almost half of the patients. Histologically Lichen Planus was the most common lesion (32.5%), followed by chronic nonspecific inflammation in (22.5%), keratosis without dysplasia (10%), keratosis with dysplasia (8.8%), Pemphigus vulgaris (7.5%), fungal infestation (5%) and Squamous cell carcinoma (3.8%). **Conclusion:** Oral Lichen Planus was the most common oral white lesion in our set up, with buccal mucosa involved in majority of the cases. Association between histo-pathological diagnosis with age and gender was insignificant. However, significant association was observed between histopathological diagnosis and site. Among risk factors significant association was seen between snuff dippers and pan users.

**Keywords:** Dysplasia, Keratosis, Lichen Planus

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## INTRODUCTION

The term “Oral white lesion” is used to describe the appearance of a lesion presenting as white areas on the oral mucosa. Oral white lesions constitute a major clinical problem in Pakistan and South Asian countries. A variety of premalignant and malignant lesions of the oral cavity appear white, such as leukoplakia, oral lichen planus, oral candidiasis, tobacco pouch keratosis, carcinoma in situ and oral squamous cell carcinoma. Clinical appearance of the lesion may belie the true nature of the white lesion.<sup>1</sup>

Oral cancer may develop as two stage process; first step is the appearance of premalignant lesion, and the second development of carcinoma within the lesion.<sup>2</sup> Worldwide, oral cancer accounts for 2–4% of all cancer cases. In some regions, the prevalence of oral cancer is higher; reaching the 10% of all cancers in Pakistan, and around 45% in India.<sup>3</sup> Oral cancer includes a group of neoplasms affecting any region of the oral cavity, pharyngeal regions and salivary glands. However, this term tends to be used interchangeably with oral squamous cell carcinoma (OSCC), which represents the most frequent of all oral neoplasms. It is estimated that more of 90% of all oral neoplasms are OSCC.<sup>4</sup>

A change in the normal reddish colour of oral mucosa to white constitute one of the most frequently encountered oral presentation in clinical set up.<sup>5</sup> Most of the time, the reason for a lesion’s white appearance can be determined clinically, but at times, the final and reliable diagnosis of the lesion depends on histo-pathological diagnosis.

## MATERIAL AND METHODS

A total of 80 patients presenting with oral white lesions were included in this cross sectional descriptive study. Age, gender, site, size and associated risk factors were recorded. The biopsy sample was fixed in 10% formalin and after standardized processing, slides were prepared, stained by Hematoxylin and Eosin, with special stains when required.

The histo-pathological diagnosis of lesion was recorded. Mean and standard deviation were calculated for quantitative variable. Frequency and percentages were calculated for qualitative variables. Chi-square test was applied to study association of histological evaluation with gender and site. Analysis of variance (ANOVA) was applied to compare age in different types of histological evaluation while size was compared using Kruskal-Wallis H test.  $p$ -value  $\leq 0.05$  is considered significant.

**RESULTS**

Mean age of cases was 47.92 years (SD=14.32) with minimum age of 20 years and maximum age of 80 years. The most common age group in this study was 30–39 years accounting for 63.2% patient. Out of 80 patients 43 (53.8%) patients were females while 37 (46.2%) were males; with female to male ratio of 1.16:1.

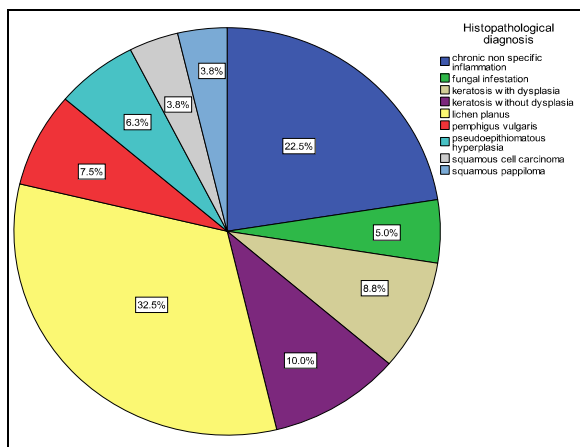
No risk factor had been observed in almost half of the patients, i.e., 43 (53.8%) patients. Twenty-six (32.5%) patients were smokers, 8 (10%) were *naswar* users, 7 (8.8%) were snuff dippers and 3 (3.8%) were pan users.

Majority of the patients were *Punjabi*, i.e., 43 (53.8%) followed by 24 (30%) *Pathan*, 6 (7.5%) *Hindkowans*, 3 (3.8%) were *Kashmiri* and Urdu speaking each and only 1 (1.2%) was *Sindhi*.

In majority of the patients frequently involved site was buccal mucosa, i.e., in 44 (55%) patients, followed by lateral border of tongue in 14 (17.5%) patients, lip mucosa in 7 (8.8%) patients, retro-molar pad area in 3 (3.8%) and ventral border of tongue in 2 (2.5%) patients.

Mean size of the lesion was 0.4315 cm (SD=0.661) with minimum size of 0.008 cm and maximum size of 4 cm. Lichen planus was the major histopathological diagnosis, i.e., in 26 (32.5%) patients followed by chronic nonspecific inflammation in 18 (22.5%) patients, keratosis without dysplasia in 8 (10%) patients, keratosis with dysplasia in 7 (8.8%) patients. (Figure-1).

Various risk factors are believed to be associated with oral white lesions. No, significant association was found between histo-pathological diagnosis and smoking ( $p=0.614$ ). However significant association was seen between snuff dippers and pan users  $p=0.003$  and  $0.040$  respectively (Table-1; Table-2).



**Figure-1: Description of histopathological diagnosis of patients (n = 80)**

**Table-1: Association between smoking and histopathological diagnosis**

Histopathological Diagnosis	Non-smokers	Smokers
Chronic nonspecific inflammation	12 (22.2%)	6 (23.1%)
Fungal infestation	4 (7.4%)	0 (0%)
Keratosis with dysplasia	3 (5.6%)	4 (15.4%)
Keratosis without dysplasia	6 (11.1%)	2 (7.7%)
Lichen planus	16 (29.6%)	10 (38.5%)
Pemphigus vulgaris	4 (7.4%)	2 (7.7%)
Pseudoepitheliomatous hyperplasia	4 (7.4%)	1 (3.8%)
Squamous cell carcinoma	3 (5.6%)	0 (0%)
Squamous papilloma	2 (3.7%)	1 (3.8%)

$p=0.614$  (Insignificant)

**Table-2: Association between snuff dippers and histopathological diagnosis**

Histopathological Diagnosis	Snuff dippers	
	No	Yes
Chronic nonspecific inflammation	18 (24.7%)	0 (0%)
Fungal infestation	4 (5.5%)	0 (0%)
Keratosis with dysplasia	7 (9.6%)	0 (0%)
Keratosis without dysplasia	7 (9.6%)	1 (14.3%)
Lichen planus	25 (34.2%)	1 (14.3%)
Pemphigus vulgaris	5 (6.8%)	1 (14.3%)
Pseudoepitheliomatous hyperplasia	2 (2.7%)	3 (42.9%)
Squamous cell carcinoma	2 (2.7%)	1 (14.3%)
Squamous papilloma	3 (4.1%)	0 (0%)

$p=0.003$  (Significant)

**DISCUSSION**

Oral white lesions are a day to day challenge which constitutes a major clinical problem in Pakistan and South Asian countries. The term oral white lesion is used to illustrate the appearance of lesion presenting as white area on the oral mucosa. Mainly white lesions of the oral mucosa attain their distinctive look from the spreading of light through an altered mucosal surface. Such changes could be the consequence of a thickened layer of keratin (hyperkeratosis), thickening of spinous layer of the epithelium (acanthosis), reduced vascularity of subjacent connective tissue and intracellular oedema of epithelial cells.<sup>6</sup> White or yellowish-white lesions might also be due to fibrin exudates covering an ulcerated surface, fungal colonies or surface debris.<sup>1</sup> The cause for a lesion’s white appearance can possibly be determined clinically but at times the concluding reliable and definitive diagnosis depends upon a precise histo-pathological examination.

In the present study a total number of eighty biopsies were included, with a vague clinical diagnosis of a white patch or lesion. The definitive explicit diagnosis of white lesion was made after a thorough microscopic examination. There was female predominance seen in this study with 43 (53.8%) of female patients and 37 (46.2%) male patients, female to male ratio being 1.16:1. In a similar study by Rana *et al.* female predominance was seen.<sup>5</sup> However, Gurung *et al.* and Baig *et al.* found out that white lesions were more common in males.<sup>1,7</sup>

Among eighty patients, average age of cases was 47.92 years (SD=14.32) with minimum age of 20

years and maximum age of 80 years. The most common age group in this study was 30–39 years accounting for 63.2% patients. In a Pakistani study by Baig *et al.* the age ranged from 9–70 years with mean age being 38 years and the common age group was 21–30 years.<sup>7</sup> There were variety of white lesions which were considered in this study and hence they report in different ages so this might be the reason for wide age distribution. However Spleith *et al.* have reported a higher prevalence in older age groups (40–81), but their studies were epidemiological and samples were much larger than this study.<sup>8</sup> A variety of oral white lesion have been identified to exist in conjunction with oral habits or substance abuse. In present study no risk factor had been observed in almost half of the patients, i.e., 43 (53.8%) patients. 26 (32.5%) patients were smokers, 8 (10%) were *naswar* users, 7 (8.8%) were snuff dippers and 3 (3.8%) were pan users. However, some studies have indicated a strong relationship of tobacco, sopari, pan and *naswar* with incidence of oral mucosal lesions.<sup>7,9</sup> In present study majority of the patients were *Punjabi*, i.e., 43 (53.8%) followed by 24 (30%) *Pathan*, 6 (7.5%) *Hindkowan*s, 3 (3.8%) were *Kashmiri* and Urdu speaking each and only 1 (1.2%) was *Sindhi*. The data reflects the specific patient population reporting to the hospitals of Rawalpindi/Islamabad; however the results might vary, if the study is conducted in different regions of Pakistan.

In present study buccal mucosa was the most frequently effected site 44(55%), followed by lateral border of tongue 14 (17.5%), this observation was similar to that of Baig *et al.* and Bokar-Bratic *et al.*<sup>7,10</sup>

In this study, Lichen planus was the major histopathological diagnosis, i.e., in 26 (32.5%) patients with buccal mucosa as the most favoured site. The results were analogous to other studies conducted in Pakistan.<sup>7,11</sup> Among these 26 patients, 15 (40.5%) were males and 11 (25.6%) were females with the majority of patients in 30–39 age group. Other studies found out that this entity was more common in females with maximum number of patients in 41–50 years age group.<sup>7,12</sup> In present study keratosis without dysplasia was seen in 8 (10%) patients, while keratosis with dysplasia in 7 (8.8%) patients presenting with a white patch, with males more frequently effected. Buccal mucosa was the site most frequently involved. These figures were comparable to the other international studies.<sup>1,10</sup> Pemphigus vulgaris an autoimmune blistering disease involving the skin and mucous membrane was also found, in the present series 6 (7.5%). Oral mucosa is frequently affected in patients with pemphigus vulgaris, and oral lesions may be the first sign of disease in majority of the patients. Therefore, timely recognition and therapy of oral lesions is critical as it may prevent skin involvement.

In present study buccal mucosa was involved most frequently with male to female ratio 1:1, which was similar to the study conducted by Reddy *et al.*<sup>13</sup> In present study, 5 (6.3%), of the patients came up with the histo-pathological diagnosis of pseudoepitheliomatous hyperplasia (PEH), which is characteristically an exuberant down growing proliferation of rete pigs into the submucosa, where hyperplastic cells fail to demonstrate cytologic signs of malignancy, although they may show reactive atypia. In present study buccal mucosa was the frequently involved site and female predominance was seen amongst these patients with the maximum patients in 60–69 years age group. In a Canadian study by Kleib and Rapheal showed somewhat similar results, with females outnumbering males in older age groups.<sup>14</sup>

In 18(22.5%) cases with the clinical diagnosis of either Lichen planus or Pemphigus vulgaris, the histopathological diagnosis revealed chronic nonspecific inflammation. In these cases surface erosions existed, with destruction of epithelium, leaving only the fibrin covered granulation at the floor of the lesion. This finding was reported earlier by Bokar-Bratic and his colleagues, who also emphasized that a biopsy should be taken from the representative lesion, taken a few millimeters away from the ulcerated mucosal lesion so that the specimen's epithelium and connective tissue remains intact.<sup>10</sup> Chronic hyperplastic candidiasis most commonly presents as a white plaque that cannot be rubbed off.<sup>15</sup> In present study 4 (5%) of the patients showed fungal infestation. All the patients were females, in their 5<sup>th</sup> and 6<sup>th</sup> decade. Dorsal surface of tongue and buccal mucosa was most commonly involved. In a similar study by Gurung *et al* 6 (9%) of oral candidiasis was seen among 61 biopsies with males outnumbering females.<sup>1</sup>

Among 80 cases, well differentiated oral squamous cell carcinoma was found in 3 (3.8%) of the patients presenting clinically as a white lesion with no associated symptoms. All were females belonging to older age groups. The posterior third of the oral cavity (both buccal mucosa and retromolar pad area) was predominantly affected. In an Indian study done by Mishra *et al*, 18 (85.7%) proved to be invasive squamous cell carcinoma on histopathological examination with buccal mucosa involved in majority of the cases.<sup>16</sup> Significant association was observed between histopathological diagnosis and site ( $p=0.004$ ). Buccal mucosa was the most frequently involved site in almost all of cases. Lima and his colleagues found out that a significant association between lesion anatomical site and dysplastic lesion was observed ( $p=0.001$ ).<sup>17</sup>

Various risk factors are believed to be associated with oral white lesions, the more frequently

blamed factor is tobacco utilized in different ways, i.e., smoking and chewing tobacco alone or included in the pan, snuff dipping, areca nut, spicy food and alcohol consumption.<sup>5</sup> In present study no significant association was found between smoking and histopathological diagnosis ( $p=0.614$ ) but snuff dipping showed a significant association ( $p=0.003$ ). Lima *et al.* were also of the opinion that there was no association between the smoking habits and development of oral white lesion ( $p=0.520$ ).<sup>17</sup> In this study significant association was observed between pan use and development of oral white lesions ( $p=0.040$ ). This was reported earlier by other studies also.<sup>5,16</sup>

## CONCLUSION

Oral Lichen Planus was the most common oral white lesion in our set up, with buccal mucosa involved in majority of the cases. Association between histopathological diagnosis with age and gender was insignificant. However, significant association was observed between histopathological diagnosis and site. Among risk factors significant association was seen between snuff dippers and pan users.

## AUTHOR'S CONTRIBUTION

WUN: contributed in data collection and SH: helped in literature review.

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