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Original Article

Clinicopathological Features of Oral Leukoplakia Among Snuff Users and Non-Users: An Analytical Study

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ABSTRACT

Oral leukoplakia refers to a white lesion of questionable risk excluding other lesions carrying a risk of conversion into malignancy. Tobacco is regarded as the most common risk factor and may affect the clinicopathological aspect of the said lesion. **Objectives:** To assess the clinicopathological features of oral leukoplakia among snuff users and non-users. **Methods:** The present analytical study was done on 60 oral leukoplakia cases and was further subdivided into 30 cases of snuff users and 30 non users. Clinicopathological features were assessed in all the cases. Data analysis was done by using SPSS-20. **Results:** The observed male cases were 43 (71.7 %) and female cases were 17 (28.3%). The ratio was found to be 2.5:1. All the 30 snuff users were males. Among non-users 13/30 (43.3%) were males and 17/30 (56.7%) were females. The relationship was found to be statistically significant with a p-value of <0.01. The mean age among cases who used snuff was 56.97 (SD ± 14.71) while the mean age among non-users was found to be 47.43 (SD ± 13.44). In snuff user's buccal mucosa was affected in 12/30 (40%) cases whereas in non-user buccal mucosa was also the most common site 18/30 (60%) cases showing a non-significant relationship p-value 0.59. **Conclusions:** Oral leukoplakia was more prevalent among males with a mean age range of more than fifty years and buccal mucosa and buccal sulcus being the most common sites. Dysplastic epithelium was more common among those cases that used snuff and this showed that chances of malignant transformation are more in such cases.

INTRODUCTION

Oral leukoplakia is a white lesion of questionable risk excluding other lesions carrying a risk of conversion into malignancy. Its global prevalence ranges from 0.2% to 3.6%. According to the studies conducted in Pakistan the prevalence ranges from 5-7% [1]. Oral leukoplakia is a clinical entity having two forms including homogeneous and non-homogeneous leukoplakia [2]. The most common sites are buccal mucosa tongue, lip and floor of the mouth [3]. Oral leukoplakia is a multifactorial disorder. Tobacco use either in smoked or smokeless form, mechanical trauma, electro galvanic shock, are some of the related etiological factors however tobacco is ranked as the main factor in the development of the said pathology [4, 5]. There are many carcinogens in tobacco which includes tobacco specific nitrosamines TSNA. Four compounds are included in this group. Two compounds are found to be more carcinogenic 1 N-Nitrosonornicotine NNN and 2. 4-(methyl nitrosamine)-1-(3-pyridyl)-1-butanone or Nicotine derived nitrosamine Ketone NNK [2]. Cancers of the oral cavity develop from premalignant form and oral leukoplakia

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is also included in the list of such entities. Dysplasia is thought to be a sign that a lesion may become cancerous [6]. Histopathologically the lesion consists of hyperplastic epithelium, hyperkeratosis and epithelial dysplasia may or may not be present. And if present it ranges from mild to severe grade [7]. Diagnosis of dysplasia is done on certain cytological changes as well as change in the epithelial architecture [8]. The gender distribution varies in different regions however oral leukoplakia occurs predominantly in males [9, 10]. Oral leukoplakia usually affects adults in the middle age and its prevalence increases with advanced age. According to studies conducted globally age ranges from 3rd–5th decade of life [9, 11]. Buccal mucosa is the most common site for the development of oral leukoplakia, followed by tongue, retromolar area and buccal sulcus [12]. For the laboratory diagnosis of oral premalignant lesions, histopathological examination of biopsy samples remains the gold standard. History, clinical examination along with histopathological assessment of biopsy material taken from the suspected area are the basis of definite diagnosis. Biopsy is mandatory for all the lesions which clinically appear to be leukoplakia for confirmation of diagnosis and planning of the treatment [13]. Oral leukoplakia and other oral potentially malignant disorders OPMDs may greatly help in early detection and prevention of cancers of oral cavity. The current study was performed to evaluate and report the clinicopathological features of oral leukoplakia with regards to snuff use and non-use to observe the diverse behavior of the lesion moreover histological dysplastic epithelium is a warning sign for transformation of oral leukoplakia into cancer and in time remedy can prevent this phenomenon.

METHODS

The current analytical research was performed at Peshawar Medical College and Khyber college of Dentistry and data collection were done from August 2016 - March 2017 (7 months) on 60 cases of oral leukoplakia which were diagnosed clinically and microscopically confirmed. The sample size was calculated by using Epi-Tool online calculator. Sampling technique was non probability convenient sampling. Permission from Institutional review board was taken before start of the study. 60 oral leukoplakia cases were divided into two groups. Group A comprising of 30 cases of snuff users and Group B 30 cases of non-users. The definition of tobacco user (smoking or smokeless) was a person who had used tobacco (smoking or smokeless) every day or at once a week for a year. Non user was an individual who never used either form of tobacco [14]. Inclusion criteria for the snuff users and non-users included biopsied and histopathologic ally diagnosed cases of oral leukoplakia with a history of snuff use and non-use. Cases of oral leukoplakia receiving treatment, alcohol users, and smokers were excluded from the study. Laboratory procedure was performed for biopsy specimen of Group A and B. The steps were grossing of the specimen, tissue processing and finally slides were stained by Eosin and Hematoxylin. The slides were then examined under the microscope and histopathological findings like dysplasia, hyperplasia, and hyperkeratosis were noted. All the relevant data which included age, gender of the patients, site of the lesion, snuff use or no use habit, duration of snuff use in years and histopathological findings were recorded on a predesigned proforma. Data analysis were carried out by using Statistical Package for Social Sciences SPSS version 20.0. For continuous variables for example age mean and standard deviation was calculated for categorical variables, for example history of snuff use percentage was calculated. Chi-square test was applied to find the relationship among snuff users and non-users. p-value of ≤ 0.05 was considered statistically significant.

RESULTS

Out of the 60 cases of oral leukoplakia males' cases were found to be 43 (71.7 %) and female patients' percentage was 17 (28.3%) The calculated ratio was 2.5:1 (Table 1).

Table 1: Gender wise distribution of oral leukoplakia cases

Gender	Number of cases (%)
Male	43(71.7)
Female	17(28.3)
Total	60(100.0)

All the 30 snuff users were males. Among non-users 13/30 (43.3%) were males and 17/30 (56.7%) were females (Table 2). The relationship was found to be statistically significant with a p-value of 0.01. The age group ranged from 14-95 years with the mean age of 50.3 years. In snuff users the mean age was 56.97 (SD ± 14.71) while in non-users the mean age was 47.43 (SD ± 13.44).

Table 2: Gender wise number of oral leukoplakia in snuff use and nonuse cases

Gender	Snuff Users	Non snuff users	p-value
	Number of cases (%)	Number of cases (%)	
Male	30(100)	13(43.3)	< 0.01
Female	0(0)	17(56.7)	
Total	30(100)	30(100.0)	

In snuff user maximum patients diagnosed in oral leukoplakia were in the age range of 61-75 years whereas in non-snuff user maximum patients diagnosed in oral leukoplakia were in the age range of 31-45 years (Table 3).

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Table 3: Age wise distribution among cases of snuff use and nonuse of oral leukoplakia

Age Groups (yrs.)	Snuff users F(%)	Non snuff users F(%)
15-30	0(0)	2(6.7)
31-45	8(26.7)	13(43.3)
46-60	9(30)	9(30)
61-75	11(36.7)	6(20)
76-90	2(6.7)	0(0)
Total	30(100)	30(100)

The observed most common site was buccal mucosa with 30/60 (50%) cases followed by buccal sulcus (20%), tongue (18.3), alveolar ridge (5%), retromolar area (3.3%), floor of the mouth+ ventral surface of tongue (1.7%) and alveolar ridge + labial sulcus (1.7%) (Table 4).

Table 4: Site distribution of oral leukoplakia cases

Site of lesion	Number of cases (%)
Buccal mucosa	30(50)
Buccal sulcus	12(20)
Alveolar ridge	3(5)
Tongue	11(18.3)
Retromolar area	2(3.3)
Floor of mouth+ ventral surface of Tongue	1(1.7)
Alveolar ridge + labial sulcus	1(1.7)
Total	60(100)

In snuff user buccal mucosa was affected in 12/30 (40%) cases whereas in non-user buccal mucosa was also the most common site 18/30 (60%) cases (Table 5) showing a non-significant relationship. P-value 0.59.

Table 5: Site distribution in snuff use and nonuse cases

Groups	Site of the lesion No of cases (%)								p-value
	Buccal mucosa N(%)	Buccal sulcus N(%	Tongue N(%)	Alveolar ridge N(%)	Retro-molar area N(%)	Floor of mouth & tongue N(%)	Alveolar ridge + labial sulcus N(%)	Total	
Snuff users	12(40)	8(26.7)	5(16.7)	3(10)	1(3.3)	1(3.3)	0(0)	30	0.59
Non snuff users	18(60)	4(13.4)	6(20)	0(0)	1(3.3)	0(0)	1(3.3)	30	
Total	30	12	11	3	2	1	1	60	

Dysplastic feature was observed in (30%) individuals who used snuff followed by combined features (21.6%), hyperkeratotic epithelium (16.7%) and hyperplastic epithelium (3%). In individuals who did not use snuff features of hyperplastic epithelium was (36.7%), followed by hyperkeratotic epithelium (23.3%) dysplastic epithelium (20%) and combined features (20%) respectively. The relationship was observed to be significant statistically and the probability value (p-value) was found to be 0.04 (Table 6).

Table 6: Comparison among patients of oral leukoplakia using and not using snuff

Histopathology	Snuff users N(%)	Non snuff users N(%)	p-value
Dysplastic epithelium	9(30)	6(20)	0.04
Hyperplastic epithelium	3(10)	11(36.7)	
Hyperkeratotic epithelium	5(16.7)	7(23.3)	
Combined features	13(21.6)	6(20)	
Total	30(100)	30(100)	

DISCUSSION

Oral malignancies are commonly related to potentially malignant conditions and lesions including oral leukoplakia [7]. Oral leukoplakia is a white patch of oral mucosa and its malignant transformation rate ranges from 0.13%-34% [15]. In our study oral leukoplakia affected more males than females. This finding is consistent with the international studies [16, 17]. The reason for this may be that traditionally males are more likely to have the habit of consuming tobacco either smoking or smokeless [18]. The present study showed old age predominance among most cases of oral leukoplakia. This is consistent with the study done by Khan *et al.*, and Mello *et al.*, according to Mello increasing age may be a risk factor for oral premalignant lesions [14, 18]. According to the present studies the most predominant sites are buccal mucosa, buccal sulcus, retromolar area and tongue. This is consistent with researches done by Hosagadde *et al.*, Mondal *et al.*, and Warnakulasuriya [12, 19, 20]. However, it was not associated with snuff and in contrast to studies done in Italy and China [7, 21]. Another international study reported floor of the mouth as the most commonly occurring site [22]. The reason for the site predilection in our study may be these are the placement and adjacent sites of snuff so have the maximum contact with snuff and in turn develops oral leukoplakia. Changes in genetic makeup of epithelial cells of oral mucosa results in dysplastic epithelium leading to development of oral leukoplakia of that specific site. Dysplasia is regarded as a marker of transforming a benign lesion into malignant lesion. In the present study dysplastic epithelium was exhibited in 9(30%) cases This is in accordance to an Indian study [23]. An international research showed dysplasia in 60 cases with smoking and chewing as major risk factors however these cases were not associated with snuff [24]. There was a statistically significant relationship of above-mentioned feature among snuff users and non-users. p value was found to be 0.04. Statistically significant relationship of other histopathological features of oral leukoplakia could not be found. Although tobacco in smokeless form is used world over however oral snuff is most commonly used in Pakistan and the procedure how to manufacture and applying snuff in oral cavity differs among various areas. Therefore, international literature in this context could not be found on

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extensive literature review. To our knowledge the current study is among the pioneer studies to reveal the clinicopathological features and snuff usage trends among oral leukoplakia cases.

CONCLUSIONS

Oral leukoplakia is more prevalent among males with a mean age range of more than fifty years and buccal mucosa and buccal sulcus being the most common sites. Dysplasia was more common among those cases who used snuff and this showed that chances of malignant transformation are more in such cases so follow up and timely treatment may prevent conversion of such cases into malignant form.

Authors Contribution

Conceptualization: TN
Methodology: SA, FI
Formal analysis: ASK, NM, HMY, SM, UM
Writing-review and editing: ASK, TN, HMY, SM, UM

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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