A Longitudinal Study on Oral Potentially Malignant and Malignant Lesions in a Tertiary Care Teaching Hospital

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Abstract

Objectives: This study aims to qualitatively and quantitatively over five years using a clinical spectrum of presentation and frequency distribution, prevalence, and malignant transformation rates of Potentially malignant disorders.

Methods: This study follows a longitudinal prospective study design which was conducted in the Department of Oral Medicine, Oral Diagnosis and Radiology, at SCB Dental College and Hospital, Cuttack over 5 years, from January 2013 to December 2017.

Results: The frequency of OPMDs was 55% with 36.88% males. The most and least frequently encountered OPMDs included Pouch keratosis (30.96% of OPMDs) and Discoid Lupus Erythematosus (0.002% of OPMDs). The mean age of malignant transformation was 41 years with a male predilection (68%) and was largely habit associated (72%). Over the 5 years, the highest rate of malignant transformation was observed for actinic cheilitis (20.66%) and the least for oral lichen planus (0.35%).

Conclusion: The significantly higher rate of transformation noted in our population can be attributed to late presentation for treatment, rampant production and continued use of smokeless forms of tobacco. To the best of our knowledge, this study is one of the few to recruit a large population presenting with varied lesions.

Keywords: Potential malignant disorders, Malignant lesions, Head and neck cancer.

Introduction

Potentially malignant disorders (PMDs) of the oral mucosa, with the risk of conversion to oral squamous cell carcinoma (OSCC), are described in the literature as 'pre-cancer'[1,] 'precursor lesions'[4], 'premalignant', 'intraepithelial neoplasia'[5], and 'potentially malignant'[6]. The clinical concept of malignant transformation in oral mucosa has been proposed for more than 100 years. Sir James Pagetfirst described the malignant transformation of an oral lesion into tongue carcinoma in 1870.[7] Schwimmeralso reported the same finding in 1877. [8] Several years later, the term "potentially malignant disorders" [6] was defined by the World Health Organization (WHO) as the risk of malignancy is present in a lesion or condition either during the time

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of initial diagnosis or at a future date. WHO earlier has also classified PMDs into two subgroups[9] as follows: a) precancerous lesion, a benign lesion with morphologically altered tissue, which has a greater than normal risk of transforming into malignancy; b) precancerous condition, a disease or patients' habit that does not necessarily alter the clinical appearance of local tissues but is associated with a greater than normal risk of precancerous lesion or cancer development in that tissue.

Despite the ability to identify PMD, clinicians have been unable to predict the behaviour of lesions or quantify the risk of malignant transformation. Overall estimates of outcomes are mostly anecdotal and retrospective. Moreover, the natural history of PMDs is, unfortunately, not only inconsistent but also unpredictable.This study aims to address the above shortcoming qualitatively and quantitatively over 5 years using the clinical spectrum of presentation and frequency distribution, prevalence, and malignant transformation rates respectively, following a longitudinal prospective study design.

Material and Methods

The present longitudinal study was conducted in the Department of Oral Medicine, Oral Diagnosis and Radiology, at SCB. Dental College and Hospital, Cuttack.The period of study was 5 years, from January 2013 to December 2017. This study aims:

- To observe the clinical spectrum of the presentation of OPMDs
- To document the 5-year frequency distribution of various OPMDs and malignant lesions of the head and neck region
- To estimate the prevalence of these lesions in the presenting population
- To observe the gender predilections of the above OPMDs and malignant lesions
- To estimate the malignant transformation rates of various OPMDs into OSCC
- To put forth a comparative evaluation of malignant transformation rates amongst the studied OPMDs
- To calculate the net 5-year cancer burden

Patients presenting with any OPMD as per the new classification proposed by Sarode et. al[10] were included in the study. Also included were patients who presented with malignant pathologies of the head and neck region. The present follow-up study was based on clinical, cytological, histopathological, radiographic, haematological or other needful investigations, all part of the routine treatment and follow-up protocol. The follow-up time for this study is defined as the duration between the initial diagnosis and the occurrence of confirmed oral cancer. Institutional Review Board recommended that ethical approval was not deemed necessary as protocols adopted were part of routine patient care and follow-up. The patients were treated under the domain of implied consent. However, due information was provided to each patient about the nature of the disease, treatment protocols and its effects.

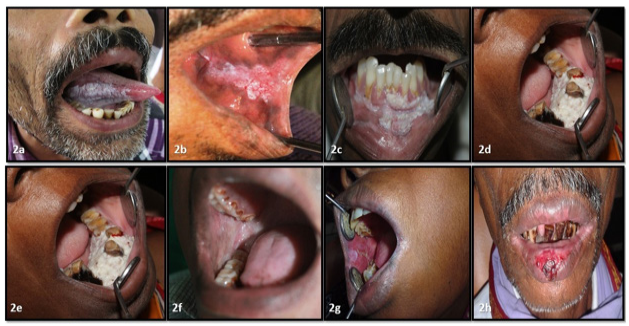

Figure 1: Spectrum of clinical presentation of various OPMDs; 2a: Homogenous Leukoplakia, 2b: Nonhomogenousnodulo-speckled Leukoplakia, 2c: Verrucous Leukoplakia, 2d: Proliferative Verrucous Leukoplakia, 2e: Oral Submucous Fibrosis, 2f: Tobacco pouch keratosis, 2g: Erosive Oral Lichen Planus, 2h: Actinic Cheilitis

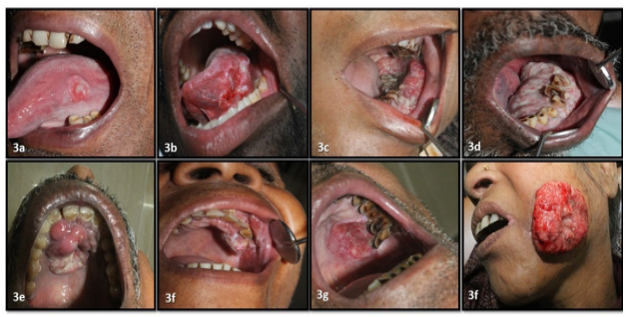

Figure 2: Varied clinical presentations of oral squamous cell carcinoma; 3 a,b: OSCC tongue, 3 c,d: OSCC mandibular gingivobuccal complex, 3 e,f,g: OSCC palate, 3h: OSCC left buccal mucosa perforating left cheek

Results

The study included all patients who were clinically and/or histopathologically diagnosed as any one of the OPMDs (Figure 1, 2). Patients lost to follow-up were excluded from the study. The net patient inflow over 5 years (January 2013 to December 2017) was 2,51,702. The frequency distribution has been depicted in Table 1. The frequencyof patients with OPMDs was 55% with 17.06% females and 36.88 % males. The lesions with a male predominance included Leukoplakia (74.24%), Oral Submucous Fibrosis (83.55%), Pouch keratosis (71.26%) and Actinic cheilitis(82.75%) while Oral lichen planus (77.63%)had a female preponderance (Figure 4). Cases of Discoid Lupus Erythematosus occurred exclusively in females. In our study, patients with Epidermolysis Bullosa were equitably distributed among males and females.

Table 1: Annual and 5-year frequency distribution with 5-year prevalence.

Year	Leukoplakia	Oral submucous fibrosis	Pouch keratosis	Oral lichen planus	Actinic cheilitis	Smokers palate	Discoid Lupus Erythematosus	Epidermolysis Bullosa
2013	5307	5565	7400	4866	4	1098	0	1
2014	6060	5937	9533	5171	5	2380	0	0
2015	6342	4139	8578	5241	6	2036	2	0
2016	6450	5964	8633	5370	6	2206	1	1
2017	7253	6168	8731	5392	8	2617	0	2
5 yr Burden	31412	27763	42875	26040	29	10337	3	4
5 yr Prevalence	12.47%	11.03%	17.03%	10.34%	0.011%	4.10%	0.001%	0.002%

The most and least frequently encountered OPMDs included Pouch keratosis (30.96% of OPMDs) and Discoid Lupus Erythematosus (0.002% of OPMDs)respectively while Oral Submucous Fibrosis (20.05% of OPMD's) and Oral Lichen Planus (18.80% of OPMD's) presented nearly equally in patients reporting at our tertiary care centre. The male:female ratio of various OPMDs reported was 2.88 for Leukoplakia, 5.08 for Oral Submucous Fibrosis, 3.16 for Pouch keratosis, 0.28 for Oral Lichen Planus, 4.8 for Actinic cheilitis, 23.96 for Smokers Palate, and 1 for Epidermolysis Bullosa(Figure 3). The mean age of presentation of OPMDs was 33.6years. Amongst males, the mean age was 29.6 years while for females it was 37.5years. The age group most commonly affected by any of the OPMDs was 20-40 years. Patients with lichen planus presented early (mean age 28 years) while cases with leukoplakia presented late (mean age 36 years). Smokers palate was more of an incidental finding (79%) than a primary presentation(21%).

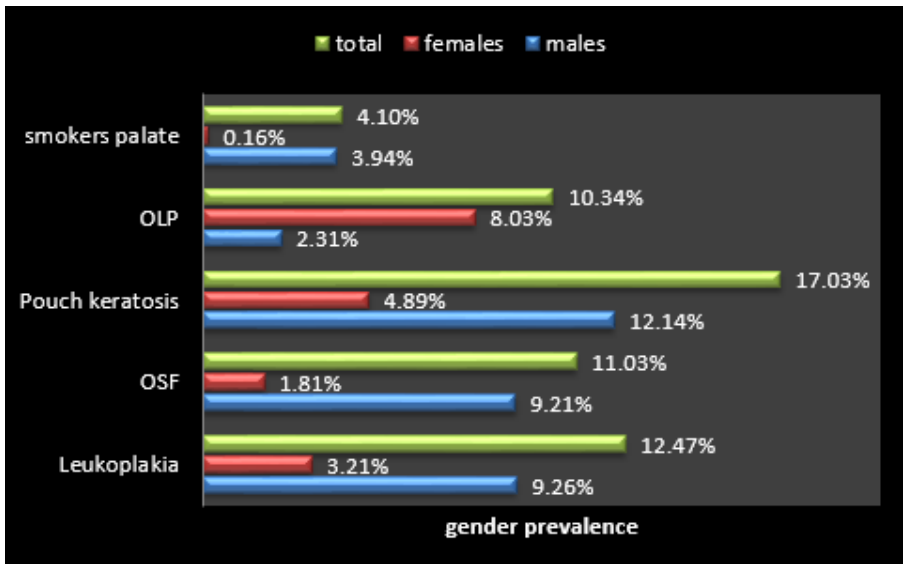

Figure 3: Gender distribution of various OPMDs.

Concerning site predilection, the lower left buccal vestibule (53%) and left buccal mucosa(28%)were the chief sites for Leukoplakia, lower left buccal vestibule was the primary site for Pouch keratosis(77%), bilateral buccal mucosa (42%) and gingivae(32%) for Lichen planus and lower lip for Actinic cheilitis (100%). The remaining patients had involvement of multiple intraoral sites. Oral submucous fibrosis had more pastoral involvement. About 47% of the OPMDs showed candidal colonization. The various predictors for malignant transformation in our study included age, gender, site, appearance and presence of deleterious habits. The net 5-year malignant transformation rates of various OPMDs to oral squamous cell carcinoma have been depicted in Figure 4.

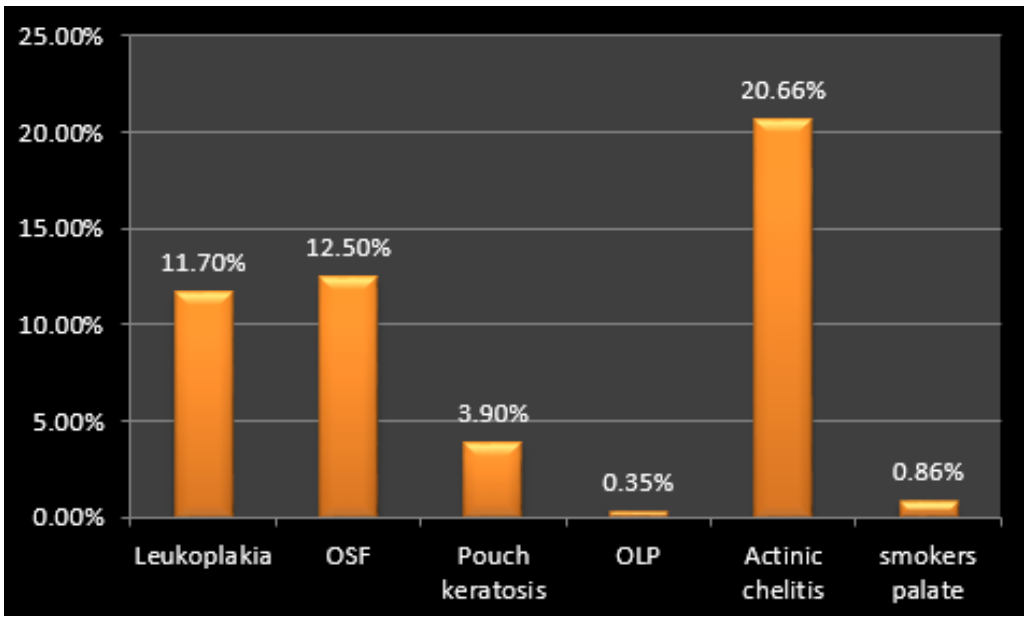

Figure 4:5-year malignant transformation rates of various OPMDs.

The lesion with the highest rate of malignant transformation wasActiniccheilitis (20.66%) while Oral lichen planus (0.35%) hadthe least conversion in our population. 2 cases of idiopathic OSMF and 3 cases of cryptogenic leukoplakia were encountered throughoutthe study. The mean age of malignant transformation was 41 years with a male predilection (68 %) and was largely habit associated (72%). The type of tobacco consumed and other relevant attributes have been summarized in Table 2. Smokeless tobacco forms were consumed by 66.25% while smoking by 35.08%. Overall, 22.99% were addicted to both. Cessation of tobacco habits was reported in 8.24%. Lesions presenting with erosions, ulcerations, surface elevations, nodularity or other features contributing to clinical non-homogeneity in the appearance of the lesions were more susceptible to malignant transformation (66%). Cases presenting primarily as malignancy were 6.34%. Out of these, 8(0.05%) were of salivary origin, 2(0.012%) melanoma, 1(0.006%) metastatic carcinoma, 2(0.012%) lymphoma, 3(0.018%) malignant ameloblastoma. The remaining cases 15949 (99.9%) presented as a primary intraoral malignancy (Figure 4).

Table 2: Type of tobacco consumed and other relevant attributes

SMOKING FORMS OF TOBACCO	Age of initiation	Duration since	Average number/ day	The predominant type of smoking
USERS	<20Y 18062	1-3Y 9312	1-5 18992	Crude 36520
	20-30Y 20173	3-5Y 10462	5-10 17609	Filtered 12056
	>30Y 10341	5-10Y 11340	>=I pack 11975	
		10-20Y 12622		
		>=20Y 4840		

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EX-USERS Cessation since	**Age of initiation**	**Duration since**	**Average number/ day**	**Type of smoking**
Few days 674	<20Y 1588	1-3Y 597	1-5 3688	Crude 2647
Few wks 908	20-30Y 3609	3-5Y 3422	5-10 1533	Filtered 3066
Few mon 2991	>30Y 516	5-10Y 972	>=I pack 492	
Few yrs 1140		10-20Y 593		
		>=20Y 129		
Smokeless Forms of Tobacco	**Age of initiation**	**Duration since**	**Average frequency/day**	**Mode of use of smokeless tobacco**
USERS	<20Y 36106	1-3Y 11059	1-5 24375	Sw 14934
	20-30Y 41530	3-5Y 18153	5-10 37305	Po 21215
	>30Y 14107	5-10Y 24618	>10 30063	Sp 12876
		10-20Y 27112		All 42718
		>=20Y 10801		
EX-USERS Cessation since	**Age of initiation**	**Duration since**	**Average frequency/day**	**Mode of use of smokeless tobacco**
Few days 233	<20Y 671	1-3Y 1740	1-5 1204	Sw 562
Few wks 562	20-30Y 3802	3-5Y 506	5-10 3008	Po 2254
Few mon 2650	>30Y 1228	5-10Y 2628	>10 1489	Sp 452
Few yrs 2256		10-20Y 455		All 2433
		>=20Y 372		

SW-swallow, po-pouch, sp-spit

Discussion

During the 5 year study period (January 2013 to December 2017), 55.01% were OPMD and 6.34% were head and neck cancers (HNCA). According to various studies, the estimated prevalence of HNCA concerning total body malignancies varies from 9.8% to 42.7%.[11-13]The diverse spectrum of clinical presentations of various oral potentially malignant disorders was encountered. The overall prevalence over 5 years was 55% with a mean yearly prevalence of 11%. This was higher than the rates observed in other studies.[14-16]

The most frequently encountered OPMD was leukoplakia (12.47%). The majority cases of the cases were habit associated with only 3 being idiopathic. The 5-year malignant transformation rate was 11.70%. The transformation occurred in the habit-associated group and 1 case in the cryptogenic group. The noted malignant transformation rate (5.374%) was higher compared to the study by Tung-YuanWang et al.[17] According to a study by Gupta PC et al, the overall malignant transformation rates were very low (0.3%–2.19%)[18]. Warnakulasuriyaand Ariyawardana[19]carried out a systematic review of 24studies and found an overall malignant transformationrate of 0.13% to 34% making our observation conformant to this range.

The next most common disorder encountered was oral sub-mucous fibrosis (11.03%). All but 2 cases were habit associated. The 2 idiopathic cases gave no history of tobacco habits, both presented in females in the late second decade, with 1 giving a similar familial history. None of the idiopathic cases showed malignant transformation. The five-year transformation rate was documented as 12.50%, in agreement with the often cited metric of a 7-13% malignant transformation rate of OSF stems from a Taiwanese study.[20]As demonstrated in a long-term follow-up study in India, scrutinizing 99 patients with OSF for 17 years, a malignant transformation rate of 7.6% was documented.[21] In contradistinction, more recent, larger studies have suggested a lower rate; in a recent review by Ray et al the transformation rate varied from 1.9% to 7.6%.[22] The significantly higher

rate of transformation noted in our population can be attributed to late presentation for treatment, rampant production and continued use of smokeless forms of tobacco, ease of availability at cheaper costs and lower tax rates and ill belief that smokeless tobacco is good for health increasing appetite and vigour.

Oral lichen planus, presented in our population with a prevalence rate of 10.34%, chiefly manifesting amongst women (77.63%). The overall 5-year malignant transformation rate documented was only 0.35% entirely sparing the reticular variant. As reported by Sana Maher Hasan Aghbariet al[23], 1.1% of OLP patients developed OSCC, while the rate of malignant transformation among OLL cases was 2.5%. Studies by IngafouM et al[24], Carbone M et al[25]. During this study, dysplastic changes were also documented in lesions originally diagnosed as tobacco pouch keratosis (3.90%).

Conclusion

To the best of our knowledge, this study is one of the few to recruit a large population presenting with varied lesions. It serves to present an overview of a few epidemiologic associations between disease, gender, site, age and deleterious habits. However, owing to large sample recruitment, various parameters remain unaddressed which can be a potential ground for future research. Association between the diseases studied and various systemic co-morbidities can be introspected. Chances of underestimation of transformation rates do exist which can be ruled out with a longer follow-up period. Also,the integration of chairside screening and histologic prognostic factors into routine diagnostic and treatment procedures might serve to change the natural course of the disease.

Conflict of Interest: There is no conflict of interest

Source of funding: Nil

Ethical clearance: Approved by Institutional Ethics Committee

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