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A Research Study on Tobacco Associated Oral Potentially Malignant Disorders (OPMDs) Prevalent in Oral Mucosa of Lumbini Province/District Rupandehi Population of Nepal

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***Background**: Tobacco associated Oral mucosal lesions (OML) oral potentially malignant disorders (OPMDs) that comprise of oral sub-mucous fibrosis, oral leukoplakia, tobacco pouch keratosis, chewer's mucositis, pan encrustation are the most prevalent diseases in Rupandehi District, Lumbini province (Province Five) of Nepal. These OPMDs are usually caused by the consumption of both smokeless and smoked forms of tobacco. Smoking, chewing of the tobacco products including alcohol consumption are the common prevalent habits in Nepal and have been positively associated with such lesions. **Aim of the Research Study**: With this background, a research study has been conducted to assess the prevalence of OPMDs and their association among the patients visiting the outpatient department in Rupandehi district of Nepal. **Research Methods and Material**: This descriptive, cross-sectional prevalence study included five hundred participants who visited the Outpatient Department and fulfilled the inclusion criteria. The study data was carried out from August 2003 till April 2024. Institutional Review Committee (IRC) provided the ethical clearance to the study, which was duly obtained along with patient consent that were part of the study. Standardised proforma was used for recording demographic details, and WHO Assessment form for oral mucosal lesions were used to record the tobacco use status and findings of the clinical and laboratory investigations. Statistical analysis was performed using IBM SPSS version 23, and the results were calculated along with the level of significance. **Research Study Results**: The final sample was comprised of 500 cases of which 392 were males and 108 were females. The mean age of the study population was 58.19 ± 12.33 years ($p<0.001$). Leukoplakia in its varied forms (OPMD) accounted for almost 82% of the sample cases. The lesions from patients aged from 41 to 80 years presented moderate and severe dysplasia more often than lesions from patients in other age groups. The prevalence of tobacco use among study participants was 41.25% and that of the OML (oral mucosal lesions) positively attributed with use of tobacco was 39.28%. Tobacco chewing (areca nut) were significant predictors of oral sub mucous fibrosis in this population. **Conclusion:** The prevalence study emphasizes the deleterious effects of tobacco use on oral mucosa and also serves as a path for future tobacco cessation programs that would be helpful to prevent OPMDs in the Nepalese population especially in Province V (Rupandehi District) of Nepal.*

Keywords: *OPMDs, oral diagnosis, oral leukoplakia, oral sub mucous fibrosis, chewer's mucositis, tobacco cessation*

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Introduction

Oral potentially malignant disorders (OPMDs) are tissue changes that may precede squamous cell carcinoma (SCC) (Villa and Gohel 2014, Johnson 2011, El-Naggar 2017). SCC is a malignant neoplasm that accounts for 80-90% of all cancers in the oral cavity. The most common disorders in this group are leukoplakia, speckled leukoplakia, erythroplakia, and oral submucous fibrosis (Warnakulasuriya 2016, Scully 2017, Johnson 2011, Sarmento 2014).

Considering the various characteristics of OPMD in different populations, knowledge of their clinical-pathological profile is an important diagnostic tool. Therefore, it may play a pivotal role in preventing malignant transformation of these lesions in oral mucosa.

Given the low number of epidemiological studies about this topic in the Nepalese population especially in Rupandehi District region, this study aimed to analyze the clinical-pathological features of OPMD diagnosed in Province Five of Nepalese population.

Material and Methods

A descriptive, cross-sectional prevalence study has been done among five hundred patients with histopathlgically diagnosed oral potentially malignant disorders, from the period of August 2023 to December 2023 duration, attending the outdoor clinic of Department of Oral Medicine, Diagnosis and Radiology, Universal College of Medical Sciences (UCMS), Bhairahawa, Lumbini Province of Nepal.

Exclusion Criteria

A consecutive sampling technique was used and patients who were already operated on for oral cancer, underwent radio/chemo therapy for oral cancer, with recurrent cancer and patients who failed to submit sufficient information were excluded from the study.

Specific Objectives of the study were to identify current demographics of oral cancer with risk factors, types, histopathological types and presenting varied and as well as specific grades and stages.

Ethical clearance was duly obtained from the Institutional Review Board of Universal College of Medical Sciences and Departmental permission for the study was granted. The informed written consent was taken from each patient included in the study. A standardized data collection sheet was used to collect the data. Collected data was summarized and analyzed by Statistical Package for the Social Sciences (SPSS) Version 24.0 and results were presented and tabulated in table form and the level of significance Chi square test was used to test the statistically significant differences with level of p-value<0.05 considered to be statistically significant.

Results

The study was carried out in 500 patients of which 78.26% were male patients and 21.74% were female patients. The most common site was buccal mucosa 97(59.9%). Other characteristics are duly depicted in Table 1.

Table 1. *Gender Characteristics of Patient and Prevalent Site of OPMD*

Gender Characteristics & Site Prediction		**n (%)**
Gender	Male	78.26%
	Female	21.74%
Intraoral site and location of OPMDs Oral Potentially Malignant Disorders	Mandibular Lower alveolus	10.5%
	Buccal mucosa	19.0%
	Gingivobuccal sulcus	15.4%
	Lower lip	20%
	Lip and palate	23%
	Lateral border of Tongue	13%
	Retromolar area	16%
	Maxillary alveolar mucosa	10%

The lateral border of the tongue was the most frequently affected anatomical site 13%, followed by the lower lip 20%, buccal mucosa/vestibule 19.0%, mandibular alveolar mucosa 10.5%, and maxillary alveolar mucosa 10% respectively.

Leukoplakia predominantly represented 82% of the sample, followed by actinic chelitis 12%, and speckled leukoplakia 6%. Pure erythroplakias were not found in the sample. Ulceration was described in 10%.

The mean size of the leukoplakias was approximately 13 mm (ranging from 1 to 100 mm) and the mean size of speckled leukoplakias was 15 mm (ranging from 5 to 30 mm) (p=0.460). With regard to smoking and drinking, 53% of the patients were smokers/ex-smokers and 30% were drinkers.

Approximately 63% of the males and 46% of the females reported smoking (p=0.001), and approximately 48% of the males and 15% of the females reported drinking (p<0.0001).

Histological analysis showed that 49% showed no dysplasia, and 28%, 12%, and 11% showed mild, moderate, and severe epithelial dysplasia, respectively. The anatomical distribution of lesions showed statistically significant differences according to the sex of the patient (p<0.0001).

The mean age of the patients did not show statistically significant difference with regard to the anatomical location of the lesions (p=0.207). The anatomical distribution of the lesions according to the final diagnosis showed statistically significant difference between leukoplakia and speckled leukoplakia (p<0.001).

Among the OPMDs diagnosed oral leukoplakia, speckled leukoplakia, and actinic cheilitis presented ulceration in 9%, 10%, and 18% of the cases, respectively (p=0.03). The distribution of the different degrees of dysplasia showed statistically significant difference between the various anatomical sites were the lesions were found (p=0.002). The floor of the mouth and ventral tongue were the anatomical sites with the greatest percentage of cases with moderate and severe dysplasia.

Oral leukoplakias and speckled leukoplakia's presented moderate or severe dysplasia in 15% and 41% of the cases, respectively (p<0.0001).

The distribution of the different degrees of dysplasia among the various age groups showed that patients aged between 41-60 years, 61-80 years, and older than 80 years presented moderate and severe dysplasia in 24%, 27%, and 30% of the lesions, respectively, contrasting with the patients younger than 40 years old (p<0.001).

Discussion

OPMDs are relatively common, with a worldwide prevalence of 4.4%, while leukoplakia alone has a prevalence of 4.1%.

Numerous studies on OPMDs have been conducted worldwide in the past few years (Kumar 2015, Kavarodi 2014, Hassona 2014, Foy and Bertulos 2018, Dionne 2015, Muller 2018), though not much of these studies focused on Nepalese populations in Province V region.

Knowledge of the social-demographic profile of patients with OPMDs in a given population is important for understanding the most prevalent risk factors and for outlining prevention and early diagnosis strategies (Mello et al. 2018a, Queiroz 2014, Liu et al. 2011, Porter 2018, Pires 2013).

In the present study, male patients made up 78.26% of the sample the predominance of male patients has also been observed in previous studies on Indian and South East Asian subcontinent populations conducted by Adhikari et al. (2015), Rahman et al. (2018), Habib et al. (2017), in other worldwide studies conducted by Liu et al. (2011), Mello et al. (2018b), and Hussein (2017). However, this predominance was not observed in several studies involving different populations (Gheno 2015).

Over 80% of the patients were aged between 41 and 80 years, which highlights the connection between age and increased risk for developing OPMDs, as previously reported in the scientific literature (Queiroz 2014, Pires 2013).

It is important to note that the age distribution observed in the present study was similar to a descriptive study that evaluated 346 cases of SCC between 2005 and 2012 in accordance with Avon and Klieb (2012). In our study, the age of the patients did not show a statistically significant difference with regard to the anatomical site where the lesions were found.

Leukoplakias are the most common oral OPMDs, with a worldwide incidence between 2 and 4% (Martin 2012, Nun 2009, Saba et al. 2011). In the present study, 82% of the patients had a diagnosis of leukoplakia, similarly to a previous study on a South East Asian Bangladeshi population in accordance with findings from Kumar et al. (2016), and Sultana and Malik (2014).

None of the cases in our sample were diagnosed as pure erythroplakia, possibly due to the lack of precise clinical correlation required for a lesion to be classified as pure erythroplakia. Cases of oral lichen planus were excluded from our sample, due to the difficulties in distinguishing its clinical features from other OPMDs. Some earlier studies have included cases diagnosed as dysplastic oral lichen planus

(Shah 2009, Anis 2013, Dhanuthai 2017), but lacked detailed individual histological information to document the malignant transformation process in those lesions.

In the present sample, leukoplakia and speckled leukoplakia were more frequent in females in all anatomical sites, except for the lips. Furthermore, the frequency of moderate/severe dysplasia in lesions of the lower lip was greater than the frequency of moderate/severe dysplasia in most of the other anatomical sites, which corroborates the findings from previously done studies (Adhikari 2015, Rahman 2018, Rai et al. 2016).

A comparison between the mean size of leukoplakias and speckled leukoplakias did not show a statistically significant difference. This finding suggests that the presence of erythroplakia does not appear to be part of the natural evolution of OPMD. Therefore, the size of the lesion alone is not an indicator of its potential for malignant transformation. Nonetheless, Speight et al. (2018) listed lesion size greater than 200 mm^2 as a clinical parameter associated with increased risk of malignant transformation in OPMDs.

The tongue – especially the lateral border – was the most frequently affected anatomical site, a finding that is in agreement with other studies. This site was also most frequently affected by SCC, according to an earlier study carried out with the same population. Other studies including from Anis (2013). However, reported greater frequencies of buccal mucosa or alveolar mucosa involvement.

This may be due to population variations, difficulty in distinguishing leukoplakia from other lesions (for example, reactional hyperkeratosis) clinically or pathologically, or even inclusion of oral lichen planus lesions in the sample.

The degree of dysplasia is based on structural and cytological characteristics of the epithelium and is one of the findings commonly used to evaluate the risk of malignant transformation in OPMDs.

Half the lesions included in this study showed no epithelial dysplasia on histological analysis but were still considered OPMDs as the clinical aspect was compatible with leukoplakias or leuko-erythroplakias and they could not be diagnosed as any other oral lesions. In the present study, comparison of the anatomical location and degree of dysplasia showed that most of the lesions found on the lateral border of the tongue either did not present dysplasia or only presented mild dysplasia 52% and 28% of the cases, respectively.

The floor of the mouth and ventral tongue were the anatomical sites with the greatest percentage of moderate 23% and severe dysplasia 16%. These results are in agreement with previous studies on South East Asian population and reinforce the notion that OPMDs located on the tongue and on the floor of the mouth have higher risk of malignant transformation (Kumar 2016, Sharma 2018).

Accordingly, these anatomical sites deserve special attention because they are the most commonly affected by squamous cell carcinoma (SCC) in this population.

The frequency of severe epithelial dysplasia increased as patient age increased; no correlation with age was observed for lesions with mild or moderate dysplasia. This finding supports the theory that the malignant transformation process is slow and gradual over the years, and that older patients are at greater risk for malignant transformation than their younger counterparts.

In addition, analysis of the degree of dysplasia based on the clinical aspect of the lesions revealed that leukoplakias and speckled leukoplakias presented moderate or severe dysplasia in 15% and 41% of the cases, respectively ($p<0.0001$), similarly to the findings from previous studies (Pires 2013, Saba et al. 2011, Dhanuthai et al. 2017, Sharma et al. 2018).

Conclusion

In conclusion, in Nepalese population oral leukoplakias were the most commonly observed OPMDs, followed by oral submucous fibrosis. The lateral border of the tongue, the lower lip, and the buccal mucosa/vestibule were the most frequently affected anatomical sites. Lesions found on the floor of the mouth/ ventral tongue presented the highest frequency of severe epithelial dysplasia, and the highest frequency of severe epithelial dysplasia was observed in older patients.

The prevalence study emphasizes the deleterious effects of tobacco use on oral mucosa and also serves as a path for future tobacco cessation programs that would be helpful to prevent OPMDs in the Nepalese population, especially in Province V (Rupandehi District) of Nepal.

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