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The description of diagnosed cases of oral epithelial dysplasia at the Tygerberg Oral Health Centre

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NC Nkomo,[1] A Jeftha,[2] F Kimmie-Dhansay,[3] J Opperman[4]

ABSTRACT

Oral epithelial dysplasia (OED) is a growth anomaly which occurs due to atypical proliferation, change in the architectural and cytological features of cells of epithelial origin, resulting in the formation of a lesion with disturbed differentiation and maturation.

The purpose of this study was to describe the OED cases diagnosed at Tygerberg Hospital in a seven-year period (from 2012 until 2019) and to determine the demographics and clinical location of these cases. The patients' medical records from the National Health Laboratory Service (NHLS) were reviewed. All diagnosed cases of OED were identified, and the data retrieved for further assessment and comparison.

Seventy cases of OED were diagnosed in the period assessed. Of those cases, the median age was 58 and the interquartile range was between 48 and 62. Thirty-six of the diagnosed patients were female and 34 were male. Most of the lesions diagnosed with OED were found on the tongue, floor of the mouth and buccal mucosa. Majority of the mild cases of OED existed in smokers (59.4%) and non-alcohol consumers (60%); however, there was no association between smoking (p=0.607) and OED severity. There was a statistically significant association between alcohol consumption and OED severity (p=0.021) (Table I).

From the results, it was derived that majority of the cases were mild and the most common location was on the tongue. Moreover, there was an association between alcohol consumption and OED severity (p=0.021).

Authors' information
1. Dr Nocwaka Charlotte Nkomo, *BChD*, *PG dipl*. aesthetic dentistry, *Msc* Oral medicine (UWC), Junior dentist, Department of Oral Medicine and Periodontology, University of the Witwatersrand, Johannesburg, South Africa
   ORCID: 0009-0007-3854-1696
2. Prof Anthea Jeftha, *BChD*, *MChD* (Oral Medicine and Periodontology) (UWC), Department of Oral Medicine and Periodontology, Faculty of Dentistry, University of the Western Cape, Cape Town, South Africa
   ORCID: 0000-0003-0910-5899
3. Dr Faheema Kimmie-Dhansay, Department of Community Dentistry, Faculty of Dentistry, University of the Western Cape, Cape Town, South Africa
   ORCID: 0000-0003-2919-6193
4. Dr Johan Opperman, Department of Craniofacial Biology, Pathology and Radiology, Faculty of Dentistry, University of the Western Cape and NHLS
   ORCID: 0000-0002-9684-6670

Corresponding author
Name: Dr N Nkomo
Email: nocwaka.nkomo1@wits.ac.za

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INTRODUCTION

Oral potentially malignant disorders (OPMDs) are defined by the WHO Collaborating Centre for Oral Cancer Workshop in 2020 as "any oral mucosal abnormality that is associated with a statistically increased risk of developing oral cancer". The term embraces precancerous lesions and conditions referred to in earlier World Health Organization (WHO) definitions.[1]

Some OPMDs may present with oral epithelial dysplasia (OED), and it has been widely used as a marker for risk assignment, in the prediction of malignant transformation and, consequently, the prognosis of OPMDs. The common lesions that may present with OED include, but are not limited to, oral submucous fibrosis, oral leukoplakia, erythroplakia, palatal lesions in reverse smokers, proliferative verrucous leukoplakia, lichen planus, discoid lupus erythematosus, actinic chelitis and certain genetic disorders, for example Xeroderma pigmentosum and Dyskeratosis congenita.[2]

The prevalence of OED is infrequently reported. In a retrospective study by Singh et al 2020 the mean prevalence of OED in the Indian population was 5.7%, while a study by Hsue et al 2007 reported a rate of 8.85% in the Taiwan population.[3,4] The variation in this reported prevalence could be attributed by variable risk behaviour across different geographic locations.[5] A retrospective study of 173 cases by Pereira et al 2011 from Brazil reported a rate of 1.8%.[5]

Most oral cancers are preceded by potentially malignant disorders; 50% of all cancers develop from precursor lesions.[7] The five-year survival rate of oral cancers in most countries is below 50%.[6] This high failure rate is due to the delay in the diagnosis and the emergence of secondary tumours.[6] Enhancing understanding of the progressive, multistep genetic changes involved in tumour formation, invasion and metastasis, as well as raising awareness about the epidemiology of OED and OSCC, is crucial. It is equally important for clinicians to identify, diagnose and monitor OPMDs, which can lead to more effective treatment plans, ultimately reducing mortality and improving quality of life.[7]

Aims and objectives

This cross-sectional study aimed to describe OED cases over a seven-year period and analyse the link between the clinical appearance of the cases with other factors such as patient demographics and risk indicators.

Design, materials and methods

This cross-sectional study analysed all OED diagnoses at Tygerberg Hospital National Health Laboratory Service between 2012 and 2019. All cases of diagnosed OED were identified, and the files of patients seen at UWC Faculty of

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Dentistry, Oral Health Centre were retrieved. The individual medical records were assessed. All patients who were diagnosed with OED by an oral pathologist between 2012 and 2019 were included in this study. Patients previously diagnosed with head and neck cancer and those with incomplete data were excluded.

The following data were extracted from pathology reports and available patient files – OED grading, the patients' demographics (age and sex), smoking and drinking habits, relevant clinical information which included the date of diagnosis and location of lesion.

The pathology diagnosis for the OED cases was done by different oral pathologists. A smoker was defined as one who smoked tobacco cigarettes at the time of diagnosis, and an alcohol user was defined as any individual who consumed alcoholic beverages, regardless of the frequency and type. The age referred to the chronological age, recorded in years. Age was presented across four groups (<44, 45-54, 55-64, >65 years) for easier reporting. The grading of OED was done using the WHO 2017 classification. The three-tier WHO 2017 classification classifies dysplasia into mild, moderate and severe. In mild dysplasia, the architectural and/or cytological changes are confined to the lower third of the epithelium, while moderate dysplastic changes extend to the middle third of the epithelium and severe dysplastic changes extend beyond the middle third and may affect the entire epithelial thickness.[1]

Summary statistics was performed using frequencies and percentages. Associations between the variables were performed using a Chi-squared or Fishers' exact test. A multinomial regression was performed to detect associations between risk indicators and the severity of OED. All tests were deemed statistically significant at $p<0.05$. All statistical tests were conducted using StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC.

Approval to conduct this study was obtained from the Biomedical Research Ethics Committee of the University of the Western Cape, BM19/10/4 and from the NHLS.

Results

Overall, 99 cases of OED were diagnosed in the 2012 to 2019 period. However, 29 cases were excluded due to incomplete data (smoking history, missing files or incomplete information in the file). Only 70.7% (n=70) of the overall cases were analysed. The median age of the participants was 58, with an interquartile range from 48 to 62. The youngest participant was 11 and the eldest was 82. OED was classified as mild (40 (57.1%)), moderate (19 (27.1%)) or severe (11(15.7%)). The WHO 2017 classification was used in the grading.

Table I: Degree of oral epithelial dysplasia and various factors

		DEGREE				
		MILD	MODERATE	SEVERE	Total	p-value
Sex	Female	21 (58.3)	10 (27.8)	5 (13.9)	36 (51.4)	0.911
	Male	19 (55.9)	9 (26.5)	6 (17.7)	34 (48.6)	
Age category	<44	11 (73.3)	3 (20)	1 (6.7)	15 (21.4)	0.246
	44-54	13 (68.4)	2 (10.5)	4 (21.1)	19 (27.1)	
	55-64	9 (45)	7 (35)	4 (20)	20 (28.6)	
	65+	7 (43.75)	7 (43.8)	2 (12.5)	16 (22.9)	
Location	Alveolar ridge	1 (50)	0 (0)	1 (50)	2 (2.9)	0.683
	Buccal mucosa	10 (71.4)	3 (21.4)	1 (7.1)	14 (20.0)	
	FOM	4 (50)	2 (25)	2 (25)	8 (11.4)	
	Gingiva	2 (50)	2 (50)	0 (0)	4 (5.7)	
	Lower lip	4 (80)	1 (20)	0 (0)	5 (7.1)	
	Maxilla	0 (0)	0 (0)	1 (100)	1 (1.4)	
	Oral mucosa	2 (50)	2 (50)	0 (0)	4 (5.7)	
	Palate	1 (50)	1 (50)	0 (0)	2 (2.9)	
	Retromolar area	1 (50)	1 (50)	0 (0)	2 (2.9)	
	Tongue	14 (51.9)	7 (25.9)	6 (22.2)	27 (38.6)	
	Upper lip	1 (100)	0 (0)	0 (0)	1 (1.4)	
Alcohol	N	27 (60)	15 (33.3)	3 (6.7)	45 (64.3)	0.021
	Y	13 (52)	4 (16)	8 (32)	25 (35.7)	
Smoker	N	21 (55.3)	12 (21.6)	5 (13.2)	38 (54.3)	0.607
	S	19 (59.4)	7 (21.9)	6 (18.8)	32 (45.7)	

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There were 51.4% (n=36) females, and the majority of the participants were older than 44 years of age. The most common location was the tongue, the exact location on the tongue was not specified. Almost 36% (n=25) were alcohol consumers and almost 46% (n=32) were smokers. There was no statistically significant association between degree of OED and age ($\chi2 = 0.946$), sex ($\chi2 = 0.1866$), alcohol usage ($\chi2 = 0.021$) or age category ($\chi2 = 0.561$).

Table II: Degree of oral epithelial dysplasia diagnosis by risk indicators

Degree	Odds ratio (95% Confidence Interval)	p>z	95% conf. interval	
Smoker Yes	0.756 (0.26 to 2.24)	0.613	0.255	2.236
Sex Male	0.966 (0.4 to 2.28)	0.949	0.339	2.751
Alcohol Yes	2.026 (0.7 to 5.94)	0.198	0.691	5.940
Age 44-54	1.309	0.731	0.283	6.051
55-64	3.079	0.127	0.726	13.069
65+	2.366	0.264	0.522	10.729
/cut 1 /cut 2	1.001 2.478		-0.208 1.146	2.210 3.811

There was no association between smokers, non-smokers and OED degree OR 0.756 (0.26-2.2.4). There was no association between sex and OED degree OR 0.966 (0.4-2.28). There was also no association between alcohol usage and age category.

For subjects who are in the 55-64 year age group relative to subjects who are below 44, the OR for moderate and severe dysplasia to mild dysplasia would be expected to increase by a factor of 3.079.

The tongue has the highest prevalence at 27 (38.57%), followed by the buccal mucosa at 14 (20%), then the FOM at 8 (11.43%). The upper lip and maxilla presented the least frequently with OED of 1 (1.43%) each. The tongue presented with the highest number of cases, but the three degrees of dysplasia was equally represented ($\chi2=0.683$).

Forty-five (64.3%) of the patients did not consume alcohol while 25 (54.3%) of the patients consumed alcohol. Therefore, there were more non-alcohol consumers diagnosed with OED than alcohol consumers. Thirty-eight (54.29%) of cases were found in non-smokers while smokers had 32 (45.71%) of the cases.

DISCUSSION

The difficulty of accurately classifying and diagnosing OED has been repeatedly highlighted and identified as an inherent limitation of any OED study.[2,3,7,9-11] The inconsistencies among observers and within the same observer are largely due to the challenges of accurately classifying and diagnosing OED, as pathologists' evaluation of specimens depend heavily on their training and past experiences.[8] The validity, uniformity and reproducibility is therefore affected. Most pathologists are familiar with the WHO 2005 grading system; this interferes with correlative accuracy and subjective judgment.[9,10] The current data set was diagnosed by various oral pathologists and hence no inter or intra observer calibration could be conducted due to the retrospective study design.

Moreover, the lack of reproducibility and consistency affects the predictive and prognostic value of grading OED. Inadequate biopsy sampling and cytological alteration due to sampling methods also affects the grading. Field mapping, the use of blade biopsies and taking multiple biopsies have been suggested to overcome this.[9-11]

The WHO 2017 and binary systems (which categorises OED into high risk and low risk) are the most reproducible systems when used between calibrated pathologists. It has also been suggested that continuous and ongoing calibration and consensus meetings, the merging of severe OED and carcinoma in situ categories, holding internal and external quality assurance programmes and the use of single centre design for OED-related studies can help improve reproducibility.[9-11]

In our study OED cases peaked in the fifth and sixth decades and had a female predilection. The age peak differs from most studies except that of Mincer et al, 2020 which reported a similar peak pattern.[3] The sex predilection of OED is consistent with the study done by Pereira et al, 2011, but in contrast with most studies that reported a male predilection.[5]

In a study of South African-related cancer statistics between 2008 and 2018, the cancer incidence was found to have reduced in the above-mentioned period; however, the associated mortality rate seems to be rising.[12] It is therefore important for clinicians to continually screen patients they see daily to allow for early detection and treatment, therefore improving the cancer-related morbidity and mortality rates. According to Stats SA, in 2018 the lip, oral cavity and pharynx accounted for 2.6% of all malignancies.[12]

Alcohol and smoking are known risk factors for the development of oral squamous cell carcinoma and have a synergistic effect when combined.[8] However, alcohol consumption does not appear to be an independent risk factor. The risk of OED development declines with smoking cessation.[8]

In our study, there were no statistically significant associations with smoking or with alcohol. In the literature, there are inconsistent results, with both negative and positive relationships.[13,14] This has led to the conclusion that the relationship between alcohol and OED, therefore, is not well established. The risk associated then depends on the level of alcohol consumption; the type of alcohol is irrelevant.[13,14] This is a limitation of our study, as the level of alcohol consumption was not measured.

Forty-one percent of patients with OED were identified as non-smokers and non-alcohol consumers. This was much higher than the 4.4% reported by Farshadpour et al, 2007.[15] Wey et al, on the other hand, reported a much higher figure at 31%[16] – this was, however, still lower than our study.

Human papillomavirus (HPV) infection is well known to be associated with head and neck cancers. HPV-associated head and neck cancers are related to sexual behaviour.[17]

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The prevalence of oral and oropharynx HPV infections has been studied globally, but there is a lack of substantial data from sub-Saharan Africa, specifically South Africa.[18] There is an increasing trend of HPV associated cancers among young individuals; there is, therefore, a need for general public awareness programmes and clinician-based patient education on the link between sexual behaviour, high risk HPV transmission and cancer development.[21]

The use of potentially carcinogenic leaf products such as areca nut, with/or without tobacco, adds to the complexity of aetiological factors for oral cancer in South Africa. It has been reported that up to 93% of adult South African Indian women chew areca nut/quid.[23]

Despite advances in research and surgical techniques, the five-year survival rate for OSCC remains low, with a rough estimate of 50%.[19,20] The high morbidity and mortality rates emphasise the importance of routine systematic extraoral and oral mucosal examinations in dental practices, screening programmes and techniques for early detection of malignancy. Although screening programmes have been highly criticised and often found to be ineffective, they have good outcomes in poor health resourced areas.[21]

Routine oral mucosal examinations should place an emphasis on the systemic tactile and visual oral examination, the use of adequate illumination (bright light), proper use of the dental mirror, retraction of the tongue and adequate prompt referrals should any abnormalities be detected.[21,22] Clinicians should be on the lookout for change in colour and soft tissue texture and consistency, the presence of high risk OPMDs, altered taste and non-healing ulcers. The presence of patient associated risk factors such as smoking, alcohol consumption, betel nut chewing, family history of oral cancer and chronic sun exposure should also be considered. By remaining vigilant about these clinical features and monitoring high risk lesions, clinicians can significantly contribute to the early detection and management of OPMDs.[21,22]

Rigorous follow-up of patients diagnosed with oral epithelial dysplasia is essential to assess for malignant transformation, early detection and intervention.[19,20] Early diagnosis and intervention, in turn, improves the overall life expectancy and quality of life due to less invasive treatment regimes.[19,20] Moreover, South Africa has a major health disparity challenge. Approximately 20% of the population has access to private medical care, while 80% of the population uses public (government) healthcare facilities.[12] The public sector system is therefore overburdened. Currently, most patients present quite late[19,20] and those diagnosed with OED do not follow rigorous follow-up protocols because this follow-up is often difficult in resource poor settings and among patients who hail from resource constraint backgrounds. This also poses diagnostic challenges and the implementation of screening programmes due to lack of resources.

A mobile health platform (VULA app) was created in South Africa to link health care workers with specialists, facilitate screening, encourage early and timely referrals and, ultimately, support early diagnosis and improved prognosis outcomes. However, majority of healthcare workers are not using the platform.

Although our study did not link OED development to risk indicators, the study came with limitations and the role that risk factors play in the development of OED cannot be ruled out. There is, therefore, a need for effective preventive measures and public health interventions to educate the community about the importance of prevention, limiting exposure to risk factors and the importance of follow-up visits. Moreover, oral health promotion can help increase screening and facilitate earlier detection of lesions.

CONCLUSION

Despite the decrease in the number of diagnosed OSCC cases, the mortality rate remains high in South Africa. There is, therefore, a need for more studies on associated risk factors, especially the prevalence of the highly rising oral and oropharynx HPV infections. The public and health care practitioners need to be educated on the importance of early detections of OPMDS, with rigorous follow-up to allow for assessment of malignant transformation and early intervention.

Declaration

The study was self-funded and there are no possible financial interest/s or incentives in products or service.

Conflict of interest

There are no conflicts of interest

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