



## **Association of Microbiota with Oral Potential Malignant Disorder: A Mini Review**

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### **Authors' contributions**

*This work was carried out in collaboration between both authors. Both authors designed the experiments and wrote the manuscript. Both authors read and approved the final manuscript.*

### **Article Information**

DOI: 10.9734/JPRI/2021/v33i47A33064

*Editor(s):*

(1) Takashi Ikeno, National Institute of Mental Health, National Center of Neurology and Psychiatry, Japan.

*Reviewers:*

(1) Nalini Doppalapudi, CHC, USA.

(2) Cláudia Roberta Leite Vieira de Figueiredo, Universidade Federal da Paraíba, Brazil.

Complete Peer review History: <https://www.sdiarticle4.com/review-history/76531>

**Mini-Review Article**

**Received 24 August 2021**

**Accepted 28 October 2021**

**Published 29 October 2021**

### **ABSTRACT**

Most of the oral squamous cell carcinoma (OSCC) are often preceded by oral potentially malignant disorders (OPMDs). OPMDs are defined as oral mucosal lesions and conditions which are at increased risk for undergoing alteration to oral cancer. OPMDs grow in a complex tissue microenvironment to acquire oral squamous cell carcinoma (OSCC) characteristics. Oral microbiota associated with OPMD may appear as potential biomarkers as these species may help in the diagnosis and prognosis of OPMD to OSCC. This association of microbiota to OPMD and may be helpful in the early treatment before the initiation of oral cancer. This article reviews the literature on association between microbiota and Oral potential malignant disorders.

*Keywords: Oral potential malignant disorders (OPMD); microbiota; pre-cancer; biomarkers.*

### **1. INTRODUCTION**

92-95% of carcinoma of oral cavity are squamous in nature [1]. Most of the OSCC are

preceded by oral potentially malignant disorders [2,3]. World Health Organization defined potentially malignant disorders (PMDs) as Oral mucosal disorders with increased risk of cancer

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transformation [3] Oral potentially malignant disorders (OPMDs) are defined as oral mucosal lesions and conditions which are at increased risk for undergoing alteration to oral cancer [4]. OPMDs includes Leukoplakia Erythroplakia, oral lichen planus, oral submucous fibrosis, discoid lupus erythematosus, actinic cheilitis, palatal keratosis associated with reverse smoking, epidermolysis bullosa and dyskeratosis congenital [5]. The more frequent oral potential malignant disorders are leukoplakia, erythroplakia, and oral submucous fibrosis. The cancer transformations of oral mucosal disorders including leukoplakia [6], erythroplakia [7], and submucous fibrosis [8] are well recorded.

Oral microbiota associated with OPMD may appear as potential biomarkers as these species allow the diagnosis of OPMD and may even permit early treatment before the start of oral cancer [9,10]. The malignant

transformation of OPMDs to oscc may be prevented by correct diagnosis and timely intervention [11].

OPMD exhibits diagnostic challenges and with the increased risk of cancer development not only complicates prognosis but also decreases treatment effectiveness [12-14].

It was noticed from the study that *F. nucleatum* can potentially promote tumor growth [15,16]. Even though microbes such as *F. nucleatum* can increase tumor development, many studies observed these lesions late in the malignant process and as there are lesser studies on review of oral microbiota associated with OPMD than with oral cancer, this review was done to know the association between oral microbiota and OPMD with the key question: "association of microbiota with oral potential malignant disorder".

**Table 1. Studies on association of microbiota and oral potential malignant disorder**

Authors	Year	Sample type	Microbial assessment platform	Major finding
MOK Shao Feng et al. [17]	2017	oral swab	16s rDNA Sequencing	<i>Prevotella melaninogenica</i> , <i>P. veroralis</i> <i>Megasphaera micronuciformis</i> in OPMD lesions
Divya Gopinath et al. [18]	2020	WMF	16s rRNA metagenomics	higher levels of <i>Bacteroidetes</i> were noticed in oral leukoplakia (LKP) samples
Abdrzak Amer et al. [19]	2017	Oral swab	qpcr	lower levels of <i>Firmicutes</i> and an increased levels of <i>Fusobacteria</i> in the oral leukoplakia patients
G. Decsi et al. [20]	2019	oral biopsy	metagenome sequencing	relative abundance of <i>Fusobacterium nucleatum</i> , was elevated and relative abundance of <i>Streptococcus mitis</i> was decreased in OPMD lesions.
Wang K et al. [21]	2016	Saliva	MiSeq sequencing	More levels of <i>Porphyromonas</i> and <i>Solobacterium</i> and <i>Prevotella melaninogenica</i> and with a significantly less <i>Cellulosimicrobium</i> , and <i>Campylobacter</i> were found in OLP patients
He Y et al. [22]	2017	Buccal scraping	high-throughput 454 pyrosequencing.	more levels of <i>Fusobacterium</i> , <i>Leptotrichia</i> and <i>Lautotrophia</i> in OLP lesions
M y chen et al. [23]	2020	saliva	high-throughput sequencing of the bacterial 16S rRNA gene	higher prevalence of <i>Fusobacterium</i> genera in pre- cancers
Pushkar et al. [24]	2012	oral tissue	16s rRNA Sequencing	<i>Megasphaera micronuciformis</i> in the tumor tissue in the oral cavity of patients with OPMD
MOK Shao Feng et al. [25]	2017	Oral swab	culture-independent 16S rRNA approaches	OPMD is associated with <i>firmicutes</i> and <i>bacteroidetes</i>
Sakamoto et al. [26]	2005	oral cavity	16S rRNA gene sequence analysis	OPMD is associated with <i>Prevotella multiformis</i>
Iwamo et al. [27]	2010	oral tissue	16s rDNA Sequencing	OPMD is associated with <i>Lactobacillus salivarius</i>

Authors	Year	Sample type	Microbial assessment platform	Major finding
mager et al. [28]	2005	whole unstimulated sample	checkerboard DNA-DNA hybridization	OPMD is associated with <i>Prevotella nigrescens</i>
Hooper et al. [29]	2007	aseptically macerated tissue	PCR	OPMD is associated with <i>Prevotella melaninogenica</i> , <i>Prevotella veroralis</i> in the tumor tissues positive for <i>Helicobacter. Pylori</i>
Oral cavity	pcr	Total of 23.6% of OLP and 20% of OL were		
Rajendran et al. [31]	2009	plaque sample	rapid urease test	Positive correlation between <i>Helicobacter. Pylori</i> load in plaque samples and mucosal inflammation in OSMF

## 2. CONCLUSION

Through this review, the main findings of the studies on oral microbiota associated with with oral potential malignant disorder have been summarized and with the results showing the association of bacteria with OPMD, it is concluded that oral microbiota have been found to be associated with oral potential malignant disorders. The studies summarized in this review has provided a lot of relevant data on the association of bacteria with OPMD and also help in improving the design of further studies.

## CONSENT

It is not applicable.

## ETHICAL APPROVAL

It is not applicable.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

## REFERENCES

- George A, Sreenivasan BS, Sunil S, Varghese SS, Thomas J, Gopakumar D, Mani V Potentially malignant disorders of oral cavity. OMPJ. 2011;2:95-100.
- Andre K, Schraub S, Mercier M, Bontemps P Role of alcohol and tobacco in the aetiology of head and neck cancer: A case-control study in the Doubs region of France. Oral Oncol Eur J Cancer 1995;31:301-309.
- Warnakulasuriya S, Johnson NW, van der Waal I: Nomenclature and classification of potentially malignant disorders of the oral mucosa. J Oral Pathol Med. 2007;36:575-580, .
- I. van der Waal, Potentially malignant disorders of the oral and oropharyngeal mucosa; terminology, classification and present concepts of management, Oral Oncology. 2009;45(4-5):317-323.
- Warnakulasuriya S, Johnson NW, van der Waal I: Nomenclature and classification of potentially malignant disorders of the oral mucosa. J Oral Pathol Med. 2007;36:575-580.
- Gupta PC, Mehta FS, Daftary DK, et al. Incidence rates of oral cancer and natural history of oral precancerous lesions in a 10-year follow-up study of Indian villagers, Community Dentistry and Oral Epidemiology. 1980;8(6):287-333.
- Bouquot JE, Whitaker SB. Oral leukoplakia—rationale for diagnosis and prognosis of its clinical subtypes or phases, Quintessence International. 1994;25(2):133-140.
- Murti PR, Bhonsle RB, Pindborg JJ, Daftary DK, Gupta PC, Mehta FS. Malignant transformation rate in oral submucous fibrosis over a 17-year period, Community Dentistry and Oral Epidemiology. 1985;13(6):340-341.
- Markopoulos AK, Michailidou EZ, Tzimagiorgis G. Salivary markers for oral cancer detection. Open Dent J. 2010;4: 172-8.
- American Cancer Society. Cancer Facts & Figures 2009. Atlanta: American Cancer Society. 2009;16.
- George A, BSS BSS, SS SS, Varghese SS, Thomas J, Gopakumar D, Mani V.

- Potentially Malignant disorders of oral cavity. OMPJ. 2011;2:95–100.
12. Jayam R. Oral Field Cancerization: A review. JIAOMR. 2010;22:201-5.
  13. Feller LL, Khammissa RR, Kramer BB, Lemmer JJ. Oral squamous cell carcinoma in relation to field precancerisation: pathobiology. Cancer Cell Int. 2013;13: 31.
  14. Slaughter DP, Southwick HW, Smejkal W. Field cancerization in oral stratified squamous epithelium; clinical implications of multicentric origin. Cancer. 1953;6:963-8.
  15. Rubinstein MR, Wang X, Liu, W, Hao Y, Cai G, Han YW. Fusobacterium nucleatum promotes colorectal carcinogenesis by modulating E-cadherin/b-catenin signaling via its FadA adhesin. Cell Host Microbe. 2013;14:195–206.
  16. Binder Gallimidi A, Fischman S, Revach B, Bulvik R, Maliutina A, Rubinstein AM, et al. Periodontal pathogens Porphyromonas gingivalis and Fusobacterium nucleatum promote tumor progression in an oral-specific chemical carcinogenesis model. Oncotarget, 2015;6:22613–22623.
  17. MOK Shao Feng, KARUTHAN Chinna, CHEAH Yoke Kqueen, NGEOW Wei Cheong, ROSNAH Binti Zain, YAP Sook Fan and Alan ONG Han Kiat, The oral microbiome community variations associated with normal, potentially malignant disorders and malignant lesions of the oral cavity. Malaysian J Pathol. 2017;39(1):1–15.
  18. Divya Gopinath, Rohit Kunnath Menon, Chong Chun Wie, Moinak Banerjee, Swagatika Panda, Deviprasad Mandal, Salivary bacterial shifts in oral leukoplakia resemble the dysbiotic oral cancer bacteriome, Journal of Oral Microbiology. 2020;13(1):1857998.
  19. Abdrazak Amer, Sheila Galvin, Claire Healy and Gary P. Moran .The Microbiome of Potentially Malignant Oral Leukoplakia Exhibits Enrichment for Fusobacterium, Leptotrichia, Campylobacter, and Rothia Species, Front. Microbiol. 2017; 8:2391
  20. Decsi G, et al. Chicken or the Egg: Microbial Alterations in Biopsy Samples of Patients with Oral Potentially Malignant Disorders, Pathology & Oncology Research,. 2019;25(3):1023-1033.
  21. Wang K, Lu W, Tu Q, Ge Y, He J, Zhou Y, et al. Preliminary analysis of salivary microbiome and their potential roles in oral lichen planus. Sci Rep. 2016;6:22943.
  22. He Y, Gong D, Shi C, Shao F, Shi J, Fei J. Dysbiosis of oral buccal mucosa microbiota in patients with oral lichen planus. Oral Dis. 2017;23(5):674–82.
  23. Chen MY, Chen JW, Wu LW, Huang KC, Chen JY, Wu WS, et al. Carcinogenesis of Male Oral Submucous Fibrosis Alters Salivary Microbiomes. J Dent Res. 2020;22034520968750
  24. Pushalkar S, Ji X, Li Y, et al. Comparison of oral microbiota in tumor and non-tumor tissues of patients with oral squamous cell carcinoma. BMC Microbiol. 2012; 12:144.
  25. Shao Feng, KARUTHAN Chinna, CHEAH Yoke Kqueen, NGEOW Wei Cheong, ROSNAH Binti Zain, YAP Sook Fan and Alan ONG Han Kiat, The oral microbiome community variations associated with normal, potentially malignant disorders and malignant lesions of the oral cavity, Malaysian J Pathol. 2017;39(1):1–15.
  26. Sakamoto M, Huang Y, Umeda M, Ishikawa I, Benno Y. Prevotella multiformis sp. nov., isolated from human subgingival plaque. Int J Syst Evol Microbiol. 2005;55:815-9.
  27. Iwamoto T, Suzuki N, Tanabe K, Takeshita T, Hirofuji T. Effects of probiotic Lactobacillus salivarius WB21 on halitosis and oral health: An open-label pilot trial. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2010;110:201-8.
  28. Mager DL, Haffajee AD, Devlin PM, Norris CM, Posner MR, Goodson JM. The salivary microbiota as a diagnostic indicator of oral cancer: A descriptive, non-randomized study of cancer-free and oral squamous cell carcinoma subjects. J Transl Med. 2005;3:27.
  29. Hooper SJ, Crean SJ, Fardy MJ, et al. A molecular analysis of the bacteria present within oral squamous cell carcinoma. J Med Microbiol. 2007;56: 1651-9.
  30. Kazanowska-Dygdala M, Duś I, Radwan-Oczko M. The presence of Helicobacter pylori in oral cavities of patients with leukoplakia and oral lichen planus. J Applied Oral Science. 2016;24:18–23.

31. Rajendran R, Rajeev R, Anil S, Alasqah M, Rabi AG. Helicobacter pylori coinfection is a confounder, modulating mucosal inflammation in oral submucous fibrosis. Ind J Dent Res. 2009;20(2):206-211.

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