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Review Article

Systematic Review on Oral Cancer

Kanwaldeep Singh Soodan[1]*, Pratiksha Priyadarshni[2], Mamit Kumar[1] and Siddhant Sharma[3]

[1]*Department of Oral and Maxillofacial Surgery, M M College of Dental Sciences and Research, Mullana, Haryana, India*

[2]*Dental Surgeon, India*

[3]*Post Graduate Student, M M College of Dental Sciences and Research, Mullana, Haryana, India*

***Corresponding Author**: Kanwaldeep Singh Soodan, Department of Oral and Maxillofacial Surgery, M M College of Dental Sciences and Research, Mullana, Haryana, India.

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Abstract

Oral cancer is the sixth most common cancer worldwide with a high prevalence in South Asia. The incidence varies widely reflecting geographic differences in exposure to risk factors. Genetic predisposition to oral cancer has been found in certain cases but its components are not yet entirely clear. The recent rise in younger age groups and females seen in many countries is of particular concern. Treatment and management of complications, local regional recurrence and further primary tumors result in high morbidity and mortality especially when the disease is advanced stage at initial diagnosis. The natural history of oral cancer seems to gradually evolve through transitional precursor lesions from normal epithelium to a full-blown metastatic phenotype.

Keywords: *Oral Cancer; Complications; Recurrence*

Introduction

Although the incidence of oral cavity cancer is not well documented since it is unfortunately often grouped with oropharyngeal subsites, it is thought to be the 8th most frequent cancer in the world among males and the 14th among females accounting for nearly 3% of all cancer cases [1]. Oral cancer is the sixth most common cancer worldwide. Life style, habits, and demographic as well as genetic factors influence geographic variations in incidence of oral cancer [2]. More than 92% of oral and pharyngeal cancers occur in individuals older than 40 years, with the average age being 63. Its incidence increases until the age of 70 to 74 and then declines slightly [3]. Once, a predominantly male disease, females have experienced a steady rise in the incidence of oral cancer since the increase in female smokers began in the 1950s [4-7]. Pain is a common symptom in oral cancer patients, representing 30 - 40% of their main complaints. Although pain is the main symptom, it usually arises only when the lesions have reached a remarkable size and is the time when the patient requests medical assistance. Thus, early carcinomas often go unnoticed because they are asymptomatic [8]. OSCC (oral squamous cell carcinoma) may appear in any location although there are certain areas in which it is more commonly found. The most common locations are the tongue and the floors of the mouth [9-13]. Advances in cancer research have provided abundant knowledge about cellular processes and molecular biology in OSCC. Oral cancer is twice as likely to develop in women as in men given the same amount of tobacco consumption [14]. It is thought that exposure to carcinogens leads to malignant transformation of cells. The deleterious effects of tobacco use and excessive alcohol consumption are well known [15]. There are approximately 1.1 billion smokers worldwide with 80% living in developing countries. The prevalence of OSCC in cigarette smokers is 4 - 7 times greater than in non-smokers [16, 17]. The majority of patients in whom oral cancer develops are consumers of alcohol. Multiple viruses have been implicated in the etiology of oral cancer including Epstein-Barr virus, herpes simplex viruses, retroviruses, and human papilloma viruses (HPVs). Human herpesvirus-8 is recognized as the most important pathogen in Kaposi sarcoma; although presence of the virus alone is not sufficient to cause malignancy [18]. The literature shows a broad range of oral HPV prevalence in oral cavity cancer because of the multiple techniques used for detection of the virus

which vary in sensitivity [19]. Detection rates are also higher in samples taken from frozen tissue than from paraffin embedded tissue [20]. The chronic iron deficiency seen in patients with Plummer-Vinson syndrome has been associated with a higher incidence of oral and hypopharyngeal cancer [21]. A deficiency in vitamins A, C and E has been associated with oral cancer [22]. Oral cancers have also been associated with low intake of fruits, vegetables and a protective role may be afforded by diets high in fruits, vegetables, and fiber [23,24].

Genetic evolution and tumor suppressor genes

Oral leukoplakia is a clinical diagnosis that describes white patches or plaques that cannot be attributed to any other disease. It is common especially in older men and is associated with a variable risk of underlying epithelial alterations depending on its location. Approximately 10 - 15% of oral leukoplakias will be diagnosed as mild or moderate dysplasia and another 5% may be diagnosed as severe dysplasia or carcinoma in situ [25]. Oral lichen planus is believed to be an autoimmune disease and the mechanism of its malignant conversion is not yet well understood. Oral erythroplakia is rare but has a very high risk of progression (14 - 50%) and is frequently diagnosed histologically as carcinoma in situ or severe epithelial dysplasia.

Another important area involves tumor suppressor genes that prevent cells from acquiring malignant characteristics and usually act in regulating discrete checkpoints during cell cycle progression, monitoring DNA replication and mitosis [26]. Inactivation of tumor suppressor genes can occur via epigenetic or genetic mechanisms.

Chemical carcinogens in tobacco smoke may contribute to the genetic mutations in TP53 [27]. The inactivation of the TP53 tumor suppressor signaling pathway is seen in most human cancers including OSCC.

Studies have also suggested that inherited genetic polymorphisms in the p53 pathway influence tumor formation, progression, and/or response to therapy [28]. In the same way, the expression of p16INK4A protein encoded by the CDKN2A suppressor gene is negative or low in up to 83% of OSCCs and up to 60% of pre-malignant lesions. Several studies have shown frequent CDKN2A gene mutations or the frequent loss of gene expression in oral lesions suggesting that it is an early step in oral carcinogenesis [29].

Toluidine blue and Lugol's iodine have been used as clinical aids to identify occult mucosal abnormalities and to demarcate the extent of a potentially malignant lesion prior to excision [30].

A variety of molecular tumor markers have been studied in the clinic for their potential to predict disease outcome or response to therapy in OSCC. However, none of these markers appears to provide definitive prognostic or predictive information. Additionally, it is unlikely that any one molecular factor determines the complete behaviour of a tumor and that the complex interaction among oncogenes and tumor suppressor genes cannot be ascertained through the analysis of a few molecular markers.

Most OSCCs exhibit limited responsiveness to chemotherapy involving cytotoxic drugs due to mechanisms that either block intracellular transport of these agents or interfere with their intracellular molecular targets [31]. In OSCC, surgery remains the primary treatment modality of choice except for inoperable cases. A better understanding of the molecular and biological profiles of OSCC and the molecular heterogeneity of the disease could facilitate the development of more efficient targeted therapies.

Conclusion

Oral cancer is the sixth most common cancer worldwide. Life style, habits and demographic as well as genetic factors influence geographic variations in incidence of oral cancer. Oral cancer is predominantly a disease of older age. Oral cancer is twice as likely to develop in women as in men given the same amount of tobacco consumption. Advances in treatment plan and diagnosis have slowly evolved with time that would help in management of cancer.

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