PAKISTAN JOURNAL OF HEALTH SCIENCES
https://thejas.com.pk/index.php/pjhs
Volume 1, Issue 1(Jan-Jun 2020)

Review Article

Risk Factors for Oral Squamous Cell Carcinoma

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How to Cite
Rafi, U. ., Kabir, M., Asif, H., & Kanwal, S. (2020). Risk Factors for Oral Squamous Cell Carcinoma. *Pakistan Journal of Health Sciences*, *1*(01). Retrieved from https://www.thejas.com.pk/index.php/pjhs/article/view/13

ABSTRACT

Oral Squamous Cell Carcinoma (OSCC) is a common cancer worldwide. Regular oral checkup is recommended for smokers and drinkers and preventive measures should be taken for discouraging and giving up the smoking. Persons who don't use tobacco and alcohol individually but in the combined form, they are at more risk, because the combination which raises the risk of oral cancer 15 times in users than non-users. Although tobacco smoking and alcohol intake are risk factors of oral cancer but their combined effects are more harmful as compare to individual ones. After tobacco smoking, HPV is the most common causative agent for oral cancer in the United States. Different types of HPV are associated with infections. Skin warts are also caused by human papillomavirus (HPV). The HPV infection is transmitted through many ways. The most important of which are prenatal. genital infections, through blood, shared objects and hands. If the objects are contaminated with HPV infection, and they are shared to one person to the other, then there is a possible chance of transmission of HPV. Fingers-genital contact is a unlikely to be a significant source but it is a possible way of HPV to be transmitted.

Keywords: HPV, Skin warts, Risk factors, Oral cancer, Smoking

INTRODUCTION

Squamous cells carcinoma of head and neck region is the 6th most common cancer about 12% worldwide [1]. Biologically nasal cavity, lip, oral, pharynx and larynx cancers are similar. Globally, with the passage of time a gradual increased incidences rate is observed [2]. The factors of developing HNSCC are both environmental and related to lifestyle that comprehends excessive alcohol and drug consumption, tobacco smoking(in forms of cigarettes and bubble pipes) [3], certain chemicals, ultraviolet light and strains of human papillomavirus [4]. Incidence rate of head and neck cancer among younger adults is also high. The chance of disease development gradually increases with age, 85% cancer patients in UK are more than the age of 50 [5].

According to the recent facts and figures issued by reliable sources risks of oral cavity cancers in French population are tobacco smoking (78.6%) and alcohol consumption (80.7%). Regular oral checkup is recommended for smokers and drinkers and preventive measures should be taken for discouraging and giving up the smoking [6]. It is not possible to conduct epidemiological study based on long term strategy because of non-

availability of records (of registration) of cancer cases at country level. According to the data, presence of HNSCC at locally based areas in Pakistan which highlights the HNSCC as the most common among all the malignancies [7].

Risk Factors

Cigarette Smoking and Alcohol Consumption

In western world, the tobacco and alcohol administration are main contributors of oral cavity cancers [8]. People who use to smoke tobacco are at risk six times higher than the people who don't smoke as it relates with the 75% of all cases of oral cancer, similarly alcohol drinkers carry 6-times more risk of oral cancer development than non-drinkers. Persons who don't use tobacco and alcohol individually but in the combined form, they are at more risk, because the combination which raises the risk of oral cancer 15 times in users than non-users. Although tobacco smoking and alcohol intake are risk factors of oral cancer but their combined effects are more harmful as compare to individual ones [9].

If alcohol and tobacco are taken in the combined form, then the combined effect of alcohol and tobacco exceeds the sum of their individual effects in causing HNSCC [10]. In a study conducted by Levi, it has been suggested that the use of cooked and raw vegetables gives the protection against HNSCC, in contrary to this the tumors of HNSCC proliferates by the excessive use of processed meat and red meat [11]. In another study on adult smokers, it has been seen that for the prevention of the development of HNSCC, vitamin E was not found [12].

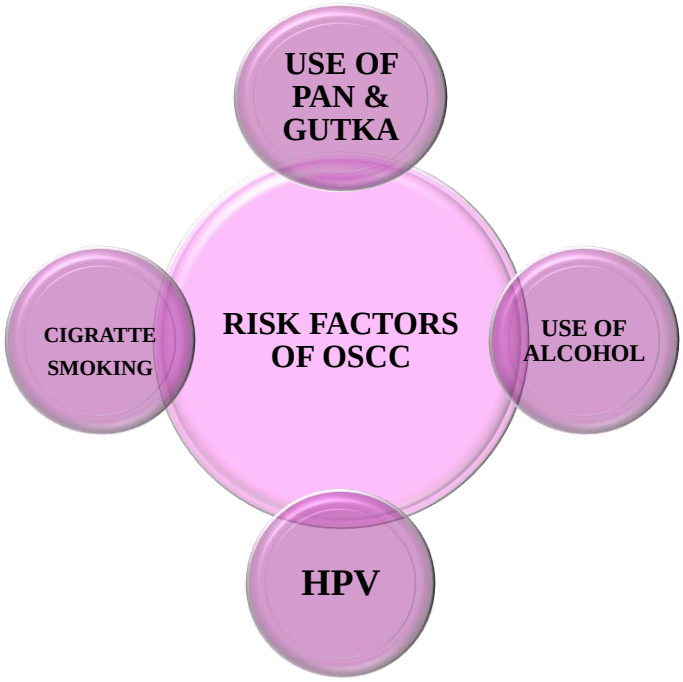

Figure 1: Major risk factors of OSCC

Use of Pan, Gutka and Other Chewing Tobacco

Oral cancer occurs more frequently among who use to chew gutka, areca nuts, pan andbetal nutsin, tobacco and alcohol (a common practice among some people in India and Asia).

Human Papilloma Virus (HPV)

A small virus of DNA is named as Human papillomavirus. It is composed of an icosahedral viral particle. It has a genome of 8000 base pairs approximately surrounded by a protiencapsid [13]. In sexually transmitted infections and veneral diseases including vaginal intercourse, oral sex and anal sex, human papillomavirus has become more common in adults and accounts for 11% of cancer incidence in women worldwide [14,15].

Signs and Symptoms

The signs and symptoms of HPV are cancers, skin warts, respiratory papillomatosis, genital warts & in the immunocompromise [16].

Cancers

After tobacco smoking, HPV is the most common causative agent for oral cancer in the United States [17]. Globally HPV is major common cause of infectious cancers. A study conducted in 2002, from 5.2% of all new cancers, the approximate estimation comes out that the 561,200 new cases of cancers were caused by HPV throughout the world. Until now, there are many types of HPV, about more than 100 types have been discovered while over 40 types are those viruses which can cause infections in genital areas. In comparison of about 50% of all new cancers, 84% of cervical cancers were in the developing countries due to HPV cancers [18]. In HNSCC, HPV-positive oropharengeal cancers have found to be linked with HPV type 16 [19]. They are categorized by their association with cancer. These two different types comprehend different cancers i-e "High-risk" (are found on the cancer cells) types are oncogenic and can cause cervical cancer, oropharengeal cancer, cancer, penile cancer, vulvar & intraepithelial neoplasia of the anogenital region whereas common skin warts as well as genital warts along with their conditions are associated with "Low-risk" types of HPV (produce skin lesions). "Low-risk" types are non-onogenic & they can also cause the disease of the respiratory tract called respiratory papillomatosis, abnormalities of cervical cancer (benign or low grade) &anogenital warts. "Low-risk" types include type 6 & 11 while "High-risk" types include type 16, 18, 31, 33, 35, 39, 45, 51, 55, 58 and 59 [20,21].

Skin Warts

Different types of HPV are associated with infections. Skin warts are also caused by human papillomavirus (HPV) [22]. Skin warts are of different types i-e Plantar warts, Anogenital warts, Common warts, flat warts, Butcher's warts and Heck's disease. All these types are caused by the infections of different types of HPV. The types of HPV cause these types of infections are given in the following table:

SKIN WARTS	HPV TYPES
1. COMMON WARTS	HPV TYPES 2 & 4
2. PLANTAR WARTS	HPV TYPES , 3, 4, 27, 28, 58
3. FLAT WARTS	HPV TYPES 3, 10, 28
4. ANOGEITAL WARTS	HPV TYPES 6, 11, 42, 44
5. BUTCHER'S WARTS	HPV TYPE 7
6. HECK'S DISEASE	HPV TYPES 7 & 32

Table 1: Different HPV types that causes skin warts

In the immunocompromised

In some cases, human papillomavirus (HPV) has adverse effects due to the abnormal susceptibility of HPV of the skin. HPVs of the skin causes a highly autosomal recessive genetic skin disorder which is known as Epidermodysplasia verruciform is that results in the appearance of small sacle-like macules & papules on hands and feets. This hereditary skin disorder has the association with carcinoma of the skin at high risk. Epidermodysplasia verruciform is also called as Lewandowsky-Lutz dysplasia and is associated with HPV type 5 & 8 [22,23].

Respiratory Papillomatosis

Respiratory papillomatosis (Laryngeal papillomatosis or glottal papillomatosis) is a chronic disease caused by the HPV type (6 and 11) that occurs in both children and adults with no known cure [24]. Its distinctive feature lies in the proliferation of benign squamous papillomas within the compounded tissues and organs of the respiratory tract and digestive tract (aerodigestive tract) [25]. In this disease warts appears on many parts of the respiratory tract, skin and respiratory mucosal surfaces and is the most common cause of childhood hoarseness [26]. In some rare cases, these papillomas (warts) can progress to cancer but in some cases they need repetitive injury[27].

Genital Warts

About ninety percent genital warts are caused by HPV 6 and 11. They can also cause by many varieties of HPV types. In the United States, million cases of genital papillomatosis come out each year approximately. Genital warts are also called as anal warts or condylomataacuminata or venereal warts and they can give the clear visualizations, signs and symptoms of the genital HPV infections [28]. According to the histopathological view, the characteristic features of genital warts are the increase in size of dermal papillae which have perakeratosis and nucleur alterations that shows HPV infection. There are no DNA tests applicable for genital warts diagnosis because DNA tests has been used for the diseases [29].

Transmission of HPV

The HPV infection is transmitted through many ways. The most important of which are prenatal. genital infections, through blood, shared objects and hands [30].

Figure 2: Transmission of HPV

GENITAL INFECTIONS

Genital infections are those infections which occurs in the genital mucosa. There are 120 known species of human papillomavirus and the number of species which infect the genital mucosa is 51 and 3 sub types(Schmitt, Depuydt et al. 2013). Sexual activity is the main transmission of infections in genital area(Burchell, Winer et al. 2006).

Prenatal

Transmission of genital HPV-related disease from mother to child is rare, although during birth genital HPV diseases can be transmitted from mother to child. Juvenile-onset recurrent respiratory papillomatosis (JORRP) is a rare type of HPV infection that can be caused by the prenatal transmission of HPV types 6 and 11 with a rates of about 2 cases per 100,000 in the United States. In children, JORRP is normally present before the age of 5(Sinal and Woods 2005; Dyrstad and Rao 2008).

Blood

The common mean of non-sexual transmission of HPV infection is through blood transfusion. Blood transfusion is the most common mean in non-sexual transmission, although other non-sexual transmission means of HPV infections are not very common [30].

Hands

Hernandez studied the dominant hand and genitals of each person in 25 couples every other month for an average of 7 months. She concluded in her study that some couples are those in which the man's genitals infected the woman's hands, and in some cases in which the woman's hand infected the man's genital, one case where woman's genitals infected man's hand, some cases in which man infected his own hands and woman infected her own. This study of Hernandez shows that HPV is transmited between hands and genitals of the same person and sexual partners [30].

Shared Objects

If the objects are contaminated with HPV infection, and they are shared to one person to the other, then there is a possible chance of transmission of HPV. Fingers-genital contact is a unlikely to be a significant source but it is a possible way of HPV to be transmitted [31]. Sexual intercourse is the main reason of transmission of HPV infection in female genitals [32].

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