

Review Article

Epidemiological and clinical presentation of head and neck neoplasia: a review

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ABSTRACT

Head and neck squamous cell carcinoma (HNSCC) stand at the sixth position most, amongst all the malignancies worldwide. Neoplasms arising in the oral cavity, larynx, pharynx, salivary gland and nasal cavity are all included in the head and neck malignancies. More than 90% of malignancies of the oral cavity are squamous cell carcinomas (SCC). Among the four head neck cancer sub-sites combined, the mean age at the time of diagnosis has risen, in the last four decades. Studies have documented a male predilection. A small percentage of SCC cases are inherited or are familial. Cigarette smoking, alcohol consumption, betel quid chewing, poor nutrition, poor oral hygiene, HPV, Epstein-Barr virus and *Candida albicans* infections are the etiological agents who have the ability to cause HNSCC. Non healing ulcer, difficulty in swallowing, change in voice, swelling, sore throat- that doesn't get better- are the symptoms of head and neck cancers. Moreover, there may be unusual bleeding, facial swelling or difficulty in breathing.

Keywords: Head neck neoplasia, Epidemiology, Clinical presentation

INTRODUCTION

Globally, head and neck squamous cell carcinoma (HNSCC) is the sixth most frequently occurring cancer.^{1,2} Neoplasms emerging from oral cavity, salivary glands, larynx, pharynx and nasal cavity comprise the head and neck malignancies.^{2,3} Every year, approximately 63,000 new cases of HNSCC are reported.⁴ Squamous cell carcinoma is responsible for nearly 90% of the cases, among the wide spectrum of malignancies occurring in the head as well as the neck region.^{2,4} Generally it has a male predilection-with males being twice or four times more susceptible than women for the developing HNSCC.¹

The Indian council of medical research (ICMR) analysis reveals that, approximately 0.2-0.25 million new cases of

head and neck cancer are detected per year.⁵ "National cancer registry programme" provided the latest data, stating that roughly 1,392,179 patients were diagnosed with cancer in India, in 2020. Majority of the head and neck cancer cases (i.e., 66.6%), were diagnosed at the advanced stage.⁶

REVIEW OF LITERATURE

In India, one of the main health problems is head and neck carcinoma, and its management needs a strict detailed regimen and well qualified manpower.⁷ Among the total head and cancers diagnosed world-wide, 57.5% cases are from Asia, especially India.⁷ In India, head and neck cancers has a male predilection and is responsible for 30% of cancer cases among males and 11 to 16% among

females.

Carcinoma of the oral cavity is the most prevalent head and neck malignancy.^{7,8} In females, the occurrence of head and neck cancer has no specific age inclination, much variation is seen however in male majority cases are seen after the fifth decade of life, i.e., after 55 years.⁹

In 2017, a retrospective study conducted by global burden of diseases (GBD) among the total 678,900 LOCPs subjects, the most frequently reported carcinomas (57.4%) were the lip and oral cavity cancers, followed by other pharyngeal cancers (26.4%) and then nasopharyngeal carcinomas (16.2%).¹⁰ A dramatic decrease is noticed in the estimated global incidence of

Nasopharyngeal cancers, from 1990 to 2017 but an increase was observed in the incidence of lip and oral cavity cancers and other pharyngeal cancers. The incidence of head and neck cancers has a male inclination; this has been observed among all age groups.¹⁰

Geographically, the occurrence of head and cancer is varied and even varies according to site.¹¹ 90% of HPV-positive oropharyngeal malignancies are caused by HPV 16 and has a male predilection.¹²

SITES

Neoplasms emerging from oral cavity, larynx, pharynx, salivary gland and nasal cavity-all comprise the head and neck malignancies. The most commonly prevalent neoplasms are oral cavity tumors. More than 90% of the wide range of malignancies encountered in the oral cavity, is SCC. Origin of other malignant tumors could be from epithelium, connective tissue, minor salivary glands, lymphoid tissue, melanocytes or metastasis from a distant tumor.¹³

Liu et al retrospective study on 1,383 oral cavity squamous cell carcinoma subjects in Taiwan reported, that buccal mucosa (40.2%) was the most common site for the occurrence of SCC followed by tongue (30.2%).¹⁴

The Alam et al 850 head and neck cancer patient study reported, the oral cavity to be the predominant site for occurrence of cancer followed by oropharynx, larynx, hypo pharynx, nose, para nasal sinuses (PNS) and nasopharynx.¹¹

Stoyanov et al observed that the most common sites for occurrence of head and neck carcinomas in the decreasing order of prevalence was, larynx (30.37%), followed by lips and oral cavity (29.08%), pharynx (20.03%), salivary glands (10.94%), external nose and nasal cavity (4.69%), auricle and external ear canal (2.75%) and the sinuses (2.1%).

AGE DISTRIBUTION

Liu et al conducted a study on 1,383 patients of oral cavity squamous cell carcinoma in Taiwan. 52.9 years was the mean age of occurrence of oral cavity SCC.¹⁴

In study by Stoyanov et al among cases of head and neck cancer, the mean age at the time of diagnosis was 63.84±12.65 years; youngest patient was 14 years old and the eldest was 103 years of age at time of diagnosis.¹⁵

In the United States, from 1975 to 2016, Bajpai et al conducted a study on head and neck cancer patients to analyse their age distribution trends. The results revealed, that for the four HNC sub-sites combined, the mean age at the time of diagnosis increased, in the last four decades. Within each sub-site of HNC, similar trends were seen, however with the exception of oropharyngeal cancers.¹⁶

Fasnula et al conducted a study on 97 laryngeal cancer patients (mostly squamous cell carcinoma), observed 60.48±12.15 years as the mean age for occurrence of cancer.¹⁷

In a retrospective study by Gilyoma et al the results stated that at the time of diagnosis, patients were in the age range of 3-82 years; 42 years (IQR 40 to 60 years) was the median age. Majority of the cases were 24 years (69.7%).¹⁸

GENDER DISTRIBUTION

In Taiwan, Liu et al conducted a study on 1,383 oral cavity SCC patients, observed a male predilection (93.8% were males).¹⁴

In the study by Stoyanov GS et al among the cases of head and neck cancer, 76.41% were present in males and 23.59% in females; the male to female ratio was 3.24:1.¹⁵

In 2017, Stoyanov et al, observed among head and neck cancer cases, 23.59% were present in females and 76.41% in males. Thus, the male to female ratio was 3.24:1.¹⁵

In Tanzania Gilyoma et al conducted a study on 346 head and neck cancer cases, and documented their prevalence had a male predilection (67.6%).

GENETIC SUSCEPTIBILITY

A small percentage of SCC cases are inherited or are familial. Fanconi anemia, an autosomal genomic instability syndrome associated with bone marrow failure, leukemia, congenital defects and sensitivity to cross linking agents-constitute the syndrome etiology which predisposes the affected individuals to an increased risk of having HNSCC. However, initial case control studies reflected, a genetic susceptibility in non-syndromic families. The first degree relatives have a 3.5 times increased risk of developing HNSCC.¹⁹

According to genomic analysis by cancer genome Atlas (TCGA) in 2015, 17% of HIV-positive HNSCCs and 26% of HPV-negative HNSCCs cases reflected inactivating mutations in NOTCH1-3. The most common abnormalities in NOTCH 1 are miss sense mutations in functional areas, nonsense mutations in shorter proteins, and frame shift insertions or deletions. NOTCH 1 activation may play a role in the sustainability of cancer stem cell characteristics, via Wt signaling pathways, and promote recurrence and metastasis. Evidence of interaction between Notch and Wt signaling has been observed in different types of malignancies. The loss of notch signaling increased transcriptional activity of B catenin responsive reporter structure in cancer, stem and progenitor cells.

Through the catenin B-activation, NOTCH 1 and FAT1 inactivating mutations induce carcinogenesis in HNSCC. Although the loss of NOTCH signaling was shown to cause carcinogenesis in HNSCC by up regulating ANp63, but the exact pathway of Notch- ANp63 regulation remains unknown.²⁰

RISK FACTORS

Cigarette smoking, alcohol consumption, betel quid chewing, poor nutrition, poor oral hygiene, HPV, Epstein-Barr virus and *Candida albicans* infections are the etiological agents who have the ability to cause HNSCC.^{1,21,22}

Drinking alcohol and chronic smoking have been found to have a strong link with HNSCC. Because of this, approximately 80% of HNSCC patients are at increased risk.^{4,21}

The primary cause of HNSCC is the carcinogenic effect of cigarette smoking. The various forms of tobacco have harmful effects on human body including electronic cigarettes and water pipe smoking. They have a specific detrimental effect on head and neck cancers.^{23,24}

Smoking and alcohol consumption are the major risks for non HPV -associated oropharyngeal carcinomas.²²

Betel quid chewing, poor nutrition, asbestos exposure, marijuana smoking certain genetic mutations such as p53 mutation and CDKN2A (p16) mutations, diet deficient in fruits and vegetables-these all are the other risk factors for non HPV associated oropharyngeal carcinomas.²⁵

Young people, who don't drink and smoke, are more likely to have HPV- related oropharyngeal carcinomas.²⁵

Smoking, is the most significant risk factor for laryngeal carcinoma, and is accountable for nearly 70-95% of total cases.¹⁷ Patients having any history of smoking are at increased risk, although present smokers are at a relatively higher risk than ex-smokers. Smokers have a relatively higher risk of having supra glottic tumors in comparison to glottis tumors.¹⁷ Alcohol is also identified as a risk factor.

However, most of the cases have alcohol consumption accompanied with smoking, thus the independent effect of alcohol is unclear.¹⁷

Alam et al, conducted a study and observed, among the overall study population, 35.8% were males and the most common risk factor among them was tobacco smoking (37.3%), followed by tobacco chewing along with smoking (19%). Among females, tobacco chewing was the most common risk factor (34%), followed by smoking (16%), and then smoking along with tobacco chewing (14.2%).¹¹

Gilyoma et al in Tanzania conducted a study on 346 head and cancer patients and documented, cigarette smoking was the most common risk factor (76.6%) followed by heavy alcohol consumption (69.9%).¹⁸

CLINICAL PRESENTATION

Mouth, throat, larynx, sinus, salivary glands, nose cancers - comprise the group of head and neck cancers.²⁶

Non healing ulcer, difficulty in swallowing, change in voice, swelling, sore throat that doesn't get better- are the symptoms of head and neck cancers. Additionally, there may be unusual bleeding, facial swelling or difficulty in breathing.

Hoarseness is the classical symptom of laryngeal carcinoma and is usually a symptom of early presenting glottic cancers. Advanced disease is suggested by pain while swallowing and referred pain to ear.²⁷ However, the early symptom of supraglottic carcinoma could be pain while swallowing and it is the most frequently reported complaint. Hoarseness indicates advanced disease extending into glottis.

Firm, fixed, painless masses in neck represent nodal metastasis.

Aspiration, dysphasia, airway compromise, weight loss - these symptoms present late in all subtypes.²⁷

Fasunla et al conducted a study on 97 cases and documented the symptoms observed - hoarseness (97%), cough (92%), difficulty with breathing(91%) ,referred otalgia(18%) ,dysphasia (13%), feeling of lump In throat (11%), throat pain (7%), neck swelling (6%).¹⁷

Ulceration is the most common clinical complaint in the oral cavity, followed by swelling, pain and then burning sensation in oral cavity, followed by bleeding and dysphagia.²⁸ Asymptomatic erythroplakia patches may represent early oral squamous cell carcinoma, however ulcers and growth having irregular margins with induration represent advanced stages.^{1,29}

The site involved represents symptoms in oropharyngeal cancers and the common symptoms reported are ear pain, bleeding, and mobility of teeth, problems in breathing,

speech difficulty, dysphagia, trismus, parasthesia and problems using prosthesis.²⁹

In a retrospective study by Carpen et al among OPSCC patients presenting with complaints of dysphagia, neck mass pain, globus sensation. Among the HPV +/ p16+ patients, the most common presenting symptom was neck mass (53.1%). And among HPV-/p16- oropharyngeal cancers pain in head and neck area (60.0%) was the most common presenting symptom.³⁰

McIlwain et al conducted a study on oropharyngeal cancer patients and documented the most common symptoms were neck masses (44%) and sore throat (33%). Neck mass was initially more likely to be noticed by HPV- positive patients (51%) as compared to HPV-negative patients (18%). However sore throat was more likely to be noticed by HPV-negative patients (53% vs. 28%), even dysphagia (41% vs. 10%) or odynophagia (24% vs. 6%) were more prevalent in HPV-negative cases.³¹

Painless neck masses are the signs and symptoms of initial salivary gland tumors; however painful neck masses were the presenting symptoms of advanced stage patients.³²

Swelling in the area of ear, cheek, jaw, lip, or floor of mouth, difficulty in swallowing or wide mouth opening, weakness and numbness of face are other symptoms.³²

PHYSICAL EVALUATION

A complete head and neck examination should be done for patients presenting to primary care physician. Thorough examination of ears, nose, oral cavity and neck is needed. For assessing the presence of middle ear fluid or other ear pathology, otoscopic examination must be performed.³³ Serious complications may occur following the malignancies of nasopharynx namely Eustachian tube obstruction, creating negative middle ear pressure and serious effusions, which present with otalgia. In an adult, nasopharyngeal malignancy interfering with Eustachian tube function maybe suspected by the presence of unilateral otitis media. Suspicion for underlying head and neck malignancy may arise, if patient is complaining of otalgia in absence of any clinical ear abnormalities.³³

Complete detailed examination of nose and para nasal sinuses must be undertaken for patients complaining of unilateral epistaxis or unilateral nasal obstruction with a large tumor of paranasal sinuses or nasopharynx.³³

During the oral cavity examination, attention should be given to the floor of the mouth, entire tongue surface and the buccal mucosa. While examining oral cavity, denture wearers must remove their dentures. The lateral edges and dorsal surface of tongue are better visualized with; a piece of gauze is used to grasp the tongue. Proper palpation of oral cavity lesions is a prerequisite. On palpation-immobility may indicate invasion of underlying tissues and firmness an underlying mass. For palpating firm masses, a

digital oral examination is needed. It includes palpating the floor of mouth under the tongue and the tongue itself. White hyperkeratosis, non scrapable plaques or erythematous plaques represent leukoplakia and erythroplakia respectively, which are pre cancerous lesions of oral cavity.³³

Trismus, painful masses, palatal fullness, parapharyngeal fullness, overlying skin ulcerations or fistulas-these are presenting symptoms of advanced malignancies. Sub mucosal oral swelling with ulceration, nasal obstruction and bleeding are the presenting symptoms of minor salivary gland tumors occurring in nasal cavity or nasopharynx. Dysphagia, odynophagia, airway obstruction, Dyspnea on exertion and vocal hoarseness are indicative of minor salivary gland tumors in pharynx or larynx. The signs suspicious for malignancies are rapid growth, pain, facial nerve paresis and cervical lymphadenopathy.³²

ENDOSCOPIC EVALUATION

For the assessment of head and neck cancers endoscopy plays a very crucial role especially Triple endoscopy including nasal, pharynx, and larynx.^{34,35} Even for performing surgeries and biopsies endoscopy maybe used.³⁶ Endoscopy plays an important role for assessing the extent, accessibility and respectability of primary tumors.^{35,37} Pan endoscopy helps in diagnosing the altered mucosa of aero digestive tract ,which occurs post the long term exposure to certain carcinogens.^{37,38} Assessing suitability for trans oral robotic surgery, detecting the carcinoma of unknown primary, helping in tissue diagnosis, identification of synchronous tumors, staging of hypo pharyngeal and laryngeal cancers-these are the indications of endoscopy.³⁷

CONCLUSION

HNSCC the sixth position commonest, amongst all the malignancies worldwide has a predilection for the oral cavity, larynx, pharynx, salivary gland and the nasal cavity. More than 90% of malignancies of the oral cavity are SCC. A small percentage of SCC cases are inherited or are familial with presentation at a late age with a male predilection. Tobacco, alcohol, betel quid, poor nutrition, poor oral hygiene, HPV, Epstein-Barr virus and Candida albicans are etiological factors. Non healing ulcer, difficulty in swallowing, change in voice, swelling, persistent sore throat, unusual bleeding, facial swelling or difficulty in breathing are symptoms suggestive of head and neck neoplasia.

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