

A Clinical and Demographic Study on Oropharyngeal Malignancies

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Abstract

Background: The aim of the study was to determine the distribution of oropharyngeal malignancies in terms of age, sex, personal habits, symptoms, site, histopathological type, and differentiation; and the modes of treatment adopted and its results.

Materials and Methods: A total of 68 patients treated previously in the Department of Ear, Nose, and Throat of MNR Medical College and Hospital were included in this study. Patients of all age groups and gender were included in the study. Patients with persistent mass of the neck or throat or with symptoms suggesting oropharyngeal cancer were included in the study. Patients with symptoms of chronic throat pain, difficulty swallowing, weight loss, earache, voice change, and blood-tinged saliva were included in the study. Patients with severe cardiac, renal and pulmonary diseases were excluded from the study. Patients with immunodeficiency diseases were excluded from the study. All the patients were initially evaluated by a detailed medical history and comprehensive head and neck examination, which included flexible endoscope examination of the pharynx and larynx in an outpatient department setting. Patients with suspicious looking lesions (tumors) of the oropharynx were biopsied for histopathological evaluation. All patients with a confirmed diagnosis of oropharyngeal squamous cell carcinoma were subjected to evaluation by a multidisciplinary treatment team. Imaging was done to evaluate the primary tumor, involvement of lymph nodes in the neck, and for evidence of metastatic cancer spread beyond the head and neck. The patients were subjected to either computed tomography scan or magnetic resonance imaging of the neck to evaluate the pharynx and lymph nodes in the neck.

Observations and Results: Among the 68 patients, there were 41 males (60.29%) and 27 females (39.70%), with a male to female ratio of 1.51: 1. The mean age was 55.63 ± 5.70 years. Thirty-seven patients (54.41%) were in 55–65 years, 24 patients (35.29%) in 45–55 years, and 7 patients (10.29%) were aged above 65 years. Malignant tumors of the tonsil were observed in 21/68 (30.88%), posterior one-third of the tongue in 17/68 (25%), soft palate in 10/68 (14.70%), valleculae in 10 (14.70%), and suprahyoid epiglottis in 6 (8.82%), and posterior pharyngeal wall in 4 (105.88%) of the patients.

Conclusions: Oropharyngeal cancers are one of the most common malignant tumors of the aero-digestive tract. Males are more commonly affected than females and usually in the 5th–6th decade of life. The incidence is rising in females also because of using smokeless tobacco products. The most common site was tonsil followed by posterior one-third of the tongue; the least common site was posterior pharyngeal wall. Well-differentiated carcinoma was the most common histopathological finding.

Key words: Malignancies, Oropharynx, Radiotherapy and chemotherapy, Staging, TNM classification

INTRODUCTION

The risk factors causing oropharyngeal malignant tumors are habits, social customs, diet, occupational exposure, climate, geography, and difference in race and

genetic factors.^[1] Even though the malignant neoplasms of the oral cavity, oropharynx, and hypopharynx put together account for 45% of all cancers in India, the prevalence of only oropharyngeal malignancies is least forthcoming in the literature.^[2] The incidence of oropharyngeal malignant tumors is not only common in India but also in the populations of Indian origin elsewhere; especially it was reported in Malaysia.^[3] The malignant tumors of oropharynx are easily diagnosed by ear, nose, and throat (ENT) clinical examination but more than 80% of these patients report at a very late stage. Direct bone involvement takes place early and is

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seen in nearly two-third of the cases.^[3] Multicentricity of the tumors and field cancerization in the mucosa has been noted by several workers.^[4] Human papillomavirus (HPV) infection was found to be responsible for onset of oropharyngeal cancers that arise predominantly from the lingual and palatine tonsils within the oropharynx.^[5] Gillison stated that oral HPV infection has recently been associated with sexual behavior; particularly with number of multiple oral sex partners.^[6] The vast majority of primary oropharyngeal tumors are squamous cell carcinomas (SCCs) on histopathological examination, but other varieties arising from minor salivary tumors (adenomas/adenocarcinomas), primary lymphoid tumors, undifferentiated tumors, various sarcomas, and “mixed cellularity” neoplasms occurring primarily in the oropharynx are not uncommon.^[7] Review of recent literature shows that many of these tumors (at least in the United States) are associated with HPV infection and potentially more amenable to curative treatment.^[8] Literature also shows in retrospective studies that nearly 60% of oropharyngeal SCCs are found to be moderately differentiated, 20% well differentiated, and 20% poorly differentiated.^[7] Genomics and proteomics are likely to modify the methods of sub-classification of many cancers, including SCCs of the head and neck, as increasingly specific molecular markers and patterns of gene expression are identified.^[9] The etiological agents of oropharyngeal SCC are tobacco use and excess alcohol use. Alcohol abuse acts not only independently as a risk factor for oropharyngeal SCC but also seems to potentiate the carcinogenic nature of tobacco smoke in the oropharynx. Moreover, the carcinogenic effects of both alcohol and tobacco smoke on the oropharynx appear to function in dose-dependent manners.^[10] The change in the trends of occurrence of SCC of oropharynx among the younger age groups in USA is mainly attributed to HPV seropositivity, oral HPV infection, or both. For reasons not yet understood, most HPV-associated oropharyngeal SCCs originate in the tonsil. Although HPV18 and HPV-16 are associated with genital cancers, the vast majority (84%) of HPV-associated head and neck cancers are associated with HPV-16 only.^[11-13] Few authors have suggested that HPV associated oropharyngeal cancers may be less aggressive than those not associated with the virus; specifically, HPV association tends to confer much better survival rates. The biologic/molecular reasons for these clinical observations have not been clearly elucidated.^[14,15] In this context, the present study is undertaken to determine the distribution of oropharyngeal malignancies in terms of age, sex, personal habits, symptoms, site, histopathological type, and differentiation; and the modes of treatment adopted and its results.

MATERIALS AND METHODS

Sixty-eight patients treated previously in the Department of ENT of MNR Medical College and Hospital was included in this study. The medical records of these patients were retrieved from the medical records section and analyzed. An Institutional Ethical Clearance was obtained before commencement of the study.

Inclusion Criteria

(1) Patients of all age groups and gender were included in the study. (2) Patients with persistent mass of the neck or throat or with symptoms suggesting oropharyngeal cancer were included in the study. (3) Patients with symptoms of chronic throat pain, difficulty swallowing, weight loss, earache, voice change, and blood-tinged saliva were included in the study.

Exclusion Criteria

(1) Patients with severe cardiac, renal, and pulmonary diseases were excluded from the study. (2) Patients with immunodeficiency diseases were excluded from the study. All the patients were initially evaluated by a detailed medical history and comprehensive head and neck examination, which included flexible endoscope examination of the pharynx and larynx in an outpatient department (OPD) setting. Patients with suspicious looking lesions (tumors) of the oropharynx were biopsied for histopathological evaluation. In those patients, where it was not possible to perform biopsy in OPD, and if a lesion was not easily accessible either directly through the mouth or through flexible endoscopy, an additional examination and biopsy under general anesthesia in an operating room was done. In patients presenting with neck masses an adequate tissue for diagnosis through a needle biopsy (fine-needle aspiration, or FNA) was done. All patients with a confirmed diagnosis of oropharyngeal SCC were subjected to evaluation by a multidisciplinary treatment team. Imaging was done to evaluate the primary tumor, involvement of lymph nodes in the neck, and for evidence of metastatic cancer spread beyond the head and neck. The patients were subjected to either computed tomography scan or magnetic resonance imaging of the neck to evaluate the pharynx and lymph nodes in the neck. These scans were done with intravenous contrast in nearly all cases, with the exception of patients with impaired kidney function or an allergy to contrast dye. CT scan of the chest was also done in most cases, to evaluate for the presence of metastatic cancer in the lungs or lymph nodes of the chest. Positron emission tomography scan was done 6 patients for pretreatment evaluation, particularly for patients with advanced-stage disease. All the data were analyzed and tabulated using standard statistical methods.

OBSERVATIONS AND RESULTS

Sixty-eight patients attending the Department of ENT in MNR Medical College and Hospital, Sangareddy, Telangana, who were diagnosed with malignancy of oropharynx, were included in this study. There were 41 males (60.29%) and 27 females (39.70%), with a male to female ratio of 1.51: 1. The patients belonged to the age group of 45 to above 65 years with a mean age of 55.63 ± 5.70 years. There were 37 patients (54.41%) in the age group of 55–65 years, 24 patients (35.29%) in the age group of 45–55 years, and 7 patients (10.29%) were aged above 65 years. The youngest patient was aged 56 years and the eldest patient was aged 69 years [Table 1].

The personal habits of the study group were studied and found that 38/41 (92.68%) of the males and 8/27 (29.62%) of the females had the habit of smoking. Alcohol consumption was observed in 27/41 (65.85%) of the males and 16/27 (59.25%) of the females. Tobacco in the form of gutkha or chewing pan was noted in 34/41 (82.92%) of the males and 22/27 (81.48%) of the females. Consumption of alcohol and tobacco in the form of smoking or chewing was noted in 14/41 (34.14%) of the males and 12/27 (44.44%) of the females. About 3/41 (7.31%) of the males and 2/27 (7.40%) of the females had no risk factors as habits [Table 2].

About 54/68 (79.41%) patients showed ulceroproliferative growths as the presenting lesions in this study followed by 12/68 (17.64%) of the patients showed ulcerative lesions, and 2/68 (2.94%) of them showed infiltrative type of lesions. The incidence of site of lesions of various subsites is tabulated in Table 3. Malignant tumors of the tonsil were observed in 21/68 (30.88%), posterior one-third of the tongue in 17/68 (25%), soft palate in 10/68 (14.70%), valleculae in 10 (14.70%), and suprahyoid epiglottis in 6 (8.82%), and posterior pharyngeal wall in 4 (105.88%) of the patients [Table 3].

Histopathological study of all the biopsy specimens was done and it was observed that well-differentiated SCC was reported in 49/68 (72.05%) of the patients followed by poorly differentiated SCC in 11 (16.17%) and anaplastic carcinoma was observed in the remaining 8 (11.76%) of the patients.

DISCUSSION

In India malignant tumors of the oropharynx and oral cavity account for the third most common cancer in men and women but when only oropharynx is considered it is the 7th most common cancer among both the genders.^[16] In the present study, the male to female ratio was 1.5:1 which

Table 1: The age and gender incidence of the study (n=68)

Age group	Male – 41	Female – 27
45 – 55 years – 24	15	9
55 – 65 years – 37	23	14
Above 65 years – 7	3	4

Table 2: The incidence of risk habits in the study group (n=68)

Personal habits	Male – 41 (%)	Female – 27 (%)	P value
Smoking	38 (92.68)	8 (29.62)	0.031
Alcohol	27 (65.85)	16 (59.25)	Not significant
Tobacco	34 (82.92)	22 (81.48)	Not significant
chewing (Pan, Gutka)			
Alcohol and tobacco	14 (34.14)	12 (44.44)	Not significant
(smoking, pan, gutka)			
None of the above	3 (7.31)	2 (7.40)	Not significant

Table 3: The site of lesions according to the gender in the study group (n=68)

Site of lesion	Male – 41 (%)	Female – 27 (%)
Tonsil – 21 (30.88%)	13 (19.11)	8 (11.76)
Posterior one-third tongue – 17 (25%)	11 (16.17)	6 (8.82)
Soft palate – 10 (14.70%)	7 (10.29)	3 (4.41)
Valleculae – 10 (14.70%)	5 (12.51)	5 (18.51)
Supra-hyoid epiglottis – 6 (8.82%)	3 (4.41)	3 (4.41)
Posterior pharyngeal wall – 4 (5.88%)	2 (2.94)	2 (2.94)

is comparable to other parts of India; in one report from Kerala the incidence in males was 57.8% in males and 42.2% in females.^[17] The higher incidence of oropharyngeal malignancies in males may be as a result of increase in the consumption of tobacco and alcohol. Tobacco is consumed by males in both smoking and chewing form in India, whereas native females usually do not smoke. This difference can also be attributed to more males seeking early medical consultation.^[18] In the present study, it was found that 38/41 (92.68%) of the males and 8/27 (29.62%) of the females had the habit of smoking which is statistically significant with $P = 0.031$ (P significant at <0.05). There were 41 males (60.29%) and 27 females (39.70%), with a male to female ratio of 1.51: 1. The patients belonged to the age group of 45 to above 65 years with a mean age of 55.63 ± 5.70 years. There were 37 patients (54.41%) in the age group of 55–65 years, 24 patients (35.29%) in the age group of 45–55 years, and 7 patients (10.29%) were aged above 65 years. The youngest patient was aged 56 years and the eldest patient was aged 69 years [Table 1]. Ahluwalia *et al.*^[19] reported from their study that the peak incidence of oropharyngeal malignancy was among males in the 6th decade of life (40.89%), while in females it was 5th decade comprising 37.31%. Patel and Pandya reported that 12.9%

of oropharyngeal malignancies were below 35 years of age, 23.8% between 35 and 45, and 63.3% cases over 45 years of age.^[20] The mean age in the present study was 55.63 ± 5.70 years when compared to the study done by Durazzo *et al.* was 57.4 years, and only 8.6% of the patients were 40 years or less.^[21] In the present study, 38/41 (92.68%) of the males and 8/27 (29.62%) of the females had the habit of smoking. Alcohol consumption was observed in 27/41 (65.85%) of the males and 16/27 (59.25%) of the females. Tobacco in the form of gutkha or chewing pan was noted in 34/41 (82.92%) of the males and 22/27 (81.48%) of the females. Consumption of alcohol and tobacco in the form of smoking or chewing was noted in 14/41 (34.14%) of the males and 12/27 (44.44%) of the females. About 3/41 (7.31%) of the males and 2/27 (7.40%) of the females had no risk factors as habits [Table 2]. It was reported that women have substantially high level of chewing habits than men in many rural areas, as they believe that tobacco has magical and medicinal properties.^[16,17] In comparison to this study in the study by Dias and Almeida, 57.8% were tobacco users, 50% were alcoholics, and 43.8% were both alcoholics and smokers.^[22] In another study by Durazzo *et al.*^[21] reported tobacco smoking in 80.8% of the patients, history of alcohol intake was observed in 56.6% of the patients. More recently in Western world, HPV infection is emerging as a common etiological factor for oral and oropharyngeal malignancies, mostly as a result of oral sex.^[11] However, in India, alcohol and tobacco usage are still the most common risk factor. Risk of oral and oropharyngeal malignancy is higher for hard liquor and beer.^[23] It is presumed that alcohol may act as a solvent to enhance mucosal exposure to carcinogens, apart from being a direct carcinogen. Acetaldehyde, an alcohol metabolite, can form DNA adducts that interfere with DNA synthesis and repair.^[24] Rodu and Jansson^[25] postulated a relationship between use of smokeless tobacco products and oral cancers as a complicated phenomenon due to the heterogeneity in smokeless tobacco, containing tobacco-specific nitrosamines. However, in India, smokeless tobacco is often mixed with other carcinogenic substances such as betel, areca nut, and lime making the smokeless tobacco products much stronger and in dose-response relationships with increased intensity, and when used for longer durations resulting in the risk of premalignant and malignant lesions of the oral cavity and oropharynx.^[26] Malignant tumors of the tonsil was observed in 21/68 (30.88%), posterior one-third of the tongue in 17/68 (25%), soft palate in 10/68 (14.70%), valleculae in 10 (14.70%), and suprahyoid epiglottis in 6 (8.82%), and posterior pharyngeal wall in 4 (5.88%) of the patients [Table 3]. Lin *et al.*, observed 70–80% of oropharyngeal SCC originate in the tonsillar complex as similar to the present study tonsillar tumors (30.88%) were the most common. They concluded that although these tumors are often asymptomatic initially,

the majority of patients report odynophagia, dysphagia, or both.^[9] Late symptoms include otalgia, bleeding, decreased tongue mobility, and trismus (usually due to invasion of the pterygoid plate).^[9] Lin *et al.* observed that SCC of the tongue base was second most frequent sub-site to develop tumors and tends to be locally, regionally, and systemically aggressive and they are poorly differentiated. The incidence in their study was 29.30% which is similar to the present study of 25%. Malignant tumors of the soft-palate are also relatively uncommon but tend to be diagnosed at early stages, because the soft palate is the most amenable oropharyngeal subsite to direct visual inspection and manual palpation.^[7] In the present study, the incidence of soft palate was 14.70% the third most common site. Cohan *et al.*^[27] observed that tumors originating from the posterior pharyngeal wall are rare because they tend to remain asymptomatic until they gain considerable bulk. In the present study, the incidence of posterior pharyngeal wall tumors was 5.88% which was least common tumor. It was observed in this study that well-differentiated SCC was reported in 49/68 (72.05%) of the patients, followed by poorly differentiated SCC in 11 (16.17%) and anaplastic carcinoma was observed in the remaining 8 (11.76%) of the patients. Similarly, Mehrotra *et al.*^[28] also noticed moderately differentiated SCC as the most prevalent type in males (13%), and well-differentiated was common in females (5.3%). However, there are several studies reporting well-differentiated SCC as the most prevalent.^[19,22,29,30]

CONCLUSIONS

Oropharyngeal cancers are one of the most common malignant tumors of the aero-digestive tract. Males are more commonly affected than females and usually in the 5th–6th decade of life. The incidence is rising in females also because of using smokeless tobacco products. The most common site was tonsil followed by posterior one-third of the tongue; the least common site was posterior pharyngeal wall. Well-differentiated carcinoma was the most common histopathological finding.

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