Research Article

Prevalence and major causative factors of upper aerodigestive tract malignancies

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Received July 15, 2015. Accepted September 5, 2015

Abstract

Background: The upper aerodigestive tract (UADT) malignancies vary with geography. Data on epidemiology of UADT are few in India, especially southern states such as Kerala.

Objective: To estimate the prevalence and major causative factors of UADT malignancies.

Materials and Methods: In this cross-sectional study, 60 patients (54 male and 6 female subjects) who showed proven UADT malignancies were included. Main epidemiological factors such as age, distribution, site, histopathological types, symptoms, and levels of lymph nodes were determined. The clinical and radiological stages of each site at the time of presentation were also assessed and statistically analyzed.

Result: The male to female ratio was 9:1, with peak incidence in 50% cases at the 60–69 years age group. Most common symptom at presentation was change in voice with hoarseness (21/60) and neck swellings (18/60) with lymph node metastasis at the time of presentation. The most commonly involved site was glottis (19/60) with T1 presentation (15/19). Oral cavity lesions found in 11 of 60 cases with seven cases in T4 presentation. Hypopharyngeal malignancies were found in eight cases. Other sites found to be involved were oropharynx, nasopharynx, maxillary sinus, and salivary gland with lesser frequency. Fifty-three cases showed addictions such as tobacco smoking, alcoholism, or tobacco chewing.

Conclusion: The distribution of UADT cancers was the highest in the 60–69 years age group with male:female ratio of 9:1. Glottic malignancy showed the highest frequency. Smoking and alcoholism were the major causative factors identified. Hence, the need for education and awareness that are aimed at reducing exposure habit forming substances are emphasized. This study showed limitations such as small sample size and short duration, which warranted further multicenter studies for a longer duration.

KEY WORDS: Upper aerodigestive tract malignancies**,** smoking, alcoholism, lymph node, glottis, oropharynx, nasopharynx, maxillary sinus, salivary gland

Introduction

The upper aerodigestive tract (UADT) includes mainly the nose and paranasal sinuses, oral cavity, pharynx, larynx, and salivary glands. The prevalence of head and neck cancer differs with geography, with high rates being recorded in France, India, South America, and Eastern Europe.[1] According to the National Cancer Institute's Surveillance, Epidemiology, and End Results program of the United States, between 1975 and 2001, the incidence for the most head and neck cancer sites has globally decreased, except for tongue (up to 16%), tonsil (up to 12%), nasal cavity and sinuses (up to 12%), salivary glands (up to 20%), and thyroid (up to 52%). Oral and pharyngeal lesions are the sixth most common in European union and third most common among men and fourth most common among women in developing countries such as India.[1] Oral cancer remains the eighth most common malignancy.[2] High rates of oral cancer are reported for the

Access this article online	
Website: http://www.ijmsph.com	Quick Response Code:
DOI: 10.5455/ijmsph.2016.1507201595	

Indian subcontinent and parts of Asia (male incidence rates in excess of 10 per 100,000 per annum),[3] and head and neck cancer accounts for 45% of all malignancies.[4] Even Indian immigrants in other countries have also been found to have higher incidence of oral malignancies.[1]

Studies are essential for education and awareness aimed at reducing exposure to habit-forming substances. The latency between the appearance of symptoms and the patient approaching a tertiary center has to be studied to show the importance of screening. Data on epidemiology of the UADT cancers are few in India, especially in Kerala. Clinical and radiological staging at presentation and duration of symptoms are all variables and are found to be important in secondary prevention by early identification. This study was aimed to evaluate the epidemiological factors such as age, distribution, site, histopathological types, symptoms, and levels of lymph nodes and the clinical and radiological stages of each site at the time of presentation.

Materials and Methods

Subjects and Material

In this retrospective cross-sectional study, all the patients who attended outpatient or admitted in the wards of *Department* of Otorhinolaryngology (ENT), Amala Institute of Medical Sciences, Thrissur, Kerala, India, with UADT cancer diagnosed by cytology or biopsy during the period of 9 months were included. Patients without diagnosis of UADT cancer by cytology or biopsy and those who were not the patients of ENT department were excluded from the study. The study protocol was approved by Institutional Ethical Committee, Amala Institute of Medical Sciences. The data on the description of UADT cancers by their age- and gender-wise distributions, histological and clinical grading, presentations, and major causative agents were collected and statistically analyzed.

Statistical Analysis

The statistical analysis was performed using SPSS (version 16.0). Fisher's exact test was done to find the significant difference between the groups. *P* less than 0.05 was considered as significant.

Results

Sixty patients (54 male and six female subjects) attended ENT with histologically proven UADT malignancies [Figure 1]. The male to female ratio was 9:1, with peak incidence at the 60–69 years age group, constituting 50% cases [Figure 2]. The most common symptom at the presentation was change in voice with all of them having hoarseness (21/60 cases). Eighteen cases presented with neck swellings, which were lymph node metastasis at the time of presentation. Other presenting complaints were odynophagia, mouth ulcer, nasal bleed, nasal obstruction, dysphagia, and trismus occurring with lesser frequency. Only two cases presented with stridor. On eliciting detailed history, 26 cases showed loss of weight, and 10 of them revealed otalgia. Duration of symptoms were also lesser in those with hoarseness, while those with nasal obstruction, nasal bleed, or mouth ulcer showed longer duration of presenting illness before they came to our tertiary-care center.

The site most commonly involved was glottis, with 19 of 60 cases, followed by oral cavity with 11 cases. Hypopharyngeal malignancies followed with eight cases. Other sites found to be involved were oropharynx, nasopharynx, maxillary sinus, and salivary gland with lesser frequency [Table 1]. Radiologically, 15 of 60 cases were stage I, while 14 cases were stage IVb and 26 cases with IVc. There was a statistically significant difference among the various stages of presentation and sites ($P = 0.0001$) [Table 1]. Four cases with metastasis were identified only radiologically.

TNM staging at presentation was assessed. Glottic malignancies showed T1 presentation in 15 of the 19 cases. Oral cavity lesions revealed T4 presentation in seven of 11 cases. All the three cases of maxillary sinus presented at T4. All nasopharyngeal lesions showed T1 and T2 presentations. Among the 60 cases, 19 were in T4 stage. Two cases were in Tis stage as they showed only metastatic nodes with no identifiable primary site clinically or radiologically at the time of presentation and were diagnosed with biopsies from tonsils [Table 2]. Both revealed N2a nodes at level II. Clinical staging by TNM showed 16 of the cases were in stage I with none of the cases in stage IVb or IVc. None of the cases were found to show metastasis clinically.

Glottis malignancy revealed earlier stage of presentation at stage I in 13 of the 19 cases. All the hypopharyngeal malignancies presented at stage IV with two cases presenting with metastasis. Oral cavity malignancies also presented at stage III or later. Significant lymph node metastasis at the time of presentation was found radiologically in 43 of the 60 cases. Level II lymph nodes were most commonly involved in 15 cases. This was followed by levels III and I with 14 and 13 cases, respectively. Level V node with primary site in nasopharynx was found in five cases. All the cases with no lymph node involvement belonged to those with primary site in glottis [Table 3]. There was a statistically significant difference among the various levels of lymph nodes and sites ($P = 0.0001$).

Addictions such as smoking alcoholism or tobacco chewing were found in 53 of 60 cases. Smoking was seen in 44 cases. Eighteen of the 19 cases of glottis malignancy were smokers. Cigarette was used more commonly than beedi. Smoking was also prevalent in hypopharyngeal malignancies. Alcoholism was seen in 32 cases, and all were either smokers or tobacco chewers. Twenty-nine cases were both chronic smokers and consumed alcohol. Five cases revealed tobacco chewing alone with no other addictions [Table 4]. There was a statistical association among the addictions and sites ($P = 0.0001$). Most smokers revealed 30–60 pack-years [Table 5] (pack-years being product of number of packs of cigarettes per day and years of smoking). Most had been smoking for over 40 years of duration. Alcohol intake was >180 mL/day over

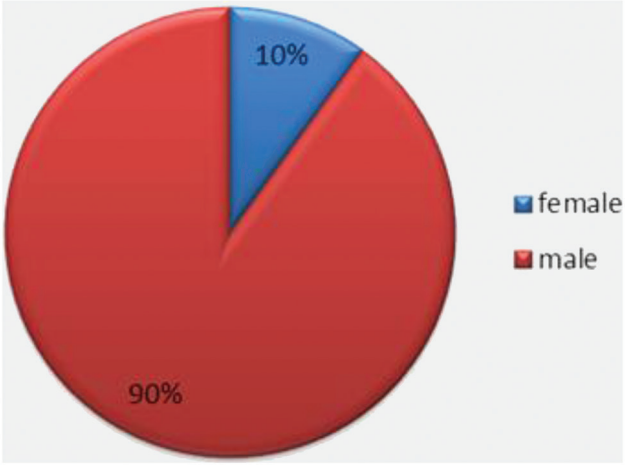

Figure 1: Gender-wise distribution of upper aerodigestive tract malignancies.

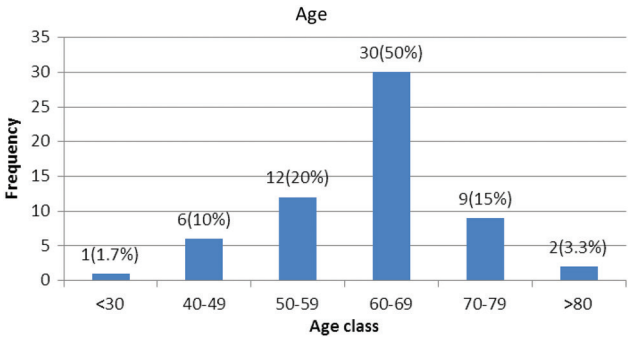

Figure 2: Age-wise distribution of upper aerodigestive tract malignancies.

Table 1: Radiological grading of upper aerodigestive tract cancers

Site	Radiological						Total
	I	II	III	IVa	IVb	IVc	
Glottis	13	0	4	0	0	2	19
Oral cavity	0	0	2	5	4	0	11
Oropharynx	2	0	2	0	2	0	6
Nasopharynx	0	5	2	0	0	0	7
Hypopharynx	0	0	0	3	3	2	8
Salivary gland	0	2	2	2	0	0	6
Maxillary sinus	0	0	0	2	1	0	3
Total	15	7	12	12	10	4	60

$P = 0.0001$.

40 years, with most of them taking brandy or less commonly toddy. Among the tobacco chewers, all of them used piper betel leaf smeared with slaked lime (called *chunnamb* colloquially in Kerala) and areca nut and dried tobacco as a quid for keeping on either gingivobuccal sulcus. History of irradiation was present in eight cases and 10 cases were recurrences, mainly in glottis, nasopharynx, hypopharynx, and oral cavity.

Table 2: TNM staging of upper aerodigestive tract cancers

Site	T staging						Total
	Tis	T1	T2	T3	T4a	T4b	
Glottis	0	15	0	2	2	0	19
Oral cavity	0	2	0	2	3	4	11
Oropharynx	2	0	0	2	2	0	6
Nasopharynx	0	7	0	0	0	0	7
Hypopharynx	0	0	4	0	3	1	8
Salivary gland	0	0	5	0	1	0	6
Maxillary sinus	0	0	0	0	2	1	3
Total	2	24	9	6	13	6	60

Discussion

In India, among head and neck cancers, oral cavity malignancies were reported to show maximum incidence.[2] But, in our study, larynx showed peak incidence, followed by oral cavity lesions. This may be because the traditional habit of pan chewing, which is implicated in premalignant and malignant conditions of oral cavity, is diminishing among the population in Kerala. On the other hand, nationwide, the incidence of smoking is on the rise owing to better economical facilities and accessibility to cigarettes, leading to an increase in laryngeal cancers.[5,6] Another distinct finding is that prevalence of nasopharyngeal carcinoma (NPC) was also found to be higher in our population. As the management of NPC is essentially by radiotherapy, this might be because of crowding of cases in our setup as we have the latest intensity-modulated radiation therapy techniques, which is available only in a few tertiary centers in Kerala.

According to the socioeconomic status scale, majority of cases were from upper middle class, followed by lower and lower middle classes; 81.7% showed mixed diet. Comorbidities were seen in 70% cases, with 21.7% of cases revealing diabetes mellitus. Histopathology report of squamous cell carcinoma was positive in 85% cases. Lymphoma and adenoid cystic carcinoma were found in four cases each, and one case of mucoepidermoid tumor was seen. Grading was well differentiated in 48.3% cases, and 36.7% cases showed poorly differentiated carcinoma.

Overall, the age distribution was highest in the 60–69 years age group. This is consistent with the worldwide statistics of occurrence in above 40-year-old group.[4] Only one case of 60 cases was below 40 years. The sex distribution was 9:1, male:female ratio. Globally, male subjects are said to have more than two to three times higher incidence of head and neck malignancies than female subjects.[4] The lower occurrence of malignancies noted among women in Kerala compared with the world. This may be because of the cultural differences tabooing them from addictions such as smoking

Table 3: Presence of lymph node metastasis at the time of presentation

Site	Level								Total
	None	I	I, II	II	II, III	II, V	III	V	
Glottis	17	0	0	2	0	0	0	0	19
Oral cavity	0	7	4	0	0	0	0	0	11
Oropharynx	0	0	0	1	2	0	3	0	6
Nasopharynx	0	0	0	2	0	2	0	3	7
Hypopharynx	0	0	0	2	0	0	6	0	8
Salivary gland	0	2	0	4	0	0	0	0	6
Maxillary sinus	0	0	0	0	3	0	0	0	3
Total	17	9	4	11	5	2	9	3	60

$P = 0.0001$.

Table 4: Causes for upper aerodigestive tract cancers

Site	None	Addictions					Total
		Smoking	Tobacco chewing	Alcoholism and smoking	Alcoholism and tobacco	Smoking and tobacco chewing	
Glottis	1	6	0	12	0	0	19
Oral cavity	4	0	4	1	0	2	11
Oropharynx	2	0	1	1	2	0	6
Nasopharynx	0	2	0	5	0	0	7
Hypopharynx	0	1	0	7	0	0	8
Salivary gland	2	2	0	1	1	0	6
Maxillary sinus	0	0	0	2	1	0	3
Total	9	11	5	29	4	2	60

$P = 0.0001$.

Table 5: Distribution of pack years among the patients with upper aerodigestive tract cancers

Pack-years[a]	Frequency	%
0	14	23.3
<10	2	3.3
10–30	5	8.3
30–60	16	26.7
60–90	8	13.3
90–120	10	16.7
120–150	3	5.0
>150	2	3.3
Total	60	100.0

[a]Pack-years is the product of number of packs of cigarettes per day and years of smoking.

and alcoholism. Among the six female cases, five showed oral cavity malignancies, mainly of buccal mucosa, probably owing to the habit of tobacco chewing among women in Kerala. All those cases were >60 years of age.

Because glottic malignancy showed the highest frequency, hoarseness was also the main complaint with highest frequency. Those with glottic malignancies presented earliest at stage I itself as opposed to pyriform fossa and oral cavity lesions, which presented as advance carcinomas at stage T3 or worse, paralleling the data of existing literature.[7–9] Mouth ulcers of oral or oropharyngeal malignancies were treated as aphthae by general practitioners from outside for a prolonged duration before being referred to our tertiary center or before attempting a biopsy. Four of 11 cases of oral cavity malignancies showed trismus before they presented to our center. Two cases who presented with level II lymph node enlargement with fine needle aspiration cytology from node showing squamous cell carcinoma and no recognizable lesion in panendoscopy underwent FDG-PET in our nuclear medicine department and were found to show a primary site in tonsil in both the cases. Around 25% of the carcinomas of previously unknown origin are proven to show their primary site in tonsils according to literature. Levels II and III nodes are most commonly involved in head and neck cancers by lymph node metastasis in accordance with literature.[10]

Fifty-three cases of 60 cases revealed addictions. Smoking was found to be present in 44 among them, and 32 cases revealed alcoholism. Both smoking and alcoholism was seen in 29 of the 53 cases. Alcoholism was associated either with smoking or tobacco chewing. Eighteen of the 19 cases of glottic malignancy were smokers; this is identical to the statistics of

98% of those with glottic malignancies being smokers.[11] The crypts of tonsil, glossotonsillar sulcus, and tongue base are bathed with carcinogens in saliva to a greater extent than soft palate and posterior pharyngeal wall. Hence, carcinomas in these sites are more associated with causative agents such as smoking, alcoholism, or pan chewing. In Kerala, piper betel leaf, slaked lime, and arecanut are mixed with oral tobacco and are used as quid called paan. Lime lowers the pH, which accelerates the release of alkaloids from both tobacco and arecanut. This also leads to submucosal fibrosis where the tobacco chewers keeps the quid. Submucosal fibrosis was present in most of the patients with oral cavity malignancies in our study.

Although there is no association between smoking and nasopharyngeal carcinoma,[12] in our study, all of the cases of NPC were smokers. This is probably owing to high prevalence of smoking in our community. Poor socioeconomic status is said to be associated with more head and neck cancers, especially owing to dietary factors. We classified our patients based on Kuppuswami's socioeconomic status scale based on education occupation and income. But, in our study, the upper middle class was found to show the highest frequency, probably because our center belongs to the private sector and the affordability will be lesser for those in lower classes.

Eighty-five percent of the cases were squamous cell carcinomas as per histopathological examination, followed by lymphomas and adenoid cystic carcinomas, identical to the literature that squamous cell carcinomas occur mostly in head and neck malignancies.[13] One case of mucoepidermoid carcinoma of parotid was also present; 48.3% cases showed well-differentiated tumors. Relative rarity of tumors of many head and neck subsites leads to the problem of small numbers, which, in our study, was managed by the grouping together of tumors from different sites. While this increased the power of the study, it showed the effect of obscuring important effects that may be present for one site but not another. This study has limitations such as small sample size and short duration, warranting further multicenter studies for a longer duration. A comparison of the prevalence of causative agents in general population has to be evaluated to know their significance as in head and neck malignancies.

Conclusion

Overall, the age distribution of UADT cancers was highest in the 60–69 years age group, with male:female ratio was 9:1. Glottic malignancy showed the highest frequency. Smoking and alcoholism were the major causative factors identified. Therefore, the need for education and awareness that are aimed at reducing exposure to habit-forming substances are emphasized.

Acknowledgment

We acknowledge the valuable help of Dr. Ajith TA, Professor, Department of Biochemistry, Amala Institute of Medical Sciences; Thrissur, Kerala, India, during the preparation of this article.

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How to cite this article: Pooja P, Andrews CJ, Arjun GM, Vinayakumar AR. Prevalence and major causative factors of upper aerodigestive tract malignancies. Int J Med Sci Public Health 2016;5:651-655

Source of Support: Nil, **Conflict of Interest:** None declared.