

## Original Research Article

# Anatomical site-wise distribution of upper aerodigestive tract malignancies in a rural population

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**Received:** 03 October 2018

**Revised:** 19 October 2018

**Accepted:** 20 October 2018

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### ABSTRACT

**Background:** Upper aerodigestive tract malignancies constitute approximately 4% of all malignancies. These include cancers of the various sites of the upper aerodigestive tract where malignant lesions can be found such as the nasal cavity, paranasal sinuses, nasopharynx, oral cavity and its sub-sites, oropharynx, larynx and hypopharynx. Malignancies of these sites are found to be common in people from lower socio-economic strata. Tobacco and alcohol are considered as risk factors for its development.

**Methods:** A cross-sectional study was conducted in the outpatient section of Department of ENT, at Chamarajanagar Institute of Medical Sciences and Hospital, Chamarajanagar, India, for a period of 1 years 10 months from October 2014 to July 2016. During the study period, 100 cases that were diagnosed as having upper aerodigestive tract malignancy by histopathology were included in the study group. The aim of this study is to determine the epidemiology, clinical features and anatomical site-wise distribution of malignancy in the study group.

**Results:** Oral cavity was the commonest site where malignancy developed in the upper aerodigestive tract followed by the larynx. Malignant disease was more common in males and in the elderly. Majority of the patients who developed malignancy had history of tobacco and alcohol consumption.

**Conclusions:** Oral cavity malignancy is common in rural population, is associated with tobacco chewing and is more common in elderly male.

**Keywords:** Upper aerodigestive tract, Oral cavity malignancy, Nasal cavity malignancy, Pharyngeal malignancy, Laryngeal malignancy

### INTRODUCTION

Head and neck cancer is the sixth most prevalent primary malignant neoplasm in the world, accounting for 5% of all cancers in men and 2.5% in women.<sup>1</sup> The most affected anatomical site in head and neck by cancer is the upper aerodigestive tract, distributed among the oral cavity (35%-40%), oropharynx (30%), larynx (25%) and hypopharynx (7%).<sup>2</sup> The most prevalent histological type of cancer located in the upper aerodigestive tract is the Squamous cell carcinoma (SCC) in 90% of the cases, and its main etiological factors are tobacco smoking and alcohol consumption.<sup>3,4</sup> Infection by the human papilloma

virus (HPV) has been responsible for at least 10% to 30% of oropharyngeal cancers.<sup>5</sup> Clinical staging at the time of diagnosis is the most important prognostic factor affecting survival but it is advanced in around 75% of cases, especially in developing countries. As a result, about 40% to 60% of patients with SCC have locoregional recurrence and 20% to 30% progress with distant metastases.<sup>5</sup>

Various factors amongst the rural population such as poor educational background, lower socio-economic status, lack of healthcare facilities, addiction to various substances found amongst the people from rural areas has

led to increased incidence of cancer amongst rural population. The purpose of this study was to determine the frequency with which the various regions of upper aerodigestive tract are affected with malignancy, in people from rural background and to establish the epidemiological profile of these patients.

## METHODS

A cross-sectional study was conducted in the outpatient department of ENT, at Chamarajanagar Institute of Medical Sciences and Hospital, Chamarajanagar, India, for a period of 1 year 10 months from October 2014 to July 2016. 100 patients who were diagnosed as having upper aerodigestive tract malignancy by histopathology were included in the study group. A detailed history was taken and clinical examination including ear, nose, throat, neck, general and systemic examination was carried out in all patients suspected to be having upper aerodigestive tract malignancy. FNAC (Fine Needle Aspiration Cytology) of neck masses if present was carried out. Complete haematological evaluation was carried out. Specialized investigations like upper gastro-intestinal endoscopy, computerized tomography (CT), MRI (magnetic resonance imaging) of the head and neck region, diagnostic imaging of chest and abdomen was carried out if required. Direct laryngoscopy and hypopharyngoscopy was carried out and tissue specimen obtained by biopsy of the growth in various parts of the upper aerodigestive tract. Biopsy specimen of lesions in the oral cavity was taken by direct visualization of oral cavity. The specimen were sent for histopathological

examination which was done using hematoxylin and eosin staining to establish the diagnosis of Carcinoma and its grade. Data was collected from the patients included in the study. Data consisted of personal details of the patient, socio-economic details and habits of the patients. Data was collected with the aid of a proforma. Standard statistical analysis was done and the data was presented in number and percentages. The aim of this study was to determine the epidemiology, clinical features and anatomical site-wise distribution of Malignancy in the study group.

## RESULTS

During the study period 100 patients presented with Upper Aerodigestive tract malignancy. All the cases had Squamous cell Carcinoma on histopathological examination of the biopsy specimen.

Oral cavity is the commonest site of malignancy followed by the larynx. None of the patients in our study had nasopharyngeal malignancy. Majority of the patients with upper aerodigestive tract malignancy were male.

Most common site of malignancy in the oral cavity is the buccal mucosa. In the larynx, supraglottis was the commonest site. In the oropharynx, base of tongue was the commonest site. In the laryngopharynx, pyriform fossa was the commonest site of malignancy.

**Table 1: Anatomical site and sex-wise distribution of upper aerodigestive tract malignancies.**

Tumor site	Male	Female	Total
Nasal cavity	1	1	2
Paranasal sinuses	-	2	2
Oral cavity	32	14	46
Larynx	20	4	24
Nasopharynx	-	-	-
Oropharynx	8	6	14
Laryngopharynx	6	6	12
Total	67	33	100

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

Tumor site	0-20 years	21-40 years	41-50 years	51-60 years	61-70 years	71-80 years	>80 years	Total
Nasal cavity	-	-	-	-	2	-	-	2
Paranasal sinuses	-	-	-	-	2	-	-	2
Oral cavity	-	2	8	20	12	4	-	46
Laryngeal	-	-	2	16	4	2	-	24
Nasopharyngeal	-	-	-	-	-	-	-	-
Oropharyngeal	-	-	-	8	6	-	-	14
Laryngopharyngeal	-	-	-	8	4	-	-	12
Total	-	2	10	52	30	6	-	100

**Table 3: Socio- economic status of patients with upper aerodigestive tract malignancies.**

Socio-economic status	No. of cases	Percentage (%)
Upper class	8	8
Middle class	32	32
Lower class	60	60
<b>Total</b>	<b>100</b>	<b>100</b>

60% of the patients with upper aerodigestive tract malignancy were from the lower socio-economic strata. Only 8% of the cases belonged to upper socio-economic class.

Exposure to tobacco either in the form of smoking or oral consumption was seen in most of the patients. Alcohol consumption was seen in 58 patients. Majority of the oral cavity malignancy (42 out of 46 patients) patients had the habit of tobacco chewing. Domestic exposure to smoke from solid fuels in 44 patients.

**Table 4: Personal habits associated with upper aerodigestive tract malignancies.**

Tumor site	Smoking	Tobacco chewing	Alcohol consumption	Solid fuel smoke	Use of snuff	Non-vegetarian food
Nasal cavity	1	2	-	-	2	1
Paranasal sinuses	2	-	2	2	2	1
Oral cavity	24	42	28	10	6	22
Laryngeal	20	8	14	18	2	14
Nasopharyngeal	-	-	-	-	-	-
Oropharyngeal	8	8	8	4	-	8
Laryngopharyngeal	6	6	6	10	2	6
<b>Total</b>	<b>60</b>	<b>66</b>	<b>58</b>	<b>44</b>	<b>14</b>	<b>52</b>

**Table 5: Symptomatology of upper aerodigestive tract malignancies.**

Symptoms	Nasal cavity	Paranasal sinus	Oral cavity	Larynx	Naso-pharynx	Orop-harynx	Laryngo-pharynx	Total
Bleeding from nose	2	2	-	-	-	-	-	4
Non-healing ulcer in mouth	-	-	40	-	-	-	-	40
Difficulty in swallowing	-	-	8	14	-	8	8	38
Painful swallowing	-	-	10	16	-	6	6	38
Difficulty in breathing	-	-	-	18	-	4	-	22
Change in voice	-	-	-	22	-	6	-	28
Neck lump	-	-	6	16	-	5	7	34
Ear pain	-	-	5	15	-	4	5	29

**Table 6: TNM stage of upper aerodigestive tract malignancy at the time of presentation.**

Anatomical site	Stage	No.	Percentage (%)
Nasal cavity	I	1	1
	II	1	1
	III	-	-
	IV	-	-
Paranasal sinuses	I	1	1
	II	1	1
	III	-	-
	IV	-	-
Oral cavity	I	10	10
	II	18	18
	III	12	12
	IV	6	6
Laryngeal	I	2	2
	II	6	6
	III	12	12
	IV	4	4

Continued.

Anatomical site	Stage	No.	Percentage (%)
Nasopharyngeal	I	-	-
	II	-	-
	III	-	-
	IV	-	-
Oropharyngeal	I	1	1
	II	4	4
	III	7	7
	IV	2	2
Laryngopharyngeal	I	1	1
	II	3	3
	III	6	6
	IV	2	2

Non-healing ulcer in the oral cavity was the commonest symptom in our study, being seen in 40 patients as oral cavity was the commonest site of malignancy in our study. Difficulty and pain during swallowing were common symptoms in our study.

Majority of the patients with oral cavity malignancy (28 patients) presented in the early stages of the malignant disease. Most of the patients with oropharyngeal, hypopharyngeal and laryngeal malignancy presented in the later stages of the malignant disease.

## DISCUSSION

In our study, Oral cavity was the commonest site of malignancy in the upper aero-digestive tract (46 patients) followed by the larynx (24 patients). There were no cases of nasopharyngeal malignancy in our study. These findings were similar to a study by Nair et al.<sup>6</sup>

Compared to the rest of the world, the incidence of Head and Neck Squamous Cell Carcinoma is far more common in India and accounts for up to 30% of the country's cancer burden.<sup>7</sup> The site wise distribution of this malignancy is different in various parts of the world. Laryngeal cancers are more common in the Western world whereas oral cancers are more common in India.<sup>8</sup> These differences between India and Western world may be due to the difference in tobacco consumption pattern in these populations. As tobacco chewing is common in India, oral cancers are more common in India. Whereas tobacco chewing is uncommon in Western countries and is used only for smoking, exposing larynx, lungs to high risk for development of malignancy.

According to World Health Organization, 40% of the oral cancers diagnosed worldwide occur in India, Pakistan, Bangladesh and Sri Lanka. India has one of the highest rates in the world; accounting for one-third of the total cancers and unfortunately this figure continues to rise.<sup>9</sup> The frequency of head and neck cancer varies with the specific anatomical location.<sup>10</sup> In a study by Chen et al, the most common site amongst oral and pharyngeal

carcinoma was oral carcinoma, this was comparable with studies conducted in other countries where betel-quid chewing is popular.<sup>11-13</sup> According to some studies, Oral cancer is a leading cause of death among the 10 most common cancers, with highest rates being reported in Indian and French population. In India, among head and neck cancers, oral cavity malignancies were reported to show maximum incidence.<sup>14</sup> The various sub-sites of oral cavity and oropharynx are bathed with carcinogens from tobacco mixed in saliva, during chewing. Hence, carcinomas in these sites are associated with chewing of causative agents such as tobacco or pan.<sup>15</sup>

In 24 patients, malignant lesion was seen in the larynx. Hence, larynx was the second most common site to be involved by malignancy in the upper aero-digestive tract in our study. Larynx is exposed to carcinogens in tobacco smoke rather than the carcinogens mixed with saliva. Laryngeal malignancy was associated with smoking. Exposure to smoke from solid fuels used for cooking purposes in rural areas is also a risk factor for the development of laryngeal malignancy. As Larynx is an important part of the airway, the inhaled air passes through it. The various carcinogens and toxins present in the inhaled tobacco or solid fuel smoke come in contact with the larynx leading to its significant damage and development of malignancy.

Majority of the cases in our study presented in the 6<sup>th</sup> decade of life (52 patients), followed by 30 patients presenting in 7<sup>th</sup> decade of life. These findings were similar to a study by Pooja et al.<sup>15</sup> This is also consistent with the worldwide statistics of occurrence in above 40-year-old group.<sup>16</sup> None of the cases presented in the first 2 decades of life. 2 cases of oral cavity malignancy presented at 36 years and 39 years of age. 36 years was the youngest age of presentation in our study. Both these patients had the habit of tobacco and gutkha chewing since childhood.

In our study, 67% of the patients were male which was consistent with most of the studies.<sup>16</sup> Globally, male subjects are said to have more than two to three times higher incidence of head and neck malignancies than

female subjects.<sup>16</sup> According to Santos et al, malignant lesions were common in males, men being more exposed to carcinogens in tobacco and alcohol which lead to the development of upper aerodigestive tract malignancy.<sup>17</sup> According to Suba, oral and pharyngeal cancers among men and women occur in the ratio 4:1.<sup>18</sup>

Oral cancer is the fourth most common cancer in men and the eighth most common cancer in women.<sup>19</sup> According to Parkin, upper aerodigestive tract malignancy is more frequent in men than in women and has its highest incidence in the sixth decade of life.<sup>9</sup>

Hypopharyngeal malignancy was seen in both males and females equally in our study, which could be because of fewer cases of malignancy affecting this site amongst patients in our study. A large number of female patients had oral cavity malignancy and all of these patients had the habit of chewing tobacco. Smoking and Alcohol consumption by females is considered a taboo in Indian population especially in rural areas. Hence the overall incidence of upper aerodigestive tract malignancy is lower in females.

60% of the patients belonged to the lower socio-economic class in our study. Poor socio-economic status is said to be associated with more head and neck cancers, especially owing to dietary factors and poor nutrition.<sup>15</sup> The causes for high prevalence of cancer in rural India are a combination of lack of awareness among people regarding health issues, self-neglect, late presentation, lack of infrastructure at rural areas, lack of information about benefits of early diagnosis, prevalence of alternative systems and quacks who do not have any knowledge of cancer and its management, prevalent tobacco and alcohol use, poverty and resource crunch. In the rural areas, many people consider cancer as a communicable disease and consider it a taboo, which could lead to isolation of the individual and their family due to lack of knowledge.<sup>20</sup> The distance of the residence from a healthcare facility and poor connectivity are also responsible for the late presentation and poor survival in cancer patients.<sup>21</sup> Patients from distant rural areas of many countries have been found to have more advanced stage of the disease at the time of diagnosis and poor prognosis and survival.<sup>22</sup> The addiction to tobacco smoking and chewing among youth in the rural areas further increases the risk. According to Conway et al, the risk of upper aerodigestive tract malignancy for those of low socio-economic status was 2.41 times higher when compared with those of high income.<sup>23</sup>

Majority of the patients had exposure to tobacco in our study. 24 patients with laryngeal malignancy were smokers, 42 patients with oral cavity malignancy had the habit of tobacco chewing. A total of 58 patients consumed alcohol. All the cases of nasal cavity and paranasal sinus malignancy had the habit of using snuff. 28 patients had the habit of both chewing tobacco and smoking. 22 patients used to consume alcohol and had

exposure to tobacco as well. The risk of oral and pharyngeal cancer is increased in smokers of all tobacco products, with a higher risk found in smokers of cigarettes without filters such as beedi, which is commonly used in rural areas than in smokers of cigarettes with filters.<sup>24</sup> Beedi is used for smoking by a large number of people from rural areas because of lower cost, local production and easy availability.

Epidemiological studies that analyzed the influence of smoking and alcohol consumption on cancer development at various sites of the larynx found that the risk was higher for cancer in the area of the larynx which is located above the vocal cords and closest to the throat like the supraglottis, than in the area around the vocal cords, the glottis. This observation suggests that the risk of laryngeal cancer is highest in those areas of the larynx that come into closest contact with alcohol and tobacco smoke.<sup>24,25</sup>

According to the International Agency for Research on Cancer (IARC) monographs, chewing of tobacco is associated with cancer of the oral cavity whereas smoking is associated with cancer of all subsites of the head and neck region, there is an association between cancer of the PNS (paranasal sinuses) and smoking, whereas there is no association between cancer of the PNS and tobacco chewing.<sup>27</sup>

The risk was higher among chain-chewers of tobacco, prolonged chewers and chewers who started the habit at an early age. According to Hirayama, in most cases the side of the mouth affected by cancer was found to be the same as the side in which the quid was usually kept (side correspondence) and there was a correspondence between the anatomical location of the oral malignancy lesion and the place where the tobacco quid was habitually kept (site correspondence).<sup>28</sup>

Use of products such as pan masala and gutkha, is increasing not only among men but among children, teenagers and women as well, which has been associated with increased risk leading to increasing incidence of oral cavity malignancy in females and younger age group. Micronutrient deficiencies and poor oral hygiene has also been associated with increased risk. High incidence of oral cancer in India is due to high prevalence of betel quid (with or without tobacco) chewing, smoking and alcohol.<sup>29</sup> People who drank heavily and smoked have a 300 times higher risk of oral and pharyngeal cancer than people who neither drank nor smoked.<sup>30</sup> An international pooled analysis found that among smokers who have never used alcohol, the risk of oral and pharyngeal cancer is 2.13 times higher than persons who have never used alcohol or smoked.<sup>31</sup>

According to certain studies, approximately 80 percent of oral and pharyngeal cancer cases in men and about 65 percent of cases in women can be attributed to alcohol and tobacco use.<sup>31,19</sup> 24% of oral and pharyngeal cancers

could be attributed to tobacco use among those who have never consumed alcohol, while approximately 7% of cases can be attributed to alcohol use among those who have never used tobacco.<sup>32</sup> Studies found that even in people who do not smoke, drinking is directly associated with the risk of upper aerodigestive tract malignancy and the risk increases with the level of alcohol consumption.<sup>25</sup>

Poor diet, namely low consumption of fruits and/or vegetables, is another risk factor for oral and pharyngeal cancers. Consumption of fruit and vegetables has been found to decrease the risk of developing upper aerodigestive tract malignancy. Intake of red meat, pork and processed meat is associated with a significantly increased risk of oral and pharyngeal cancers.<sup>33</sup> Regular vegetable and fish consumption in the diet have been shown to be protective.<sup>34</sup> Majority of the patients in our study were non-vegetarians.

Symptoms of upper aerodigestive tract malignancy depend on the site where the malignant lesion is located. 40 patients of oral cavity malignancy presented with non-healing ulcer in the oral cavity. Bleeding from nose was seen in the cases with nasal and paranasal sinus malignancy. Neck lump was a complaint in 34 patients.

The main symptoms in order of frequency with which the patients with oral cavity malignancy presented were lesion in the mouth being reported by the patient, pain and difficulty in swallowing, earache. In patients with laryngeal malignancy, the main symptoms were change in voice, pain and difficulty in swallowing, difficulty in breathing. For lesions in the hypopharynx, the main complaints were pain and difficulty in swallowing and change in voice.

According to Tromp et al, early diagnosis of malignancy in the upper aerodigestive tract may be hampered by the fact that the initial lesions, with few symptoms, are not appreciated either by the individual or by healthcare workers.<sup>35</sup> Some authors suggest that these symptoms can be confused with other common diseases affecting the population. More so when these symptoms have never been presented to them as cancer indicators.<sup>36,37</sup>

In many cases, paranasal sinus cancers grow fairly large before they are diagnosed. This is because the tumors have room to grow before they block the sinuses or nasal passages or cause other symptoms. But these patients presented early in our study as they had history of blood-stained nasal discharge which was an alarming symptom to the patient.

28 cases of oral cavity malignancy presented in stage I and II of the disease. However, majority of the cases with malignant lesion in the larynx, oropharynx and laryngopharynx presented in an advanced stage of the disease (Stage III and IV). This was similar to a study by Santos.<sup>17</sup> 51 cases presented in stage III and IV of the disease, showing that most of the cases presented in

advanced stage of the disease. This was similar to a study by Pooja et al.<sup>15</sup> Cases with nasal cavity and paranasal sinus malignancy presented early as they had complaints of nasal bleeding. Majority of the cases where malignant lesion was found in other sites of upper aerodigestive tract presented late, in advanced stages of the disease as the symptoms which were produced from these lesions were not alarming. Most of the oral cavity malignancy patients presented with non-healing ulcer, early in the course of illness.

Physical examination is an important mean of detecting lesions of the upper aero-digestive tract. Initial assessment usually indicates the site of lesion, severity of the disease. Additional investigative modality such as nasal endoscopy, hypopharyngoscopy, direct laryngoscopy help in detailed evaluation of various sites in upper aero-digestive tract and also in obtaining the tissue specimen for histopathological examination. Ultrasonography of neck and fine needle aspiration cytology (FNAC) of enlarged neck node if present have to be undertaken to rule out metastases to cervical lymph node. Computerised tomography and magnetic resonance imaging of the involved site helps in staging of the disease and its severity and this in turn helps in assessing the prognosis of the disease. Due to the frequent occurrence of multiple primary tumors in patients with a head and neck tumor, careful evaluation of the entire upper aerodigestive tract is necessary at the time of diagnosis. The examination should always follow a systematic approach.

All the cases in our study were squamous cell carcinoma on histopathological examination. Squamous cell carcinomas (SCC) constitute more than 90% of all upper aerodigestive tract malignancies. Other malignant tumors in the upper aerodigestive tract can arise from the epithelium, connective tissue, minor salivary glands, lymphoid tissue and melanocytes or metastasis from a distant tumor.

The most common site of upper aerodigestive tract malignancy in rural population as seen in our study, is the oral cavity. It has been shown that the most commonly affected individuals are males in the elderly age group. Tobacco and alcohol consumption are implicated as habits that increase the risk of upper aerodigestive tract malignancy. People from rural areas, due to personal habits, lower socio-economic status and lack of education are exposed to various factors that increase the risk of upper aerodigestive tract malignancy.

Health education about the ill-effects of smoking, tobacco chewing and alcohol consumption needs to be delivered to the people from rural areas. People should be informed regarding the warning signs of cancers of the upper aerodigestive tract and the importance of a healthy, active life-style, consumption of a nutritious and balanced diet. Improvement of socio-economic status of people from rural areas is also likely to bring about significant

improvement in the nutrition, self-care, concern and awareness about health issues amongst people. A detailed clinical examination of patients presenting with upper aerodigestive tract symptoms should be undertaken especially in high-risk groups.

## ACKNOWLEDGEMENTS

The author is thankful to the Faculty members and Residents of the Department of Otorhinolaryngology and Head and Neck Surgery and also the Faculty members of the Department of Pathology of Chamarajanagar Institute of Medical Sciences and Hospital, Chamarajanagar for their assistance during the study.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

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**Cite this article as** Shariff MA. Anatomical site-wise distribution of upper aerodigestive tract malignancies in a rural population. *Int J Otorhinolaryngol Head Neck Surg* 2018;4:1394-401.