

A Study to Evaluate Clinicopathological Parameters in Patients with Carcinoma Pharynx



Medical Science

KEYWORDS : squamous cell carcinoma, nasopharynx, oropharynx, hypopharynx.

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ABSTRACT

Pharyngeal cancer is cancer of the head and neck region. It is divided into three parts the nasopharynx, oropharynx and hypopharynx. Smoking and alcohol act synergistically in the development of carcinoma pharynx. The aim of this study was to evaluate clinico-pathological parameters in patients with carcinoma pharynx and to compare clinico-pathological parameters between patients aged less than and more than 40 years age. Majority of patients had smoke tobacco, smokeless tobacco and alcohol consumption in both age groups with no statistical difference. Involvement of oropharynx, hypopharynx was more commonly seen in > 40 years age group, whereas, cancer nasopharynx was more common in < 40 years age group with no statistical difference in involvement of three parts of pharynx was seen between the two age groups.

INTRODUCTION

Pharyngeal cancer includes cancers of the nasopharynx, oropharynx and hypopharynx. Nasopharyngeal carcinoma (NPC) is a tumor arising from the epithelial cells that cover the surface of the nasopharynx. In India, NPC is rare, except for the Hill States of Northeast India. In cases of nasopharyngeal carcinoma neck mass is the commonest complaint, followed by bleeding from the nose and headache.

Oropharyngeal squamous cell carcinoma is usually poorly differentiated and locally advanced at the time of clinical presentation. The overall incidence of cervical lymph node metastasis is 50–70% [7]. The clinical features of oropharyngeal cancer include trismus, dysphagia, odynophagia, altered tongue mobility, otalgia or all [8]. The commonest sites of cancers in the oropharynx are the tonsil and the tongue base [9]. The incidence of oropharyngeal cancers worldwide is 1.2% [10].

Hypopharynx is the longest of the three segments of pharynx. The incidence of hypopharynx carcinoma in India is 5.9 per 100,000 populations. Clinically, cancers of the hypopharynx tend to be aggressive and demonstrate a natural history that is characterized by diffuse local spread, early metastasis, and a relatively high rate of distant spread. More than 50% of patients with hypopharyngeal cancer have clinically positive cervical nodes at the time of presentation. In 50% of these individuals, a neck mass is the presenting symptom. The clinical features of hypopharyngeal cancer other than neck mass include dysphagia, odynophagia, voice change, and otalgia.

MATERIALS AND METHODS

The present study was carried out in the department of Otorhinolaryngology, at Himalayan Institute of Medical Sciences, Swami Ram Nagar, Dehradun over a period of 12 months. A total of 98 patients newly diagnosed with carcinoma nasopharynx, oropharynx or hypopharynx were included in this study after taking informed consent from the patient and clearance from the ethics committee. Previously treated pharynx cancer patients with recurrence were excluded.

The patients selected for this study were subjected to a detailed history and complete Otorhinolaryngology and head and neck clinical examination after detailed informed consent. Detailed personal history included consumption of smoke tobacco, smokeless tobacco and alcohol intake. As per patients history, smokeless tobacco consumption was calculated as packets per day and smoke tobacco consumption was calculated in pack years (number of bidis/cigarettes smoked per day divided by the number of bidis/cigarettes in 1 pack and then multiplied by the number of years the person has smoked). Alcohol consumption was calculated in grams per day (Alcohol by volume (%) × Volume consumed per day (ml) divided by 1000 and then multiplied by 10). Energy was calculated in Kcal/day, fat in grams/day and proteins in grams/day based on patients regular diet.

General examination and vitals of all patients were recorded. Systemic examination was done to detect distant metastasis. The oral cavity was examined in detail with help of a tongue depressor using head mirror and bull's eye lamp to look for second primary. Suspected area was evaluated by digital palpation. Detailed examination of larynx and pharynx (oropharynx and hypopharynx) were done by indirect laryngoscopy mirror (No. 3-7) and by diagnostic laryngeal endoscopy using Karl Storz 700 rigid wide angle laryngeal endoscope (7mm) and findings were recorded using Imimo software and printed records were obtained. Nasopharynx was examined by posterior rhinoscopy and findings were confirmed by Karl Storz 00 Hopkins rod rigid nasal endoscope (4mm).

Detailed examination of neck was done including laryngeal framework, laryngeal tenderness, laryngeal crepitus and lymph nodes from level I to level VI. Clinical staging of the tumor was done as per American Joint Committee on Cancer (AJCC) (2012) classification (20). Fine Needle Aspiration Cytology (FNAC) was done by standard technique either using aspiration (Thompson 1982) or without aspiration (Zadela 1987) under all aseptic precautions with a 22 gauge needle for neck swelling. All patients underwent biopsy for histopathological examination under general anaesthesia (GA) or local anaesthesia (LA). Patients diag-

nosed as carcinoma nasopharynx, oropharynx or hypopharynx was grouped into < 40 years of age patients and > 40 years of age patients. Patients aged 40 years were included in < 40 years age group. Records were maintained for future references.

OBSERVATION

In present study, the age distribution of patients ranged from 24 to 80 years of age. There were 98 patients with cancer pharynx, out of which, 38 (38.77%) patients were in < 40 years age group and 60 (61.22%) patients in > 40 years age group. (Table-1)

Table: 1 showing distribution of cases according to age and sex.

Carcinoma N=98	Age (years)	Sex	No of cases
Oropharynx N=53(54.08%)	<40	Female	3
		Male	23
	>40	Female	9
Nasopharynx N=12(12.24%)	<40	Female	2
		Male	2
	>40	Female	1
Hypopharynx N=33(33.67%)	<40	Female	0
		Male	21
	>40	Female	4

In carcinoma nasopharynx,(n=12) 75% of patients were young (< 40 years age group) and rest were above 40 years of age(25%) and majority were males. There were 53 patients (54.08%) with carcinoma oropharynx,, majority were male(77.35%) and majority were above 40 years of age(60.37%). There were 33 patients (33.67%) with carcinoma hypopharynx, out of which, 25(75.75%) were above 40 years and 29 were males (87.87%).

Table: 2 Presenting symptoms in cancer pharynx patients (n=98)

Symptoms	No. of patients	
	Age < 40 years (n=38)	Age > 40 years (n=60)
Pain on swallowing	31 (81.57%)	59 (98.33%)
Ulcer/growth in mouth	5 (13.15%)	4 (6.66%)
Change in voice	23 (60.52%)	23 (38.33%)
Difficulty in swallowing	22 (57.89%)	44 (73.33%)
Swelling in the neck	24 (63.15%)	35 (58.33%)
Difficulty in breathing	14 (36.84%)	14 (23.33%)
Earache	19 (50%)	26 (43.33%)
ENT bleed	14 (36.84%)	11 (18.33%)
Decreased hearing	7 (18.42%)	2 (3.33%)

In our study, pain or difficulty on swallowing,change invoice, swelling in neck and earache was the commonest complaints. (Table-2)

Table: 3 Showing distribution of cases according to habit.

Habit	Age		Percentage
	<40 yrs	>40 yrs	
Smoke tobacco	32	56	89.79
Smokeless tobacco	11	17	28.57
Alcohol	30	57	88.77

Smoke tobacco consumption,tobacco chewing and alcohol intake were commonest habits responsible for causation of carcinoma pharynx. Statistically there was insignificant difference in habits below and above 40 years of age. (Table-3)

Table: 4 Showing distribution of cases according to diet intake.

Dietary intake	Age (years)			
	<40		>40	
	M	F	M	F
Protein	14 (<100 g/day)	3 (<100 g/day)	23 (100-150 g/d)	5(100-150 g/d)
Fat	11 (41-50 g/d)	3 (31-40 g/d)	26(41-50 g/d)	6 (41-50 g/d)
Energy intake	17 (2001-3000 kcal/d)	4(<2000 kcal/d)	32(2001-3000 kcal/d)	9(<2000 kcal/d)

In < 40 years of age group, it was found that intake of protein, fat and calorie was than age group > 40 years and could be implicated as one of the causative factor of pharyngeal carcinoma. (Table-4)

Table: 5 Subsite distribution in cancer pharynx patients (n=98)

Subsite	Site wise no. of patients	
	Age< 40 years (n=38)	Age > 40 years (n=60)
	Nasopharynx (n=12)	
Fossa of Rosenmuller	9 (23.68%)	3 (5%)
Torus tubaris	9 (23.68%)	3 (5%)
Posterior choanae	9 (23.68%)	2 (3.33%)
Superior and posterior wall	9 (23.68%)	3 (5%)
Eustachian tube	7 (18.42%)	3 (5%)
Oropharynx (n=54)		
Soft palate	3 (7.89%)	7 (11.66%)
Uvula	3 (7.89%)	8 (13.33%)
Tonsillar pillar	6 (15.79%)	7 (11.66%)
Tonsillar fossa	8 (21.05%)	19 (31.66%)
T-L sulcus	7 (18.42%)	12 (20%)
Posterior pharyngeal wall	3 (7.89%)	3 (5%)
Posterior one third tongue	14 (36.84%)	32 (53.33%)
Vallecula	6 (15.79%)	14 (23.33%)
Lateral pharyngeal wall	6 (15.79%)	4 (6.66%)
PEF	4 (10.52%)	28 (46.66%)
Hypopharynx (n=32)		
Pyriform fossae	6 (15.79%)	29 (48.33%)
Post-cricoid region	2 (5.26%)	16 (26.66%)
Posterior pharyngeal wall	1 (2.63%)	9 (15%)

Cancer pharynx patients in our study had involvement of more than one subsite. Majority of patients with carcinoma oropharynx had involve base of tongue and tonsillar area in both age group while in carcinoma hypopharynx pyriform fossa was the commonest site in both age group. (Table-5)

Table.6: Level of cervical lymphadenopathy in cases (n=98)

Level of Lymph nodes involved	Site wise no. of patients	
	Age < 40 yrs (n=38)	Age > 40 yrs (n=60)
Level Ia	0	0
Level Ib (n=5)	0	0
Level II (n=104)	23	30
Level III (n=41)	8	15
Level IV (n=17)	5	12
Level V (n=6)	2	3
Level VI (n=0)	0	0

In both age group most common lymph node spread was level II nad III. (Table-6)

Table: 7 Tumor staging of cancer patients (except cancer nasopharynx) (n=86)

Tumour staging	No. of patients			
	Cancer Oropharynx (n=53)		Cancer Hypopharynx (n=33)	
	Age < 40 years(n=20)	Age > 40 years (n=33)	Age < 40 years (n=7)	Age > 40 years (n=25)
T1	3	4	0	1
T2	11	15	5	7
T3	5	9	2	1
T4a	1	5	0	13
T4b	0	0	0	3

Table: 8 Nodal staging in cancer patients (except cancer nasopharynx) (n=86)

Node stage	No. of patients			
	Cancer Oropharynx (n=53)		Cancer Hypopharynx (n=33)	
	< 40 years (n=20)	> 40 years (n=33)	< 40 years (n=7)	> 40 years (n=25)
N0	12 (57.14%)	15 (45.45%)	5(7.14%)	14(56%)
N1	6(28.57%)	11(33.33%)	2(28.57%)	9(36%)
N2a	2 (9.52%)	4(12.12%)	0(0%)	0 (0%)
N2b	0 (0%)	1(3.03%)	0 (0%)	1(4%)
N2c	0 (0%)	1(3.03%)	0 (0%)	1(4%)
N3	0(4.76%)	1(3.03%)	0 (0%)	0 (0%)

In our study most common presentation of tumor size in carcinoma oropharynx and hypopharynx was T1 and T2 and most common nodal involvement was N0 and N1 in both age groups. (Table-7 & 8)

Table: 9 Tumor staging of Cancer Nasopharynx (n=12)

Tumour staging	No. of patients	
	Age < 40 years (n=9)	Age > 40years (n=3)
T1	3 (33.33%)	0 (0%)
T2	4 (44.44%)	2 (66.66%)
T3	1 (11.11%)	1 (33.33%)
T4	1 (11.11%)	0 (0%)

Table: 10 Nodal staging in cancer nasopharynx (n=12)

Node stage	No. of patients	
	<40 years (n=9)	>40 years (n=3)
N0	2 (22.22%)	1 (33.33%)
N1	1 (11.11%)	0 (0%)
N2	5 (55.55%)	2 (66.66%)
N3a	1 (11.11%)	0 (0%)
N3b	0 (0%)	0 (0%)

In our study most common presentation of tumor size in carcinoma nasopharynx was T1 and T2 and most common nodal involvement was N0 and N2 in both age groups. (Table-9 & 10)

Table: 11 Showing distribution of cases according to histopathological presentation.

Histopathological parameter	No of cases	
	<40 yrs	>40 yrs
Squamous cell carcinoma	35	60
Non Hodgkins lymphoma	3	-
SCC+ Necrosis	27	44

Most common cancer variant present was squamous cell carcinoma seen in 95 (96.93%) patients. In < 40 years age group, squamous cell carcinoma was present in 35 (94.91%) patients followed by Non Hodgkins lymphoma in 3 (5.08%) patients. In > 40 years age group, squamous cell carcinoma was present in 60 (100%) patients. In < 40 years age group, moderately differentiated squamous cell carcinoma was the most common finding present in 20 (57.14%) patients and poorly differentiated squamous cell carcinoma was present in 15 (42.85%) patients. In > 40 years age group, moderately differentiated squamous cell carcinoma was mostly found present in 36 (60%) patients followed by poorly differentiated squamous cell carcinoma was present in 22 (36.66%) patients and well differentiated squamous cell carcinoma was present in 2 (3.33%) patients. Among other histopathological parameters, necrosis was the most common parameter present in 27 (77.14%) patients in < 40 years age group and 44 (73.33%) patients in > 40 years age group. (Table-11)

Most of the patients with distant metastasis had lung involvement present in 6 (6%) patients. In cancer nasopharynx, 2 (50%) patients in < 40 years age group and 1 (100%) patient in > 40 years age group had lung involvement. In cancer oropharynx, 1 (100%) in < 40 years age group and 2 (66.66%) patients in > 40 years age group had lung involvement. In patients with cancer pharynx, majority of patients presented with stage III cancer in 18 (47.36%) patients in < 40 years age group and 35(58.33%) patients in > 40 years age group. Total 40 (38.02%) cases with cervical lymphadenopathy who underwent fine needle aspiration cytology, 28 (70%) patients had metastatic deposits of squamous cell carcinoma, 9 (22.5%) patients had metastatic deposits of poorly differentiated carcinoma and 3 (7.5%) had Non hodgkins lymphoma.

Discussion

There were 98 patients with cancer pharynx, out of which, 38 (38.77%) patients were in < 40 years age group and 60 (61.22%) patients in > 40 years age group. Pain on swallowing was present in 31 (81.57%) patients with cancer pharynx in < 40 years age group and in > 40 years age group, pain on swallowing was present in 59 (98.33%) patients. In a study by Bhagat S et al [1] on tumors of hypopharynx, dysphagia for 2.6 months followed by neck mass and throat pain 2 months duration was the commonest symptoms. Yerma A et al [2] found hoarseness of voice (73.92%) as commonest complaint followed by dysphagia (50.95%) and pain in throat (25.59%) in patients with cancer larynx and hypopharynx. Licitra L et al [3] found odynophagia (72%) as the common presenting symptoms in oropharyngeal cancer patients. In a study by Morales Anquilo C et al [4] in cancer nasopharynx patients, most common presenting complaint was neck mass present in 47% of patients. In our study, it was observed that most patients presented to hospital within 3 months of onset of symptoms or at the most, between 3 to 6 months duration. It was because symptoms of cancer pharynx are noticed early by the patients as these symptoms hinder in day to day activity of patients which leads them for early consultation at the hospital. Smokeless tobacco consumption was present in 28 (28.57%) patients with cancer pharynx, out of which 11 (39.28%) patients were in < 40 years age group and 17 (60.71%) patients were in > 40 years age group. In a report by Arzola RA et al [5], 5.5% of high school students in U.S. reported current use of smokeless tobacco. It was observed that increased prevalence of smokeless tobacco was seen in young patients in < 40 years age group as compared to patients > 40 years of age leading to increased incidence of oropharyngeal cancer in younger age groups. More nicotine is absorbed by smokeless tobacco use than that by smoke tobacco.

Alcohol consumption was present in 87 (88.77%) patients, out of which 30 (34.44%) patients were in < 40 years age group and 57 (65.51%) patients were in > 40 years age group. In a study by

Choi SY et al [6] heavy drinkers (males who consumed 90 grams daily of ethanol) had an 11-fold risk of pharyngeal cancer. In our study, it was revealed that maximum number of chronic alcoholic patients were in > 40 years age group as compared to < 40 years age group. However, it is observed that the development of squamous cell carcinoma at a young age can be related to chronic alcohol consumption along with tobacco usage as many patients belonged to lower socioeconomic status who had poor oral hygiene and poor diet. Poor survival in many young patients is due to self-neglect and failure to seek medical care early in the course of disease.

In < 40 years age group, 14 (36.84%) male patients and 3 (7.89%) female patients with less than 100 grams per day protein intake was the commonest. 11 (28.94%) male patients with 41 to 50 grams per day fat intake and 3 (7.89%) female patients with 31 to 40 grams per day fat intake was most commonly seen and 17 (44.73%) male patients with 2001 to 3000 kcal/day energy intake and 4 (10.52%) female patients with less than 2000 kcal/day energy intake was found in majority of patients. Whereas, in > 40 years age group, 23 (38.33%) male patients and 5 (8.33%) female patients with 100 to 150 grams per day protein intake was seen in most of patients. 26 (43.33%) male patients and 6 (10%) female patients with 41 to 50 grams per day fat intake was found in majority of patients and 32 (53.33%) male patients with 2001 to 3000 kcal/day energy intake and 9 (15%) female patients with less than 2000 kcal/day energy intake was most commonly seen. Schmidt KN et al [7] concluded that advanced tumor stage, pain, loss of appetite, and difficulty swallowing significantly lowered dietary intake and caused more than 5% weight loss over 6 months. In a study by Sanchez MJ et al [8], a significant inverse association with the risk of oral and oropharyngeal cancer was found for total consumption of total green vegetables and total fruits with significant trends in risk.

The most common site in pharynx observed in present study was oropharynx present in 54 (55.10%) patients followed by hypopharynx present in 32 (32.65%) patients and then nasopharynx in 12 (12.24%) patients. Similar findings were seen by Lee YC et al [9] found oropharynx along cases were 922 (47.22%) patients followed by hypopharynx cases were 854 (40.61%) patients. Bhattacharjee et al [10] observed that oropharyngeal cancer (28.62%) was the commonest site in elderly patients. According to our study, base of tongue was the commonest subsite involved in oropharynx in both < 40 years of age present in 14 (36.84%) patients and > 40 years of age present in 32 (53.33%) patients. This finding was in accordance with Ramqvist T et al [11] Pyriform fossa was the commonest subsite involved in hypopharynx in both < 40 years of age present in 6 (15.79%) patients and > 40 years of age present in 29 (48.33%) patients. Bhagat S et al [1] in their study observed that pyriform fossa (80%) was the commonest subsite involved in hypopharynx which was similar to our study. In cancer pharynx patients, ulceroproliferative growth pattern was seen in 74 (75.51%) patients, out of which there were 24 (63.15%) patients in < 40 years age group and 50 (83.33%) in > 40 years age group. Rousseau A et al [12] observed that cancer oral cavity, pharynx and larynx usually presents as ulceroproliferative lesion. The cervical lymphadenopathy was present in 82 (47.12%) patients with cancer pharynx. Most common site of cervical lymph node involvement was level II lymph node present in 46 (46.93%) patients. Mukherji S K et al [13] observed that mostly level II cervical lymphadenopathy was seen in cancer nasopharynx (82%), base of tongue (88%), palatine tonsil (97%), soft palate (86%) and pyriform sinus (72%). N1 nodal staging was most common presentation in our study among cancer patients with cervical lymphadenopathy except N2 nodal stage was mostly seen in cancer nasopharynx patients with cervical lymphadenopathy. Majority of patients with cancer nasopharynx presented with N2 nodal stage present in 5 (55.55%) patients in < 40 years age group and 2 (66.66%) pa-

tients in > 40 years age group. Cancer oropharynx patients had N1 nodal stage present in 6 (28.57%) patients in < 40 years age group and 11 (33.33%) patients in > 40 years age group. Among patients with cancer hypopharynx, N1 staging was present in 2 (28.57%) patients in < 40 years age group and 9 (36%) patients in > 40 years age group. Liu MT et al [14] suggested N2 stage as commonest presentation in cancer nasopharynx patients. Gunn GB et al [15] found that N1 stage presentation among cancer oropharynx patients was most common. Taha MS et al [16] found N1 node presentation in 9 (39.1%) patients as commonest among cancer hypopharynx patients with cervical metastasis. Patients presented to hospital late because of less awareness among them and late referral by primary treating doctor. Among patients with cancer nasopharynx, majority of patients presented with T2 stage present in 4 (44.44%) patients in < 40 years age group and 2 (66.66%) patients in > 40 years age group. Cancer oropharynx patients mostly presented with T2 stage present in 11 (52.38%) patients in < 40 years age group and 15 (45.45%) patients in > 40 years age group. T2 stage presentation was most common among cancer hypopharynx patients, in < 40 years age group T2 stage was present in 6 (75%) patients, whereas, in > 40 years age group had T3 stage presentation was common present in 14 (56%) patients. In a study by Liu MT et al (14), T2 stage was the most commonly seen in cancer nasopharynx patients present in 35 (42.16%) patients. Markou K et al [17] observed T3 stage (32%) as the most common presentation in cancer larynx patients. Gunn GB et al [15] observed that T2 stage tumors (64%) as most common presentation in oropharyngeal cancers. Taha M S et al [16] observed that T3 and T4 as most common presentation in cancer hypopharynx patients. In cancer nasopharynx, 2 (50%) patients in < 40 years age group and 1 (100%) patient in > 40 years age group had lung involvement. In cancer oropharynx, 1 (100%) in < 40 years age group and 2 (66.66%) patients in > 40 years age group had lung involvement. Patients with distant metastasis usually present in late stage of disease as most of them belong to rural area with poor medical facility, transportation, and belief in religious ritual and traditional medicines. Majority of patients with cancer pharynx presented with stage III cancer present in 18 (47.36%) patients in < 40 years age group and 35 (58.33%) patients in > 40 years age group. These findings were consistent with Liu MT et al (14), Markou K et al [17] Gunn GB et al [15] and Taha MS et al [16] Total 40 (38.02%) cases with cervical lymphadenopathy who underwent fine needle aspiration cytology, 28 (70%) patients had metastatic deposits of squamous cell carcinoma, 9 (22.5%) patients had metastatic deposits of poorly differentiated carcinoma and 3 (7.5%) had Non Hodgkins lymphoma. Patients with cervical lymphadenopathy had primary tumour involving the nasopharynx, oropharynx, hypopharynx, supraglottis and/or oral cavity which have rich lymphatic supply.

Most common cancer variant present was squamous cell carcinoma seen in 95 (96.93%) patients. In < 40 years age group, squamous cell carcinoma was present in 35 (94.91%) patients followed by Non Hodgkins lymphoma in 3 (5.08%) patients. In > 40 years age group, squamous cell carcinoma was present in 60 (100%) patients. In < 40 years age group, moderately differentiated squamous cell carcinoma was the most common finding present in 20 (57.14%) patients in < 40 years age 36 (60%) patients in > 40 years age group. Among other histopathological parameters, necrosis was the most common parameter present in 27 (77.14%) patients in < 40 years age group and 44 (73.33%) patients in > 40 years age group. Busquets JM et al [18] conducted a study on head and neck squamous cell carcinoma and concluded that most of the patients (55.5%) had moderately-differentiated squamous cell carcinoma. Bhattacharjee et al [10] concluded in his study that squamous cell carcinoma was the commonest histological type seen in 99.37% with hypopharyngeal cancer, 97.5% with cancer oropharynx. Necrosis in histopathological reporting is associated with high T classification and high N classification and thus poor prognosis of disease.

Conclusion

- Majority of patients of carcinoma pharynx had presenting symptom of pain on swallowing.
- Tobacco and alcohol consumption was the most common etiological factor in our study.
- Higher consumption of smoke tobacco, smokeless tobacco and alcohol was seen in > 40 years age group was seen as compared to < 40 years age group.
- Majority of patients had inadequate dietary intake as per recommended dietary allowance.
- The most common clinical presentation was ulceroproliferative growth pattern.
- More than half of the patients had cervical lymphadenopathy which were positive for metastasis deposits on FNAC.
- Most of the patients were diagnosed at stage III of cancer.
- Squamous cell carcinoma was the most common histopathological type seen and moderately differentiated squamous cell carcinoma was the most common differentiation variant observed.
- Involvement of nasopharynx was more commonly seen in < 40 years age group and involvement of oropharynx and hypopharynx was more common in > 40 years age group.

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