

Original Article

Head-and-neck cancer: Survival analysis of patients treated in a tertiary cancer hospital in Mumbai

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ABSTRACT

Objectives: The main objective of this study is to report on the survival rates of head-and-neck cancer cases seen in Tata memorial hospital (TMH).

Materials and Methods: In the present study comprises of a large number of head-and-neck cancer cases seen in TMH, Mumbai, during the years 2012–14. The study included 4351 oral cancer, 766 oropharyngeal cancer, 612 hypopharyngeal cancer, 544 laryngeal cancers, and 244 nasopharyngeal cancer. TNM group staging was used to determine the clinical extent of disease.^[2]

Results: In the study, a major proportion of patients were diagnosed in Stage III and stage IV, except in vocal cord and to a lesser extent in lower lip and anterior tongue. Thus, the treatment offered is either only surgery or in combination with radiotherapy or chemotherapy. The overall 3-year survival rates for oral cancer were 26–43%, 23–33% for oropharyngeal cancer, 22–28% for hypopharyngeal cancer, 28–53% for laryngeal cancers, and 44% for nasopharyngeal cancer.

Conclusion: Prognosis differed by site of disease and subsites in this study. The differences in outcome are an indicator of the scope of prevention activities that could be reiterated for better prognosis of head-and-neck cancer.

Keywords: Head-neck cancer, Survival rates, India

INTRODUCTION

As per the GLOBOCAN^[1] estimates, there are approximately 200,000 (17%) head-and-neck cancer cancers diagnosed annually. There is a male pre-dominance in this cancer. Of the head-and-neck cancers, oral cancers contribute a major proportion, followed by Pharyngeal cancer. The data emanating from the 36 population-based registries and six hospital based cancer registries indicate that, irrespective of the geographical location in India, oral cancers are leading cancers in all the registries as reported by National Centre for Disease Informatics and Research (NCDIR).^[2] The main risk factor for these cancers is tobacco-consumption, as is well-known and established time and again through various epidemiological studies.

The Tata memorial hospital (TMH), a premier cancer hospital in India, registers more than 50,000 cancers annually, of which 35% are head-and-neck cancers. The present study

is an effort of conducting a cohort study of patients seen and diagnosed at TMH during the years 2012–14. The study reports on survival rates of head-and-neck cancers.

The present study aims at reporting cancer survival rates of head-and-neck cancer, by subsites as well, seen and diagnosed during the years 2012–14 at TMH, a tertiary Cancer hospital in Mumbai.

MATERIALS AND METHODS

The present study is a retrospective study, based on head-and-neck cancer cases seen in TMH between 2012 and 14.

The eligibility criteria for inclusion in the study were those with (i) no previous cancer-directed treatment given before registration at TMH, (ii) only histologically confirmed epithelial cancer, (iii) those treated with chemotherapy in combination with surgery or radiotherapy and not as the

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only treatment, and (iv) only those subsites of head-and-neck cancers which report at least 50 cases. Some of the cancer subsites excluded were upper lip, commissure of lip, tongue not otherwise specified (NOS), salivary gland, palate NOS, and subglottic larynx, which reported <50 cases each. Primary site and secondary site (International Classification of Diseases for Oncology,) of cancer, histology of primary and secondary site, tumour node metastasis (TNM) staging by UICC,^[3] type of treatment given within 6 months from diagnosis, and follow-up details were abstracted from the electronic medical record of the hospital. The staging of disease was classified into four stages, namely, Stage I comprising of T₁N₀M₀ status, Stage II comprising T₂N₀M₀, Stage III comprising T₃N₀M₀, T₃N₁M₀, T₁N₁M₀, T₂N₁M₀, Stage IV comprising of T₄N₀M₀, T₄N₁M₀, any T, N₂ or N₃ M₀, and any T any N M. Active follow-up was undertaken to obtain information at periodic intervals, by emails, telephonic contact and postcards. In all 9934 cases were diagnosed, of which 929 cases had prior treatment and 1981 cases had no treatment before attending TMH. Of 7024 cases, 6412 were with curative intent and 612 were palliative intent. However, of 7024 new cases, 507 did not complete treatment (incomplete) and the reasons for incomplete treatment were due to various social factors, such as affordability, residing in far off places, no-family support, etc. Thus, 6517 cases who undertook full complete treatment were considered for analysis. The follow-up included both demographic (electronic method) and clinical follow-up (hospital visits). Patients were followed up for minimum of 3-years. Response rate to such methods was 50%. The Municipal Corporation of Greater Mumbai provided of dead patients. The closing date of study was December 31, 2017. The study population comprised of 6517 cancer cases. Duration of follow-up was minimum 3-years. In this study of 6517 patients, 760 (11.7%) patients were known to have died and 2688 patients were known to be alive at the end of 3-years from their date of diagnosis.

Methods

Actuarial life-table method was applied to compute survival rates for 1, 2, and 3 years. Patients lost to follow-up with disease were considered as censored and survival information available up to that point was used for analysis. Observed survival rates are reported. Since 60% of patients in the study population were from Maharashtra State in India, life-table for Maharashtra published by Government of Maharashtra, by registrar general of India (RGI)^[4] was used to estimate the relative survival rates (RSR). Statistical software SPSS Ver21^[5] was used for analysis.

RESULTS

Patient's characteristics of all cases by sub-sites are shown in [Tables 1 and 2]. It includes distribution of number of cases,

sex ratio, stage of disease, treatment modalities, and survival rates (%). [Table 1] comprises of Oral cavity (OC) cancer and [Table 2] comprises of pharyngeal (PHY) cancers.

It is seen in [Table 1] that buccal mucosal cancers ($n = 2032$) and anterior tongue ($n = 1313$) cancers constitute a major proportion of OC cancers, while floor of mouth showed the least number of cases. The average age among the OC cancers ranges between 48.5 years (anterior tongue) and 53.8 years (lower alveolus). In all the sub-sites, more than 65% of the cases were diagnosed in Stage (III + IV) cancers. Those treated with only surgery ranged between 14.4% in anterior tongue to 27.3% in lower lip cancers, and treatment with only radiotherapy ranged between 2.1% in anterior tongue and 20.5% in retromolar cancers. The most favored treatment was combination therapy of surgery, radiotherapy, and chemotherapy, which constituted more than 70–80%. This clearly indicates the role of radiotherapy as a major contributor to combinative therapy.

3-year survival rates for OC cancers are shown in [Table 1]. It is observed that the 3-year survival rates for all the OC cancers were below 50%; the highest 3-year survival rates were observed among those with lower-lip (43%) and hard-palate cancers (43%), and the lowest survival rates were seen in those with floor-of-mouth cancers (26%). The median survival times are also shown.

[Table 2] shows the details of pharyngeal cancers as number of cases, stage distribution, treatment, and survival rates. Among the PHY cancers, pyriform fossa constituted highest number of cases ($n = 470$), followed by vocal cord ($n = 275$), sub-glottis ($n = 269$), and base-tongue ($n = 264$) among others. Nasopharyngeal cancers constituted 244 cancer cases. The average age ranged between 38.7 years in nasopharynx and 59.9 years in pyriform fossa cancer patients. Among all the sub-sites in pharyngeal cancers, more than 70–75% of cases were diagnosed in Stage (III + IV), except in soft-plate and vocal cord cancers; only in vocal-cord cancers, 57% of cancers constituted Stage (I + II).

As seen in [Table 2], unlike in OC cancers, those treated with only surgery were very minimal (<5%), except in hypopharyngeal cancer (28.7%) and nasopharyngeal cancer (16%). Majority of them were treated with radiotherapy. 3-year survival rates were highest in those with vocal cord cancers (53%), followed by nasopharyngeal cancers (44%), tonsil (33%), pyriform fossa (28%), and sub glottis (28%), among others. Lowest survival rates were observed in hypopharyngeal cancers (22%). In general, patients with OC cancers have better prognosis than those with PHY cancers.

[Table 3] shows 3-year survival rates by different treatment modalities for various sub-sites of head-and-neck cancers. It is observed that the best prognosis for most of the sub-sites those that have been treated with surgery combined with radiotherapy. Consistently, in vocal cord cancers, the

Table 1: Patient characteristics and 3-year observed survival rates (%).

Sites (ICD-10)	Lower lip	Anterior tongue	Lower alveolus	Upper alveolus	Floor mouth	Buccal mucosa	Hard palate	Retro molar
Number of cases	99	1313	473	105	69	2032	115	145
Average age (years)	53.4	48.5	53.8	53.7	54	49.6	52.6	51.6
Stage (%)								
I	20.2	19.5	2.5	6.7	8.7	7.9	6.1	2.8
II	14.1	24.1	5.5	7.6	13	10.6	18.3	8.3
III	19.2	15.4	7.6	7.6	17.4	14.5	14.8	15.9
IV	42.4	36.7	81.4	73.3	52.2	62.4	53	69
NOS	4	4.3	3	4.8	8.7	4.6	7.8	4.1
	100	100	100	100	100	100	100	100
Treatment summary								
SX	27.3	14.4	15.2	24.6	19.3	27	16.6	1.1
RT	3	2.1	9.5	5.8	3	13	4.8	20.5
CH	5.5	11.4	10.5	13	13	7	9	8.3
SX+RT	30	39.3	22.9	24.6	27.6	32.2	21.4	1.1
SX+CH	1.7	1.7	1.9	1.4	3	0.9	2.8	0
RT+CH	5.8	3	11.4	10.1	5.3	7.8	13.1	64
SX+RT+CH	26.4	27.1	26.7	20.3	28.2	11.3	30.3	1.5
Others	0.3	1.1	1.9	0	0.6	0.9	2.1	3.4
	100	100	100	100	100	100	100	100
Survival (%)								
1	71	71	65	57	52	66	73	65
2	58	54	52	44	36	50	51	50
3	43	37	40	29	26	37	43	36
Median survival times (in months)	29	22	30	25	13	22	17	32

SX: Surgery, RT: Radiotherapy, CH: Chemotherapy, ICD-10: International Classification of Diseases 10, NOS: Not otherwise specified, Survival time, Bold value: The median survival time

3-year survival rates have been above 50% with any form of treatment. Among those treated with only surgery, vocal cord (62%), hard palate (54.8%), and buccal mucosa (50.6%) have better prognosis with this modality; lower lip (53.3%) and vocal cord (51.1%) showed better outcomes when treated with only radiotherapy. Among those treated with combinative therapy, better outcomes were observed in lower lip (SX + RT = 69.2%), retromolar (SX + RT = 61.3%), vocal cord (SX + RT = 55%), hard palate (SX + RT + CH = 53.8%), and nasopharynx (RT + CH = 51.8%). In summary, combination therapy shows better outcomes, in general, than single modality of treatment.

3-year RSR are shown in [Table 4] of sub-sites by gender and stage of disease in head-and-neck cancer site. Among women, reasonably and distinctively better 3-year RSR were observed in hard palate (M = 56.8%, F = 64%), retromolar (M = 48.6%, F = 60.2%), base tongue (M = 32.3%, F = 54.2%), soft palate (M = 48.9%, F = 67.8%), tonsil (M = 44.6%, F = 56.1%), post-cricoid (M = 23.4%, F = 38.2%), pyriform fossa (M = 37.2%, F = 53.1%), and hypopharynx (M = 25.9%, F = 47.4%), than that among men in this study.

There were not many patients that were diagnosed in Stage I disease. In [Table 4] it is observed that the prognosis worsen

with the progression of stage of disease and this is reflected in the survival rates by stage of disease for each of the sub-sites; it is seen that in Stage I patients, among the OC cancer patients, the RSR is between 55% and 98%, between 75.2% and 92.0% in PHY cancers, 80% for laryngeal cancer. The rates indicate that the treatment provided has shown good outcomes, especially in Stage I disease patients and there is a potential for better outcomes if detected in early stage of disease.

In Stage II, RSR ranged from 57.5% to 78.8% in OC cancers, 44.1%–65% in PHY cancer, and 61.2%–63.3% in laryngeal cancer; in Stage III, RSR ranged from 49.1% to 66.3% in OC cancers, 25.5%–58.2% in PHY cancer, 41.9%–61.9% in laryngeal cancer, and 53.8% in nasopharyngeal cancer; in Stage IV, RSR ranged from 19.2% to 52.3% in OC cancers, 24.1%–37.5% in PHY cancer, 34.2%–71.6% in laryngeal cancer, and 60.1% in nasopharyngeal cancer.

DISCUSSION

Cancer cases in India have shown an increasing trend over the decades; the incidence rates have not shown any substantial increase/decrease over the years. India is a vast country and has people following different religions, lifestyle practices, and food habits. Some of the cancers which are

Table 2: Patient characteristics and 3-year observed survival rates (%).

Sites (ICD-10)	Base tongue	Soft palate	Tonsil	Oro pharynx	Post cricoid	Pyriiform fossa	Hypo pharynx	Vocal cord	Sup glottis	Naso pharynx
Number of cases	264	90	183	229	57	470	85	275	269	244
Average age	58	54.6	54.2	57.8	49.8	59.9	56.9	57.4	58.3	38.7
Stage (%)										
I	0	8.9	4.9	1.3	3.5	2.3	0	43.3	1.1	2.9
II	7.6	27.8	12	9.6	12.3	7.2	3.5	13.5	10	2
III	15.9	16.7	12.6	20.1	35.1	24.7	31.8	26.9	29.4	16.8
IV	73.9	44.4	62.3	66.8	42.1	63.4	64.7	9.8	56.9	70.5
NOS	2.7	2.2	8.2	2.2	7	2.3	0	6.5	2.6	7.8
	100	100	100	100	100	100	100	100	100	100
Treatment summary										
SX	2.2	1.6	0.9	3.5	1.7	1.2	28.7	3	0.4	16
RT	28.9	28.4	26.2	17.5	21.1	17.6	34.2	17.5	6.1	9.7
CH	2.2	6	7	8.8	13.8	20	1.8	8.9	7.8	9.6
Sx+RT	2.2	0.5	1.3	0	3.2	3.5	7.3	5.9	1.2	20.6
Sx+CH	0	0	0	3.5	0.4	0	0.7	0.4	0.4	1.6
RT+CH	60	58.5	57.6	56.1	52.1	54.1	24	54.3	80.7	22.1
Sx+RT+CH	2.2	3.3	4.4	5.3	5.7	2.4	3.3	5.9	1.6	19.1
Others	2.2	1.6	2.6	5.3	1.9	1.2	0	4.1	1.6	1.2
	100	100	100	100	100	100	100	100	100	100
Survival (%)										
1	57	62	68	55	53	58	48	84	60	77
2	35	36	45	37	28	40	28	72	40	61
3	25	23	33	27	25	28	22	53	28	44
Median survival times (in months)	14	9	21	29	13	19	12	24	12	17

SX: Surgery, RT: Radiotherapy, CH: Chemotherapy, ICD-10: International Classification of Diseases 10, NOS: Not otherwise specified, Survival time, Bold value: The median survival time

Table 3: 3-year observed survival rates (%) by treatment modalities.

Sites (ICD-10)	SX	RT	CH	SX+RT	SX+CH	RT+CH	SX+RT+CH
Lower lip	40.7	53.3	-	69.2	-	0	33.3
Anterior tongue	45.4	23.1	0	46.7	0	19.7	33.1
Lower alveolus	42.6	0	0	51.6	0	-	43
Upper alveolus	31.3	0	0	50	0	-	32.1
Floor mouth	41.2	0	-	47.1	-	-	0
Buccal mucosal	50.6	23	0	50.3	23.3	13.1	38.6
Hard palate	54.8	0	-	51.4	-	0	53.8
Retromolar	37.5	0	0	61.3	0	0	38.6
Base tongue	0	20.4	-	0	-	27.8	0
Soft palate	0	23.1	-	0	-	24.1	-
Tonsil	0	34.6	0	-	-	35.5	0
Ot oropharynx	0	16.7	0	0	-	32.6	0
Post-cricoid	0	-	0	-	0	31.3	0
Pyriiform fossa	0	17.2	0	40	0	36.7	37
Hypo pharynx	-	0	0	0	-	28.3	0
Vocal cord	62	51.1	-	55	0	50	0
Sup glottis	0	23.4	-	31.3	-	36.3	0
Nasopharynx	-	0	0	0	-	51.8	0

SX: Surgery, RT: Radiotherapy, CH: Chemotherapy, ICD-10: International Classification of Diseases 10

more prevalent are also predominant in India as well, namely, breast cancer in women and lung cancer in men.

There is a traditional practice of chewing tobacco in India for ages and it is more prevalent in rural India. There are various

Table 4: Three-year relative survival rates (%).

Sites (ICD-10)	Gender		Stage			
	Male	Female	I	II	III	IV
Lower lip	61.1	58.1	55.2	0	50.8	49.2
Anterior tongue	51.4	54.8	65.8	63.6	49.1	38.6
Lower alveolus	58.7	43.7	92	63.7	65.1	52.3
Upper alveolus	42.1	34.8	59.2	69	0	39.4
Floor mouth	56.1	32.2	0	0	57.5	19.2
Buccal mucosal	54	40.7	85.4	64.8	66.3	41.2
Hard palate	56.8	64	98.5	78.8	56.8	42.9
Retromolar	48.6	60.2	0	57.5	65.9	41.4
Base tongue	32.3	54.2	-	62.1	39.4	31.2
Soft palate	48.9	67.8	0	44.1	0	24.1
Tonsil	44.6	56.1	92	62.8	48	37.5
Ot oropharynx	37.4	40.7	0	56.4	36	32.4
Post-cricoid	23.4	38.2	0	0	41.4	0
Pyrimiform fossa	37.2	53.1	75.2	65	58.2	26.9
Hypo pharynx	25.9	47.4	-	-	25.5	35.2
Vocal cord	75	63.8	80	63.3	69	71.6
Sup glottis	37.9	41.4	-	61.2	41.9	34.2
Nasopharynx	61.1	62.5	0	0	53.8	60.1

forms of tobacco use, namely, chewing, smoking, nasal snuff, masher, etc. Chewing is more prevalent than smoking in most of the population groups. Head-and-neck cancers are among the top 10 most frequent cancers in the world and are observed to be common in regions with a high prevalence of tobacco use and alcohol habits. They account for one-fourth of male and one-tenth of female cancers in India. In general, in India, head-and-neck cancers are more common in men than in women because men tend to chew and smoke tobacco and consume alcohol. The data from GLOBOCAN^[1] also show male predominance in head-and-neck cancers in India.

The present study is a hospital based, retrospective and follow up study of patients seen and treated in TMH during 2012-14 which comprised of 4351 oral cavity cancers, 2166 pharyngeal and naso-pharyngeal cancers, totaling up to 6517 head and neck cancers. A periodical follow-up was done for subjects, either by email or telephonic communication.

A similar study of such voluminous data was published by TMH in 1998 by Rao *et al.*^[6] This study reported observed survival rates by subsites. The findings are similar to the present study. A large study was reported by Yeole *et al.*^[7] of head-and-neck cancer, comprising of 6311 cases in Mumbai; they reported 5-year RSR of 74.5% for the lip, 42.7% for the anterior tongue, 25.5% for the posterior tongue, 45.1% for the mouth, 29.7% for the oropharynx, 38.7% for the nasopharynx, 29.1% for the hypopharynx, and 41.2% for the larynx. There were disparities in survival rates between sites.

Another hospital-based, retrospective, and record-based study of 454 head-and-neck cancer cases treated during 2013–2016 by Saxena *et al.*^[8] reported that the TNM staging

distribution of head-and-neck cancer in the hospital over 3-years indicated higher proportion of cases reported in the hospital at an advanced stage of disease. The present study showed similarly large percentage of patients reported in Stage 4 in most of the subsites. However, in this study, those diagnosed at an early stage of cancers (I and II) tended to have a better survival; it was also seen in the present study in all of the subsites. Patients treated with surgery and radiation, surgery, radiation, and chemotherapy had better outcomes. Similar outcomes were reported by Nandakumar.^[9]

In a large voluminous study conducted earlier in TMH, they reported survival rates for various subsites of head-and-neck cancer seen during 1987 and 89 (Rao *et al.*,^[6]). In this earlier study, the overall 5-year survival rate ranged between 20% and 43% for oral cancer, 8–25% for pharyngeal cancers and 25–62% for laryngeal cancer. Comparing the results of 1987–89 to the present study registered between 2012 and 14, it shows that the overall 3-year observed survival for oral cancer was between 26% and 43% for oral cancer, 22–33% for pharyngeal cancer and between 28% and 53% for laryngeal cancer. Further, the results of the RSR of present study are better than those reported earlier by Rao *et al.* (1998), for head-and-neck cancers.

A study based on Surveillance, Epidemiology, and End Results (SEER) database stated that survival has substantially improved for head-and-neck cancer patients over the past decade, increasing from 54.7% in 1992–1996 to 65.9% in 2002–2006, the greatest improvement was seen in tonsillar and tongue cancers as reported by Pulte and Brenner.^[10] Similar observation is seen in improvements in survival rates reported by Rao *et al.*,^[6] and the present study as well. The present study also highlights the poor survival associated with higher stages at the time of diagnosis; however, since the present study included patients from all over India, the finding of the study can be generalized.

In the present study, a subgroup analysis showed improvement in survival rates for cancers of the OC, tongue, tonsils, and nasopharynx, with the greatest improvements observed in tonsillar carcinoma and carcinoma of the tongue, compared to earlier study by Rao *et al.*^[6]

In India, laryngeal cancer contributes to approximately 3–6% of all cancers in men. The age-adjusted incidence rate of cancer larynx in males varies widely among Indian registries, between 1.26/100,000 in Nagaland to 8.18/100,000 in Kamrup Urban District. The 5-year survival for laryngeal cancer in India as reported by Bobdey *et al.*,^[11] to be 28%, while in the present study, the observed survival ranged between 28 and 53% compared to 5-year relative survival for supraglottis, all SEER stages combined, was 46%, vocal cord 49% and 35% for hypopharyngeal cancer, as reported by the American Cancer Society Surveillance Research Program (ACS).^[12]

CONCLUSIONS

In the present study, 3-year relative survival was 75% in males and 63.8% in females, for vocal cord, 37.9% in males and 41.4% in females for supra glottis, and 25.9% in males and 47.45% in females for hypopharyngeal cancers. The overall observed survival rates in present study were comparable to studies done in India and elsewhere. Despite the limitations of the study in terms of follow-up and censoring, the best has been achieved by demographic follow-up methods. Due to incomplete death registration system in India, censoring was done and could be considered as one of the limitations of the study.

This study highlights the fact that long-term follow-up of cancer patients is difficult due to poor socioeconomic status and lack of awareness among the general public. Most of the patients in our hospital do not come for follow-up due to various factors such as the home being far away from the treatment center, costs involved in traveling and staying in the city, etc. The outcomes of the study suggest that since tobacco is a key risk factor, prevention, and activities in terms of awareness, education could be beneficial in terms of reduction in number of cases and also better prognosis, if they seek cancer care facilities in early stage of disease.

Ethical statement

The study is approved by Ethics Committee of Tata Memorial Centre.

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Declaration of patient consent

Patient's consent not required as patient's identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

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