Original Research Article

A descriptive study to understand how severity of symptoms after completion of treatment impact on the life of oral cancer patients

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ABSTRACT

Background: Oral cancer is a commonly occurring cancer among Indians, who are mostly habituated to chewing tobacco. It accounts for around 30–40% of all malignant tumors in India and has one of the lowest five years survival rates, as most of them are diagnosed in advanced stages. More so, after the treatment is completed, the patients' still suffers from a number of symptoms, which are often not taken seriously. The objective of this study was to evaluate the impact of severity of symptomatology of oral cancer after completion of cancer treatment.

Methods: EORTC (European organization for research and treatment of cancer) H and N 35 questionnaire (Marathi version) was used to assess the severity of clinical symptoms. 100 consecutive patients of oral cancer who had completed their treatment and came for follow up after 1 to 3 months of treatment completion were enrolled for the study after taking informed written consent. The study was initiated after obtaining ethical approval from the institutional ethics committee. Statistical analysis was done using R software.

Results: Age of the patient, status of insurance, time gap between symptom onset and diagnosis, socio-economic status and stage of oral cancer were included in the final model of multivariate analysis. Time gap between symptom onset and diagnosis (in months) was also found to be associated significantly to head and neck symptoms. Participants from higher socio-economic status were found to have fewer head and neck symptoms and this association was found statistically significant.

Conclusions: Assessment of severity of symptomatology should be routinely practiced among patients who had completed their treatment and come for follow up. This needs to be followed by guidance and individualized interventions for improving the quality of life of the treated patients.

Keywords: Oral cancer, EORTC QLQ H and N 35, Symptoms, Quality of life

INTRODUCTION

Oral cancer is a significant public health problem in our country. Consumption of tobacco in the chewable form is the most important causal factor for the occurrence of this disease.[1] Though it is a disease that can be detected early but due to poor knowledge, attitude and practice of the poor Indian masses, most of the tumors of oral region are diagnosed at a later stage.[2] It accounts for over 30% of all cancers in India. Age adjusted rate of oral cancer in India is high, that is, 20 per 100 000 population.[3]

According to WHO, quality of life is "an individual's perception of their position in life, in the context of the culture and value systems in their life and in relation to their goals, expectations, standards and concerns".[4] Irrespective of tremendous improvement in the field of cancer diagnosis and treatment, oral cancer is still a disease, which shows a lower five-year survival rate, may

be because of its late diagnosis.[5] The treatment also results in tremendous pain and suffering, more so in the cancers occurring in the oral cavity, as oral cavity is associated with eating, speaking and also cosmetic soundness.[6]

The patients of oral cancer who have undergone the full treatment complains of a variety of symptoms like dryness of mouth, pain, drooling of saliva, problem in producing sound and talking and many more that severely affects their daily day to day life and significantly decreases their quality of life.[7] Though the treating physicians prescribe symptomatic management, yet a detailed assessment of the severity of these symptoms lack behind. There are many studies conducted on the quality of life of oral cancer patients but very few of them worked on understanding the severity of symptomatology of the post treated oral cancer patients. That is the reason why we planned to conduct this study with the patients attending the hospital for their first follow up after the treatment completion using a self-administered EORTC QLQ H and N 35 (Marathi language) questionnaire.

METHODS

This is a cross sectional study. It was conducted in a tertiary care center of Wardha, Maharashtra. The study was continued from September 2015 to August 2017. The study population included the patients diagnosed histopathologically with squamous cell cancer of lip, tongue, buccal mucosa, alveolus and GB mucosa who came to the radiotherapy unit of the hospital for follow-up after 2 to 3 months of completion of their treatment.

Study subjects were recruited till a sample size of 100 was reached. This was adequate to report proportions with an error of 10%. A consecutive sampling approach was used till the desired sample size was achieved within the period of data collection. Sampling was done with replacement for non-response. Both males and females were enrolled for the study. We did not put any age barrier for selecting the study participants. Severely debilitated oral cancer patients who were not in a condition to fill up the questionnaire and those who did not give consent were excluded from the study. The questionnaire was mostly filled up by the study participants themselves and in few cases; the investigator helped them to clarify few of the terminologies used in the questionnaire. The caregiver was allowed to sit in the room where the study was undertaken but he/she was not allowed to prompt or give any hint or make any influence on the patients while marking the answers. Informed written consent was taken from each of the patients before recruiting them for the study. The patients attending the hospital understand Marathi, so we have adopted the Marathi version of the questionnaire that is freely available and is already validated.

EORTC developed this tool to provide an integrated approach for assessing the severity of clinical symptoms of head and neck (oral) cancer.[8] This tool comprised of 35 questions. This questionnaire incorporates seven multiple-item scales that assess the symptoms of pain, swallowing ability, senses (taste/smell), speech, social eating, social contact, and sexuality. Also included are six single-item scales, which survey the presence of symptomatic problems, associated with teeth, mouth-opening, dry mouth (xerostomia), sticky saliva, coughing, and feeling ill. All the questions ask about the head and neck symptoms experienced by the oral cancer patient during the past week. This questionnaire captured the impact of the disease on the psychosocial life of the oral cancer patients. It was chosen for this research, as it is one of the most widely implemented questionnaires, with over 10 years of research invested to develop an integrated, modular approach. All scales pertaining to the EORTC QLQ-H and N 35 range from 0 to 100. A high score for a symptom scale represents the presence of a symptom or problem/s.

EORTC QLQ-H and N 35 questionnaire used Likert scale, which we converted into a score from 0 to 100 using the following method that was already mentioned in the manual of EORTC questionnaires:

Step 1: calculation of the raw score (RS); in practical terms, if items $I1$, $I2$, In are included in a scale then RS was calculated as RS= $(I1+I2+……In)/n$

Step 2: a linear transformation method was used to standardize the RS so that the scores range from 0 to 100; in practical terms, if items $I1$, $I2$, In are included in a scale the procedure is as follows:

The RS (raw score) was calculated as RS= $(I1 + I2+……In)/n$

The linear transformation was applied to 0–100 to obtain score S,

S= $[\{RS–(\text{minimum score in the Likert scale})/\text{range}*\} ×100$

*Range is the difference between the maximum and minimum possible value of RS.

This technique has been designed so that all items in any scale take the same range of values (0 to 100). Therefore, the range of RS equals the range of the item values.

Data entry was done in EPI INFO version 7 and analysis was done using R.[9,10] The study was initiated after obtaining approval from the institutional ethics committee.

RESULTS

The characteristics of the 100 oral cancer patients included in our study are summarized in Table 1. The mean age of the study population was 48.7 years (range,

30–72 years), with majority of the study participants being male (81%). 83% of the patients stayed with their spouse and 48% of them stayed in nuclear families. We have noted the years of schooling of the study participants and it was found that 19% of them did not go to school ever, while 15% of them studied till class six. Majority of the participants studied for 7 to 12 years and only 6% of them ever went to college.

Table 1: Characteristics of patients (n=100).

Variables	N (%)
Age (in years)	
<40	22 (22)
40-60	59 (59)
>60	19 (19)
Sex	
Male	81 (81)
Female	19 (19)
Years of schooling/education	
0	19 (19)
1-6	15 (15)
7-12	60 (60)
>12	6 (6)
Category	
SC	23 (23)
ST	11 (11)
OBC	43 (43)
Open	17 (17)
Others	6 (6)
Ration card	
Antyodaya	13 (13)
BPL	34 (34)
APL	47 (47)
No card	6 (6)
Marital status	
With spouse	83 (83)
Without spouse	17 (17)
Socio economic status (modified BJ Prasad scale)	
Class I	13 (13)
Class II	21 (21)
Class III	33 (33)
Class IV	32 (32)
Class V	1 (1)

On the basis of monthly per capita income, the study population were divided into five income groups as per modified BG Prasad classification, where we found 13%, 21%, 33%, 32% and 1% of the population were from were from upper (per capita monthly income>6253 INR), upper middle (per capita monthly income 3127-6253 INR), middle (per capita monthly income 1876–3126 INR), lower middle (per capita monthly income 938–1875 INR) and lower class (per capita monthly income<938 INR) respectively.

In this study we have included patients diagnosed with squamous cell carcinoma of lip, tongue, buccal mucosa, gingiva-buccal mucosa and alveolar cancer as shown in Figure 1, where majority of the participants of both sexes were suffering from cancer of buccal mucosa. All four stages of oral cancers were included in our study where we found 13%, 23%, 23% and 41% were in stage I, II, III and IV respectively.
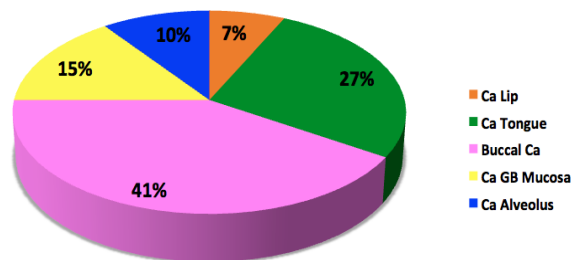

Figure 1: Distribution of different types of oral cancer among the study subjects (n=100).

Table 2 shows the calculated scores for the EORTC H and N 35 for the different symptoms of oral cancer. In this head and neck module, having pain in the mouth, dry mouth, feeling ill, difficulty in opening mouth, and having sticky saliva are the worst problems. All the oral cancer patients included in the study complained of pain in the mouth during the past week for which they had to use analgesics. Figure 2 displays the findings of the head and neck symptom scores.
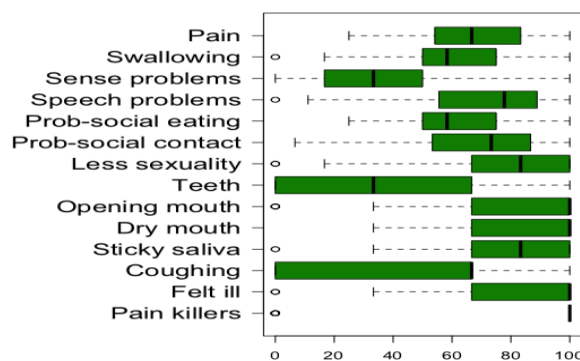

Figure 2: Boxplot showing head and neck symptom score.

Figure 3 shows the boxplots for head and neck score according to the stage of the disease. The symptom score was found to be highest in stage IV oral cancer. Table 3 shows the change in the head and neck score with the site of oral cancer. The mean head and neck symptom scores were highest in the patients with GB mucosa cancer (64.2±13.2) followed by patients of cancer alveolus (60.6±12.9).

Table 2: Calculated scores of EORTC H and N 35 for the oral cancer patients (n=100).

Scales	Mean (SD)	Median (IQR)	Range
Pain (HNPA)	66.±18.8	66.7 (56.2, 83.3)	25.0-100.0
Swallowing (HNSW)	60±23.4	58.3 (47.9, 75)	0.0-100.0
Senses problem (HNSE)	31.8±26	58.3 (47.9, 75)	0.0-100.0
Speech problem (HNSP)	72.±23.5	77.8 (55.6, 88.9)	0.0-100.0
Trouble with social eating (HNSO)	62.2±17.8	58.3 (50.0, 75)	25.0-100.0
Trouble with social contact (HNSC)	67±23.8	73.3 (53.3, 86.6)	6.7-100.0
Less sexuality (HNSX)	75.5±29.1	83.3 (66.7, 100)	0.0-100.0
Teeth (HNTE)	41.3±37	33.3 (0.0, 66.7)	0.0-100.0
Opening mouth (HNOM)	79.±29.4	100.0 (66.7, 100)	0.0-100.0
Dry mouth (HNDR)	84±20.9	100.0 (66.7, 100)	33.3-100.0
Sticky saliva (HNSS)	78.7±24.8	83.3 (66.7, 100)	0.0-100.0
Coughing (HNCO)	47±35.8	66.7 (00.0, 66.7)	0.0-100.0
Feeling ill (HNFI)	80.3±25.5	100.0 (66.7, 100)	0.0-100.0
Pain killers (HNPK)	86±34.8	100.0 (100, 100)	0.0-100.0
Nutritional supplements (HNNU)	40±49.2	0 (0, 100)	0.0-100.0
Feeding tube (HNFE)	28±45.1	0 (0, 100)	0.0-100.0
Weight loss (HNWL)	61±49	100 (0, 100)	0.0-100.0
Weight gain (HNWG)	39± 49	0 (0, 100)	0.0-100.0

SD: standard deviation; IQR: inter quartile range.

Patients of oral cancer were treated with combinations of surgery, radiotherapy, chemotherapy and palliative therapy. None of the included study participants were treated by single treatment modality. Table 4 shows the distribution of treatment pattern among the 100 oral cancer patients according to the stage of the disease. We found that 62% of the patients were treated by combination of surgery, chemotherapy and radiation therapy and this combination was mostly used for the stage IV cancer patients. 10 patients (10%) received combination of chemotherapy and radiotherapy and 10 patients (10%) received combination of radiation therapy

and surgery. Palliative therapy was used in 18% of the patients, where it was advanced oral cancer only, that is stage III and IV disease. The mean duration of completion of treatment (gap between completion of treatment and interview) of oral cancer patient was found to be 3 months. The last column shows the change in the H and N symptom scores as per the change in treatment modalities. The head and neck symptom score were found to be highest in the patients who received combination of chemotherapy, radiotherapy, surgery and palliative therapy. Table 5 shows the correlations between the different head and neck scores used in EORTC QLQ H and N 35.
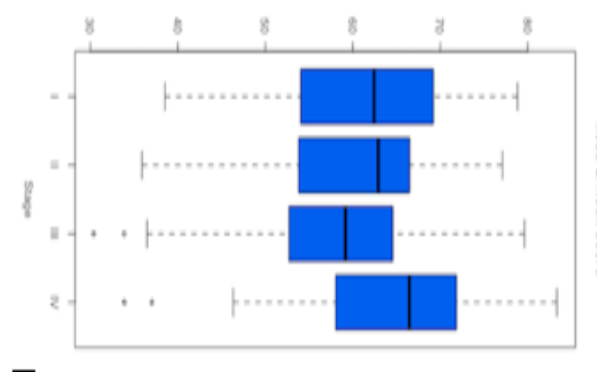
Figure 3: Stage wise different EORTC H and N 35 score.

To understand the relationship between the different relevant independent variables and head and neck symptom scores, we conducted a multiple linear regression. The independent variables included in the model were age of patient, sex of patient, years of schooling, type of ration card, socio economic group (as per modified BJ Prasad's classification), type of family, stage of the disease, time gap between symptom onset and diagnosis (in months), duration since completion of treatment (in months), the marital status of the patient, status of insurance, presence of any cut down of expenses as a result of continuing the cancer treatment and the type of treatment modalities–chemotherapy, surgery, radiotherapy and palliative therapy. We have shown only final model of multiple linear regressions developed in R in Table 6 for the head and neck symptom score. Age of the patient, status of insurance, time gap between symptom onset and diagnosis, socio-economic status and stage of oral cancer were included in the final model. Like quality of life score, function and symptom scores, time gap between symptom onset and diagnosis (in months) was also found to be associated significantly ($p<0.05$) to head and neck symptoms. And participants from higher socio-economic status (SES I) were found to have fewer head and neck symptoms and this association was found statistically significant ($p<0.05$).

Table 3: Comparison of head and neck scores with site of cancer occurrence.

Cancer site	Lip	Tongue	Buccal mucosa	GB mucosa	Alveolus
Head and neck symptom score (Mean±SD)	54.6±9.9	58.7±11.7	55.7±13.7	64.2±13.2	60.6±12.9

SD: Standard deviation.

Table 4: Distribution of oral cancer patients of all the stages as per the treatment received and their respective head and neck symptom score.

Treatment combination	Stage					Head and neck symptom score
	I	II	III	IV	Total	
CT RT	00	04	03	03	10	59.9±10.6
RT+SX	03	03	02	02	10	60.7±7.7
CT+RT+SX	10	16	12	24	62	61.3±12.4
CT+RT+Pall	00	00	03	06	09	58.6±14.4
RT+SX+Pall	00	00	02	02	04	56.6±14.3
CT+RT+SX+Pall	00	00	01	04	05	63.7±10.1

CT: Chemotherapy, RT: radiotherapy, SX: surgery, Pall: palliative therapy.

Table 5: Correlation between the head and neck symptom scores (EORTC QLQ H and N 35).

	HNPA	HNSW	HNSE	HNSP	HNSO	HNSC	HNSX	HNTE	HNOM	HNDR	HNSS	HNCO	HNFI	HNPK
HNPA	1.00													
HNSW	0.51	1.00												
HNSE	0.20	0.36	1.00											
HNSP	0.28	0.29	0.09	1.00										
HNSO	0.21	0.35	0.08	0.51	1.00									
HNSC	0.31	0.33	0.07	0.70	0.54	1.00								
HNSX	0.05	0.27	0.10	0.45	0.32	0.47	1.00							
HNTE	0.14	0.34	0.39	0.03	0.06	0.02	0.04	1.00						
HNOM	0.10	-0.00	-0.23	0.16	0.01	0.21	0.02	-0.19	1.00					
HNDR	0.18	0.16	0.00	0.28	0.22	0.40	0.32	-0.09	0.32	1.00				
HNSS	0.34	0.21	0.08	0.02	0.10	0.13	0.20	-0.12	0.24	0.35	1.00			
HNCO	0.16	0.33	0.38	0.45	0.21	0.22	0.32	0.28	-0.25	0.07	-0.07	1.00		
HNFI	0.14	0.20	0.19	0.43	0.31	0.35	0.44	0.08	0.10	0.30	0.02	0.24	1.00	
HNPK	0.12	0.11	0.10	0.22	0.18	0.32	0.12	0.03	0.02	0.15	0.11	0.08	0.10	1.00

Table 6: Multivariate analysis for head and neck symptom score of oral cancer patients.

Variables	β	SE	t- value	p value
Intercept	78.70	13.5	5.8	9.58e-08***
Age	0.1	0.1	1.8	0.07
Insured: yes vs. no	-6.6	3.2	-2.0	0.04*
Time gap between symptom onset and diagnosis (months)	-0.93	0.3	-3.0	<0.01*
Socio economic status				
SES IV	-10.8	11.0	-0.97	0.33
SES III	-16.2	11.0	-1.4	0.14
SES II	-16.8	11.1	-1.5	0.13
SES I	-22.8	11.3	-2.0	0.04*
Stage of oral cancer (reference: stage I)				
Stage II	-0.8	3.8	-0.2	0.82
Stage III	-3.2	3.7	-0.8	0.30
Stage: IV	5.4	3.6	1.5	0.14

β: unstandardized regression coefficient; SE: standard error; residual SE: 10.9, multiple R squared: 0.3; adjusted R squared: 0.2; F statistics: 3.5; p<0.01.

DISCUSSION

According to Globocan, in India oral cancer is the second most common cancer in terms of mortality and morbidity among the males while it ranks third in occurrence both sexes combined. In our study, we found a male predominance of oral cancer.[11] Other studies, e.g. Shavi et al in a study conducted in Bhopal found male: female ratio to be 4:1.[12] According to the consolidated report of hospital-based cancer registry in India, like most other adult cancers, oral cancer occurs mostly in the older adults and in our study, around 60% of the patients were found to be in the age group of 40 to 60 years.[13]

Majority of the study participants included in our study were suffering from cancer of buccal mucosa followed by cancer tongue. This is in accordance with the findings of the study conducted by Shavi et al.[12] Mathur et al explained the reason for increased occurrence of oral cancer in the buccal mucosa and tongue in both sexes.[14] Buccal mucosa is the most obvious part inside oral cavity that comes in direct contact with the oral tobacco when it is being consumed. This raw tobacco, which is often consumed with raw lime is an irritant for the soft buccal mucosa that results in ulcer formation gradually leading to carcinomatous changes. Narwal et al in their epidemiological and clinico-pathological study of oral cancer patients in Haryana found increased occurrence of oral cancer in alveolus followed by buccal mucosa and tongue.[15] According to their study betel quid is habitually put in alveolar region; i.e., in the inner aspect of the lips that causes a regular irritation resulting in cancer formation in the alveolar region.

Coelhi in his review article on the challenges of oral cancer burden in India stated that though oral cancer can easily be diagnosed by simple visual inspection, yet in India 60 to 80% of the patients present for the first time with advanced disease.[16] This finding was in accordance with our study where 64% of the patients presented with advanced (stage III and IV) oral cancer disease.

Pain, fatigue, and insomnia were the most important complains recorded in EORTC questionnaire in our study; while dry mouth, sticky saliva, decreased opening of mouth and problems of feeding tube were other problems that the patients shared during their interviews.[8] Different treatment modalities are available for oral cancer including surgery, radiation and chemotherapy and it depends upon stage of the disease. In advanced stage of the cancer, palliative therapy is required that may include supportive therapy including palliative radiotherapy and chemotherapy. Shuman et al studied the end of life care among head and neck cancer patients and stated that palliative therapy increases the end of life experience in the terminally ill cancer patients.[17] Christopher et al found that each treatment option has its own advantages and side effects that have an impact on the psychosocial well-being of the patients.[18] They found that patients who received chemo-radiation experienced the lowest overall quality of life, those who had a combination of surgery and radiation experienced the highest reported pain; and those treated with only surgery experienced the highest overall quality of life. The study participants with advanced cancer who had received combination of surgery, chemotherapy, radiation and palliative therapy had high symptom scores.

CONCLUSION

Like any other cancers, patients of oral cancer also suffer from the adverse effects of radiation, chemotherapy and surgery, but the quality of life of the oral cancer patients are affected more severely as compared to any other cancer. The top symptoms that were reported after the completion of treatment were pain, fatigue and insomnia apart from dry mouth, problem in speaking and mouth opening. Many of the patients avoided the questions related to their sexual life.

The findings of this study gives us a ray of hope for improving the quality of life and better symptom management of the post treated patients of oral cancer. It can be done by routinely monitoring the symptomatology and assessing them using a valid tool, which should be followed by guidance and individualized interventions for improving the quality of life of the treated patients. A counseling center can also be set up by the side of the follow up clinic not only for the patients but also for their caregivers, that will provide them with adequate knowledge regarding the expected symptomatology of the oral cancer patients after their treatment has been completed and will also empower the caregivers with the basic first aid management skills.

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