

Original Research Article

Proportions, five-year survival rates of hypopharyngeal cancer and its associated factors among head and neck cancer patients at a tertiary care hospital in Northern Tanzania

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ABSTRACT

Background: Hypopharyngeal cancer is a rare, aggressive form of cancer of the hypopharynx. It is one of the public health problems with a high burden in low and middle-income countries (LMICs). Despite the advancement in cancer management, mortality associated with cancer continues to rise mostly in LMICs like Tanzania. Yet, the contribution of hypopharyngeal cancer to the observed outcome is not known.

Methods: A hospital based cohort study was conducted at a tertiary care hospital in northern Tanzania, Kilimanjaro Christian Medical Center (KCMC), from January 2015 to December 2019. Kaplan-Meier estimates were used to determine the survival rate. Cox regression analysis assessed factors associated with survival status. A p value <0.05 was considered statistically significant.

Results: A total of 1,259 participants with head and neck cancer were included in this study. Among them, 97 (7.7%) had hypopharyngeal cancer. Participants with hypopharyngeal cancer were followed for five years. The median survival time was 32.0 months at the end of follow-up, and 45 (46.4%) participants had died. Participants with stage IV cancer had a 3.82 times higher hazard of mortality compared to those with stage II. Additionally, those with distant metastasis had a 9.90 times higher hazard of death.

Conclusions: The study reported a poor survival rate with a five-year mortality rate of 46.4%. Participants with cancer at stage IV, and those with the presence of distant metastasis, had a higher hazard of mortality compared to their counterparts.

Keywords: Hypopharyngeal cancer, Five-year survival, Survival rate, Proportion, Associated factors, Head and neck cancers

INTRODUCTION

Hypopharyngeal cancer is a rare and yet, aggressive form of head and neck cancer, known for the development of malignant cells in the tissues of the hypopharynx.¹ Hypopharyngeal cancer is ranked as the 25th most common cancer globally with a prevalence and mortality rate both at 0.4%.² In Africa, the report showed an overall hypopharyngeal cancer prevalence of 1.4%.³ Based on the anatomical feature of the pharynx, hypopharyngeal cancer

mostly affects the pyriform sinus area followed by the posterior pharyngeal wall and post-cricoid region.⁴ Due to this anatomical area, diagnosis management requires extensive surgical procedures such as the removal of adjacent larynx for clear margins.⁵

Depending on the prognosis of the cancer, hypopharyngeal can be categorized into five stages; stage 0 (carcinoma in situ), stage I, stage II, stage III, and stage IV.⁶

Risk factors of hypopharyngeal cancer include Smoking and chewing tobacco, heavy alcohol use, poor nutrition, and infections such as human papillomavirus (HPV), and human immunodeficiency virus (HIV) infections.⁷⁻⁹ Hypopharyngeal cancer can be managed through chemotherapy, radiotherapy, surgery, or combinatorial therapy, depending on the disease stage and subsite of the affected anatomical area.^{6,10} Yet, hypopharyngeal cancer has been reported to have poor prognosis and survival outcomes when compared to other cancers. This is mainly due to the anatomical complex of the affected area causing late diagnosis of the disease and complexity in management.¹¹ Globally, an estimated five-year survival rate of hypopharyngeal cancer ranges from 30% to 35%.¹

Despite advances in cancer management approach, hypopharyngeal cancer remains a significant challenge in most LMICs, including Tanzania.¹² This is mostly due to lifestyle and limited healthcare resources, leading to difficulties in early diagnosis and access to comprehensive treatment options.^{12,13} Yet, there is limited information on the survival status of hypopharyngeal cancer and its predictors, limiting assessment of the effectiveness of the management approach used. The present study aims to determine the proportion of hypopharyngeal cancer, 5-year survival rates, and its associated factors among head and neck cancer patients in KCMC Hospital in Tanzania from January 2015 to December 2019. In general, the study aims to improve management practices of hypopharyngeal cancer by providing factors that limit the good outcome.

METHODS

Study design, population and area

This was a hospital-based cohort study conducted among individuals diagnosed with head and neck cancer at a tertiary care hospital in northern Tanzania (KCMC). This retrospective study used data from the cancer registry database of KCMC Hospital from January 2015 to December 2019. Among individuals with head and neck cancer, those diagnosed with hypopharyngeal cancer were followed up for a period of five years (30 months) to assess survival status. The management of hypopharyngeal cancer at KCMC Hospital involves cancer diagnosis through clinical examination, imaging, and pathological tests. Treatment used mainly depends on the stage of the disease and may be through surgical, radiotherapy, chemotherapy, or combinatorial therapy. Follow-up is mainly made to understand disease progression and the effectiveness of the management approach. Advanced stages of hypopharyngeal cancer are mainly managed with palliative care.

Eligibility criteria

All Head and neck cancer patients admitted or diagnosed at KCMC Hospital from January 2015 to December 2019 were included in the current study whereby, participants

with missing information and those with another tumor apart from hypopharyngeal cancer were excluded.

Sample size and sampling

Due to the low prevalence of hypopharyngeal cancer reported in previous studies, a convenient sampling technique was used whereby, all participants with head and neck cancer from January 2015 to December 2019 at KCMC were included in the study.

Study variables

Dependent variables of the study were hypopharyngeal cancer (yes/no) and five years survival status (alive/dead). Independent variables were social demographic characteristics (age, and sex), HIV status (positive, negative, and unknown), stage of the disease (stage I, II, III, IV), anatomical subsite (post-cricoid region, posterior pharyngeal wall, and pyriform sinus), presence of distance metastasis.

Data collection tools and procedures

A well-structured data extraction sheet was used in data collection using the hospital database and patients' files. The tool comprises 5 sections; general information, demographic characteristics, cancer-related information, treatment information, and outcome section. Data were extracted from the patient registry book and hospital database from January 2015 to December 2019.

Information regarding social demographic characteristics, type of cancer, stage of the disease, and type of treatment was recorded from the patient's file and hospital database. Each year new patient was followed for 5 years to determine the survival rate. Patients with missing information and those with metastatic tumors from other sites apart from head and neck were excluded from the study.

Data management and analysis plan

Data were cleaned, summarized, and analyzed using statistical package for the social sciences (SPSS) version 25.0. Descriptive statistics was performed, with categorical variables presented using frequencies and proportions, and numerical variables presented using means or medians along with their respective measures of dispersion. Kaplan Meier's estimate was used in the estimation of survival rate, with a log-rank test used in comparing the survival status of different variables. Univariable and multivariable Cox regression analysis was used to assess the factors associated with the survival status. Variables that were significant in univariable analysis were included in the final multivariable analysis. Variables with a p value <0.05 were considered statistically significant and associated with the survival status of hypopharyngeal cancer. Crude and adjusted

hazard ratio (HR) with their corresponding 95% confidence interval (CI) were reported.

Ethical consideration

Ethical approval for this study was obtained from the KCMC-Research Ethics Committee. Formal letters were written to the management of KCMC hospital, oncology, and ENT department for data collection approval. The study adheres to all basic ethics principles. Privacy and confidentiality were assured throughout the study.

RESULTS

Enrollment of the study participants

A total of 1,277 head and neck cancer cases were recorded at KCMC Hospital from January 2015 to December 2019. Among them, 10 had missing information and 8 were duplicates, all were excluded. The remaining 1,259 cases were used in the final analysis to determine the proportion of hypopharyngeal cancer, 5-year survival rate and its associated factors (Figure 1).

Socio-demographic characteristics of the study participants

A total of 1,259 study participants with head and neck cancer were included in the present study. The median

(Interquartile range) age of all participants was 59 (48, 69) years whereby, the majority of the participants were aged above 60 years old 576 (45.8%). Most of the participants were male 847 (67.3%), making a male-to-female ratio of 2:1.

Table 1: Socio-demographic characteristics of the study participants (n=1,259).

Variables	Frequency	Percentages
Age categories (years)		
<30	73	5.8
30-45	188	14.9
46-60	422	33.5
>60	576	45.8
Median (IQR)	59 (48, 69)	
Sex		
Male	847	67.3
Female	412	32.7

IQR-Interquartile range

Proportions of hypopharyngeal cancer among head and neck cancer patients

From 1,259 study participants with head and neck cancer, 97 (7.7%) were presented with hypopharyngeal cancer. There was no significant difference in proportion of hypopharyngeal cancer regarding age categories and sex of the participants.

Table 2: Proportions of hypopharyngeal cancer by participants' characteristics (n=1,259).

Variables	N (%)	Hypopharyngeal cancer		P value
		No	Yes	
Age categories (years)				
<30	73 (5.8)	63 (5.4)	10 (10.3)	0.062
30-45	188 (14.9)	173 (14.9)	15 (15.5)	
46-60	422 (33.5)	384 (33.0)	38 (39.2)	
>60	576 (45.8)	542 (46.6)	34 (35.1)	
Sex				
Male	847 (67.3)	787 (92.9)	60 (7.1)	0.236
Female	412 (32.7)	375 (91.0)	37 (9.0)	

Clinical characteristics of the participants with hypopharyngeal cancer

Of 97 participants diagnosed with hypopharyngeal cancer, the majority were from pyriform sinus 61 (62.9%), and most of the participants had hypopharyngeal cancer at stage III 25 (25.8%). 5 (5.2%) of the participants were HIV positive. 36 (37.1%) of the participants with hypopharyngeal cancer received chemotherapy, and 29 (29.9%) received radiotherapy.

Sixteen (16.5%) of the participants had lymph node involvement, and 9 (9.3%) had the presence of distant metastasis.

Five-year survival rates of hypopharyngeal cancer

From 97 participants with hypopharyngeal cancer, follow-up was made for the period of 5 years (60 months). At the end of the follow up 45 (46.4%) participants were dead, and the remaining 52 (53.6%) were either alive or censored. The median survival time was 32.0 months (SE=5.544, 95% CI (21.1, 42.9)). Kaplan Meir survival curve showed poor survival status in female participants compared to males. Also, participants with stage IV of cancer compared to those with stage II. A significant good outcome was observed in participants receiving radiotherapy.

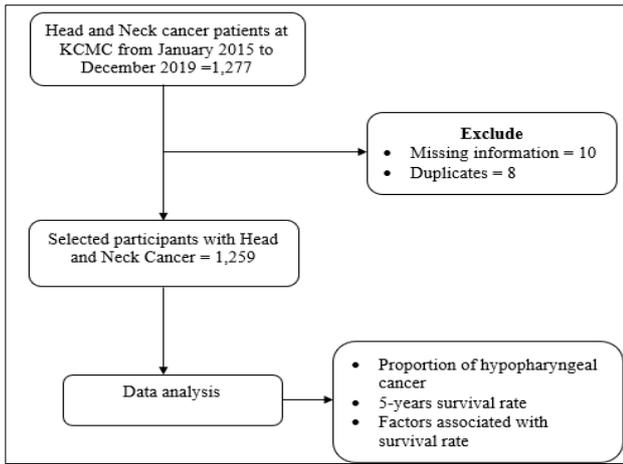


Figure 1: Enrolments of the study participants.

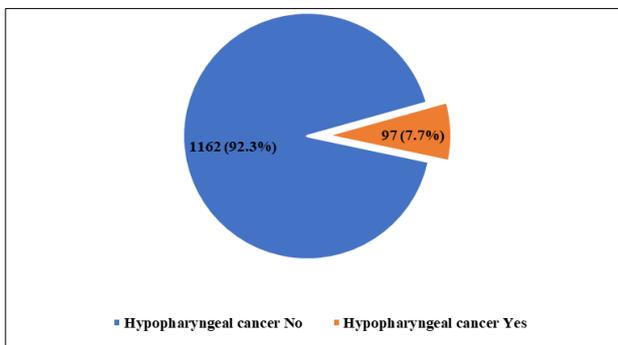


Figure 2: Proportions of hypopharyngeal cancer among head and neck cancer patients (n=1,259).

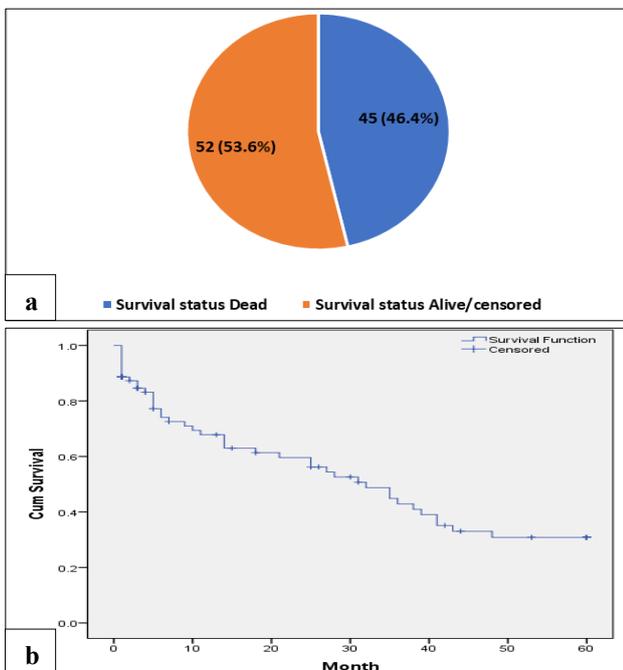


Figure 3 (a and b): 5-year survival status of participants with hypopharyngeal cancer (n=97).

Factors associated with the five-year survival rate of hypopharyngeal cancer

Factors associated with 5-year survival status were determined using Cox regression analysis. In univariable analysis; sex, stage, chemotherapy, radiotherapy, and presence of distance metastasis were significantly associated with survival status.

Whereas, in the final multivariable analysis only the cancer stage and presence of distance metastasis were significantly associated with survival status (p value <0.05).

Participants with cancer stage IV had a 3.82 times higher hazard of mortality compared to those with stage II (HR=3.84 95% CI (1.47-9.95), p value=0.006). Also, participants with presence of distance metastasis had 9.90 times higher hazard of mortality compared to those with no distance metastasis (HR=9.90 95% CI (1.02-16.10), p value=0.048).

Table 3: Clinical characteristics of the participants with hypopharyngeal cancer (n=97).

Variables	Frequency	Percentages
Subsite		
Post-cricoid region	9	9.3
Posterior pharyngeal wall	27	27.8
Pyramidal sinus	61	62.9
Stage		
II	20	20.6
III	25	25.8
IV	18	18.6
Unknown	34	35.1
Chemotherapy		
No	28	28.9
Yes	36	37.1
Unknown	33	34.0
Radiotherapy		
No	26	26.8
Yes	29	29.9
Unknown	42	43.3
HIV status		
Negative	37	38.1
Positive	5	5.2
Unknown	55	56.7
Involvement of lymph nodes		
No	13	13.4
Yes	16	16.5
Unknown	68	70.1
Presence of distance metastasis		
No	9	9.3
Yes	9	9.3
Unknown	79	81.4

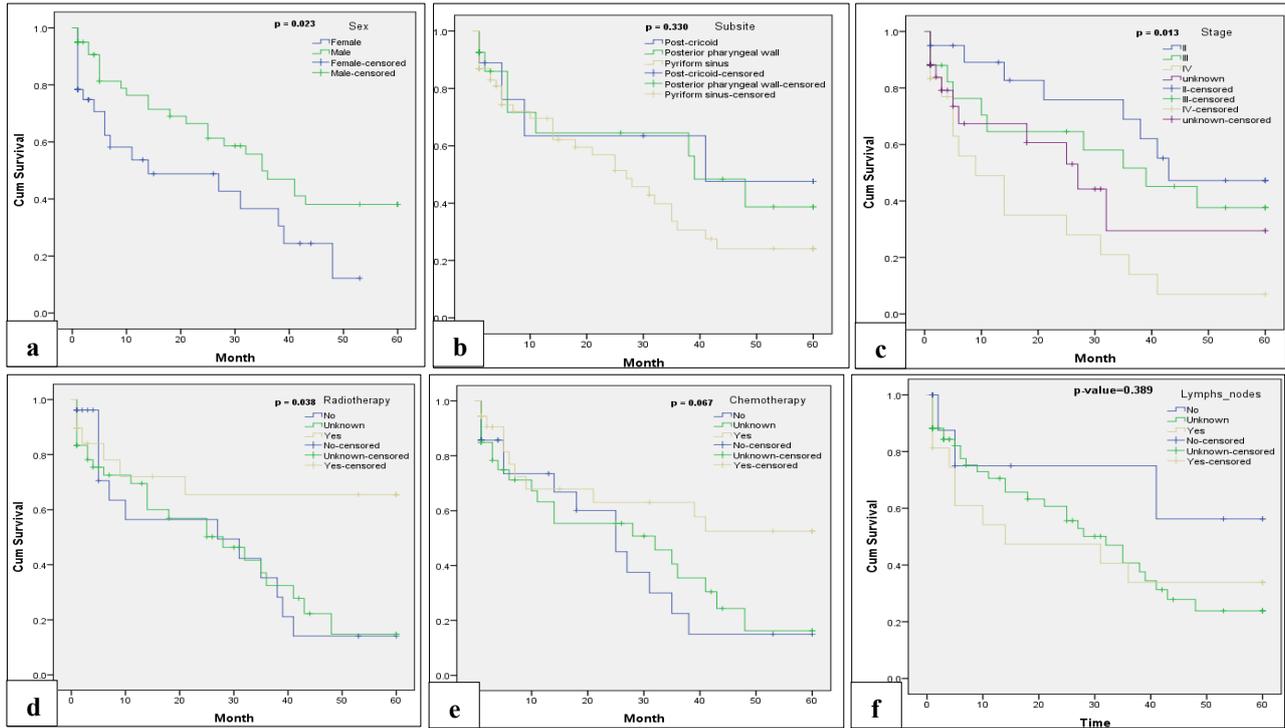


Figure 4 (a-f): 5-year survival curve in relation to participants' characteristics (n=97).

Table 4: Factors associated with the five-year survival rate of hypopharyngeal cancer.

Variables	Univariable analysis		Multivariable analysis	
	HR	P value	HR	P value
Age categories				
<35	Ref			
35-54	0.69 (0.23-2.06)	0.506		
>54	1.09 (0.46-2.62)	0.841		
Sex				
Male	Ref		Ref	
Female	1.94 (1.07-3.51)	0.029	1.67 (0.84-3.34)	0.146
Subsite				
Post-cricoid region	Ref			
Posterior pharyngeal wall	1.12 (0.35-3.65)	0.850		
Pyramidal sinus	1.74 (0.61-4.95)	0.298		
Stage				
II	Ref		Ref	
III	1.51 (0.61-3.75)	0.378	1.80 (0.69-4.68)	0.229
IV	3.68 (1.52-8.89)	0.004	3.82 (1.47-9.95)	0.006
Chemotherapy				
No	Ref		Ref	
Yes	0.43 (0.19-0.96)	0.039	0.81 (0.30-2.17)	0.674
Radiotherapy				
No	Ref		Ref	
Yes	0.37 (0.14-0.93)	0.034	0.65 (0.21-2.01)	0.454
HIV status				
Negative	Ref			
Positive	0.36 (0.05-2.67)	0.315		
Involvement of lymph nodes				
No	Ref			
Yes	2.23 (0.61-8.09)	0.197		

Continued.

Variables	Univariable analysis		Multivariable analysis	
	HR	P value	HR	P value
Presence of distance metastasis				
No	Ref		Ref	
Yes	20.10 (2.34-32.03)	0.006	9.90 (1.02-16.10)	0.048

Age was categorized due to few participants with hypopharyngeal cancer being aged 20 to 34 years old

DISCUSSION

Hypopharyngeal cancer is a global public health problem, mostly in low- and middle-income countries including Tanzania.¹² The main objective of the present study was to determine the proportion of hypopharyngeal cancer, five-year survival rates, and its associated factors among head and neck cancer patients at KCMC from January 2015 to December 2019. The key findings are that the study reported a hypopharyngeal cancer proportion of 7.7% among head and neck cancer cases from January 2015 to December 2019. The median survival time was 32.0 months in which, at the end of the follow-up time, 45 (46.4%) participants were dead and the remaining 52 (53.6%) were either alive or censored. Participants with cancer stage IV had a higher hazard of mortality compared to those with stage II. Also, those with presence of distance metastasis had a higher hazard of mortality compared to those with no presence of distance metastasis.

The current study reported a hypopharyngeal cancer proportion of 7.7% among head and neck cancer patients during the study period whereby, the findings of this study deviate from those reported in previous studies conducted elsewhere. The observed proportion of hypopharyngeal cancer is relatively high compared to the findings of the studies conducted in Nigeria, yet lower than the findings of the studies from India, and Egypt.¹⁴⁻¹⁸ The observed variation could be due to differences in; socioeconomic factors of the different populations, prevalence in regional-specific risk factors, development of the healthcare system, and study design.^{19,20}

However, a high proportion of hypopharyngeal cancer in participants aged above 45 years old, shows the risk of age in the development of hypopharyngeal cancer. This was also reported in a previous study conducted in Korea.²¹ An increase in age is directly proportional to the increase in exposure to risk factors for hypopharyngeal cancer. Also, reduced immune surveillance among older individuals increases the risk of hypopharyngeal cancer.^{22,23}

In the present study, participants with hypopharyngeal cancer were followed up for a period of 5 years (60 months). At the end of the follow-up time, the median survival time was 32.0 months of which 45 (46.4%) participants were dead, and the remaining 52 (53.6%) were either alive or censored. These findings are in line with those of the studies conducted in Taiwan and India.^{24,25} Results however differ from those of the studies conducted in the Netherlands, United States, and Denmark.²⁶⁻²⁸ Variations in findings could be attributed to differences in population characteristics, development in the healthcare

system, and study design. While the current study focuses on five years of data, the referenced studies focused on 10- and 20-year data on hypopharyngeal cancer. The poor outcome of hypopharyngeal cancer can be due to late diagnosis of the disease due to anatomical structure, and early metastasis.^{29,30}

Regarding factors associated with survival status, participants with cancer stage IV had a high hazard of mortality compared to those with stage II. Also, those with presence of distance metastasis had a higher hazard of mortality compared to those with no presence of distance metastasis. Similar findings were reported in studies conducted in India and Denmark.^{25,27} Consistency in findings with other studies shows the common factors affecting the prognosis of hypopharyngeal cancer. Participants at stage IV experience poorer outcomes due to the advanced stage of the disease which spreads to more parts of the body. This applies also to those with the presence of distance metastasis mostly due to systemic dissemination of the disease to the vital organs, which limits the effectiveness of the treatment and led to poor outcomes. Hence, participants with no distance metastasis experienced good outcomes and offering more treatment options.

Overall, the study reported poor survival status of hypopharyngeal cancer whereby, at five years follow-up nearly half of the participants with hypopharyngeal cancer died. The late stage of the disease and the presence of distance metastasis significantly impact the outcomes. Participants at cancer stage IV and with the presence of distance metastasis experienced poor outcomes.

Strengths and limitations of the study

While the strength of the present study is that, it is the first report in Tanzania to provide comprehensive information about the proportion of hypopharyngeal cancer, five-year survival rates, and its associated factors among head and neck cancer patients. The limitations are that using secondary data and a retrospective study design limits the completeness of the clinical information due to many incomplete variables and may also introduce selection bias. Also, being conducted in a single centre limits generalizations of the findings to other regions with different population characteristics.

CONCLUSION

The study reported a poor survival rate of hypopharyngeal cancer with a five-year mortality rate of 46.4%. Participants with hypopharyngeal cancer at stage IV, and

those with the presence of distance metastasis had higher hazard of mortality compared to their counterpart.

Recommendations

Further efforts should be implemented towards enhancing the early detection and management of hypopharyngeal cancer, in order to tackle the disease at the early stage for better outcomes. Further multicentered, prospective cohort study should be conducted to give more representative data for the generalizability of the findings across all regions in Tanzania.

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