Clinico-Pathological Profile of Hypopharyngeal Cancer at Two Largest Tertiary Hospitals in Tanzania

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Abstract

BACKGROUND

Hypopharyngeal cancer being one of the upper aerodigestive malignancies has a very poor prognosis due to its late presentation, delay in diagnosis and initiation of treatment. The study aimed to determine the clinicopathological profile of hypopharyngeal cancer at the two largest tertiary hospitals in Tanzania.

MATERIALS AND METHODS

This study was conducted at Muhimbili National Hospital (MNH) and Ocean Road Cancer Institute (ORCI) both located in Dar es Salaam, Tanzania and it was conducted from September 2019 to February 2020 where 119 patients were recruited after a thorough clinical evaluation and histopathological confirmation of the tissue biopsies. Structured questionnaires were used to collect data and it was analyzed using the Statistical Package for Social Sciences (SPSS) version 20. The chi-square test was used to determine the relationship between independent and dependent variables and a p-value <0.05 was considered statistically significant.

RESULTS

The study depicted male preponderance (male to female ratio being 2.6:1) and the majority of the patients (87.23%) were aged above 60 years. Progressive dysphagia and persistent sore throat (100%) were the predominant clinical features. Regarding the involvement of anatomical subsites of the hypopharynx by cancer, the majority of patients had more than one anatomical subsite involvement (89.08%) followed by the pyriform fossa (5.88%) posterior pharyngeal wall (3.36%) and least affected site is the post cricoid space (1.68%). Postcricoid space was found to affect women only. The majority of the patients (88.2%) were diagnosed at advanced stages. Histopathologically, the predominant subtype was found to be carcinoma (98.5%) with invasive squamous cell carcinoma (95.8%) predominating.

CONCLUSION

Progressive dysphagia and persistent sore throat were the predominant clinical features whilst the majority of patients had more than one anatomical site involved. Most patients presented at advanced stages due to delayed diagnosis and similarly, the predominant histopathological subtype was carcinoma.

Keywords: *Clinico-Pathological; Hypopharynx; Cancer; Tanzania*

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Introduction

Hypopharyngeal cancer is a subtype of head and neck cancer where malignant cells grow/arise from the mucosa of either one or the three anatomical subsites of the hypopharynx [1-3]. Head and neck squamous cell carcinoma is the sixth leading cancer globally with an annual incidence of more than 550,000 cases and around 300,000 deaths per year and generally accounts for about 5% of all head and neck cancers [2-4]. The incidence of head and neck cancer has been increasing in the last few decades just as hypopharyngeal cancer cases have kept on increasing with increasing incidence in younger patients having been described in some literature [1].

Cancer survivorship in high-income countries has shown an increasing trend which may be attributed to earlier cancer detection via screening, insights into tumor biology and pathogenesis, as well as improved treatments and supportive care [3].

The most frequently affected anatomical subsite of the hypopharynx is the pyriform sinus representing 70% of cases, followed by the postcricoid space (15- 20%) and the posterior pharyngeal wall (10-15%) [1]. Hypopharyngeal carcinomas are generally more common in males, aged around 55 years except for postcricoid cancer seen generally in about 30% of women and unrelated to alcohol consumption or cigarette smoking, which are the two main risk factors for hypopharyngeal cancer. The commonest implicated risk factors for hypopharyngeal cancer which are cigarette smoking and alcohol consumption are predominant in males than females however there have been changes in dynamics in the current era where such habits are becoming commoner in women too [5]. Other risk factors include diet lacking nutrients, women with Plummer-Vinson syndrome, genetic predisposition, people working in metal industries, construction, ceramic industry, food industry, coal mines, acid reflux, Human Papillomavirus infection, previous head and neck irradiation or previous history of head and neck cancer [4-15].

Hypopharyngeal cancer is diagnosed at advanced stages owing to its late symptomatic presentation [9]. Progressive dysphagia, persistent sore throat, voice change, neck mass, and referred ear pain are some of the clinical features of hypopharyngeal cancer [1,10,11,16-19].

Given the late presentation of symptoms and considerable submucosal spread of the malignant tumour, hypopharyngeal squamous cell carcinoma is usually detected in advanced stages (III and IV) often with locoregional and/or distant metastases [4,9]. Similarly, hypopharyngeal cancer has the worst prognosis compared to other head and neck cancers due to its late presentation and delayed initiation of treatment [3,12].

Treatment options include radiotherapy, chemotherapy and surgery, alone or multimodality treatment. Early hypopharyngeal cancers can be treated with radiotherapy alone. In terms of loco-regional control and survival rates, results are comparable to those of partial surgery though radiotherapy alone does not appear to provide a satisfactory outcome in advanced cancers compared to radical surgery and eventual adjuvant radiotherapy [19]. To date, no study in our settings has described the clinical and histopathological profile of hypopharyngeal cancer as one of the subtypes of head and neck cancer. The study's objective was thus to address such an existing gap by determining the clinical and pathological profile of hypopharyngeal cancer at Muhimbili National Hospital and Ocean Road Cancer Institute.

Materials and methods

Study design, area and study duration

This was a hospital-based descriptive cross-sectional study that was conducted at two hospitals serving the largest number of patients with cancers including head and neck cancer

(hypopharyngeal cancer). These hospitals were MNH and ORCI in Tanzania. The study data was collected from September 2019 to February 2020.

Study population and sampling

The study targeted all inpatients and outpatients with histopathologically proven hypopharyngeal cancer. Cochran's formula [$N=4Za^2P(1-P)$ (W^2)] was used to estimate the sample size [13]. Applying a margin of error of 5%, confidence level of 95% (z-score=1.96) and prevalence of 14.3% a sample size of 119 patients from the two selected hospitals was obtained. To obtain the desired sample size, a convenient sampling technique was utilized where the sample was specific to those patients with histopathologically proven hypopharyngeal cancer.

All outpatients and inpatients who were histopathologically proven to have hypopharyngeal cancer at any stage of the disease from the two selected hospitals during the study period were included. On the other hand, patients who did not consent to participate and those with head and neck cancers other than hypopharyngeal cancer were excluded.

Data collection

Data were collected using structured questionnaires from patients on an outpatient and inpatient basis provided hypopharyngeal cancer was confirmed by histopathology. The principal investigator to ascertain the size of the lesion, subsites involved and clinical staging of the patients performed rigid/flexible hypopharyngoscopy. Imaging studies (computerized tomography scan, magnetic resonance imaging) and the results /reports were obtained through hospital registries, computerized databases and patients' files.

Data analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS) version 20. The chi-square test was used to determine the relationship between independent and dependent variables and a p-value <0.05 was considered to be statistically significant.

Ethical considerations

Ethical approval was obtained from the MUHAS Ethical and Research Publication Committee and granted ethical approval with reference number Ref.No.DA.287/298/01A/ and the permission to collect data was provided by the administration of the two selected hospitals.

Results

Age and sex distribution of the study participants

In this study, 119 patients were enrolled where the majority were males (72.27%) with a male-to-female ratio of 2.6:1.

The age of patients ranged from 18-82 years with a mean age of 54.9 years and a standard deviation of 13.2 years. The majority of the patients (87.23%) were aged above 60 years and the most affected age group was 60+ years (39.5%). (Table 1)

Table 1:
Distribution of study participants by age and sex (N=119)

Age group (years)	Sex		
	Female N(%)	Male N(%)	Total N(%)
10-20	2 (100)	0 (0)	2 (1.68)
21-30	3 (27.28)	8 (72.72)	11 (9.24)
31-40	5 (50)	5 (50)	10 (8.40)
41-50	6 (46.15)	7 (53.85)	13 (10.92)
51-60	11 (30.55)	25 (69.44)	36 (30.25)
60+	6 (12.77)	41 (87.23)	47 (39.5)
Total	33 (27.73)	86 (72.27)	119 (100)

Clinical features of hypopharyngeal cancer among the study participants

In this study, the predominant clinical features were difficulty in swallowing (100%) and persistent throat pain (100%) while koilonychia (1.68%) and glossitis (1.68%) were the least encountered clinical features. (Figure 1)

Distribution of anatomical subsites for hypopharyngeal cancer by age of patients

A majority (98.1%) of patients in this study above 30 years had involvement of more than one anatomical subsite of the hypopharynx. The p-value was 0.000, thus the relationship between the distribution of anatomical subsites of the hypopharynx affected by hypopharyngeal cancer by age was found to be statistically significant. (Table 2).

Distribution of anatomical sub sites for hypopharyngeal cancer by sex of patients

In this study, both males and females had involvement in more than one anatomical subsite of the hypopharynx 106(89.08%) while postcricoid subsite was involved only in females, 2 (6.06%).

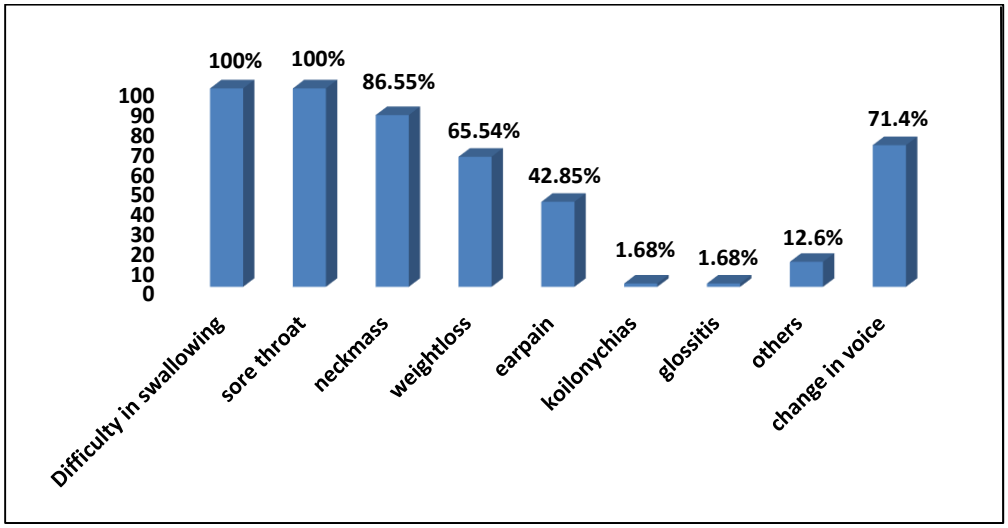

***Figure 1*:**
Distribution of clinical features of hypopharyngeal cancer

Table 2:
Distribution of anatomical subsites of the hypopharynx involved by hypopharyngeal cancer by age of patients

Age (years)	Subsites Pyriform fossa N(%)	Post cricoid space N(%)	Posterior pharyngeal wall (PPW) N(%)	More than one subsite N(%)	Total N(%)
10-20 years	0	2 (100)	0	0	2 (1.68)
21-30 years	5 (45.5)	0	4 (36.36)	2 (18.2)	11 (9.24)
31-40 years	0	0	0	10 (100)	10 (8.40)
41-50 years	0	0	0	13 (100)	13 (10.92)
51-60 years	2 (5.6)	0	0	34 (94.4)	36 (30.25)
60+	0	0	0	47 (100)	47 (39.49)
Total	7 (5.88)	2 (1.68)	4 (3.36)	106 (89.08)	119 (100)

The p-value for the distribution of anatomical subsite of the hypopharynx by sex was found to be 0.154, thus not statistically significant. Similarly, amongst those with single subsite involvement (13 patients), the commonest involved subsite was the pyriform fossa 7(53.8%) followed by the posterior pharyngeal wall 4(30.8%) and the least involved subsite was the post cricoid space 2(15.4%). (Table 3)

Distribution of stage of hypopharyngeal cancer at diagnosis by age of patients

Majority of patients aged 10-30 years presented in the early stage of hypopharyngeal cancer while patients aged 31+ years presented at the late stage of the disease. The distribution between the stages of hypopharyngeal cancer at diagnosis by age of patients was found to have a statistically significant p-value of 0.000 (Table 4).

Distribution of stage of hypopharyngeal cancer at diagnosis by sex of patients

In this study, both male (89.5%) and female (84.84%) patients presented to the two hospitals while in an advanced stage of hypopharyngeal cancer.

Table 3:
Distribution of anatomical subsites of the hypopharynx involved by hypopharyngeal cancer by sex

Anatomical subsite	Pyriform fossa N(%)	Post cricoid space N(%)	Posterior pharyngeal wall (PPW) N(%)	More than one subsite N(%)	Total N(%)
Female	2 (1.68)	2 (6.06)	1 (3.03)	28 (84.85)	33(27.73)
Male	5 (5.81)	0 (0)	3 (3.49)	78(90.70)	86(72.26)
Total	7 (5.88)	2 (1.68)	4 (3.36)	106 (89.08)	119(100)

Table 4:
Distribution of stage of hypopharyngeal cancer at diagnosis by age of patients

Age group (years)	Early stage N(%)	Advanced stage N(%)	Total N(%)
10 – 20	2 (100)	0	2 (1.68)
21 - 30	9 (81.8)	2 (18.2)	11 (9.24)
31 – 40	1 (10.0)	9 (90.0)	10 (8.40)
41 – 50	0	13 (100)	13 (10.92)
51 – 60	2 (5.6)	34 (94.4)	36 (30.25)
60+	0	47 (100)	47 (39.49)
Total	14 (11.8)	105 (88.2)	119 (100)

Table 5:
Distribution of stage of hypopharyngeal cancer at diagnosis by sex of patients

Sex	STAGE OF HYPOPHARYNGEAL CANCER		
	Early stage N(%)	Advanced stage N(%)	Total N(%)
Female	5 (15.15)	28 (84.84)	33 (27.73)
Male	9 (10.5)	77 (89.5)	86 (72.26)
Total	14 (11.8)	105 (88.2)	119 (100)

The observed relationship between the stage of the disease at diagnosis and the sex of patients was not statistically significant P-value of 0.336 (Table 5).

Histopathological types and grades of hypopharyngeal cancer from the study population

The predominant histopathological type for hypopharyngeal cancer in this study was found to be carcinoma, (98.32%) with squamous cell carcinoma being the commonest subtype 114(95.8%) and the two other histopathological subtypes were adenocarcinoma 3(2.52%) and lymphoma 2(1.68%). Of the 114 patients with squamous cell carcinoma, their grades are as follows; well-differentiated carcinoma, 69(60.5%), moderately differentiated carcinoma, 24(21.05%) and poorly differentiated carcinoma, 21(18.4%).

Histopathological grades of hypopharyngeal squamous cell carcinoma by sex of patients

Of the 82 males with squamous cell carcinoma, the majority 57(69.5%) had well-differentiated squamous cell carcinoma while 18(22.0%) had moderately differentiated squamous cell carcinoma and 7(8.5%) had poorly differentiated squamous cell carcinoma. Similarly, of the 32 females with squamous cell carcinoma, the predominant histological grade of squamous cell carcinoma among females was poorly differentiated subtype 14(43.8%) followed by well-differentiated subtype 12(37.5%) and moderately differentiated squamous cell carcinoma 6(18.18%). The p-value for the relationship between histopathological grade and sex of patients was found to be 0.000, thus statistically significant

Discussion

Hypopharyngeal cancer being one of the head and neck cancers has a very poor prognosis because it's mostly diagnosed in advanced stages and there is no study from the two selected hospitals that has characterized such cancer. The study thus aimed to describe the clinicopathological profile of hypopharyngeal cancer at MNH and ORCI.

In this study, a total of 119 patients with histopathologically proven hypopharyngeal cancer were enrolled and such cancer was commonly seen in those in the 5th decade and above. Male preponderance for the malignant neoplasms of the hypopharynx was also found and the age range of patients was 18-82 years (Mean=54.9, SD=13.2). These findings were consistent with those from India where the disease was found to be predominant in those above the 5th decade of life and with male preponderance [9]. Similarly, a study from Kenya found the affected patients to be mostly in their 6th and 7th decades of life [1]. However, the demographic findings from our study appear to be dissimilar to those from Senegal where females were more affected than males by hypopharyngeal cancer with a mean average of 33 years [6]. Such observed differences may be attributed to chronic anaemia (iron deficiency anaemia) seen in 30% of the studied patients and thus one of the possible predisposing factors in those with Plummer-Vinson syndrome. On top of that, two studies from Nepal found no sex predominance in patients with hypopharyngeal cancer since both sexes in the study were equally exposed to predisposing risk factors like heavy cigarette smoking, chewing tobacco and excessive alcohol consumption [20,21].

Regarding the clinical features of hypopharyngeal cancer, all patients in this study presented with progressive dysphagia (100%) and persistent sore throat (100%) followed by neck mass (86.55%), change in voice (80.7%), weight loss (65.54%) and otalgia (42.85%) while the least features were glossitis (1.68%) and koilonychia (1.68%). These findings appear to be similar to what was found in Bangladesh where the commonest clinical features for hypopharyngeal cancer were found to be

dysphagia (96.6%), neck mass (96.6%), change in voice (79%) and otalgia (75%) [14]. Similarly, a study from Kenya found dysphagia (100%) and change in voice (82.8%) to be the commonest features [1]. On the other hand, a study from Senegal found no patients presenting with a neck mass thus no metastasis to cervical lymph nodes [6].

Regarding anatomical sites involved by hypopharyngeal cancer, the majority of patients (89.08%) in our study had more than one anatomical site of the hypopharynx being involved and amongst those with single subsite involvement (13 patients), the commonest involved subsite was the pyriform fossa 7(53.8%) followed by the posterior pharyngeal wall 4(30.8%) and the least involved subsite was the post cricoid space 2(15.4%) and with the later being involved exclusively in females. Such findings appear to be in line with what has been found in other countries like Senegal, Korea, India and Pakistan where hypopharyngeal cancer was observed to involve multiple sites and with the pyriform fossa being the commonest involved anatomical subsite of the hypopharynx ranging from 41% to 100% and the post cricoid space being involved only in females [6,9,12,14,22,24]. Pyriform fossa is the commonest anatomical subsite because this area is large and acts like a smuggler's fossa thus harboring food particles and carcinogenic materials leading to chronic irritation of the mucosal lining and eventually pathogenesis of cancer.

Regarding the stage of the disease and the age of the studied patients, our study found younger patients aged 10-31years (10.92%), presented with early-stage hypopharyngeal cancer at diagnosis while those aged 31+ years presented at a late stage of the disease (82.2%). Such findings mirror what has been observed in other studies globally [25-27]. The reasons for the delayed diagnosis may be due to the capacity of the hypopharynx where there is usually a considerable tumor growth in the pyriform fossa before a patient starts to exhibit symptoms.

In this study, the commonest histopathological type of hypopharyngeal cancer was squamous cell carcinoma (95.88%). Such finding appears to be similar to those found in other countries like Nigeria, India and Kenya [1,22, 26]. Such similarity may be attributed to the mucosal lining of the hypopharynx from which hypopharyngeal cancer, is lined by stratified squamous non-keratinized epithelium hence the most common histopathological type is squamous cell carcinoma.

Regarding the degree of cellular differentiation, the majority of the squamous cell carcinomas were well differentiated, most of which were amongst males while females had predominantly moderately and poorly differentiated cancers. Such findings appear to resemble what was found in India and Kenya where the majority of the patients with hypopharyngeal cancer had a well-differentiated pattern [1,18].

Conclusion

Hypopharyngeal cancer has been found to peak in the 6th decade of life and is more common in males. The predominant clinical features were dysphagia and persistent sore throat and the commonest involved anatomical subsite of the hypopharynx was found to be the pyriform fossa though most patients had involvement of more than one anatomical site at the time of diagnosis. On the other hand, the predominant histopathological subtype was found to be squamous cell carcinoma.

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Conflicts of Interests: The authors have declared that no competing interests exist

Authors' contributions: All others contributed significantly to the study. Joyce M.K., Aveline A.K. and Zephania S.A designed and computed

the study. Enica R.M., Edwin L. and John K. designed the study. All authors participated in the preparation of the manuscript.

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