

# Clinical Profile and Treatment Outcome of Laryngeal Cancer in a Nigerian Tertiary Hospital

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## Abstract

**Background:** Laryngeal cancer is one of the most common malignancies of the upper aerodigestive tract worldwide, and its management may sometimes be challenging, especially in developing countries due to late presentation, poverty and limited resources. **Aim:** This study aims to highlight the clinical profile and treatment outcome of laryngeal cancer in our centre. **Patients and Methods:** This was a retrospective review of patients who were managed for laryngeal cancer between January 2011 and December 2020. **Results:** There were 90 (89.1%) males and 11 (10.9%) females, with a male-to-female ratio of 8.2:1. The age ranged from 22 to 82 years, with a mean age of  $57.2 \pm 12.7$  years. Fifty patients (49.5%) presented more than 1 year after the onset of the symptoms. Squamous cell carcinoma (SCCA) was the only histological diagnosis observed in our patients. The laryngeal cancer was transglottic in location in 45 (44.6%) patients, while 50 (49.5%) patients presented with Stage III disease. Twenty-one (20.8%) patients had total laryngectomy. Amongst the patients managed, 17 (17.0%) were still on follow-up. Up to 37 (37.0%) were referred for radiotherapy elsewhere after chemotherapy. Forty-one of the patients (40.0%) died during the course of their management. There was a statistically significant association between having definitive surgical management and survival beyond 5 years (Chi-square test = 8.635,  $P = 0.003$ ). **Conclusion:** Majority of the patients presented late with transglottic SCCA. Surgical extirpation of the lesion was associated with better prognosis in our patients.

**Keywords:** Clinical profile, laryngeal cancer, outcome, squamous cell carcinoma

## INTRODUCTION

Laryngeal cancer is one of the most common malignancies of the upper aerodigestive tract worldwide.<sup>[1]</sup> In 2017, about 210,606 new cases (2.76 new cases/100,000 inhabitants) of laryngeal cancers were reported worldwide, with associated 126,471 death (1.66/100,000 inhabitants).<sup>[2]</sup> In Europe, 35,981 cases and 18,069 deaths were reported.<sup>[2]</sup> Furthermore, in the United States of America alone, 13,150 cases were reported in 2018 with associated 3710 deaths.<sup>[1]</sup> In Nigeria, larynx was the third most common site of head-and-neck cancers following nasopharynx and sinonasal region.<sup>[3]</sup> Laryngeal cancer has a male preponderance and is more commonly seen amongst people between 45 and 70 years of age.<sup>[4]</sup> Tobacco smoking and alcohol ingestion are two independent and most common

risk factors for development of laryngeal cancer. Furthermore, the risk of developing laryngeal cancer may be increased by 50% in people who smoke cigarette and also ingest alcohol.<sup>[5]</sup> Laryngopharyngeal reflux, exposure to asbestos, polycyclic aromatic hydrocarbons, wood dust, coal dust and cement dust were also recognised as risk factors, especially in non-smokers.<sup>[6,7]</sup> Squamous cell carcinoma (SCCA) is the most common histological variety of laryngeal cancer accounting for 85%–90%. About 60% of cases of laryngeal cancers occur in the glottis followed by supraglottic (35%) and subglottic (5%).<sup>[8]</sup> However, some cases of laryngeal

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cancers may present as transglottic, where more than 1 subsite is involved. A tumour is said to be transglottic if it crosses the laryngeal ventricle or anterior commissure, and when it spread along the arytenoid cartilage or through paraglottic space.<sup>[9]</sup> Laryngeal cancer can spread locally along tissue planes or via lymphatics. Spread via lymphatic channels was more commonly observed in supraglottic and subglottic tumours, and is one of the most important prognostic factors in laryngeal cancer.<sup>[10]</sup>

Most cases of glottic cancers present early due to hoarseness. In contrast, patients with supraglottic cancers may ignore initial early non-specific symptoms and present later with dysphagia, haemoptysis, hoarseness, referred otalgia, cervical lymphadenopathy and airway obstruction. Difficulty in breathing and stridor may be the main presenting features of subglottic cancers.<sup>[11]</sup> Assessment of patients with laryngeal cancers starts with thorough history and examination including flexible nasopharyngoscopy to visualise the larynx and surrounding structures and to characterise the lesion and the status of vocal cord. Computed tomographic scan (CT scan), magnetic resonance imaging (MRI) and chest radiograph may play a vital role in patient's assessment. These imaging tests are important in identifying the site and size of primary tumour, involvement of laryngeal cartilage and surrounding extralaryngeal structures, state of airway and nodal status.<sup>[12]</sup> Modalities for treating laryngeal cancer may include surgery, radiotherapy and chemoradiotherapy or combination of modalities. The choice of modality may be influenced by the stage of the disease, patient's performance status, availability of facilities and expertise. While early stages may be treated with radiotherapy or surgical extirpation, the advanced disease may be managed with laryngectomy and chemoradiotherapy.

In Nigeria, the treatment of laryngeal cancer may be challenging owing to late presentation, patients' desire to keep their voice and few functioning radiotherapy centres. Although laryngeal cancer is a common head-and-neck cancer in our environment, there is paucity of literature on outcome of management of laryngeal cancer in the study area. The aim of this study was to highlight the clinical presentation and treatment outcome of patients managed for laryngeal cancer in our centre.

## PATIENTS AND METHODS

This was a retrospective, descriptive study of patients managed for laryngeal cancers at the Department of Radio-Oncology and Division of Otorhinolaryngology of Ahmadu Bello University Teaching Hospital (ABUTH), Zaria, over a 10-year period between January 2011 and December 2020. ABUTH is a tertiary health centre that receives patients from various parts of the country, with majority coming from Northwestern Nigeria.

After obtaining approval from the Health Ethics Committee of ABUTH, Zaria, with protocol number: ABUTHZ/HREC/224/2020 on 12 October 2020, the records of all concerned patients were retrieved by the staff of the Health Information Department of the hospital. Patients

with insufficient data as well as missing files were excluded from the study. Information retrieved from the patients' case file included demographics, risk factors, clinical characteristic such as duration of symptoms, main presenting symptoms, main examination findings including flexible and direct laryngoscopy, radiological investigation, need for tracheostomy, surgical and non-surgical treatment, histological diagnosis and outcome.

At presentation, all patients underwent thorough history and examination including flexible nasopharyngolaryngoscopy/indirect laryngoscopy to arrive at initial diagnosis. They all had radiological and laboratory investigations, and direct laryngoscopy and biopsy. Patients who presented with upper airway obstruction had tracheostomy before direct laryngoscopy and biopsy to arrive at histological diagnosis. Following histological diagnosis, patients were counselled on various treatment modalities including chemoradiotherapy alone or surgery and post-operative chemoradiation. A large number of patients presented with histological diagnosis, following evaluation and biopsy, tracheostomy or laryngectomy in their primary centre before referral to our hospital. Due to large volume of patients being referred to our centre for radiotherapy, patients usually undergo chemotherapy for 6 months first and then radiotherapy afterwards. Cisplatin and 5-fluorouracil were the drug combination of choice in our patients. Patients who could not get the radiotherapy from our centre for various logistic reasons were referred to another centre with similar facilities after receiving 6 courses of chemotherapy. The usual external beam radiotherapy (cobalt 60) cumulative dose in our centre was 65 cGy at the rate of 2 cGy/day for 5 days in a week for a period of 6 weeks. Following chemoradiation, patients are followed up for a period of 5 years.

## Statistical analysis

The data collected were entered into spreadsheet and analysed using SPSS version 23 (SPSS Inc., Chicago, Illinois, USA). Qualitative data were summarised as frequencies and percentages and presented as tables. Statistical relationships were analysed using Chi-square test and Fisher's exact tests. *P* value was set at <0.05.

## RESULTS

Within the period under review, 116 patients presented with laryngeal cancer and only 101 fulfilled the inclusion criteria. There were 90 (89.1%) males and 11 (10.9%) females, with a male-to-female ratio of 8.2:1. The age ranged from 22 to 82 years, with a mean age of 57.2 years and standard deviation of 12.7 years ( $57.2 \pm 12.7$ ) and a median age of 59 years. The peak age of occurrence was in the age group of 60–69 years [Table 1]. Majority of the patients were civil servants (32, 31.7%) and farmers (32, 31.7%) while carpentry was the least common occupation observed in 1 (1%) patient [Table 1]. Most of the patients emanated from the northwest geopolitical zone accounting for 50 (49.5%) patients, followed by north central 26 (25.8%) and north east

**Table 1: Characteristics of the study population**

Variable	n (%)
Age	
20-29	2 (2)
30-39	9 (8.9)
40-49	14 (13.9)
50-59	26 (25.7)
60-69	32 (31.7)
70-79	16 (15.8)
80-89	2 (2)
Total	101 (100)
Gender	
Male	90 (89.1)
Female	11 (10.9)
Total	101 (100)
Occupation	
Civil servant	32 (31.7)
Farmers	32 (31.7)
Trading	22 (21.8)
Homemaker	10 (9.9)
Driving	2 (2)
Student	1 (1)
Priest	1 (1)
Carpentry	1 (1)
Total	101 (100)
Geopolitical zone	
Northwest	50 (49.5)
North central	26 (25.8)
Northeast	13 (12.9)
Southeast	8 (7.9)
Southwest	3 (2.9)
South south	1 (1.0)
Total	101 (100)
Tribe	
Hausa	65 (64.4)
Igbo	8 (7.9)
Yoruba	3 (2.9)
Others	25 (24.8)
Total	101 (100)

13 (12.9%) geopolitical zones. Hausa was the predominant tribe of most of the study population accounting for 65 (64.4%) patients [Table 1].

Hoarseness was the most common presenting complaint accounting for 101 (100%) patients. It is closely followed by difficulty in breathing observed in 91 (90.1%) patients. Haemoptysis was the least common symptom seen in only 1 (1.0%) patient [Table 2]. The duration of symptoms before presentation ranged from 1 to 36 months with a mean of  $16.9 \pm 9.9$  months. Majority of our patients (50, 49.5%) presented more than 1 year after the onset of the symptoms. Only 10 (9.9%) presented before 6 months of the onset of the symptoms [Table 2]. Hypertension was the most common comorbid condition observed in 21 (20.8%) patients. HIV/acquired immunodeficiency syndrome was

**Table 2: Clinical characteristics**

Variable	n (%)
Presenting complaints	
Hoarseness	101 (100)
Difficulty in breathing	91 (90.1)
Dysphagia	22 (21.8)
Odynophagia	13 (12.9)
Cough	9 (8.9)
Foreign body sensation	8 (7.9)
Neck pain	7 (6.9)
Otalgia	5 (5)
Haemoptysis	1 (1)
Duration of symptoms (months)	
<6	10 (9.9)
6-12	41 (40.6)
13-24	37 (36.6)
>24	13 (12.9)
Total	101 (100)
Medical conditions	
None	65 (64.3)
Hypertension	21 (20.8)
Diabetes	11 (10.9)
HIV/AIDS	4 (4.0)
Total	101 (100)

the least common comorbid condition seen in 4 (4.0%) patients [Table 2].

SCCA was the only histological diagnosis observed in our patients, and the most common histological grade was well-differentiated SCCA seen in 57 (56.4) followed by moderately differentiated SCCA in 32 (31.7%) patients. Only 12 (11.9%) patients presented with poorly differentiated SCCA [Table 3]. Transglottic tumour was the most common accounting for 45 (44.6%) patients. This was closely followed by glottic subsite observed in 36 (35.6%) patients. Involvement of the subglottic subsite was noted in only 1 (1%) patient [Table 3]. Majority of the patients presented with late disease, with 50 (49.5%) and 31 (30.7%) of them having Stage III and IV diseases, respectively. One patient presented with Stage I disease [Table 3]. Cervical lymph node enlargement was noted amongst 35 (34.7%) patients. Amongst the patients with vocal fold palsy, the left was the most commonly involved seen in 36 (35.6%) patients followed by right seen in 28 (27.8%) patients [Table 3].

Amongst the risk factor (s) for laryngeal cancer identified in our patients, smoking of cigarette only was noted in 30 (30%) patients, alcohol ingestion and smoking of cigarette was observed in 26 (26%) patients, family history of cancer was found in 1 (1%) patient and in 40 (39%) patients no risk factor was identified. Plain radiograph of the neck and chest was the most commonly requested investigation accounting for 74 (73.3%) patients, followed by CT scan and MRI in 19 (18.8%) and 1 (1.0%) patients, respectively.

Majority of our patients (92, 91.1%) presented with upper airway obstruction necessitating tracheostomy to secure their

airway. Total laryngectomy was observed amongst 21 (20.8%) patients. Cordectomy was the least common surgical procedure noted on 1 (1.0%) patient. Most of our patients (43, 42.6%) had chemoradiotherapy while 37 (36.6%) had chemotherapy only before they were referred for radiotherapy elsewhere. Up to 19 (18.8%) patients had surgery and post-operative chemoradiotherapy [Table 4]. Amongst the patients managed, 17 (17%) were still on follow-up at the time of review. Up to

37 (37.0%) were referred for radiotherapy elsewhere after chemotherapy. Many of the patients (41, 40.0%) died during the course of their management [Figure 1].

Chi-square test showed a significant association between having definitive surgical management and surviving beyond 5 years. Furthermore, patients younger than 50 years tend to have better chance of survival compared to those above 50 years of age (Chi-square test = 8.635  $P = 0.003$ ) [Table 5].

**Table 3: Laryngeal tumour characteristics**

Variable	n (%)
<b>Histology</b>	
Well-differentiated SCCA	57 (56.4)
Moderately differentiated SCCA	32 (31.7)
Poorly differentiated SCCA	12 (11.9)
Total	101 (100)
<b>Subsites</b>	
Supraglottic	19 (18.8)
Glottic	36 (35.6)
Subglottic	1 (1)
Transglottic	45 (44.6)
Total	101 (100)
<b>Tumour stage</b>	
Stage I	1 (1)
Stage II	19 (18.8)
Stage III	50 (49.5)
Stage IV	31 (30.7)
Total	101 (100)
<b>Cervical lymph node</b>	
None	66 (65.3)
Level II, III	11 (10.9)
Level II, III, IV	8 (7.9)
Level III, IV	7 (6.9)
Level II	4 (4.0)
Level IV	4 (4.0)
Level I, II, III	1 (1.0)
<b>Vocal fold palsy</b>	
None	30 (29.7)
Left	36 (35.6)
Right	28 (27.8)
Bilateral	7 (6.9)
Total	101 (100)

SCCA: Squamous cell carcinoma

**Table 4: Modalities of treatment**

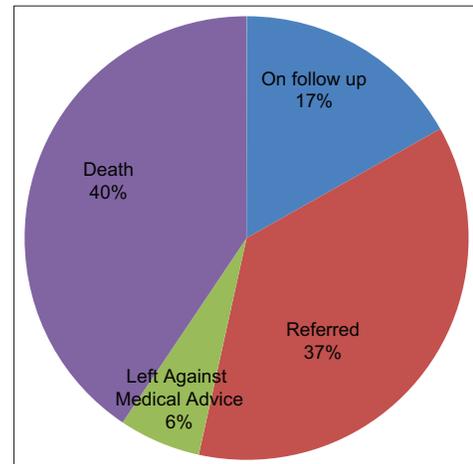
Variable	n (%)
<b>Surgical procedure</b>	
Tracheostomy	92 (91.1)
Total laryngectomy	16 (20.8)
Total laryngectomy and selective neck dissection	5 (5.0)
Cordectomy	1 (1.0)
<b>Combination of modalities of treatment</b>	
Chemoradiotherapy	43 (42.6)
Chemotherapy alone	37 (36.6)
Surgery and chemoradiotherapy	19 (18.8)
Surgery and chemotherapy only	2 (2)

**DISCUSSION**

Laryngeal cancer is one of the most common head-and-neck cancers worldwide. It is the twentieth most common cancer worldwide.

The mean age of 57 years observed amongst our patients was in agreement with several other studies.<sup>[13-15]</sup> However, other researchers reported a mean age ranging from 60 to 62 years.<sup>[16-18]</sup> About 24% of our patients were in the fifth decade at the time of presentation. A study has shown that African American patients with laryngeal cancer present at younger age compared to Caucasians, Hispanics and Asians.<sup>[19]</sup> Majority of our patients were male with a male-to-female ratio of 8:1. This is similar to the findings in Germany,<sup>[13]</sup> India<sup>[15]</sup> and Slovakia<sup>[17]</sup> where the male-to-female ratio of 9:1, 9:1 and 12:1 was reported, respectively. However, reports from another part of Nigeria and Israel found increasing number of females presenting with laryngeal cancer.<sup>[16,20]</sup>

Hoarseness was the most common symptom at presentation in all our patients. This finding was corroborated by other workers where they also reported 100% of their patients presenting with hoarseness.<sup>[20,21]</sup> This may be due to the fact that majority of our patients presented with advance disease with involvement of the vocal cord. The duration of symptoms at presentation in our study is consistent with the report by Nwaorgu *et al.*<sup>[22]</sup> and da Lilly-Tariah *et al.*<sup>[23]</sup> who observed a mean duration of symptoms of 13.8 and 13.5 months, respectively. However, our findings differ from that of another study in Nigeria which reported an average of 7.3 months as duration of symptoms



**Figure 1: Outcome of the patients after treatment**

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**Table 5: Factors associated with survival**

Factors	<5-year survival	>5-year survival	$\chi^2$	P
Age (years)				
<50	13	5	3.898	0.048
$\geq 50$	42	4		
Vocal cord palsy				
Yes	36	5	0.651	0.420
No	19	4		
Cervical lymph node				
Yes	18	5	0.471	0.493
No	37	4		
Tracheostomy				
Yes	50	1	0.037	0.847
No	5	8		
Clinical stage				
Early	8	2	0.436	0.557
Late	47	7		
Definitive surgical management				
Yes	11	6	8.635	0.003
No	44	3		
Complication				
Yes	10	4	3.122	0.077
No	55	5		

before presentation.<sup>[16]</sup> A large number of our patients were farmers living in rural areas where access to healthcare facility and availability of trained health personnel may be limited.

All of our patients had histological diagnosis of SCCA. Jyoti *et al.*,<sup>[15]</sup> Calkovsky *et al.*<sup>[17]</sup> and Daneshi *et al.*<sup>[24]</sup> also reported SCCA as the only histological finding. However, Fasanla *et al.*<sup>[16]</sup> from Nigeria reported SCCA in 96.9%, with the remaining having synovial sarcoma, chondrosarcoma and adenoid cystic carcinoma. Muhoka *et al.*<sup>[21]</sup> from Tanzania also found SCCA in 98.6%, with the remaining having adenocarcinoma. Our finding of well-differentiated SCCA was contrary to those of other authors,<sup>[17,20,25]</sup> who reported moderately differentiated SCCA as the most common. This may be due to the relatively smaller sample size in our study. Transglottic was the most commonly involved subsite in our patients. This is in accordance with the findings of Fasanla *et al.*,<sup>[16]</sup> Calkovsky *et al.*<sup>[17]</sup> and da Lilly-Tariah *et al.*<sup>[23]</sup> However, Karatzanis *et al.*,<sup>[13]</sup> Gourin *et al.*<sup>[14]</sup> and Jyoti *et al.*<sup>[15]</sup> all reported supraglottic as the most common subsite. On the other hand, Peller *et al.*<sup>[18]</sup> and Nachalon *et al.*<sup>[20]</sup> found glottis as the most common subsite in their series.

In agreement with several other studies,<sup>[14,17,21,24]</sup> majority of our patients presented late with Stage III disease. In sharp contrast to this, Nachalon *et al.*<sup>[20]</sup> reported that most of their patients presented with Stage I and II disease. Resemblance of the initial symptoms to upper respiratory tract infection, lack of awareness and paucity of trained personnel to suspect and diagnose laryngeal cancer may be the reason for late presentation in our environment. Cervical lymphadenopathy is most commonly found in patients with supraglottic tumours

due to the presence of rich lymphatic channels. In this study, cervical lymphadenopathy was found in 34.7% of our patients. This finding is similar to that of Calkovsky *et al.*<sup>[17]</sup> who also reported cervical lymphadenopathy in 35% of their patients. Contrary to this, Fasanla *et al.*<sup>[16]</sup> found up to 58.8% of their patients having cervical lymphadenopathy. This may be due to large number of patients with transglottic disease in their series.

Tobacco smoking and alcoholism are the two most commonly documented risk factors for laryngeal cancer. The risk may double when one combines the two at the same time. Smoking was the most common risk factor in this study. Similarly, Jyoti *et al.* and Nachalon *et al.* also reported smoking as the most common accounting for 79% and 82%, respectively.<sup>[15,20]</sup> Contrary to this, other studies reported concurrent alcoholism and smoking as the most common risk factor.<sup>[21,26,27]</sup> Most of our patients presented with upper airway obstruction necessitating tracheostomy. This is also the finding of a similar study from Southwestern Nigeria where 91% of their patients also had tracheostomy.<sup>[16]</sup> In most of the patients, difficulty in breathing and noisy breathing were the main reasons necessitating presentation to the hospital.

Amongst the patients who had definitive surgery, total laryngectomy was the most common. This was also the reports of other workers.<sup>[21,28,29]</sup> In another study by Gourin *et al.*,<sup>[14]</sup> 57% of their patients had surgery as primary treatment. Only one of our patients had cordectomy, as majority of them presented with advance disease. Cordectomy was also the second most common laryngeal surgery in other studies.<sup>[17]</sup> Amongst the non-surgical treatment of laryngeal cancer, Muhoka *et al.*<sup>[21]</sup> reported

chemoradiotherapy as the most common. Our study corroborated this finding. However, 18.8% of our patients had combination of surgery and chemoradiation, as was similarly reported by other workers.<sup>[13]</sup> Platinum-based concomitant chemoradiotherapy is one of the most effective organ preservation modalities used in the treatment of advanced laryngeal cancers.<sup>[30,31]</sup> Only one of our patients had concomitant chemoradiotherapy due to large volume of patients depending on few facilities.

Of the 101 patients reviewed, 41 died, giving a mortality rate of 40%. This is comparable to the findings of Fasanla *et al.*<sup>[16]</sup> where they reported a 46.5% mortality rate. A relatively lower mortality rate of 34% was reported by Nachalon *et al.*<sup>[20]</sup> from Israel. Late presentation coupled with the inadequate functional oncology centres in our environment may have affected the outcome of laryngeal cancer. Up to 37% of our patients were referred elsewhere due to faulty radiotherapy machine. Subsequently, all the patients who presented with laryngeal cancer within that period had only chemotherapy for 6 months before referral. We could not account for the outcome in these patients. Seventeen per cent of our patients are still on follow. These were the patients at various stages of follow-up after completing chemoradiotherapy. Overall, the median duration of survival of our patients was 1 year. Another study from Cameroun found 1.4 years as the median duration of survival after treatment.<sup>[32]</sup> Definitive surgery and age <50 years were found to be associated with better survival in this study. Several other studies also reported similar findings.<sup>[13,14,33]</sup> The fact that majority of our patients had well-differentiated SCCA which is mostly amenable to surgical excision may explain the better survival of the patients.

### Limitation

This study was retrospective in nature, and some patients had to be excluded due to incomplete information. The study could not account for the outcome of up to 37 patients referred for radiotherapy elsewhere.

### CONCLUSION

Majority of the patients were male and presented late with transglottic SCCA. Cigarette smoking was the most common risk factor. Surgical extirpation of the lesion was associated with better prognosis in our patients.

### Recommendation

Performing laryngectomy in patients with advanced disease as well as provision of additional oncology centres in the country may go a long way in improving the outcome of laryngeal cancer.

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### Conflicts of interest

There are no conflicts of interest.

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