

Chemoradiation in head and neck tumours in patients receiving treatment tertiary hospital in Nigeria: A ten-year review

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Abstract

Background: Head and neck tumours are diverse, heterogeneous, and are relatively difficult to diagnose/stage. The use of chemoradiation for these cancers has been associated with better outcomes but has not been fully studied in this environment. Thus, this study aims at describing the pattern of presentation and mode of management of patients with head and neck cancers while exploring the impact of chemoradiation on treatment outcomes and survival in these patients.

Methods: Using a retrospective study design, clinical data was obtained for 406 patients who were treated for head and neck cancers between January 2001 and December 2011.

Results: The mean age was 49 ± 17.1 years with a 2:1 male to female ratio. More tumours were located in the nasopharynx (18.0%) than anywhere else, and the bulk of patients presented with stage 4 diseases (48.5%). Most patients (37.5%) presented with a neck mass, then nasal blockage (23.4%). Squamous cell carcinoma was more prevalent (57.4%) and 73.6% had biopsy before and during surgery, while 26.4% had definitive surgical procedures done. Radiotherapy was the sole treatment in 41.4% and 29.1% had chemoradiation. Post-treatment, 63.1% experienced complete response; 28.3% partial response, and 14% recurrence. Most patients (39.8%) survived for six months post-treatment, 30.7% for 7-12 months, and 17.5% for 13-24 months and patients who received chemoradiation had longer survival.

Conclusion: Early presentation for diagnosis and treatment will definitely improve treatment outcome and survival duration. In addition, concurrent use of chemoradiation improves the treatment outcomes.

Keywords: Chemoradiation, cancer, Nigeria, head and neck, radiotherapy

Résumé

Contexte: Les tumeurs de la tête et du cou sont diverses, hétérogènes et relativement difficiles à diagnostiquer / classer. L'utilisation de la chimioradiothérapie pour ces cancers a été associée à de meilleurs résultats, mais n'a pas été entièrement étudiée dans cet environnement. Cette étude vise donc à décrire le schéma de présentation et le mode de gestion des patients atteints de cancers de la tête et du cou, tout en explorant l'impact de la chimioradiothérapie sur les résultats du traitement et la survie de ces patients.

Méthodes: En utilisant une structure d'étude rétrospective, les données cliniques ont été obtenues pour 406 patients traités pour un cancer de la tête et du cou entre janvier 2001 et décembre 2011.

Résultats: L'âge moyen était de $49 \pm 17,1$ ans avec un ratio hommes / femmes de 2:1. Plus de tumeurs étaient localisées dans le nasopharynx (18,0%) que partout ailleurs et la majorité des patients présentaient des maladies de l'étape 4 (48,5%). La plupart des patients (37,5%) ont présenté une masse au cou, puis un blocage nasal (23,4%). Le carcinome épidermoïde était plus prévalent (57,4%) et 73,6% avaient subi une biopsie avant et pendant la chirurgie, tandis que 26,4% avaient subi une intervention chirurgicale définitive. La radiothérapie était le seul traitement chez 41,4% des patients et 29,1% avaient une chimioradiothérapie. Après le traitement, 63,1% ont eu une réponse complète; 28,3% de réponse partielle et 14% de récurrence. La plupart des patients (39,8%) ont survécu six mois après le traitement, 30,7% de 7 à 12 mois et 17,5% de 13 à 24 mois, et les patients ayant reçu une chimioradiothérapie ont eu une survie plus longue.

Conclusion: Une présentation précoce pour le diagnostic et le traitement améliorera définitivement le résultat du traitement et la durée de survie. En outre, l'utilisation simultanée de la chimioradiothérapie améliore les résultats du traitement.

Mots-clés: Chimioradiothérapie, cancer, Nigéria, tête et cou, radiothérapie

Each patient was assessed and staged based on information on clinical examinations and radiological investigations such as head and neck CT scan, abdominal ultrasound, and chest x-rays. Patients were treated on the linear accelerator machine (6MV) where radiotherapy field and techniques depended on the anatomical location of the tumour but encompassed the primary disease and all regional lymph nodes. The given treatment dose was 60-70 Gray as 2-Gray daily fractions over 6-7 weeks. For concurrent chemoradiation: radiotherapy was given with concurrent weekly intravenous cisplatin 40mg/m² with weekly reaction review. For other patients who received chemotherapy alone or as adjuvant therapy, a variety of cytotoxic drug combinations were used for them or in adjuvant therapy.

Results

Sample characteristics.

The records of four hundred and six (406) patients with head and neck carcinomas seen at the radiotherapy clinic of Lagos University Teaching Hospital (LUTH) between 2001 and 2011 were reviewed. The patients' ages ranged from 2 to 90 years (Fig. 1). The mean age was 49 years (SD 17.1), while the median age was 50 years. There were two hundred and fifty six (256) males (63%) and one hundred and fifty (150) females (37%), with a male to female ratio of about 2:1.

The locations of the tumours are shown in Table 1. The majority of tumours were located in the nasopharynx (18.0%), followed by maxillary antrum (11.3%), and larynx (10.3%). Other major sites include the parotid (8.9%), orbit (8.6%), and mandible (7.4%).

At the time of presentation, majority of patients (48.5%) presented with stage 4 disease. Stage 3 disease followed closely with 37% of the patients presenting at this stage. Only 1% and 14% of the patients presented with stages 1 and 2 respectively. The most common pattern of presentation (Table 2) was neck mass in 37.5% of the respondents, and followed by nasal blockage in 23.4%. The histopathological types of the different cancers seen are shown in Table 3. Squamous cell carcinoma (57.4%) was the most common subtypes of this group.

Treatment modalities

A significant proportion of the patients (73.6%) had biopsy before and during surgery, while 26.4% had definitive surgical procedures done. Radiotherapy was the sole treatment in 41.4%. The results in table 4 show that most of the patients had either

radiotherapy alone or radiotherapy in combination with chemotherapy. Just 8.1% had chemotherapy alone.

After the required course of treatment, the nature of the patients' response to treatment (two months after completion of treatment) is reflected in Table 5. Complete response is defined as total disappearance of all clinical disease while partial response represent a greater than 50% reduction in size of some or all lesions. No response is defined as a reduction in size of less than 50% of some or all lesion or progressing disease. For those with recurrence it is defined as the reappearance of cancer in the same location or distant after patient has been disease free for a time interval 1 year after having complete response to treatment. A significant proportion of the patients (n=256, 63.1%) had complete response following treatment; while 28.3% had partial response and required more treatment. In addition, 35 patients (8.6%) had progression of disease despite the treatment, and 57 (14%) had recurrence.

Table 1. Anatomical locations of the tumours

Site	No	%
Nasopharynx	73	18.0
Maxillary antrum	46	11.3
Larynx	42	10.3
Parotid	36	8.9
Orbit	35	8.6
Mandible	30	7.4
Neck	19	4.7
Nasal	18	4.4
Oral cavity	18	4.4
Tongue	17	4.2
Palate	16	3.9
Cancer of Unknown Primary	16	3.9
Submandibular	14	3.4
Salivary Gland	7	1.7
Ear	7	1.7
Oesophagus	6	1.5
Lip	5	1.2
Parietal	1	0.2
Total	406	100

It is important to note that 14% of the patients experienced recurrence after treatment. The disease recurrence in these patients in relation to the treatment modalities were as follows: radiotherapy alone (n=34, 59.6%), chemotherapy alone (21, 36.8%), and chemoradiation (n=2, 3.5%). The outcome of patients following treatment also varied. Up to 240 patients (59.1%) were lost to follow up or

Introduction

Tumours of the head and neck are the sixth most common malignancy globally with annual incidence of 533,100 cases.[1] They are a diverse and heterogeneous group of diseases arising in all structures cephalad to the clavicles except for the brain, spinal cord, base of skull and usually skin. Each tumour has its own distinct epidemiologic, anatomic and pathologic feature. About 90-95% of head and neck cancers are squamous cell carcinomas. [2-13] The staging of head and neck cancer is complex and depends on the anatomic location of the tumour and there are three clinical stages: early, loco-regionally advanced, and metastatic or recurrent.[6,7,14]

One of the earliest references to head and neck cancers in Nigeria was made by Elmes and Baldwin [15] who reported cases of nasopharyngeal cancer but noted it was rare. Later, cases of oesophageal carcinoma and salivary tumours were reported, although they were also found to be rare in Nigeria [16,17]. However, it has been established that cancer of the nasopharynx is not uncommon in Nigeria as previously reported [18]. Presently, the prevalence of head and neck tumour is on the increase in Lagos, Nigeria; and late presentation is a major problem [18-24]. Similar to foreign studies, there is a male preponderance of head and neck cancers in Nigeria [10-12].

The risks of developing head and neck cancers have been associated with cigarette smoking (by 25-fold) and alcohol use (by 2-6-fold) [13,14,25]. Other risk factors include infections with Epstein Barr virus and Human Papilloma virus especially in younger age groups [13,14]. The common sites of occurrence are in the oral cavity, pharynx, nasopharynx, larynx, and hypopharynx while paranasal sinuses and salivary gland tumours are less common. Also, sarcomas, lymphomas and melanomas of the head and neck region are less common.[3,-5,12,19] Most patients with tumours of the head and neck present with advanced local disease with lymph node metastasis already present in many cases. Salivary gland and nasopharyngeal tumours occur in younger age groups at about the age of 40 years [26] and approximately one-third of these patients are females.[27] As the age increases, the incidence of head and neck cancers increases.[14,28]

Presenting features depend on the primary site involved. Usually, the early symptoms do not produce functional limitations or cosmetic problems because they are mostly vague and non-specific, and are therefore often ignored or not suspected. This makes many patients in this environment present at advanced stage of the disease.[18-20] Ignorance,

poverty and late referral additionally contribute to the dismal state of late presentation. In Nigeria, patients consulting traditional healers and spiritual faith healers also tend to contribute to delay in presentation.

The diagnosis of head and neck cancers requires a good knowledge of disease pattern and a high index of suspicion. Also, treatment depends on the initial localization of tumour on patients, occurrence of co-morbidities, and/or the potential side effects of treatment. Surgical resection, radiotherapy, chemoradiation radio-biotherapy with anti-epidermal growth factor receptor (EGFR) such as cetuximab, and other anti-EGFR are the therapeutic methods used in locally advanced cases.

Chemotherapy can be used singly, depending on stage or in combination to achieve a better outcome. It is also used as an adjunct and can be given as induction chemotherapy or adjuvant to surgery or radiotherapy or given concurrently with radiotherapy which is called "chemoradiation" and this has been observed with better outcome in patients and improves the rate of curability.[29] There is some paucity in knowledge with regards to head and neck cancers in the local Nigerian population. This study focuses on documenting the pattern of presentation and mode of management of patients with head and neck cancers; and to compare treatment outcome and side effects of different treatment modalities: chemotherapy alone, chemotherapy with radiotherapy given either as induction chemotherapy or adjuvant to radiotherapy in comparison with chemoradiation (concurrent chemotherapy and radiotherapy CCRT).

Methods

This ten-year (1st January 2001 – 31st December 2011) retrospective study reviewed the case files of four hundred and six (406) patients with head and neck cancers in the hospital.

Data extracted for analysis include: Age and sex of the patients, Clinical staging of the cancer, histopathologic diagnosis, tumor site, diagnosis and investigations, mode of treatment given and outcomes.

Selection Criteria.

All patients with head and neck cancers who had biopsy and histological confirmation and receiving any form of treatment i.e. chemotherapy, radiotherapy, or concurrent chemoradiation (CCRT) at the radiotherapy clinic in LUTH were included in this study. The exclusion criteria include: (i) absence of histological confirmation, (ii) non-commencement of treatment for histologically confirmed disease, (iii) defaulting or non-completion of treatment.

the peak incidence is in the 6th decade of life [4,9]. This variation in age may be due to geographical and environmental differences. The predominance of males noticed in this study is similar to the sex ratios seen in previously reported studies, locally and international [3-6,8,10-12,15,24,30,31].

The nasopharynx was found to be the commonest site of head and neck cancers. This is similar to reports in many studies [3-5,19,31]. About 4% of the patients presented with metastatic spread to a cervical lymph node, for which the primary site or origin remained undetermined. There has been similar report which described unknown metastatic neck nodes without an obvious primary source [3,4,6,7,19,32,33]. Also, carcinoma of the lip was observed to be a hundred percent in females. This is not in agreement with reports in the literature where lip carcinomas were 8 times commoner in males. In this study, cancer of the ear was also observed to be few which is similar to previous studies in literature [5,8,19,31].

The pattern of histologic types of head and neck cancers found in this study was not different from those previously reported. The most common histological type was squamous cell carcinoma which accounted for 61.3% of the total cases in this study. Other studies have reported a 66.7% incidence for squamous cell carcinoma. [3,5-7,9,19,31]. Adenoid cystic carcinoma (9.9%) was the second most frequent cell type, with sarcoma being the third most frequent type (7.3%). This finding was at variance with the studies of Nwawolo *et al* [3], Lilly-Tariah [25], Okoye *et al* [8] and Ajayi *et al* [28] who all reported sarcomas as the second most common occurring histological type. Reports from other health institutions within the country showed that lymphoma was the second most frequent cell type [5,6,16,19,30]. This was not so with the review study where lymphomas accounted for 5.2% representing the 4th most common histologic type.

The presenting features depended on the primary site of the disease. At presentation, enlarged cervical lymphadenopathy was the predominant symptom accounting for 54%. This is similar to existing presentation patterns. Similarly, late presentation in this environment may have contributed to bulky diseases and extensive nodal involvement at presentation. This late presentation has also been identified in similar studies as most patients usually present in the hospital after failure of traditional and spiritual treatments. By the time they finally present in the hospital for care, the disease would have often progressed significantly to an advanced stage and sometimes with distant

metastasis which makes such tumours become almost unresectable. The stage of disease at the time of presentation varied among the patients. The majority presented with stage IV (48.5%) [18,19,30].

The manner of treatment of these patients with head and neck cancers varied, as the major influencing factors were the stage and location of the tumour; which is similar to what has been previously reported by Bernier *et al* [34] and other researchers [35,36]. Many tumours of the head and neck are not surgically accessible and, in some cases, where surgery may play a role, late presentation makes it unsuitable or cosmetic results are taken into consideration.

As a result, surgical treatment will be limited to biopsy alone. Radiotherapy is the main stay of treatment in most head and neck tumours. Chemotherapy can be used to down stage the disease in those with locally advanced disease and this can be used concurrently with radiotherapy. Combinations consisting of cisplatin, taxane and 5FU have given satisfactory results in previous studies. It has also been observed that chemoradiation has a better outcome and improves the rate of curability and survival of patients also depends on stage and treatment modalities and outcome [29,37,34]. In this study, patients with head and neck cancer who receive chemoradiation had the least number of recurrences and also had better overall survival (Table 5 and 6).

One major challenge of this study was follow up as many patients abandoned hospital treatment and follow up once they experienced slight improvement in symptoms. Other patients who were referred from far centres or location are lost when they decide to go to their referral centres due to proximity, thereby abandoning follow up.

Conclusion

From the findings of this study, head and neck cancers are commoner in males, and the commonest symptom is neck mass. The commonest type found was nasopharyngeal carcinoma with squamous cell carcinoma being the commonest histopathological type seen. Most patients presented late with advanced and metastatic disease. The advent of concurrent chemotherapy and radiotherapy has improved rate of curability and survival outcome. Despite the treatment options available, factors like, the grade of disease, histological type, age, presence of metastasis and the type of treatment and other comorbid factors, should be considered when treating patients.

Table 2. Pattern of presentation

Presentation	Frequency	%
Neck mass	93	37.5
Nasal blockage	58	1.6
Epistaxis	50	20.2
Hoarseness	20	8.1
Metastasis	20	8.1
Dysphagia	7	2.8
Total	268	100

Table :3. Histopathological types of head and neck cancers

Type	Freq	%
Squamous cell carcinoma		
SCC Moderately differentiated	82	20.2
SCC Well differentiated	70	17.2
SCC Poorly differentiated	65	16
Adenoid cystic	40	9.9
Mucoepidermoid	21	5.2
Undifferentiated	15	3.7
Adenocarcinoma	15	3.7
Non Hodgkins	12	3.0
Rhabdomyosarcoma	10	2.5
Hodgkins lymphoma	9	2.2
Lymphoepithelioma	8	2.0
Pleiomorphic adenoma	7	1.7
Anaplastic	6	1.4
Others	46	11.3
	406	100

Table: 4. surgical procedures and types of treatment modalities

	Frequency	%
<i>Surgical Procedures</i>		
Definitive surgery	107	26.4
Biopsy	299	73.6
<i>Types of Treatment Modalities</i>		
Radiotherapy alone	168	41.4
Chemoradiation	118	29.1
Radiotherapy before chemotherapy	46	11.3
Chemotherapy before radiotherapy	41	10.1
Chemotherapy alone	33	8.1
Total	406	100

Table: 5. Nature of response, recurrence and treatment outcomes

	Frequency	%
<i>Response</i>		
Complete response	256	63.1
Partial response	115	28.3
No response	35	8.6
<i>Recurrence after . . .</i>		
Radiotherapy alone	34	20.2 (34/168)
Chemotherapy alone	21	63.6 (21/33)
Chemo radiation	2	1.7 (2/118)
<i>Treatment Outcomes</i>		
On follow-up	136	33.5
Lost to follow-up	240	59.1
Dead	30	7.4

Table 6. Overall survival following individual treatment modalities

Periods			Radiotherapy	Chemoradiation	Chemotherapy
1 - 6 months	66	39.8%	23	38	5
7 - 12 months	51	30.7%	19	30	2
13 - 24 months	29	17.5%	10	18	1
25 - 36 months	11	6.6%	3	8	0
37 - 48 months	5	3%	2	3	0
49 - 60 months	4	2.4	2	2	0
	166	100%	59 (35.6%)	99 (59.6%)	8 (4.8%)

defaulted, 136 (33.5%) were on regular follow up at the clinic while 30 patients (7.4%) died.

The survival period following treatment in this study ranged from two weeks to five years. 66 (39.8%) survived for six months after treatment, 51 (30.7%) survived for seven to twelve months after treatment, 29 (17.5%) survived for thirteen to twenty-four months, 11 (6.6%) survived for twenty-five to thirty-six months, 5 (3%) survived for thirty-seven to forty-eight months while 4 (2.4%) survived for forty-nine to sixty months (Table 6).

Discussion

This study showed that most of the patients were within the age range of 40-49 and 50-59 years, which represents the 4th and 5th decades of life. This suggests that head and neck cancer is most common around the age of 50, a statistic that has been highlighted in similar studies from Lagos and Ilorin, Nigeria [3,7]. However, studies conducted in northern Nigeria showed that the peak incidence was in the 3rd and 4th decade [5,9,30] while in Ibadan

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This study has shown the pattern of presentation and treatment modalities employed in managing head and neck cancers in LUTH. Concurrent use of chemotherapy and radiotherapy in the management of head and neck cancers improves the treatment outcomes. For developing nations like Nigeria, more radiotherapy centres are needed to improve accessibility to treatment since most patients in this study had to travel far distances to get treatment. Also, there is need for more awareness of the importance or necessity of presenting to an orthodox medical practitioner immediately whenever any persistent mass or symptom is noticed in the head and neck region.

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