PATTERNS OF CERVICAL LYMPH NODE METASTASIS AMONG LARYNGEAL CANCER PATIENTS AT THE KENYATTA NATIONAL HOSPITAL, NAIROBI, KENYA

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ABSTRACT

Background: Cervical lymph node metastasis is common in laryngeal carcinoma and is the most important prognostic factor of the disease. In patients with histologically confirmed head and neck cancer including cancer of the larynx, the presence of an ipsilateral metastatic cervical node reduces the 5-year survival rate by 50%. Presence of bilateral metastatic cervical nodes reduces the 5-year survival rate further to 25%. Ideally, cervical lymph node metastasis is confirmed by Fine Needle Aspirate Cytology (FNAC), however, in routine clinical practise, evaluation by palpation of the nodes and a Contrast-enhanced CT scan of the neck is acceptable for decision making.
Objective: To determine the patterns of cervical lymph node metastasis among laryngeal cancer patients presenting for treatment at the Kenyatta National Hospital (KNH).
Design: A hospital based descriptive cross-sectional study.
Methods: Seventy nine patients with a pre-treatment histological diagnosis of laryngeal cancer were examined for presence and patterns of cervical lymphadenopathy. Data on their direct laryngoscopy examination findings was also collected. Primary and nodal disease stage was confirmed by a contrast-enhanced CT scan of the neck.
Results: Trans-glottic cancer was 81.0%, subglottic 10.1% and glottic 8.9%. N+ neck nodes status was 54.6% and N0 status 45.6%. T4 primary cancer and poor grade of differentiation on histology were significantly associated with N+ neck node status P=0.001 and P=0.010 respectively.
Conclusion: Locally advanced primary cancer and poor grade of histologic differentiation are significantly associated with N+ neck node status, while glottic primary is significantly associated with N0 status.

Key words: Cervical lymph nodes, Laryngeal cancer, Kenyatta National Hospital

INTRODUCTION

Cancer of the larynx is one of the commonest head and neck cancers in Kenya and globally[1]. Onyango *et. al.*[2,3] reported a prevalence of 39% of laryngeal cancer among patients with head and neck cancer while Sandabe *et. al*4] reported a prevalence of 20% of all head and neck cancers. It is predominantly a disease of the elderly male in their 7th decade of life with a male to female ratio varying from 5.2:1 to 24:1[2,4-7]. Among patients with head and neck cancer, lymph node metastasis is one of the most important prognostic factors. In patients with histologically proven head and neck cancer, including cancer of the larynx, the presence of an ipsilateral metastatic cervical node reduces the 5-year survival rate by 50%, whereas the presence of bilateral metastatic nodes reduces the 5-year survival further to 25%[8].

Advanced laryngeal cancer may involve multiple anatomic subsites but the disease progression is predictable based on the presence of natural barriers and pathways which may prevent or facilitate the spread of the cancer as depicted on Figure 1[9].

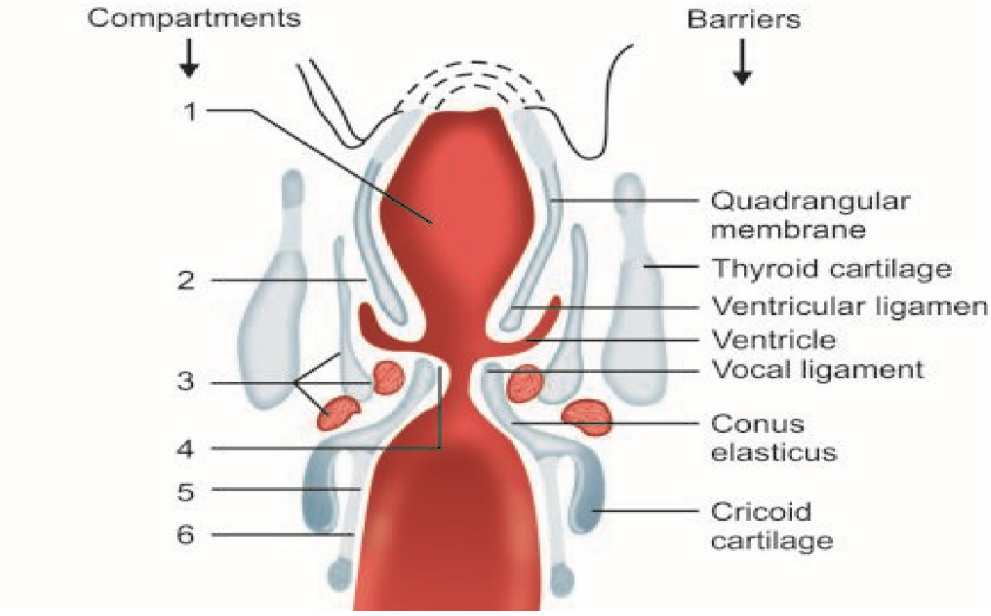

Figure 1: Coronal view of the larynx

Coronal view of the larynx demonstrating the natural barriers to spread of laryngeal tumours along with spaces through which tumours can spread. (i) Supraglottis, (ii) Portion of the pre- epiglottic space continuous with the PGS, (iii) PGS, (iv) Reinke's space, (v) Subglottis, (vi) Cricoid area[9].

Some of the natural barriers which limit the spread of laryngeal cancer include: the thyroid and cricoid cartilages, the hyoepiglottic ligament, the conus elasticus, the quadrangular membrane, the thyrohyoid membrane and the cricothyroid membrane[9].

There are also natural pathways within the larynx that facilitate the spread of laryngeal cancer within and without the larynx. The thyroepiglottic ligament and the anterior commissure provide minimal if any resistance to tumour spread thus allowing cancers of the anterior commissure to invade the thyroid cartilage due to a deficiency of the thyroid perichondrium at the insertion of the anterior commissure.

The pre-epiglottic and paraglottic spaces provide pathways of spread of laryngeal cancer within the laryngeal framework. Cancers that involve the infrahyoid epiglottis will almost always invade the pre-epiglottic space. Laterally, the pre-epiglottic space is continuous with the paraglottic space on either side providing a pathway for cancer to spread submucosally to involve the glottis and subglottis. Spread of cancer through the pre-epiglottic space also predisposes to cancer spread into the soft tissues of the neck via the superior laryngeal neurovasculature.

The paraglottic space binds the laryngeal ventricles bilaterally and its medial limit is the quadrangular membrane, the ventricles and the conus elasticus. Laterally, the paraglottic space is bound by the thyroid cartilages and the piriform sinus mucosa. Invasion of laryngeal cancer into the paraglottic space can lead to the spread of the cancer into the extra-laryngeal soft tissue and the thyroid gland by penetrating through the cricothyroid membrane[9,10].

Save for some little variations; the lymph fluid is drained along relatively predictable and constant lymph vessels into certain lymph node groups. This forms the basis for dividing lymph nodes in the head and neck region into groups. In the year 2002, The American Head and Neck Society committee neck dissection issued an updated classification which has aided and improved assessment of lymph nodes by regions and improved the nomenclature of selective neck dissection as summarized in Table 1[11].

Table 1: American Head and Neck Society (2002 Updates) classification of neck nodes

Level	Lymph node group	Boundaries of neck levels
IA	Submental	Between
IB	Submandibular	Between the boundaries of the anterior belly of the digastric muscle, the stylohypoid muscle and the mandible
II	Upper jugular	Includes nodes located around the upper third of the internaljugular vein and spinal accessory nerve.This extends from the skull base above to the inferior border of hyoid bone below.The anterior boundary is the stylohyoid muscle, and the posterior boundary is the posterior border of sternomastoid muscle
IIA		anterior to the vertical plane defined by thespinalac-cessory nerve
IIB		posterior to the vertical plane defined by the spinal accessory nerve
III	Middle jugular	Includes nodes located around the middle third of the internaljugular vein extending from the inferior border of the hyoid bone above to the inferior border of cricoid cartilage below. The anterior (medial) boundary is the lateral border of the sternohyoid muscle,and the posterior (lateral) boundary is the posterior border of sternocleidomastoid muscle
IV	Lower jugular	Includes nodes located around the lower third of internal jugular vein extending from the inferior border of the cricoid cartilage above to the clavicle below
V	Posterior triangle	Includes nodes located along the lower half of the spinal accessory nerve and the transverse cervical artery.The supraclavicular nodes are also included in the posterior triangle group. The superior boundary of this level is the apex formed by convergence of sternomastoid and trapezius muscles
VA		Above a horizontal plane marking the inferior border of the anterior cricoid
VB		Below a horizontalplane markingthe inferior border of the anterior cricoid
VI	Anterior compartiment	includes pre and paratrachealnodes,precricoid (Delphian node),and the perithyroidal nodes including the nodes along the recurrent laryngeal nerves.The superior boundary is the hyoid bone,the inferior boundary is the suprasternal notch. The lateral boundaries arethe common carotid arteries.

Every effort should be made to accurately evaluate and stage regional lymph nodes as they bear a great prognostic significance. While performing a pre-therapeutic evaluation for lymph node metastasis, clinical palpation remains the basic method applied [12]. Palpation criteria to consider a node metastatic include: a firm to hard consistency of the lymph node, size more than 10mm and fixation to underlying structures[12].

The sensitivity of exclusive inspection and palpation in detecting cervical lymph nodes ranges from 60% - 70%[12]. Application of CT scanning and MR Imaging is complementary with sensitivity ranging from 65% - 88% in literature[13].

Globally, the most significant procedure currently used to detect lymph node metastasis is B mode ultrasonography combined with ultrasound guided node aspiration cytology[13]. Based on a comparative meta-analysis, this modality has a sensitivity of 80% and a specificity of 98% and is superior to both CT scanning and MR imaging[13]. However, this technique is time consuming and suffers from wide inter-operator variability making its clinical use difficult. To forestall the difficulties associated with ultrasonography and ultrasound guided FNAC, CT scanning and MRI are more commonly used in pre-treatment staging of nodal disease.

Contrast-enhanced CT scanning of the neck has found wide and practical use in the radiological staging of both the primary cancer of the larynx and metastasis to regional cervical lymph nodes and even distant metastasis. CT scanning eliminates inter-operator variability which affects Ultrasound guided FNAC.

Contrast enhanced CT scans allow for characterization of the cervical nodes in detail. The CT scan criteria used to define a node as metastatic include: nodes with central necrosis regardless of size in the absence of clinical infection, heterogeneous density of the node, aggregation of lymph nodes, evidence of extra capsular spread as shown by irregular borders, presence of contrast material surrounding the node. Size criterion may vary from 10-15mm. Computed tomography has improved the accuracy of diagnosis of cervical metastasis. It has limitations of being expensive and has hazards of radiation exposure[13].

Pathologic or metastatic lymphadenopathy is radiologically defined as a node greater than 10mm in its transverse diameter or one that contains central necrosis[13,14]. Central nodal necrosis has been variously proven to be the most accurate marker of metastatic lymphadenopathy with up to 100% sensitivity and specificity on CT and ultrasound examination when compared against histological examination of the lymph nodes[15-17].

MATERIALS AND METHODS

The study was designed to determine the patterns of cervical lymph node metastasis among laryngeal cancer patients presenting for treatment at the Kenyatta National Hospital (KNH). The specific objectives were: to determine the distribution of sub-sites of the larynx from which primary cancer of the larynx arose, to determine the correlation between the sub-site(s) of origin of primary laryngeal cancer and level(s) of metastatic cervical nodes involved on CT scan, and to determine the correlation between the histological type and grade of the primary cancer of the larynx with the metastatic cervical nodes detected on CT scan.

The study was carried out at the ENT and Radiology Departments between October 2018 and June 2019. Seventy-nine patients were recruited by consecutive sampling. The inclusion criteria included patients with confirmed laryngeal carcinoma on histology, had radiological imaging, and gave written consent to participate. Neck node status was determined by clinical palpation and confirmed by contrast-enhanced CT scan of the neck. The exclusion criteria were patients who did not have a histological confirmation of laryngeal carcinoma, patients who had undergone any form of treatment whether curative or palliative for the disease, and patients who declined to give a written consent.

The sample size was determined using Fisher's formula with finite population correction taking an estimate of 60.0% as expected proportion of patients with cervical node metastases in laryngeal cancer patients[14].

Approval to conduct the study was obtained from the Kenyatta National Hospital/University of Nairobi Ethics and Research Committee.

The principal investigator did a complete ENT examination on all the study subjects. All direct laryngoscopy examinations were either done by the principal investigator or fellow ENT surgery residents in the department who completed a standard reporting form provided by the principal investigator. All the patients had a contrast-enhanced CT scan of the neck done and reported within 6 weeks. All the CT scans were reported by one consultant radiologist at the hospital for consistency.

The incidence of cervical lymph node metastasis was determined by calculating the proportion of laryngeal cancer patients in the sample with confirmed metastatic node involvement on CT scan of the neck. Frequencies and percentage showing Nodal (N) staging of cancer of larynx were also calculated. The Chi squared and Fisher's exact tests were used to determine the association between the primary tumour sub-site and level(s) of cervical nodes involved, and in determining the association between the histologic grade of cancer and radiological N stage of the disease. All analyses were performed with Statistical Package for Social Sciences (SPSS) version 22, and P-values of <0.05 were considered statistically significant.

RESULTS

Males constituted 98.7% of the patients with females accounting for 1.3%. Most of the patients were in the 7th decade of life accounting for 45.6% (Table 1).

Table 2: Demographic characteristics of the study patients

Characteristic	No.	(%)
Age (years)		
31 – 40	1	1.3
41 – 50	11	13.9
51 – 60	17	21.5
61 – 70	36	45.6
71 – 80	8	10.1
81 – 90	6	7.6
Sex		
Male	78	98.7
Female	1	1.3

The examination and imaging findings are displayed in Figure 2.

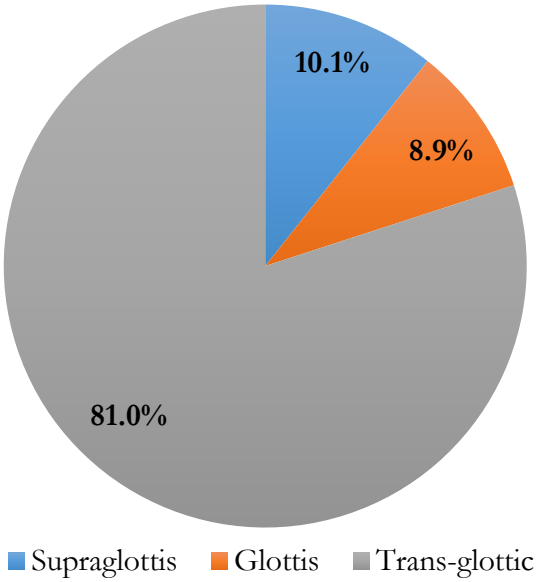

Figure 2: Percentage distribution of laryngeal cancer by subsites

Multiple subsite involvement was predominant with both clinically and radiologically trans-glottic cancers accounting for 81.0% of all the patients.

Table 3: Overall clinical and radiological nodal stage of the patients

Stage	No.	(%)
N0	36	45.6
N1	9	11.4
N2a	5	6.3
N2b	8	10.1
N2c	13	16.5
N3	8	10.1

Overall, 36 patients had no cervical nodes detected either on clinical examination or on CT scan, thus, patients with N0 nodal status accounted for 45.6% of the patients. Forty-three patients had cervical nodes detected either clinically or on imaging, thus, patients with N+ nodal status accounted for 54.4% (Table 3).

Table 4: Association of laryngeal subsite of primary cancer and the cervical nodal status

Subsite	Total	N+	N0	P-value
Supraglottic	8 (10.1)	6 (14.0)	2 (5.6)	0.280
Glottic	7 (8.9)	0 (0.0)	7 (19.4)	**0.003**
Clinical Transglottic	60 (75.9)	33 (76.7)	27 (75.0)	0.857
Transglottic with subglottic extension	4 (5.1)	4 (9.3)	0 (0.0)	0.121

All the patients with the glottis as the origin of their primary cancer had an N0 neck and the difference observed in this subsite was statistically significant (p=0.003) (Table 4).

Table 5: Subsite of primary cancer versus the level of cervical nodes detected

Cervical node group(s) & Cancer subsites	Total	II	II, III	II, III, IV	III	III, IV	IV	P-value
Supraglottic	6	4	0	1	1	0	0	0.179
Clinical Transglottic	33	4	9	5	10	2	3	0.067
Radiological Transglottic	4	2	1	1	0	0	0	0.688
Total for node groups	43	10	10	7	11	2	3	-
Percentage	100.0	23.3	23.3	16.3	25.6	4.6	6.9	0.204

For Patients with N+ cervical nodal status, all the nodes were detected at levels II, III, and IV. On testing for the association between the sub-site of origin of the primary cancer of the larynx and the predilection to any specific levels of cervical nodal groups, the differences noted were not statistically significant, with p-values of 0.179, 0.067 and 0.688 for supraglottic as well as clinical and radiological trans-glottic cancers respectively. There was no significant differences for the combination of patterns of nodal level distribution (p=0.204). In this study there was no involvement of level I, V, or VI cervical nodes detected.

Table 6: Association between laryngeal primary site and laterality of neck nodes

Subsite of primary cancer	Total	Ipsilateral	Bilateral	P-value
Supraglottic	6	4	2	0.699
Clinical transglottic	33	17	16	0.728
Radiological transglottic	4	2	2	1.000

Among patients studied with N+ neck node status, 53.5% had ipsilateral lymphadenopathy while 46.5% had bilateral cervical lymphadenopathy. Zero percent had contralateral cervical lymphadenopathy. There was no significant association between the subsite of primary laryngeal cancer to either a predilection to ipsilateral or bilateral cervical lymphadenopathy. However, the finding that as high as 46.5% of patients who had N+ neck nodes status had bilateral cervical lymphadenopathy is clinically significant in the care of these patients.

Table 7: Overall clinical and radiological T stage of primary laryngeal cancer

Stage	No.	(%)
T1	5	6.3
T2	2	2.5
T3	30	38.0
T4a	36	45.6
T4b	6	7.6

In the study, 53.2% of patients presented with T4 primary laryngeal cancer. Patients with locally advanced primary disease at T3 and T4 accounted for 91.2% of all patients in the study.

Table 8: Association between primary stage of laryngeal cancer and neck node status

	Total	N+	N0	P-value
T1	5 (6.3)	1 (2.3)	4 (11.1)	0.110
T2	2 (2.5)	0 (0.0)	2 (5.6)	0.117
T3	30 (38.0)	12 (27.9)	18 (50.0)	0.044
T4	42 (53.2)	30 (69.8)	12 (33.3)	0.001

T4 primary laryngeal cancer accounted for 69.8% of all N+ neck disease and 33.3% of N0 neck disease (p=0.001). T3 primary laryngeal cancer accounted for 27.9% of all patients with N+ neck disease and 50.0% of all the patients with N0 neck disease (p=0.044) (Table 8).

Table 9: The T stage of primary cancer versus cervical nodal stage

T stage of primary cancer	Total	N1 (%)	N2/N3 (%)	P-value
T1	1	1(11.1)	0 (0)	0.209
T3	12	5(55.5)	7(20.6)	0.088
T4	30	3(33.3)	27(79.4)	0.014

Patients with T4 primary laryngeal cancer constituted 79.4% of those who presented with advanced cervical lymph node metastasis N2/N3 nodal stage and 33.3% of those with early cervical lymph node metastasis N1 nodal stage (p=0.014) (Table 9). Advanced primary laryngeal cancer at stage T4 is significantly associated with advanced cervical lymph node metastasis of the disease (Table 10).

Table 10: Grade of differentiation of primary cancer

Grade of cancer differentiation	No.	(%)
Grade 1: Well differentiated SCC	24	30.4
Grade 2: Moderately differentiated SCC	41	51.9
Grade 3: Poorly differentiated SCC	14	17.7

All patients in this study (100.0%) had squamous cell carcinoma of the larynx. There were 51.9% who had moderately differentiated grade, 30.4% with well differentiated, and 17.7% who had the poorly differentiated grade. There was no patient with grade 4 (undifferentiated) laryngeal carcinoma (Table 11).

Table 11: Association between grade of differentiation of primary cancer and nodal status

	Total	N+	N0	P-value
Grade 1: Well differentiated	24 (30.4)	14 (32.6)	10 (27.8)	0.645
Grade 2: Moderately differentiated	41 (51.9)	17 (39.5)	24 (66.7)	0.016
Grade 3: Poorly differentiated	14 (17.7)	12 (27.9)	2 (5.6)	0.010

Patients with a poorly differentiated squamous cell carcinoma of the larynx accounted for 27.9% of all the N+ cervical nodal status and 5.6% of all the N0 cervical nodal status (p=0.010), while those with moderately differentiated squamous cell carcinoma of the larynx accounted for 39.5% of the N+ cervical nodal status and 66.7% of the N0 cervical nodal status (p=0.016). Those patients with well differentiated carcinoma of the larynx accounted for 32.6% of the N+ cervical nodal status and 27.8% of the N0 cervical nodal status (Table 11).

Table 12: Grade of differentiation versus cervical nodal stage

Grade & Nodal stage	Total	N1	N2/N3	P-value
Grade 1: Well differentiated	14	1	13	0.045
Grade 2: Moderately differentiated	17	7	10	
Grade 3: Poorly differentiated	12	1	11	

Among the patients with N+ neck node status, 9 (20.9%) had early nodal/ regional disease N1, while 34 (79.1%) had late/ advanced nodal disease N2/ N3. Overall, when this observation was tested against the grade of differentiation of primary laryngeal carcinoma, it was statistically significant (p= 0.045) (Table 12). Thus, a worsening grade of histology of primary laryngeal cancer may be a significant predictor of a more advanced cervical nodal diseases.

DISCUSSION

Cancer of the larynx is the most common head and neck cancer whose incidence ranges from 20% to 40%[2,4]. It predominantly affects the male gender with the male to female ratio varying from 5.2:1 to 24:1, and the peak age is in the 7th decade of life[2,4,5]. This heavy male preponderance is comparable to studies elsewhere since males tend to consume more alcohol and smoke cigarettes more than females as was found also in a Kenyan survey[6]. In the survey, 2% of women used tobacco in its various forms, whereas 1% smoked cigarettes which may explain the low prevalence of laryngeal squamous cell carcinoma in the females. Studies in other centres have shown up to 100% prevalence of laryngeal squamous cell carcinoma among males[7].

In this study, 81.0% of the patients had multisite primary laryngeal cancer being trans-glottic in origin, 10.1% had isolated supra-glottic carcinoma and 8.9% isolated glottic cancer. Overall, subglottic cancer was observed in 4 out of the 79 patients (5.06%), however, this sub-site was not involved in isolation, but as part of the trans-glottic malignancies of which it constituted 6.3%. The finding differs slightly with those in the study by Sandabe *et al*[4] who reported the sub-site distribution as 43% trans-glottic, 37.6% supra-glottic, 9.7% glottic and 9.7% sub-glottic in the sub Saharan Africa population. This difference may be explained by the fact that the patients in our study presented late and thus a clear delineation of the exact sub-site of origin of primary cancer was difficult.

The sub-site of origin of the primary laryngeal cancer has also been postulated to have an association with the cervical nodal status of the patients. In this study, patients with isolated supra-glottic carcinoma of the larynx were 10.1% while isolated glottic carcinoma patients made up 8.9% of all the patients. An overwhelming majority had laryngeal cancer of trans-glottic origin indicating that multisite involvement of the primary carcinoma is more common. Isolated cancer of the subglottic larynx was not observed.

Trans-glottic cancer of the larynx (multisite) was associated with a 76.6% detectable cervical nodal metastatic rate. This compares with the results in the studies by *Ahsan et al*[18] and Kirchner[19] who reported 72% and 65% incidence of detectable cervical nodal metastasis respectively. Isolated carcinoma of the sub-glottis was not observed in this population; however, 4 patients out of 64 with trans-glottic laryngeal cancer had sub-glottic involvement of the primary cancer. All patients who had sub-glottic extension of the primary laryngeal cancer also had positive neck node metastasis, thus 9.3% of all N+ patients were patients with sub-glottic extension of laryngeal cancer. This finding differs with the findings by Ahsan *et al*[18] and Kirchner[19] who both reported 0% incidence of neck node metastasis in sub-glottic laryngeal cancer. The methodology in this study and that of both Ahsan *et al*[18] and Kirchner[19] were similar and, therefore, the difference in the findings may warrant further research involving a larger population of patients.

In this study, carcinoma of the glottis was significantly associated with lack of cervical nodal metastasis (N0 nodal status), p=0.003. This finding significantly differs with those of Ahsan *et al*[18] who found 30% N+ neck node status and Kirchner[19] who found a 25% N+ neck node status. The methodology of this study was comparable to that by Ahsan *et al*[18] and Kirchner[19] and therefore, the marked difference may be explained by racial and regional variation in the populations that may need to be investigated in a larger study.

The stage of primary laryngeal cancer (T stage) has also been postulated to be associated with presence or absence of cervical lymph node metastasis. In this study, 6.3% of patients presented with stage T1 disease, 2.5% with stage T2 disease, 38.0% stage T3 disease and 53.2% stage T4 disease. This compares with the findings of the studies by Luca *et al*[20] and Wenyue *et al*[21] especially for T1, T3 and T4 stages. However, in this study, stage T2 patients only accounted for 2.5% of

the patients which was significantly much lower than the 31% -60% reported by Luca *et al*[20] and Wenyue *et al*[21], this difference may be due to a subjective definition for T2 laryngeal cancer which leads to lack of uniformity in staging.

It was also observed in this study that T3 laryngeal cancer accounted for 27.9% of all patients with N+ cervical nodal status while T4 laryngeal cancer accounted for 69.8% of N+ cervical nodal status. Both T3 and T4 primary laryngeal cancer were significantly associated with presence of cervical lymph node metastasis (p=0.044 and 0.001 respectively). This observation compares with those by Wenyue[21] who documented 38.0% N+ status for T3 and 25% N+ status for T4 laryngeal cancer. Nevertheless, these findings are much lower than the metastatic rates reported by Ahsan[18] at T1 14.3%, T2 41.2%, T3 81.8% and T4 100%. Attempts have also been made to establish the association between the sub-site of origin of primary laryngeal cancer and the level(s) of metastatic cervical nodes. In this study, only levels II, III and IV were detected to have metastatic disease. However, when statistical test of association was done, this association between sub-site of origin of laryngeal primary cancer and the levels of cervical neck node metastasis was insignificant. In spite of this, the observation is still comparable to the findings by Ahsan *et al*[18], Akhter *et al*[22] and Luca *et al*[20] who all demonstrated a predilection of levels II, III and IV cervical nodes to be the ones involved in loco-regional metastasis of laryngeal cancer.

All the patients in this study (100%) had squamous cell carcinoma of the larynx. This finding is in keeping with multiple studies that have found that squamous cell carcinoma constitutes over 95% of all head and neck cancer histology including cancer of the larynx[22]. The study has also demonstrated a statistically significant association between poorly differentiated histology of the primary cancer with the presence of cervical neck node metastasis. There has also been a statistically significant association demonstrated for the moderately differentiated squamous cell carcinoma histology. Though, this study was a cross-sectional descriptive hospital-based study, its findings are comparable to several other retrospective studies[23-25] which also found some association. Kowlasky *et al*[24] for example in his study demonstrated an Odds Ratio of 4 showing that grade 3 (poorly differentiated) laryngeal cancers were four times more likely to manifest with cervical nodal metastasis which is both clinically detectable as well as occult than grade 1 (well differentiated) cancer.

CONCLUSIONS

(i) Laryngeal cancer patients presenting at the Kenyatta National Hospital predominantly have trans-glottic primary disease.
(ii) A majority of these patients present with T4 primary laryngeal cancer and the advanced primary disease is significantly associated with presence of detectable cervical lymph node metastasis.
(iii) Grade 3 poorly differentiated laryngeal squamous cell carcinoma is significantly associated with presence of detectable cervical lymph node metastasis.
(iv) Glottic laryngeal cancer is significantly associated with N0 neck node status.
(v) For patients with N+ neck node status, advanced grade of differentiation of primary laryngeal cancer is associated with more advanced cervical nodal disease N2/ N3.
(vi) For N+ neck node status, levels II, III and IV neck nodes were detected to be the sites of cervical metastasis, however, there is no significant association between the sub-site of primary laryngeal cancer to metastasis to any cervical lymph node level or groups of node levels.

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