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PHARYNGO-CUTANEOUS FISTULA POST TOTAL-LARYNGECTOMY: A LOCAL EXPERIENCE

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ABSTRACT

Background: Pharyngo-cutaneous fistula is a major complication of total laryngectomy. Despite its significant impact on thepatients' nutrition and management outcome, there is lack of consensus forrecognising high-risk patients andfactors associated with fistula formation.Hence, this study was aimed at determining the incidence ofpharyngo-cutaneous fistula and factors associated with fistula formation.
Methods: A retrospective collection of data on all cases of laryngeal cancer diagnosed histologically and had total laryngectomy, in the Otorhinolaryngology Department of a tertiary centre in Southwestern, Nigeria, from 2007 – 2016. The data collected includeage, gender, tumour stage, tracheostomy, adjuvant therapyextent of laryngectomy procedure and factors for pharyngocutaneous fistula.
Results: Forty-two patients had total laryngectomy, male to female ratio was 7.4:1 andmean age was 52.3 ± 2.1 years. All patients had pathological diagnosis of stage 3 (83.3%) and stage 4 (16.7%) laryngeal cancer, respectively. The incidence of pharyngo-cutaneous fistula was11.9% and the factors related to fistula formation were prior radiotherapy treatment and diabetes. Age, gender, neck dissection procedures, site of primary tumor and emergency tracheostomy did not contribute to fistula formation. Spontaneous fistula closure was achieved in all cases except one patient who had surgical closure.
Conclusion: Pharyngo-cutaneous fistula formation post-surgery is related to the presence of co-morbidities. The high percentage of spontaneous closure underscores the need for a conservative management approach.
Keywords: Laryngeal Cancer, Laryngectomy, Neck dissection, Pharyngo-cutaneous fistula, Post-surgery, Radiotherapy.

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INTRODUCTION

Post laryngectomy pharyngo-cutaneous fistula is an abnormal connection between the skin and pharyngeal mucosa, with leakage of oral feeds and saliva due to dehiscence of the pharyngeal repair.[1] it is associated with surrounding tissue necrosis. The fistulas can also occur higher in the neck, at the level of the junction between the pharyngeal mucosa and the base of the tongue. The leakage of saliva into the surrounding tissue results in infection and micro-venous thrombosis with tissue necrosis, partly due to impaired wound healing as a result of micro-angiopathy, and poor immune response.[2]Pharyngo-cutaneous fistula could be a debilitating condition that may significantly increase the morbidity and mortality of the patient.[3]

The incidence of pharyngo-cutaneous fistula after total laryngectomy ranges from 3% to 65%, with an average time of appearance of 10 days after surgery.[3,4]Identified factors contributing to the wide disparity in the prevalence of pharyngo-cutaneous fistula include the use of radiation in organ preservation.[4, 5]Radiation therapy reduces blood supply and causes tissue fibrosis; in addition, it impairs leukocytesmigration and hinders wound healing. Deficiencies of vitamins and micronutrients in patients with head and neck cancers could also be responsible for the development of pharyngocutaneous fistula due to poor wound healing.[6]The variation in the fistulae rate seen in different studies may be due to the differencesin the tumour stage and extent of pharyngeal resection at surgery.[7]Despitethe description of a large number of factors associated with the development of pharyngo-cutaneous fistula no set of factors is consistently significant.[8,9]

Diagnosis of pharyngo-cutaneous fistula is exclusively clinical, though the occurrence of fever in the first postoperative day is significant predictor for pharyngo-cutaneous fistula development.[10] Pharyngo-cutaneous fistula can be diagnosed by dye test (methylene-blue) or by observing a salivary leak in the neck.Other clinical

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methods of early diagnosis includes - skin flap oedema, neck erythema[3], sinus tract on barium swallow study[5],fever (101.5° F) in the first 48 hours post operatively[10] and an elevated wound amylase concentration.[11]

Pharyngo-cutaneous fistula is associated with increased morbidity, prolonged hospital admission, increased health care costs, delay of oral feeding, delay in initiating radiotherapy and voice rehabilitation with subsequent hindrance of the adjunct postoperative care.[12,13]The impact of pharyngo-cutaneous fistula underscores the importance of identifying factors associated with pharyngo-cutaneous fistula formation. Moreover, complicated pharyngo-cutaneous fistula has significant impact on the patients' quality of life, and could escalate to pharyngeal stenosis, dysphagia, carotid artery rupture, sepsis, mediastinitis, pneumonia and even death. Conservative management of small fistula results in spontaneous closure without sequelae; however, there is significant reduction in pharyngeal dimensions in large fistula which may necessitate a reconstruction surgery with local or free flaps. We conducted an audit of total laryngectomy procedures in our hospital to determine the factors associated with pharyngo-cutaneous fistula formation in other to improve the care of patients with laryngeal carcinoma.**Patients and Methods:** This is a retrospective study using the hospital records of patients with laryngeal carcinoma and who had total laryngectomy between January 2007 and December 2016, in the Department of Otorhinolaryngology, University College Hospital, Ibadan. Hospital admission records, case notes and operative theatre records were retrieved.Data extracted were demographic indices, smoking and alcohol consumption, medical history, tumour stage, laboratory investigations, details of surgical procedure and post-operative care. A pharyngo-cutaneous fistula was defined as wound dehiscence resulting in a fistula, and it was diagnosed clinically in this study using methylene-blue dye test or by observation of a salivary leak in the neck. The laryngeal cancer staging was done using the International Union Against Cancer (UICC) TNM classification system.[14] The participant's socioeconomic status was assessed by their occupation, while the last job was used to assess the economic status of those that had retired.[15]Statistical analysis was performed using IBM- SPSS 20, continuous variables were analyzed with t-test and categorical variables were analyzed with Fisher's exact test, with level of significance set at p =0.05 t 95% confidence interval.

RESULTS: Forty-two patients had total laryngectomy during the study period, the male to female ratio was 7.4:1 (Table 1). The patients' age ranged from 36 years to 77 years, mean age was 56.9 ± 11.8 years. The incidence of pharyngo-cutaneous fistula in this study was 11.9%. Fistula development occurred between day 6 and day 10 post-surgery(mean:6.8day±1.7).

All the patients had histological diagnosis of squamous cell carcinoma laryngeal tumor and had similar preoperative/ and postoperative care. The duration of laryngeal symptoms prior to hospital presentation ranged from 3months to 3 years. (Median: 6months).

Twenty-six (61.9%) patients had emergency tracheostomy prior to total laryngectomy, of which 2(7.7%)had pharyngocutaneous fistula. The interval between tracheostomy and total laryngectomy varied between 20 days and 8 months. Medical-comorbid conditions like hypertension 5 (11.9%), diabetes mellitus 3(7.1%), chronic obstructive pulmonary disease 1(2.3%) occurred in the patients. The primary tumor was supra-glottic in 5 patients (11.9%), glottic in 19 (45.2%), trans-glottic in 16 (38.1%), and pharyngo-laryngeal in 2 (4.8%). The disease was stage 3 in 35(83.3%) and stage 4 in 7(16.7%), as shown in table 1.

Thirty-nine (92.9%) patients had total laryngectomy as the primary treatment for the laryngeal cancer, while 3(7.1%) patients had received radiotherapy prior to total laryngectomy.

The surgeries were performed by 5different surgeons with similar experience, and their operative techniques were consistent. The pharyngoesophageal repair was in 2 layers. The first layer was closed continuouslywith Vicryl suture and the second layer was closed interruptedly with vicryl suture. The patients were fed via nasogastric tube feeding 24 to 48 hours post-surgery, while oral feeding was initiated on post-surgery day 5 to 10 after a negative dye test.

The integrity of the pharyngeal repairs was tested using a dye test (methylene blue) at the time of surgery in 13(31.0%) patients, and in case of dye leak the affected mucosal area were re-apposed to prevent a leak, this method was used by one of the surgeons to prevent pharyngocutaneous fistula.

Chemo-radiation therapy was received by 3out of 42 patients, in a period ranging from 8 months to 3 years before total laryngectomy, among which 1 developed pharyngocutaneous fistula. The other patients with pharyngo-cutaneous fistula had pharyngeal extension of the laryngeal cancer and diabetes, respectively.

The fistulas were managed conservatively in 4(9.5%) patients, and 1(2.4%) patient had surgical closure by using pectoralis major myocutaneous flap.There was no association between pharyngo-cutaneous fistula and age (p = 0.23) or gender (p = 0.24), pre-laryngectomy tracheostomy (p = 0.29), the surgeons that perform the surgery (p = 0.19)and time of post-operative feeding (p = 0.24),but it was associated with low socioeconomic status (p = 0. 02). As shown in table 2.

DISCUSSION

The male predominance in this study was similar to earlier reports that laryngeal tumour is prevalent among men.[16,17]All the patients had histological diagnosis of squamous cell carcinoma, buttressing reports of high prevalence of squamous cell carcinoma of the larynx in sub-Saharan Africa.[17] The mean age of the patients in this study is similar to the reported mean age of patients with laryngeal tumour in Nigeria.[18]

The incidence of pharyngo-cutaneous fistula (11.9%) in this study falls within the range of 5.2% to 14% reported in previous studies[3,17,19,20],but lower than 65% reported by Bresson et al.[21] The wide variation in the prevalence of pharyngo-cutaneous fistula may be due to prior radiotherapy with aim of organ preservation seen in patient populations who presents early to the hospital but who subsequently had failed treatment and thus required surgery.[3,22]Virtaniemi et al. reported low incidence of pharyngo-cutaneous fistula in patients who had

laryngectomy without prior adjunct radiotherapy.[3]

Advanced tumour stages seen in this study were due to delay in hospital presentation, and are similar to previous reports from sub-Saharan Africa.[16,18]However, there was no association between the advanced disease and occurrence of pharyngo-cutaneous fistula in this study, corroborating observations that rate of fistula formation does not increase with advancing tumor stage.[3,23]The prevalence of pre-laryngectomy tracheostomywas high in this study, this was probably related to late hospital presentation,similar to other local report from sub Saharan Africa.[16,17,24] Though pre-laryngectomy tracheostomy was associated with pharyngo-cutaneous fistulae in some studies, probably due to tumour seedling in advanced lesions.[7] However, our experience was similar to other authors who did not observe an association between occurrence of tracheostomy and the duration of tracheostomy before total laryngectomy with the development pharyngo-cutaneous fistula.[3]

There were no significant differences between the surgeon's ability (evaluated on the basis of postgraduate training experience and surgical technique of determining the integrity of pharyngeal repair using dye test) and occurrence of pharyngo-cutaneous fistula in this study thoughsurgical experience is an important determinant factor in fistula formation.[25] The pharyngeal repair in this study was a vertical line repair; this type of repair is associatedwith low pharyngo-cutaneous fistula formation[26] andmay contribute to the low fistula incidence in this study. Conversely the "T" or "Y"-shaped pharyngeal closure is potentially weak at the three-point junction, and this is associated with fistula formation.[27,28] Suture materials used in pharyngeal repair contributes to the wound healing process and could potentially influence pharyngo-cutaneous fistula formation. Vicryl suture used in the surgical procedures in this study is strong, stimulates less inflammatory response, and has a long half-life, these properties will likely reduce the incidence of pharyngo-cutaneous fistula.[29,30]The extent of surgery (standard laryngectomy ± neck dissection) did not have any relationship with pharyngocutaneous formation, though combining neck dissection with total laryngectomy has been associated with development of pharyngo-cutaneous fistula.[7]Advanced laryngeal tumour may lead to extensive resection of the pharyngeal mucosa, this may lead to pharyngeal closure under tension, and subsequent wound break down with fistula formation.[3,31,32] Antibiotic prophylaxis against anaerobes and gastroesophageal reflux prophylaxis postoperatively are associated with reduced incidence of fistula formation.[3,33,34]This regimen is standard practice in our hospital and may have contributed to the low pharyngo-cutaneous fistulas incidence seen.The presence of concomitant medical diseases such as diabetes, radiationtherapy of= 30Gray's and above, prior to laryngectomy or an interval less than 3months between radiation and subsequent laryngectomy is associated with fistula formation.[2,3] Although, pharyngo-cutaneous fistula observed in the patients with diabetes, post-radiation therapy and advanced laryngeal tumours in this study were not statistically significant.

The factors for pharyngo-cutaneous fistula formation remain unclear.[35]After accounting for tumour and patients' factor, the extent of surgery and malnutrition, no factor significantly influenced the occurrence of postoperative fistulae in this study except patients with low socioeconomic status who had higher incidence of fistula formation. This is similar to other studies whereby there was lack of significant association between pharyngo-cutaneous fistula formation and defined factors.[19,31]Theassociation of fistula with low socioeconomic factor may be due to poor hygiene and malnutrition, but this is beyond the scope of this study.

Conclusion: our records showed thatpharyngo-cutaneous fistula formation does not significantly associated with tumour staging or extent of surgery, however prior radiotherapy treatment, diabetes and low socioeconomic status predisposes to fistula formation. Our experience established that most fistulascan be successfully managed with conservative care.

Table1:Demographicandclinicalfeaturesofthepatientsthathadtotallaryngectomy

Factors		Pharyngo-cutaneous fistula	
		No n = (88.1%)	Yes n = 5 (11.9%)
Age	Mean age (years)	...	58.1±3.0
Sex	Male	32(76.1%)	5(11.9%)
	Female	5 (11.9%)	0(0%)
Socioeconomic status	Low	29(69%)	4(9.5%)
	Middle	6(14.2%)	1(2.3%)
	High	2(4.6%)	0(0%)
Histology	Poorly differentiated	4(9.5%)	2(4.6%)
	Moderately differentiated squamous carcinoma	1(2.3%)	0(0%)
	Well differentiated squamous carcinoma	32(76.2%)	3(9.5%)
Radiotherapy prior to laryngectomy	No	35(3.3%)	4(9.5%)
	Yes	2(4.6%)	1(2.3%)
Concurrent neck dissection	Nil	22(52.3%)	4(9.5%)
	Functional	1(2.3%)	0(0%)
	Modified	19(45.3%)	1(2.3%)
Site of tumour	Supraglottic	5(11.9%)	0(0%)
	Glottis	18(42.7%)	1(2.3%)
	Subglottic	0(0%)	0(0%)
	Transglottic	12(28.5%)	4(9.5%)
	Pharyngo-larynx	2(4.6%)	0(0%)
Diabetes	Yes	3(7.1%)	1(2.3%)
	No	34(81.0%)	4(9.5%)
Tumour staging	T3	35(83.3%)	4(9.5%)
	T4	7(16.7%)	1(2.3%)
Type of laryngectomy	Standard	36(85.7%)	4(9.5%)
	Extended	1(2.3%)	1(2.3%)

Table2:Factors responsible for pharyngo cutaneous fistula formation

Factors	p- value(s)
Age	0.23
Gender	0.24
Low Socioeconomic Status	0.02
Tumour staging	0.98
Diabetes	0.40
Pre-laryngectomy tracheostomy	0.29
Time of post-operativecommencement of feeding	0.24
Surgeon's expertise	0.19

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