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Clinicopathological analysis of 33 cases of laryngeal carcinoma with their response to COVID19 virus

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Background: laryngeal carcinoma is a common cancer of the head and neck region. Lifestyle, signs and symptoms, including those of COVID-19, clinical and histological features of the lesions were highlighted in this study to increase the understanding of this fatal cancer, which will decrease the high morbidity and mortality rates associated with it. **Methods:** This study was conducted at the Department of Otorhinolaryngology, 33 cases of laryngeal cancer presented from January 2017 to July 2019 were included in this study. **Results:** the leading age group of subjects was 51-60 years. Smoking was a significant risk factor in 100% of cases. Most of the patients presented with hoarseness of voice followed by dysphagia. The glottic area was the commonest site (72.7%) for laryngeal cancer and squamous cell carcinoma seen in 100% of patients. Most of the cases showed a well-differentiated tumour with 39.9% of patients and presented in stage I (42.4%). Only a few cases (9%) had cervical lymph node metastasis at the time of presentation. And only four patients developed COVID-19 infection post laryngectomy, their symptoms were mild upper respiratory tract infection, and their chest x-rays were clear. All of them healed without any severe complication of CVOID-19. **Conclusions:** Early detection of laryngeal cancer is associated with a good prognosis. This early detection is based on good history, clinical examination, and invasive and non-invasive investigation. Post laryngectomy care may play an essential role in protecting the patient from serious complications of COVID-19 infection.

Keywords: COVID-19, Laryngeal carcinoma, Smoking

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Background

Laryngeal carcinoma is one of the most common head and neck cancer [1], with a high rate of morbidity and mortality worldwide [2]. The main risk factors associated with laryngeal carcinoma are smoking and alcoholism [3-4-5]. Many literatures connected the chronic use of tobacco, either smoking, chewing tobacco or snuff, with increased risk of laryngeal malignancy. Many previous studies showed that this risk is many times higher in individuals who smoke and drink alcohol simultaneously [5]. Furthermore, the association between alcoholism and smoking with laryngeal carcinoma is proved by the significantly low rate of laryngeal cancer in females due to the low rate of smoking and drinking of alcohol [6]. Other risk factors include age above 60s, specific inherited syndromes, such as Fanconi anemia, exposure to certain toxins and chemicals, include silica dust [7], asbestos and therapeutic radiation [3-4-5-6-7-8-9] and viral infections (especially Human papillomavirus (HPV) [10-11]. More than 90% of laryngeal carcinomas are conventional squamous cell tumours with rare cases of adenocarcinomas that arise from the mucous glands of the larynx [12]. The prognosis for small laryngeal growth, which is not associated with lymph node metastasis, is usually very good with high cure rates.

In contrast, an advanced disease with lymph node metastasis has a poor prognosis. In general, the survival rates depend on the tumour location (whether supraglottic, glottic or subglottic), the size of the lesion, the histopathological type, the grading of the tumour, the presence of metastasis and, to a large extent, a good management plan [13]. The novel COVID-19 pandemic nowadays is associated with variable clinical manifestations, and the effects of the virus on laryngectomy patients is still underdetermination. This study aims to highlight the factors that affect the prognosis of laryngeal carcinoma to increase the understanding of this fatal tumour to prolong the life of the patient and improve its quality.

Methods

A prospective study was performed on 33 cases of laryngeal cancer at the department of otorhinolaryngology, Head and Neck Surgery. All cases of laryngeal cancer presented from January 2017 to July 2019 were included in this study. A detailed clinical history was taken, mainly emphasizing main symptoms, exposure to a toxin, and recent history of smoking and alcohol. The careful general examination followed by an examination of the ear, nose, nasopharynx, oral cavity, and oropharynx was done. Routine investigations, including soft tissue x-ray of neck and chest x-ray and indirect mirror examination, were done in all patients. CT scan of the larynx was routinely done in all cases. Direct laryngoscopy with tissue biopsy (for diagnosis and grading) was also done for all subjects. FNAC confirmed metastasis in patients with cervical lymph node swelling. All tumours were classified according to the TNM staging system. During the follow-up, all cases were tested for CVOID-19 several times, even in the absence of any symptoms.

Statistical analysis: The obtained data were statistically analyzed and were demonstrated as numbers and percentages using statistical graphs.

Ethical Approval and consent to participate: The Ethics Board of Scientific Research accepted this study, and it was conducted following the Helsinki Declaration. The written informed consent was obtained from all the patients.

Results

A total of 33 cases were analyzed in this study; all of them were males (Figure 1) as malignant tumours diagnosed no females. The records showed that all the females presented by vocal cord masses were suffering from benign laryngeal nodules.

The range of the age in this study was 40-87 years, the mean age of the patients was 60.09±3.75 (SD) years. Most of the cases belonged to the age group of 51-60 years, followed by 61-70 years, with a low incidence of the disease in 40-50 years. No cases were reported in patients less than 40 years of age (Figure 2).

All the patients were smoking, none of them gave any history of additions or alcohol consumption. The main presenting complaint was hoarseness of voice, seen in 51.52% of cases, followed by dysphagia (27.27%) and then neck swelling (21.21%) (figure 3A). The most common site for the detected laryngeal growth was a glottic area, then the supraglottic. Only a few cases showed subglottic growth (Figure 3B).

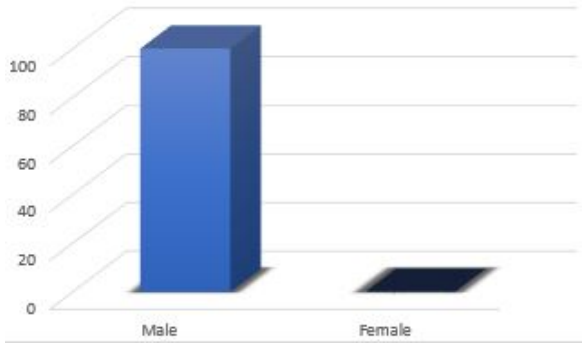

Figure 1. Sex distribution. All the reported cases were male, no female cases were reported.

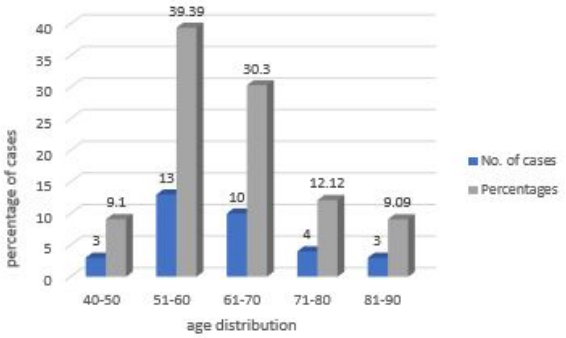

Figure 2: Age distribution. Most of the cases were between 51 and 60 years of age, followed by 61 to 70 years. The incidence of the disease was low, below 50 years and above 70 years.

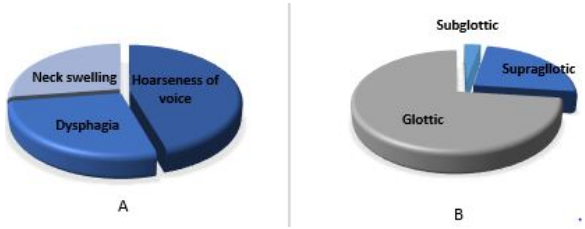

Figure 3: The main presenting symptoms and sites of laryngeal carcinoma. A) 51.52% of cases presented with a change in voice quality, 27.27% presented with difficulty in swallowing and 21.21% presented with a neck mass. B) The most common site of the tumour was the glottic area.

CT evaluated the stage of the tumour in all patients. 5 cases (15.15%) were stage 0 (carcinoma *in situ*), 14 cases (42.43%) were stage I, 7 cases (21.21%) stage II, 4 cases (12.12%) stage III and T4 in 3 cases (9.09%) (Figure 4). A representative CT is shown in figure 5.

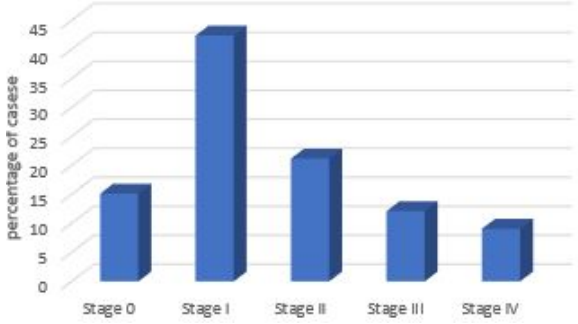

Figure 4: Tumour staging. 15.15%, stage 0 (carcinoma *in situ*), 42.42% stage I, 21.21% stage II, 21.21% stage III and 9.09% stage IV with lymph node metastasis.

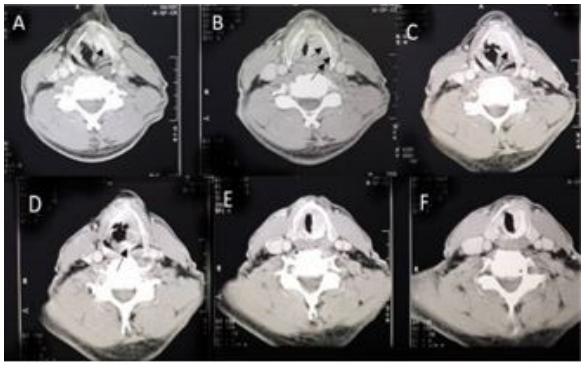

Figure 5: CT imaging transverse section of the head and neck. A) tumour growth destroys the thyroid cartilage (arrow). B) double-headed arrow showed destructed, mispositioned cartridge. C) subglottic infiltration by the tumour. D) circumferential growth of the tumour. E) and F) showed narrowing of the tracheal lumen by the tumour growth.

Figure 6: Percentage of histopathological grade: 39.3% was well-differentiated, followed by moderately differentiated tumour (27.27%). The poorly differentiated tumours account for 18.18% of cases while carcinoma in situ forms only 15.16% of the studied cases.

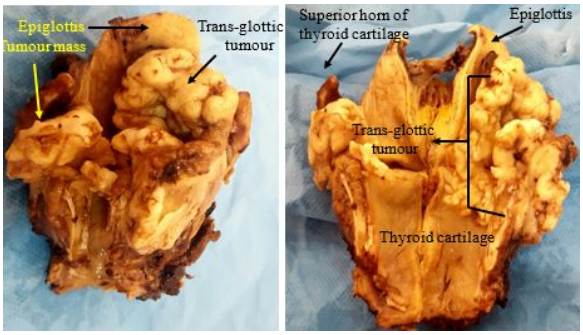

Figure 7: gross morphology of large trans-glottic tumour involves glottic, supra and subglottic areas extended to thyroid cartage.

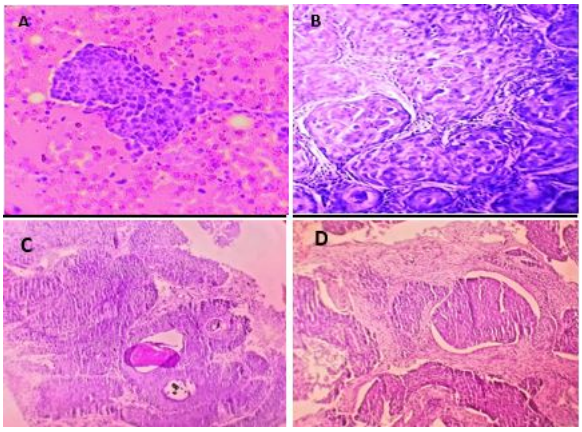

Figure 8: Microscopic picture of selected cases of laryngeal cancer. A) cytological features of metastatic laryngeal carcinoma in aspirated cytology from the enlarged cervical lymph node. B, C, and D are selected pictures that demonstrated different histological grades of squamous cell carcinoma, B) differentiate nests of malignant squamous cells. C) sheets of moderately differentiated malignant squamous cells. D) sheets of poorly differentiated malignant squamous cells.

All cases underwent direct laryngoscopy, and the histopathological examination of the provided punch biopsies revealed squamous cell carcinoma in all cases. The grading was as follows: (39.39%) well differentiated, (27.27%) moderately differentiated tumour, 18.18% poorly differentiated tumours, and 5 cases (15.16%) were carcinoma i*n situ* (Figure 6). FNAC investigated the three cases presented with neck mass; all of them were positive for metastatic squamous cell carcinoma. Figure 7 showed a representative gross morphology of a large trans-glottic tumour, and figure 8 showed representative pictures of the FNAC and the histological finding.

During the follow-up, all 33 cases were tested for COVID-19 infection several times, even without any signs or symptoms of COVID-19. Only four patients were positive for COVID-19 disease, which PCR proved 2-4 months post laryngectomy. Their symptoms were mild upper respiratory tract infection, including headache, mild fever and mild cough. Their chest x-rays were clear, all of them healed without any serious complications of CVOID-19.

Discussion

Larynx carcinoma is a very common head and neck malignancy, especially in males [14]. In this study, all of the patients were male, and most of them were above 50 years of age, few cases were above the 70s, and no cases were seen below 40s. Similar results have been observed by Saedi et al. [15] and Lam et al. [16]. All cases of laryngeal mass in females, in this study, showed benign vocal cord nodules, the data for benign nodules is not demonstrated in this study, some other studies have recorded laryngeal carcinoma in females, but they are still few compared to male patients [6 &17-18]. The complete absence of female cases in our study, compared to the few cases in other studies, is probably related to the differences in the environments and social habits. In Libya, absences of laryngeal carcinoma in females are associated with the low rate or complete absence of smoking and alcohol consumption in females in the Libyan community. Predisposing factors for laryngeal cancer, other than smoking and alcoholism, include chemical carcinogens and viral infection [7]. In the present study, all the patients were heavy smokers. However, they all denied alcoholic consumption, most of them were alcoholic, but they refused it due to the social stigma associated with alcoholism in muslin society such as in Libya. The association between laryngeal cancer alcoholism and smoking in the study was in agreement with many previous studies [19-20-21], where they found that smoking and alcohol consumption were predisposing factors in the majority of the cases. No link can be found between any of the patients in this study and any viral infection of any type. Furthermore, no history of chemical hazard has been given by any of the patients

The main presenting symptoms in this study was hoarsening of voice with the change

Of the voice quality, which was seen in more than 50% of cases, followed by dysphagia and different degrees of difficult swelling, in about 27% of cases. Patients who presented with neck mass form only 21.2% of cases. Other studies also showed that voice changes and dysplasia were the main presenting symptoms of many laryngeal cancer patients [22-23]. As in another survey by Patrick Sheahan [24], the largest percentage of our cases, 39.3%, showed well-differentiated squamous cell carcinoma, followed by moderates differentiated squamous cell carcinoma in 27.2% and approximately a close percentage of poorly differentiated carcinoma and carcinoma in situ by 17% and 15% respectively, only one case of spindle cell carcinoma which is considered and classified in a poorly differentiated category, other histological types were also rare in other studies [25]. In the present study, more than 70% of cases were with glottis tumours, 24.23% had supraglottic, and only 3 % had subglottic laryngeal cancer. Other studies showed different data where the supraglottic lesion was more common, followed by the glottic region and then the subglottic area [17&26].

Most of our cases presented with early stages with glottic tumours because of the alarming symptoms such as voice changes and dysphagia. Thekdi et al. [22] also found that patients with glottic tumours usually presented with early-stage because of the notable changes in voice. In our study, 42% was stage I and 21% were stage II, only a few cases presented as a late stage of III and VI; this also can be explained by the site of the tumour itself. This is also seen by another study that showed metastasis of laryngeal carcinoma is associated with the primary site of the tumour, and a high incidence of metastasis was found in patients with supraglottic tumours due to rich lymphatics supply in the supraglottic region [27].

During the follow-up, and in contrast to other studies [28], only four patients were infected by COVID-19, their signs and symptoms were mild, and none of them showed serious complications or evidence of pneumonia or any opportunistic infections. The rest of the patients were harmful to COVID-19 until the writing of this article. The low incidence of COVID-19 in our patients was related to the post laryngectomy care, which included an early diagnosis of infection, immediate intervention with proper treatment any correctly the use of chemotherapy. Unaffected patients can Be explained by the good follow of the prevention protocols and the low incised of the COVID-19 in our community.

Conclusions

Early detection of laryngeal cancer is associated with a good prognosis. Any changes in voice quality, especially in smoking males, should be taken as an early symptom of laryngeal cancer. The early detection of laryngeal carcinoma is based on good history, clinical examination, and some invasive and noninvasive investigations, such as direct laryngoscope, CT scan and histopathological examination. Post laryngectomy care may play an essential role in protecting the patient from serious complications of COVID-19 infection. This study has been done to improve the awareness of laryngeal carcinoma and highlight the risk factors which allow early detection of the tumour to prevent fatal stage at presentation and to put a base for the analysis of post laryngectomy COVID-19 infection.

What this study added to existing knowledge?

In this study, we highlight the main risk factors of laryngeal carcinoma in a north African country and showed that post-operative care may protect the patients from serious complications of COVID-19.

Contribution by different authors: First author: Dr Houssein Elmatri: clinical data collection, data analysis and writing. **Second author**: Dr Nabeia Gheryani: preparing of histological data, writing and proofreading.

Abbreviations:

FNAC: Fine needle aspiration cytology.

CT: Computed tomography.

TNM: Tumour staging system.

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