

Squamous cell carcinoma of larynx in northwestern Iran

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ABSTRACT

The aim of this study was investigation of laryngeal cancer in northwestern Iran, Urmia to have a clear roadmap for planning the next health policy programs. This study was conducted in the largest tertiary center, northwestern Iran. Of all 23474 patients referred to the clinics of ENT in the Hospital, totally 267 cases were admitted as inpatients with laryngeal problems, 196 patients (73.4%) underwent laryngoscopy, of whom 145 (54.3%) were biopsied. Of these biopsied specimens, 103 cases (71%) were non-malignant lesions and the rest 42 specimens (29%) had malignancies. During the period of study, for five years, totally 0.1% of the cases had laryngeal cancer, which was confirmed by pathological studies. All of the cases were pathologically detected as squamous cell carcinoma. 35 cases of detected 42 patients (83.3%) had at least a smoking history of daily 20 cigarettes for ten years. Any other risk factors were not detected as significant ($p>0.05$). The locations involved by the tumor included as 16 cases (38%) supraglottic, 18 cases (42.8%) glottic, and 8 cases (19%) were reported with unknown location. The main clinical manifestations of the patients were dysphonia, dysphagia, weight loss, dyspnea, laryngalgia, cervical lymphadenitis, stridor, hemoptesis, coughing. As a conclusion and due to the relatively high incidence of the laryngeal cancer in the population (0.1%), and higher rate among the inpatients admitted in the ENT ward (15.7%), we suggest comprehensive planning and measurements to be implemented in the society level for this hidden public health problem.

Keywords: ENT, laryngeal cancer, squamous cell carcinoma, Middle-East.

INTRODUCTION

Laryngeal cancer, also called cancer of the larynx or laryngeal carcinoma, are commonly squamous cell carcinomas (SCCs). SCC reflects the origin of the squamous cells which form the majority of the laryngeal epithelium. Cancer can develop in any part of the larynx, but the cure rate is affected by the location of the tumor. For the purposes of tumor staging, the larynx is divided into three anatomical regions: the glottis (true vocal cords, anterior and posterior commissures); the supraglottis (epiglottis, arytenoids and aryepiglottic folds, and false cords); and the subglottis. Almost laryngeal cancers originate in the glottis. Supraglottic cancers are less common, and subglottic tumors are least frequent. Laryngeal cancer may spread by direct extension to adjacent structures, by metastasis to regional cervical lymph nodes, or more distantly, through the blood stream. Distant metastases to the lung are most common. Of the main risk factors, we may enumerate the smoking as the most important risk factor for laryngeal cancer. Death from laryngeal cancer is 20 times more likely for heaviest smokers than for nonsmokers. Heavy chronic consumption of alcohol, particularly alcoholic spirits, is also significant. When combined, these two factors appear

to have a synergistic effect. Some other quoted risk factors are likely, in part, to be related to prolonged alcohol and tobacco consumption. These include low socioeconomic status, male sex, and age greater than 55 years. People with a history of head and neck cancer are known to be at higher risk (about 25%) of developing a second cancer of the head, neck, or lung. This is mainly because in a significant proportion of these patients, the aerodigestive tract and lung epithelium have been exposed chronically to the carcinogenic effects of alcohol and tobacco. In this situation, a field change effect may occur, where the epithelial tissues start to become diffusely dysplastic with a reduced threshold for malignant change. This risk may be reduced by quitting alcohol and tobacco [1-2].

The major symptoms of laryngeal cancer (depending on the size and location of the tumor) may include: hoarseness or other voice changes, a sore throat or feeling that something is stuck in the throat, stridor, persistent cough, a lump in the neck, bad breath and the earache. Incidence of laryngeal cancer is five in 100,000 (12,500 new cases per year) in the USA. Each year, about 2,200 people in the U.K. are diagnosed with laryngeal cancer [3].

The diagnosis is made by the doctor on the basis of a medical history, physical examination, and special investigations which may include a chest x-ray, CT or MRI scans, and tissue biopsy. The examination of the larynx requires some expertise, which may require specialist referral. The physical exam includes a systematic examination of the whole patient to assess general health and to look for signs of associated conditions and metastatic disease. The oral cavity and oropharynx are examined under direct vision. The larynx may be examined by indirect laryngoscopy using a small angled mirror with a long handle and a strong light. Indirect laryngoscopy can be highly effective, but requires skill and practice for consistent results. For this reason, many specialist clinics now use fiberoptic nasal endoscopy where a thin and flexible endoscope, inserted through the nostril, is used to clearly visualize the entire pharynx and larynx. Nasal endoscopy is a quick and easy procedure performed in clinic. Local anesthetic spray may be used. If there is a suspicion of cancer, biopsy is performed, usually under general anesthetic. This provides histological proof of cancer type and grade. If the lesion appears to be small and well localized, the surgeon may undertake excision biopsy, where an attempt is made to completely remove the tumor at the time of first biopsy. In this situation, the pathologist will not only be able to confirm the diagnosis, but can also comment on the completeness of excision, i.e., whether the tumor has been completely removed. A full endoscopic examination of the larynx, trachea, and esophagus is often performed at the time of biopsy. The final management plan will depend on the site, stage (tumor size, nodal spread, distant metastasis), and histological type. The overall health and wishes of the patient must also be taken into account [4].

Specific treatment depends on the location, type, and stage of the tumor. Treatment may involve surgery, radiotherapy, or chemotherapy, alone or in combination. This is a specialized area which requires the coordinated expertise of ear, nose and throat (ENT) surgeons (otolaryngologists) and oncologists [5].

According to our best knowledge, there were no reports about the profile of laryngeal cancer in northwestern Iran, Urmia. We tried to investigate this disorder in this important part of country, to have a clear roadmap for planning the next health policy programs.

MATERIALS AND METHODS

It was a transverse cross-sectional study that was undertaken from November 1 1991 to October 31st 1996. The study was conducted at the ENT wards of Imam and Madani Teaching Hospitals of the Urmia University of Medical Sciences. This hospital is the largest tertiary center with 450 bed spaces, in West Azerbaijan province, northwestern Iran. They serve as referral centers for the neighbor provinces with an overall approximate population size of about 14 million people (2006 National population census). Of all 23474 patients referred to the clinics of ENT in the Hospital, totally 267 cases were admitted as inpatients with laryngeal problems within the study period, who were included in the study. A pre-tested and validated study protocol was used for the data collection. The study protocol which was filled by trained interviewers elicited the following information; socio-demographic profile of the patients and parents, family history surveying both paternal and maternal aspects particularly family history of laryngeal problems (we did not evaluate family history of other congenital anomalies), dietary/nutritional history, patient's antenatal and delivery history. Specifically, the protocol explored the following antenatal events' parental history of alcohol ingestion, cigarette smoking, cooking method, drug use during pregnancy and exposure to irradiation. Approval for this study was obtained from the Ethics committee of the Urmia University of Medical Sciences. The rights of patients to participate or not was respected, and the study was carefully explained to the patients or their parents and their informed consent obtained before they were recruited into the study. All information obtained was recorded on the data collection sheet designed for the study. The coded data were then fed into the computer using the SPSS statistical software and analysis was conducted. This consisted of univariate and bivariate analysis and comparisons of identified relationships. Test of the statistical significance was based on 95%

confidence interval using Chi square test with the Yates or Fischer exact correction where applicable. Odds ratio and confidence interval was then calculated to determine the association between the risk factors and laryngeal cancers.

RESULTS

Of all 23474 patients referred to the clinics of ENT in the Hospital, totally 267 cases were admitted as inpatients with laryngeal problems within the study period, who were included in the study. 196 patients (73.4%) underwent laryngoscopy, of whom 145 (54.3%) were biopsied. Of these biopsied specimens, 103 cases (71%) were non-malignant lesions and the rest 42 specimens (29%) had malignancies. During the period of study, for five years, totally 0.1% of the cases had laryngeal cancer, which was confirmed by pathological studies. All of the cases were pathologically detected as squamous cell carcinoma. The absolute and relative frequencies of laryngeal SCC prevalence based on the age groups of the patients has been summarized in **Table 1**. The male:female ratio of the patients was 20:1, meaning 4.7% female and the rest 95.3% male. This may be related to the social situations of this population that the smoking is more common among men than the women. 35 cases of detected 42 patients (83.3%) had at least a smoking history of daily 20 cigarettes for ten years. Any other risk factors were not detected as significant ($p>0.05$). The locations involved by the tumor included as 16 cases (38%) supraglottic, 18 cases (42.8%) glottic, and 8 cases (19%) were not exactly located (reported as unknown). The main clinical manifestations of the patients were dysphonia, dysphagia, weight loss, dyspnea, laryngalgia, cervical lymphadenitis, stridor, hemoptesis, coughing. See **Table 2** for the frequency of the main and subsidiary clinical manifestations in the patients with laryngeal cancer. **Figure 1** depicts the main clinical complaints of the patients with laryngeal cancer.

Age groups	prevalence	
	frequency	percentage
35-44 y	4	9.5%
45-54 y	10	23.8%
55-64 y	16	38%
65-74 y	10	23.8%
75-84 y	2	4.7%
Total	42	100%

Table 1: The absolute and relative frequencies of laryngeal SCC prevalence based on the age groups of the patients in the studied population

manifestations	signs	
	main	subsidiary
dysphonia	38 (88%)	0 (0%)
dysphagia	3 (7%)	20 (47.6%)
weight loss	0 (0%)	15 (35.7%)
dyspnea	0 (0%)	8 (19%)
laryngalgia	1 (2.3%)	7 (16.6%)
cervical lymphadenitis	0 (0%)	6 (14.2%)
stridor	0 (0%)	5 (11.9%)
hemoptesis	0 (0%)	5 (11.9%)
coughing	1 (2.3%)	5 (11.9%)

Table 2: The main and subsidiary clinical manifestations in the patients with laryngeal cancer

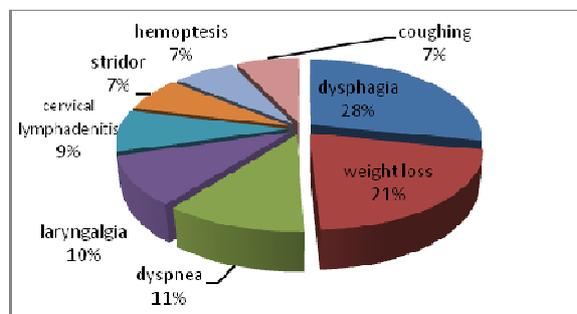


Figure 1: The percentage of main clinical complaints of the patients with laryngeal cancer

DISCUSSION AND CONCLUSION

Squamous cell carcinoma represents more than 90 percent of all head and neck cancers. In the United States, squamous cell carcinoma of the head and neck comprises about 4 percent of all malignancies. This type of cancer is formed from reserve cells, which are the cells that replaced injured or damaged cells in the epithelial cells. Five-year survival rates average about 60 percent. If the tumor is treated at an early stage before it has grown or spread significantly, survival rates are better—as high as 80 percent [6].

Males have this type of cancer about twice as often as females. Tobacco products, especially smokeless tobacco, are a primary cause. Females are more commonly experiencing this type of cancer as they use tobacco products. Squamous cell carcinoma is more common among individuals in their 50s, 60s, and older. Excessive alcohol use also is considered a risk factor in the development of squamous cell carcinoma, especially when coupled with tobacco products. In addition, Epstein-Barr virus; human papillomavirus (HPV) infection; gastroesophageal reflux disease (GERD); and exposure to paint fumes, plastic by-products, wood dust, asbestos, and gasoline fumes are considered possible risk factors [7].

The primary symptoms of squamous cell carcinoma of the larynx are sore throat, ear pain, and trouble swallowing. This type of cancer is located in one or all of these three areas, including: supraglottis: the upper part of the larynx above the vocal cords, including the epiglottis; glottis: the middle part of the larynx where the vocal cords are; and subglottis: the lower part of the larynx between the vocal cords and the trachea.

A physician may gather a biopsy specimen for the pathologist to examine. A computed tomography (CT) and/or PET (positron emission tomography) scan also can help the pathologist to see the nature and extent of the primary tumor and whether or not it has spread to the lymph nodes, lungs, or liver. These tests help the pathologist assess the location, spread, and stage of the cancer. Stage 1 squamous cell tumors of the larynx are confined to the location of the original tumor. Stage 2 tumors are confined to the larynx but may have begun to affect the vocal cords or may be present in two different parts of the larynx. Stage 3 and 4 have spread beyond the larynx into other parts of the body [3].

Radiation therapy uses high-energy, pinpointed x-rays to kill cancer cells. This type of treatment is directed at specific areas. It can be used to treat small tumors, minimizing the damage to normal cells or tissue surrounding the tumor, or can be used to destroy cancer cells that remain after surgery.

Surgical procedures used to treat cancer of the larynx include cordectomy (vocal cords removal), supraglottic laryngectomy (supraglottis removal), hemilaryngectomy (removal of half the voice box, saving the voice), partial laryngectomy (partial voice box removal, saving the ability to talk), total laryngectomy (removal of whole larynx), thyroidectomy (removal of thyroid gland), and laser surgery to remove a surface tumor through a bloodless cut in the tissue [8].

In addition, a surgeon may perform neck dissection to remove malignancies in the lymph nodes. This kind of surgery can significantly improve the chances of patient survival. In any type of surgery, surgeons take special care to preserve as much nerve, circulatory and muscular function in the neck and spine as possible. Reconstructive surgery accompanied by rehabilitation is used to retain or recover speech and swallowing function after the cancer is removed.

Chemotherapy treatments deliver drugs or hormones throughout the body and reduce the risk of the cancer spreading further or coming back. Physicians focus chemotherapy on specific areas as much as possible to improve effectiveness and reduce toxicity to normal parts of the body. Photodynamic and photothermal therapies activate chemotherapy drugs with light or heat to cause cancer cell death.

According to the results of our study, the smoking, in the absence of any major factors, considered as the leading risk factor in almost of our patients with laryngeal cancer. We suggest the cultural activities to decrease the smoking over the society level. As the dysphonia is the most common early sign of the laryngeal cancer, we suggest the precise examination of any voice changes for more than two weeks, especially in greater ages. Almost of our patients, in spite of their eminent signs and explicit clinical signs did not refer or had not the financial possibilities to refer to the therapeutic centers. We suggest the authorities involved in heal policy making, to plan screening programs to detect the potential patients prior to occurrence of the malignancy. According to the results of this study, and due to the relatively high incidence of the laryngeal cancer in the population (0.1%), and higher rate

among the inpatients admitted in the ENT ward (15.7%), we suggest comprehensive planning and measurements to be implemented in the society level for this hidden public health problem.

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