

## An etiological study of the laryngeal cancer in the patients admitted in Imam Hospital of Urmia, Northwestern Iran

Hassan Latifi <sup>1</sup>, Peyman Mikaili <sup>2\*</sup>, Majid Kassiyanzadeh <sup>3</sup>, Kaveh Latifi <sup>4</sup>

<sup>1</sup>.Department of Otolaryngology, Imam Khomeini Hospital, Faculty of Medicine, Urmia University of Medical sciences, Urmia, Iran

<sup>2</sup>.Department of Pharmacology, Faculty of Medicine, Urmia University of Medical Sciences, Urmia, Iran

<sup>3</sup>.Student of Medicine, Faculty of Medicine, Urmia University of Medical sciences, Urmia, Iran

<sup>4</sup>.Student of Medicine, Faculty of Medicine, Teheran Azad University, Tehran, Iran

[peyman\\_mikaili@yahoo.com](mailto:peyman_mikaili@yahoo.com)

**Abstract: Introduction:** Laryngeal cancer accounts for 2% of total human cancers and also 30-35% of cancers of head and neck. Before 1860s, laryngeal cancer was rarely recognized. Different types of neoplasms involve laryngeal region, including sarcoma, adenocarcinoma, cylindroma, lymphoma, histiocytoma etc. Although the laryngeal cancer seems to be common in the northwestern Iran, to our best knowledge, it has been poorly documented. The aim of this study is evaluating the clinical and statistical profile of laryngeal cancer in northwestern Iran in detail, including information about etiology, clinical manifestations and usual treatment methods in a three year long study. **Subjects and Methodology:** This study was performed in the period of three years on the all referred patients (n=50, male to female ratio: 48:2) with laryngeal cancer, accepted in the major state Imam hospital of Urmia. The medical documents of all accepted patients were completely recorded. They all underwent laryngoscopy and biopsy samples were collected. Their laryngeal cancer was approved by pathological tests in the medical center. Of all 50 patients, 46 cases (92%) underwent surgery and/or radiotherapy. Only 4 patients (8%) after primary diagnosis discharged or transferred to other medical centers, thus, we missed them and we could not follow them up anymore. **Results:** Almost all of 50 studied patients (m=48, f=2) were in 7th and 8th age decades. The average of malignancy occurrence age was 65.5 years for female and 62.3 for male patients. In the drawn age graph, 31 cases are located above and 17 cases below the average value. Regardless the gender, the average age of malignancy occurrence is 62.5. The results showed that 90% of the patients were smokers and only the rest 10% had no smoking history. More than the half of the patients had signs of voice changes. 98% (n=49) of pathological lesions of laryngeal cancer were detected as SCC and only one case (2%) was as adenocystic carcinoma. The results of our study showed the incidence of cancers of glottis origin are 56% and the supraglottic, was 40%, with no cases (0%) of infraglottic origin. In our study, 90% of the cases were smokers and 70% of latter had 20-year long smoking history. Statistically, there was a significant relation between smoking and laryngeal cancer ( $r > 0.89$ ;  $p < 0.01$ ). **Conclusion:** For about 90 percents of the patients, we may consider a survival of 5 years. But if the cancer spread to the infraglottic or inner posterior parts of the larynx, the five-year survival decreases to 70 percents of them. The patients should be educated so that they do the follow-up visits, although the surgery has been successfully done. This is because, sometimes the tumor, even after a radical excision, may proliferate and remised, and then the common therapy will fail. We propose educational programs for the patients after laryngeal cancer surgery.

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### 1. Introduction

Information on cancer statistics is important for better planning and to ensure the most economical use of professional and financial resources toward tumor control within a certain region (Firat, 1995). Laryngeal cancer accounts for 2% of total human cancers and also 30-35% of cancers of head and neck. Before 1860s, laryngeal cancer was rarely recognized. After then, using laryngoscope by Garcia and the histological tests by Wirshaw, the condition was diagnosed. The first total laryngectomy was done by

Bilrouth in 1873. Totally 103 laryngectomies were reported up to the end of 1887. The conventional treatment of patients with locally advanced laryngeal cancers has consisted of surgery and/or radiation therapy. Many of these patients lose their larynx. In the early 1980s, we observed that patients who respond to cisplatin-based combination chemotherapy respond further with subsequent radiation therapy and, conversely, those who do not respond to initial chemotherapy, even after six

courses, will not respond to radiation therapy (Al-Sarraf, 1995).

Although like other malignancies, the exact cause of laryngeal cancer is unknown, but some etiologies have been suggested, including smoking, alcoholism, concomitant second cancers, gender, race, age and occupation.

Different types of neoplasms involve laryngeal region, including sarcoma, adenocarcinoma, cylindroma, lymphoma, histiocytoma etc. The most eminent form of laryngeal cancer, however, is called squamous cell carcinoma (SCC), which accounts for 95% of laryngeal cancer. Other forms include *in situ* (2%) and other miscellaneous forms (2-3%).

The localization of the above-mentioned pathological forms includes supraglottic, glottic and subglottic. Laryngeal cancer is characterized by a variant clinical manifestations including dysphonia, pain, dysphagia, mass sensation in the throat, dyspnea, hemoptysis, discharges, anorexia, weight loss and coughing.

Involvement of the local lymph nodes also is common. Supraglottic metastasis is the most common malignancy in the larynx.

The radical or palliative treatments of the malignancy include surgical removal along with radiotherapy and chemotherapy.

In industrialized countries, men are affected two to three times as often as women, largely due to their higher indulgence of alcohol and tobacco for intra-oral and laryngeal cancer and higher exposure to sunlight for lip cancer among those who work outdoors (Johnson, 2001).

Within the continental United States, there is a greater than fivefold regional variation by state in mortality rates due to ethnic differences, socioeconomic status, and differences in risk factors, including the use of oral smokeless tobacco in the South. Striking variations are also seen across the European Union (EU). There is likely to be a doubling in deaths from oral cancer in the EU between 1970 and 2020, fueled by younger age groups and therefore continuing well into the next century. The highest mortality rates in the world for laryngeal cancer in men are in Hungary, Poland, Slovakia, and Romania (Zatonski, 1996).

Part of the urban/rural difference in incidence of head and neck cancer also relates to atmospheric pollution. Mean sulphur dioxide and smoke concentrations in the atmosphere are positively correlated with SCC of the larynx and, to a lesser extent, the pharynx in parts of England. The importance of fossil fuel combustion at work is confirmed in a large study in four areas in the United States (1,114 cases, 1,268 controls), with ORs of approximately 2.0 for pharyngeal sites. Asbestos,

pesticide exposures, and mists from strong inorganic acids (OR 95 percent CI 1.1-2.9 for the latter) were shown for laryngeal cancer in Uruguay. The risk of laryngeal cancer from acid mists in the steel industry is confirmed in a United States study of 1,031 exposed men (Streenland, 1997).

La Vecchia et al. estimate that approximately 15 percent of oral and pharyngeal cancers in Europe can be attributed to dietary deficiencies or imbalances, perhaps accounting for 5,000 avoidable deaths per year. Similar conclusions can be drawn from studies of laryngeal cancer. In the presence of tobacco and/or alcohol, low intake of fruit and vegetables has been estimated to account for 25-50 percent of cases among men (McLaughlin, 1988).

Although the laryngeal cancer seems to be common in the northwestern Iran, to our best knowledge, it has been poorly documented. The aim of this study is evaluating the clinical and statistical profile of laryngeal cancer in northwestern Iran in detail, including information about etiology, clinical manifestations and usual treatment methods in a three year long study.

## 2. Material and Methods

This study was performed in the period of three years on the all referred patients (n=50, male to female ratio: 48:2) with laryngeal cancer, accepted in the major state hospital of Urmia, Imam Khomeini.

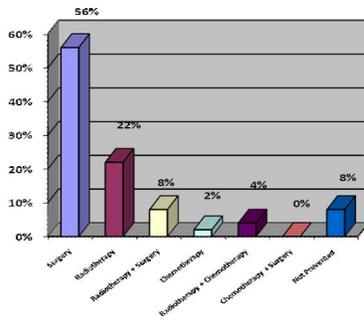
The medical documents of all accepted patients were completely recorded. They all underwent laryngoscopy and biopsy samples were collected. Their laryngeal cancer was approved by pathological tests in the medical center. Of all 50 patients, 46 cases (92%) underwent surgery and/or radiotherapy. Only 4 patients (8%) after primary diagnosis discharged or transferred to other medical centers, thus, we missed them and we could not follow them up anymore.

## 3. Results

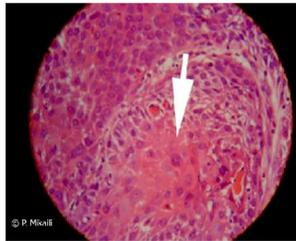
Almost all of 50 studied patients (m=48, f=2) were in 7th and 8th age decades. The average of malignancy occurrence age was 65.5 years for female and 62.3 for male patients. In the drawn age graph, 31 cases are located above and 17 cases below the average value. Regardless the gender, the average age of malignancy occurrence is 62.5. According to the results of descriptive analysis of the data, the majority of the patients were above the average value. The results showed that 90% of the patients were smokers and only the rest 10% had no smoking history.

The radical or palliative treatments of the malignancy included surgical removal, radiotherapy and chemotherapy, or concomitant usage (Figure 1). More than the half of the patients had signs of voice changes. Due to the high prevalence of voice change, this symptom was separately studied and differentiated from dysphonia. 98% (n=49) of pathological lesions of laryngeal cancer were detected as SCC and only one case (2%) was as adenocystic carcinoma.

Histologic findings include squamous cell carcinomas with varying degrees of tissue differentiation and well-defined cell borders (intercellular bridges) and eosinophilic cytoplasm due to production of keratin, enlarged nucleoli and occasionally, keratin pearls (Figure 2).



**Figure 1:** The graph shows the relative frequency (percentage) of different therapeutic measurements on the patients with laryngeal cancer, including surgery; radiotherapy; radiotherapy + surgery; chemotherapy; radiotherapy + chemotherapy; chemotherapy + surgery; not prevented.



**Figure 2:** The pathological sections from the patients with laryngeal cancer after surgical excision, showed Squamous Cell Carcinoma (SCC) (arrow), a carcinoma that mimic squamous epithelium, exhibiting filamentous eosinophilic cytoplasm, sharply demarcated cell borders, and keratinization. Tissue patterns in this type of squamous cell carcinoma is in a highly differentiated forms, exhibiting layers of cells that tend to keratinize and forming cornified clumps that are layered like an onion; H&E, x100.

#### 4. Discussions

As mentioned above, the exact etiology of laryngeal cancer is unclear, but in 1950 it was shown that, it is associated with smoking. In 1950, Wynder *et al.* reported smoking as the most important risk factor for supraglottic and glottis cancers. In 1970 Auerbach *et al.* histopathologically studied the necropsies collected from 941 cadaver, who were dead due to any causes other than laryngeal cancer. 99% of them who smoked during different periods of their life, had a degrees of epithelial atypias and 16% of them had carcinoma in situ. Only 25% of the rest non-smoking cases, however, had mucosal atypias.

In 1971, Yussawla and Shotefeld suggested a direct relationship between laryngeal cancer (especially in supraglottic region) and simultaneous smoking and consumption of alcoholic beverage. They also reported a positive concomitance of laryngeal cancer (specially supraglottic) along with secondary cancers in the oral and pharyngeal regions due to smoking and alcoholism.

Moore *et al.* showed that there is a direct and positive relationship between cigarette numbers and smoking elongation with laryngeal and second cancers. Of 102 patients in this study who were continuing smoking, 61 cases suffered second cancers. On the other hand, only two cases of the patients who quit smoking, suffered second cancer. High incidence of laryngeal cancer in Italy, France and Spain reveals the relationship with high consumption of alcoholic beverage and cigarette smoking in these countries. It notices the importance of synergism between smoking and carcinogenesis of the larynx, comparing other types of cancers in the head and neck region (Dong, 2002).

In our study, 90% of the cases were smokers and 70% of latter had 20-year long smoking history. Statistically, there was a significant relation between smoking and laryngeal cancer ( $r > 0.89$ ;  $p < 0.01$ ). But considering the two female cases with laryngeal cancer, who neither were smokers but having laryngeal cancer; we may consider other importance of other involving factors in the pathogenesis of laryngeal cancer, including herpes II virus infections, HIA and other genetics factors. The race also is an important factor. According to the literature, race factor may affect the incidence of this neoplasia. For instance, the incidence of laryngeal cancer among Hawaii nations is as 8.1 in ten thousand. This rate is five times more than Chinese among community (1.4 in ten thousand), four times more than Philippians' community (2 in ten thousand) and finally 3 times more than Japanese resident in USA. The American blacks are more predisposed to laryngeal cancer than white American.

In spite of incidence variations of this malignancy worldwide, but the overall incidence rate is high in male comparing to the females. This difference is the least in Canada 6:1 (Hoekstra, 1990) and the highest in Italy 22:1. But in the years 1968-72 and 1978 and 1983 the rate of female cases increased. It may be due to the increasing numbers of female smokers, during years of World War II in the country. The region of higher risk is the supraglottic (comparing to glottis) (Stell, 1990) and according to the statistics, the m:f ratio in UK and USA are 9:1 and 10:1, respectively. As said above the world rate of m:f ratio ranges between 6 to 22. According to the results of our study this ration was 24:1, that it is due to smoking in northwestern Iranian is more common among males.

The age of laryngeal cancer occurrence is higher in the middle ages and according to the Ladderman, the among age for men and women are 61.5 and 60.6, respectively. Reviewing literature, the reports studied in Iranian people. Salehi et al. reported the average occurrence age in northeastern Iran (Mashhad) were 59.4 and 51.4 for men and women, respectively. According to the studies 80% of SCCs occurred in the fifth, sixth and seventh decades of the ages. The results of our study (regardless the gender) showed 86% of the SCC cases occurred in the fifth, sixth and seventh age decades, which our results is approximately consistent with other studies. The average laryngeal cancer occurrence age was 62.5 regardless the age and the majority of the patients were upper than the average rate.

The average age of laryngeal cancer occurrence for women and men were 65.5 and 62.3, respectively, and according to the statistical results, 31 male cases and 17 female cases were lower the average value.

Reviewing the world statistics of localization and regional origins of laryngeal cancer, supraglottic cancers account for 30% of the laryngeal cancers, of which 60% originate from epiglottis, 30% from false cord and 10% from aryepiglottis (Rodriguez-Cuevas, 1998). The average world situation of glottis and infraglottic rates are 50-60% and 10-20%, respectively.

The results of our study showed the incidence of cancers of glottis origin are 56% and the supraglottic, was 40%, with no cases (0%) of infraglottic origin.

## 5. Conclusion

Laryngeal cancer is characterized by discernible localization to be easily differentiated, poor and rare metastasis, and a nearly good prognosis and life expectancy for the patients. As mentioned

above, in our study, 90% of the cases were smokers and 70% of latter had 20-year long smoking history. Statistically, there was a significant relation between smoking and laryngeal cancer. But considering the two female cases with laryngeal cancer, who neither were smokers but having laryngeal cancer; we may consider other importance of other involving factors in the pathogenesis of laryngeal cancer, including herpes II virus infections, HIA and other genetics factors (Morris, 2000).

This neoplasm may be soon diagnosed to decrease the subsequent complications. For about 90 percents of the patients, we may consider a survival of 5 years. But if the cancer spread to the infraglottic or inner posterior parts of the larynx, the five-year survival decreases to 70 percents of them.

Educating the patients plays an important role for the prognosis and elongation of the survival. The patients should be educated so that they do the follow-up visits, although the surgery has been successfully done. This is because, sometimes the tumor, even after a radical excision, may proliferate and remised, then the common therapy will fail. We propose educational programs for the patients after laryngeal cancer surgery.

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## Corresponding Author

Dr. Peyman Mikaili  
Dept. of Pharmacology, Faculty of Medicine,  
Urmia University of Medical Sciences,  
Nazloo Road, Urmia, Iran  
E-mail: [peyman\\_mikaili@yahoo.com](mailto:peyman_mikaili@yahoo.com)

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