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LARYNGEAL CANCER: SOCIODEMOGRAPHIC, LIFE STYLE AND CLINICAL RISK FACTORS AMONG PATIENTS UNDERWENT TOTAL LARYNGECTOMY

E. A. EL-MOSELHY, Y. M. SALEH, M. M. EL-SAWY*,
E. S. ABD-ALLAH Y. A. BARKA, and T. M. FARGHALY***
Departments of Community Medicine;
Ear, Nose and Throat* and Community Health Nursing**
Faculty of Medicine and Nursing, Al-Azhar and Zagazig University

Abstract

Introduction: Laryngeal cancer (LC) is an important health problem. It is one of the most common respiratory cancers. The prevalence of this cancer is increasing all over the world.

Objectives: The aim of the present study is to determine the clinical features of the laryngeal cancer patients underwent total laryngectomty (TL); to define the characteristic features of surgery in these patients; and to define the life style, health behavioral, sociodemographic and clinical risk factors of the patients.

Subjects and methods: A total of 90 laryngeal cancer patients and a control group of the same number were enrolled in the study. A case-control, hospital based study design was used. **Results**: The most important clinical features of the studied laryngeal cancer cases underwent TL were; most lesions site was glottis (56.7%), presented with hoarseness of voice (85.6%) and most of the patients were in stage III (63.3%). Also, the most important characteristics of the surgery in these cases were 64.4% had TL and primary tracheoesophageal puncture, 88.9% underwent thyroidectomy and 25.6% had preoperative tracheostomy. The +ve reflux symptoms index was significant clinical risk factor (OR=6.77). Factory worker occupation was significant risk factor (OR=4.65). The most important sociodemographic risk factors for laryngeal cancer were male sex, urban residence, old age, low social level and low occupational level (ORs= 52.59, 2.43, 2.43, 1.99 and 1.97; respectively). Further, the most important significant health behavioral risk factors were cigarette smoking, goza smoking and no healthy food intake (ORs= 4.44, 4.25 and 2.74; respectively).

Recommendations: Population based studies are needed in different areas in Egypt and on large numbers of patients to understand the full epidemiology of the laryngeal cancer and quality of life of these patients.

Introduction

Laryngeal cancer (LC) is the second most common respiratory cancer after lung cancer. Moreover, the prevalence of LC is increasing over time in much of the world **(Cattaruzza, 1996)**. It is estimated that 12,600 new cases of LC were diagnosed in the United States (US) during 1993 and an estimated 3,800 deaths were due to this cancer **(Boring et al., 1993)**.

Also, in the US the highest incidence was recorded for black men aged 65-69, while the highest incidence among white men occurred for those in age group 70-74 years. Incidence rate was also higher

among black women compared with white women **(Miller, 1990)**. Further, the incidence rates are substantially lower among women than men throughout the world **(Parkin, 1992)**. In Egypt, LC represents 5.7% of all body malignancies and 38.7% of the head and neck malignancies **(Farghaly, 1991)**.

Social class, which reflected by occupation and education, is an important determinant of LC risk **(Hirayama, 1990** and **Maier & Tisch, 1997)**. Low social class was associated with an increased risk of developing LC **(Elwood et al., 1984)**. Also, laryngeal cancer mortality was higher fourfold among subjects in the lowest occupational category (laborers/transport/ production) compared with those in professional and technical occupations (2.1 deaths per 100,000 person-years vs. 0.5 deaths). At the same time, relative risk for LC was higher among those in the least skilled social class compared with those in the professional and most skilled social classes **(Pearce and Howard, 1986)**.

Epidemiologic studies over the last half century cleared the deleterious effects of tobacco use on health. These studies established unequivocally that tobacco use, particularly manufactured cigarette smoking, causes most cancers of the larynx. Geneticists increasingly study tobacco use as a model for environmental carcinogenicity **(Thun et al., 2002)**. Tobacco and alcohol consumption by the cancer patients was roughly twice as great as in their controls **(Maier et al., 1997)**. They act synergistically in elevating the risk of development of laryngeal cancer **(Guenel et al., 1988)**.

The effect of dietary nutrients on the risk of developing laryngeal cancer was evaluated; the dietary intake of vitamins A and C **(Graham et al., 1981)**, fibers, carbohydrates and vitamin E **(Tavani et al., 1994)** and fish **(Hirayama, 1990)** were found to be protective against development of laryngeal cancer.

Laryngopharyngeal reflux (LPR) is a potential predisposing factor for laryngeal cancer **(Lewin et al., 2003)**.

Occupational exposure to asbestos, mustard gas, the strong-acid process of isopropyl alcohol manufacturing, nickel refining, nickel compounds, soot, tars, and certain mineral oils have been identified as likely carcinogens to the larynx. An association was suspected for diethyl sulfate, but it has not been confirmed **(Merletti et al., 1984)**. Acid mists have also been identified as potential carcinogens. Bischloromethyl ether and beryllium have also been associated with increased risk for laryngeal cancer **(Boring et al., 1993)**. On the other hand, no association was found between exposure to man-made mineral fibers and laryngeal cancer **(Gardner et al., 1986)**.

The aim of the present research is to determine the clinical features of the LC patients underwent total laryngectomty (TL); to explore the characteristic features of surgery in these patients; to define the most important etiological risk factors of LC; and to assess the sociodemographic, life style, health behavioral and clinical risk factors of these patients with LC.

Material and Methods

This study was carried out on the patients, with LC underwent TL, attending the Ear, Nose and Throat Outpatient Clinics, Al-Azhar University Hospitals as well as some private hospitals asking for medical advice, treatment and/or follow up. The patients group in this study was diagnosed, enrolled and managed as having LC. All the patients' sheets were reviewed; the patient with incomplete data was excluded from the study. A total number of 90 patients with LC underwent TL and an equal number of controls were enrolled in this study. The control group was chosen randomly from patients attending the clinics and proved to be free from malignancies and laryngeal diseases. A case-control, hospital based study design was chosen to

carry out this research. The laryngeal cancer patients and controls were adults. The aims and procedures of the study were explained to the patients and controls. A verbal consent of both of them, to participate in the study, was given.

Clinical examinations had been done for the patient and control groups. Also, the required investigations had been done for them. Laryngeal cancer was diagnosed through specific protocol according to **El-Moselhy et al. (2004)**. The reflux symptoms index (RSI) was used to determine presence of reflux symptoms. Subjects were classified +ve, if scored ≥10 and –ve, if scored <10 of the index score. Positive RSI was suggested to be related to presence of laryngeal pathologies as laryngeal cancer **(Belafsky et al., 2002)**.

A comprehensive questionnaire was also designed to contain data relevant to the topic of the study.

Chi-square (χ^2) and odds ratio (OR) were used as tests of significance. The significance level for χ^2 was accepted if P-value <0.05. While, OR was weighted according to value of the 95% confidence interval (CI) or exact confidence limits (ECL).

Results

Table **(1)** clears the characteristics and clinical features of the studied patients with laryngeal cancer. Hoarseness of voice was the main presenting symptom of the LC patients; 85.6%. Also; 74.4% and 25.6% of the cancers were glottic and supraglottic, respectively. Further, all (100.0%) lesions were squamous cell carcinoma. Regarding tumor size, 65.6%, 32.2% and 2.2% of the masses were T3, T4 and Tx (can not be assessed due to severe edema), respectively. At the same time; 71.1%, 18.9% and 8.9% of the cases had N0, N1 and N2, respectively. Further, 100.0% of the patients had no distant metastasis at time of surgery. Collectively, 63.3% and 34.4% of the patients their lesions were in stage III and IV, respectively. Lastly; 26.4%, 16.7% and 14.4% of the patients had chronic obstructive disease, hepatitis C virus infection and diabetes mellitus, respectively.

Table **(2)** shows distribution of the laryngeal cancer patients underwent TL. All the patients had TL; 64.4% of them had TL and primary tracheoesophageal puncture (TEP), 31.2% had TL and secondary TEP and only 4.4% had TL alone. Also, selective neck dissection (SND); right and left were done for 78.9% and 65.6% of the patients, respectively. While, right and left radical neck dissections (RNDs) were done for 1.1% and 3.3% of the patients, respectively. Further, thyroidectomy was done in 80 (88.9%) patients with high incidence of thyroid gland invasion; 74 (82.2%) patients underwent thyroid lobectomy and 6 (6.7%) underwent total thyroidectomy. Also, preoperative tracheostomy was done for 25.6% of the patients. As regarding surgery complications, 15.0% of the patients had pharyngocutaneous fistula (PCF). Lastly, 4.4% of the patients had developed distant metastasis at follow up; pulmonary (3.3%) and esophageal (1.1%).

Table **(3)** details distribution of the laryngeal cancer patients and control group according to reflux symptom index. RSI was found to be a significant risk factor for a subject to be a laryngeal cancer patient (OR=6.77, 95% ECL: 1.43-63.57).

Table **(4)** shows distribution of the laryngeal cancer patients and control group according to their occupational type risk factors weights'. Some occupations were found to be risk factors for cancer larynx, but the significant one was factory worker (OR=4.65, 95% ECL: 1.41-19.80). On the other hand, house wife occupation was found to be the only significant protective factor (OR= 0.02, 95% ECL: 0.00-0.16).

Table **(5)** illustrates distribution of the laryngeal cancer patients and control group according to their life style and health behavioral risk factors. As regard smoking, in general it was found to be a significant risk factor for LC (OR= 63.03, 95% ECL: 14.90-548.04). In details, the risk of cigarette smoking was significant (OR=4.44, 95% CI: 2.27-8.75). The risk increases significantly with increasing

number of smoked cigarettes per day (≥3 pack/day) and by increasing duration of smoking (≥40 year) (ORs=3.63, 95% ECL: 1.06-15.83 and 17.88, 95% ECL: 4.17-158.79, respectively). Also, goza smoking had nearly the same significant risk as cigarettes (OR=4.25, 95% ECL: 1.42-15.27). Also, the risk increases significantly with increasing duration of smoking (≥35 year) (OR=7.43, 95% ECL: 1.59-69.22). Further, passive smoking was found to be significant risk factor for laryngeal cancer (OR=42.31, 95% ECL: 6.55-1746.95). Also, alcohol intake and simultaneous smoking and alcohol taking were found to be non significant risk factors for LC (OR= 4.14, 95% ECL: 0.40-206.11 for each of them). Lastly, no healthy food intake was found to be significant risk factor for LC (OR=2.74, 95% CI: 1.06-7.32).

Table **(6)** details distribution of the patients with laryngeal cancer and control group according to their sociodemographic risk factors. As respect age, old age (60-75 years) is significant risk factor for laryngeal cancer (OR= 2.43, 95% CI: 1.18-5.02). As regard sex, male sex was found to be significant risk factor for LC (OR=52.59, 95% ECL: 12.48-457.71). While, low and high education levels were found to be non significant risk factors for LC (ORs=1.81, 95% CI: 0.96-3.45 and 1.23, 95% CI: 0.27-3.29). On the other hand, low occupational level was found to be significant risk factor (OR=1.97, 95% CI: 1.04-3.75). So, collectively low social class was significant risk factor for LC (OR=1.99, 95% CI: 1.05-3.79). Lastly, urban residence was significant risk factor for laryngeal cancer (OR=2.43, 95% CI: 1.01-5.99).

Discussion

The prevalence of laryngeal cancer is increasing over time in much of the world countries **(Cattaruzza, 1996)**.

Hoarseness of voice is the main presenting symptom for our patients with LC. This finding is expected and accepted as the main function of the larynx is phonation **(Rosen and Murry, 2000)**. Tumors arising in the glottis site usually produce hoarseness at an early stage, while in advanced lesions it can produce pain of varying severity, sore throat, referred otalgia and airway obstruction especially if there is subglottic extension. Dysphagia and sore throat are the most frequent initial symptoms with cancer of the supraglottic larynx, with hoarseness and odynophagia usually indicating spread to the glottis and hypopharynx respectively **(Gluckman, 1994)**. Ninety six percent of LC patients had dysphonia **(Farghaly, 1991)**.

Laryngeal cancer may originate in the glottis, supraglottis or subglottis **(Lehmann et al., 1991)**. Glottic carcinomas constitute the majority of the laryngeal malignancies, accounting for 55.0% to 75.0% of primary sites. Supraglottic tumors accounts for 25.0% to 45.0% **(Gluckman, 1994)**. Primary subglottic tumors are rare, constituting 1.0% to 5.0% of laryngeal primary sites and most of the lesions are due to extension from glottic or supraglottic sites **(Gluckman, 1994** and **Bahar et al., 2002)**. In Egypt, 54.0%, 41.0% and 5.0% of the cancer sites' were supraglottis, glottis or subglottis **(Farghaly, 1991)**.

About 95.0% of LCs is squamous cell carcinomas (SCCs) and about 5.0% of all carcinomas of the larynx are not squamous. The more common non squamous tumors of the larynx include those of salivary, cartilaginous and neuroendocrine origin **(Landis, 1999)**. On the other hand, **Farghaly (1991)** reported that SCC represented 78.4% in his cases.

In this study TL was indicated in advanced stages of LCs or after radiation therapy (stage X). Since Billroth performed his first laryngectomy in 1873, TL still the most widely accepted surgical treatment for advanced LC (stage III and IV) **(Silver & Ferlito, 1996** and **Fagan et al., 2002)**. It considered the last resort in the management of laryngeal cancer, especially when other conservative measures are not applicable **(Silver and Ferlito, 1996)**.

Thyroid gland involvement in LC patient can occurs in two conditions, either through direct extension of the laryngeal carcinoma through the thyroid cartilage to involve the thyroid gland or by indirect extension of the laryngeal carcinoma

through intrathyroid lymphatics or veins **(Fagan and Kaye, 1997)**. Therefore; thyroid gland invasion is expected in glottic cancer with subglottic extension, preoperative tracheostomy, fixed vocal fold with paraglottic space involvement, anterior commissure involvement and transglottic tumors to avoid local and stomal recurrence **(Zhao et al., 2009)**.

Pharyngocutaneous fistula (PCF) still one of the most serious postoperative complications following TL. PCF is defined as a breakdown of the mucosal closure of the pharynx, which results in dissemination of saliva into the peripheral neck. This may leads to elevation of the skin flaps with ultimate wound dehiscence, followed by necrosis of the flaps, and in the worst case scenario, carotid exposure and blowout **(Mäkitie et al., 2003)**. The reported incidence of PCF is extremely variable, ranging from 7.0% to 65.0%. A percent between 13.0% and 25.0% has been often reported and only few reports had a percent of less than 10.0% **(Javed et al., 2006)**. In this study the authors found that the suspected risk factors for PCF in this study were patient with supraglottic tumor, had preoperative tracheotomy, low hemoglobin level, diabetic and underwent preoperative radiation therapy.

Neck metastasis is critical in guiding therapy and predicting prognosis. In all laryngeal carcinomas the incidence of cervical metastasis was between 24.0% and 49.0%. Occult cervical nodal metastasis occurs in 16.0% to 28.0%. Negative clinical examination and imaging, exclusively, does not rule out the presence or absence of cervical nodal metastases. In patients who are most likely to have occult nodal metastases, selective neck dissection (SND) has been advocated as both a therapeutic and a staging modality. Radical neck dissection (RND) was reserved for advanced neck metastases **(Tu, 1999)**. In this study, TL was done in patients with advanced stages laryngeal cancer; III and IV. In these patients high incidence of neck metastasis is expected. So, SND (taking level II, III & IV) was done in 95.6% of the patients for N0 and N1 and RND (taking level I-V in addition to sternocleidomastoid muscle, internal jugular vein and spinal accessory nerve) in 4.4% of the patients.

Distant metastases are usually reported as uncommon incidence in laryngeal cancer. The most common site for distant metastases is the lung, bone, liver and esophagus. It is noted that the incidence of distant metastasis increases with the initial stage of the disease. Also, the overall incidence of distant metastasis is 6.0% with stage I, 20.0% with stage II, 32.0% with stage III and 43.0% with stage IV disease **(Kotwall et al., 1987).**

Positive RSI was risk factor for LC. Laryngopharyngeal reflux (LPR) went unrecognized as a clinical entity until it has been implicated in the etiology of LC **(Koufman, 1991)**. But, LPR considered as a modest risk factor for LC **(El-Serag et al., 2001)**. Further, gastroesophageal reflux is often present in patients with neoplastic lesions of the larynx **(Galli et al., 2002** and **Lewin et al., 2003)**. Also, premalignant and malignant changes in the larynx occur more among patients with gastric surgery as duodenogastroesophageal reflux is common after total or partial gastrectomy **(Cianci et al., 2003)**. Further, +ve RSI was more common among LC patients compared with the controls (OR=37.82, 95% CI: 11.29-152.64) **(El-Moselhy et al., 2004)**.

Retired persons are the most common occupation to be a risk factor for laryngeal cancer **(Herrington-Hall et al., 1988)**. Laryngeal cancer may be expected in this group due to the old ages of the retirees. In the present study we didn't included this occupation, but we mentioned the actual previous occupations. Retirement is mainly related to age and/or effects of the disease on the patients. Also, majority of the cancer patients were workers exposed to a variety of hazardous working materials like polycyclic aromatic hydrocarbons, cement dust, metal dusts, asbestos, varnish, lacquer, etc. Further, environmental exposure to airborne carcinogens like fossil fuel single stove emissions may increase the relative risk of laryngeal cancer **(Farghaly, 1991; Maier et al., 1997; Maier & Tisch, 1997** and **Maier et al., 2002)**. Occupations involved dust and fumes exposure as fertilizers factories,

construction and building workers, carpenters, miller and drivers were more present among laryngeal cancer cases **(Farghaly, 1991)**. Also, the factory worker occupation was noticed as one of the most common risky occupations exposing the subject to LC. It was suggested that the working conditions that require breathing irritants in the air are possible causes of vocal pathology in this population **(Herrington-Hall et al., 1988)**. In Egypt, 42.1% of LC cases were farmers. This figure was accepted as they were the majority of these cases **(Farghaly, 1991)**. Farmers presented commonly with LC and this can be explained by the fact that the hospitals with good health care are relatively far from rural areas and this may direct patients with difficult curable diseases that need special medical care for specialized centers **(Herrington-Hall et al., 1988)**. Also; textile processors, laborers, machinists and farmers who had worked at least 15 years, excluding the last 5 years before diagnosis, were identified to be at increased risk of laryngeal cancer **(Flanders et al., 1984)**. Further; workers in plastics manufacturing industries, exposed to bichloro-methyl-ether, were at increased risk of LC **(Zagraniski et al., 1986)**. Also, workers who heavily exposed to nickel, chromium and formaldehyde were found to have fourfold increased risk of LC. Mechanics, drivers of light trucks, spray paint machine operators, metal and plastic working, machine operators, plumbers and pipe fitters, carpenters, construction workers, decorators and bartenders were also identified at increased risk of LC **(Wortley et al., 1992)**. At the same time, bartenders and workers exposed to wood dust and diesel fumes were found at increased risk of LC **(Muscat and Wynder, 1992)**. Also, it was found that workers in the chemical and allied industries have double the risk of developing LC **(Coggon et al., 1986)**. In analysis, and compared occupations and industries of 90 LC cases with patients with other cancers that were not suspected to be associated with occupational exposures; sheet metal workers, mechanics, operators, sailors and laborers had elevated risks as well as workers employed in general construction, rail transportation and lumber manufacturing **(Flanders and Rothman, 1982)**. Also, hotel and restaurant workers found to have elevated risks for LC **(Olsen et al., 1985)**. Further, exposure to diesel oil, mineral oil and gasoline were risk factors for LC. Textile and leather workers were found to be at the highest risk, followed by shippers, stock clerks and service workers. Risk increased with increasing length of employment for most occupations **(Ahrens et al., 1991)**. There is significant elevated risks adjusted for non-occupational variables (as smoking, alcohol consumption and diet) and other occupational exposures were consistently found for organic solvents (OR=1.7, 95% CI: 1.1-2.5) and asbestos (OR=1.6, 95% CI: 1.0-2.5). Analyses restricted to subjects aged 55 or more did not show elevated risks, with the exception of wood dust (OR=1.8, 95% CI: 1.3-2.7) **(Berrino et al., 2003)**. When controlling for age only, LC was associated with ever versus never manual work occupation (OR=2.54, 95% CI: 1.78-3.62) and when adjusted for alcohol and tobacco consumption the risk decreased (OR=1.91, 95% CI: 1.23-2.95) **(Menvielle et al., 2004)**. Glass wool production was found to be associated with increased mortality from LC **(Bertazzi et al., 1986)**. But, a negative association existing was found between exposure to man-made mineral fibers and LC **(Gardner et al., 1986)**. On the other hand, some occupations were found to be protective factors, but the house wife was the only significant occupation. This may be expected and accepted in this group due to their presence in homes far away from hazardous pollutions and irritants. Also, they relatively non smokers and drinkers compared to men.

Smoking is risk factor for LC. Further, its prevalence is increasing in much of the world and this increase is generally accepted to be related to changes in tobacco consumption **(Cattaruzza, 1996)**. The studies establish that tobacco use causes most cancers of larynx. Tobacco smoke contains many carcinogens. Also, it is chronically irritating to the laryngeal mucosa and at the extreme it can provoke

cancer. Most of studies indicate that risk increases with increasing amounts of tobacco use **(Hanson & Jiang, 2000** and **Thun et al., 2002)**. Further, it is postulated that the high incidence of LC observed in Varese, Italy, relative to the average for all Italian provinces can be explained by the higher prevalence of smoking among this population. In addition, a higher proportion of Varese smokers started smoking before the age of 18 **(Berrino and Crosignani, 1992)**. So, it is predicted that the incidence rates of LC will continue to increase until the cohort born in 1940 reaches age 70 in 2010. Thereafter, there will be a decrease in rates, which reflect the decrease in the proportion of smokers in Italy **(Ferrano, 1992)**. Also, it is mentioned that the risk of LC steadily decreased from 3 years after stopping smoking **(Altieri et al., 2002)**. Further, passive smoking was found to be a significant risk factor for LC. The effects of passive smoking is evident in elevated levels of protein adducts in exposed non-smokers **(Phillips, 2002)**. Results of two studies on LC showed that relative risk (RR) estimates from the earlier study **(Wynder et al., 1956)**, included cases with carcinoma of the pyriform sinus, was substantially higher for smoking than from the later study **(Wynder et al., 1976)**. The higher tar content of cigarettes and the inclusion of pyriform sinus cases may explain, in part, this higher RR estimates. Exclusive use of filter cigarettes had been found to be protective relative to exclusive use of plain cigarettes. Also, use of black tobacco has been reported to be associated with at least a doubling in risk for LC compared with use of blond tobacco. Black tobacco is richer in aromatic amines and tobacco-specific nitrosamines than blond tobacco. Non-inhalers of smoke also had a decreased risk for LC relative to inhalers **(Pequignot et al., 1988** and **Sancho-Gamier & Theobald, 1993)**. Further, black tobacco and no filter cigarettes yield higher tar content than blond tobacco and filter cigarettes. Smokers of cigarettes with tar-yields of ≥22 mg/cigarette were twice as likely as smokers of cigarette brands with <22 mg tar-yield to develop LC **(La Vecchia et al., 1990)**. Smoking of hand-rolled cigarettes had 2.7 times the risk to have LC relative to smoking commercially manufactured cigarettes **(De Stefani et al., 1992)**. Also, pipe and cigar smoking were associated with a threefold increase in risk **(Wynder and Stellman, 1977)**. On the other hand, pipe and cigar smoking were not associated with increased risk for LC **(Freudenheim et al., 1992)**. Further, studies have confirmed that risk of developing LC decreases with increasing time since cessation of smoking **(De Stefani et al., 1992)**. This evidence indicates that tobacco acts as a promoter as well as an initiator in carcinogenesis **(Sankaranarayanan et al., 1990)**. Also, it was found that current smokers had a 32.5 RR for LC compared with nonsmokers. This risk dropped to 15.1 after adjusting for socioeconomic status **(Hirayama, 1990)**. Differences have been observed for mortality rates from LC with gender differences following closely the smoking time trends within each population **(La Vecchia et al., 1993)**. In Egypt, smokers were more common among LC group compared with controls; 93.7% vs. 22.8% **(Farghaly, 1991)**. Further, smoking was found to be a significant risk factor for LC (OR=37.82, 95% CI: 11.29-152.64) **(El-Moselhy et al., 2004)**.

Alcohol intake emerged as a risk factor for LC. The prevalence of LC is increasing in much of the world and this increase is generally accepted to be related to changes in alcohol consumption **(Cattaruzza, 1996)**. Relative risk estimates for LC was substantially high for alcohols intake **(Wynder et al., 1976** and **Rothman et al., 1980)**. The risk for LC reaches more than 5 fold in case of alcohol intake (OR= 5.15, 95% CI: 1.17-19.25) **(El-Moselhy et al., 2004)**. Compared with nondrinkers, men drinking >4 glasses daily had 11 times the risk of developing LC. Women had a 700 times increase in risk when drinking 1-2 glasses daily compared with a 22 times increase among men drinking equivalent amounts. The difference between men and women is most likely due to the low background exposure to other risk factors in women **(Choi and Kahyo, 1991)**. Also, differences have been observed for

mortality rates from laryngeal cancer with gender differences following closely the alcohol drinking time trends within each population **(La Vecchia et al., 1993)**. It is concluded that decline in LC risk was observed only 20 years or more after stopping drinking **(Altieri et al., 2002)**.

Further, tobacco and alcohol consumption by the cancer patients was roughly twice as great as in their controls **(Maier et al., 1997)**. Tobacco and alcohol act synergistically in elevating the risk of development of LC, because joint exposure results in much higher relative risk estimates than would be expected if alcohol and tobacco acted independently **(Guenel et al., 1988)**. Moreover, the effects of alcohol and tobacco on cancer risk were multiplicative rather than merely additive **(Maier et al., 1997)**.

Non healthy diet consumption proved to be risk factor for occurrence of laryngeal cancer. However, the results of epidemiological studies have been mixed. On the one hand, vegetables and fruits have been shown to be inversely associated with several forms of cancers including LC. On the other hand, the information concerning specific macro- or micro-nutrients in relation to particular forms of cancer has been very limited and mostly inconclusive **(Lagiou et al., 2002)** or failed to reveal any clear differences tending to incriminate any particular food **(Maier et al., 1997)**. High intake of fruits and vegetables has been associated with reduced risk of cancer **(La Vecchia et al., 1993)**. Phytochemicals in fruits and vegetables are suggested to be the major bioactive compounds for the health benefits **(Sun et al., 2002)**. Also, high intake fish found to be protective against developing LC **(Hirayama, 1990)**. So, the regular and frequent intake of fruits, salad and dairy products that contain considerable amounts of tumor protective micronutrients may decrease the risk of LC **(Maier & Tisch, 1997** and **Maier et al., 2002)**. The consumption of at least 5 fresh vegetables and/or fruits per week is protective against cancer **(WHO, 2001)**. Also, a high consumption of plant foods was protective (OR=0.42, 95% CI: 0.21-0.84). Subgroups of plant foods, fruits and raw vegetables were more protective (OR= 0.29, 95% CI: 0.15-0.56). Subjects whose intake was ≤1/3 of the recommended daily allowance (RDA) of vitamin A or ≤1/2 the RDA for vitamin C were at more than 2-fold the risk of developing LC, compared with those whose intake was at least the RDA for these nutrients **(Graham et al., 1981)**. Further, the joint effect of heavy smoking and the low intake of vegetables and fruits displayed an increased risk (OR=19.2, 95% CI: 5.7-64.9) **(De Stefani et al., 2000)**. Also, higher intake of vitamin E, carbohydrates and fiber were protective, relative to those in the lower intake categories for these nutrients **(Tavani et al., 1994)**. Further, higher zinc levels in nail tissue were associated with lower relative risks **(Rogers et al., 1993)**. Moreover, a significant risk was found for high consumption of fried meat, fish, eggs and potatoes (ORs=1.6, 3.1, 1.9 and 1.9, respectively) **(Bosetti et al., 2002)**. Further, the amount of alcohol consumed is inversely related to the intake of numerous nutrients (protein, vitamins A, B1, B2, riboflavin, niacin, calcium, iron and fiber). Also, smoking is inversely related to the intake of several nutrients as well as to levels of some important nutrients in blood. Thus, some of the associations found between nutrients intake and risk of LC may reflect, in part, residual confounding by smoking and drinking habits **(Kelly, 2002)**.

The peak incidence of the LC was 50-60 years of age **(Maier et al., 1997)**. LC equally affects the 45-64 and ≥65 year's age groups **(Herrington-Hall et al., 1988)**. Also, it affects commonly the 45-64 and ≥65 year's age groups **(Coyle et al., 2001)**. The highest incidence was recorded for black men aged 65-69. While, the highest incidence for white men occurred for those aged 70-74 **(Miller, 1990)**. In Egypt, 60.0% of laryngeal cancer cases were in the sixth and seventh decades **(Farghaly, 1991)**. Also, LC affects commonly the oldest age, ≥65 years **(El-Moselhy et al., 2004)**.

The incidence rates of laryngeal cancer are substantially higher among men

than women throughout the world **(Parkin, 1992)**. The cases of laryngeal cancer occurring predominantly in males have been speculated to result from the different susceptibilities of the tumor cells to steroid sex hormones. The sex hormone action is mediated by specific cellular receptors. The data on the receptor status for androgen, estrogen and progesterone receptors in laryngeal carcinomas are controversial. But, the assured absence of male and female sex hormones receptors strongly argues against that laryngeal carcinomas being sex hormone-dependent tumors **(Hagedorn and Nerlich, 2002)**. LC was found to be more occurred significantly among males **(Herrington-Hall et al., 1988** and **Coyle et al., 2001)**. But, LC is becoming frequent in females; the male to female ratios have decreased from 15/1 in 1947 to 7/1 in 1978 **(Dorn & Cutler, 1959** and **American Cancer Society, 1978)**. In Egypt, male to female ratio was 23:1 **(Farghaly, 1991)**. Male sex was associated with high risk (OR=10.61, 95% CI: 41.56-25.90), but the prevalence of females in our earlier group was higher than this group, 7.1% vs. 2.2% **(El-Moselhy et al., 2004)**. These results are attributed to increased smoking and working in women **(Stellman and Stellman, 1981)**.

Low educational standard is associated with high risk for laryngeal cancer **(Maier & Tisch, 1997** and **El-Moselhy et al., 2004)**. The educational level in LC group was significantly lower than controls (P<0.001) **(Maier et al., 2002)**. Further, the proportion of laryngeal cancer patients who had completed technical college or university education was significantly lower than in the controls (9.6% vs. 24.4%; P<0.001) **(Maier et al., 1997)**. Also, in Egypt the educational level in laryngeal cancer group was low **(Farghaly, 1991)**. The low educational standard is associated with 2-fold risk for laryngeal cancer (OR=2.21, 95% CI: 1.23-4.00) **(El-Moselhy et al., 2004)**. Further, when controlling for age, laryngeal cancer was strongly associated with low educational level (OR=3.22, 95% CI: 2.01-5.18) **(Menvielle et al., 2004)**.

Laryngeal cancer was strongly associated with low occupational level (manual worker) and with all indicators based on occupation (OR=2.54, 95% CI: 1.78-3.62) **(Menvielle et al., 2004)**. Also, relative risk for LC was higher among workers in the least skilled work class compared with those in the professional and most skilled work classes **(Pearce and Howard, 1986)**. The majority of the LC patients were blue-collar workers who were exposed to a variety of hazardous working materials. Also, low occupational training was associated with high risk. **(Maier and Tisch, 1997)**. About 17.0% of laryngeal cancer patients and 7.0% of control persons had not completed their professional training. The percentage of so-called blue-collar workers was significantly higher in the cancer group (20.9% vs. 7.3%; P<0.002) **(Maier et al., 2002)**. In Egypt, the occupational level in laryngeal cancer group was low **(Farghaly, 1991)**. Further, low occupational level was associated with high risk for LC (OR=3.58, 95% CI: 1.92-6.72) **(El-Moselhy et al., 2004)**.

Collectively, social inequalities for laryngeal cancer were observed **(Menvielle et al., 2004)**. Our result agreed with many other studies, which cleared that socioeconomic status and social class are important determinants of laryngeal cancer risk **(Hirayama, 1990; Menvielle et al., 2004** and **El-Moselhy et al., 2004)**. The risk for laryngeal cancer reaches up to 3-folds in case of low social level (OR= 2.99, 95% CI: 1.64-5.48) **(El-Moselhy et al., 2004)**. Also, low socioeconomic status was associated with an increase in risk of developing LC after controlling for tobacco and alcohol consumption, marital status, dental care, and history of tuberculosis **(Elwood et al., 1984)**. On the other hand, refusal to participate could be associated with selection bias, as controls of lower socioeconomic class may be less likely to agree to be interviewed **(Giordano et a1., 1990)**.

Incidence rates of laryngeal cancer appear to be highest among men in urban areas **(Pequignot et al., 1988** and **Sancho-Gamier & Theobald, 1993)**. Also, it is

suggested that factories that produce irritants in the air are possible causes of laryngeal cancer in urban areas **(Herrington-Hall et al., 1988)**.

Conclusions and recommendations

It could be concluded that the most important clinical features of the studied LC patients were most lesions was glottis (56.7%), presented with hoarseness of voice (85.6%) and in stage III (63.3%). Also, the most important characteristics of surgery in the patients were most cases had TL and primary TEP (64.4%), had thyroidectomy (88.9%) and had preoperative tracheostomy (25.6%). Positive RSI was significant risk factor (OR=6.77). Also, factory worker occupation was significant risk factor (OR= 4.65). The most important health behavioral risk factors were cigarette smoking, goza smoking and no healthy food intake (ORs= 4.44, 4.25 and 2.74; respectively). Further, the most important sociodemographic risk factors for LC were male sex, urban residence, old age, low social class and low occupational level (ORs=52.59, 2.43, 2.43, 1.99 and 1.97; respectively). Population based studies are needed in different areas in Egypt and on large number of patients to determine the full epidemiology of the laryngeal cancer and quality of life of these patients.

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Table (1): Characteristics and clinical features of the studied patients with laryngeal cancer.

Characteristics and clinical features of the patients with laryngeal cancer	N=90	%
Presenting symptom(s):		
Hoarseness of voice	77	85.6
Referred otalgia	54	60.0
Stridor	34	38.8
Dysphagia	33	36.7
Odynophagia	31	34.4
Cough and/or heamoptesis	31	34.4
Site of the lesion:		
Glottis	67	74.4
Supraglottis	23	25.6
Histopathological features:		
Squamous cell carcinoma	90	100.0
Tumor size (T):		
T3	59	65.6
T4	29	32.2
Tx (can not be assessed)	2	2.2
Lymph node (N):		
N0	64	71.1
N1	17	18.9
N2	8	8.9
N3	1	1.1
Metastasis (M):		
M0 no distant metastasis at time of surgery	90	100.0
Stage of the lesion:		
Stage III	57	63.3
Stage IV	31	34.4
Stage X (can not be assessed)	2	2.2
Associated diseases:		
Chronic obstructive disease	24	26.4
Hepatitis C virus infection	15	16.7
Diabetes mellitus	13	14.4
Hypertension	12	13.3
Coronary heart disease	9	10.0

Table (2): Characteristic features of surgery in patients underwent total laryngectomy.

Patients' characteristics	Patients (N=90)	%
Total laryngectomy (TL)	90	100.0
TL + primary tracheoesophageal puncture (TEP)	58	64.4
TL + secondary TEP	28	31.2
TL without primary or secondary TEP	4	4.4
Selective neck dissection (SND):		
Yes:	86	95.6
Right II, III, IV	71	78.9
Left II, III, IV	59	65.6
Radical neck dissection (RND):		
Yes:	4	4.4
Right RND	1	1.1
Left RND	3	3.3
Thyroidectomy:		
Yes:	80	88.9
Right lobectomy	29	32.2
Left lobectomy	45	50.0
Total	6	6.7
Preoperative tracheostomy:		
Yes	23	25.6
Pharyngocutaneous fistula (PCF):		
Yes	14	15.6
Distant metastasis (at follow up):		
Yes:	4	4.4
Pulmonary	3	3.3
Esophageal	1	1.1

Table (3): Distribution of the patients with laryngeal cancer and control group according to their reflux symptoms index (RSI).

Positive reflux symptoms index	Laryngeal cancer (n=90)		Control group (n=90)		OR (95% ECL)
	NO.	%	NO.	%	
Yes	12	13.2	2	2.2	6.77 (1.43-63.57)*

Table (4): Distribution of the patients with laryngeal cancer and control group according to their occupational type risk factors weights'.

Occupation	Laryngeal cancer group (n=90)		Control group (n=90)		OR (95% CI) OR (95% ECL)*
	NO.	%	NO.	%	
Factory worker	16	17.8	4	4.4	4.65 (1.41-19.80)*
Sale man	12	13.3	5	5.6	2.62 (0.81-9.87)*
Construction worker	5	5.6	3	3.3	1.71 (0.32-11.29)*
Driver	9	10.0	6	6.7	1.56 (0.47-5.55)*
Other	9	10.0	6	6.7	1.56 (0.47-5.55)*
Farmer	10	11.1	7	7.8	1.48 (0.49-4.57)
professional	12	13.3	12	13.3	1.00 (0.39-2.56)
House wife	1	1.1	28	31.1	0.02 (0.00-0.16)*
Teacher	5	5.6	7	7.8	0.70 (0.17-2.67)*
Skilled worker	11	12.2	12	13.3	0.91 (0.35-2.36)

Table (5): Distribution of the patients with laryngeal cancer and control group according to their life style and health behavioral risk factors.

Variable	Laryngeal cancer group (n=90)		Control group (n=90)		OR (95% CI) OR (95% ECL)*
	NO.	%	NO.	%	
Smoking:					
Yes	88	97.8	37	41.1	63.03 (14.90-548.04)*
Cigarettes:	63	70.0	31	34.4	4.44 (2.27-8.75)
Pack/day:					
0.5-	19	21.1	14	15.6	1.45 (0.64-3.33)
1.5-	9	10.0	3	3.3	3.22 (0.76-19.03)*
2-	22	24.4	10	11.1	2.59 (1.08-6.34)*
≥3	13	14.4	4	4.4	3.63 (1.06-15.83)*
Duration (years):					
<25	13	14.4	17	18.9	0.72 (0.31-1.71)
≥25-	24	26.7	12	13.3	2.36 (1.03-5.47)
≥40	26	28.9	2	2.2	17.88 (4.17-158.79)*
Goza:					
Hagar/day:	18	20.0	5	5.6	4.25 (1.42-15.27)*
3-6	12	13.3	4	4.4	3.31 (0.95-14.57)*
≥7	6	6.7	1	1.1	6.36 (0.74-295.63)*
Duration (years):					
<35	5	5.6	3	3.3	1.71 (0.32-11.29)*
≥35	13	14.4	2	2.2	7.43 (1.59-69.22)*
Cigarette and Goza:					
Yes	7	7.8	1	1.1	7.51 (0.92-342.00)*
Passive smoking:					
Yes	89	98.9	61	67.8	42.31 (6.55-1746.95)*
Alcohol intake:					
Yes:	4	4.4	1	1.1	4.14 (0.40-206.11)*
Social	1	1.1	1	1.1	1.00 (0.01-79.37)*
Heavy	3	3.3	0	0.0	Undefined
Duration (years):					
<15	3	3.3	1	1.1	3.07 (0.24-162.89)*
≥15	1	1.1	0	0.0	Undefined
Smoking & alcohol intake:					
Yes:	4	4.4	1	1.1	4.14 (0.40-206.11)*
Healthy diet intake:					
No	82	91.1	71	78.9	2.74 (1.06-7.32)

Table (6): Distribution of the patients with laryngeal cancer and control group according to their sociodemographic risk factors.

Variable	Laryngeal cancer group (n=90)		Control group (n=90)		OR (95% CI) OR (95% ECL)*
	NO.	%	NO.	%	
Age at diagnosis (years):					
30-44	9	10.0	31	34.4	0.21 (0.09-0.51)
45-59	47	52.2	41	45.6	1.31 (0.70-2.45)
60-75	34	37.8	18	20.0	2.43 (1.18-5.02)
Sex:					
Male	88	97.8	41	41.6	52.59 (12.48-457.71)*
Female	2	3.2	49	54.4	0.02 (0.00-0.08)*
Educational level:					
Low	45	50.0	32	35.6	1.81 (0.96-3.45)
Middle	33	36.7	48	53.3	0.51 (0.27-0.96)
High	12	13.3	10	11.1	1.23 (0.46-3.29)
Occupational level:					
Low	48	53.3	33	36.7	1.97 (1.04-3.75)
Middle	30	33.3	45	50.0	0.50 (0.26-0.95)
High	12	13.3	12	13.3	1.00 (0.39-2.56)
Social class level:					
Low	46	51.1	31	34.4	1.99 (1.05-3.79)
Middle	32	35.6	47	52.2	0.50 (0.27-0.96)
High	12	13.3	12	13.3	1.00 (0.39-2.56)
Residence:					
Urban	80	88.9	69	76.7	2.43 (1.01-5.99)
Rural	10	11.1	21	23.3	0.41 (0.17-0.99)

سرطان الحنجرة: عوامل الخطورة الاجتماعية - الديموجرافية والإكلينيكية وأسلوب الحياه لدى المرضى المعالجين بالاستئصال الكلى للحنجره

عصام عبد المنعم المصيلحى – يحيى محمد صالح – محمد محمود الصاوى*–
إيمان شكرى عبد الله – يحيا عبد العظيم بركه –**
طلعت محروس فرغلى*
قسم طب المجتمع - أنف وأذن وحنجرة* - تمريض طب المجتمع**
كلية الطب - جامعة الأزهر وكلية التمريض – جامعة الزقازيق

يُعتبر سرطان الحنجرة واحداً من أهم أورام الجهاز التنفسى. كما أن معدل انتشار هذا المرض يزداد فى كل انحاء العالم. كما أنه يمثل مشكلة صحية هامة وله تأثيرات ضارة على نوعية حياة هؤلاء المرضى . إن الهدف من هذا البحث هو تحديد الخصائص الإكلينيكية لمرضى سرطان الحنجرة و أشكال علاجهم وتحديد عوامل الخطورة الاجتماعية-الديموجرافية والسلوكية و الإكلينيكية و كذلك دراسة نوعية الحياة لمرضى سرطان الحنجرة. و قد أُجريت هذه الدراسة على 90 مريضاً ممن يعانوا من مرض سرطان الحنجره وكذلك على عدد مساوٍ من الأشخاص السالمين كمجموعة ضابطة. وقد أُستخدم نمط دراسة الحالة الضابطة بالمستشفى لإجراء هذا البحث.

وكانت أكثر الخصائص الإكلينيكية شيوعاً لمرضى سرطان الحنجره: وجود سرطان الحنجره على الثنيات الصوتية (56.7%)، بُحَّة الصوت (85.6%) و المرحلة الثالثة للمرض (63.3%). وكانت أكثر خصائص العلاج شيوعاً لمرضى سرطان الحنجرة: استئصال كُلى للحنجرة (64.4%)، استئصال الغدة الدرقية (88.9%) و إجراء شق حنجرى قبل إجراء العملية (25.6%). وقد كان معامل ارتجاع الحامض المعوى بالحنجرة والحلق الايجابى عامل خطورة (نسبة أودز = 6.77) . ومثلت وظيفة عامل بمصنع عامل خطورة (نسبة أودز =4.65). وكانت أهم مظاهر السلوك الصحى السلبى شيوعاً لمرضى سرطان الحنجرة: تدخين السجائر والجوزة وعدم تناول طعام صحى (نسبة أودز = 4.44 ، 4.25 ، 2.74 على الترتيب) . وكانت أهم عوامل الخطورة الاجتماعية-السكانية ذات الدلالة الاحصائية لمرضى سرطان الحنجرة: المرحلة العمرية المتقدمه (60-75 عام)، الرجال كجنس، المستوى الوظيفى المتدنى، المستوى الاجتماعى المتدنى، و سكنى المدينة (نسبة أودز = 52.59،2.43 ، 1.97، 1.99 و 2.43 على الترتيب). وأخيراً فإن هناك حاجة لمزيد من الدراسات بين السكان فى مناطق مختلفة من مصر وعلى أعداد كبيرة من المرضى للتحديد الكامل لوبائيات هذا المرض وتأثيره على جودة حياة هؤلاء المرضى.