ORIGINAL STUDY

Clinical-demographic characteristics of laryngeal cancer at a third level of care

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ABSTRACT

BACKGROUND. Cancer is currently one of the greatest challenges in public health. In Mexico, cancer has remained in second or third place, as one of the leading causes of death.

OBJECTIVE. To describe the clinical and demographic characteristics of laryngeal cancer.

MATERIAL AND METHODS. We performed a retrospective, analytical, observational, cross-sectional study with the review of records in patients with laryngeal cancer in a period of 5 years. The variables age, sex, state of origin, occupation, clinical data were taken. A descriptive analysis of the variables and inferential statistics were carried out with Chi2 and Fisher's exact test in search of association between tobacco and alcohol, occupation and stages of cancer. A p-value <.05 was considered statistically significant.

RESULTS. From January 2015 to December 2019, 62 records were selected, the male sex was involved in a 5:1 ratio, with an average age of 67 years. Squamous cell carcinoma was the most common pathological finding, the most frequent sub-site was glottis, stages III-IV present with greater constancy, dysphonia the most common symptom. Smoking alone or combined with alcoholism was associated with more advanced steps.

CONCLUSION. Male in the seventh decade of life who presents with dysphonia of long evolution, of day labor occupation and history of smoking with or without alcoholism, is the clinical pattern of a patient with glottic squamous cell carcinoma in advanced stage.

KEYWORDS: characteristics, clinical, demographic, laryngeal cancer, third level of care.

INTRODUCTION

Laryngeal cancer ranks first among head and neck tumors, accounting for the second most common respiratory tract cancer in the world, only behind the lung cancer[1-4]. It accounts for 2.8% of new cases of cancer in men worldwide, corresponding to the tenth most frequent malignancy in this gender[2].

During 2018, an incidence of 177,422 cases and 94,771 associated deaths were reported worldwide, at all ages and both sexes[5].

Head and neck cancer encompasses a group of related neoplasms that arise in the oral cavity, pharynx and larynx, being the sixth in frequency worldwide[6].

The incidence of laryngeal cancer varies throughout the world, where the most affected countries are those considered industrialized, increasing by approximately 3% each year, especially high in Spain, France, Italy, Brazil, Poland[7]. The highest mortality from laryngeal cancer was reported in France, Uruguay, Spain, Italy, Cuba, Argentina, Brazil, Colombia and Greece[7].

In 2018, the Caribbean region reported an incidence of 2,678 cases, 2,344 men and 334 women, and a mortality of 1,475, 1,294 men and 181 women, Central America reported an incidence of 1,969 cases, 1,634 men and 335 women, while South America reported 12,397 new cases of which 10,332 men and 2,065 women[5].

In Latin America, cancer is positioning itself as the second cause of death after diseases of the circulatory system, although in men it is, since 2000, the first cause of death. By 2012, three out of 10 deaths in men and two out of 10 in women were from cancer[8-10].

In Mexico, during 2006, malignant tumors were the third cause of death; out of 63,888 (12.9%) deaths registered, 2.5% in men and 0.4% women corresponded to laryngeal cancer. Cancer of the larynx occupies the first

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site in frequency of the total number of upper aerodigestive tract cancers, followed by that of the oral cavity. 95% correspond to squamous cell carcinoma, most often diagnosed in men of 60-70 years of age with a history of smoking and intake of alcoholic beverages, chronic exposure to substances such as paints, metals and plastics. In young patients of both sexes, in association with the human papillomavirus, the most frequent site of cancer is the glottis 59%, supraglottis 40% and subglottis 1%[11].

Aldaco-Sarvide et al. found that, in relation to the cases of cancer mortality per 100,000 inhabitants, the 10 states with the highest mortality were: 1) Mexico City 117, 2) Sonora 79.4, 3) Nuevo Leon 77.4, 4) Sinaloa 76.4, 5) Colima 75.8, 6) Chihuahua 74.4, 7) Jalisco 74.3, 8) Veracruz 72.6, 9) Tamaulipas 71.8, 10) Yucatan 71.6 deaths per 100,000 inhabitants[12]. According to the histological registry of malignancies of the Ministry of Health in Mexico, in 2000 there were 936 cases of laryngeal cancer, representing 1% of the malignancies diagnosed that year and occupies the sixth place of the total malignancy pathology, being more common in male patients over 65 years[13]. The classic risk factors for the development of laryngeal cancer are tobacco and alcohol[14,15].

The larynx can harbour different histologic types of primary malignancies (adenocarcinomas, sarcomas, lymphomas, carcinoid tumors), but the most common is the squamous cell carcinoma. In fact, the larynx is the second most common region in the primary site of epithelial carcinomas[16].

Since 1979, both the quality of the cancer registry and the classification of death certificates in Mexico have improved considerably. A database with mortality and 22 other variables is currently available. However, there is no national registry of new cases, so it is not possible to identify the incidence, distinguishing its compensatory effect on the analysis of survival and cancer mortality attributable to tobacco use[17].

Cancer death has steadily increased in the last decade, from a rate of 59 to 66 events per 100,000 inhabitants. Changes in lifestyle and population dynamics in the coming years are expected to have an unfavourable impact on mortality[17].

Some authors have studied, particularly, a group of patients with cancer of the larynx, not related to tobacco and alcohol. The distribution by gender did not present significant difference and the most frequent location site of the cancer was the glottic region[18].

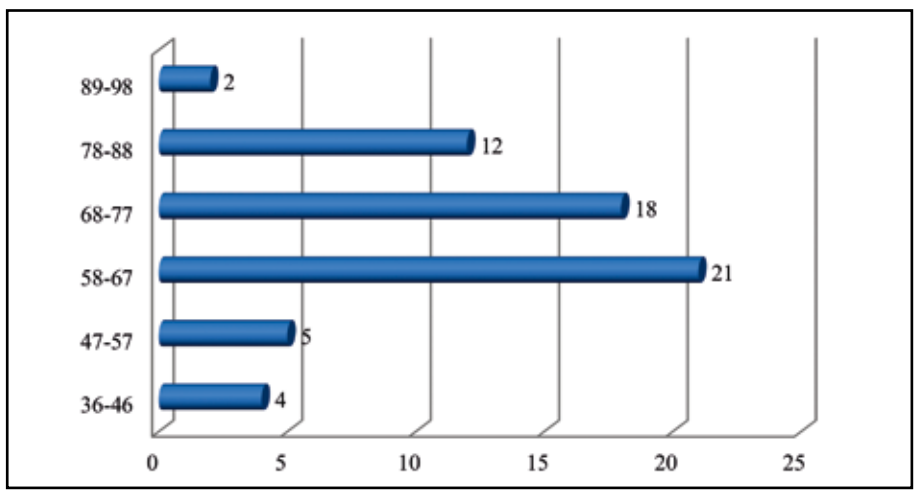
Our objective was to describe the demographic data of the patients treated at our institution with a diagnosis of laryngeal cancer from 2015 to 2019, as well as to search for the association of some risk factors.

MATERIAL AND METHODS

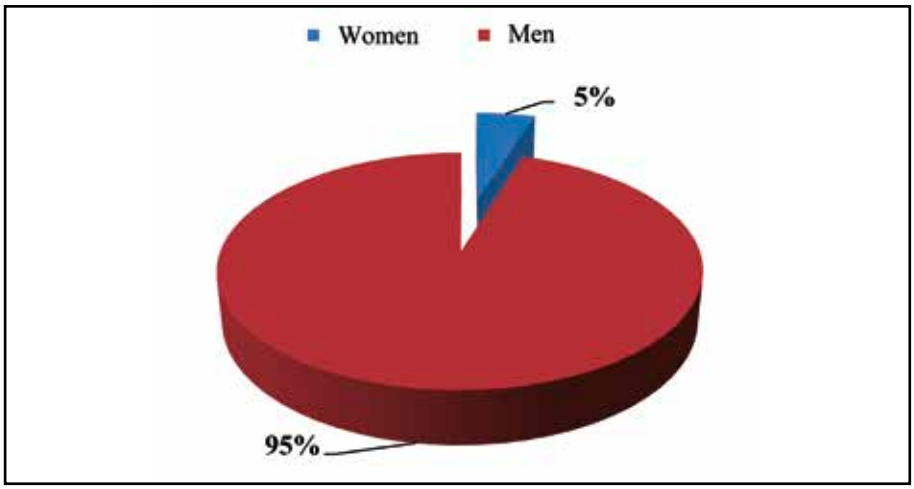
An observational, analytical, retrospective, cross-sectional study was carried out, with the review of records of patients with laryngeal cancer in the Otolaryngology Service of the Specialty Hospital No. 2 of the Mexican Institute of Social Security, Ciudad Obregón, Sonora, between 2015-2019. Demographic data were obtained for each patient included in the study: age, sex, occupation, smoking, alcoholism, time of evolution, symptoms, location of the neoplasm, clinical stage, definitive histological diagnosis. Our study population included all those entitled to social security in the states of Baja California Norte and Sur Sinaloa and Sonora, who are sent to perform biopsy at our service for laryngeal tumors.

Statistical analysis

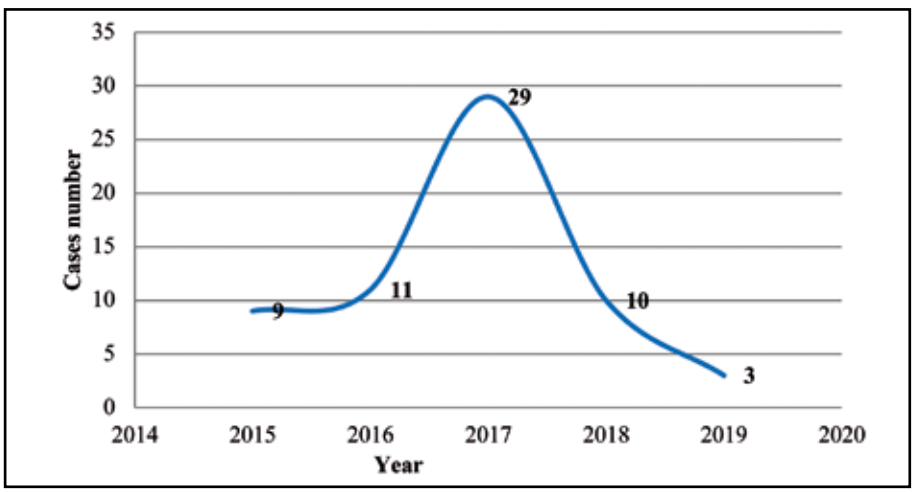
The variables we monitored were: age, sex, state of



Graphic 1. Distribution of the patients from the study group according to age (Source: Otolaryngology Service, Specialty Hospital No. 2, IMSS, Ciudad Obregón, Sonora, 2015-2019).



Graphic 2. Distribution of the patients from the study group according to sex (Source: Otolaryngology Service, Specialty Hospital No. 2, IMSS, Ciudad Obregón, Sonora, 2015-2019).



Graphic 3. Distribution per year of the patients from the study group (Source: Otolaryngology Service, Specialty Hospital No. 2, IMSS, Ciudad Obregón, Sonora, 2015-2019).

origin, clinical data, smoking, alcoholism, occupation, time of evolution, symptoms, clinical stage, histopathological diagnosis, location. A descriptive analysis of the variables was carried out with central tendency drugs, as well as an inferential statistic with Fisher's exact test in search of association between tobacco, alcohol or both, occupation, main symptoms and the stages of cancer in its diagnosis. A p-value <.05 was considered statistically significant. The pre-designed Excel sheets were used and later exported to the SPSS version 22 statistical program for Windows.

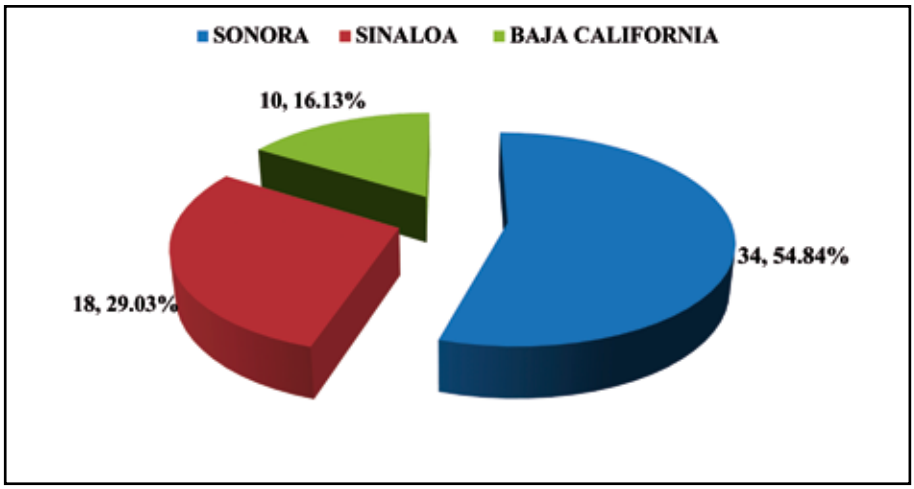
RESULTS

Of a total of 130 records considered in the study period for laryngeal symptoms reviewed, 62 complete files were located from January 2015 to December 2019, for an incidence of 62 cases in 5 years. The average age was 67.91 years (range 36 to 91), the most affected age group was the decade 58 to 67 with 21 cases, followed by the 68 to 77 decades with 18 cases (Graphic 1). Male gender was found in 59 cases (95%), and female in 3 cases (5%), the male-female ratio of 5:1 (Graphic 2).

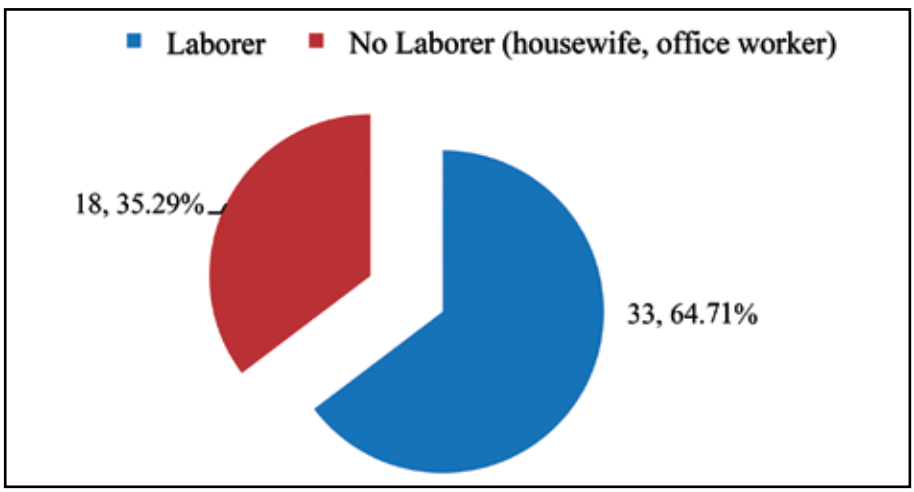
Regarding the distribution by year, in the period of 5 years, the highest number of cases - 29 - was found that in 2017, followed by 2016 with 11, 2018 with 10 and 2019 with 3 (Graphic 3).

The distribution by state was as follows: 34 cases (54.84%) in Sonora, followed by Sinaloa with 18 (29.03%) and Baja California south and north with 10 (16.13%) (Graphic 4).

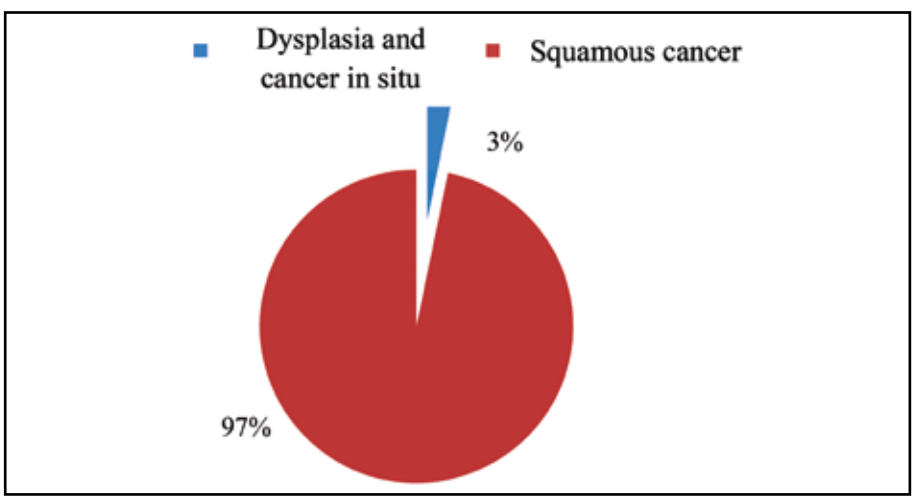
The occupation was registered in 51 cases and we divided them into day laborers and non-day laborers



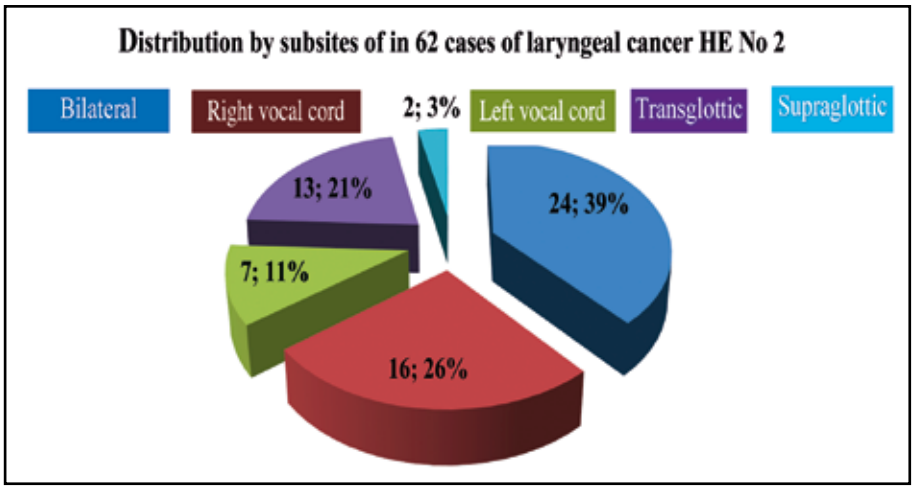
Graphic 4. Distribution by State of the patients from the study group (Source: Otolaryngology Service, Specialty Hospital No. 2, IMSS, Ciudad Obregón, Sonora, 2015-2019).



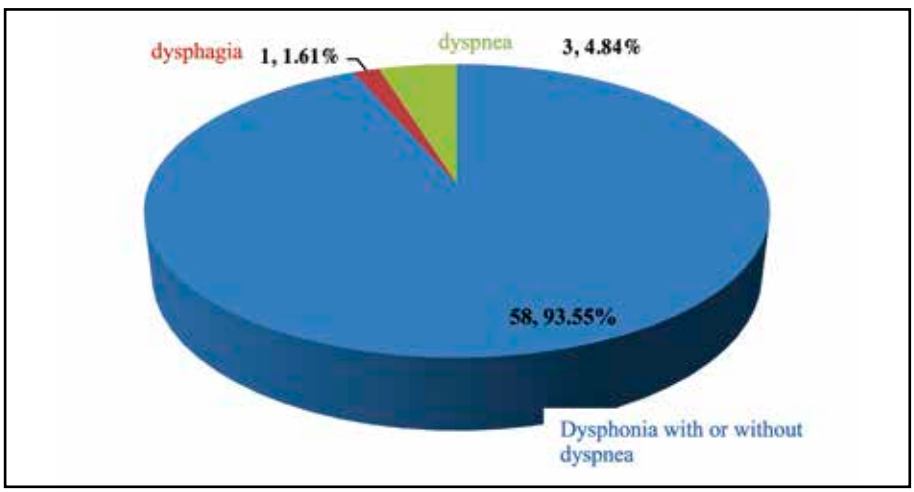
Graphic 5. Distribution of the patients from the study group according to their occupation (Source: Otolaryngology Service, Specialty Hospital No. 2, IMSS, Ciudad Obregón, Sonora, 2015-2019).



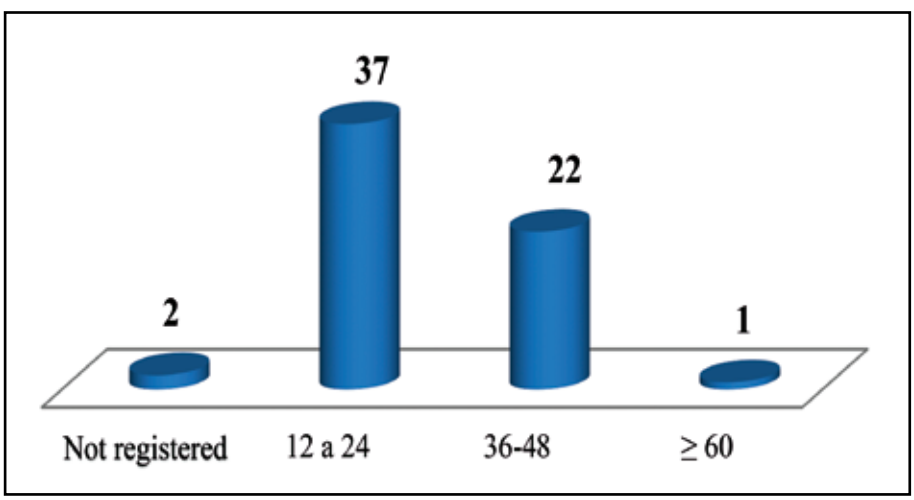
Graphic 6. Distribution of the patients from the study group according to histological type (Source: Otolaryngology Service, Specialty Hospital No. 2, IMSS, Ciudad Obregón, Sonora, 2015-2019).



Graphic 7. Distribution of the patients from the study group according to the tumoral subsites (Source: Otolaryngology Service, Specialty Hospital No. 2, IMSS, Ciudad Obregón, Sonora, 2015-2019).



Graphic 8. Distribution of the patients from the study group according to the symptoms (Source: Otolaryngology Service, Specialty Hospital No. 2, IMSS, Ciudad Obregón, Sonora, 2015-2019).



Graphic 9. Distribution of the patients from the study group according to the time of symptoms evolution in months (Source: Otolaryngology Service, Specialty Hospital No. 2, IMSS, Ciudad Obregón, Sonora, 2015-2019).

(domestic workers, office workers and workers), finding 18 (35.29%) non-day laborers and 33 (64.71%) day laborers (see Graphic 5).

Among the results of the histopathological study, squamous cell carcinoma was found in 60 cases (97%), one case of dysplasia and one of carcinoma in situ (Graphic 6).

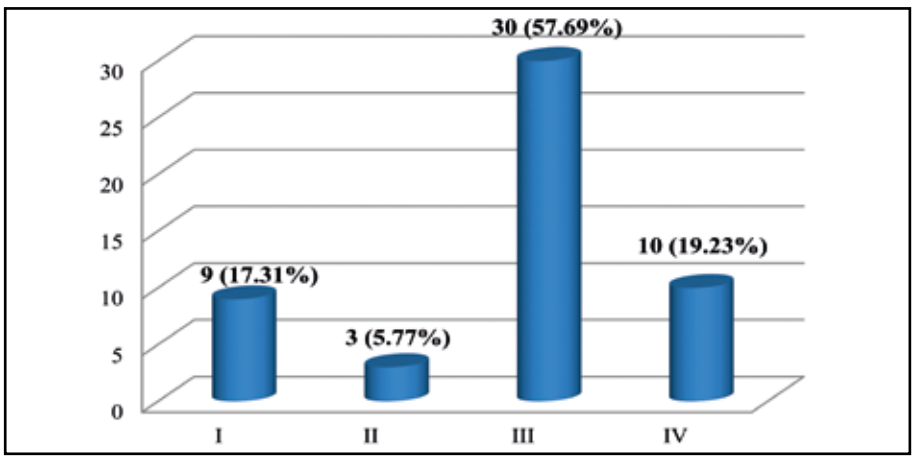
The most involved laryngeal sub-site was the glottic space (both vocal cords) with anterior commissure involvement - 24 cases (39%), followed by right vocal cord in 16 cases (26%), trans-glottic region (a variety in which the paraglottic space is affected; it infiltrates the three floors of the larynx) in 13 cases (21%), left vocal cord – 7 (11%) and supraglottic region with 2 cases (3%) (Graphic 7).

The most frequent symptom was dysphonia with or without dyspnea in 58 cases (93.55%), followed by dyspnea alone in 3 patients (4.84%) and dysphagia in one case (1.61%) (Graphic 8).

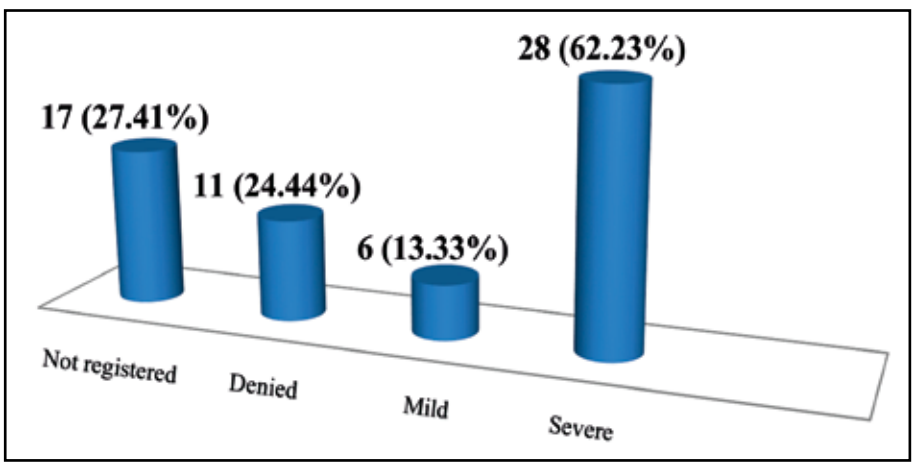
Regarding the time of evolution of the symptoms, they were not recorded in 2 cases; of those registered, 37 patients (61.67%) had a period of 12 to 24 months, followed by 22 cases (36.67%) with a period of 36 to 48 months, and 1 single case with ≥60 months, with an average of 29.03 months (Graphic 9).

Following the TNM classification criteria of the American Joint Committee for cancer Staging and End Results Reporting (AJCC), the tumors were classified in stages I to IV. This variable was recorded in only 52 files, where the most frequent was stage III, in 30 patients (57.69%), followed by stage IV with 10 patients (19.23%), stage I 9 patients (17.31%) and stage II with 3 patients (5.77%) (Graphic 10).

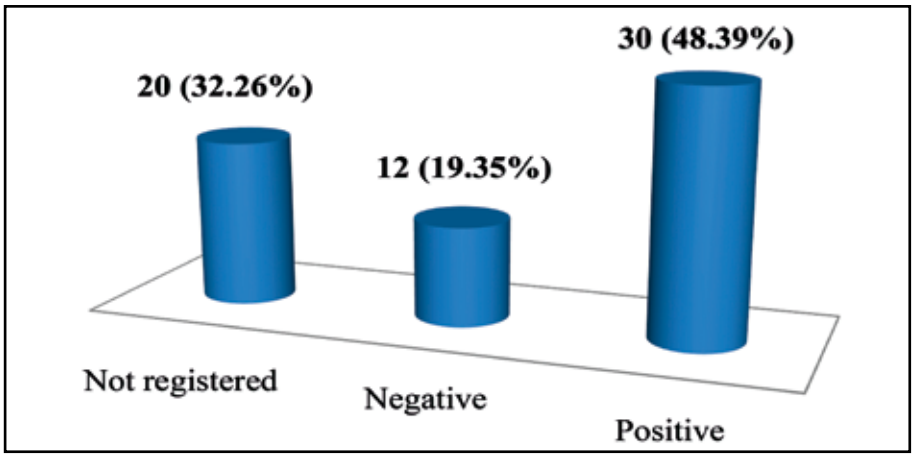
We define heavy smoking as a consumption of ≥20 cigars per day, per year, and light smoking as <20 cigars per day, per year. An adult who has never smoked or who has smoked less than 100 cigarettes in his or her lifetime is considered a non-smoker. Analysing the data, we found that tobacco use was not recorded in the registry in 17 (27.41%) patients, it was registered in 45 cases - 11



Graphic 10. Distribution of the patients from the study group according to the tumoral stage (Source: Otolaryngology Service, Specialty Hospital No. 2, IMSS, Ciudad Obregón, Sonora, 2015-2019).



Graphic 11. Distribution of the patients from the study group according to smoking (Source: Otolaryngology Service, Specialty Hospital No. 2, IMSS, Ciudad Obregón, Sonora, 2015-2019).



Graphic 12. Distribution of the patients from the study group according to alcohol consumption (Source: Otolaryngology Service, Specialty Hospital No. 2, IMSS, Ciudad Obregón, Sonora, 2015-2019).

(24.44%) denied, 6 (13.33%) reported mild consumption and 28 (62.23%) severe one (Graphic 11).

In the record of alcohol consumption, we found a lack of consignment in 20 cases (32.26%), 30 patients answered positively (48.39%) and 12 denied (19.35%) (Graphic 12).

Inferential Analysis

The division of clinical stages was considered as early (I and II) and advanced (III and IV). The association between positive and negative smoking and the level of cancer progression in 47 cases, in which tobacco users had more advanced stages III-IV compared to non-smokers, with a value of p=0.005 (in $p < 0.05$) from Fisher's exact test, was significant.

Alcohol consumption alone was not associated with more advanced stages of cancer at diagnosis, with a p=0.159241 value ($p > 0.05$) when using Chi2 test.

The combination of tobacco with alcohol was associated with more advanced stages of cancer, with a value of p=0.0333 ($p<0.05$.), with Fisher's exact test. Likewise, the intensity of tobacco use had a significant association with more advanced stages of cancer, with a value of $p = 0.0085$ ($p < 0.05$).

According to the occupation and stage of the cancer, in 51 of the cases, we divided them into two groups of occupation - day laborers and non-day laborers. We found a significant difference with a value of $p = 0.0018$ ($p < 0.05$), that is, the occupation of day labourers had a greater association with more advanced stages compared to non-day laborers.

DISCUSSIONS

In our series, we found an average age of 67.91 years (range from 36 to 91 years) similar to that reported by Herrera-Goméz et al.[19] and other authors[20,21]. Male patients were predominant (59 males, representing 95%, and 3 females, 5%), compared to what was reported by Herrera-Goméz et al.[19] and others[22,23]. Regarding the male-female relationship, we presented a 5:1 ratio, different from that reported by Herrera-Goméz et al.[19], with 10.6:1 male/woman in a series of 500 cases. The most affected age group was 58 to 77 years, similar to that described by Herrera-Goméz et al.[19] in Mexico and Cattaruzza et al.[24], with 56 to 70 years in Europe, and Lence et al.[25], 50 to 74 in Cuba.

The histopathological result was squamous cell carcinoma in 96.77% of the cases, similar to those reported in the literature[19,22,23,25,26].

The tumor was diagnosed in stage III, in 30 patients (57.69%), followed by stage IV, with 10 patients (19.23%), stage I in 9 patients (17.31%) and stage II in 3 patients (5.77%). Our results were similar to those reported by Menach et al.[23] in series of 50 cases, where the advanced stages III (46%) and IV (27%) were the most frequent, followed by stages II (20%) and I (6.4%). Unfortunately, most patients are diagnosed in advanced stages, that is, more than 75% in stage III or stage IV. However, Lance et al.[25] reported, in a series of 30,748 cases in Cuba, from 1988 to 2003, stages I-II were the most common in 58% of the cases, advanced stages III-IV in 19% and unknown in 23%. The results are possibly related to timely detection in their country.

The most frequent sites in our 62 cases were the following: glottic region including the anterior commissure in 24 cases (39%), followed by right vocal cord in 16 cases (26%), trans-glottic in 13 cases (21%), left vocal cord in 7 cases (11%) and supraglottic in 2 cases (3.22%). The results were different from those reported by Markou et al.[26]. On a sample of 1,638 cases, the location was glottic in 633 patients (60.2%), supra-glottic in 345 patients (32.8%), trans-glottic in 62 patients (5.9%) and sub-glottic in only 11 patients (1.1%)[26]. A study performed in Mexico by Herrera-Goméz et al.[19] reports a glottic distribution in 308

patients (61.6%), supraglottis in 166 patients (33.2%) and the subglottis in eight patients (1.6%). In a similar manner, Lence et al.[25] found a proportion of glottic cancer of 74%, followed by supra-glottic with 25%, in a sample of 3,074 cases from 1988 to 2003.

In our study group, the most frequent symptom was dysphonia with or without dyspnea in 58 cases (93.55%), followed by dyspnea in 3 patients (4.84%) and dysphagia in 1 patient (1.61%), similar to that reported by Herrera-Goméz et al.[19], where the symptoms were dysphonia in 458 patients (91.6%), dysphagia in 110 patients (22%), dyspnea in 103 patients (20.6%), odynophagia in 37 patients (7.4%) and bleeding in 11 patients (2.2%). Dechaphunkul et al.[21] refer to dysphonia in 97.2% of the patients included in their study, accompanied by dyspnea in 24.4% of cases and odynophagia in 13.3%.

In relation to the time of evolution of the symptoms, in 60 registered cases, we had an average of 29.03 months, range from 12 to ≥ 60 months, greater than that reported by Herrera-Goméz et al.[19] who describes an average time of 12.2 months, with a range of 0 to 84 months.

Regarding the occupational distribution of our patients, the majority of the study population belonged to day laborers 33 cases (64.71%) and non-day laborers (office workers, housewives and laborers) 18 cases (35.29%), similar to that described by Mallis et al.[27] in a series of 209 patients in Greece. In their study, agricultural day laborers predominated with 89 cases (42.5%), followed by those related to construction occupations (n = 54, 25.8%)[27]. In Mexico, they describe a correlation that is inverse. Regarding the socioeconomic status, states with higher mortality rates from lung cancer have lower rates of marginalization. This is probably due to greater access to goods and tobacco, higher economic income and differences in lifestyle between communities with different levels in their social and economic development[17]. It would be interesting to evaluate these characteristics in a population of laryngeal cancer. Carreras et al. found that higher body mass index may increase the risk of certain types of lung cancer, particularly squamous cell and small cell carcinoma. The data is somewhat controversial, given the obesity epidemic that prevails in our country. However, it would be important to review that association[28].

The association between smoking and the stage level of the cancer at the time of diagnosis was found to be significantly differentiated, where tobacco users had a more advanced stage of cancer compared to non-smokers. Our findings are similar to those reported by Trigg et al.[29] in a series of 499 cases at the University of Illinois at the American Union. De Stefani et al., on the other hand, found that smoking dark tobacco was the strongest risk factor, with a risk ratio (RR) 2.5 times higher than that shown by light tobacco smokers and 35 times higher than that of non-smokers. Alcohol exposure showed minor effects, but its interaction with smoking resulted in very high risks (more than 100 times higher)[15].

Overall, alcohol consumption versus non-alcohol consumption was associated with an approximately 2-fold increase in the risk of laryngeal cancer (RR = 1.90; 95% CI: 1.59-2.28)[30]. Light alcohol consumption (drinking 1 drink/day) did not show any significant association with laryngeal cancer risk (RR = 0.88; 95% CI: 0.71–1.08), moderate consumption (> 1 to <4 drinks/day) was associated with a 1.5-fold increased risk (RR = 1.47; 95% CI: 1.25–1.72) and excessive alcohol consumption (⩾4 drinks/day) was associated with a 2.5-fold increased risk (RR = 2.62; 95% CI: 2.13-3.23)[30]. Several studies have confirmed a dose-response relationship, in which the risk of laryngeal cancer increases with increasing daily alcohol consumption. A case-control study of laryngeal cancer in São Paulo found an adjusted risk index of 7.5 times higher for heavy smokers and 3.7 times more for heavy drinkers[31]. Wynder and Stellman observed higher smoking habits and lower rates of tobacco cessation among the lowest socioeconomic groups, suggesting that these groups of low socioeconomic and cultural status will bear an increasing proportion of the burden of care for tobacco-related cancer[32].

Smoking has long been recognized as one of the leading causes of cancer of the larynx and especially of the endolarynx[20,24].

Finally, we presented an under-registration of variables in a range of 27.41% to 30% in the 62 cases, similar to that reported by Villamizar in Manizales Colombia in a series of 72 cases with 33.33%[33].

CONCLUSIONS

In our series, we found an average age of 67.91 years (range from 36 to 91 years), the male gender being the most affected in a 5:1 ratio to the female gender; the most involved age group was from 58 to 77 years, while squamous cell carcinoma was the most found lineage. Advanced stages (III-IV) were the most common at the time of diagnosis, the most frequent sub-site in our 62 cases being the glottis. The most common symptom was dysphonia with or without dyspnea. In relation to the time of evolution of symptoms, it was an average of 29.03 months. As for the occupational distribution of our patients, the majority of the study population belonged to day laborers.

Tobacco use alone or in combination with alcohol was more associated with advanced stages of cancer compared to non-smokers.

It is very important to point out that it is necessary to improve the records and organizations of the clinical record, because we have a high proportion of under-registration of the data and this hinders a more truthful analysis in our studies.

Contribution of authors: All authors have equally contributed to this work.

Conflict of interests: The authors declare no conflict of interests.

REFERENCES

1. Bressmann T. Self-inflicted cosmetic tongue split: a case report. J Can Dent Assoc. 2004;70(3):156-7.
2. Sartor SG, Eluf-Neto J, Travier N, Wünsch Filho V, Arcuri ASA, Kowalski LP, et al. Occupational risks for laryngeal cancer: a case-control study. Cad Saude Publica. 2007;23(6):1473-81. DOI: 10.1590/s0102-311x2007000600022.
3. Granell Navarro J, Puig Rullán A. Registro de cáncer de cabeza y cuello: estudio prospectivo de incidencia a dos años. Oncologia (Barc.). 2004;27(1):33-9.
4. Goiato MC, Fernandes AÚR. Risk factors of laryngeal cancer in patients attended in the oral oncology center of Araçatuba. Brazilian J Oral Sci. 2005;4(13):741-4.
5. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394-424. DOI: 10.3322/caac.21492.
6. Xavier F, Henn LA, Oliveira M, Orlandine L. Smoking and its relation to the histological type, survival, and prognosis among patients with primary lung cancer. Sao Paulo Med J. 1996;114(6):1298-302.
7. Paré CA, Paré KE, Sanabria BVR, Tagle JF, Chamorro AP. Cancer de laringe: revision. Rev Posgrado la VIa Cátedra Med. 2009;192(11):17-22.
8. Black RJ, Bray F, Ferlay J, Parkin DM. Cancer incidence and mortality in the European union: Cancer registry data and estimates of national incidence for 1990. Eur J Cancer Part A. 1997;33(7):1075-107. DOI: 10.1016/S0959-8049(96)00492-3.
9. Bustamante ALM, Marín OSJ, Cardona AD. Mortalidad por cáncer: segunda causa de muerte del adulto mayor en Medellín, 2002-2006. Rev Fac Nac Salud Pública. 2012;30(1):17-25.
10. Pichiule M, Gandarillas A, Ordobás M, Servicio de Epidemiologia Comunidad de Madrid. Mortalidad general y por causas en la Comunidad de Madrid , 2009. [Internet]. 2011. Available from: https://www.comunidad.madrid/sites/default/files/doc/sanidad/epid/informe_mortalidad_2009.pdf.
11. Secretaría de Salud. Guía de Práctica Clínica Diagnóstico y Tratamiento del Carcinoma Epidermoide de Laringe. [Internet]. 2010. Available from: https://www.imss.gob.mx/sites/all/statics/guiasclinicas/471GER.pdf.
12. Aldaco-Sarvide F, Pérez-Pérez P, Cervantes-Sánchez G, Torrecillas-Torres L, Erazo-V AE. Cancer mortality in Mexico 2000-2010: the counting of the damages. Gac Mex Oncol. 2012;11(6):371-9.
13. Meneses-García A, Ruiz-Godoy LM, Beltrán-Ortega A, Sánchez-Cervantes F, Tapia-Conyer R, Mohar A. Main malignant neoplasms in Mexico and their geographic distribution, 1993-2002. Rev Investig Clin. 2012;64(4):322-9.
14. Altieri A, Bosetti C, Talamini R, Gallus S, Franceschi S, Levi F, et al. Cessation of smoking and drinking and the risk of laryngeal cancer. Br J Cancer. 2002;87(11):1227-9. DOI: 10.1038/sj.bjc.6600638.
15. De Stefani E, Correa P, Oreggia F, Leiva J, Rivero S, Fernandez G, et al. Risk factors for laryngeal cancer. Cancer. 1987;60(12):3087-91. DOI: 10.1002/1097-0142(19871215)60:12<3087::aid-cncr2820601238>3.0.co;2-6.
16. Shah JP, Karnell LH, Huffman HT, Ariyan S, Brown SG, Fee WE, et al. Patterns of care for cancer of the larynx in the United States. Arch Otolaryngol Head Neck Surg. 1997;123(5):475-83. DOI: 10.1001/archotol.1997.01900050021002.
17. Tovar-Guzmán VJ, Barquera S, López-Antuñano FJ. Tendencias de mortalidad por cánceres atribuibles al tabaco en México. Salud Publica Mex. 2002;44(Suppl 1):20-8.
18. Agudelo D, Quer M, León X, Díez S, Burgués J. Laryngeal carcinoma in patients without a history of tobacco and alcohol use. Head Neck. 1997;19(3):200-4. DOI: 10.1002/(sici)1097-0347(199705)19:3<200::aid-hed6>3.0.co;2-6.
19. Herrera-Gómez Á, Villavicencio-Valencia V, Rascón-Ortiz M, Luna-Ortiz K. Demography of laryngeal cancer at the Instituto Nacional de Cancerologia in Mexico City. Cir Cir. 2009;77(5):353-7.
20. Ramroth H, Schoeps A, Rudolph E, Dyckhoff G, Plinkert P, Lippert B, et al. Factors predicting survival after diagnosis of laryngeal cancer. Oral Oncol. 2011;47(12):1154-8. DOI: 10.1016/j.oraloncology.2011.08.003.
21. Dechaphunkul T. Epidemiology, risk factors, and overall survival rate of laryngeal cancer in Songklanagarind Hospital. J Med Assoc Thail. 2011;94(3):355-60.
22. Arsenijevic S, Pantovic V, Gledovic Z, Stojanovic J, Belic B. Demographic characteristics of patients with laryngeal cancer and their socioeconomic status. J BUON. 2010;15(1):131-5.
23. Menach OP, Patel A, Oburra HO. Demography and histologic pattern of laryngeal squamous cell carcinoma in Kenya. Int J Otolaryngol. 2014;2014:507189. DOI: 10.1155/2014/507189.
24. Cattaruzza MS, Maisonneuve P, Boyle P. Epidemiology of laryngeal cancer. Eur J Cancer B Oral Oncol. 1996;32B(5):293-305. DOI: 10.1016/0964-1955(96)00002-4.
25. Lence Anta JJ, Fernandez Garrote LM. Trends of laryngeal cancer incidence in Cuba, 1988-2003. Rev Cubana Salud Publica [online]. 2008;34(3). Available from: http://scielo.sld.cu/scielo.php?pid=S0864-34662008000300003&script=sci_abstract&tlng=en.
26. Markou K, Christoforidou A, Karasmanis I, Tsiropoulos G, Triaridis S, Constantinidis I, et al. Laryngeal cancer: epidemiological data from Northern Greece and review of the literature. Hippokratia. 2013;17(4):313-8.
27. Mallis A, Jelastopulu E, Mastronikolis NS, Naxakis SS, Kourousis C, Papadas TA. Laryngeal cancer and passive smoking: the neglected factor? Eur Arch Otorhinolaryngol. 2011;268(5):727-31. DOI: 10.1007/s00405-010-1403-z.
28. Carreras-Torres R, Haycock PC, Relton CL, Martin RM, Smith GD, Kraft P, et al. The causal relevance of body mass index in different histological types of lung cancer: A Mendelian randomization study. Sci Rep. 2016;6:31121. DOI: 10.1038/srep31121.
29. Trigg DJ, Lait M, Wenig BL. Influence of tobacco and alcohol on the stage of laryngeal cancer at diagnosis. Laryngoscope. 2000;110(3 Pt 1):408-11. DOI: 10.1097/00005537-200003000-00014.
30. Islami F, Tramacere I, Rota M, Bagnardi V, Fedirko V, Scotti L, et al. Alcohol drinking and laryngeal cancer: overall and dose-risk relation – a systematic review and meta-analysis. Oral Oncol. 2010;46(11):802-10. DOI: 10.1016/j.oraloncology.2010.07.015.
31. Filho VW. The epidemiology of laryngeal cancer in Brazil. Sao Paulo Med J. 2004;122(5):188-94. DOI: 10.1590/s1516-31802004000500002.
32. Wynder EL, Stellman SD. Comparative epidemiology of tobacco-related cancers. Cancer Res. 1977;37(12):4608-22.
33. Omar Robert Z, Camejo Carbonell AB, Neyra Barros RM. Características clinicoepidemiológicas de pacientes con cáncer de laring. Medisan [Internet]. 2020;24(1):57-64. Available from: https://www.redalyc.org/journal/3684/368462717006/html/.