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Occupational Risk Factors for Laryngeal Cancer in Tunisia: A Case Control Study

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Abstract

Background: *Tobacco use and alcohol consumption are the primary risk factors for laryngeal cancer (LC). In most populations, occupational exposures are likely to play a minor role in laryngeal carcinogenesis. We aimed to investigate the association between occupational exposure and laryngeal cancer.* **Methods:** *It is a case-control study that included 140 cases diagnosed between January 2013 and December 2016 and 140 controls matched by sex, age, alcohol consumption, and tobacco consumption.* **Results:** *Significantly increased risks were found amongst workers of the building sector (OR=4.621; 95% CI [1.826-11.693]) and the mechanical industry sector (OR=5.074; 95% CI [1.425-18.072]). Significant association of laryngeal cancer with various carcinogens was observed such as asbestos (p=0.009; OR=3.68; 95% CI [1.29-10.46]), paint vapors (p=0.005; OR=3.35; 95% CI [1.37-8.16]), solvents (p=0.001; OR=3.29: 95% CI [1.61-6.68]) and cement dust (p=0.003; OR=3.19: 95% CI [1.43-7.12]). After binary logistic regression, cement dust was independently correlated with LC (p=0.042; OR=3.93; 95% CI [1.04-14.78]. The administration sector was associated with decreased risk (p=0.001; OR=0.07; 95% CI [0.03-0.15]) as well as the health sector (p=0.001; OR=0.098; 95% CI [0.02-0.43]).* **Conclusions:** *Our results supported the role of occupational factors in developing LC. Further studies enabling an in-depth analysis of occupational exposures are necessary to provide a clearer definition of the etiological associations between single agents and circumstances of exposure and the genesis of LC.*

1. Introduction

Laryngeal cancer (LC) poses a significant public health challenge in Tunisia, ranking among the foremost cancers of the Ear-Nose-Throat (ENT) region [1]. The predominant histological form is squamous cell carcinoma, and it manifests with common symptoms such as hoarseness, dysphagia, odynophagia, neck mass, referred otalgia, and dyspnea [2]. Treatment options encompass surgery, radiation therapy, and chemotherapy, which can be employed individually or in combination [3].

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Understanding the full spectrum of lifestyle and environmental risk factors, especially occupational factors, is crucial for developing effective prevention strategies against this malignancy. While alcohol and tobacco are well-recognized as the primary risk factors for LC [4], a comprehensive work history and an inventory of associated products, coupled with vigilant monitoring of potentially exposed individuals, can aid in assessing the occupational contribution to this risk.

Asbestos (all forms) [5] and strong inorganic acid mists [6] have been identified by the International Agency for Research on Cancer (IARC) as two carcinogens potentially involved in the occurrence of LC (group 1) while hard bitumen emissions during mastic asphalt work and working in the rubber manufacturing industry [6] have been classified by IARC as agents with limited evidence in humans about carcinogenicity for the larynx.

Exploring the role of occupational and environmental factors in laryngeal cancer remains a relatively understudied area, particularly in middle and low-income countries. In this context, our study aimed to investigate the association between occupational exposure and LC in the context of the Tunisian population. Specifically, we focused on patients treated at the ENT department of the University Hospital Farhat Hached in Sousse, Tunisia.

2. Methods

It is a case-control study of occupational risk factors, which gained approval from the Ethics and Research Committee of the University Farhat Hached Hospital (IRB 00008931 as provided by OHRP). The study participants were recruited from a university hospital in Sousse, Tunisia. All patients diagnosed clinically with primary CL, confirmed by pathological examination, and followed either at the outpatient clinic and/or at the ENT department were eligible for inclusion as cases. Cases were recruited between 01 January 2013 and 31 December 2016. The inclusion criteria were professional activity (patients who were currently employed or who have worked previously) and agreement to answer the questionnaire were included in the study. Patients who passed away before the survey or who developed secondary laryngeal carcinoma were excluded. Cases were individually matched according to age, gender, tobacco consumption, and alcohol consumption to healthy participants with no history of cancer and selected randomly among the consultants of the Occupational Medicine department of the same hospital during the same period. At first, a random selection was made from the consultants' files. Matched controls were invited to participate in this survey and were informed that an investigator would shortly contact them. Exclusion criteria for controls were death or refusal of participation. All controls initially recruited were included in the survey.

Personal data and medical characteristics were filled out from the medical records in a standardized synoptic sheet. All participants were interviewed face-to-face by specially trained interviewers. Detailed occupational history was recorded by direct contact with the patient alone or with one of his relatives. The participants completed a questionnaire that included items related to occupational activity, performed tasks, number of years of work, use of carcinogenic products (cement dust, wood dust, asbestos...), analysis of possible exposure to the agents implicated in the literature in the development of LC, and a semi-quantitative estimation of this exposure. This estimate was made using the daily exposure frequency, work hours (H), years of exposure (D), and level of exposure (E). The level of exposure was rated, based on the nature of occupational activities and work environment, from 0 to 3, as follows: 0= minimally safe exposure; 1= indicates little product contact; 2= denotes moderate product contact; 3= contact with the product frequently.

An exposure index (I) for each product was calculated to approximate the cumulative exposure to that product: $I = H \times D \times E$. Tobacco consumption was quantified by "pack year" (PY), based on how many packs are smoked daily and for how many years. We defined a "current smoker" as a patient who has smoked at least 100 cigarettes in their lifetime and is currently smoking cigarettes. Alcohol consumption was assessed using the question: "Do you drink alcohol?". The main occupational exposures were defined according to the International Standard Classification of Occupations (ISCO 88) [7].

Univariate, multivariate, analytic, and descriptive statistical analyses were conducted. We used the chi-2 (χ^2) test and Student t-test in the univariate analysis. To identify the determinants of laryngeal cancer, we conducted a binary logistic regression method, and we included all variables with a p-value of less than or equal to 20% in the univariate analysis. The association was quantified using odds ratios (OR) presented with their 95% Confidence Intervals.

3. Results

During the study period, 252 patients were diagnosed with histologically confirmed laryngeal cancer. Many patients did not meet the inclusion criteria primarily due to being lost to follow-up or reported as deceased before the interview. The remaining cases included 140 patients who agreed to participate and were interviewed either directly during their hospitalization, during their consultation, or through their relatives.

We identified 140 LC cases meeting the inclusion criteria matched with controls. The mean age was 60.12±9.50 years, ranging from 39 to 82 years. There was a male predominance with a percentage of 95%, resulting in a sex ratio of 19. Alcohol consumption was reported by 31% of patients. The mean tobacco consumption was 46.4±18.4 PY, and 80% were current smokers. Notably, 28 patients (71.4%) had a family history of cancer, with the most common types being lung (71.4%), liver (14.3%), colon (7.2%), and brain (7.1%) cancers. Additionally, 21 patients (15%) had a family history of ENT cancer. The disease was detected incidentally in only one patient. The predominant symptom reported among cases was dysphonia, observed in 94.3% of cases. Dyspnea was the second most frequently noted symptom, occurring in 30% of cases, followed by dysphagia in 22.9%. Thus, glottic involvement was found in 116 patients (82.9%), supraglottic involvement in 100 patients (71.4%), and subglottic involvement in 62 patients (44.3%). Squamous cell carcinoma was the predominant histological type (97.1% of cases).

Verrucous carcinoma and sarcomatoid Carcinoma (1.45% each) were the other types reported. The majority of patients were manual workers (80.7%). The average seniority of workers in their last jobs was 17.28±10 years, with extremes of 2 and 45 years. An occupational seniority equal to or greater than 20 years was found in 37.9% of cases. A quarter of cases were working in the agricultural sector. Those working in the building sector and mechanical industry represented 17.1% and 10% of the cases (Figure 1). According to ISCO, the most represented occupational subgroup in our population were farmers and

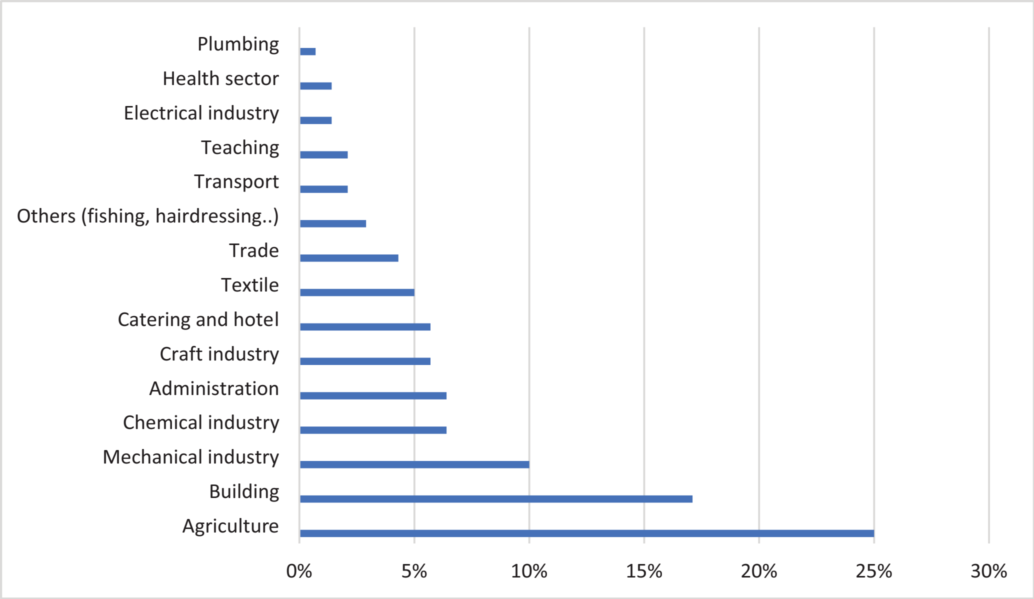

Figure 1. Distribution of patients according to their occupational sector.

Table 1. Distribution of patients according to the frequency of exposure to the considered agents and circumstances of exposure.

Handled Products	Exposure		
	Yes N (%)	**No N (%)**	**Don't know N (%)**
Cement Dust	25 (18)	114 (81.3)	1 (0,7)
Diesel Exhausts	15 (10.7)	125 (89.3)	0 (0)
Welding Smokes	13 (9.3)	127 (90.7)	0 (0)
Asbestos	15 (10.7)	109 (77.9)	16 (11.4)
Silica	18 (12.9)	117 (83.6)	5 (3.6)
Man-made Mineral Fiber (glass fibers, mineral wools)	18 (12.9)	107 (76.4)	15 (10.7)
Work in Plastic or Rubber Industry	7 (5)	132 (94.3)	1 (0.7)
Strong Inorganic Acid Mists	3 (2.1)	135 (96.4)	2 (1.4)
Cutting Fluids and Mineral OIL	9 (6.4)	127 (90.7)	4 (2.9)
Wood Dust	7 (5)	133 (95)	0 (0)
Textile Dust	8 (5.7)	132 (94.3)	0 (0)
Vapours from Solvents, Degreasers, and Diluents	33 (23.6)	107 (76.4)	0 (0)
Arsenic	6 (4.3)	117 (83.6)	17 (12.1)
Nickel	14 (10)	126 (90)	0 (0)
Chrome	13 (9.3)	125 (89.3)	2 (1.4)
Cadmium	5 (3.6)	125 (89.3)	10 (7.1)
Paint Vapours	21 (15)	119 (85)	0 (0)
Formaldehyde	3 (2.1)	129 (83.2)	8 (5.7)
Pesticide	27 (19.3)	113 (80.7)	0 (0)

skilled workers in commercial agriculture (21.4%), followed by skilled building workers (17.1%). Exposure to vapors from solvents, degreasers, and diluents was the most frequent and reported by 23.6% of patients. Pesticides were mentioned in 19.3% of cases, followed by cement dust in 18% (Table 1). The cumulative exposure was higher for pesticides, with a mean exposure index IE of 325.51±199.87.

According to the laryngeal tumor location, cancer was present in one anatomical region in 35% of cases. It invaded two and three regions in 31.4% and 33.6% of cases, respectively.

We studied the relationship between tumor size and frequency of exposure to risk products and there were no statistically significant differences between patients with one region location and those with more than one region location.

Table 2 summarizes the distribution of cases and controls according to their occupational category. Cases were significantly more frequently assigned to the construction, agriculture, trade, chemical industry, and textile sectors than controls. In contrast, controls were significantly more assigned to the administration, health, and direct services to individuals, protection, and security sectors.

The seniority of cases in their jobs was significantly more important in the administration, construction, agriculture, and health sectors (Table 2). An increased risk of LC was found for exposure to cement dust, asbestos, solvents, and paint vapors. As for the cumulative exposure, the exposure index to cement dust and asbestos was significantly higher in the cases than in the controls (Table 3).

After binary logistic regression, the only independent factor associated with LC was exposure to cement dust (OR=3.93; 95% CI [1.43-7.12]), whereas the area of administration was the only

Table 2. Distribution of cases and controls according to their occupational sector and seniority in their jobs.

		Cases	Controls	P	OR	95%CI
Administration	Frequency	9 (6.4)	68 (47.6)	**10^{-3}**	**0.07**	**[0.03-0-15]**
	Seniority	24.33±6.46	17.33±5.29	**10^{-3}**		
Building	Frequency	24 (17.1)	6 (42)	**10^{-3}**	**4.62**	**[1.82-11.69]**
	Seniority	19.66±7.82	17.5±0.7	0.20		
Agriculture	Frequency	32 (22.9%)	0 (0)	**10^{-3}**	-	-
	Seniority	24.9±9.59	-	-		
Transport	Frequency	6 (4.3)	4 (2.9)	0.520		
	Seniority	20.16±10.38	12.75±1.5	0.202		
Trade	Frequency	11 (7.9)	0 (0)	**10^{-3}**	-	-
	Seniority	16.27±5.96	-	-		
Chemical Industry	Frequency	5 (3.5)	1 (0.7)	0.214		
	Seniority	18.6±8.14	11	0.62		
Mechanical Industry	Frequency	14 (10)	3 (2.1)	**0.006**	**5.07**	**[1.42-18.72]**
	Seniority	16.28±6.24	12.33±2.521	0.68		
Textile	Frequency	7 (4.9)	0 (0)	**0.02**	-	-
	Seniority	18.85±5.33	-	-		
Craft Industry	Frequency	7 (4.9)	1 (0.7)	0.07		
	Seniority	20.85±9.51	12	0.417		
Health Sector	Frequency	2 (1.4)	18 (12.9)	**10^{-3}**	**0.09**	**[0.02-0.43]**
	Seniority	25±7.07	16.38±3.85	**0.011**		
Teaching	Frequency	3 (2.1)	5 (3.6)	0.473		
	Seniority	22.33±3.51	20.20±2.28	0.329		
Catering/Hotel	Frequency	6 (4.3)	3 (2.1)	0.498		
	Seniority	26.5±7.2	14±9.89	0.095		
Direct Service to Individuals/ Security	Frequency	7 (5)	22 (15.7)	**0.003**	**0.28**	**[0.11-0.68]**
	Seniority	15.85±4.29	15.8±6.02	0.98		
Electrical industry	Frequency	1 (0.7)	5(3.5)	0.214		
	Seniority	17	19.16±5.03	0.707		
Plumbing	Frequency	1 (0.7)	3 (2.1)	0.622		
	Seniority	17	16.66±5.8	0.96		
Others (Fishing, Hairdressing...)	Frequency	5 (3.6)	1 (0.7)	0.214		
	Seniority	25±9.4	19	0.59		

protective factor identified in our study (OR=0.15; 95% CI [0.06-0.38]).

4. Discussion

In our study, we identified several industries and chemicals associated with an increased risk of LC among Tunisian workers. However, this study has limitations. Given that this is a hospital-based case-control study rather than a population-based one, it could be susceptible to selection bias. However, it is noteworthy that the hospital where our patients were recruited is the biggest of the center of Tunisia and receives patients from urban and rural regions.

Table 3. Distribution of cases and controls according to the frequency of exposure to the considered agents and circumstances of exposure.

Risk Products		Cases	Controls	P	OR	95%CI
Cement Dust	Frequency	25 (18)	9 (6.4)	**0.003**	**3.19**	**[1.43-7.12]**
	IE	176.3±127.9	69.3±42.5	**0.012**		
Diesel Exhausts	Frequency	15 (10.7)	7 (5)	0.07	0.9	[0.6-.1]
	IE	116.0±82.2	92.6±65.3	0.51		
Welding Smokes	Frequency	13 (9.3)	6 (4.3)	0.09	0.8	[0.7-1.1]
	IE	123.1±95.3	105.3±48.0	0.67		
Asbestos	Frequency	15 (12.1)	5 (3.6)	**0.009**	**3.68**	**[1.29-10.46]**
	IE	161.1±99.3	36.0±72.0	**0.027**		
Silica	Frequency	18 (13.3)	9 (6.4)	0.05	0.9	[0.7-1.3]
	IE	163.1±135.0	68.0±57.6	0.11		
Man-Made Mineral Fiber	Frequency	19 (13.6)	0(0)	0.001	-	-
	IE	132.6±118.2	-	-		
Work in Plastic or Rubber Industry	Frequency	7 (5)	1 (0.7)	0.06	0.7	[0.5-0.9]
	IE	156.6±86.9	56	0.32		
Strong Inorganic Acid Mists	Frequency	3 (2.1)	2 (1.4)	0.68	1.0	[0.6-1.8]
	IE	168.0±207.5	140.0±5.6	0.86		
Cutting Fluids and Mineral OIL	Frequency	9 (6.6)	3 (2.1)	0.06	1.5	[1.2-2.1]
	IE	155.0±107.3	208±115.4	0.48		
Wood Dust	Frequency	8 (5.6)	3 (2.1)	0.12	0.7	[0.6-0.9]
	IE	133.9±114.8	68.0±57.6	0.19		
Textile Dust	Frequency	8 (5.7)	0 (0)	**0.007**	-	-
	IE	245.7±138.15	-	-		
Solvents, Degreasers, and Diluents	Frequency	33 (23.6)	12 (8.6)	**0.001**	**3.29**	**[1.61-6.68]**
	IE	178.4±134.8	154.7±51.4	0.76		
Arsenic	Frequency	6 (4.3)	1 (0.7)	0.12	0.8	[0.6-1]
	IE	256.0±163.0	152	0.58		
Nickel	Frequency	14 (10)	11 (7.9)	0.53	1.0	[0.7-1.6]
	IE	88.0±73.7	67.63±71.58	0.49		
Chrome	Frequency	13 (9.3)	7 (5)	0.16	1.4	[0.9-2.3]
	IE	84.3±.80.8	68.6±72.1	0.67		
Cadmium	Frequency	5 (3.6)	2 (1.4)	0.44	0.8	[0.5-1.1]
	IE	105.6±113.1	208.0±181.0	0.38		
Paint Vapours	Frequency	21 (15)	7 (5)	**0.005**	**3.35**	**[1.37-8.16]**
	IE	177.1±117.1	75.2±79.9	0.07		
Formaldehyde	Frequency	3 (2.1)	1 (0.7)	0.36	0.7	[0.7-1.0]
	IE	226.7±83.3	144	0.48		
Pesticide	Frequency	27 (19.3)	0 (0)	10^{-3}	-	-
	IE	336.3±200.93	-	-		

Population heterogeneity may influence the comprehension of posed queries. To address this bias, the questions asked were simplified, and each time, we ensured a genuine understanding of the question and its meaning. The assessment of occupational exposure was conducted in a semi-quantitative manner, which may not allow an objective consideration of exposure variability among different jobs.

It is often difficult to determine the fraction attributable to occupational exposure in the genesis of occupational cancers, mainly because of the multiple activities with variable workstations and exposures. Inhalation is the main entry route for many agents in the workplace, which makes the upper airway tract an anatomical region directly in contact with these nuisances. In France, the fraction of LC attributed to occupational exposure was 7.6% [8].

Most of our patients were blue-collar workers, either in their last job (80.7%) or in their previous job (77.3%). Through a literature review, LC was often associated with manual occupations. Indeed, according to a meta-analysis [9] combining the results of 21 case-control studies (6,906 cases and 10816 controls) with the same occupational exposures, there was a significant increase in the risk of LC for blue-collar workers (OR=1.3; 95% CI=[1.2-1.4]), whereas administrative and managerial staff and office and related workers had less frequent laryngeal cancer.

In our study, we found that most of the cases worked in the agriculture sector, building sector, and mechanical industry. In Turkey, the sector of textile and construction was mentioned as a risk sector of association with LC [10]. In Finland, working in the food industry increased this cancer risk by 30% [11].

4.1. Asbestos

In our study, asbestos exposure was found in 9.3% of cases in the current job and 12.5% in the preceding job, with a statistically significant increase in the risk of laryngeal cancer (OR=3.68; 95% CI=[1.29-10.46]). Laryngeal cancer and its association with asbestos exposure have been assessed in several studies. Indeed, Occupational risk factors for laryngeal cancer with a sufficient level of evidence include asbestos, which has been classified as a group 1 carcinogen for the larynx by the International Agency for Research on Cancer (IARC) since 2009 [5], as well as mists from strong inorganic acids, which have been classified as group 1 carcinogens since 2012 [6]. Two case-control studies were conducted in France [12] and Germany [13], showing that asbestos exposure increased the risk of LC, and this depended on the duration and intensity of exposure. A more recent French study focused on cases of work-related laryngeal cancers confirmed the role of asbestos in laryngeal carcinogenesis and showed that it was the laryngeal cancer risk factor most reported in the network from 2001 to 2016 [14].

4.2. Strong Mineral Acid Mists and Sulfuric Acid

Strong inorganic acid mists have been classified as a group 1 carcinogen with sufficient evidence for the larynx since 2012 [6]. Colin L. et al. reported that the effects related to sulfuric acid are increased by the duration of exposure and the degree of exposure [15]. Our study couldn't prove the relationship between exposure to acid mist and CL.

4.3. Cement Dust

Our study showed that exposure to cement dust had a significant association with an increased risk of LC (p=0.003; OR=3.19; 95% CI=[1.43-7.12]). In the multivariate study, this factor was independently associated with the occurrence of LC (pa=0.042; OR=3.93; 95% CI=[1.04-14.78]). Similarly, most of the studies conducted in many countries found a relationship between the risk of LC and exposure to cement dust [16, 17]. In a Swedish study, Purdue MP and coll. [18] observed a slight dose-response relationship depending on the intensity of exposure in construction workers exposed to cement dust.

Cement dust could pose a carcinogenic risk because it may contain hexavalent chromium, a known carcinogen [19], found in certain types of cement. Additionally, the lime content in cement, may potentially induce the production of reactive oxygen species [20]. However, exposures to asbestos, cement dust, and silica are strongly interconnected. Given the identification of an association between asbestos and LC in our data, it is difficult to investigate the individual impact of each exposure.

4.4. Wood Dust

According to IARC, wood dusts, which are carcinogenic to human (group 1), have an established role in the occurrence of cancers of the sino-nasal cavities [17]. The role of wood dusts in the occurrence of LC has been the subject of considerable research and speculation. In fact, our study did not show a statistically significant association (p=0.12). A meta-analysis done in 2012 showed a non-significant decreased risk of LC in wood workers (OR=0.95; 95% CI 0.80 to 1.14) [21]. On the other hand, in a cohort of workers exposed to softwood [22], the SIR (standardized incidence ratio) for larynx cancer was elevated (SIR 1.4, 95% CI 0.6 to 2.6).

4.5. Pesticides

Several pesticides are classified as potential (group 1) or probable (group 2) carcinogens by IARC. A recent case-control study [23] found a statistically significant association between pesticide exposure and LC after controlling for age, sex, and smoking (OR=9.33; 95% CI 1.65 to 52.68) with a dose-response pattern. In our study, the cases were more exposed to pesticides with a statistically significant difference but no association with LC was proven.

4.6. Man-made Mineral Fiber

Refractory ceramic fiber is classified as possible human carcinogens, whereas mineral wools are unclassifiable for humans [24]. In a meta-analysis of risks of cancers of the lung and head and neck from exposure to rock wool and glass wool, the summary RR for LC was 1.3 (95% CI 1.1 to 1.6) [25]. In a French cohort, the incidence of cancer was determined among workers employed in a French man-made mineral fiber production plant. It was significantly higher for the larynx (SIR 2.3) [26]. In our study, we were unable to assess the association between LC and exposure to these fibers because it was only observed among cases.

4.7. Work in the Rubber Industry

Work in the rubber industry is also classified as a Group 1 carcinogen by IARC but with limited evidence for human LC [5]. In a review to examine the epidemiological evidence on cancer risk among workers in the rubber industry, overall, the findings indicate the presence of a widespread moderate increased risk for LC [27]. In a meta-analysis, significantly increased meta-relative risk was obtained considering working in the rubber industry (meta-RR 1.39; 95% CI 1.13 to 1.71). However, working in the rubber industry involves complex and variable exposures, which depend on processing, work area, and period. The risk was increased for production workers, while the OR for tire makers and vulcanizers was equal to 1 [9]. A meta-analysis was conducted on observational studies published until April 2016 on work in the rubber industry and cancer risk. An increased risk was found for LC [standardized incidence ratio (SIR) [1.46; 95% CI 1.10 to 1.94] [28]. In our study, exposure to rubber was exclusively found among the cases. Consequently, we could not establish an association between the risk of exposure to these products and LC.

4.8. Silica

Known for its pulmonary carcinogenic effect, the role silica exposure in laryngeal cancer has been widely studied. A significantly increased risk of laryngeal cancer (OR=1.39, 95% CI 1.17 to .67) among workers exposed to silica dust was observed in a meta-analysis by combining six case-control studies with adjustment for smoking and alcohol consumption [29]. A hospital-based case-referent study was conducted to identify occupational risk factors for laryngeal cancer in Turkey [30]. A high risk was observed in workers potentially exposed to silica dust (OR=1.8; 95% CI 1.3 to 2.3). From our study, a role of silica dust exposure doesn't emerge.

4.9. Textile Dusts

Paget-Bailly et al. [9], reported a significant meta-RR of 1.4 for LC among textile workers. It was higher for textile work (meta-RR 3.20; 95% CI 1.72 to 5.98) than for textile dust exposure (Meta –RR 1.25; 95% CI 0.93 to 1.69). According to Elci OC et al. [30], specific exposure to cotton dust has an OR equal to 1.3 for exposed subjects with significant dose-response relationship. In a Finnish study, Kyyronen et al. [31] found an increased SIR with high cumulative exposure to textile dusts. Our results showed a statistically significant difference in textile dust exposure between cases and controls, with cases being significantly more exposed. However, no conclusive risk could be established because absence of textile dust exposure among the control group.

4.10. Solvents

Several authors have studied the association between exposure to organic solvents and LC, but the specific role of each type of solvent is poorly investigated. Our results have demonstrated that cases were significantly more exposed to solvents than the controls, with a statistically significant difference associated with a substantial increase in risk (p=0.001, OR=3.29; 95% CI=[1.619-6.683]). In a multicenter case-control study, Shangina et al. [32] found a significant increased risk associated with exposure to chlorinated solvents in men (OR=2.18; 95% CI 1.03 to 4.61). A case-control study conducted in France [33] observed a statistically significant association between cumulative exposure to Perchloroethylene (PCE) and LC (p=0.04). The OR was 3.86 (95% CI 1.30 to 11.48) for those exposed to the highest levels of PCE.

4.11. Welding Fumes

In 2017, welding fumes were recognized as a cause of lung cancer in humans [34]. In a Swedish case-control study, Gustavsson et al. [35], found an increased risk of LC in association with exposure for more than eight years to welding fumes (OR=2.0; 95% CI 1 to 3.7). In a meta-analysis of occupations and LC, Bayer et al. [36] found a meta-RR of 1.17 (95% CI 0.98 to 1.39) for welders and plumbers. From our study, a role of the exposure to welding fumes exposure doesn't emerge.

4.12. Diesel Exhausts

Paget-Bailly S et al. [9], from their meta-analysis on the risks of occupational cancers of the larynx have highlighted significant but moderate associations for exposure to engine exhaust and LC (Meta –RR 1.17; 95% CI 1.05 to 1.30]. No statistically significant association between diesel exhausts exposure and LC occurrence emerged from our study.

4.13 Metals

Many heavy metals seem to be involved in the development of several types of cancer. In our study, no significant association between exposure different types of metals has been proven. In a previous prospective study conducted in Sfax, Tunisia [37], there was a statistically significant association between the different metals and the incidence of LC and nasopharyngeal cancer. The ORs were 2.41 for arsenic; 4.95 for cadmium; 2.09 for chromium; 8.87 for nickel.

4.14. Formaldehyde

Formaldehyde is a proven human carcinogen by the IARC in relation to leukaemia and nasopharyngeal cancer [38]. For the laryngeal location, the results are less conclusive. Although some studies, found positive associations between occupational exposure to formaldehyde and LC [39], the meta-analysis carried out by Paget-Bailly et al. [9] did not support this hypothesis. In our study only three patients were exposed to this agent without a statistically significant association p=0.361.

5. Conclusions

Overall, several occupational risk factors have been incriminated in LC. In our study, the most incriminated chemical occupational substances were asbestos, cement dust, solvents, and paint vapors. The definite carcinogens were exposure to asbestos and strong inorganic acid mists. The rubber industry is the only work sector classified as a definite carcinogen by IARC for this cancer site. Otherwise, smoking and alcohol consumption are the most incriminated lifestyle factors, with a convincing level of evidence.

Preventing this cancer starts with fighting against these bad lifestyle habits and the intervention in the occupational factors. Further studies enabling an in-depth analysis of occupational exposures are necessary to provide a clearer definition of the etiological associations between single agents and circumstances of exposure and the genesis of LC.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

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