ORIGINAL ARTICLE

Epidemiological study on nasopharyngeal cancer in Morocco: Case of the University Hospital Center Mohammed VI in Marrakech

Etude épidémiologique sur le cancer du nasopharynx au Maroc : Cas du Centre Hospitalier Universitaire Mohammed VI de Marrakech

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Abstract

Introduction: Globally, nasopharyngeal cancer has a varied geographic distribution, occurring more frequently in certain areas and less often in others (1).
Aim: This article presents the epidemiological situation of this cancer in the Marrakech-Safi region, Morocco.
Methods: Our retrospective study analyzed the epidemiological profile of nasopharyngeal cancer in the Marrakech-Safi region (Morocco) based on 226 cases evaluated at the University Hospital Center MOHAMMED VI of Marrakech from 2014 to 2018. We used descriptive and analytical statistics to create this profile.
Results: The cases studied were 61.9% male (140 cases), and 38.1% female (86 cases), with a mean age of 47.95 ± 16.54 years and a sex ratio of 1.62 (p <0.001). The majority, 76.5%, were married, 16.4% single, 5.8% widowed and 1.3% divorced. The Medical Assistance Plan (RAMED) was the most widespread medical coverage (86.73%). The provinces most affected were Marrakech (42.92%), Safi (10.62%) and El Kelaa (9.73%). These cases were without profession (55.31%), housewives (13.72%), farmers (7.08%), and workers (3.98%). This may be due to the multifactorial etiology of the disease, including occupational exposure to chemical carcinogens.
Conclusions: The study reveals the incidence of nasopharyngeal cancer and identifies the age group most affected in the region studied, highlighting a link with formaldehyde. Further studies are recommended to determine the probable risk factors for this cancer.

Key words: Nasopharyngeal carcinoma, Formaldehyde, Epidemiology, Marrakech-Safi, Morocco.

Résumé

Introduction: Globalement, le cancer du nasopharynx a une distribution géographique variée, plus fréquente dans certaines régions et moins fréquente dans d'autres (1).
Objectif: Cet article présente la situation épidémiologique de ce cancer dans la région de Marrakech-Safi, au Maroc.
Méthodes: Notre étude rétrospective a analysé le profil épidémiologique du cancer du nasopharynx dans la région de Marrakech-Safi (Maroc), en se basant sur 226 cas évalués au Centre Hospitalier Universitaire MOHAMMED VI de Marrakech entre 2014 et 2018. Pour établir ce profil, nous avons utilisé des statistiques descriptives et analytiques.
Résultats: Les cas étudiés étaient à 61,9% des hommes (140 cas), et à 38,1% des femmes (86 cas), avec un âge moyen de 47,95 ± 16,54 ans et un sex-ratio de 1,62 (p <0,001). La majorité soit 76,5 %, étaient mariés, 16,4 % étaient célibataires, 5,8 % veufs et 1,3 % divorcés. Le Régime d'Assistance Médicale (RAMED) est la couverture médicale la plus répandu (86,73%). Les provinces les plus touchées étaient Marrakech (42,92%), Safi (10,62%) et El Kelaa (9,73%). Ces cas étaient sans profession (55,31%), femmes au foyer (13,72%), agriculteurs (7,08%) et ouvriers (3,98%). Cela peut être dû à l'étiologie multifactorielle de la maladie, notamment à l'exposition professionnelle à des cancérigènes chimiques.
Conclusions: L'étude révèle l'incidence du cancer du nasopharynx et identifie le groupe d'âge le plus touché dans la région étudiée, mettant en évidence un lien avec le formaldéhyde. Des études complémentaires sont recommandées pour déterminer les facteurs de risque probables de ce cancer.

Mots clés: Carcinome nasopharyngé, Formaldéhyde, Épidémiologie, Marrakech-Safi, Maroc.

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What is known
Nasopharyngeal carcinoma is remarkably distributed worldwide.
Environmental, genetic, and viral factors contribute to the etiology of the disease.
Men are more likely than women to get this cancer.
the relationship between nasopharyngeal cancer and formaldehyde as a toxic and carcinogenic substance.

What this article adds
The study analyzed the epidemiological profile of nasopharyngeal cancer in the public sector of Marrakech-Safi, Morocco, from 2014-2018.
The results of the study confirm current knowledge of the epidemiological status of NPC in endemic areas.
The low socioeconomic status of the local population is the main reason of the rise in this disease's incidence.

Introduction

The nasopharynx, the upper part of the pharyngeal cavity, is located under the base of the skull, forming a musculoaponeurotic wall that limits an odd, median cavity behind the nasal fossae (2).
Nasopharyngeal carcinoma (NPC) is an epithelial carcinoma that originates from the nasopharyngeal mucosa and is typically identified in Rosenmüller's fossa in the pharyngeal cavity (3).
A remarkable geographical distribution distinguishes this disease; it is rare in some countries while frequent in others (1). In reality, there are three areas worldwide, consisting of South China (Canton), where the incidence is 30-80/100 000/year, and North China, where the incidence is 2-3/100 000/year, which form a very high-frequency zone, then a medium-frequency zone consisting of Taiwan, Vietnam, Thailand, Malaysia, the Philippines, the Caribbean, the Mediterranean basin, Alaska, and Greenland (8-12/100 000/year), and the United States and Europe (0.5-2/100 000/year), which constitute the low-frequency zone (1).
The disease affects more people from endemic areas in a specific global region than residents of the same region. For example, immigrant populations of North African and Polish origin are primarily affected in France; the incidence of NPC in French people who lived in Morocco was 5.7 times higher than in those who lived in France (1). Local populations in England, Brazil, Australia, France, the United States, Uruguay, and Canada are less affected than Italians who emigrated there (1).
The risk of NPC in indigenous southern Chinese is similar to that of south Chinese living in Malaysia, Japan, and Singapore. However, the incidence of NPC among Chinese Americans is about half that observed in South China, although it is still 10 to 20 times higher than that of whites and blacks in the USA; this is also observed among Chinese emigrating to Australia and the United Kingdom (4).
The incidence of NPC is highest in Morocco and the Maghreb countries, and is endemic in North Africa and Southern China (1-5). According to the International Cancer Research Center (2010), in Morocco, the Age-Standardized incidence Rate of nasopharyngeal carcinoma (ASR (W)) is 2.3 (671 cases) and mortality is 1.5 (414 cases) (6). According to GLOBOCAN(7), in 2018, Morocco reported 844 new cases of NPC (2.2 ASR (W)) and 361 deaths (0.97 ASR (W)).
Nasopharyngeal cancer is a multifactorial disease characterized by three key factors: Infection with the Epstein-Barr virus, which is identified as a class I oncogenic virus by the World Health Organization, is associated with the appearance and development of the disease (8), a genetic susceptibility (1), and an environmental factor (9-10). Among these factors, Exposure to chemical substances like formaldehyde, commonly used in various consumer products and industries, has become a significant research topic.

Methods

This retrospective descriptive study aims to provide an overview of the nasopharyngeal cancer situation in the Marrakech-Safi region, Morocco. It was carried out at the Oncology Center of the University Hospital Center MOHAMMED VI in Marrakech, from 2014 to 2018. All patients with nasopharyngeal cancer diagnosed at this center from 2014 to 2018 were included. We used data from the medical records of patients at the study center. A file is created for each new patient, containing the patient's telephone number and home address, marital status, tumor location, nature and degree of extension, treatment protocol and follow-up, payment method, and management information.
The variables of interest were: The sex, the age of the new cases, the profession, the origin of the consultations, the environment (urban/rural), the tumor location, and the medical coverage. Only patients for whom the most relevant data were complete and available were retained after data processing. We analyzed 9 272 medical records of cancer patients treated at the center between 2014 and 2018. Of these, 226 were records of patients with nasopharyngeal cancer. Duplicates were removed during data processing. Excel was used for data processing, and SPSS version 21 was used for statistical analysis.
Descriptive and analytical statistics were used to study our sample's epidemiological profile of nasopharyngeal cancer. This involved identifying the frequencies and characteristics of each parameter studied (mean, minimum, maximum, etc.). Quantitative variables (mean age of patients) were presented as means ± standard deviation, while qualitative variables (gender, year, and age class) were presented as raw values. We used association tests, including the Chi2 test, which calculates the difference between theoretical and observed frequencies. This test was used to compare the two sexes. Missing data have been eliminated beforehand.

Results

Nine thousand two hundred and seventy-two cancer cases were studied; nasopharyngeal cancer occupies the tenth position in the public sector, with 226 cases or 2.4% of cancer cases.
Among the nasopharyngeal cancer cases, 140 (61.9%)

are male, and 86 (38.1%) are female, with a sex ratio of 1.62 (p <0.001). Seventy-six point five percent of cases are married, 16.4% are single, 5.8% are widowed, and 1.3% are divorced.

Figure 1 shows that most of our patients have the Medical Assistance Plan (RAMED) as medical coverage (86.73%), followed by the National Caisse of Social Prediction Organizations (CNOPS) (4.42%), the National Social Security Fund (CNSS) (3.10%), and the Mutual fund of the Royal Armed Forces (FAR) (0.88%).

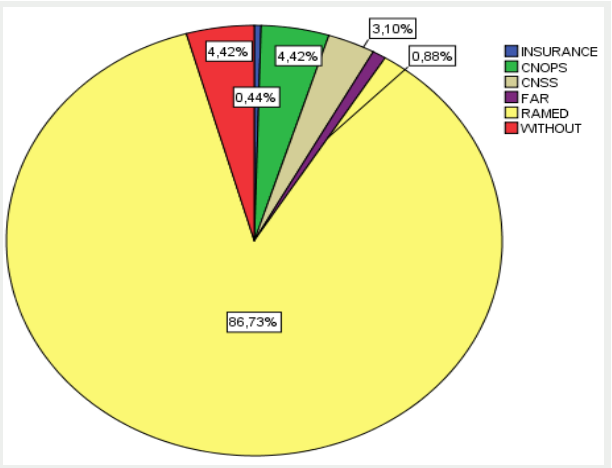

Figure 1. Distribution of new cases of nasopharyngeal cancer studied at Marrakech's University Hospital Center (UHC) MOHAMMED VI during 2014-2018, according to medical coverage

Figure 2 shows a stabilization of the annual distribution of the number of new cases between 2014 and 2015, followed by a significant increase between 2015 and 2018.

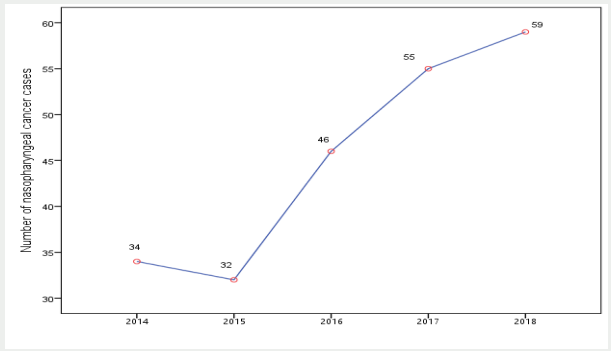

Figure 2. Annual distribution of new cases of nasopharyngeal cancer studied at Marrakech's University Hospital Center (UHC) MOHAMMED VI during 2014-2018

Sixty-eight point six percent (155 cases) of nasopharyngeal cancer cases reside in urban areas and 31.4% (71 cases) in rural areas. with Marrakech province having the highest frequency (42.92%), followed by Safi (10.62%), and El Kelaa (9.73%) (Figure 3).

Concerning the age of nasopharyngeal cancer cases treated at the studied center, according to the five-year age groups, we noticed that the age group [55-60 years] was the most affected by this cancer (Figure 4) and that the average age was 47.95 ± 16.54 years (Table 1).

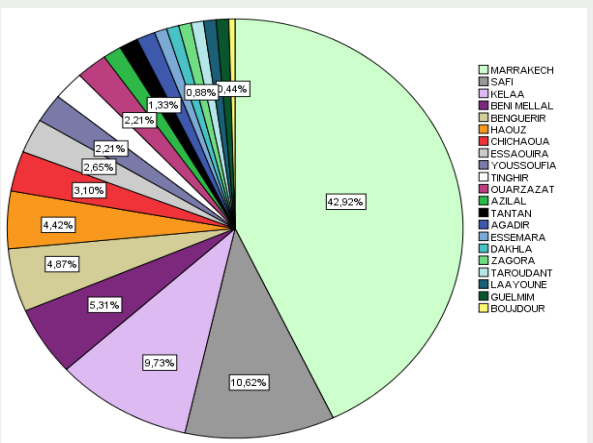

Figure 3. Distribution of new cases of nasopharyngeal cancer studied at Marrakech's University Hospital Center (UHC) MOHAMMED VI during 2014-2018, according to the origin of the consultations

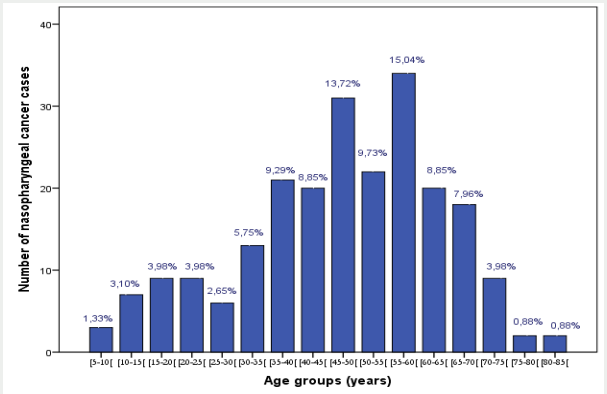

Figure 4. Distribution of nasopharyngeal cancer percentages according to age groups at Marrakech's University Hospital Center (CHU) MOHAMMED VI during 2014-2018

Table 1. Age differences between men and women treated for nasopharyngeal cancer at Marrakech's University Hospital Center (UHC) MOHAMMED VI during 2014-2018

	Age (years)			Chi2 (1dof)
	Average	Minimum	Maximum	
Male (active n = 140)	49.04 ± 16.14	6	85	12.903 (P <0.001)
Female (active n = 86)	46.17 ± 17.12	6	75	
Total (active n = 226)	47.95 ± 16.54	6	85	

The cases of nasopharyngeal cancer treated in the center are without profession (55.31% of cases), housewives (13.72%), farmers (7.08%), and workers (3.98%) (Figure 5). These occupations may indirectly indicate exposure to toxic products such as pesticides, solvents, fumes, or dust.

Discussion

These results provide an epidemiological profile of nasopharyngeal cancer in the population of the Marrakech

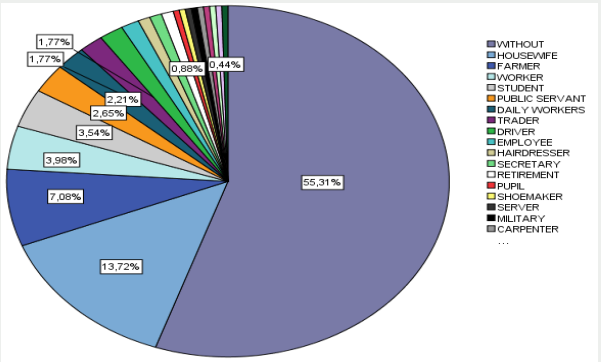

Figure 5. Distribution of new cases of nasopharyngeal cancer studied at Marrakech's University Hospital Center (CHU) MOHAMMED VI during 2014-2018, by profession

-Safi region.

Nasopharyngeal cancer is predominant in men (61.9%) compared to women (38.1%), with a sex ratio of 1.62 (p <0.001). These results are roughly similar to those of the study of Maamri(11), which is a retrospective epidemiological study carried out during 2005-2010 in the eastern region of Morocco, where the sex ratio is 1.61, in favor of men who are more affected than women. It differs from the literature data, where the sex ratio varies between 2 and 3.5 in favor of men (1-11-12).

In our sample, both sexes are affected by nasopharyngeal cancer at an older age (six years), which is different from the results of the study by Arfaoui,Soulaymani(1), which is a retrospective epidemiological study that took place in the Al Azhar center specializing in the treatment of cancer and located in Rabat during the period 1994-2004, where we notice that the early age in men is 11 years old and in women is ten years old. In children, NPC represents 1% to 5% of all primary malignancies (13).

Ammor,Baali(14) noted that among the high-risk populations, children, their attainment of NPC in Morocco could be explained by the fact that they stay outside for a long time in summer when ozone levels increase, and the fact that their respiratory system is still in growth age. In addition, they mainly belong to low-income urban groups.

Men are more likely than women to develop nasopharyngeal cancer, specifically in endemic areas (15). According to Feng,Chang(15), male age-standardized NPC (per 100 000) in 2012 were two to three times higher than female rates in various countries, including Zhongshan, China (25.0 vs. 7.7), Hong Kong (12.8 vs. 4.0), East Asia (2.5 vs. 1.0), Shanghai, China (3.1 vs. 1.0), Europe (0.6 vs. 0.2), and North Africa (2.3 vs. 1.0). According to Feng,Chang(15), the difference in incidence between men and women is associated with the unequal distribution of environmental factors between the two sexes (smoking and certain occupational exposures), differences in sex steroid hormone levels, and differential genetic susceptibility. The same authors suppose that the development of NPC could be influenced by the X chromosome or a sex-dependent variation in gene expression, which could interact with the Epstein-Barr virus infection.

Between 2015 and 2018, the number of new cases of nasopharyngeal cancer increased significantly, from 32 to 59 annually. This can be explained by the attendance at the center studied, which increased with the introduction of RAMED.

Most of our patients have RAMED as medical coverage (86.73%). The Medical Assistance Plan was generalized in 2012 (16), founded on the ideals of national unity and social help for the benefit of the underprivileged. This suggests that the majority of our patients come from low socioeconomic backgrounds. Indeed, the socioeconomic level of individuals and, consequently, of the community influences their health status. A stable and appropriate income might ensure a proper and healthy environment, an adequate, balanced diet, and access to health services and medical treatment (17).

The majority of cases in our sample belong to urban areas (68.6%), and the highest frequency of nasopharyngeal cancer cases observed is in Marrakech (42.92%), followed by Safi (10.62%) cases, and El Kelaa (9.73%). This can be explained by the fact that Marrakech and Safi concentrate more than 67% of the region's urban population (18) and by easy access in urban areas to health facilities, education, financial and social resources, and illness awareness (17). Mimi & Yuan(12) found no differences in NPC risk between urban and rural populations in southern China, as well as those in Southeast Asia, and noticed that non-Hispanic white residents of urban counties in the United States, on the other hand, have higher NPC mortality rates than those in rural counties.

Nasopharyngeal cancer is most frequent in cases belonging to [55-60 years [with (15.04%). Figure 4 shows that the incidence of this cancer increases between the ages of 30 and 60 years, and after 60 years, the incidence decreases. These results align with the findings of Sekarutami,Gondhowiardjo(19). They found that in high-risk populations, the incidence of nasopharyngeal cancer rose from the age of thirty, peaked between 40 and 60 years, and then started to decline (19). Also, in this figure, we notice an early incidence peak between 10 and 20 years and a second high between 40 and 60 years, which agrees with the literature; it is a bimodal distribution by age that characterizes the Maghreb countries (20-22).

On the other hand, this study shows that most cases are without profession (55.31%), housewives (13.72%), farmers (7.08%), and workers (3.98%). Notably, most patients (55.31%) are day laborers who report not having a job (they do not have an official job).

The Marrakech-Safi region is known for its cultural heritage, diversity, and essential artisanal manufacturing; indeed, the souks of the Medina of Marrakech constitute an important artisanal market. Marrakech is famous for its wood, clay, copper, stone, and weaving materials (23). Marrakech occupies the 3rd place in Moroccan handicrafts with 8.9% of total employment in the sector; it is the central export pole of the kingdom with more than 50% of sales of artisanal products abroad, and handicrafts have a vital role in the economic and social life of the population of the city (23). The province of Safi is also famous for its pottery. Marrakech is a source of income, contributes to creating employment opportunities, and supports more than 40 000 artisans (23). These artisans

are exposed to carcinogenic substances in dyes, pigments to color textiles, leathers, papers, inks, paints, wood, and cotton dust. Leather dust, tetrachloroethylene, and trichloroethylene (used in dyes) are considered by the International Agency for Research on Cancer as possible carcinogens (24). Exposure to cotton, wood dust, combustion in the textile industries, work in poorly ventilated rooms, and inhalation of formaldehyde in the printing industry can create procarcinogens, activate detoxification processes, and increase the risk of NPC (25). This artisanal sector attracts many day laborers and workers from the region.

Thirteen point seventy-two percent of nasopharyngeal cancer cases in our sample are housewives; unhealthy diets and cooking methods can explain this. The Moroccan diet is known for using spices, the consumption of salted and spicy dried meat such as quadid, and khlii, which is meat prepared with salt and then preserved in its fat or olive oil, smen (fermented butter), and brines such as preserved lemon. For example, the combination of the amines piperidine and pyrrolidine present in black pepper and paprika with sodium nitrite in the nasal mucosa of rats and mice produces nitrosamines, which cause tumors, the butyric acid contained in smen (butyric fermentation of butter) is intensely involved in the in vitro reactivation of the Epstein Barr virus (9). The results of the study by Feng,Khyatti(26) found that the use of traditional cooking facilities like kanoun, which is an ancient brazier originating from Morocco and is essential for cooking and especially keeping food warm, seems to have less impact in adulthood, but in childhood, it increases the risk of NPC almost twofold. Cooking with wood fires in youth and poor kitchen ventilation were linked to a 30-40% increase in the risk of NPC, but these factors are not statistically significant. The same authors reported that a multivariate analysis affirms these results and suggests that in North Africa, young exposure to household emissions is a risk factor for NPC. Using tagine (a cooking utensil made of terracotta, sometimes varnished, widespread in traditional Moroccan cuisine) and a pressure cooker as a cooking method is unhealthy. It can lead to the formation of nitrosamines, which result from a reaction of fat to heat and are accelerated by cooking at high heat (14). Heterocyclic amines can also be formed, often through the consumption of grilled or pan-fried canned meat, which increases the risk of NPC (27).

According to the Ministry of the Interior Directorate General of Local Authorities, the Marrakech-Safi Region (2015), about 53% of the region's working population is absorbed by the agricultural sector (18). Farmers use pesticides, fertilizers, and insecticides that contain carcinogens; indeed, pesticide exposure is cited as the cause of certain cancers (24). Exposure to toxic substances and agricultural life is significantly associated with NPC (14). Indeed, lymphoma cases and cancer of the maxillary sinus, NPC, and cancer of the larynx and skin predominate among farmers and are caused by exposure to fertilizers, pesticides, dust, and solvents formaldehyde ultraviolet radiation, and organophosphate insecticides or phenoxyacetic acid herbicides (14). This explains why 7.08% of the cases in our sample are farmers.

Relationship between chemicals and NPC

Among the substances studied, formaldehyde, a substance widely used in various industries and consumer products, has been associated with nasopharyngeal cancer (9-24). Epidemiological research suggests a potential correlation between prolonged exposure to this substance and a higher risk of NPC in certain populations (9-24-28).

Formaldehyde is a well-known carcinogen. In 2004, the International Agency for Research on Cancer (IARC) officially designated formaldehyde as a “definite human carcinogen” concerning NPC (28). Denmark, Malaysia, Taiwan, and France have established lists of recognized occupational diseases, including formaldehyde-related malignancies (28). The European Union's Classification of Occupational Diseases, Labelling, and Packaging of Substances and Mixtures Directive and the American Conference of Governmental Industrial Hygienists are among the authorities to have recognized the potential carcinogenicity of formaldehyde (28).

Kwon,Kim(28) study found an increase in mortality from goldsmithing or metal processing, but the IARC committee found no significant risk of NPC associated with formaldehyde.

Chang and Adami(29) observed that, although there is little epidemiological data in humans, laboratory observations in rats confirm the increased risk of NPC after exposure to formaldehyde in the workplace. The same author notes that exposure to formaldehyde increases the risk of NPC by a factor of 2 to 4, but that most studies have not found a significant association, and that a recent IARC evaluation showed the carcinogenicity of this substance, with excess mortality due to NPC in 25000 American workers. According to IARC, formaldehyde is classified as a Group 1 human carcinogen distributed through indoor air (24). Kwon,Kim(28) noted that, the relationship between formaldehyde exposure and NPC is not clearly carcinogenic, but exposure to this substance can induce genotoxicity in human nasal cells and the in vitro production of DNA-protein cross-links.

Understanding the impact of formaldehyde on nasopharyngeal cancer epidemiology is crucial for industrial practices and public health policies, with stricter laws potentially reducing the risk of this cancer.

Ammor,Abdellatif(9) carried out a study, which is a questionnaire involving 32 NPC patients from the private sector in Marrakech between 1997 and 1999, as well as 48 controls taken at random from a population showing the same socio-economic characteristics as the patients. This study revealed a statistically significant relationship between this cancer and certain factors related to the environment (contact with agriculture or with toxic substances and livestock), diet (consumption of smen (fermented butter), khlii (meat prepared with salt and then preserved in its fat or olive oil), and alcohol)).

Limitations of the study: Limitations of the study include the lack of information on the exact occupation of most patients, highlighting the importance of understanding their occupation to identify potential risk factors and disease etiology.

Conclusions

In the public sector of the Marrakech-Safi region of Morocco between 2014 and 2018, this retrospective epidemiological study revealed a higher incidence of nasopharyngeal cancer in men, identifying the age group most affected. The study also highlighted the link between formaldehyde and this cancer.
Further studies are recommended to determine the probable risk factors for nasopharyngeal cancer in this region.

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