Open Access Research Journal of
Biology and Pharmacy
Journals home page: https://oarjbp.com/
ISSN: 2782-9979 (Online)

(RESEARCH ARTICLE)

Prevalence of oral premalignant lesions in the area with the highest prevalence of gastrointestinal cancer

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Open Access Research Journal of Biology and Pharmacy, 2023, 08(02), 008–016

Publication history: Received on 25 May 2023; revised on 05 July 2023; accepted on 07 July 2023

Article DOI: https://doi.org/10.53022/oarjbp.2023.8.2.0024

Abstract

Objective: According to research conducted in Iran, from 141450 cases of reported cancer between 2003-2006, 1896 cases of oral and lip cancer have been reported. The timely and prompt diagnosis of this disease reduces mortality, increases longevity, reduces damage to adjacent structures, reduces financial costs, and unwanted side effects. The current study aimed to investigate the prevalence of oral premalignant lesions in the oral cavity and the factors related to it in Golestan province.

Methods: In this descriptive-analytic cross-sectional study, 1900 Iranian subjects living in Golestan province, regardless of gender, aged 40 and above, participated voluntarily and randomly. Initially, a questionnaire containing demographic information, assessment of habits and risk factors was completed for each patient in an interview form, followed by oral examination on all patients. Statistical analysis of data was done by SPSS 22.

Results: The mean age of these individuals was 49.5 ± 10.3 years and the highest premalignant lesions were observed in the age range of 70-80 years. Of the 1900 participants, 69 (3.6%) had pre-malignant lesions. Among the pre-malignant lesions, the prevalence of lichen planus was 49.28%, leukoplakia was 14.49%, and the suspected malignancy was 18.8%. In addition, there was a significant relationship between the use of tobacco with the development of pre-malignant lesions ($p < 0.01$). Cigarette alone showed the highest association with the development of pre-malignant lesions.

Conclusions: In this study, there was a significant relationship between risk factors such as age, ethnicity and smoking with the development of premalignant lesions in people. However, risk factors such as alcohol consumption and family history did not show a significant relationship.

Keywords: Mouth Neoplasms; Precancerous Conditions; Gastrointestinal Neoplasms; Tobacco Products

1. Introduction

Head and neck cancer is the eighth most common cancer, which has grown significantly in the last few decades(1). Head and neck cancers refer to several cancer sites, including squamous cell carcinoma, mucoepidermoid carcinoma, adenoid cystic carcinoma, adenocarcinoma, lymphoma, sarcoma, melanoma, etc. These malignant neoplasms appear in the oral cavity, nasal cavity, oral mucosa, skin, Paranasal sinuses, salivary glands, larynx, and pharynx (2). Oral squamous cell carcinoma (OSCC) is the most common form of oral cancer, including more than 90% of oral cancers (3, 4). The most common location of OSCC is on the lateral surface of the tongue, the ventral side of the tongue, and then the floor of the mouth. It has also been reported in other areas such as lip, front of tongue, gums, cheek mucosa, floor of mouth, soft

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palate, and hard palate (4). The appearance of these lesions is white, red, white, and red, raised or scarred (5). They include leukoplakia, erythroplakia, erythroleukoplakia, lichenoid reactions, lichen planus, oral submucous fibrosis, reverse smoker's palate, and actinic cheilitis(6). They can turn to OSCC without any specific change in their shape and appearance (5,7).

Oral cancer is also a common public health challenge with a relatively high incidence and prevalence in Iran (8, 9). According to the previous researches in Iran, out of 131,191 new cancer cases reported in 2020, 1139 cases were related to mouth and lip cancer (10). In Golestan province, the prevalence of this cancer is significant and 3,100 cases per 100,000 people were reported in 2016 (9). Tobacco smoking, alcohol use and old ages are the main risk factors that are known in squamous cell carcinoma etiology (11). Growing pattern in tobacco smoking particularly in youth and women along with aging of the population and some risk factors like opium use may increase burden of oral cancer in the near future in Iran and particularly Golestan province (12). Therefore, early diagnosis of oral premalignant lesions is too important as it could improve survival rate, and reduce mortality rate oral cancer cases (13). It can also provide financial benefits for both patients and health system. However, there is no clear understanding regarding prevalence of oral premalignant lesions (OPML) and its associated risk factors among the Iranian adults (14). The current study aimed to investigate the prevalence of oral premalignant lesions lesions in the oral cavity and the factors related to it in Golestan province.

2. Material and methods

We conducted a cross-sectional study on 1900 people of Iranian adults (age≥40) residing in different cities of Golestan province from April 2018 to March 2019. Testing was done in the form of information obtained through the health centers of Gorgan and Gonbad cities and neighboring cities, and the testing in all centers lasted four months and was done at no cost to the subjects. The sample collection method was based on several dental clinics, hospitals, and comprehensive urban and rural centers (health houses) in the cities of Gorgan and Gonbad. We also performed a household base survey to cover some remote rural areas of the province. Patients suspected of oral premalignant lesions were referred to the dental clinic for final diagnosis and followed up.

On the day of the examination, we explained the purpose of the study to the participants. Written informed consent was completed for each participant. Then, we completed a questionnaire containing demographic information and a few other questions about previous history of cancer and other maxillofacial disease. It should also be noted that this questionnaire was evaluated in an expert panel by eight experts (two assistant Professor of Biostatistics, one associate Professor of Epidemiology, one assistant Professor of Community Oral Health, two assistant Professor of Oral and Maxillofacial Surgery and two assistant Professor of Oral & Maxillofacial Medicine). We performed a pilot study on 30 patients before the primary research to check the validity and reliability of the questionnaire. The Cronbach's alpha was 80%, which was acceptable. A dentist performed examinations under the supervision of a maxillofacial specialist using different oral examination techniques (observation, palpation of the lesion) and tools such as a unit light, mirror, probe, gauze, and flashlight in the examination room(15, 16). First, an extra-oral examination was performed for each person, which included the following: a) head and neck examination: in terms of distortion or facial deformity and swelling of the face b) examination of the lymph nodes of the head and neck: in terms of size, consistency, mobility or stability, and pain, and then an intra-oral examination was performed, which included the examination of the oral mucosa, especially the areas such as the lateral and ventral surface of the tongue, the floor of the mouth, the soft palate, and the lips, where the possibility of the formation of these lesions is higher(15).

At this stage, if there was no suspicious lesion in the mouth and no risk factor, the person left the examination center and was advised to participate in oral cancer screening every five years. In the case of founding a lesion, participants were examined in terms of a) the involved area, b) size, c) color (white, red) and diffusion pattern (homogeneous, non-homogeneous), d) external border of the lesion: clear or unclear e) consistency: (soft, hard) k) surface characteristics of the lesion (granular, verrucous, wound or scar)(17).

After the final diagnosis, the lesions were divided into the following categories (15): 1) Leukoplakia, 2) Erythroplakia, 3) Erythroleukoplakia, 4) lichenoid reactions, 5) lichen planus, 6) Submucosal fibrosis, 7) Actinic cheilitis, 8) Palatal keratosis caused by reverse smoker's palate(18). For the final diagnosis, all cases of lesions were consulted with an oral and maxillofacial specialist (The questionnaire and consent letter are attached in the supplementary material).

2.1. Sample size

The sample size was estimated, assuming that the prevalence of OPML was 4% (19, 20). We used the following equation for sample size estimation where Z1-α/2= 1.96 and d was 0.01. Accordingly, the sample size was estimated to be 2305. The final estimated sample size was 2500 considering 10% drop in the study samples.

$$n = \frac{Z^2_{1-\alpha/2}\, P(1-P)}{d^2} \quad \text{……. Equation 1}$$

During the study, 2305 people were referred for the oral examination. Of this number, 1900 people agreed to be interviewed and filled out the questionnaire (Response rate= 75%).

2.2. Inclusion criteria were

All people aged 40 and above who voluntarily participated in the research.

2.3. Exclusion criteria were

People taking systemic medications that have oral side effects;

People with lupus and systemic diseases with oral complications;

People with traumatic lesions.

2.4. Statistical analysis

The statistical analysis of the data was performed by chi squared, Student t-test and One-Way ANOVA tests, and P values <0.05 were considered significant. Finally, the resulting data were analyzed using SPSS (version 22) statistical software

3. Results

1900 people participated in this study, 719 men (37.8%) and 1181 women (62.2%). The samples were in the age range of 40 to 100 years and the average age of these people was 49.5 years. The largest numbers of participants were in the age range of 40-50 years (1207 people). Most of the women were housewives, agriculture, and self-employment were the most shared occupations between women and men. 89% of the participants did not show any risky behavior. 10.6% of the people used tobacco and 1.4% people used alcohol. Also, cigarettes were the most commonly used smoking substance, and the most common type of alcohol consumed by people was wine. Among 1900 participants, 69 people (3.6%) had OPML lesions. The frequency of these lesions was higher in men. In women it was 3.1% of the total female population and in men it was 4.5% of the total male population. Despite this difference, no significant difference was observed between the two groups (p=0.88). The average age of people with OPML is 54.8 ± 13.78 and it was significantly higher than healthy subjects. Also, ethnicity had a significant relationship with the occurrence of OPML (p=0.05). In the Turkmen race, men were more susceptible than women. (p=0.01) In Turkmen ethnicity, smoking has a direct relationship with OPML lesions (P=0.00). The prevalence of OPML lesions has a significant relationship with the level of education; it was observed that patients with a bachelor's level of education had a higher probability of having OPML lesions than the entire population (12.7%). Also, this relationship is more common in men (p=0.00).

Smoking tobacco was the most commonly used substance in affected people (11.6%). Also, Marijuana, Snuff and Crystal meth were not used by any of the research participants (Table 1).

Table 1 The frequency of the type of Tobacco products used among people over 40 years old in Golestan province

The type of Tobacco products used by the affected person	The frequency of Tobacco products used in the affected person	The percentage of Tobacco products in the affected person
Opium	1	1. 4
Cigarettes	8	11.6
Hookah	2	2.9
Opium + Cigarettes	1	1.4
Cigarettes + Hookah	1	1.4

Also, these lesions were more common in men who used tobacco (p=0.04). Smoking had a very important and significant role in developing OPML lesions, (p=0.01), but alcohol consumption as another risk factor had no significant relationship with OPML lesions in both genders (p=0.243). Positive family history of oral cancer or other cancers had no significant relationship with the occurrence of OPML lesions (p=0.68). Also, this relationship did not show a significant difference in both genders (p=0.561). OPML lesions in the tongue area were more common than other areas of the mouth (29%). After that, the most frequently observed area was the buccal mucosa (26.1%) and maxillary gingiva (8.1%) (Table 2).

Table 2 Frequency of OPML lesions in people over 40 years old by the involved area

Lesion site	Percentage	Frequency
Dorsal surface of tongue	29.0	20
Buccal mucosa	26.1	18
Maxillary gingiva	8.7	6
Upper vestibule	7.2	5
upper lip	5.8	4
floor of the mouth	5.8	4
Lower lip	4.3	3
Ventral surface of tongue	2.9	2
mandibular gingiva	2.9	2
jaw bone	2.9	2
toothless ridge	2.9	2
corners of the lips	1.4	1
Total	100.0	69

Table 3 Types of OPML lesions and the frequency of these lesions in the population of people over 40 years-old in Golestan province

OPML lesion type	Frequency	Percentage
Lichen planus	34	49.2
Suspicious to OSCC	13	18.8
Leukoplakia	10	14.4
Lichenoid reactions	7	10.1
Erytroplakia	3	4.3
Erytroleukoplakia	2	2.8
Actinic chelitis	0	0
Oral submocous fibrosis	0	0
Total	69	100.0

It was also observed that the frequency of this lesion is higher in the center of the province (Gorgan) (58%) than in other cities of the province (Figure 1).

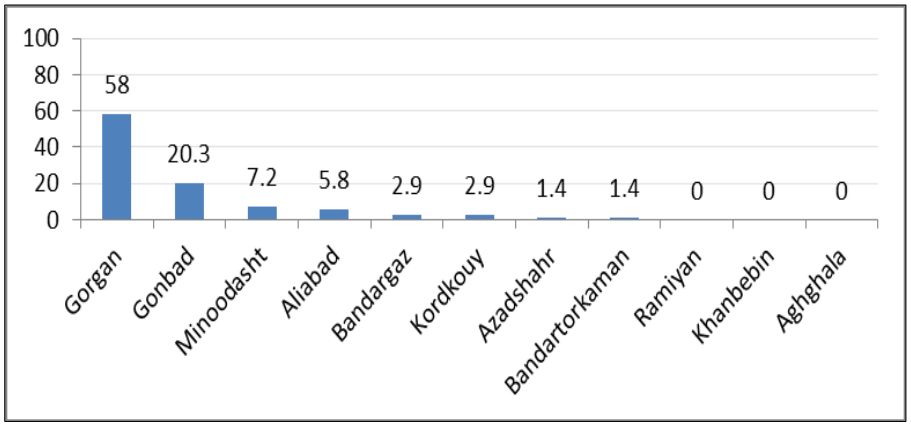

Figure 1 Frequency of OPML in different cities of Golestan province

4. Discussion

Among oral diseases, oral cancer has caused the most concern for the dental community. Two thirds of this cancer is seen in developing countries(21). Oral cancer often starts from an OPML(22, 23). Early detection of OPML before biopsy, by considering the WHO guidelines for oral cancer screening and dysplasia diagnosis tools, can help in the prognosis of cancer treatment or in preventing its transformation into malignancy(19). Cancer is the third cause of death due to disease in Iran(24). Head and neck cancers are very common in the northern region of Iran and have many deaths every year due to poor prognosis. So that in 10-year study, conducted in 2018, Taziki and his colleagues, reported the incidence of cervical cancer in Golestan province was 4%, and it was calculated 8% among cancer patients (22). Also, squamous cell cancer was found specifically in the oral cavity of 1,500 people per 100,000 people in both sexes (22). Studies have shown that 18% of OPML become cancer(25). It is worth noting that in the region where Roshandel and his colleagues investigated the prevalence of malignant lesions, the prevalence of OPML was higher(26).

In the current research, according to the investigations, the prevalence of OPML in Golestan province, which has the highest statistics in the field of gastrointestinal cancers in the country, was equal to 3.6%. This result was consistent with the prevalence of 3.7% in the Pahwa study (21). The frequency of lesions in the order of highest to lowest is: lichen planus (49%), leukoplakia (14.4%), lesions suspected of squamous cell cancer (18.8%), lichenoid lesions (10.1%), erythroplakia (4.3%) and erythroleukoplakia (2.8%). In many studies, erythroleukoplakia was investigated along with

leukoplakia(27). But in this study, we tried to examine these two lesions separately. In the study of Chher and his colleagues, the prevalence of leukoplakia was found to be equal to 60% of OPML lesions. However, the prevalence of leukoplakia in the present study was equal to 14.4%, which can be justified by the difference in the studied society, geographical distribution, risk factors and people's habits (28). In the present study, the prevalence of lichen planus was obtained as 49.2%, while this number was 30.8% in the Chher study(28). On the other hand, in Mathew's study, as in the current study of Lichen Plan, OPML was the most common lesion in the population(23). Lichenoid lesions are one of the important premalignant lesions that have the possibility of turning into malignancy in these lesions(29). In the study of Robledo and his colleagues, the prevalence of this lesion among other lesions was calculated to be 2.4%(30). But in our study, this prevalence reached 10.1%. In this study, we did not separate lichenoids because it was difficult to distinguish contact lichenoids from drugs. According to the results obtained in this study, most OPML were found in the dorsal surface of the tongue, which again shows a higher prevalence of lichen planus. But in the study of Chher and his colleagues, the buccal mucosa was more affected by OPML (28).

In the present study, there was no significant difference in the gender of OPML patients. But in other studies, OPML has a significant difference in male gender compared to female (21, 23, 28). In this study, it was found that with increasing age, the possibility of OPML increased, which was in line with other researches (28, 31, 32). In the comparison of the prevalence of OPML between Turkmen and non- Turkmen ethnic groups, OPML was more common in Turkmen. Two separate studies conducted by Marjani and his colleagues and Roshandel and his colleagues in relation to the comparison of risk factors for esophageal cancer (tobacco, cigarette, snuff and other drugs and food and hot liquids) showed differences between Turkmen and non-Turkmen groups. But they were not significant. Many of these risk factors are common with oral cancer and OPML, so it can be concluded that the higher prevalence of OPML, like digestive cancers, in this ethnic group can be due to genetic factors and family history of cancer (9, 21, 26). Men were also more affected than women in both ethnic groups. In this study and many other studies, education level had a significant relationship with OPML. But in some studies, no significant relationship was found(33). In the present study, people with a higher level of education were exposed to more lesions than the whole population. In this way, it is justified that people with a higher literacy level were identified earlier because they had more knowledge. In this study, one of the most important types of smoking that showed the highest risk of OPML was smoking Cigarettes, with the increase in the number of smokers (heavy smokers), the probability of OPML increases twice compared to smokers and four times compared to non-smokers(21, 28, 34-36). In a study in 2018, the result was that chewing betel plant can be the strongest known risk factor among the population studied (21, 28, 37, 38).

Also, in the study of Mathew and his colleagues, chewing areca nut seeds were assigned the highest risk among the population(23). In the present study, as in the study by Chher et al. and Petti et al., we did not find a significant relationship between the prevalence of OPML in alcohol users, but in Warnakulasuriya's study in 2009, the synergistic effect of smoking and alcohol use was proven(21, 28, 39-41) In the study of Gavarello and his colleagues in 2008, the existence of a family history of cancer was considered as an important risk factor for OPML, while in our study, like the study of Pahwa and his colleagues, this relationship was not significant (21, 42). In some studies, risk factors such as consumption of hot food and liquids (43, 44) and spicy foods (45) as well as poor oral hygiene (46), low consumption of fruits and vegetables (47) and trauma(48, 49) to the oral tissue are also known as a risk factor for cancer.

5. Conclusion

In this study, a significant relationship between risk factors such as age, ethnicity and smoking was seen with the development of OPML in people ($p<0.05$). But risk factors such as alcohol consumption alone, and family history did not show any significant relationship.

Compliance with ethical standards

Acknowledgments

We would like to express our appreciation to Research Center of Gastroenterology and Hepatology of Golestan University of Medical science of Golestan, Iran.

Disclosure of conflict of interest

The authors declare that they have no competing interests in this section.

Statement of ethical approval

This study was approved by ethical committee of Golestan university of medical sciences, Gorgan, Iran (code: IR.GOUMS.REC.1397.023). All methods were carried out in accordance with relevant guidelines and regulations. Informed consent was obtained from all subjects. Participants had the right to unconditionally withdraw at any stage of the study, with no fear of physical, mental, social, legal and economic harm. At the collecting stage, transferring and storing information, attention was also paid to keeping the confidence of the patients. Besides, the effective results in the health process of the patients and the necessary guidance for the next steps were provided to the participants of this study.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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