

Epidemiological Aspects in Lip Tumors in Oltenia Region of Romania During 2012-2016

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ABSTRACT: Purpose. The objective of this study was to review lip tumor diagnosed subjects from Oltenia region, in the past 5 years according to gender, age, home environment, profession, geographic area, smoking habit, associated diseases, tumor location, macroscopic aspect and histological type. Material and Methods. The study was done at the Oral and Maxillo-Facial Clinic of the Emergency Clinical County Hospital of Craiova, and involved the analysis of patient file records, surgical registers, histopathological bulletins, from 2012-2016. Results. Of the 175 subjects included in this study, all of them diagnosed with lip tumor pathology, 109 (62.29%) were men, and 66 (37.71%) were women, all of them with ages between 6 and 92 years, with a mean age of 61 years. Distribution of study participants according to the home residence showed that majority of the subjects lived in rural area. The most frequently localization of lip tumors in study participants was at the lower lip-140 cases (80%), than at the upper lip-35 cases (20%). According to histological characteristics, distribution of the malignant lip tumors was 87.39%-squamous cell carcinoma (SCC), 5.41%-basal cell carcinoma (BCC) and 7.20%-other type of tumors. Conclusions. The lower lip was the most affected, by lip cancer, and squamous cell carcinoma represents the most frequently histological type of these tumors.

KEYWORDS: lip cancer, lip tumor epidemiology, lip histopathology, lip study

Introduction

Lip cancer is the most frequent tumor of the oral-maxillary region [1], representing 1/5 of upper aerodigestive tract cancers and 15-30% of all encephalic extremity cancers [2].

In the US, 3500-4000 new lips cancer cases are diagnosed every year, being a 2 per 100000 incidences and 500000 new cases worldwide [3]. High male lip cancer rates are reported for regions of North America (12.7 per 100 000 per annum), Europe (12.0 per 100 000 per annum) and Oceania (13.5 per 100 000 per annum), while it is virtually unknown in parts of Asia [4].

About 90 per cent of tumors arise in the lower lip with 7 percent occurring in the upper lip and 3 per cent at the oral commisure [5].

In Romania, lip cancer accounts for about 1% of the nearly 60,000 new cases of malignant tumors detected annually [6]. In Dolj county, 1,5% of cancers are lip cancers [7].

Squamous cell carcinoma (SCC) is the commonest histological tumor type in lip cancers, followed by basal cell carcinoma [5].

Squamous cell carcinoma is accounting for more than 95% of lip cancers in all published case series. However, most malignant neoplasms of the upper lip are basal cell carcinomas (BCC) [8]. The most common non-mucosal form of lip cancer arises from tumors of the minor salivary glands [5].

The International Agency for Research on Cancer (IARC) report, however, states that: "Assessment of the carcinogenicity of solar radiation for the lip is complicated by the fact that carcinoma of the lip is actually diagnosed as a mixture of cancers of the external lip and cancers of the buccal membranes" [9].

The aim of the study was to highlight the epidemiological aspects, associated with lip tumors as gender, age, home residence, profession, geographic area, smoking habit, associated diseases, tumor location, macroscopic aspect and histological type on a sample of subjects from Oltenia region, treated at the Oral and Maxillo-Facial Clinic of the Emergency County Hospital of Craiova.

Material and methods

The study was performed on 175 subjects, diagnosed with lip tumors, who presented between 2012-2016 at the Oral and Maxillo-Facial Surgery Clinic within the Emergency Clinical County Hospital of Craiova. The study was approved by the Ethical Committee of the University of Medicine and Pharmacy of Craiova. All study participants were informed on study objectives and they gave the informed consent. The patients were analyzed according to the age, gender, profession, home environment, geographic area, smoking habits, localization of the lesions, associated systemic diseases and histopathological type of tumor. The relationship between these features and etiological factors

was also evaluated. The collected data were analyzed by descriptive statistics and the relationship between lip tumors and risk factors was evaluated using Chi-square test, with $\alpha=5\%$. In this case, any p value lower than 0.05 showed that there was a clear relationship between the risk factor and the pathology, so there is a dependence between the two.

Results

Of the 175 subjects that were diagnosed with tumor lip pathology, 109 (62%) were men and 66 (38%) were women, all of them with ages between 6 and 92 years, with a mean age of 61 years.

Distribution of study participants according to the home residence showed that majority of the subjects lived in rural area (Fig.1).

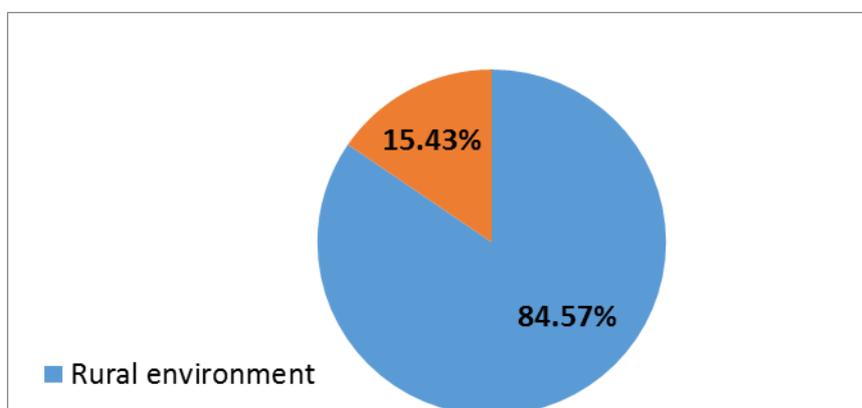


Fig.1. Study participants distribution according to home environment

The dominant profession in the study group was worker in agriculture (64%) (Fig.2).

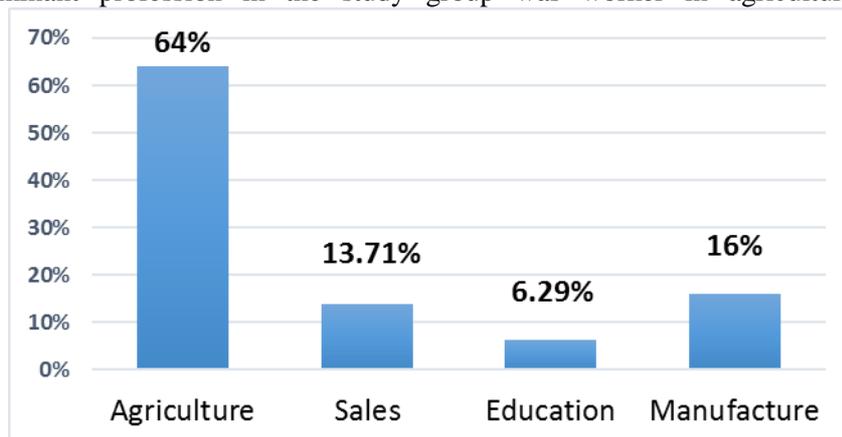


Fig.2. Distribution of subjects according to profession

In this study, the connection between benign or malignant status and the subjects' profession was observed. A Chi-square test of independence (Table 1,2) was calculated, comparing the relationship between subjects'

profession and histopathological type of tumors. The results found [χ^2 (3)=11.84, $p=0.007$] revealed that subjects that work in agriculture, because they are more exposed to UV radiation,

are more predisposed to malignant lip tumors (Fig.3).

	AGRICULTURE	SALES	EDUCATION	MANUFACTURE	Total
MALIGNANT	74	11	7	19	111
BENIGN	10	7	5	8	30
Total	84	18	12	27	141

Table 1. The observed distribution between subjects' profession and histopathological type

	AGRICULTURE	SALES	EDUCATION	MANUFACTURE	Total
MALIGNANT	66.13	14.17	9.45	21.26	111
BENIGN	17.87	3.83	2.55	5.74	30
Total	84	18	12	27	141

Table 2. The expected distribution between subjects' profession and histopathological type

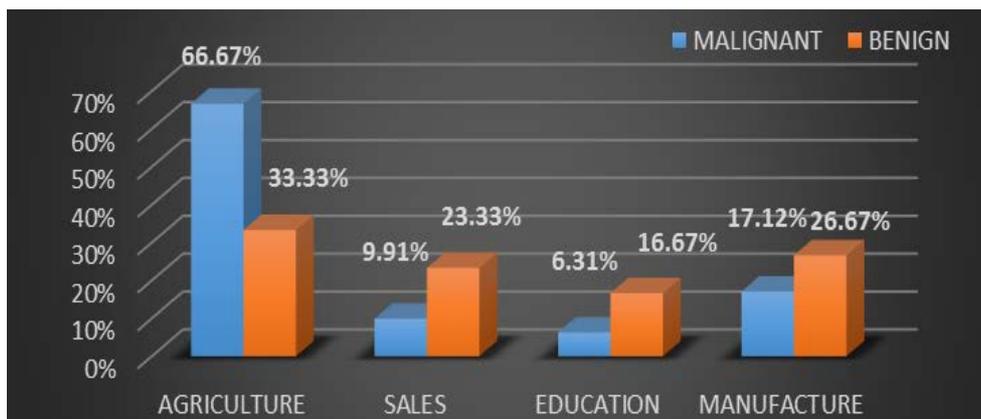


Fig.3. The correlation between subjects' profession and histopathological type

According to the geographic area for the study participants, most of them lived in the south area of Oltenia, a region of south-south-west Romania.

Of the 109 male subjects of this study, data analyzed showed that 66.97% of them smoke tobacco, with an average of 20 cigarettes per

day. In terms of women, of 66 subjects studied, 54.55% are smokers (Fig.4).

A Chi-square test of independence was calculated comparing the smoking habit in men and women. No significant interaction was found [$\chi^2(1)=2.70, p=0.100$] (Table 3,4).

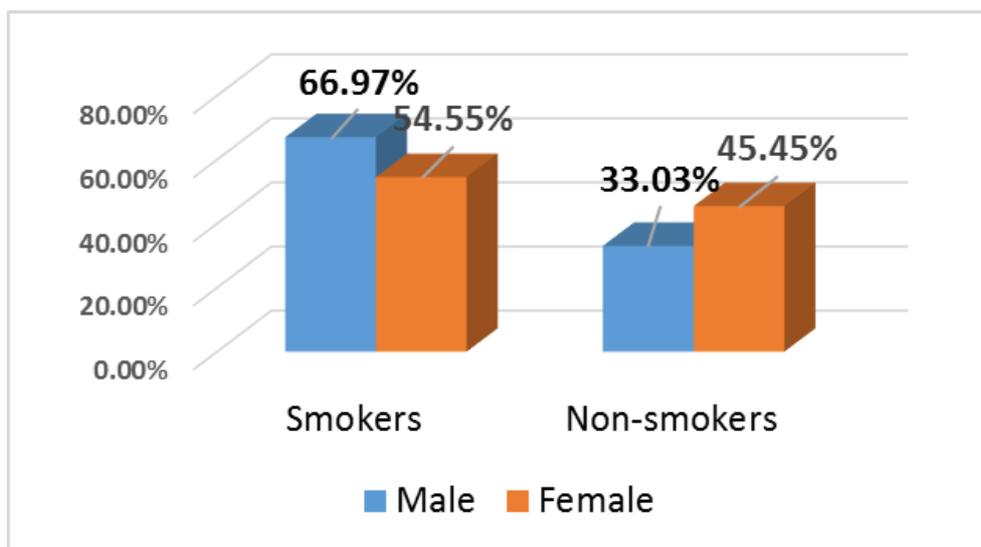


Fig.4. Distribution of subjects according to smoking habit and gender

Table 3. Distribution of observed subjects according to smoking habit and gender

	SMOKERS	NON-SMOKERS	Total
MALE	73	36	109
FEMALE	36	30	66
Total	109	66	175

Table 4. Distribution of expected subjects according to smoking habit and gender

	SMOKERS	NON-SMOKERS	Total
MALE	67.89	41.11	109
FEMALE	41.11	24.89	66
Total	109	66	175

Regarding association with systemic diseases, most encountered was hypertension, followed by diabetes (Fig.5).

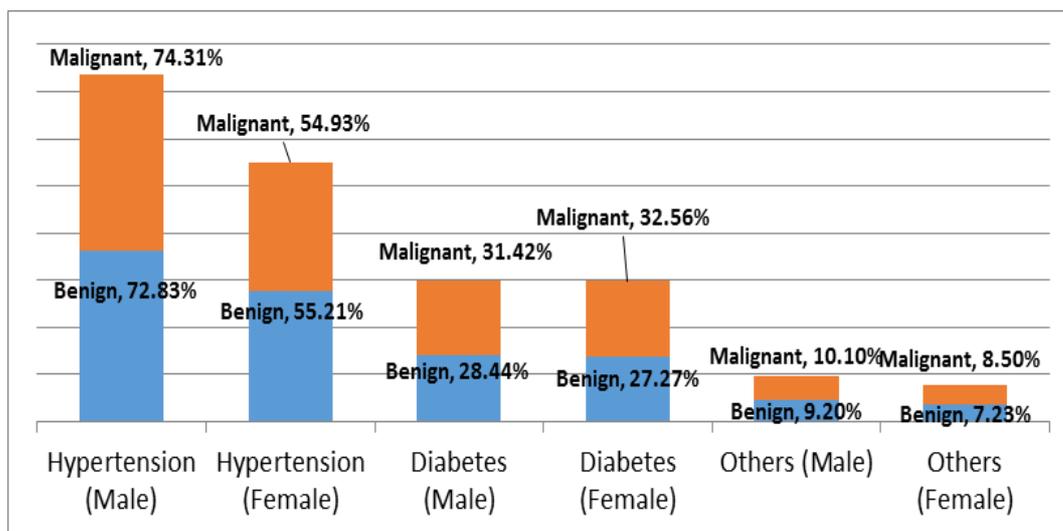


Fig.5. Association with systemic diseases

The most frequently localization of lip tumors in study participants was at the lower lip-140 cases (80%), then at the upper lip-35 cases (20%). This should be a consequence that the lower lip is more exposed to solar radiations and

other oncogenic factors. Regarding the macroscopic aspect of the tumors, most of the subjects presented an ulcerative form (18.29%-upper lip and 36.82%-lower lip) (Fig.6,7).

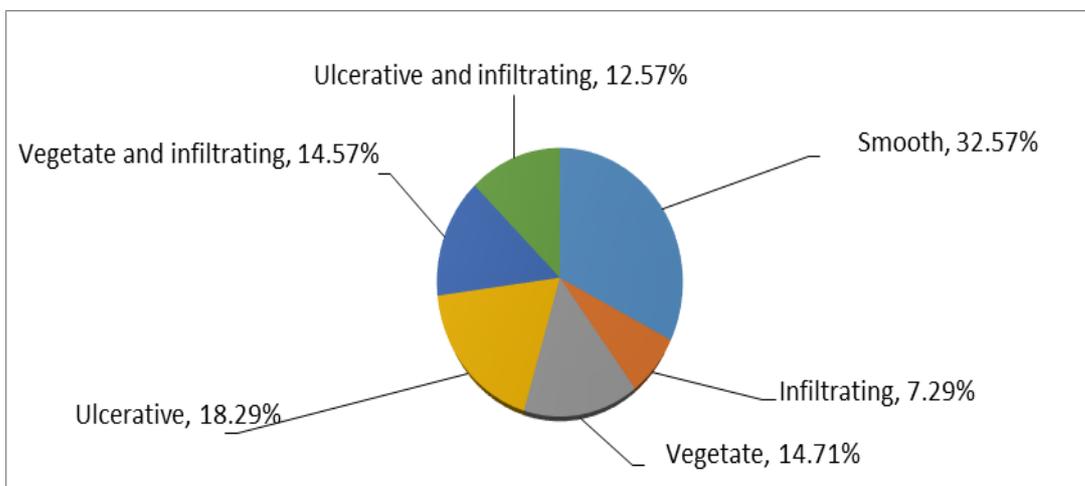


Fig.6. Distribution of subjects according to macroscopic aspects of tumors of the upper lip

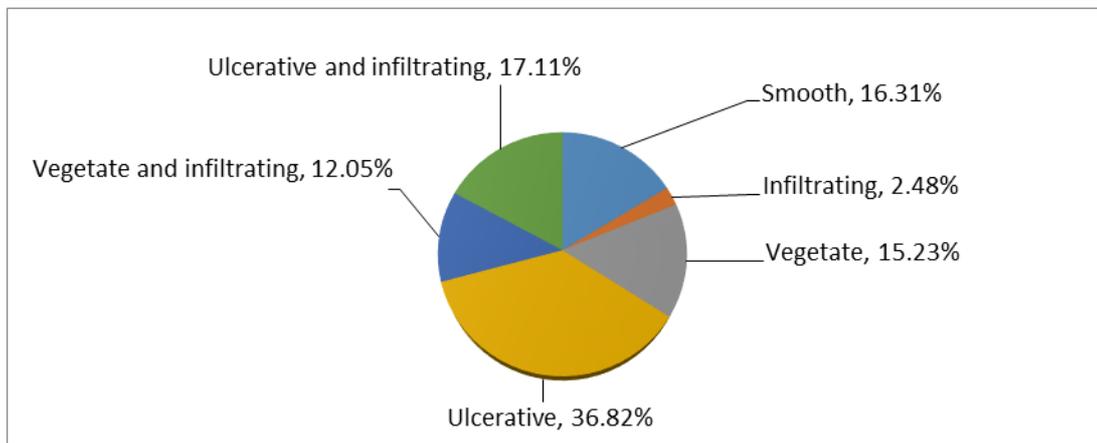


Fig.7. Distribution of subjects according to macroscopic aspects of tumors of the lower lip

Regarding the connection between the macroscopic aspects of tumors and smoking habit, a Chi-square test of independence was calculated.

The results [$\chi^2 (5)=1.20, p=0.944$] showed that no significant interaction was found between the two (Table 5,6).

Table 5. Distribution of observed macroscopic tumor aspects and smoking habit

	Ulcerative-infiltrating	Vegetate-Infiltrating	Ulcerative	Vegetate	Infiltrating	Smooth	Total
SMOKERS	22	16	45	20	6	22	131
NON-SMOKERS	10	5	12	7	2	8	44
Total	32	21	57	27	8	30	175

Table 6. Distribution of expected macroscopic tumor aspects and smoking habit

	Ulcerative-infiltrating	Vegetate-Infiltrating	Ulcerative	Vegetate	Infiltrating	Smooth	Total
SMOKERS	23.95	15.72	42.67	20.21	5.99	22.46	131
NON-SMOKERS	8.05	5.28	14.33	6.79	2.01	7.54	44
Total	32	21	57	27	8	30	175

Of the 175 subjects, 111(63.43%) presented malignant lip tumors, 30 (17.14%) of them were diagnosed with benign tumors and 34 (19.43%) with pseudotumoral lesions.

A Chi-square test of independence was calculated comparing smoking habit with the benign or malignant type of tumors. A

significant interaction was discovered following the results: $\chi^2 (1)=7.69, p=0.005$.

The possibility of developing malignant tumors is much higher for smokers than for non-smokers (Fig.8) (Table 7,8). Subjects diagnosed with malignant tumors were smokers in 81.08% cases.

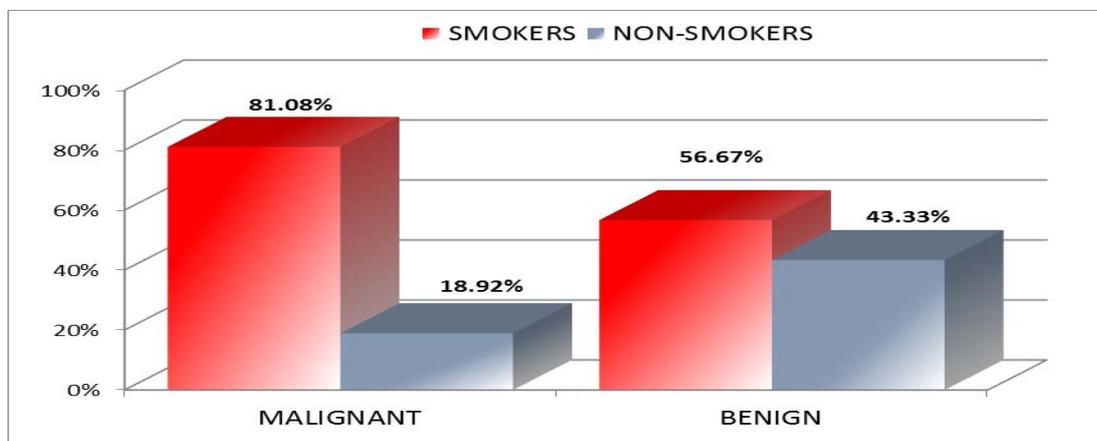


Fig.8. Histopathological tumor type correlated with smoking habit

Table 7. Observed distribution according to histopathological tumor type correlated with smoking habit

	SMOKERS	NON-SMOKERS	Total
MALE	73	36	109
FEMALE	36	30	66
Total	109	66	175

Table 8. Expected distribution according to histopathological tumor type correlated with smoking habit

	SMOKERS	NON-SMOKERS	Total
MALE	67.89	41.11	109
FEMALE	41.11	24.89	66
Total	109	66	175

According to histological characteristics, distribution of the malignant lip tumors was 87.39%-squamous cell carcinoma (SCC),

5.41%-basal cell carcinoma (BCC) and 7.20%-other type of tumors (Fig.9).

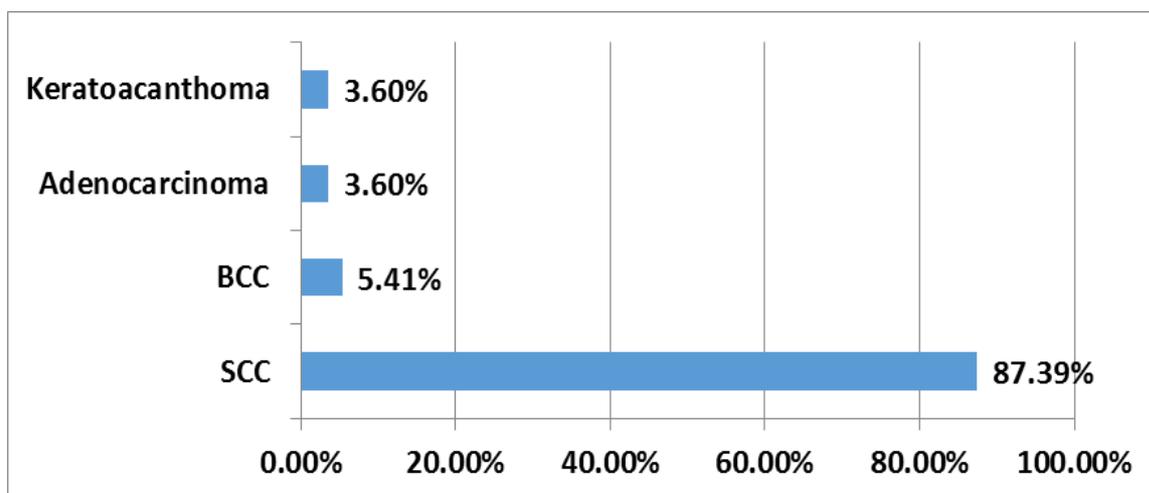


Fig.9. Distribution of subjects with malignant lip tumors according to histological characteristics

Regarding the correlation between histological characteristics and smoking habit, a Chi-square test of independence was calculated. The results revealed that there is no significant

interaction [χ^2 (2)=0.26, p=0.877] (Fig.10) (Table 9,10).

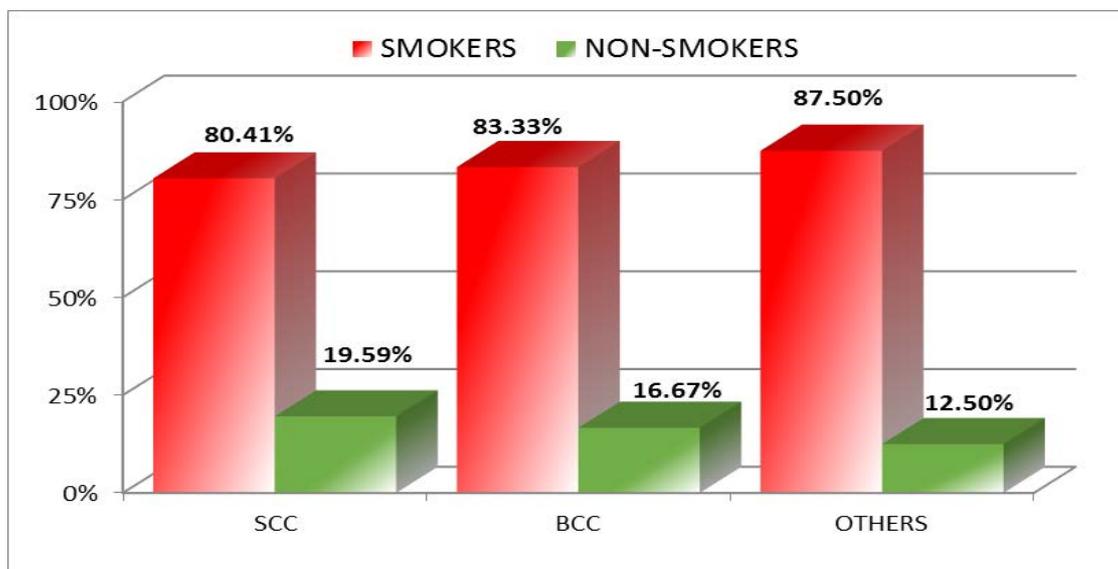


Fig.10. Distribution of subjects with different types of malignant lip tumors and smoking habit

Table 9. Distribution of observed subjects with different types of malignant lip tumors and smoking habit

	SCC	BCC	OTHERS	Total
SMOKERS	78	5	7	90
NON-SMOKERS	19	1	1	21
Total	97	6	8	111

Table 10. Distribution of expected subjects with different types of malignant lip tumors and smoking habit

	SCC	BCC	OTHERS	Total
SMOKERS	78.65	4.86	6.49	90
NON-SMOKERS	18.35	1.14	1.51	21
Total	97	6	8	111

Discussion

The results of present study highlighted that lip tumors were more frequently in men and in subjects aged higher than 60 years. These results are confirmed by other studies. Shield KD *et al.* showed that the incidence of lip cancer was consistently elevated among men relative to women. The male: female (M: F) rate ratio was 2.5, with this ratio ranging from 5.4 for central and eastern Europe to 1.0 for eastern/southeast [10]. Another study on lip and oral cavity carcinomas realized by Cracana A *et al.* in North-East Romania showed that of all patients hospitalized in the period 2011-2015, 675 (83.3%) were male, while 136 (16.7%) female [11]. In this study, 62% of the subjects were males and 38%-women.

A study published by Perea-Milla Lopez E *et al.* Showed lip cancer was found more common among older men, in people of rural residence, and especially on the lower lip [12]. Regarding home residence, Abreu L *et al.* found other results. They reported that of all cases reported, 73.2 per cent were metropolitan residents, 25.6 per cent rural and the remainders were unknown. Same authors sustained that crude and age-standardized rates for lip cancer are higher among rural dwellers than among metropolitan people [13]. According to this study, 84.57% were subjects living in the rural areas, and 15.43% in the metropolitan areas and mean age of subject was 61 years.

Regarding lip cancer etiology, the most commonly factors cited include solar radiation, tobacco smoking and viruses [4]. The combination of long-term exposure to ultraviolet (UV) radiation from sunlight and a fair skin has been proposed as one of the etiological factors in the epidemiology of lip cancer [6,14]. Some studies mention that certain professions are linked with exposure to solar radiation.

For example, Kachuri L *et al.* showed in one of their studies that agricultural workers are exposed to a higher risk of lip cancer (HR=2.14, 95% CI=1.70-2.70) [15]. In other studies, Pătrașcu V and Ciurea R showed that regarding their profession, most of their study subjects were farmers too (76,32%) [7].

In the present study, 112 subjects (64%) were agriculture workers, so the prevalence of lip cancer was higher in subjects more exposed to solar radiation.

This is demonstrated by the Chi-square test of independence calculated to compare the relationship between subjects' profession and histopathological type of tumors. The results were: $\chi^2(3)=11.84$ and $p=0.007$. This means that there is a strong connection between the subjects' profession and lip tumors pathology. Working in agriculture means that the subject was exposed 8-10 hours per day to UV radiation and the probability to develop malignant lip tumors is increased.

Concerning the geographic area where the study participants live, the present research indicated that most of them were from the South of Oltenia region. In this region, the number of sunny days is higher than in the north of same region. Results of other researches revealed that in Dolj county, situated in Oltenia region, lip cancer is about 40% of oral squamous carcinomas in this geographical area [7]. A study realized by Crăcană A *et al.* in North-East of Romania showed that the lip and oral cancer prevalence was 42% among hospitalized subjects in the period 2011-2015 in the Oral and Maxillofacial Surgery Clinic, "Sf. Spiridon" Hospital Iasi [11].

Lip cancer is associated frequently with tobacco smoking. This etiological factor is always studied in researches. For example, Biasoli ER *et al.* studied a group of subjects on a 25-year period and obtained that tobacco

smoking history was positive in 87 cases (60.41%), with 19 ex-smokers (13.18%), 8 light smokers (5.55%), 28 moderate smokers (19.45%), and 32 severe smokers (22.23%) [16].

Data resulted from this study made in Oltenia region revealed that 66.97% of male subjects smoke tobacco, and, regarding female subjects 54.55% are smokers. Also, a Chi-square was calculated for this hypothesis, obtaining the following results: $\chi^2(1)=2.70$, $p=0.100$.

Another factor associated with a higher risk of lip cancer was hydrochlorothiazide (HCTZ), a common treatment in hypertension. Pedersen SA *et al.* have observed clear dose-response patterns for both BCC and SCC, with a more than a 7-fold increased risk of SCC for a cumulative use of 200,000 mg or more of HCTZ. In addition, for both BCC and SCC, the associations with HCTZ use became stronger with increasing lag time before diagnoses [17]. In this study, analyzed data showed that 74.31% of the male study subjects and 54.93% of the female study subjects diagnosed with malignant lip tumors were medicated with antihypertensive medication. Concerning benign lip tumors, 72.83% of the male study subjects and 55.21% of the female study subjects were medicated with antihypertensive medication. Also, other studies, like the one performed by Végh D *et al.* demonstrated a close connection between diabetes, another frequent associated systemic disease, and lip cancer [18].

In this study, the most frequently localization of lip cancer was found on lower lip, 80% of the subjects. Also, other authors highlighted same results Han AY *et al.* showed that most of the tumors were found in the lower lip [19].

Regarding macroscopic aspect of lip tumor, majority of subjects included in this study presented an ulcerative lip cancer form. Pătrașcu and Ciurea have encountered the following clinical forms: ulcerative and vegetate (42.10%), nodular (21.05%), keratotic (15.79%), ulcerative and infiltrating (9.72%), vegetate (5.92%), in situ carcinoma (4.60%) and fissuring (1.32%) [7]. The Chi-square test calculated showed that there was no significant interaction found between smoking habit and macroscopic tumors' aspects [$\chi^2(5)=1.20$, $p=0.944$].

The correlation between benign or malignant type of tumor and smoking habit was analyzed by calculating a Chi-square independence test.

The results [$\chi^2(1)=7.69$, $p=0.005$] showed that a very important relationship exists between histopathological type of tumors and smoking, smoker subjects diagnosed with malignant lip

tumors representing 81.08% of the total number of malignant cases. On the other side, from the total cases of subjects diagnosed with benign lip tumors, 56.67% of them were smokers.

About the histological type of malignant lip tumors, a lot of studies were made. Bozan *et al* showed in their work that squamous cell carcinoma is encountered in 89.01% of the subjects analyzed and basal cell carcinomas in only 10.99% [20]. In this study, it was found out that 87.39% of the subjects diagnosed with malignant tumors, had SCC, 5.41% BCC and 7.20% other type of malignant tumors.

The Chi-test calculated revealed the following results: [$\chi^2(2)=0.26$, $p=0.877$].

Conclusion

Overall, lip tumors were encountered more frequently in men, in subjects aged over 60 years, in rural area habitants, in subjects more exposed to solar radiation, in smokers. The lower lip was the most affected by lip cancer and squamous cell carcinoma represents the most frequently histological type of these tumors.

Acknowledgements

These authors contributed equally to this article.

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