

PREVALENCE AND NON-INVASIVE EARLY DIAGNOSIS OF ORAL PRE-MALIGN LESIONS IN EXTENDED EDENTULOUS PATIENTS TREATED WITH REMOVABLE DENTURES

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Declarations

•Ethical approval: CECS38/12.04.2022 Ethical Committee University of Medicine and Pharmacy "Victor Babes" Timisoara Romania. All the participants signed an Informed Consent that they agreed to participate in this study. The Informed Consent was according to Helsinki Declaration. 'Clinical trial number: not applicable

• Ethics and Consent to Participate declarations: not applicable'

•Availability of data and materials Data resulted in the study are presented in results. The informed consent signed by the patients included in the study and signed by two experienced clinicians is attached as auxiliary file. The data is available in the Research Center TADERP, Department of Prosthodontics and Occlusology, Faculty of Dentistry, University of Medicine and Pharmacy "Victor Babes" Timisoara.

• Consent for publication: All authors consent for the publication of this study

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• Authors' contributions; Assoc. Prof.Dr. Goguta Luciana Maria has written the manuscript, reviewed the manuscript, worked in the clinical trial

Ass.Prof Dr Topala Florin made the pictures

Prof.Dr.Anca Jivanescu had the idea of the study and reviewed the manuscript.

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ABSTRACT

Intro: Early detection and diagnosis of premalignant oral lesions is important for the quality of life of patients

Methods: 113 patients wearing complete or partial dentures were included in the study after signing an Informed Consent in accordance with the Ethical Committee from University of Medicine and Pharmacy "V Babes" Timisoara, Romania (CECS38/12.04.2022). The interview for each patients included: age, gender, smoking tobacco, drinking alcohol, oral hygiene, and general health condition. The clinical intraoral examinations included: the lips, the oral mucosa, the tongue, the floor of the mouth, the labial sulcus in maxilla, the mandibular labial and lingual sulcus, the palatal vault and the oropharyngeal isthmus. In cases where there was clinically found at least one lesion, the patient was examined by using auto-fluorescent light (VELscope)

Results: The advanced age affected health condition ($p < .001$), drinking alcohol ($p < .001$), smoking tobacco ($p < .001$) and poor oral hygiene ($p = 0.02$) are influencing the occurrence of premalignant oral lesions. Also wearing the complete and partial removable dentures can affect the health oral mucosa.

Conclusion Age, general health, personal habits, local hygiene and removable denture wearing are influencing the presence of oral premalignant lesions. Auto-fluorescence light was useful in early diagnosis of oral premalignant lesions.

INTRODUCTION

According to the latest WHO data published in 2018 Oral Cancer Deaths in Romania reached 2,272 or 0.97% of total deaths. The age adjusted Death Rate is 7.16 per 100,000 of population ranks Romania #20 in the world [1]. The data include dentate and edentate patients. As prosthodontists, working in the field of gerontology our main concern is the complete and removable denture denture wearers. Many times this patients are coming for the first time in the office dentist with lesions in the oral cavity.

Complete and extended partial edentulous patients are often wearing their removable dentures too long without any follow-up. So, flanges of the dentures become unadapted and generates mucosal lesions like oral ulcers and epulis fissuratum. Mechanical stress underneath the rigid dentures as hydrostatic pressure, compressive, tensile and shear stress are considered by some researchers carcinogenic factors [2- 4]

Some of these patients have bad oral hygiene [5], others have bad habits like tobacco smoking, [6,] alcohol consumption, and majority have general health conditions. All these factors are well known as oral cancer risk factors [7, 8].

Screening the oral mucosa by using non invasive devices is what all the dentists should do during their daily practice. Direct visual fluorescence evaluation allows the detection and screening of oral precancerous and early cancerous disorders. Some malign tumors like carcinoma, intercepted and treated in its initial phase allows for a complete cure and five-year survival in 85% of cases.[9-12]. Unfortunately, patients wearing removable dentures are sometimes examined superficially and certain oral lesions are neglected.

Recent studies have shown that deep convolutional neural networks (CNN) are

expected to be a novel innovation as a diagnostic tool to assist clinicians, in improving the accuracy of early detection of cancerous lesions [13,14]

VELScope® (Visually Enhanced Lesion scope) (LED Apteryx, Akron, OH, USA) is a medical tool recognized by the World Health Organization in 2009, useful for early diagnosis of premalignant oral lesions mainly in risk groups of population [15- 21].

Tissue auto-fluorescence is sensitive at detecting white, red and white and red patches, and the area of fluorescence visual loss (FVL) often extends beyond the clinically visible lesion That initial diagnosis allows the dental specialists to refer the suspect cases to a surgery specialist for a local cytological exam. [22- 25].

The aim of the present study was to assess the prevalence of pre - malign lesions in senior patients wearing complete and partial removable dentures in a Romanian population in Timisoara. The first hypothesis is that age, general health, personal habits, oral hygiene and removable denture wearing are influencing the presence of premalignant lesions. The second hypothesis is that auto-fluorescence light provided by VELScope® is helpful in initial diagnosis of premalignant oral lesions.

MATERIALS AND METHODS

The study was started in the Department of Prosthodontics, Faculty of Dentistry, University of Medicine and Pharmacy, Timisoara, Romania in March 2022 and was finished in July 2024. All the patients included in the study have signed an Informed Consent in accordance with the Ethical Committee of the University and with the Helsinki Declaration. Ethics approval was CECS38/12.04.2022 Ethical Committee University of Medicine and Pharmacy “Victor Babes” Timisoara Romania”

The initial number of patients was 120 and the final number participating effectively to the research was 113.

Included criteria were:

1. Patients who were wearing at least one removable denture older than 1 year and have agreed to participate to the screening.
2. The patients must wear every day their removable dentures

Exclusion criteria: patients which have missed the questionnaire even they have agreed to participate to this clinical survey.

The interview and the clinical examination were made by two experienced prosthodontics specialists. The interview was found out the age of the patients, their gender, their oral hygiene habits, the alcohol consumption patterns and the associated general health conditions.

The clinical intraoral examinations included: the lips, the oral mucosa, the tongue, the floor of the mouth, the labial sulcus in maxilla, the mandibular labial and lingual sulcus, the palatal vault and the oropharyngeal isthmus. In cases where there was clinically found at least one lesion (Fig 1a, 2a), the patient was examined by using auto-fluorescent light

(VELscope) (Fig 1b, 2b) Patients found with suspect oral lesions were sent in an Oro-maxillo- facial surgical clinic for a histopathological examination and further treatment if necessary.

Statistical analysis

Prevalence of oral pre-malign lesions with age, gender, tobacco smoking, alcohol user, oral hygiene and general condition were calculated by using descriptive statistics

Connection between oral pre-malign lesions with age, gender, tobacco smoking, alcohol user, oral hygiene and general condition was performed by using the descriptive statistics and the e Chi-square (χ^2) analysis.

Possibility of early detection of the oral pre-malign lesions was calculated by using also Chi-square (χ^2) analysis.

RESULTS AND DISCUSSIONS

The descriptive statistics for age show that the majority of the patients fall within the age ranges of 60-70 years (32.7%) and 70-80 years (28.3%), indicating that the sample is predominantly composed of older adults. The smallest representation comes from patients aged 80-90 years, accounting for only 5.3% of the total.(Table 1)

Table 1. Age Distribution of Patients

Frequencies of AGE			
	Counts	% of Total	Cumulative %
40-50	17	15.0 %	15.0 %
50-60	21	18.6 %	33.6 %
60-70	37	32.7 %	66.3 %
70-80	32	28.3 %	94.6 %
80-90	6	5.3 %	100 %

Regarding the gender, the majority of the patients are female (55.8%), while males make up 44.2% of the total. This relatively balanced gender distribution suggests that both

sexes are represented fairly equally, although slightly more women were involved in the study. (Table 2)

Table 2. Gender Distribution of Patients

Frequencies of GENDER			
	Counts	% of Total	Cumulative %
Female	63	55.8 %	55.8 %
Male	50	44.2 %	100.0 %

The data on smoking habits reveal that 55.8% of the patients are non-smokers, while 43.4% are smokers, with only 0.9% identified as occasional smokers. This relatively high percentage of smokers highlights a significant risk factor for oral health, as smoking is known to contribute to

the development of oral lesions. The near-equal distribution between smokers and non-smokers allows for meaningful comparisons in the analysis of the influence of smoking on the presence of premalignant lesions.(Table 3)

Table 3. Smoking tobacco habits among patients

Frequencies			
	Counts	% of Total	Cumulative %
non-smokers	63	55.8 %	55.8 %
smokers	49	43.4 %	99.1 %
occasional smokers	1	0.9 %	100.0 %

The majority of the patients consume alcohol occasionally (42.5%) or moderately (26.5%), while a similar percentage (26.5%) reported no alcohol consumption at all. A small proportion of patients also reported additional health conditions linked with occasional alcohol consumption, such as hypertension (HTA) or osteoarthritis. These

figures suggest that alcohol consumption is common among the patients, with over two-thirds consuming alcohol either occasionally or moderately, which may have implications for their oral health, particularly in relation to the development of premalignant lesions.(Table 4)

Table 4. Alcohol Consumption Patterns in the Patient Population

Frequencies of alcohol consumption rarel /medium /frequent			
	Counts	% of Total	Cumulative %
Rare	48	42.5 %	42.5 %
Medium	30	26.5 %	69.0 %
Ocasional (HTA)	3	2.7 %	71.7 %
No	30	26.5 %	98.2 %
Ocasional (Artritis)	1	0.9 %	99.1 %
Ocasional (HTA, Osteoporosis)	1	0.9 %	100.0 %

In terms of oral hygiene practices, the data show that a significant majority of patients (81.4%) practice incorrect oral hygiene, while only 18.6% maintain proper oral hygiene. This imbalance suggests a concerning trend in the patient population, as inadequate oral hygiene is a well-known risk factor for the development of oral health issues, including premalignant lesions. The high percentage of improper hygiene indicates a critical area for intervention, as improving daily oral care routines could significantly reduce the risk of oral lesions.(Table 5)

Table 5. Oral Hygiene Practices in the Patient Group

Frequencies of igienizarea(corect/incorect)			
	Counts	% of Total	Cumulative %
correct oral hygiene	21	18.6 %	18.6 %
incorrect oral hygiene	92	81.4 %	100.0 %

The data on general health conditions reveal that 56.6% of the patients do not suffer from any associated medical conditions, while the remaining 43.4% present a variety of conditions. Hypertension (HTA) is the most common condition, affecting 15.9% of patients, followed by diabetes (5.3%), osteoarthritis (3.5%), and ischemic heart disease (3.5%). A variety of other conditions, including chronic obstructive pulmonary disease (COPD), arthritis, and osteoporosis, are also present in smaller percentages. The relatively high prevalence of these conditions, particularly hypertension and diabetes, highlights the importance of considering these comorbidities when assessing the overall health of the patients and their susceptibility to oral lesions.(Table 6)

Table 6. Prevalence of Associated General Health Conditions

Frequencies of afectiuni generale asociate			
	Counts	% of Total	Cumulative %
Healthy Patients	64	56.6 %	56.6 %
Ischemic heart disease	5	4,4 %	85.8 %
Type I diabetes	1	0.9 %	58.4 %
HTA	18	15.9 %	74.3 %
COPD	2	1.8 %	76.1 %
Type II diabetes	5	7.9 %	92.9 %
Arthrosis	5	1,8 %	86.7 %
Osteoporosis	2	1.8 %	96.5 %
Arthritis	2	1.8 %	88.5 %
Psoriasis	1	0.9 %	89.4 %
Asthma	2	1.8 %	94.7 %
Vascular fragility	1	0.9 %	95.6 %
Penicillin allergy	1	0.9 %	97.3 %
Gluten intolerant	1	0.9 %	98.2 %
Hearing loss	2	1.8%	100%

Table 7 Connection between age and premalignant lesions

Clinical examination	AGE	
	Value	p-value
Lips	486.824	<.001
Oral mucosa	647.103	<.001
Tongue	113	<.001
Floor of the mouth	352.477	0.002
Labial sulcus – maxilla	161.624	0.007
Labial and lingual sulcus mandibular	253.901	<.001
Palatal vault	343.77	0.981
oropharyngeal isthmus	58.953	0.963

The results for age show a clear relationship between aging and the presence of premalignant lesions in various parts of the oral cavity. For example, for the lip examination, the chi-square test yielded a value of $\chi^2=486.824$, with a p-value of $p<0.001$, indicating a significant relationship between age and the presence of lesions. Similarly, in the buccal mucosa examination, the χ^2 value was 647.103, with $p<0.001$, and in the tongue examination, $\chi^2=113$, $p<0.001$. In contrast, no significant relationship was found between age and the presence of lesions in the palatal vault ($\chi^2=343.77$, $p=0.981$) or in the oropharyngeal isthmus ($\chi^2=58.953$, $p=0.963$). (Table 7)

Table 8 Connection between tobacco smoking and premalignant lesions

Clinical examination	Tobacco smoker /non-smoker	
	χ^2 Value	p-value
Lips	7.644	0.907
Oral mucosa	13.249	0.926
Tongue	1.318	0.517
Floor of the mouth	202.1	< .001
Labial sulcus – maxilla	2.898	0.822
Labial and lingual sulcus mandibular	2.947	0.938
Palatal vault	8.429	0.989
oropharyngeal isthmus	2.817	0.589

The analysis shows that there is no significant relationship between smoking status and the presence of premalignant lesions in the oral cavity. For instance, in the lip examination, the χ^2 value was 7.644, with a p-value of 0.907, indicating no significant relationship. Similarly, in the buccal mucosa examination, $\chi^2=13.249$, $p=0.926$, and in the floor of the mouth examination, $\chi^2=7.216$, $p=0.926$. Only in the floor of mouth in the present study was found that smoking tobacco can be a factor that influences the appearance of the premalignant lesions. ($p<.001$). These results indicate that, in this specific population, smoking did not have a significant impact on oral lesions.

Table 9 Connection between alcohol consumer and premalignant lesions

Clinical examination	Alcohol consumer occasional/moderate/frequent	
	χ^2 Value	p-value
Lips	19.935	0.981
Oral mucosa	247.229	< .001
Tongue	2.791	0.732

Floor of the mouth	17.147	0.995
Labial sulcus – maxilla	115.739	<.001
Labial and lingual sulcus mandibular	118.898	<.001
Palatal vault	25.29	0.999
oropharyngeal isthmus	12.209	0.271

The data indicate that there is a significant association between alcohol consumption and the presence of premalignant lesions in the buccal mucosa and vestibular and lingual fold. In the buccal mucosa examination, the χ^2 value was 247.229, with $p < 0.001$, and for the vestibular sulcus (Mx), $\chi^2 = 115.739$, $p < 0.001$. Additionally, for the vestibular and lingual sulcus (Md), the χ^2 value was 118.898, with $p < 0.001$. In contrast, no significant relationship was found in the tongue examination ($\chi^2 = 2.791$, $p = 0.732$) or the palatal vault ($\chi^2 = 25.29$, $p = 0.999$). Table 9

Table 10 Connection between general condition and premalignant lesions

Clinical examination	General condition	
	χ^2 Value	p-value
Lips	203.937	<.001
Oral mucosa	93.699	0.999
Tongue	0.772	0.999
Floor of the mouth	54.076	0.999
Labial sulcus – maxilla	2.36	0.999
Labial and lingual sulcus mandibular	70.739	0.649
Palatal vault	474.023	<.001
oropharyngeal isthmus	126.089	<.001

The analysis reveals that patients with associated general conditions are more likely to present premalignant lesions in certain regions. In the lip examination, the χ^2 value was 203.937, with $p < 0.001$, indicating a significant relationship. Similarly, in the palatal vault examination, $\chi^2 = 474.023$, $p < 0.001$, and in the oropharyngeal isthmus, $\chi^2 = 126.089$, $p < 0.001$. These results suggest that patients with associated general conditions, such as chronic diseases, may be more prone to developing premalignant lesions in these regions. However, in other areas, such as the buccal mucosa ($\chi^2 = 93.699$, $p = 0.999$) or the tongue ($\chi^2 = 0.772$, $p = 0.999$), no significant relationship was observed. These data underline the need for rigorous monitoring of patients with chronic diseases to prevent and detect oral lesions early. (Table 10)

Table 11 Connection between oral hygiene and premalignant lesions

Clinical examination	oral hygiene (correct/incorrect)	
	χ^2 Value	p-value
Lips	5.756	0.568
Oral mucosa	10.816	0.459
Tongue	0.23	0.631
Floor of the mouth	18.969	0.008
Labial sulcus – maxilla	4.849	0.183
Labial and lingual sulcus mandibular	5.294	0.258
Palatal vault	13.05	0.221
oropharyngeal isthmus	0.276	0.871

The results show that correct oral hygiene significantly influences the presence of lesions in the floor of the mouth. In this case, the χ^2 value was 18.969, with $p=0.008$, indicating a significant relationship between correct oral hygiene and the presence of lesions in this area. In other areas, such as the buccal mucosa ($\chi^2=10.816$, $p=0.459$) or the palatal vault ($\chi^2=13.05$, $p=0.221$), no significant relationship was found. {Table 11}

Table 12 Possibility of detection of premalignant lesions by using auto-fluorescence light provided (VELScope)

Table χ^2 Test

Clinical examination by using VELScope	auto-fluorescence light provided by VELScope	
	χ^2 Value	p-value
Oral mucosa	788.95	<0.001
Floor of the mouth	227.20	<0.001
Labial sulcus (maxilla)	226.09	<0.001
Labial and lingual sulcus (Mandible)	282.11	<0.001
Palatal vault	121.28	0.218

The interpretation of the results from the chi-square test table for the use of VELScope® auto - fluorescence light suggests a significant relationship between this technique and the detection of

pre-malignant lesions in certain regions of the oral mucosa. For the buccal mucosa examination, the $\chi^2=788.95$ with $p<0.001$ indicates a strong relationship between the use of VELScope light and the diagnosis of

pre-malignant lesions in this area. Similarly, for the floor of the mouth, $\chi^2=227.20$ with $p<0.001$, the upper vestibular fold (Mx) $\chi^2=226.09$ with $p<0.001$, and the lower vestibular and lingual fold (Md) $\chi^2=282.11$ with $p<0.001$, all indicate a significant relationship between the use of autofluorescence light and the identification of lesions in these locations. However, in the case of the palatal vault, the $\chi^2=121.28$ with $p=0.218$ shows no significant relationship between the use of VELScope and the detection of lesions in this region.

Older persons often suffer from dental diseases and lesions of the oral mucosa which could have been avoided by appropriate daily oral hygiene. With increasing age the oral health risk factors and the importance of daily oral care increases, while the ability to manage the oral hygiene often decreases [26]. In the present study the majority (80%) of the patients were between 50 and 80 years old, which suggests that the study primarily involves a population in late adulthood, where the risk of pre-malignant oral lesions may be higher due to age-related factors. In this group, older individuals are more prone to developing these lesions, particularly in certain areas such as the lips and oral mucosa, highlighting the need for careful monitoring of these patients.

At the same time, the need for different oral health care support products increases [27].

The gender balance found in this study, mostly female, is important for ensuring that the findings related to pre-malignant lesions and their risk factors can be applied to both genders, although it is slightly skewed towards the female population.

Smoking tobacco use is increasing across developing nations as economic progress increases household disposable income. In developed nations, tobacco use has declined overall but increased in certain

demographics, commonly women [28, 29]. Smoking tobacco and alcohol are considered risk factors for pre-malignant and malignant tumors in oral lesions, [30, 31].

The first hypothesis was that age, general health, personal habits, local hygiene and removable denture wearing are influencing the presence of pre-malignant lesions. The results are showing that:

- a. Older individuals are more prone to developing these lesions, particularly in certain areas such as the lips and buccal mucosa, highlighting the need for careful monitoring of these patients. No important differences were found between males and females.
- b. However, smoking remains a well-known risk factor, these data suggest that other variables may play a more important role in this case. It is important to note that in practice, smokers should still be closely monitored, even if this study did not reveal a significant relationship.
- c. The results suggest that alcohol may play an important role in the development of lesions in specific regions of the oral cavity, and patients who consume alcohol should be examined more carefully in these areas- oral mucosa, labial sulcus in maxilla and labial and lingual mandibular sulcus.
- d. There is a significant association between alcohol consumption and the presence of pre-malignant lesions in the oral mucosa and labial and lingual sulcus.
- e. These results suggest that patients with associated general conditions, such as chronic diseases, may be more prone to developing pre-malignant lesions in lip, palatal vault and oropharyngeal isthmus

- f. Proper oral hygiene can reduce the risk of developing lesions in specific regions of the oral cavity, and patients, especially those wearing dentures, should be encouraged to follow a strict hygiene routine to prevent premalignant lesions. They should be also encouraged to present in the dental office for twice per year check-ups.

According to this results, the first hypothesis was confirmed.

Results of the present study strongly agree with regular dental check-ups and non – smoking recommendation for maintaining optimal oral health. Recommended oral self - care includes tooth brushing and dentures brushing more than once a day, lesser consumption of sugar containing snacks once daily or rarely and regular use of fluoride containing tooth paste in partial edentulous patients wearing removable dentures [32].

Prevention and early detection of oral lesions, in the pre- malign state is the goal of all the dentistry specialists. Most dentists have a good knowledge of the presentation and risk factors like tobacco smoking and alcohol abuse associated with oral cavity cancer. [33,34]. Sometime, delayed diagnosis often occurs due to patients and dental practitioners because many seniors with associate conditions are not coming regularly for dental check-ups, ignoring the signs and symptoms of these lesions. On the other side dentists using routine examination cannot always identify the small lesions directly in the white light or they have no time for that examination. [35-37]

The second hypothesis that auto - fluorescence light provided by VELScope is helpful in the initial diagnosis of premalignant lesions is supported in most of

the examined areas. These results suggest that VELScope is effective in early diagnosing premalignant lesions of the oral cavity. All the patients with some suspect oral lesions were referred to the oral surgery service for histopathological examination.

Autofluorescence can help a skilled doctor spot oral premalignant lesions [37], and has a real benefit of combining autofluorescence with conventional oral examination in identifying surgical margins during biopsy procedures for leukoplakia and oral carcinoma.[38-43]

Some systematic reviews are showing that the VELscope® mean value about sensitivity and specificity was 70.19% and 65.95%, respectively, by results analysis, but despite this, some studies disagree about its clinical effectiveness, and this diagnostic method is still much debated in scientific and clinical medical literature.[46,46]

Although the diagnostic accuracy of auto fluorescence in the screening work-up of oral cancer and pre-cancer was more sensitive than those of clinical examination it was not accurate enough to be used alone reliably [47, 48].

CONCLUSIONS

Within the limits of this study, the number of the patients and the single location of the examination (Timisoara, Romania, Europe), the following findings were drawn:

- Age, general health, personal habits, local hygiene and removable denture wearing are influencing the presence of oral premalignant lesions
- Auto-fluorescence light (VELscope) was useful in early diagnosis of oral premalignant lesions in patients wearing removable dentures.

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