

The Epidemiological Trend of Oral Carcinoma in Eastern Europe

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Oral and pharyngeal cancer is estimated by World Health Organization (WHO) to be the eighth most common cancer worldwide with significant regional variation with increasing and decreasing incidence trend. The aim of the study was to evaluate the oral cancer epidemiological trend, incidence and mortality in Central and East Europe (CEE), and to compare the incidence of oral cancer with other regions from the world. The analyzed data was from NORDCAN and GLOBOCAN, using ASR (age-standardize rate) incidence and mortality overall and by sexes. The incidence of oral and pharyngeal cancer is higher in CEE than the global incidence. This is in accord with specific mortality from oral and pharyngeal cancer that is higher in CEE than the regions other submitted to the current evaluation. The incidence of oral cancer is very high at man, especially in Hungary, which is the most affected from oral cancer from CEE.

Keywords: squamous cell carcinoma, head and neck, epidemiology, geographic distribution

Oral squamous cell carcinoma (OSCC), refers to a subgroup of head and neck malignancies that develop at the lips, tongue, salivary glands, gingival, floor of the mouth, oropharynx, buccal surfaces and other intra-oral locations, according to the International Classification of Diseases (ICD) [1]. Oral cancer is a major global threat to public health and increases every year in terms of both morbidity and mortality [2]. There are 300,000 new cases diagnosed worldwide, and approximately 30,000 new cases are recorded annually only in the United States, and 40,000 new cases are recorded in the European Union, on an annual basis [3]. Oral cancer is estimated by World Health Organization (WHO) to be the eighth most common cancer worldwide with significant local variation and is increasing in some parts of the world [4]. The incidence of OSCC is higher in man, the lifestyle being an important element for the occurrence of oral and pharyngeal cancer [5,6].

OSCC is supposed to be induced specially because of smoking tobacco [7-9] and alcohol consumption [10-12], but human papilloma virus infection is also incriminated (particularly serotype 16 and serotype 18) [13,14]. Epstein Barr virus infection [15], ultraviolet radiation (for lip cancer), malnutrition [16] and genetic factors [17] may also contribute to carcinogenesis of OSCC. The high morbidity and mortality rates of the OSCC have improved in last decades for the more developed countries, and these significant improvements are based mainly on early diagnosis and new treatment strategies. Also, improvements could be related to the introduction of anti-human papilloma virus vaccine [18] to prevent molecular changes of epithelial cells of the oral cavity and pharynx, associated with large campaigns against tobacco and alcohol consumption and eliminating tobacco consumption in public spaces [19,20].

The differences between incidence and mortality in different parts of the world and the well-known increasing incidence of OSCC in CEE are not well determined in order to realize more efficient prevention and treatment strategy [20]. Evaluating OSCC from epidemiological point of view

could bring new insights in the main risk factors, the diagnostic methods, prognosis and treatment. Is necessary to better understand the geographic distribution, incidence and mortality by sex of OSCC in CEE, to develop the best preventive strategy.

This study describes the epidemiological trend of oral cancer incidence and mortality in ten of the most affected countries from CEE and compared the incidence of oral cancer with other regions from the world.

Experimental part

Material and methods

To evaluate the data on the incidence and mortality of lip and oral cancer (ICD 10 C00- C08), of pharyngeal cancer (C09-10; C11, C12-14) and laryngeal cancer (C32.9) for CEE, was used from GLOBOCAN homepage (<http://globocan.iarc.fr>), which uses incidence/100000 people and mortality/ 100000 people from 2012. To analyze these data, we used the age-standardized rates (ASR), for both sexes and for all ages, or separately on man and woman. Mortality statistics evolution for oral cancer in CEE was collected from WHO for 1990-1994 and 2000-2004, and from GLOBOCAN for 2012. For some counties, the coverage of the population was incomplete, so the data of mortality rates are very low, and in other years the coverage was higher, so the rates of changes are significantly high. To compare the incidence and mortality of oral cancer in CEE with the other parts from the world we used the data for West of Europe, World in generally, more developed countries (all regions of Europe plus Northern America, Australia/New Zealand and Japan) and less developed countries (all regions of Africa, Asia (excluding Japan), Latin America and the Caribbean, Melanesia, Micronesia and Polynesia) as they are used on GLOBOCAN.

We choose to analyze the trend of evolution in ten countries from CEE as it follows: Hungary, Romania, Republic of Moldova, Ukraine, Belarus, Bulgaria, Russia Federation, Slovakia, Czech Republic and Poland where we analyzed the epidemiological trend of lip and oral cavity, larynx and pharynx cancer.

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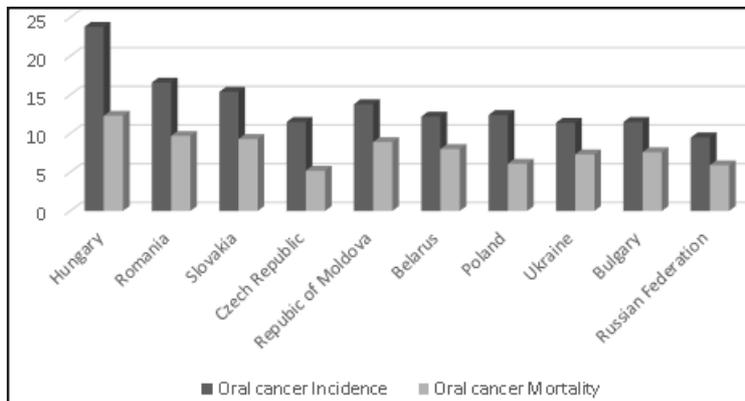


Fig. 1. Overall ASR oral squamous carcinoma cancer incidence and mortality/100000 people in countries from Central and East Europe

Table 1

ASR FOR ALL AGES AND FOR BOTH SEXES INCIDENCE AND MORTALITY ON THE CEE COMPARATIVE WITH OTHER REGIONS FROM THE WORLD AND FROM THE WORLD IN GENERAL, OF ORAL CANCER, LIPS AND CAVITY CANCER, PHARYNX CANCER AND LARYNX CANCER

REGION	Oral and pharyngeal cancer		Lip and oral cavity cancer		Pharynx cancer		Larynx cancer	
	Incidence	Mortality	Incidence	Mortality	Incidence	Mortality	Incidence	Mortality
Central and Eastern Europe	11.5	6.8	5	2.6	3	2	3.6	2.2
West of Europe	13	3.8	5.5	1.3	4.8	1.7	2.7	0.8
WORD	9.1	4.9	4	1.9	3.1	1.9	2.1	1.1
More developed countries	10.4	3.9	4.7	1.4	3.1	1.3	2.7	1.1
Less developed countries	8.7	5.4	3.7	2.1	3.1	2.2	1.9	1.1

Results and discussions

The results of the current epidemiological study of oral cavity cancer are separately presented according to their localization, for evaluating which types have higher incidence or mortality according to regions from CEE and also a comparative evaluation between men and women.

Oral cavity, laryngeal and pharyngeal cancer

Oral cavity, laryngeal and pharyngeal cancer accounted 686328 new cases in 2012 and caused 375665 deaths in the same year. The highest incidence was in West of Europe where ASR incidence/100000 people was 13, and in more developed countries as we see from table I that the incidence was higher than in the less developed countries, but the mortality was higher in the less developed countries 5.4 than in the more developed countries 3.9, (table 1). The incidence of oral, laryngeal and pharyngeal cancer of 11.5 is higher in CEE than the global incidence 9 or than incidence for the more developed countries 10.4. The mortality from oral and pharyngeal cancer is higher in CEE than the other studied regions, (table 1).

From CEE, we observe in table II the highest incidence at 100.000 people in Hungary 23.8 and on the second place is Romania 16.6. The lowest incidence was observed in Russian Federation. The mortality was highest in Hungary 12.3 and on the second place Slovakia with 9.9. The incidence of oral and pharyngeal cancer in CEE was higher at men 22.8 that the woman 3.2, with a rate than 7:1 (men: woman), (fig.1). The incidence at men in Hungary was 42.2 which is the highest ASR incidence from the world, were the second ASR man incidence is in Papua New Guinea 38.3, the third is in Bangladesh 33.1 and the fourth in Romania 32.4. (table 2). The highest changes rates between mortality at men from 2012 and mortality from 2000-2004 were found in Bulgaria 181.91%, Romania 94.19% and Poland 90.63%. The mortality rate of changes at woman was very high at all ten countries over 100%, but the highest was found at woman from Czech Republic 471.69%, Bulgaria 307.44% and 275% Poland, (table 3).

Lip and oral cavity cancer

300373 (4) of new lip and oral cavity cancer was diagnosed in the world, 199550 (3.7) in the less developed countries, 100823 (4.7) in more developed countries and 23765 and incidence 5 from CEE. (table 2). The global incidence of lip and oral cavity at men 5.5 is higher than the woman 2.5. (table 2). In CEE the incidence at men is 9.1 and is the third highest incidence from the regions on the world after Melanesia 22.9 and South- Central Asia 9.9. At woman in CEE the incidence is 2, that is the fourteen places from the world regions, and is smaller than West of Europe 3.2, more than in developed regions 2.8 or than less developed regions 2.5. From the countries of CEE, the highest incidence is in Hungary 9.7, followed by Slovakia 6.5. In Romania in 2012 was diagnosed 1847 (5.4) of new cases of lips and oral cavity and died 1001 (3), (fig. 2).

145323 people died worldwide because of lip and oral cancer that represent a mortality/100000 people of 1.9, in CEE died 12516 people (2.6). (table 1). The mortality was also higher in men that the woman, in the world 2.7:1.2, in CEE 5.1: 0.7. The highest mortality/100000 people in countries from CEE was found in Hungary 4.4, followed by Slovakia and Belarus 3.2. Hungary has the highest mortality rate from the CEE countries 23.2, followed by Romanian men 19.4 people and Slovakia men 18.4 people (fig. 3). For woman, also the highest mortality was found in Hungary 8.4 people, followed by woman from Poland 4.2 people and Slovakia 3.9 people, (table 3).

Pharyngeal cancer

229078 (3.1) new pharyngeal cancer was diagnosed in the world in 2012 and 146936 (1.9) died because of it. In CEE were diagnosed 13216 (3) people and died 9159 (2). The incidence of pharyngeal cancer in CEE, (figure 2) was lower than the incidence found in West of Europe 4.8, more developed regions incidence 3.1 and less developed regions incidence 3.2, but the mortality was higher than West of Europe 1.7, more developed regions 1.3 and lower than less developed regions 2.2, (fig. 3). The same as in lips and

Table 2

ASR INCIDENCE OF ORAL CANCER, LIP AND ORAL CAVITY, PHARYNX AND LARYNX AT MAN AND WOMAN IN THE CENTRAL AND EAST EUROPE COUNTRIES

Central and East Europe Counties	Oral and pharyngeal cancer		Lip and oral cavity cancer		Pharynx cancer		Larynx cancer	
	Man	Woman	man	Woman	Man	woman	man	woman
Hungary	42.2	8.4	15.7	4.6	14.1	2.4	12.3	1.4
Romania	32.4	2.8	10	1.6	12.1	0.9	10.4	0.4
Slovakia	29	3.9	11.4	2.4	10.7	1	6.9	0.5
Czech Republic	18.8	5	7.1	2.9	6.3	1.5	6.8	0.5
Republic of Moldova	27.7	2.7	9.9	1.2	6.4	1	11.4	0.5
Belarus	26.8	2.5	10.6	1.2	7.3	0.3	8.8	0.2
Poland	22.2	4.2	8.5	2.4	5.3	0.9	8.4	0.9
Ukraine	24.2	1.8	10.2	1.6	5.7	0.6	8.2	0.3
Bulgaria	21.1	3.3	6.8	1.9	4.3	0.9	10.2	0.5
Russian federation	19.6	2.8	8.5	1.9	4.2	0.6	5.6	0.3

oral cavity cancer Hungarian men are the second most affected people from the world (14.1), Romanian men are on the fifth positions, (figure 2).

From the CEE countries, the highest incidence was found in Hungary 7.8, followed by Romania 6.1 and Slovakia 5.5. The highest incidence of pharyngeal cancer was found at Hungarian men 14.1, followed by Romanian men 12.1 and Slovakian men 10.7, (table 2). At woman, the highest incidence was found at Hungarian woman 2.4, followed by Czech woman 1.5 and Moldavian woman, (table 2). The mortality from pharyngeal cancer in CEE countries was found in Hungary 4.9, followed by Slovakia 4.1 people and Romania 3.8. The mortality was highest at the Hungarian men 9.2, followed by Slovakian men 8.3 and Romanian man 7.4. The mortality at women in the studied countries was low, but the highest was found in Hungary 1.3, Bulgaria 0.8, Romania 0.6 and Slovakia 0.6, (table 3).

Larynx cancer

156977 (2.1) new cases of larynx cancer was diagnosed on the world and 83376 (1.1) died because of it. In CEE countries were diagnosed 16494 (3.6) people and died 2.2, this region being the fourth most affected region from the world after Caribbean (4.2), Southern Europe (3.7) and Western Asia (3.6). (Table 1). The incidence and mortality for larynx cancer is highest in CEE than the West of Europe 2.7/ 0.8, more developed countries 2.7/1.1 and less developed countries 1.9/1.1. (figure 3). The Hungarian men has the five incidences from the world 12.3 and the

Romanian men with seven incidences 10.4 and on the first place is Cuba with 10.4, (table 1).

Like at lips and oral cavity cancer and at pharyngeal cancer in Hungary are the highest incidence/ 100000 people from the CEE countries 6.3 (12.3 for men and 1.4 for woman), (figure 3). On the second place is Republic of Moldova 5.4 (11.4 for men and 0.3 for woman) and on the third place is Romania 5 (10.4 men and 0.4 woman), (figure 3). For woman, the second affected country is Poland 0.9, and third is Czech Republic 0.5. The mortality/100000 people are highest and Moldavian men 7.6 followed by Bulgarian men 6.7, Hungarian and Romanian men 6.2, (table 3).

The present study highlighted the variability of OSCC incidence and mortality rates across country of Central and East of Europe are in Hungary, Romania and Slovakia.

Oral cancer incidence CEE is lower than the incidence from Vest of Europe, but the mortality is much higher, and these can be possible from diagnostic method, with diagnosis OSCC in a higher stage, late submission of the patients to the doctor although the existence symptoms, or because of the prognosis and the treatment. This can be observed for the pharyngeal cancer at man, where the men from Bulgaria and Republic of Moldova, which has a lower incidence than the Hungarian men, has a higher mortality.

The incidence for oral cancer in CEE is higher at man that the woman and the rate incidence man: woman is higher than other parts of the world, although the

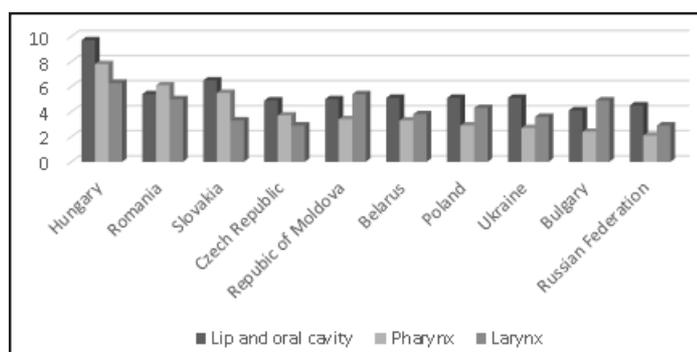


Fig. 2. Oral cancer overall ASR incidence/100000 people in countries from Central and East Europe by type of oral cancer

Table 3

TREND OF AGE-STANDARDIZED (OVERALL) MORTALITY RATES FROM ORAL CANCER AT MAN/ 100 000 PEOPLE IN TEN CENTRAL AND EASTERN EUROPEAN COUNTRIES FOR 1990-1994, 2000-2004 AND 2012, AND THE RATES OF CHANGES ARE SHOWN BELOW.

Central and East of Europe Countries	Men					Women				
	1990-1994	2000-2004	Changes 1990-1994/2000-2004 (%)	2012	Changes 2000-2004/2012(%)	1990-1994	2000-2004	Changes 1990-1994/2000-2004 (%)	2012	Changes 2000-2004/2012(%)
Hungary	17.12	21.12	23.39	23.2	9.84	2.22	3.25	46.39	8.4	158.46
Romania	6.45	9.99	54.44	19.4	94.19	1.02	1.23	20.5	2.8	127.64
Slovakia	16.01	16.85	4.93	18.4	9.19	1.1	1.19	8.18	3.9	227.63
Czech Republic	6.53	7.13	9.18	9.1	39.35	0.97	1.06	9.27	5	471.69
Republic of Moldova	10.57	11.21	6.05	18.5	65.03	1.02	1.1	7.84	2.7	145.45
Belarus	8.28	9.7	17.15	18	85.5	0.72	0.72	0	1.8	150
Poland	6.27	5.98	-4.625	11.4	90.63	1.06	1.12	5.66	4.2	275
Ukraine	9.73	10.55	8.42	16.1	52.6	0.97	0.88	-9.27	2.5	184.09
Bulgaria	4.27	4.93	14.45	13.9	181.91	0.69	0.81	17.39	3.3	307.41
Russian Federation	8.92	8.85	-0,78	12.9	45.76	1.03	1.08	4.85	2.8	159.25

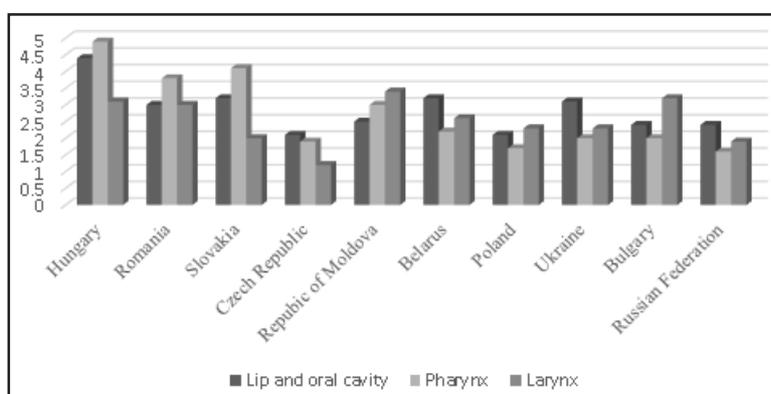


Fig. 3. Oral cancer mortality / 100000 people in Central and Eastern Europe by type of oral cancer

environmental and living conditions are similar but the life style, behaviors and the work place is different. The incidence of OSCC is higher in CEE at man because of their habits, the most of them use to combine alcohol consumption with tobacco smoking, bad oral hygiene and smaller amounts of fruits and vegetables consumption [8,21,22].

The alcohol consumption in CEE has some characteristics like: beer is currently the most consumed type of alcohol, but the spirits from home production and from the markets (like vodka) are also very frequently consumed. The Hungarian woman have the highest incidence and mortality for all type of OSCC across countries of CEE, but they are also known that they have the highest alcohol consumption [23].

Although some of the risk factors are known and there are differences in the geographical distribution of oral cavity and lip, pharyngeal and laryngeal cancer, globally, Hungary is all five in all these cancers, which may imply a genetic predisposition [24] combined with known risk factors for

this country, high alcohol consumption, smoking and low fruit consumption.

The highest incidence and mortality of oral cancer in CEE, presented in table II is at Hungarian men and women, and the Hungarian man has the highest incidence from the entire world, which can be explained by the lifestyle, where the tobacco and alcohol consumption is very high and they are incriminated for the high incidence of oral cancer in this country [25]. The incidence of pharynx cancer and lip and oral cavity at Hungarian man is the second highest incidence from the world and at the larynx cancer is the third incidence from the world. The HPV infection and the OSCC incidence is higher at Hungarian man than the Hungarian woman [26,27].

The woman OSCC incidence and mortality rates is not very high across CEE, but the trend of mortality rate is much higher in the last decade than the other decades, comparing with the penultimate decade, this can be explained by increasing the incidence of HPV+ [28]. Bulgaria and Romanian man has the highest rate of

changes of mortality in the last decade; this may be possible because of a better monitoring of morbidity in these two countries.

Our study showed that incidence of laryngeal cancer is in decrease on the world and in Europe, which is the same with the trend from US [29], but the pharyngeal cancer is increasing also in Europe and US [29].

We have limited data about the prevalence of HPV+ people in Central and East Europe, but in the last decade, all the CEE countries have introduced the immunization for HPV in the national vaccination program [30,31], so we can't define the influence of decreasing the OSCC later.

Although the risk factors for oral cancer are well known, premalignant lesions are known, oral and pharyngeal cancer appears to be easily prevented by screening [31] at regular medical checkups and preventive measures have been taken, oral cancer remains a major public health issue in CEE, where the mortality from OSCC is high.

The present study has limitation. We aimed to describe the epidemiological trend of OSCC in CEE but, we used data from GLOBOCAN, not from national registry, so it is possible to have lack of information, because the used registry is not complete. We also used data for the ten of the most affected for OSCC countries from CEE, not all of them.

Conclusions

The incidence of OSCC has an increasing trend for pharynx cancer, plate of mouth and a decreasing for larynx cancer and lip cancer. OSCC incidence and mortality in Central and East Europe has variable differences between countries, Hungary, Romania and Slovakia experiencing the highest rates from this region. The differences between sexes are also very high, males from CEE are very affected, being the third most affected males from the world, but the women are on the fourteen places. The most affected people from this region are Hungarians, especially men as shown in table 2.

The alcohol consumption and tobacco is still the mean risk factors for OSCC in this region, and most of the countries implemented the WHO recommendation for public anti-tobacco strategy and anti-alcohol consuming [32]. The very high mortality because of the OSCC in CEE can be reduced by a preventive national or regional strategy with health education for population with informed by the OSCC early symptoms, and by screening on the dentistry, or improve the diagnosis methods.

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