

## ROLE OF SMOKING IN CERVICAL ONCOGENESIS

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**Keywords:** smoking, cervical cancer, risk factor, incidence

**Abstract:** The knowledge of cervical cancer and its etiology has registered a remarkable development. Recent studies have highlighted the link between smoking and cervical cancer, this not being dependent of sexual behaviour. Smoking is, therefore, considered a risk factor in the incidence of cervical cancer. The aim of the research was to demonstrate the involvement of tobacco as an etiologic factor in the emergence and development of cervical cancer. Starting from this, I analysed the incidence of cervical cancer in the female smokers in a group of 200 patients diagnosed and operated in Sibiu Gynecology Clinic between 1998 and 2012.

### INTRODUCTION

According to the estimates of the World Health Organization (WHO), smoking is becoming the main cause of morbidity and mortality in the world. It is estimated that there are about 1.1 billion smokers worldwide.(1)

At the end of the XXI<sup>th</sup> century, cancer remains one of the most serious diseases facing humanity. Cancer incidence registered an impressive growth in recent years, currently ranking first, along with the cardiovascular diseases and accidents, regarding mortality in the worldwide countries, without exception.(2,3)

Since 1977, Winklestein found that smoking may be a cause of cervical cancer. Since then, the links between smoking and cancer have been consistently observed.(4) The situation is plausible, since the components of tobacco with a high level of teratogenicity were detected in cervical mucus, suggesting a possible biological mechanism in the development of this cancer.

Becker et al. (1994) issued the hypothesis that assumes that smoking is an etiological factor in the development of high grade cervical dysplasia, finding ethnic differences between different populations. Typically, cervical cancer develops in several years. Before the development of cancer, cervix cells often show changes, known as Cervical Intraepithelial Neoplasia (CIN).(5,6) CIN is a pre-cancerous condition. Pre-cancerous diseases do not involve an immediate risk to health, but in the future, they can fully develop in an advanced cancer.(7,8)

### PURPOSE

It was found that smoking is a risk factor in the incidence of cervical cancer. Starting from this, I analysed the incidence of cervical cancer in smokers in a group of 200 females patients diagnosed and operated in Sibiu Gynecology Clinic between 1998 and 2012.

Based on these considerations, the purpose of the research was to demonstrate the involvement of tobacco as an etiologic factor in the emergence and development of cervical cancer. For this, there has been studied the global analysis of casuistry related to female smokers, casuistry analysis in relation to the female smokers and their age, casuistry analysis in relation to the female smokers and the education level and the

casuistry analysis in relation to the female smokers and clinical staging.

### METHODS

The study material of this paper consists of the observational sheets and the surgical records of the Department of Gynecology within the Sibiu County Hospital between 1 January 1998 and 31 December 2012, counting about 200 patients diagnosed and surgically treated for neoplasm of the cervix during this period.

Statistical analysis of the data was performed using the SPSS (Statistical Program for Social Science) software, version 19. For the descriptive analysis of the data, I used frequency tables, measures of central tendency and of dispersion and in order to determine the significant differences between groups, parametric and nonparametric statistical tests were used (binomial test, chi-square, t-test, Mann-Whitney test). For data representation, I used pie charts, grouped bar graphs, box plots.(9)

### RESULTS

Regarding the consumption of cigarettes, the distribution of cases according to this indicator, shows that of the 200 persons surveyed, 141 are smokers, which represents 70.5% of the studied cases.

Regarding casuistry analysis in relation to smoking, it has been noticed that there are statistically significant differences between the female smokers patients and the non-smokers ones, as follows: the number of female smokers is significantly higher ( $p = 0.000 < 0.05$ ) than the non-smokers who belonged to our study, which strengthens the belief that smoking plays an important etiologic role in the occurrence and development of cervical cancer.

Table no. 1 and figure no. 1 show the numerical and percentage incidence of casuistry operated for cervical cancer in relation to smoking.

To analyze the incidence of smokers according to age groups, the 200 female patients belonging to our study were divided as follows: 18-23 years old – one patient (0.5%); 24 to 30 years: old - 8 patients (4%); 31-35 years old - 14 patients (7%); 36-40 years old - 31 patients (15.5%); 41-45 years old -

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24 patients (12%); 46-50 years old - 36 patients (18%); 51-55 years old - 29 patients (14.5%); 56-60 years old - 20 patients (10%); 61-65 years old - 19 patients (9.5%); 66-70 years old - 10 patients (5%); More than 70 years of age: 8 patients (4%).

**Table no. 1. Numerical and percentage incidence of casuistry operated for cervical cancer during 1998-2012 in relation to smoking**

Distribution of cases according to smoking	Total interventions for cervical cancer between 1998 and 2012		
	No. of cases	Percentage	Statistical significance
Female smokers	141	70.5%	p=0.000<0.05
Female non-smokers	59	29.5%	
<b>Total of cases</b>	<b>200</b>	<b>100%</b>	

**Figure no. 1. Numerical incidence of the operated cases in relation to smoking**

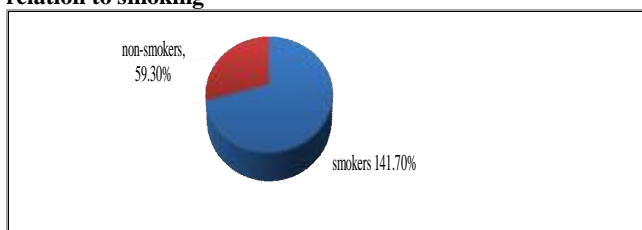
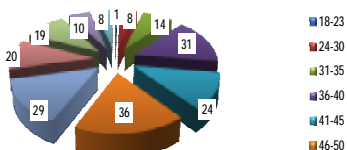


Figure no. 2 presents numerically the incidence of cervical cancer by age groups.

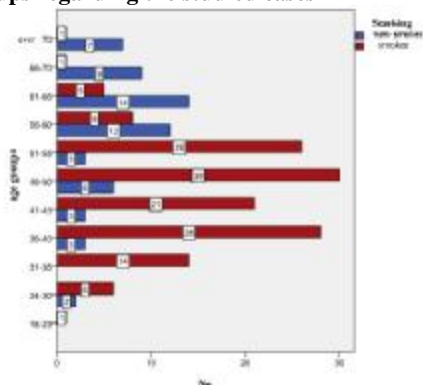
**Figure no. 2. Incidence of cervical cancer according to age groups**



Regarding the incidence of female smokers in relation to age groups, the study found that female smokers were registered in all age groups, but the highest prevalence of smokers was met in the age group of 46-50 years old with 30 cases and in the age group of 36-40 years old - 28 cases.

Figure no. 3 presents the incidence of female smokers by age groups in the studied cases.

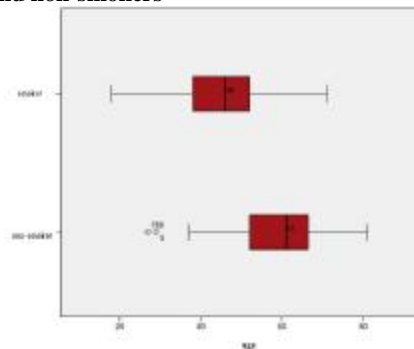
**Figure no. 3. Numerical incidence of the female smokers per age groups regarding the studied cases**



The statistical analysis of the incidence of female smokers in relation to the non-smokers found that until the age

of 55 years old, the percentage of the female non-smokers is higher than the smokers. The average age of the smokers is 44.98 (SD = 9.45) years old and the non-smokers is 58.76 (SD = 11.57) years (p = 0.000 < 0.05), as presented in figure no. 4.

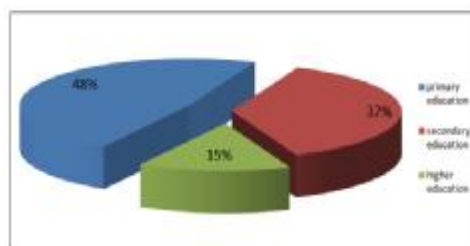
**Figure no. 4. Distribution of age values in case of female smokers and non-smokers**



The statistical analysis according to the level of education showed an increased weight for those with primary education - 48% and 37.5% of the cases with secondary education and only 14.5% had university education. This incidence rate generally reflects the weight of the education level in the general population of Romania.

Figure no. 5 presents the research data in relation to the level of education.

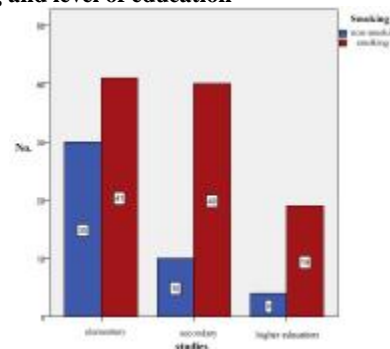
**Figure no. 5. Incidence of the operated cases in relation to the education level**



Regarding the incidence of smoking in relation to the education level, it is observed that for the people with secondary and higher education, the percentage of smokers (smokers with secondary education - 80%, smokers with higher education - 80%) is significantly higher than the non-smokers (p = 0.011 < 0.05). Also, in the case of the female patients with primary education, the percentage of the smokers (58%) is higher than the non-smokers (42%) but the difference is not significant (p = 0.235 > 0.05).

Figure no. 6 presents the research data in relation to smoking and the level of education.

**Figure no. 6. Numerical incidence of the cases in relation to smoking and level of education**



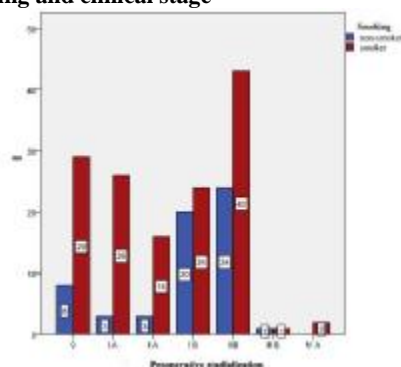
From the clinical stage distribution, I find that in stage 0, 37 patients (18.5%) were diagnosed and surgically treated. Of these, a total of 29 cases were smokers (78.4%). Of the 29 cases in stage I<sub>A</sub> (14.5%), a total of 26 were smokers, representing 89.7% of all cases of this stage. With regard to stage I<sub>B</sub>, there were 44 cases, representing 22% of the casuistry under study, of whom, 24 were smokers, representing 54.5% of the casuistry belonging to this stage. In stage II<sub>A</sub>, there were diagnosed and treated a total of 19 cases. Of these, 16 cases were smokers, representing 84.2% of the casuistry of this stage. Regarding the 67 cases of stage II<sub>B</sub> (33.5%), 43 of them were smokers, accounting for 64.2%.

In stage III, there were diagnosed and surgically treated for cervical cancer two patients of whom one was a smoker, representing 50% of the casuistry of this stage, and regarding the both patients belonging to the IV<sup>th</sup> stage, they were both smokers, representing 100% of the casuistry under study.

The statistical analysis of the smokers in relation to the clinical staging showed that the percentage of the smokers compared to non-smokers was higher in stages 0, I<sub>A</sub>, II<sub>A</sub>, II<sub>B</sub>, and in the remaining stages, the difference is not significant ( $p = 0.015 < 0.05$ ).

Figure no. 7 presents the numerical incidence of the casuistry according to smoking and the clinical stage.

**Figure no. 7. Numerical incidence of the casuistry in relation to smoking and clinical stage**



## DISCUSSIONS

Smoking has been recently considered a risk factor for cervical cancer: cancer risk is two times higher in smokers than in non-smokers, this risk is related to the duration and intensity of smoking.

In the cervical mucus of smokers, there was revealed nicotine, cotinine and other mutagens, reaching the cervical tissue by blood, where the following were detected: existing carcinogens in tobacco smoke: 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) and polycyclic aromatic hydrocarbons (PAH) and changes in cellular DeoxyriboNucleic Acid (DNA) produced by benzo(a)pyrene of tobacco smoke.

Smoking increases the risk of cervical cancer: DNA activation induced by NNK, PAHs, benzo(a)pyrene (BaP); Human papillomavirus infection favouring (HPV) and the progression of this infection to cancer.

There were suggested several possible mechanisms of carcinogenesis: a direct carcinogenic effect; an immunosuppressive effect on cell-mediated immunity.

It has been shown that smoking causes an increase in interleukin-6 (IL6) in cervical mucus, which is a risk factor, given the effects of IL-6 to promote cell growth and neoplastic proliferation. In addition, there are studies showing that reducing the number of cigarettes is accompanied by decreased

Langerhans cells responsible for the presence of antigen at cervical level.

Smoking is a major risk to health. It kills six people every minute, and one smoker in four dies of a tobacco related disease. In 2002, smoking has killed 4 million people, of whom 1.2 million were Europeans.

## CONCLUSIONS

The study shows that the incidence of cervical cancer was higher in smokers than in non-smokers.

Although it does not directly influences the clinical staging, the study demonstrates the presence of smokers in all clinical stages and in all age groups, regardless of the education level, which supports the conclusion that women who smoke have an increased risk of cancer of cervical cancer.

Smoking is an important risk factor in the incidence of cervical cancer in people who smoke as changes occur in the cells throughout the body, including the cells in the cervix, which are more susceptible to sexually transmitted oncogenic viruses.

Women who smoke risk twice regarding the likelihood to develop cervical cancer compared to the non-smokers; this may be due to the harmful effects of chemicals in tobacco on the cells of the cervix.

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