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Original article

SMOKING HABIT AS A RISK FACTOR ASSOCIATED WITH OCCURRENCE OF LUNG CANCER

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Abstract

Lung cancer is one of the most common causes of mortality in the world, right after cardiovascular diseases.

The motivation for conducting this study was the fact that the number of newly diagnosed and death cases from lung cancer has been constantly growing, especially in the last few years.

The aim of the study was to present lung cancer (LC) as a public health problem today at the global level as well as in the Republic of North Macedonia.

This is an analytical case-control study. It included all patients with a confirmed diagnosis of lung cancer (LC) with histopathological analysis (examined group) and patients who have not had any history of malignancy (control group), in a period of six months. Survey data were collected using a specially designed questionnaire.

The study included a total of 82 respondents in both, the examined and the control group. Regarding the habit of cigarette smoking, the largest percentage of examined respondents (56%) were current smokers, compared to the control group where the largest percentage (56%) were non-smokers. The results obtained showed that the two groups differed significantly with regards to the habit of cigarette smoking.

This study confirmed the association of cigarette smoking habit and lung cancer, where several variables related to smoking were examined (age at which cigarette smoking started, number of cigarettes smoked per day, duration of smoking status, type of cigarettes).

Keywords: lung cancer, epidemiology, death, risk factors

Introduction

Lung carcinoma (LC) is still one of the most common causes of mortality worldwide[1]. Despite progress in recent years with the discovery of new life-prolonging treatments, this disease continues to have high mortality rate[2].

Carcinoma is a particular problem in highly developed industrialized countries, where it is the second most common cause of death, after diseases of the cardiovascular system, and is responsible for a quarter of all deaths[3].

The most significant risk factor for the occurrence of this neoplasm is the habit of smoking cigarettes, which is associated with about 80% of all diagnosed cases[4-6]. Smoking increases the risk by 5- to 10-fold, and exposure to environmental tobacco smoke among nonsmokers increases the risk by about 20%[7].

With its frequency and high mortality, as well as with the series of etiological causes, lung cancer is a challenge for modern epidemiology. About 2,206,771 new cases and 1,509,000 deaths are diagnosed worldwide every year[8]. Globally, the number of new cases and deaths from lung cancer is constantly increasing. The increase is particularly noticeable in developing countries, where it is closely related to the habit of smoking cigarettes[9,10]. Different trends in smoking largely dictate international patterns of lung cancer incidence and mortality[9]. Despite advances in the study of risk, pathogenesis, immune control, and treatment options for lung cancer, it remains the leading cause of death from malignant neoplasms.

Because cigarettes remain the leading risk factor for lung cancer, disease prevention is largely focused on smoking avoidance and cessation. Other preventive measures include a healthy diet and maintaining a physically active lifestyle[10-12].

The reduction of the smoking rate in developed countries, the acquired knowledge about the molecular proliferation of tumors, as well as the emergence of new risk factors will lead to changes in the landscape of lung cancer epidemiology[9].

According to research conducted by Globocan in 2020 on the incidence and mortality of malignant neoplasms, lung cancer is the most commonly diagnosed cancer in both sexes. Estimates show the existence of 2.2 million new cases (11.4% of total cancer cases) and 1.8 million deaths (18% of total deaths) worldwide. According to the obtained results, the rates are 4.5% higher than in 2012, where the number of new cases was 1.8 million and the number of deaths was 1.6 million[13]. Of them, 85% were cigarette smokers[13-15].

Globally, rates are highest in regions where cigarette use began long ago, such as North America and Europe[16,17]. Mortality has gradually begun to decline in most of these countries (e.g., the United States, the United Kingdom, Australia) as a result of reduced tobacco use, particularly among men. On the other hand, it increases in countries where smoking is current and increasing, such as Russia, China and a large part of Eastern Europe, the Middle East and Southeast Asia[18]. The number of deaths in Europe in 2020 was highest in Hungary with 42.4 deaths per 100,000 inhabitants, the highest recorded mortality rate in Europe[19-22]. It is followed by Serbia with 40.0 deaths per 100,000 [19], Turkey with a rate of 35.9/100,000 deaths[19], Montenegro with 39.7/100,000[19] and Belgium with 38.3/100,000. deaths[19]. Denmark has the lowest number of deaths from lung cancer (36.8/100,000 inhabitants)[19,23]. RN Macedonia ranks third in the world in terms of mortality from lung cancer among men. The highest death rate was recorded in 2020 with 47.17/100,000 inhabitants[24].

The Reason for conducting the study

The main motive for conducting this study was the fact that lung cancer and its untimely diagnosis makes it the second leading cause of death in the world.

The aim of the study

To determine the influence of the habit of smoking cigarettes as a risk factor in the occurrence of lung cancer.

Materials and methods

Study design

This is an analytical case-control study that identified cigarette smoking as one of the potential risk factors in the occurrence of lung cancer. It included two groups of respondents:

A) Examined group (EG) represented by patients with diagnosed and pathohistologically confirmed lung cancer, selected from the Institute of Oncology and Radiotherapy in Skopje.

B) Control group (CG) which served to evaluate the epidemiological risk of the habit of cigarette smoking as a factor for the occurrence of lung cancer. This group consisted of patients recruited from several general medicine clinics in Skopje who have never had and at the time of conducting the study did not have a malignant disease.

Data for the survey was collected using a specially designed survey questionnaire over a period of four months. The questionnaire aimed to investigate the correlation of the habit of cigarette smoking as a risk factor and the occurrence of lung cancer by comparing the examined group with a control group of patients who did not suffer from lung cancer.

The survey questionnaire contains 40 questions appropriately categorized. In addition to the section with demographic and socio-economic data (age, gender, residence, level of education, profession, marital status), it also contains a section that refers to the habit of cigarette smoking and questions from the Questionnaire on the use of cigarettes, recommended by Tobacco or Health Program of the World Health Organization.

The survey questionnaire also includes a section with questions about possible exposure to other risk factors (occupation, exposure to potentially carcinogenic substances, air pollution, genetic factor, stress), as well as questions related to the diagnosed lung cancer in patients regarding the way it appears, the type of symptoms, their condition, diagnosis and therapy.

In order to reduce the risk of bias when comparing the examined group with the control group, the selection of patients in the control group was performed using the matching method, i.e. both groups were identical or similar in terms of certain accepted characteristics: age (+ 5 years) and a half.

Results

A total of 82 patients were included in both groups - the examined group and the control group. Of the respondents with LC, 53 (65%) were men, and 29 (35%) were women, while in the CG group, the majority were women - 46 (56%) and a smaller percentage were men - 36 (44%). The average age of respondents in the EG group was 66.54 ± 8.380 against CG where the average age was 58.05 ± 10.039.

The distribution of patients by the smoking habit is presented in Table 1, showing that the current and former smokers were more prevalent in EG compared to CG patients (56% *vs.* 40% and 32% *vs.* 4%, respectively). Non-smokers were significantly more present in CG (56% *vs.* 12%, respectively).

Table 1. Distribution of respondents according to the habit of cigarette smoking

Habit of cigarette smoking	Examined group		Control group		p-level
	Participant	%	Participant	%	
Current smokers	46	56	33	40	p<0.0001
Ex-smokers	26	32	3	4	
Non-smokers	10	12	46	56	
Total	82	100	82	100	

p<0.0001 Fisher's exact

The difference in the distribution of current smokers, ex-smokers and non-smokers between the two groups was statistically significant ($p<0.0001$). The habit of cigarette smoking differed significantly between patients with and without lung cancer.

The results obtained in this study showed that majority of respondents from both groups started smoking between the ages of 16 and 20 (44% and 61%, respectively), followed by those aged 15 years and younger (42% and 31%, respectively)).

There was no statistical difference in the relation to the age at which subjects with and without lung cancer started cigarette smoking ($p=0.22$).

In both groups, the lowest percentage belonged to the respondents who had started smoking after the age of 40 (examined group - 1%; control group - 3%).

Table 2. Distribution of patients from the examined and control groups in relation to the age at which they started cigarette smoking

Age at which they started cigarette smoking	Examined group		Control group		p-level
	Respondents	%	Respondents	%	
≤ 15 years	30	42	11	31	
16-20 years	32	44	22	61	
21-30 years	9	13	2	5	p=0.22
31-40	/	/	0	0	
> 40 years	1	1	1	3	
Total	72	100	36	100	

The average age at which patients with LC started cigarette smoking was 17.37 + 4.422 years, while the age of patients from CG was 17.94 + 5.865 years.

Table 3. Average age of respondents at which they started cigarette smoking

Group	Statistical parameters / Age		
	Mean ± SD	Min	Max
EG	17.5±4.4	7	35
CG	18.4±5.7	15	48

In addition to the age at which one starts smoking cigarettes, the number of cigarettes smoked per day, as well as the length of the smoking status, play a significant role in the analysis of LC.

Most (59%) of the patients smoked 21-40 cigarettes per day, while in CG 50% of patients smoked 11-20 cigarettes per day.

The study showed that there was no statistical difference ($p=0.4$) between patients from the two groups (examined and control group), no matter the number of cigarettes smoked per day.

Table 4. Distribution of respondents according to the number of cigarettes smoked per day

Number of cigarettes smoked per day	Examined group		Control group		p-level
	Respondents	%	Respondents	%	
≤ 10	3	6	2	6	
11-20	16	35	16	50	
21-40	27	59	14	44	p=0.4
> 40	0	0	0	3	
Total	46	100	32	100	

The results presented in Table 4 illustrate that patients with lung cancer smoked almost 27.15±11.745 cigarettes per day, compared to the controls, where the average was 23.61±8.299 cigarettes per day.

Table 5. Average number of cigarettes smoked per day in both groups

Group	Statistical parameters / number of smoked cigarettes per day		
	Mean ± SD	Min	Max
EG	27.15±11.745	5	60
CG	23.61±8.299	10	40

Table 6. Distribution of smokers in EG and CG according to the duration of smoking habit

Duration of smoking habit (age)	Examined group		Control group		p-level
	Respondents	%	Respondents	%	
≤15	5	7	2	5	
16-30	7	10	5	14	
31-45	21	29	19	53	p=0.052
> 45	39	54	10	28	
Total	72	100	36	100	

p=0.052

According to the results presented in Table 6, it is evident that most of the patients with LC (54%) smoked cigarettes for more than 45 years, while in the control group that percentage was 28%. The highest percentage of patients without lung cancer (53%) smoked between the ages of 31 and 45. In both groups, the lowest percentage of patients smoked less than 15 years (examined group - 7%, control group - 5%).

There **was** a statistically significant difference (p=0.052) in the duration of smoking habit between the examined and control groups.

Two types of cigarettes were included in the analysis: cigarettes with a filter and handrolled cigarettes. According to the results obtained, most of the respondents in both groups (examined - 94% and control group - 100%) smoked nicotine cigarettes with a filter. Only 4% of lung cancer patients smoked handrolled cigarettes, while 2% of them smoked handrolled cigarettes and filter cigarettes, opposite to the control group subjects who smoked only filter cigarettes.

Table 7. Structure of smokers according to the type of cigarettes they smoked

Type of cigarettes	Examined group		Control group	
	Respondents	%	Respondents	%
Handrolled cigarettes	3	4	/	/
Filter cigarettes	68	94	36	100
Handrolled cigarettes and filter cigarettes	1	2	/	/
Total	72	100	36	100

Discussion

The most significant risk factor for the occurrence of lung cancer is the habit of smoking cigarettes, which is associated with about 80% of all diagnosed cases [1]. This habit increases the risk of LC by 5 to 10 times. Exposure to environmental tobacco smoke increases the risk of this disease by about 20% in non-smokers[4-6].

This study included a total number of 82 respondents in both, the examined and the control groups. Of the respondents with LC, 53(65%) were men, and 29(35%) were women, while in the CG, the majority were women - 46 (56%) and a smaller percentage were men - 36 (44%). The average age of EG respondents was 66.54±8.380 against CG respondents

whose average age was 58.05±10.039. Similar results were obtained in the study by Yu Y, Liu H, *et al*., where the majority of lung cancer patients were males and a smaller proportion were females[25].

Regarding the smoking habit, the largest percentage of the diseased respondents (56%) were current smokers, while in the control group the largest percentage (56%) were non-smokers. Similar results were obtained in the studies by Liao W. and Wang X. et al. conducted in the USA.

In these studies, the majority of diagnosed cases with LC were current smokers, but in the control group, there were mostly non-smokers[26,27]. The two groups differed significantly regarding the habit of cigarette smoking. Although the number of diagnosed women with LC is constantly increasing globally, the male population is still the one that dominates. These data have been confirmed in the studies by Wang X, Bergman BP, Romaszko-Wojtowicz A and Djekic Malbasa J[27-30]. This is in agreement with the situation in our country where the majority of subjects with lung cancer are male.

The age at which one starts smoking cigarettes is also a very significant factor for the occurrence of LC. This has also been confirmed in the studies by Wang X. and Bergman BP. *et al*., presenting the fact that starting this habit at an earlier age increases the risk of LC onset[27,28]. The results obtained in our study showed that the largest percentage of respondents from both groups (EG-88%; KG-61%) started this habit by the age of 20. In both groups, the percentage of those who started smoking after the age of 40 was the lowest (EG-1%; CG-3%). There was no significant difference regarding the age at which respondents from both groups started smoking.

The average age at which LC patients started smoking cigarettes was 17.37+4.422 years, and of CG patients 17.94+5.86.

Despite age at which one starts smoking cigarettes, the number of cigarettes smoked per day as well as the duration of smoking habit play a significant role in the occurrence of LC. Most studies carried out in the world indicate a linear relationship between the number of cigarettes smoked per day and the length of smoking experience with the occurrence of lung cancer. One of them is the study conducted in Montreal by Remen *et al*., in which the highest percentage of subjects in both groups (EG and CG) smoked 20 to 30 cigarettes per day[31]. With reference to the results of their research, the majority (59%) of patients smoked 21-40 cigarettes per day, compared to the majority of patients without LC (50%) who smoked 11-20 cigarettes per day.

Regarding the duration of smoking habit, the results of Remen's study revealed that the largest percentage of patients and control participants smoked in the interval of 40-60 years[31]. The results of our study showed that most of the patients (54%) have been smoking cigarettes longer than 45 years, while the percentage of the control group respondents was 28%.

Strict regulations to control tobacco smoking can prevent a large number of deaths globally, especially from lung cancer. The battle between health authorities, the tobacco industry and smokers continues to haunt humanity, while the tobacco industry continues to make millions of dollars as Bergman says in his study[28].

Conflict of interest statement. None declared.

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