



Smoking Tobacco – a Risk Factor for Breast Cancer

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Abstract

Introduction: In 2009, the International Agency for Research on Cancer (IARC) stated that there was “limited evidence of a cause and effect relationship between an increased risk of breast cancer and smoking”. Environmental tobacco smoke is known to cause cancer by exerting both carcinogenic and genotoxic effects. The aim of the study was to assess the relationship between smoking (active and passive) and breast cancer risk.

Material and methods: The case/control study was conducted from 2015–2019 in the Lodz region. The case group included 384 women with breast cancer; the control group included 298 healthy women. The research tool was an anonymous questionnaire.

Results: In the group of 682 respondents, 63% have ever smoked cigarettes (65.4%/60.1% in the case/control group respectively), 22.1% were current smokers, 67% were exposed to passive smoking. In the majority of cases, women were exposed to smoking by the husband (86%), the father (55.5%) or both (43.2%). Breast cancer risk is 253–271% higher for smokers (current – past) in comparison to the group of non-smokers, never exposed to passive smoking. The risk for passive smokers is 139% higher than for those not exposed.

Conclusions: Exposure to environmental tobacco smoke increases the risk of breast cancer. Public awareness of the negative consequences of passive smoking should be raised.

Key words: tobacco smoking, passive smoking, breast cancer, tobacco-related diseases, breast cancer risk factor

Introduction

The problem of cigarette smoking (active and passive) severely affects the entire world's population. According to data on prevalence of smoking in Europe (collected in the European Health Interview Survey (EHIS)), almost one in four EU28 inhabitants smoke cigarettes (23.9% to be exact) and almost one in five women (19.5%). However, smoking varies widely from country to country – from Bulgaria, Greece, and Turkey, where more than 30% of the population smokes, to Sweden, where the percentage of smokers is 16.7%. Regarding the percentage of smokers by sex, for all EU28 countries, the percentage of smokers is higher for men than for women, with the highest difference being Lithuania (40.3/12.3% smoking men/women) and the lowest Sweden (17.4/16.0%). For Poland, the percentage of smoking men is higher than women (32.5/20.3%) [1, 2]. Kaleta research [3] shows that among professionally active people the percentage of smokers is higher (daily smoking was declared by 37.3% of men and 28.2% of women).

According to the World Health Organization (WHO), smoking kills approximately 8 million people a year (including 1.2 million deaths attributed to second-hand tobacco smoke [SHS]) [4]. The percentage of people who die of tobacco-related diseases is higher than the sum of victims of tuberculosis, malaria and HIV/AIDS. Among the smoking-related causes of deaths, the list is topped by cardiovascular diseases, respiratory failure in the course of chronic obstructive pulmonary disease (COPD), and malignant cancer, smoking is also an important risk factor for stroke, blindness, deafness, back pain, osteoporosis, and peripheral vascular disease [5]. As early as 1964, the carcinogenic properties of tobacco smoke were identified, especially those of several polycyclic aromatic hydrocarbons which featured in the Surgeon General's report on smoking and health [6]. In 2009, the International Agency for Research on Cancer (IARC) stated that there was "limited evidence of a cause and effect relationship between an increased risk of breast cancer and smoking" [7].

Breast cancer is the most frequently diagnosed cancer among women (24.2% of all cancers) in a majority (140/184) of countries worldwide, accounting for one quarter of the total. It is also a leading cause of cancer-related deaths in women (15.0%) [8]. In Poland, in 2018, breast cancer was the most common cancer among women (22.5% of all cancers) and the second (after lung cancer) cause of death due to malignant tumors (15.0% of all cancer-related deaths) [9].

The aim of the study was to assess the association between active and passive smoking and breast cancer, controlling for most of the above-mentioned factors of this disease and to establish prognostic implications if any.

Material and methods

The case/control study was conducted from 2015–2019 in the Lodz region. The case group included 494 women diagnosed with malignant breast cancer. The women from the case group were patients of the Oncological Surgery Department and the 2nd Department of Oncological Surgery, Oncological Surgery Clinics of the Provincial Specialist Hospital M. Kopernik in Łódź; the surgery department of Poddębice Health Center; and the Provincial Specialist Hospital M. Skłodowska-Curie in Zgierz. The control group included 515 women without a diagnosis of breast cancer. A detailed description of the study design and study population, including the selection of women for the case/control groups and a description of the research tool, can be found in our previous article: “Night Shift Work-A Risk Factor for Breast Cancer” [10]. The research tool was an anonymous and voluntary questionnaire.

Respondents were asked: “Have you ever smoked cigarettes for more than six months?”. If they replied positively, they were asked about their smoking status, with possible variants of responses: yes or no. For “yes” answers a further distinction was made: “former smoker” and “active smoker.” The other question: “Have you ever lived with someone who smoked regularly at home?” was asked to identify women exposed to secondhand

smoke. For “yes” answers, there were further questions about relatives who smoked (father, mother, siblings, husband). Respondents were also asked: “How many smokers together have lived with you throughout your life?”, with the answer containing the number of people [1, 2, 3, 4, 5].

Respondents also answered questions about their exposure to passive smoking (“exposed”, “not exposed”).

The study design received a positive opinion from the Bioethics Committee at the Medical University of Lodz (RNN/236/15/EC of 22 September 2015). The part of the survey concerning smoking was completed by 682 women.

The following statistical methods were used in the analysis: (1) t-test for mean value, (2) proportions – to calculate the percentage of a given category in the case and control groups; (2) simple and multiple logistic regression to estimate the odds ratio (OR). Statistical calculations were carried out in: (1) a Microsoft Excel spreadsheet (frequency distribution of the variables, contingency tables); (2) a Gretl econometric package (t-test and logit model selection); and (3) Statistica 13.3 (OR and CI for the final version of the logit model). Predictor reduction in the logit model was carried out using a backward elimination model selection procedure, which started with the most general model and eliminated one variable at a time until the best model was reached (i.e. when all right-side variables were statistically significant for $p < 0.05$).

Results

In the group of 682 respondents who completed the section on smoking, 430 (63%) have ever smoked for at least for six months in their life (65.4% and 60.1% in the case/control group respectively). Up to 279 (40.9%) of the smokers successfully quit smoking (42.7%/38.6% in the case/control group). There were 151 current smokers (22.1% of the whole sample, 22.7%/21.5% in the case/control group).

An average number of smoked cigarettes is similar in the case/control group (15.2/14.7 cigarettes per day) with no significant differences in the

group of current (15.6/14.3) and former (15.0/14.9) smokers. What significantly differences case/control group is the years of smoking which is significantly higher in the case group (31.5 vs 28.6 average years of smoking). This difference is made by former smokers who have longer history of smoking (28.2 vs 24.9 years of smoking).

The whole characteristic of the sample is presented in Table 2, which shows that the most significant differences between the case and control group occur in terms of the following factors:

- BMI > 25 – in the case group the percentage of women who are obese is 104.1% (for BMI \geq 30) and 72% (for BMI 25–30) higher than the control group;
- late menopause – in the case group, the percentage of women who had menopause at age 55+ is 88.4% higher than the control group;
- Smoking – in the case group, the percentage of women who are non-smokers not exposed to smoke is 70.2% lower than the control group;
- number of smokers with whom the respondent lived – in the case group, the percentage of women who live at home with two smoking persons is 76.1% greater than the control group.

The characteristics from Table 1 and 2 show that history of smoking in the group of current and past smokers is fairly similar. Confirmation of this can be found in the table below, where the ORs for the current and past smokers differ little, and are even slightly higher for former smokers (this is due to the longer history of smoking in the case group of former smokers than in control group of former smokers – see last row of Table 1).

The OR for smokers in contrast to the group of non-smoking women is similar for current and past smokers and equal to 1.22–1.28 and shows that risk of breast cancer is 22–28% higher in the group of smokers and past smokers, but is statistically insignificant. We observed high percentage (67%) of respondents exposed to passive smoking (456 out of 682). In the majority of cases, women were exposed to smoking by the husband (86% of all exposed to passive smoking women) or father (55.5%) or both (43.2%) – see Table 2.

Table 1. Smoking status in case and control group

	Case			Control			p-value for case/control average' equality
	N	average	stan. dev.	N	average	stan. dev.	
	Age						
Smokers	251	62.8	9.8	179	61.5	11.3	0.204
• current	87	60.4	8.4	64	59.2	9.6	0.416
• former	164	64.1	10.3	115	62.8	12	0.333
Non-smokers	133	62.3	12.4	119	60.5	9.2	0.196
	Number of cigarettes						
Smokers	251	15.2	7.0	179	14.7	5.8	0.434
• current	87	15.6	7.9	64	14.3	5.3	0.256
• former	164	15.0	6.5	115	14.9	6.1	0.897
	Years of smoking						
Smokers	251	31.5	12.6	179	28.6	13.9	0.025
• current	87	36.4	9.9	64	35.0	10.5	0.404
• former	164	28.2	12.7	115	24.9	14.2	0.043

Source: own calculations based on case-control data.

Table 2. Characteristics of the cases and control groups

Categories	Case N = 384	Control N = 298	Case %	Control %	Case/Control % difference
Smoking					
Smoker	87	64	22.7	21.5	5.6%
Former smoker	164	115	42.7	38.6	10.6%
Non-smoker	133	119	34.6	39.9	-13.3%
Passive smoking—who smoked at home					
Total	289	167	75.3	56.0	34.5%
Father	168	85	43.8	28.5	53.7%
Mother	27	18	7.0	6.0	16.7%
Husband	251	141	65.4	47.3	38.3%
Father and husband	135	62	35.2	20.8	69.2%
Passive smoking – how many smokers lived with respondent					
Total	270	157	70.3	52.7	33.4%
1	126	85	32.8	28.5	15.1%
2	127	56	33.1	18.8	76.1%
≥ 3	17	16	4.4	5.4	-18.5%
Smoking including passive smoking					
Smoker exposed to smoke	60	31	15.6	10.4	50.0%
Former smoker exposed to smoke	111	56	28.9	18.8	53.7%
Non-smoker exposed to smoke	118	80	30.7	26.8	14.6%

Smoking excluding passive smoking							
Smoker not exposed to smoke	27	33	7.0	11.1	-36.9%		
Former smoker not exposed to smoke	53	59	13.8	19.8	-30.3%		
Non-smoker not exposed to smoke	15	39	3.9	13.1	-70.2%		
Age							
35-44	17	15	4.4	5.0	-12.0%		
45-54	72	62	18.8	20.8	-9.6%		
55-64	136	114	35.4	38.3	-7.6%		
65-74	115	83	29.9	27.9	7.2%		
75+	44	24	11.5	8.1	42.0%		
Degree of urbanization							
Cities	91	69	23.7	23.2	2.2%		
Towns and suburbs	170	142	44.3	47.7	-7.1%		
Rural areas	115	73	29.9	24.5	22.0%		
No answer	8	14	2.1	4.7			
Educational level							
ISCED 0-2	51	31	13.3	10.4	27.9%		
ISCED 3-4	270	197	70.3	66.1	6.4%		
ISCED 5-8	62	68	16.1	22.8	-29.4%		
No answer	1	2	0.3	0.7			

Marital status						
Married	260	211	67.7	70.8	-4.4%	
Widow	62	33	16.1	11.1	45.0%	
Divorced (in separation)	23	19	6.0	6.4	-6.3%	
Never married	20	21	5.2	7.0	-25.7%	
No answer	19	14	4.9	4.7		
Employment history						
Ill shifts worker	148	73	38.5	24.5	57.1%	
worker	220	210	57.3	70.5	-18.7%	
Non worker	8	10	2.1	3.4	-38.2%	
No answer	8	5	2.1	1.7		
BMI						
18-25	159	193	41.4	64.8	-36.1%	
25-30	144	65	37.5	21.8	72.0%	
≥ 30.00	76	29	19.8	9.7	104.1%	
No answer (or BMI < 18)	5	11	0.8	1.7		
Age of first menstrual period						
10-12	133	74	34.6	24.8	39.5%	
13-15	208	184	54.2	61.7	-12.3%	
16-18	38	39	9.9	13.1	-24.4%	
No answer	5	1	1.3	0.3		

Age of menopause						
	20	20	5.2	6.7		
≤ 44						-22.4%
45-49	42	24	10.9	8.1		34.6%
50-54	145	139	37.8	46.6		-18.9%
≥ 55	100	41	26.0	13.8		88.4%
No answer	77	74	20.1	24.8		
Number of pregnancies						
0	44	37	11.5	12.4		-7.3%
1	81	80	21.1	26.8		-21.3%
2	145	105	37.8	35.2		7.4%
3	76	54	19.8	18.1		9.4%
≥ 4	38	22	9.9	7.4		33.8%
Sum of duration (in months) of breastfeeding						
< 6	190	104	49.5	34.9		41.8%
6-12	107	107	27.9	35.9		-22.3%
> 12	87	87	22.7	29.2		-22.3%

Source: own calculations based on case-control data.

If smokers are compared with the group of non-smoking women not exposed to passive smoking, the ORs are significantly higher (OR = 3.53–3.71). This shows that the risk of breast cancer is 253–271% higher for smokers (current–past) in comparison to the group of non-smokers who were never exposed to passive smoking. The breast cancer risk for passive smokers is 139% higher than for those not exposed (OR = 2.39). If we exclude from passive smokers current and past smokers, the OR = 3.84 and this shows the ‘clear’ effect of only passive smoking (non-smoking women exposed to smoke have a nearly three times higher risk of breast cancer than non-smoking women never exposed to smoke). Finally, we calculated the OR for non-smokers not exposed to smoke, OR = 0.27, which shows that this group have a 73% lower risk of breast cancer than all the others.

Below are the results of the multiple logistic regression, which includes all the others factor from Table 2 which, along with smoking, can affect breast cancer (a backward elimination procedure was used to reduce the model to a form with only statistically). Results from Table 4 confirm that non-smoking significantly lowers the odds of breast cancer (OR = 0.37; 95% CI: 0.19–0.71), but only if non-smokers were not exposed to passive smoking. Similar to the study [10], the most crucial risk factors of breast cancer are high BMI, which increases the risk by 147–211% and night shift work, which increases the risk nearly twofold. Late menopause and short (or non) period of breastfeeding are factors with an influence of 71 and 44% respectively. Differences between the ORs from Table 4 and [10] results from the different group sizes – here we analyzed only 682 persons who answered all the questions about smoking, so currently estimated OR = 0.37 more precisely measures the impact of non-smoking on breast cancer.

As non-smoking (with no exposure to passive smoke) occurs in a significant percentage of breast cancer cases, we were interested in which sociodemographic factors are favorable to this group. Logistic regression for non-smokers not exposed to smoke, considering the sociodemographic factors from Table 2, shows that only one of these factors signifi-

cantly increases the chances of being in this group. This was the higher education level (ISCED 5–8) for which there is an OR = 2.94, showing that women with a high educational level have twice higher odds of being non-smokers not exposed to smoke than women without high education.

Table 3. Impact of smoking on breast cancer (simple logistic regression).

Categories	OR	Se	95%	CI
Smokers vs non-smokers	1.22	0.21	0.81	1.83
Former smokers vs non-smokers	1.28	0.18	0.91	1.80
Smokers vs non-smokers not exposed to smoke	3.53	0.35	1.80	6.96
Former smokers vs non-smokers not exposed to smoke	3.71	0.33	1.95	7.04
Exposed to smoke vs not-exposed to smoke	2.39	0.17	1.72	3.30
Non-smokers exposed to smoke vs non-smokers not exposed to smoke	3.84	0.34	1.98	7.42
Non-smokers not exposed to smoke vs all the others	0.27	0.31	0.15	0.50

Source: own calculations in Statistica 13.3.

Table 4. Statistically significant odds ratios from multiple logistic regression

Variable	OR	Se	95% CI	
Constant	0.59	0.14	0.45	0.79
BMI >= 30	3.11	0.25	1.91	5.07
BMI 25–30	2.47	0.19	1.71	3.57
Night shift work	1.89	0.18	1.32	2.69
Age of menopause 55+	1.71	0.21	1.12	2.61
Breastfeeding <= 6	1.44	0.18	1.01	2.05
Non-smokers not exposed to smoke	0.37	0.33	0.19	0.71

Source: own calculations in Statistica 13.3.

Discussion

In most epidemiological studies the findings have indicated that both active and passive smoking can increase the risk of breast cancer. In our previous article [10], not-smoking was a significant factor which lowered the OR of breast cancer by 60% (OR = 0.40). Similar results have been

obtained in this study (OR = 0.37). The increased risk may be associated with smoking large quantities of cigarettes, smoking for a long duration, and passive smoking [11–15]. In a nationwide Danish Nurse Cohort Study on 21 867 female nurses, Andersen ZJ et al. found association between active smoking and breast cancer risk. The percentage of active smokers was higher to that observed in our study, 33.7% of nurses were current and 30.0% were former smokers. Authors found increased breast cancer risk of 27% in current (HR: 1.27; 95% CI: 1.11–1.46) smokers and 18% in ever (HR: 1.18; 95% CI: 1.04–1.34) smokers. The researchers observed a dose-response relationship with smoking intensity with the highest risk of breast cancer in nurses smoking > 20 pack-years (HR: 1.32; 95% CI: 1.12–1.55) and > 15 cigarettes/day (HR: 1.31; 95% CI: 1.11–1.56). Moreover, it was observed that women who smoked > 10 pack-years before first childbirth had the highest breast cancer risk (HR: 1.58; 95% CI: 1.20–2.10) [12]. Malik A. et al. examined the association between passive smoking and breast cancer risk. Out of 100 breast cancer cases, 23% were exposed to secondhand smoke. Among passive smokers, 34.8% had exposure to tobacco smoke for ≥ 10 years during childhood, 65.2% were exposed for ≥ 20 years in adulthood. Authors suggested positive association between the intensity and duration of smoking and the age at presentation and poor prognostic factors [13]. In a Chinese case/control study Tong JH et al. found the relationship between passive smoking exposure from partners and breast cancer risk. Women whose partner smoked cigarettes had an increased risk of breast cancer (OR: 1.46; 95% CI: 1.05–2.03; $P = 0.027$). Moreover, it was observed that patients who smoked > 5 cigarettes/day also had significant increased risk (OR: 1.99; 95% CI: 1.28–3.10; $P = 0.002$), as were patients exposed to environmental tobacco smoke for 16–25 years (OR: 1.87 95% CI: 1.22–2.86; $P = 0.004$), and patients smoked > 4 pack-years (OR: 1.71 95% CI: 1.17–2.50; $P = 0.004$) [14]. In a large prospective cohort study the European Prospective Investigation into Cancer and Nutrition, it was observed that both active and passive smoking increase the risk of breast cancer, and smoking in the period between the first menstruation and the first pregnancy is particular-

ly dangerous. The findings indicated that 56.7% of the women surveyed never smoked, 23.3% were former smokers, and 20% of women smoked at the beginning of the study period. Of the surveyed woman 42.6% were exposed to second-hand smoke, 14.2% were not exposed to environmental tobacco smoke (neither at work nor at home), 7.1% were current or former smokers, never exposed to second-hand smoke, and 36.1% were active smokers exposed to second-hand smoke. In our study 67% of respondents were exposed to second-hand smoke. The risk ratio was similar for current (HR: 1.06; 95% CI: 1.00–1.12) and former (HR: 1.05; 95% CI: 1.00–1.10) smokers compared to women who had never smoked [15].

Conclusions

Exposure to environmental tobacco smoke increases the risk of breast cancer. Unfortunately, many women are exposed to secondhand smoke. This exposure also occurs at home, women are most often exposed to passive smoking by their husband/partner. Public awareness of the negative consequences of passive smoking should be raised. The undoubted strengths of the study are: (1) quite a large study group, (2) an extensive questionnaire and many analyzed variables, (3) wide range of smoking definitions. The study also has a number of weaknesses. The weaknesses of the study include the fact that: (1) all data are self-reported by the respondents, which is difficult to verify, (2) questionnaire questions concerned sometimes distant events in the past of the surveyed women, (3) relatively small numbers of respondents in the detailed definitions of smoking, which did not allow for a further division of these groups.

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