THE EFFECTS OF PRENATAL FACTORS ON THE DEVELOPMENT OF NON-SMALL CELL LUNG CANCER

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ABSTRACT

Objective: *The aim of the present study was to investigate the possible effects of prenatal factors on the development of non-small cell lung cancer (NSCLC).*

Material and Method: *The study participants included 101 patients with NSCLC, who were admitted to the Medical Oncology Outpatient Clinic of the Farabi Hospital at the Karadeniz Technical University School of Medicine. A questionnaire was used in this study. The same questionnaire was given to both the patient and control groups. Prenatal factors, together with other known factors for the development of NSCLC, were addressed via this questionnaire.*

Results: *It was determined that patients with NSCLC had older parents compared to the control group ($p<0.0005$; $p<0.0005$). In addition, a lower level of education, lower income, larger families, increased prevalence of smoking in the patients, increased prevalence of smoking in the patient's father, and having more first degree relatives with a history of cancer were detected in the patient group compared to the control group ($p<0.0005$). Also, the height of the patients was shorter than the height of the control group ($p=0.003$). When the patients were classified as normo-weight, overweight, or obese according to their body mass index (BMI), a lower ratio of patients with NSCLC was overweight when compared to the control group ($p<0.0005$).*

Conclusion: *In light of the present study, having older parents is a risk factor for the development of NSCLC, in addition to other known risk factors.*

Key Words: *Non-small cell lung cancer, prenatal factors, maternal age, paternal age* ***Nobel Med 2011; 7(3): 41-45***

PRENATAL FAKTÖRLERİN KÜÇÜK HÜCRELİ DIŞI AKCİĞER KANSERİ GELİŞİMİ ÜZERİNE ETKİSİ

ÖZET

Amaç: Bu çalışmada, prenatal faktörlerin küçük hücreli dışı akciğer kanseri (KHDAK) gelişimi üzerine olası etkilerini araştırmayı amaçladık.

Materyal ve Metod: Çalışmaya Karadeniz Teknik Üniversitesi Tıp Fakültesi Farabi Hastanesi Tıbbi Onkoloji Polikliniğine müracaat eden KHDAK tanısı almış 101 hasta alındı. Çalışmaya alınan tüm hasta ve kontrollere aynı anket uygulandı. Prenatal faktörler, KHDAK gelişiminde bilinen diğer risk faktörleriyle birlikte bu sorular yoluyla kaydedildi.

Bulgular: Bu çalışmada, KHDAK'li hastaların kontrol grubuna göre, daha yaşlı anne ve babalara sahip oldukları belirlenmiştir (p<0,0005; p<0,0005). Ayrıca, hastaların eğitim düzeyinin kontrol grubuna göre daha düşük olduğu, daha düşük gelir düzeyine sahip oldukları, daha geniş ailelerden geldikleri, kendileri ve babalarının sigara içme sıklığının yüksek olduğu, babalarının sigara içme alışkanlığının daha fazla olduğu ve birinci derece akrabalarında kanser öyküsünün daha fazla olduğu tespit edilmiştir (p<0,0005). Yine bu çalışmada, hastaların boylarının kontrollere göre daha kısa olduğu belirlenmiştir (p=0,003). Ayrıca, olgular beden kitle indekslerine (BKİ) göre normal, kilolu ve obez şeklinde sınıflandırıldığında, hastaların kontrollere göre daha düşük oranda kilolu grubuna girdiği saptanmıştır (p<0,0005).

Sonuç: Bu çalışmanın ışığında, diğer bilinen risk faktörlerinin yanında, doğumda ileri anne ve baba yaşına sahip olmanın, KHDAK gelişimi için bir risk faktörü olabileceği düşünülmüştür.

Anahtar Kelimeler: Küçük hücreli dışı akciğer kanseri, prenatal faktörler, anne yaşı, baba yaşı. Nobel Med 2011; 7(3): 41-45

INTRODUCTION

Lung cancer is still the most frequently encountered cancer and the leading cause of death from cancer.[1] The effect of certain prenatal factors on the overall health of infants has been investigated for a long time. Advanced parental age, as one of the prenatal factors, is theoretically considered to predispose some diseases to the fetus. The best known correlation involves the relationship between advanced maternal age and having a child with Down syndrome. An increase in the risk of developing Acute Lymphoblastic Leukemia (ALL) or Acute Myelogenous Leukemia (AML) has been reported in children with mothers of advanced age in some limited studies. Similarly, an increased risk of retinoblastoma and breast cancer among children with elderly fathers has been reported in some studies.[2, 3]

In the current study, we compared the prenatal factors of patients with Non-small cell lung cancer (NSCLC) and healthy controls. Thus, we aimed to determine the effect of maternal and paternal age at the time of delivery, in addition to the smoking habits, family histories of cancer, levels of education, family structures, and the economic status of the patients with NSCLC and a healthy control group on the development of NSCLC.

MATERIAL and METHOD

The study participants included 101 patients with NSCLC, who were seen at the Medical Oncology Outpatient Clinic of the Farabi Hospital at the Karadeniz Technical University School of Medicine, or who were hospitalized on the Medical Oncology Service of Farabi Hospital between July 2006 and December 2006, and 202 healthy controls, who attended the General Internal Medicine Outpatient Clinic with no diagnosis of NSCLC and were of similar age and gender to the patients with NSCLC.

The same questionnaire was distributed to the NSCLC patients and the control group. Sociodemographic features, such as age, gender, marital status, level of education, total monthly income, height and weight of the patients and control subjects, the number of family members, the family members the patient lived with, the birth date of the patient's parents, and the smoking habits of the patients and their parents, were addressed in the questionnaire.

Statistical analysis

The normality of the distribution of data was evaluated by using the Kolmogorov Smirnov test for each group. The Student t-test was used for comparison of variables with a normal distribution, both in the NSCLC and control groups. Qualitative data were analyzed via a chi-square test. Quantitative (metric) data are represented as the mean±standard deviation, whereas qualitative (categorical) data are represented as percentages. p<0.05 was assumed to be the significance level. Logistic regression analysis was used to determine the factors affecting the development of NSCLC. In this analysis, having NSCLC was assumed to be a →

dependent variable, whereas the paternal and maternal age at the time of delivery, obesity, the smoking habits of the father, the smoking habits of the patient, a history of cancer among first degree family members (mother, father, and siblings), family type, educational status, and total monthly income were assumed to be independent factors. The results are presented as the odds ratio (OR) and 95% confidence interval (CI).

RESULTS

Sociodemographic features of the patients and control group

Three hundred three subjects, consisting of 101 patients with NSCLC and 202 controls, were included in this study. The distribution of NSCLC patients and the control group according to age and gender is presented in Table 1. In terms of gender, patients with NSCLC and control subjects were selected in a 1: 2 ratio (p=1.000), and no statistically significant difference was found between the age groups (p=0.645).

The distribution of the NSCLC patients and the control group according to the level of education is evaluated. Twenty (19.8%) patients and 1 (0.5%) control subject did not have a formal education; the difference between the patients and the control group was statistically significant (p<0.0005).

The distribution of the NSCLC patients and the control group according to their total monthly income is evaluated. The total monthly income of 12 (11.9%) patients and 1 (0.5%) control subject was <404 YTL; the difference between the patients and control group was statistically significant (p<0.0005).

The distribution of the NSCLC patients and the control group according to the type of family is evaluated. The families of 75 patients (74.3%) and 191 (94.6%) control subjects were of the nuclear type, whereas 26 patients (25.7%) and 11 (5.4%) control subjects had extended families; the difference between the patients and the control group was statistically significant (p<0.0005).

Comparison of the patients and the control group according to smoking habits

The distribution of the NSCLC patients and the control group according to smoking habits is evaluated. Ninety-four patients (93.1%) and 136 (67.3%) control subjects were either current or former smokers; the difference between the patients and the control group was statistically significant (p<0.0005).

Comparison of the parents of both the NSCLC patients and the control group according to smoking habits

The distribution of mothers of both the NSCLC patients and the control group according to their smoking habits is presented in Table 2. No statistically significant difference was observed between the patients and the control group in terms of their mother's smoking habit (p=0.750).

Table 1: The distribution of the NSCLC patients and control group according to the age groups and gender

	Patient		Control		p
	n	%	n	%	
Gender					1.000
Female	7	6.9	14	6.9	
Male	94	93.1	188	93.1	
Age (years)					0.645
<50	15	14.9	36	17.8	
50-59	32	31.6	69	34.2	
≥60	54	53.5	97	48.0	
TOTAL	101	100.0	202	100.0	

Table 2: The distribution of mothers of both the NSCLC patients and the control group according to their smoking habits

Smoking Habit of the Patient's Mother	Patient		Control	
	n	%	n	%
Smokers and former smokers	2	2.0	3	1.5
Non- smokers	99	98.0	199	98.5
TOTAL	101	100.0	202	100.0
p<0.750				

Table 3: The distribution of fathers of both the NSCLC patients and the control group according to their smoking habits

Smoking Habit of the Patient's Father	Patient		Control	
	n	%	n	%
Smokers and former smokers	68	67.3	43	21.3
Non-smokers	33	32.7	159	78.7
TOTAL	101	100.0	202	100.0
p<0.0005				

The distribution of fathers of both the NSCLC patients and the control group according to their smoking habits is presented in Table 3. The fathers of 68 patients (67.3%) and 43 (21.3%) control subjects were either smokers or former smokers, and the difference between the patients and the control group was statistically significant (p<0.0005).

Comparison of the patients and the control group according to the cancer history of first degree relatives

The distribution of the patients and the control group according to the history of cancer among→

Table 4: The mean ages of the mothers and fathers of the patients with NSCLC and the control group at the time of delivery

At The Time of Delivery	Patient		Control		p
	Mean	Standard deviation	Mean	Standard deviation	
Age of the patient's mother	26.5	6.3	22.5	4.0	<0.0005
Age of the patient's father	31.2	8.4	25.7	4.2	<0.0005

Table 5: The distribution of patients with NSCLC and the control group according to the age of their mothers at the time of delivery

Age of Patient's Mother	Patient		Control	
	n	%	n	%
<20	15	14.9	40	19.8
20-30	58	57.4	154	76.2
≥31	28	27.7	8	4.0
TOTAL	101	100.0	202	100.0
p<0.0005				

Table 6: The distribution of the patients with NSCLC and the control group according to the age of their fathers at the time of delivery

Age of the Patient's Father	Patient		Control	
	n	%	n	%
<25	21	20.8	81	40.1
25-29	29	28.7	88	43.5
30-34	22	21.8	24	11.9
≥35	29	28.7	9	4.5
TOTAL	101	100.0	202	100.0
p<0.0005				

their first degree relatives is evaluated. There was a history of cancer among first degree relatives of 50 patients (49.5%) and 14 (6.9%) control subjects; the difference between the patients and the control group was statistically significant (p<0.0005).

Comparison of patients and control group in terms of mean body mass index (BMI), height, and weight at the time of the diagnosis

The mean BMI, height, and weight of patients with NSCLC and the control group at the time of the diagnosis are evaluated. No statistically significant difference was found between the patients and the control group in terms of mean BMI and mean weight (p=0.789; p=0.148, respectively). The mean height of the patients was 169.2 cm, whereas the mean height of the control group was 171.2 cm, and the difference between the patients and the control group was statistically significant (p=0.003).

Comparison of the patients and the control group according to the mean ages of their mothers and fathers at the time of delivery

The mean ages of the mothers and fathers of the patients with NSCLC and the control group at the time of delivery is presented in Table 4. The mean age of the mothers of the patients at the time of delivery was 26.5 years old, whereas the mean age of the mothers of the control group was 22.5 years old, and the difference between the patients and the control group was statistically significant (p<0.0005). The mean age of the fathers of the patients at the time of delivery was 31.2 years old, whereas the mean age of the fathers of the control group was 25.7 years old, and the difference between the patients and control group was statistically significant (p<0.0005), as well.

Distribution of ages of the mothers and fathers of the patients and the control group according to the age groups at the time of delivery

The distribution of the patients with NSCLC and the control group according to the age of their mothers at the time of delivery is presented in Table 5. The age of the mothers of 28 patients (27.7%) and 8 control subjects (4.0%) was ≥31 years old, and the difference between the patients and the control group was significant (p<0.0005).The distribution of patients with NSCLC and the control group according to the age of their fathers at the time of delivery is presented in Table 6. The age of the father of 29 patients (28.7%) and 9 control subjects (4.5%) was ≥35 years old, and the difference between the patients and the control group was statistically significant (p<0.0005).

DISCUSSION

Lung cancer is still the most frequently encountered cancer and the leading cause of deaths from cancers as well. NSCLC accounts for 75-85% of all lung cancers.[1] We haven't seen any study that investigated the possible effect of prenatal factors on the development of NSCLC. In the current study, the effect of prenatal factors on the development of NSCLC was investigated.

In the present study, the mean age of the mothers of patients at the time of delivery was 26.5 years old, whereas the mean age of the mothers of the control group was 22.5 years old, and the difference between the patients and control group was statistically significant (p<0.0005). The ages of 28 (27.7%) mothers in the patient group and 8 (4%) mothers in the control group at the time of delivery was determined to be ≥31 years old, and the difference between the patients and the control group was also statistically significant (p<0.0005). Indeed, it was →

determined that NSCLC patients had older mothers than the control group at the time of delivery.

Our results are in agreement with the results of other studies about certain cancer types. In a case-control study in England and Wales, similar to our results, it has been reported that patients had older mothers at the time of delivery when compared to the control group, and children of older mothers are at increased risk for childhood leukemias (both ALL and AML).[2] In another case-control study in Korea, which was performed among 1999 patients who had breast cancer-proven histologically and 1548 controls, it was reported that female children of older mothers are at increased risk for breast cancer. In the same study, the age of the mothers of the patients and the control group at the time of delivery were classified into four groups as follows: <25, 25-29, 30-34, and ≥35 years old, which is similar with our classification, and it was reported that patients had older mothers than the control group at the time of delivery.[3] In our study, the mean age of the fathers of the patients at the time of delivery was 31.2 years old, whereas the mean age of the fathers of the control group was 25.7 years old, and the difference between the patients and the control group was statistically significant (p<0.0005). The ages of the fathers of 29 (28.7%) patients and 9 (4.5%) control subjects at the time of delivery were determined to be ≥35 years old, and the difference between the patients and the control group was also statistically significant (p<0.0005). Patients had older fathers than the control group at the time of delivery. In the case-control study performed in England and Wales, it was also reported that children of older fathers are at increased risk of bilateral retinoblastoma.[2] In a cohort study performed in Sweden, in which an increased risk for retinoblastoma and leukemia for the children of older mothers until the age 5 years old has been reported, an increased risk for leukemia and central nervous system cancers for the children of older fathers was also reported.[4] In the same study, also similar to our results, it was reported that the patients had older fathers than the control group at the time of delivery.[4]

In the literature, there are studies that have reported an increased lifetime risk for certain cancer types, mainly the childhood cancers, who have both older mothers and fathers.[2-8] However, there is no study that has investigated the same relationship in patients with NSCLC, and the present study has the features of being the first study investigating this relations.

In conclusion, this study implies that together with other known risk factors, the advanced age of the mother or father makes the child prone to NSCLC. Further comprehensive studies are needed in this subject.

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