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CLINICAL STUDY

The effect of prenatal factors on the development of colon cancer

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Abstract: *Background:* There is some evidence that prenatal factors can play a role in the development of colon cancer. Children with an old parent age at the time of birth were observed to develop certain childhood cancers more frequently
Objective: This trial was designed to investigate the effects of some prenatal factors on colon cancer risk. Particularly, investigation of the effect of advanced parent age on colon cancer development risk was targeted.
Materials and methods: In this study 117 in or out patients diagnosed with colon cancer and 234 control subjects were included. Definitive diagnostic results and dates of diagnosis were determined from pathological reports. Groups were asked for the parent age, smoking habits, sociodemographic, environmental, familial and reproductive traits. The results were compared between the patients and the control group.
Results: It was determined that children may have higher risk if mother and father are more than 30 at birth (p=0.018, p=0.020). While the mean mother age at birth was 25.6±5.72 in patients, it was 24.7±6.90 in the controls. The difference was not statistically significant (p<0.056). The mean father age at birth was 29.4±6.58 in patientsand 27.4±7.47 in the controls. The difference was statistically significant (p<0.001). Smoking of mother was one of the important risk factors of colon cancer (p=0.044).
Conclusion: Our data supports that some prenatal factors such as high parental age at birth and mother -smoker may be risk factors for some cancers in children. This is the first study to report that high parental age at birth and exposure to smoke prenatally increase the risk or colon cancer *(Tab. 7, Ref. 28).* Full Text in free PDF *www.bmj.sk.*
Key words: prenatal factors, colon cancer, father age.

Having an old mother or father is known to increase the risk of certain health problems in newborns (1). The risk of trisomies (particularly trisomy 21 – Down Syndrome) and mitochondrial DNA diseases are increased in the children of old mothers. The incidence of some hereditary diseases was detected to be increased in children with an old parent age at the time of birth (2). Children with an old parent age at the time of birth were observed to develop certain childhood cancers more frequently (1). Advanced parent age may affect the risk of cancer in children through several mechanisms. The increased incidence of germ cell mutations with the advance in the father's age and increased incidence of chromosomal aberations in the germ cells of the mother with aging may predispose newborns to cancer development (1).

There are trials reporting that advanced mother age is associated with retinoblastoma, leukemia and astrocytoma development in children. Similarly, the risk of central nervous system tumors is reported to be increased in the children of old fathers (3–9). In addition to childhood cancers, the evidence that the risk of breast cancer increases during childhood in little girls with an old mother and father at the time of birth gradually grows stronger. Most of the epidemiological trials reported that advanced parent age mildly increased the risk for breast cancer (10). This trial is designed to investigate the effects of some prenatal factors on colon cancer risk. Particularly, investigation of the effect of advanced parent age on colon cancer development risk, as in some other cancer types, was targeted.

Material and method

In this trial, 117 patients diagnosed with colon cancer, who presented to Karadeniz Technical University Medical Faculty Farabi Hospital Medical Oncology Outpatient Clinic between March 2007 and July 2008 or were hospitalized at the Medical Oncology Department between these time points, and 234 controls (2 controls corresponding to one patient) were enrolled. This study was approved by the institutional ethics committee. The exact diagnosis and the date of diagnosis were determined based on their pathology report. For this purpose, prenatal factors including the mother and father age at the time of birth, the smoking history of the mother and father, and some environmental factors were questioned through a survey and the results were compared between the patients and the control group, thereby evaluating the potential effects of prenatal factors on colon cancer development.

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Statistical analyses

The conformance of data obtained by measurements to normal distribution was investigated in each group by Kolmogorov Smirnov test. The comparisons of the variables conforming to normal distribution were made by Student t-test between the patients with colon cancer and the control group. As for the comparisons of the variables not conforming to normal distribution, Mann-Whitney U test was used. The analyses of data obtained by counting were performed by chi-square test. The data obtained by measurement were expressed as arithmetic mean ± standard deviation while those obtained by counting were expressed as number (%). The significance level was $p<0.05$. Logistic regression analysis was performed to investigate the independent factors effective on colon cancer development. In this analysis, while the presence of colon cancer was a dependent variable, marital status, family type, smoking habit of the patient himself/herself, body mass index, history of colon cancer in the first-degree relatives, the age of the mother and the father at the time of birth were considered independent variables. The results are presented with Odds Ratio (OR) and 95 % Confidence Interval (CI).

Results

Certain sociodemographic characteristics of patients and the control group

One hundred seventeen (117) patients diagnosed with colon cancer and 234 controls were included in the trial (a total of 351 participants). The comparisons between patients with colon cancer and the control group by age and gender are presented in Table 1 and Table 2. Patients with colon cancer and the control group were selected in a way to include 2 controls for one patient with respect to age and gender; there was no statistically significant difference between the patients with colon cancer and the control group with respect to age and gender.

Tab. 1. Distribution of the patients with colon cancer and the control group by gender.

	Patient		Control	
Gender	Number	%	Number	%
Female	44	37.6	90	38.5
Male	73	62.4	144	61.5
Total	117	100	234	100

p= 0.87

Tab. 2. Comparison of the patients with colon cancer and the control group by age.

Group	Number	Mean age	Standard deviation
Patient	117	57.8	13.4
Control	234	57.5	13.6

p=0.685

Tab. 3. Distribution of patients with colon cancer and the control group by smoking habit.

	Patient		Control	
Smoking habit	Number	%	Number	%
Smoker + Quit	64	54.7	83	35.5
Non-smoker	53	45.3	151	64.5
Total	117	100.0	234	100.0

p=0.001

Tab. 4. The distribution of patients with colon cancer and the control group by smoking habit of their mother.

	Patient		Control	
Smoking habit of the mother	Number	%	Number	%
Smoker + Quit	4	3.4	1	0.4
Non-smoker	113	96.6	233	99.6
Total	117	100.0	234	100.0

p=0.044

Tab. 5. The mean mother and father age of the patients and the control group at birth.

	Patient		Control		p
	Mean	Standard deviation	Mean	Standard deviation	
Mother age at birth	25.6	5.72	24.7	6.90	0.056
Father age at birth	29.4	6.58	27.4	7.47	0.001

There was no statistically significant difference between the patients with colon cancer and the control group with respect to family type (p=0.138).

Comparison of patients and the control group by smoking habits

Distribution of patients with colon cancer and the control group by smoking habit is presented in Table 3. 64 patients (54.7 %) and 83 controls (35.5 %) were smoking or had quit smoking; this difference between the patients and the control group was statistically significant (p=0.001).

Comparison of patients with colon cancer and the control group by smoking habit of their parents

The distribution of patients with colon cancer and the control group by smoking habit of their mother is presented in Table 4. The smoking rate is higher among the mothers of patients with colon cancer (3.4 %) compared to the control group (0.4 %) and the difference was statistically significant (p=0.044).

There was no statistically significant difference between the two groups by smoking habit of their father (p=0.704).

The presence of cancer history in 1st degree relatives was evaluated. 50.4 % of patients with colon cancer and 26.5 % of

Tab. 6. The distribution of the patients and the control group by mother age at birth.

	Patient		Control	
Mother age	Number	%	Number	%
< 20	16	13.7	60	25.6
20–29	65	55.6	124	53.0
≥30	36	30.8	50	21.4
Total	117	100.0	234	100.0

p=0.018

Tab. 7. The distribution of the patients and the control group by father age at birth.

	Patient		Control	
Father age	Number	%	Number	%
< 25	36	30.8	104	44.4
25–29	26	22.2	53	22.7
≥30	55	47.0	77	32.9
Total	117	100.0	234	100.0

p=0.020

the control group had cancer history in 1st degree relatives and the difference was statistically significant (p<0.0005).

The presence of colon cancer history in 1st degree relatives was evaluated. 13 % of the patients and 3.4 % of the controls had colon cancer history in 1st degree relatives and the difference was statistically significant (p<0.0005). The risk of colon cancer development increases in close relatives of patients with colon cancer.

The mean BMI, height and weight values at diagnosis of patients and the control group was evaluated. There was no statistically significant difference between the patients and the control group by mean height, weight and BMI values.

Patients and the control group were classified as normal, overweight and obese; however no statistically significant difference was detected between the two groups (p=0.103).

The presence or absence of relationship between the mother and father was evaluated. There was a relationship between the mother and father in 26.5 % of the patients and 21.8 % of the control group; the difference was not statistically significant (p<0.327).

Comparison of the patients and the control group by mean mother and father age at birth

Comparison of the patients and the control group by mean mother and father age at birth is presented in Table 5. While the mean mother age at birth was 25.6 ± 5.72 in patients, it was 24.7 ± 6.90 in the controls. The difference was not statistically significant (p<0.056). While the mean father age at birth was 29.4 ± 6.58 in patients, it was 27.4 ± 7.47 in the controls. The difference was statistically significant (p<0.001).

The distribution of patients and the control group by mother and father ages at birth by age group

The distribution of patients and the control group by mother age at birth is presented in Table 6. 30.8 % of the patients and 21.4 % of the controls had a mother = 30 years old at birth. The difference between these two groups was statistically significant (p=0.018).

The distribution of the patients and the control group by father age at birth is presented in Table 7. 47 % of the patients and 32.9 % of the controls had a father=30 years old at birth. The difference between these two groups was statistically significant (p=0.020).

Discussion

In our trial, more patients were detected to have a mother = 30 years old at the time of birth compared to the control group (p=0.018). Again in this trial, patients were detected to have a more advanced father age at the time of birth compared to the control group (p=0.001). In addition, the distribution of patients by age group revealed that more patients had a father = 30 years old at the time of birth compared to the control group (p=0.020). The trial also showed that father age was an independent risk factor for colon cancer and that each 1-year increase in the father age increased the risk of colon cancer 1.08 fold (OR=1.08, CI=1.02–1.14). Our results support the trials reporting that the risk of some cancers increases in children with an advanced mother and father age at the time of birth. In addition, this is the first trial to suggest that an advanced parent age may be a risk factor of colon cancer. There is evidence that prenatal factors may be involved in development of certain cancers. The increased incidence of germ cell mutations with the advance in the father's age and increased incidence of chromosomal aberations in the germ cells of the mother with aging render advanced parent age an interesting subject (1, 11). In children with a father at advanced age, the incidence of some abnormalities such as achondroplasia and hydrocephaly is known to be higher (12). There are also trials reporting that advanced father age increases the risk of retinoblastoma and Wilms' tumor during childhood (10, 13). The results from three trials investigating the correlation between prostate cancer and advanced father age in the literature are controversial. Henderson et al reported that an advanced father age at the time of birth is not associated with prostate cancer risk (14). Janerich et al reported a reduction in prostate cancer risk with the advance in father's age (15). Zhang et al evaluated data from 2164 male participants included in the Framingham trial, who were followed up for 42 years. This trial detected that advanced father age strongly increased the risk of prostate cancer (16). In the literature, there are trials reporting that advanced mother age at birth increases the risk of breast cancer (17). Again, in some studies, advanced father age was reported to increase the risk for breast cancer (15, 18, 19). In the literature, a trial by Henderson et al performed in 1974 investigating the risk factors for cancer in the elderly population evaluated a total of 106 patients with colon cancer including 48 males and 58 females and detected no correlation between colon cancer risk and mother and father age (14).

In the presented trial, the rate of smoking was higher in the mothers of patients with colon cancer compared to the control group (p=0.044). The mutagenic and carcinogenic substances in the cigarette can pass the placenta, thereby representing a poten-

tial risk factor for childhood cancers (20, 21). Prenatal exposure to cigarette smoking increases the risk for some cancers in the newborns (22). In the children of smoking mothers, the risk of central nervous system tumors is reported to be increased (23, 24). In another trial, an increase was reported in the incidence of childhood acute myeloblastic leukemia and lymphoma in the children of smoking mothers (25).

This trial detected no difference between the patient and the control group by smoking (p=0.704). The smoking habit of the father may exhibit carcinogenic activity directly by affecting the paternal germ cells or indirectly through passive exposure of the mother to the smoke (26). Although the results from epidemiological trials are controversial, there are also trials reporting that smoking habit of the father is associated with brain tumors, neuroblastoma and rhabdomyosarcoma during childhood (26–28). In the literature, there are no trials investigating the colon cancer development risk in newborns in their future life in correlation with smoking habit of the mother or father. Our trial detected an increase in colon cancer risk with smoking habit of the mother. However no correlation was detected between the father's smoking habit and the colon cancer risk.

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