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Obstetric Outcomes in Non-Gynecologic Cancer Patients in Remission

Remisyondaki Non-Jinekolojik Kanserli Hastaların Obstetrik Sonuçları

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Abstract

Objective: The aim of the present study was to evaluate the obstetric and perinatal outcomes in treated women who were diagnosed with non-gynecologic cancer and to compare these findings with pregnant women with no history of cancer.

Materials and Methods: This retrospective study was conducted on 21 pregnant women with non-gynecologic cancer who were in remission (study group) and 63 pregnant women with no history of cancer (control group). The women were admitted to the high-risk pregnancy clinic of Zekai Tahir Burak Women's Health Training and Research Hospital with a diagnosis of pregnancy and cancer between January 2010 and January 2015. Obstetric outcomes and demographic characteristics of the patients were recorded. Age, gravida, parity, abortus, body mass index (BMI), gestational week, smoking, mode of delivery, gestational weight, and perinatal outcomes were examined for each woman.

Results: The most common cancer types were thyroid (28.5%) and breast cancers (23.8%), which constituted just over half of the non-gynecologic cancer cases during pregnancy. The time elapsed after the diagnosis was 3.8±2.2 (1–9) years. No statistically significant differences were found between the two groups with regard to age, obstetric history, BMI, gestational week, smoking, and obstetric and perinatal outcomes (p>0.05).

Conclusion: Negative perinatal outcomes in non-gynecologic cancer patients in remission were found to be within acceptable levels.

Keywords: Cancer, female cancers, pregnancy, perinatal outcome

Öz

Amaç: Bu çalışmada amacımız non–jinekolojik kanser tanısı almış ve tedavi edilmiş kadınların obstetrik ve perinatal sonuçlarını değerlendirmek ve kanser öyküsü olmayan gebeliklerle karşılaştırmaktır.

Gereç ve Yöntem: Bu retrospektif çalışma, Ocak 2010–2015 tarihleri arasında gebelik ve kanser tanısı ile Zekai Tahir Burak Kadın Sağlığı Eğitim ve Araştırma Hastanesi yüksek riskli gebelikler kliniğine yatırılan 21 remisyondaki non–jinekolojik kanserli gebe (çalışma grubu) ile 63 kanser öyküsü olmayan gebe (kontrol grubu) dahil edilerek gerçekleştirildi. Hastaların demografik özellikleri ve obstetrik sonuçlar kaydedildi. Her bir kadın için yaş, gravida, parite, abortus, vücut kitle indeksi (VKİ), gebelik haftası, sigara, doğum şekli, doğum kilosu, perinatal sonuçlar araştırıldı.

Bulgular: En sık rastlanan kanser türlerinin tiroid (%28,5) ve meme kanseri (%23,8) olduğu ve bu kanserlerin gebelikte görülen tüm non–jinekolojik kanser olgularının yaklaşık yarısını oluşturduğu görüldü. Tanı üzerinden geçen süre, ortalama 3,8±2,2 (1-9) yıl olarak hesaplandı. İki grup arasında yaş, obstetrik hikâye, VKİ, gebelik haftası, sigara kullanımı, obstetrik ve perinatal sonuçlar açısından istatistiksel anlamlı fark yoktu (p>0,05).

Sonuç: Remisyondaki non–jinekolojik kanserli gebelerin olumsuz perinatal sonuçları kabul edilebilir düzeylerdedir.

Anahtar Kelimeler: Kanser, kadın kanserleri, gebelik, perinatal sonuç

Introduction

Cancer is a leading cause of mortality worldwide. In 2012, an estimated 14.1 million new cases were diagnosed with cancer and 8.2 million of these died of the disease. In the United States, nearly 10% of newly diagnosed female cancer patients occur in women of reproductive age, and 1 in every 1,000 pregnancies is complicated by cancer [1]. According to data from the Cancer Department of the Public Health Agency of Turkey, the age-standardized incidence rate of female cancer is 168.7/100,000 in our country, and approximately 67,000 women get cancer each year according to statistics from 2010 [2]. This report also states that the five most common cancer types in females aged 15–24 years are thyroid,

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nonHodgkin's lymphoma, Hodgkin's disease, central nervous system cancers, and ovarian cancer. However, breast, thyroid, ovarian, colorectal, and corpus uteri cancers are the most frequently diagnosed cancers in females aged 24–29 years.

Cancer is mainly a disease of older people and the incidence of many cancer types increases with age. In recent years, with advances in reproductive techniques and women postponing their pregnancies because of career plans, there has been an increase in the average pregnancy age, which in turn, has increased the co-occurrence of pregnancy and cancer [3]. Although the studies on pregnancy outcomes in patients with cancer are promising, only a small percentage of women can get pregnant after the treatment. This may be related to the chemotherapy and radiotherapy since they can cause infertility. However, patients' fear of pregnancy, or health professionals' and other people's dissuading the patients from getting pregnant, may also explain the low rates of pregnancy in these patients. Some research and meta-analysis has suggested that pregnancy is safe for patients with a history of breast cancer and does not affect the total survival rate [4]. Yet, it has been reported that only 10% of women in breast cancer treatment get pregnant [5]. Likewise, 10% of thyroid cancers develop during the reproductive age. Optimal maternal levels of thyroid hormones should be managed in pregnant women diagnosed with thyroid cancer, as these levels play a crucial role in the development of the fetal central nervous system [6].

In this study, we aimed to assess the obstetric and perinatal outcomes in treated women who were diagnosed with non-gynecologic cancers and compare these with pregnant women with no history of cancer.

Materials and Methods

This retrospective case-control study included patients who were admitted to the Zekai Tahir Burak Women's Health Training and Research Hospital's High-risk Pregnancies Clinic with a diagnosis of pregnancy and cancer between January 2010 and 2015. After obtaining the approval of the Zekai Tahir Burak Education Planning and Coordinating Committee (31/2015), 25 patients were identified from medical records and the hospital's database. Of these, 21 patients were determined as the study group after excluding patients for various reasons including being diagnosed with gynecologic cancer, diagnosed during pregnancy, having had an abortion in the early stages of pregnancy, and missing data in their medical files. Another 63 patients with no history of cancer comprised the control group and were determined by recruiting three consecutive patients giving birth in our hospital following each patient in the study group.

Remission was considered as having no temporary or permanent cancer symptoms or signs during pregnancy or at least one year after the treatment. Demographic characteristics and obstetric outcomes were recorded. Age, gravida, parity, abortus, body mass index (BMI) on admission, mode of delivery, birth weight, and perinatal outcomes were examined. Pregnancy age was calculated by the date of the last period, while ultrasound measurements were performed during the first trimester for those patients who did not know the last day of their period. Routine blood and urine tests were performed in patients during the admission, and vital findings and anthropometric measurements were recorded. Each patient was evaluated by ultrasonography and external fetal monitoring using cardiotocography. Betamethasone (12 mg) was administered every 12 hours to pregnant women at ≤34 gestational weeks and in those having the risk of a preterm delivery for fetal lung maturation. All cases were evaluated in terms of preterm delivery (<37 weeks), fetal stress during delivery, perinatal morbidity, and mortality. The need for the neonatal intensive care unit (NICU) was approved by neonatologists for some cases due to respiratory distress, low birth weight (<2,500 g), and intrauterine growth restrictions (estimated fetal weight <10%).

The Statistical Package for the Social Sciences, version 17.0 (SPSS, Inc.; Chicago, IL, USA) was used for the statistical analysis. Descriptive data and frequencies were calculated by computer. Data compliant with a normal distribution was assessed using the KolmogorovSmirnov test. Continuous and normal data were expressed as mean ± standard deviation if normally distributed; non-normally distributed continuous and normal data were expressed as medians (minimum–maximum). Categorical variables are presented as numbers (percentage). Independent-samples *t*tests were used to compare unadjusted means between groups. Non-parametric variables between groups were compared with Mann-Whitney U tests. Pearson's chi-square and Fisher's exact tests were used for categorical variables. Statistical significance was set at $p<0.05$.

Results

Of the 84 patients included in this study, 25 were admitted to our hospital with diagnoses of pregnancy and cancer. Patients excluded from the study included one patient who was diagnosed with ovarian cancer and another patient with Ewing sarcoma syndrome who had an abortion in the early stages of pregnancy. Other patients that were excluded included one patient with missing data in her files who was being followed up due to Hodgkin's lymphoma and hospitalized for twin pregnancy intrauterine ex at gestational week 21, and the other patient was diagnosed with small cell osteosarcoma during pregnancy. The most frequent cancer types were thyroid (n=6) and breast cancers (n=5), and these cancers constituted a little more than half of the nongynew-

Table 1. The distribution of cancer types

Cancer type	n (%)
Colon cancer	2 (9.5)
Thyroid / parathyroid cancer	7 (33.3)
Leukemia / lymphoma	3 (14.3)
Central nervous system malignancies	3 (14.3)
Breast cancer	5 (23.3)
Renal cell carcinoma	1 (4.8)

Table 2. Comparison of demographic and clinical characteristics of the patients

Variables	**Cancer group (n:21)**	**Control group (n=63)**	**p**
Age (years)	32.1±7.1	29.8±5.8	0.134
Gravida	2(1-6)	2 (1-7)	0.585
Parity	1 (0-3)	1 (0-3)	0.329
Alive	1(0-3)	1(0-4)	0.311
Abortion	0 (0-2)	0 (0-3)	0.534
BMI (kg/m2)	28.9±4.4	28.5±3.9	0.716
Smoker	2 (9.5)	4 (6.3)	0.637
Nulliparity	10 (47.6)	16 (25.4)	0.056
Gestational week	37.1±2.5	37.7±2.7	0.435
Preterm birth	6 (26.6)	9 (14.3)	0.139
Birth weight (g)	3100±534	3130±660	0.851
LBW (<2500 g)	3 (14.3)	5 (7.9)	0.317
Route of delivery			**0.165**
Cesarean section	14 (66.7)	32 (50.8)	
Vaginal delivery	7 (33.3)	31 (49.2)	
Indications for Caesarean section			**0.736**
Severe preeclampsia	1 (4.8)	2 (3.2)	
Repeated cesarean	4 (19)	12 (19)	
Malpresentation	1 (4.8)	2 (3.2)	
CPD	3 (14.3)	6 (9.5)	
Fetal Distress	5 (23.8)	7 (11.1)	
HELLP	0	1 (1.6)	
Pl. Previa	0	1 (1.6)	
Infant gender			**0.076**
Female	13 (61.9)	25 (39.7)	
Male	8 (38.1)	38 (60.3)	
Major malformations	**0**	**1 (1.6)**	**1.000**
NICU needs	**5 (23.9)**	**7 (11.1)**	**0.370**
IUGR+LBW	1 (4.8)	3 (4.8)	
Preterm birth+LBW	2 (9.5)	3 (4.8)	
Respiratory distress	2 (9.5)	1 (1.6)	

BMI: body mass index; NICU: neonatal intensive care unit; CPD: cephalopelvic disproportion; IUGR: intrauterine growth retardation; LBW: low birth weight.
Data are presented as mean ± standard deviation, median (minimum-maximum), and number (percent).

cologic cancer cases during pregnancy (Table 1). In the thyroid/parathyroid cancer group, one patient had a parathyroid carcinoma. Of all of the patients with cancer, four received chemotherapy, four received radiotherapy, and one received both chemotherapy and radiotherapy. The others underwent surgical excisions. The time elapsed after the diagnosis was 3.8±2.2 (range: 1–9) years. The mean age of patients with a history of cancer and those in remission (study group) was 32.1±7.1 (19–49) years, which was not significantly older than those in the control group whose mean age was 29.8± 5.8 (19–41) years (p>0.05). One patient became pregnant using an assisted reproductive technique because of poor ovarian reserve. Also, patients with a history of thyroid/parathyroid cancer were found to have received thyroid hormone replacements. No differences were observed between the two group regarding obstetric history, BMI, and smoking. The mean gestational week was determined as 37.1±2.5 (31–41) weeks in the study group, and 37.7±2.7 (26–42) weeks in the control group. Cesarean delivery, female births, and the need for the NICU were at higher rates in the study group, but these differences were also not statistically significant. One neonate in the study group was detected to have pes equinovarus. The most frequent cesarean indication was fetal distress in pregnant women with non-gynecologic cancer in remission and repeated cesarean in the control group (Table 2).

Discussion

The present study was performed to assess the effect of cancer history on pregnancy outcomes and to determine the most common cancer types in pregnant women with non-gynecologic cancer in remission. Thyroid and breast cancers were the most frequent non-gynecologic cancer types. Maternal and perinatal outcomes of patients with a history of cancer are not poor; even though they rarely manage to get pregnant.

A cancer diagnosis during pregnancy is a tragic situation for expectant mothers and fathers. It is also a very distressful process not only for the families, but also for the gynecologist, oncologist, and neonatologist. Even though the diagnosis of cancer remains rare, the treatment can be quite difficult. The acceptability of pregnancy outcomes is not always certain when a woman with a history of cancer or active cancer becomes pregnant. It is known that the radiotherapy and chemotherapy agents have teratogenic effects on people [7]. Few studies have been carried out on pregnancy outcomes in patients with cancer, but pregnancy outcomes of non-gynecologic cancers are still insufficient.

In 2013, a society-based study was conducted to evaluate the fertility of women undergoing cancer treatment. This study examined the deliveries of surviving women after non-gynecologic cancer treatments and the pregnancy durations in women who had not given birth before the diagnosis was found; the results were similar to those in the control group [8]". Although the study had some limitations such as not evaluating the number of children and the child wish, it concluded that the fertility of women surviving cancer decreased, although this effect was not observed homogenously in all cancer types.

In a study conducted by Sait et al. [9], thyroid cancer was the most common cancer in pregnancy. Also, after being exposed to the radioactive iodine used for thyroid cancer treatment, the pregnancies were safe and the effect of the radioactive iodine on gonad functions was temporary and reversible [10]. Additionally, there was no increase detected in poor perinatal outcomes. After radioactive iodine treatment, it is suggested that a woman should not become pregnant for at least one year to ensure the complete elimination of the drug [10].

Breast cancer in pregnancy is the second most common cancer type after cervical cancer [11]. Even the first studies showed that pregnancy worsens the cancer prognosis, however, other studies have demonstrated that the hormonal effect was very low and the survival rate of the non-pregnant cases with the same stage breast cancer did not differ [12]. Nevertheless, a delay in the diagnosis and the effect of pregnancy on tumor biology should be taken into consideration. A breast lump should not be missed in pregnant women, and it should be examined by mammography if needed. Ultrasonographies and biopsies should also be performed depending on the increased density of the breast. During breast cancer treatment, the fetal malformation rate was 17% after applying chemotherapy and radiotherapy with a single agent in the first trimester [13]. This rate was reduced to 6% by not administering a folate antagonist and avoiding irradiation. Increased malformations were not reported during the second and third trimesters; however, antineoplastic agents are associated with poor perinatal outcomes such as low birth weights, intrauterine growth restriction, preterm delivery, and miscarriage [13]. When examining the post-treatment period following breast cancer it has been shown that pregnancy is not a contraindication for a woman who has received breast cancer treatment. Although some clinicians recommend waiting 2 years, there is no data concerning the adverse effect of not becoming pregnant on the prognosis before 2 years [14]. However, in theory, it is worthy to note that positive tumors, particularly those with estrogen and progesterone receptors, may be worsened during a pregnancy [11]. Similar to previous studies, our study revealed that thyroid and breast cancers were the most frequent cancer types in pregnant women. A literature review evaluating pregnant women with either active cancer or cancer in remission, examined 562 pregnancies in 424 patients with different cancer types. The rates of live births, low birth weights, stillbirths, congenital defects, and

spontaneous and therapeutic abortions were 10.3%, 4.8%, 3.8%, 8%, and 10.9%, respectively [9]. Pregnancy outcomes in women with cancer in remission are not expected to be poor. Yet the patients with active cancer have a significantly greater risk of mortality. Sait et al. [9] reported that 16% of pregnant women with active nongynecologic cancer died of metastases during the pregnancy or early postpartum period.

To our knowledge, our study is one of the first studies investigating non-gynecologic cancer in remission. Having a control group with no history of cancer increases the reliability of our study. However, a limited number of patients may have caused the statistical insignificance of the negative perinatal outcome frequency. Similarly, the prevalence of hematologic malignancies such as leukemia/lymphoma, which are common in this age group, might be low due to the number of cases.

When giving preconception counseling to women with cancer, couples should be informed of the possible effects of hormone-related cancers, such as breast cancer, on both recurrence and survival during pregnancy.

To conclude, even poor maternal and perinatal outcomes in pregnant patients with active cancers have been reported, and the negative pregnancy outcomes of pregnant women with nongynecologic cancer in remission are within acceptable levels. This group of patients should not be discouraged from getting pregnant. The cooperation of the gynecologist and oncologist is essential for the proper diagnosis and determining the appropriate treatment methods. These pregnant women must be examined carefully and families should be informed in detail to better obtain optimal perinatal and maternal outcomes.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Zekai Tahir Burak 31 /3107-2015.

Informed Consent: Written informed consent was obtained from patients due to the retrospective nature of our study

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