ORIGINAL ARTICLE

Pregnancy outcome in women who survived genital or extragenital cancer

Anis Cerovac[1,2], Dženita Ljuca[3], Gordana Bogdanović[3], Gordana Grgić[3], Haris Zukić[3]

[1]Department of Gynaecology and Obstetrics, General Hospital Tešanj, Tešanj, [2]Department of Anatomy, School of Medicine, University of Tuzla, Tuzla, [3]Clinic for Gynaecology and Obstetrics, University Clinical Centre Tuzla, Tuzla; Bosnia and Herzegovina

ABSTRACT

Aim To investigate clinical and obstetrical characteristics, an outcome and a prognosis for pregnant women with diagnosed and treated genital or extragenital cancer and their newborns.

Methods This retrospective cohort study included pregnant and childbearing women with a history of cancer diagnosed before pregnancy during the period between 1 January 2014 and 31 December 2018. Data related to the course of pregnancy and childbirth were collected from medical records (mothers' disease history and partogram). The analysis covered clinical and histopathological characteristics of cancers, type of the treatment (surgery, chemotherapy, radiotherapy), demographic data, obstetric characteristics, comorbidities of women, and outcome of the newborns.

Results The study recorded 18 414 deliveries, of which 30 (0.16%) were pregnancies in women who had been diagnosed and treated earlier for genital or extragenital cancer. The average age of the women at the time of delivery was 29.43±5.97 years. There were six (20%) women with genital and 24 (80%) with extragenital cancer. The most frequent extra genital cancer was Hodgkin lymphoma, in eight (26.6%) cases; ovarian cancer was the most frequent genital cancer, in four (13.3%) cases. The average time span from the cancer diagnosis and start of the treatment to the delivery was 59.2±44.4 months (5 years) (range 12 months - 15 years). Two (6.6%) women died.

Conclusion Our data demonstrate a favourable obstetric and neonatal outcome for women who have survived cancer.

Key words: fertility, malignancy, obstetric outcome, pregnancy

Corresponding author:
Anis Cerovac
General Hospital Tešanj
Braće Pobrić 17, 74260 Tešanj,
Bosnia and Herzegovina
Phone: +387 32 650 662;
Fax: +387 32 650 605;
E-mail: cerovac.anis@gmail.com
ORCID ID: https://orcid.org/0000-0002-7209-382X

Original submission:
06 December 2019;
Revised submission:
21 January 2020;
Accepted:
17 February 2019
doi: 10.17392/1109-20

Med Glas (Zenica) 2020; 17(2): 457-464

INTRODUCTION

A delay of childbearing to the later reproductive age increases the number of women who had a cancer cured or survived a cancer (1-3). Recent advances in oncologic diagnostic methods and treatments, and better access to fertility sparing and infertility treatment imply that both pregnancy and childbirth are now real options for women with history of cancer (1,2). The most common types of cancer in women of reproductive age are breast, genital, hematologic, thyroid, and skin (melanoma) (3,4). Fertility and pregnancy rates have decreased in women with history of cancer (cancer survivors, e. g. five years after the cancer treatment; completed initial cancer treatment and no apparent evidence of active disease), especially in those with leukaemia and breast cancer (3% and 8%, respectively) (3,5). However, these rates do not significantly differ in malignant melanoma, thyroid cancer, and Hodgkin lymphoma survivors (29 %, 33 % and 32%, respectively) (6). Genital cancers (including breast, ovaries, uterine tubes and uterus) are the fourth most commonly diagnosed cancers in women of childbearing age (15–45 years), accounting for 16% of all cancers (6). Cancer therapy comprises chemotherapy with agents of high gonadotoxicity; radiotherapy treatment of the ovaries, vagina, or uterus can have detrimental effects on the patient's ability to achieve reproductive function and carry pregnancy to term (2,6). Fertility-sparing surgeries are aimed at preserving woman's fertility, providing options for girls and women of reproductive age with genital cancer. The women with low stage/grade/borderline genital carcinoma are eligible for fertility-sparing surgical techniques (6); the fertility sparing treatment in these women has not negatively affected overall women survival rate or quality of life, with good reproductive and pregnancy outcomes (6). Pregnancies of women after breast cancer do not carry a worsened prognosis, but some studies suggest an increased risk of miscarriage, preterm birth, low birth weight, increased Caesarean delivery rate and antepartum and postpartum haemorrhage (3). Haematological cancers account for 17% of all cancers diagnosed in girls and women of reproductive age (7). Thyroid cancer is the most common endocrine cancer (8). Because of half of the patients are in the reproductive age, effects of different treatments, such as radioactive iodine (RAI), on future gonadal and reproductive health are an important issue (8). Melanoma is the sixth most commonly diagnosed cancer in women; the diagnosis of melanoma is established prior to their first pregnancy in many women. The available evidence does not show an adverse effect of pregnancy on disease-free and overall survival, progression and/or mortality in melanoma patients (3).

The data about complications related to pregnancy and neonatal outcome of women with history of cancer are scarce. Some studies have reported increased risks of diverse obstetrical, perinatal, and neonatal complications concerning these pregnancies (1,2,9,10). However, larger studies are required with longer follow-up periods in order to further verify reproductive outcome following fertility-sparing techniques for women diagnosed with genital and extragenital cancers.

Despite of the increasing importance of knowledge about the course and outcome of pregnancy in cancer survivors in Bosnia and Herzegovina, there have been no such studies, except for one case report (11).

The aim of this study was to investigate clinical and obstetric characteristics, perinatal and neonatal outcome and prognosis in pregnant women with the history of cancer.

PATIENTS AND METHODS

Patients and study design

This retrospective cohort study included pregnant and childbearing women with the history of cancer diagnosed before pregnancy during the period between 1 January 2014 and 31 December 2018 at the Clinic for Gynaecology and Obstetrics, University Clinical Centre Tuzla. Inclusion criteria were: pregnant women who gave birth with the established diagnosis (histopathologically confirmed) and treatment (surgery, chemotherapy or radiotherapy) for cancer before pregnancy. Excluding criteria were: women without histopathologically confirmed diagnosis of cancer, pregnant women with histopathologically confirmed diagnosis but whose pregnancy ended with miscarriage (spontaneous or induced abortion), and women with histopathologically confirmed benign borderline tumours before and during pregnancy, and carcinoma *in situ* of uterine cervix (four patients).

The survey was approved by the Ethics Committee of the University Clinical Centre of Tuzla.

Methods

Data on the course of pregnancy and childbirth were collected on the basis of available medical records (mother's disease history and partograms). Oncologic data analysis covered clinical and histopathological characteristics of cancers, date of diagnosis, type of treatment (surgery, chemotherapy, radiotherapy), and maternal survival. Obstetrical data included the age of women at delivery, time from diagnosis and treatment to delivery, parity, week of gestation at delivery, mode of delivery, obstetric comorbidities and complications. Neonatal data included gender, birth weight and length, intrauterine growth restriction (IUGR), Apgar score (AS) at the first and fifth minute, congenital malformation, admission to the neonatal intensive care unit (NICU), stillbirths, and early neonatal death.

Statistical analysis

Descriptive statistics, mean value, standard deviation (SD), and percentage were used in statistical data processing.

RESULTS

During the observed period 18,414 deliveries were recorded, of which 30 (0.16%) were cases of pregnancy in women who had been earlier diagnosed and treated for genital or extragenital cancer. There were six (20%) women with genital and 24 (80%) with extragenital cancer.

The average women's age at the time of the diagnosis and treatment was 23.6±67.85 (range 3-36 years); the youngest woman had brain cancer (17.5 years old), and the oldest one had thyroid cancer (28.1 years old). The average women's age at the time of delivery was 29.43±5.97 (range 16-38 years).

Women with thyroid (32.5 years), haematological (31 years) and other (malignant melanoma, epipharyngeal cancer, hepatic angiosarcoma, osteosarcoma of the humerus, abdominal ganglioneuroblastoma) types of cancers (28.66 years) were older at the time of delivery than women with genital (27 years) and brain (23.5 years) cancers (Table 1).

Table 1. Obstetric characteristics of 30 pregnant women according to type of cancer

Characteristics	Genital	Extra genital			Others*	Total N(%)
		Haematological	Thyroid	Brain		
Number of women (No, %)	6 (20)	10 (33.3)	6 (20)	2 (6.66)	6 (20)	30
Age at time of diagnosis and treatment (mean SD) (years)	21±8.31	25±6.1	28.1±5.03	17.5±6.3	21.83±11.4	23.66±7.85
Age at time of delivery (mean SD) (years)	27±6.72	30.7±4.2	32.5±4.5	23.5±3.5	28.6±8.3	29.43±5.97
Time span from treatment to delivery (mean SD) (years)	4.58±3.92	5.8±3.6	4.3±2.06	6.5±2.12	8.5±5.8	5
Parity (No, %)						
Primiparous	5 (83.3)	6 (60)	3 (50)	2 (100)	4 (66.6)	19 (63.33)
Secundiparous	1 (16.6)	3 (30)	3 (50)	-	2 (33.3)	10 (33.33)
Third and multiparous	-	1 (10)	-	-	-	1 (3.33)
Weeks of gestation (mean SD)						38.13±2.02
Delivery less than 37 weeks of gestation (No, %)	1 (16.66)	1 (10)	-	-	1 (16.66)	3 (10)
Mode of delivery (No, %)						
Vaginal birth	-	5 (50)	5 (83.3)	-	2 (33.3)	12 (40)
Caesarean section	6 (100)	5 (50)	1 (16.6)	2 (100)	4 (66.6)	18 (60)
Preterm rupture of membranes (No, %)						
Yes	1 (16.6)	6 (60)	4 (66.6)	1 (50)	2 (33.3)	14 (46.6)
No	5 (83.3)	4 (40)	2 (33.3)	1 (50)	4 (66.6)	16 (53.3)
Obstetrics comorbidities (No, %)						
Miscarriages in reproductive anamnesis	1 (16.6)	2 (20)	-	-	1 (16.6)	4 (13.3)
Infertility/Assisted reproductive technology	1 (16.6)	-	-	-	1 (16.6)	2 (6.6)
Genital infection (colpitis and pelveoperitonitis)	-	2 (20)	3 (50)	-	1 (16.6)	6 (17.64)
Previous Caesarean section, uterine septum resection, myomectomy	1 (16.6)	2 (20)	1 (16.6)	-	1 (16.6)	4 (13.3)
Gestational hypertension /preeclampsia	-	-	1 (16.6)	1 (33.3)	1 (16.6)	3 (8.82)
Hypothyroidism	-	1 (10)	6 (100)	-	1 (16.6)	8 (23.52)
Other maternal comorbidities†	-	3 (30)	1 (16.6)	-	-	4 (13.33)
Maternal mortality	1 (16.6)	1 (10)	-	-	-	2 (6.6)
Type of treatment of cancers (No, %)						
Surgery	6 (100)	-	6 (100)	2 (100)	5 (83.3)	19 (63.3)
Chemotherapy	5 (83.3)	10 (100)	-	2 (100)	5 (83.3)	22 (73.3)
Radiotherapy	-	8 (80)	6 (100)	-	2 (33.3)	16 (53.3)

*malignant melanoma (2), epipharyngeal cancer (1), hepatic angiosarcoma (1), osteosarcoma of the humerus (1) and abdominal ganglioneuroblastoma (1). † varicose veins, earlier surgery of persistent ductus arteriosus, avascular necrosis of the femoral head, bilateral hydronephrosis

The most frequent were primiparous women, in all type of cancers; one woman had twins. The average weeks of gestation was 38.13±2.02 weeks (range 29- 40). The overall prevalence of deliveries with less than 37 weeks gestation was 10%. Caesarean section was a more frequent mode of delivery (60%); in genital and brain cancers it was 100%, and the lowest in women with thyroid cancer, 16.6%.

Preterm rupture of membranes was found in 14 (46.6%) pregnancies; most frequently in women with haematological and thyroid cancers, 60% and 66.6%, respectively. Miscarriages with less than 10 weeks of gestation in reproductive anamnesis were found in 13.3% women, most frequently in haematological cancers, 20% (Table 1).

Infertility and assisted reproductive technology was found in two (6.6%) women. Genital infection (colpitis and pelveoperitonitis) was found in six (17.64%) women, most frequently in women with thyroid and haematological cancers (50% and 20%). Gestational hypertension/preeclampsia was found in three (8.8%) women with thyroid (16.6%), brain (33.3%) and other cancers (16.6%). Hypothyreoidism was found in eight (23.52%) women, mostly in women with thyroid cancers (100%).

The most frequent were female newborns, in all type of cancers. The average birth weight was 3202±557.36 (range 1250- 4070 grams). The highest birth weight was found in women with thyroid cancer (3471). Average birth length was 52.76±3.4 (range −40-57 centimetres) (Table 2).

The prevalence of intrauterine growth restriction was 13.3%. The average Apgar score was 8.01±1.78 (range 2- 9) in the first minute, and 8.63±0.76 (range 6-9) in the fifth minute. Imminent fetal asphyxia (Apgar score >7) was found in 13.3% newborns, and incipient (Apgar score <7) in 16.6% newborns; 16.6% newborns were admitted to neonatal intensive care unit. No stillbirths and congenital malformations were recorded (Table 2).

The most frequently encountered cancer types were haematological, in ten (33.3%), genital, in six (20%), and thyroid cancer, in six (20 %) women. The most frequent was Hodgkin lymphoma, in eight (26.6%) women. Among genital cancers ovarian cancer was represented in four (13.3%) and breast cancer in two (6.6%) women. Among extra genital cancers, haematological (Hodgkin lymphoma, acute myeloid leukaemia, and multiple myeloma), thyroid cancer, brain cancers (cerebellar and lateral ventricle cancer), and others (malignant melanoma, epipharyngeal cancer, hepatic angiosarcoma, osteosarcoma of the humerus, abdominal ganglioneuroblastoma) were found.

One women accidentally found out that she was pregnant (20 weeks) during the treatment for relapses of acute myeloid leukaemia M4, which had previously been discovered and treated.

The average time span from the diagnosis and treatment to delivery was 59.2±44.4 months (5 years), from 12 months to 15 years, the highest in other cancers (8.5 years), and the lowest in thyroid cancer (4.3 years). Nineteen (63.3%) women underwent surgery, 22 (73.3%) chemotherapy and 16 (53.3%) radiotherapy. During the follow up period (from 1 January 2014 to 31 Decem-

Table 2. Obstetric characteristics of newborns according to type of mother cancer

Characteristics	Genital	Extra genital			Others*	Total (No, %)
		Haematological	Thyroid	Brain		
Gender (No, %)						
Male	2 (33.3)	7 (70)	2 (33.3)	1 (50)	2 (33.3)	14 (46.6)
Female	4 (66.6)	3 (30)	4 (66.6)	1 (50)	4 (66.6)	16 (53.3)
Birth weight (mean SD) (g)	3170±409.14	3144±472.02	3471.6±463.48	3345±360.62	2815.71±989.3	3202±557.36
Birth length (mean SD) (cm)	52.5±1.97	52.5±2.5	54.6±2.65	55±1.41	49.42±6.57	52.76±3.45
Intrauterine growth restriction (No, %)	1 (16.6)	1 (10)	-	-	2 (33.3)	4 (13.3)
Apgar score (AS) (mean SD) (min)						
First min.	8.5±0.83	7.4±2.01	9±0	9±0	8±2.44	8.1±1.78
Fifth min.	8.83±0.40	8.3±0.82	9±0	9±0	8.5±1.22	8.63±0.76
Condition of fetus after delivery (No, %)						
Imminent fetal asphyxia (AS>7)	1 (16.6)	2 (20)	-	-	1 (16.6)	4 (13.3)
Incipient fetal asphyxia (AS<7)	1 (16.6)	3 (30)		-	1 (16.6)	5 (16.6)
Neonatal Intensive Care Unit	1 (16.6)	3 (30)	-	-	1 (16.6)	5 (16.6)

*the same as in Table 1

Table 3. Types of cancer/stage, treatment and time span from treatment to delivery

Type/stage of cancers	**Total** (No, %)	**Type of surgery** (No of women)	**Chemotherapy** (YES/NO) (No of women)	**Radiotherapy** (YES/NO) (No of women)	**Time span from treatment to delivery**
Genital	**6 (20)**				
Ovarian cancer FIGO Ia (*Cystadenocarcinoma serosum*)	1 (3.3)	Unilateral adnexectomy (1)	NO	NO	24 months
Ovarian cancer FIGO IIIc (*Cystadenocarcinoma serosum*)	2 (6.6)	Unilateral adnexectomy, Omentectomy (2)	6 cycles (taxol/carboplatina) (2)	NO	18 and 24 months
Embryonic ovarian cancer FIGO IIIc (*Ca embrionale ovarii*)	1 (3.3)	Unilateral adnexectomy, Omentectomy	6 cycles (bleomycin, etoposid, cysplatina)	NO	8 years
Breast cancer - pT1bN0M0 (1) - pT2bN1M0 (1) (*Carcinoma ductale invasivum*)	2 (6.6)	Mastectomy (2)	6 cycles+hormonotherapy (letrosol, tamoxifen) +imunotherapy (trastuzumab) (2)	1	24 months and 11 years
Extragenital	**24 (80)**				
Cerebelar (*Astrocytoma anaplasticum*)	1 (3.3)	Craniotomy and tumour ablation	6 cycles chemotherapy	NO	8 years
Lateral ventricle (*High grade ependimoma)*	1 (3.3)	Tumorectomy, Ventriculocysternostomy, Ventriculoperitoneostomy	6 cycles chemotherapy	NO	5 years
Hepatic angiosarcoma	1 (3.3)	Tumour extirpation	6 cycles chemotherapy	NO	13 years
Osteosarcoma of the humerus	1 (3.3)	Amputation of extremity	neoadjuvant and adjuvant chemotherapy	NO	15 years
Abdominal ganglioneuroblastoma	1 (3.3)	Tumour extirpation	6 cycles	NO	13 years
Malignant melanoma pT1N0M0	1 (3.3)	Excision of the tumour	NO	NO	12 months
Malignant melanoma pT2N1M0	1 (3.3)	Excision of the tumour, lymph node extirpation	4 cycle (dacarbazine)	YES	4 years
Epipharingeal cancer pT1N0M0 (*Carcinoma planocellulare*)	1 (3.3)	NO	6 cycles (docetaxel, cisplatin, florouracil)	YES	5 years
Thyroid gland (*Carcinoma papillare invasivum glandulae thyroideae*)	1 (3.3)	Thyreoidectomy (1)	NO	Radioactive iodine treatment (1)	24 months
Thyroid gland (*Carcinoma papillare invasivum glandulae thyroideae*) pT1bN0M0 (5)	5 (16.6)	Thyreoidectomy (5)	NO	Radioactive iodine treatment (5)	3 – 8 years
Lymphoma Hodgkin IIA/B stage (*Nodular sclerosis*) (6) IIIB stage (2)	8 (26.6)	NO	ABVD regimen (adriamycin+bleomycin+Vinblastine+dacarbazine) (7) ABVD+BEA COPP regimen 4 cycle (1)	Radiotherapy of the neck and mediastinum (8)	3 – 10 years
Multiple myeloma	1 (3.3)	NO	6 cycles	NO	3 years
Acute myeloid leukaemia M4 (FAB)	1 (3.3)	NO	Before pregnancy: AD (adriamycin+dexamethason) 3+7 protocol for induction and reinduction. In pregnancy: cytosar	NO	24 months

ber 2019) two (6.66%) women died. Their deaths were caused by acute myeloid leukaemia M4 (two months after delivery) and ovarian cancer FIGO IIIC, respectively (17 months after delivery) (Table 3).

DISCUSSION

In a systematic review by Gerstl et al. (6) the women's mean age at the time they were diagnosed with genital cancer, as well as the time of delivery was 30.5 and 30.3, respectively, which is higher than 21 and 27, respectively found in our study. Approximately 12% of ovarian cancers occurred under the age of 44 (6). Gerstl et al. reported that most women with ovarian cancer had grade 1- stage IA, and underwent fertility-sparing treatment including unilateral oophorectomy with adjuvant chemotherapy, similar to our study (6). In our study we have found four women with ovarian cancer (three were with epithelial ovarian cancers). According to the stage of ovarian cancer one women was in stage FIGO IA, two in stage

FIGO IIIC, and one with embryonic ovarian cancer in stage FIGO IIIC, and all had been treated with unilateral adnexectomy and chemotherapy, and gave birth to healthy newborns. Kashima et al. (12) reported among 18 women who underwent fertility sparing surgery with epithelial ovarian cancer FIGO stage IC, seven singleton pregnancies for five women, compared to our results, four singleton pregnancies in four women; they suggest that fertility sparing surgery for ovarian cancer is a valid treatment option for women of reproductive age who strongly desire to conceive (12). Gerstl et al. (6) reported 15% of miscarriages and 10% of preterm birth rates, which is lower than in our study, 16.6% and 16.6%, respectively.

In a systematic review and meta-analysis conducted by Gerstl et al. (7) the most commonly reported haematological diagnoses were Hodgkin or non-Hodgkin lymphoma (40%), chronic myeloid leukaemia (21%), acute myeloid leukaemia (15%), and acute lymphoblastic leukaemia (7%). In our study we have found 33.3% of haematological diagnoses out of all cancers: Hodgkin lymphoma 26.6%, multiple myeloma 3.3%, and acute myeloid leukaemia 3.3%, which had been treated with chemotherapy and radiotherapy.

De Sanctis et al. reported that the median time from diagnosis to delivery was nine years, compared to 5.7 years in our study (13). The female/male ratio in the Italian study was 51% / 49% (10), which is different from our finding, 30%/70%. The median birth weight found in the Italian study was similar to our data (3220 vs. 3144) (13). De Sanctis et al. reported 12% of miscarriages, 7% of premature births, 2% of low birth weight infants in women treated for Hodgkin lymphoma, which is lower in comparison to our results (13). In the study by De Sanctis et al. two cases of congenital malformations were recorded and no cases of stillbirths, while in our study no cases of congenital malformations or stillbirths were found (13). In our study 80% of women with haematological cancer underwent radiotherapy (neck and mediastinum) and all women had chemotherapy before pregnancy, which is higher compared to the study by De Sanctis et al. (91% and 66%, respectively) (13). A Serbian study (4) reported good maternal and neonatal outcome in women with acute myeloid leukaemia M4, in contrast to our study.

Two studies (14,15) reported that the mean age during the pregnancy and at delivery for thyroid cancer women was 29.9 and 29.7 years, respectively, which means younger women compared to our data (32.5). The same studies (14,15) reported that the duration between the diagnosis of thyroid cancer and the beginning of pregnancy was 40.5 and 60.9 months, respectively, in comparison with 51.6 months in our study. In the two studies the median age of thyroid cancer diagnosis was 36 and 24.7 years, comparing to 28.1 in our study (14,16). Hirsch et al. reported 47.6% and 17.5% of women in T1 and T2 stage of the disease, respectively, whereas in our study 83.3% and 16.6% of women were in T1 and T2 stage of the disease, respectively (14). In our study all patients underwent thyroidectomy and subsequent radioactive iodine treatment (RAI) compared to 93.6% and 92%, respectively, in an Israeli study (14). No women in our study had thyroid cancer progression/recurrence during pregnancy, compared to 9.5% in the Israeli study (14). In a systematic review by Sawka et al. (8) it was found that RAI treatment for thyroid carcinoma was not generally associated with an increase of long-term risk of infertility, miscarriage, stillbirths, or congenital defects, which was the same for women with thyroid carcinoma not treated with RAI; it correlates with our results. Blackborn et al. (16) reported complications connected with increased risks for haemorrhage and diabetes/or abnormal glucose tolerance during pregnancy, childbirth, and the puerperium in thyroid cancer survivors. We did not record these complications. Our study confirms that pregnancy does not have an impact on the recurrence of the disease in women who survived thyroid cancer without evidence of disease's persistence before the conception.

A Turkish study (1) reported 68 pregnant women who survived cancer, where the most frequently encountered cancer types were thyroid (26.4%), haematological (22.1%), genital (19.1%), and breast cancer (13.2%), which slightly differs from our results (20%, 33.3%, 13.3% and 6.6%, respectively). The mean maternal age (31.7 vs. 29.4), birth weight (3030 vs. 3202) and gestational age (37.5 vs. 38.1) in Davutoğlu et al. study were very similar to our findings (1); the prevalence of nulliparity (63.3%), miscarriages (13.3% vs. 2.9%), preterm birth (10% vs. 8.8%), intrauterine growth

restriction (IUGR) (8.8% vs. 5.8%) and gestational hypertension / preeclampsia (8.8% vs. 2.9%) was higher in our study, respectively. The most probable reason for this difference is that Davutoğlu et al. excluded women with other coexisting medical conditions and any sequelae associated with chemotherapy and radiotherapy from the analysis. A Georgian study reported higher incidence of preterm delivery in breast cancer and leukaemia survivors in contrast to survivors of Hodgkin lymphoma, melanoma, and thyroid cancer (17). We reported a high incidence of Caesarean section (60 %), which correlates with Davutoglu et al. (66.6%) and Hartnett et al. studies (1,17). The high number of women with miscarriages, IUGR and Caesarean section in our study is probably a result of numerous comorbidities in pregnancies, earlier surgeries, chemotherapy /radiotherapy /radioactive iodine treatment, and older age of pregnant women. The preterm rupture of membranes was found in 46.6% of term gestations, mostly in haematological and thyroid cancers (60% and 66.6%, respectively). This is high frequency when compared to healthy adolescent and adult pregnancies (39.44% and 21.33%), probably because of comorbidities and consequences of cancer treatment (18).

The prevalence of admission to neonatal intensive care unit (NICU) in our study was higher than in the Turkish study (16.6% vs. 8.8%), mostly due to prematurity (1). There were no early neonatal deaths or congenital anomalies detected in the newborns in both studies, but the Turkish study reported one stillbirth (1). Miscarriage, preterm birth and IUGR are common findings among the offspring of female childhood cancer survivors who received chemotherapy and abdominal, pelvic or total body irradiation (9,10,15).

Women intending to become pregnant after surviving cancer should be strongly supported, their pregnancy and delivery should be monitored closely and in a multidisciplinary manner. The influence of pregnancy on the course of cancer and the risk of relapse has to be discussed individually with the patient, depending on the tumour type and its stage (1).

Davutoglu et al. (1) reported four (out of 31) maternal deaths due to the advanced stage of breast and gastrointestinal cancers, which is higher comparing to our finding, e.g. two maternal deaths (out of 30); both deaths in our study were due to late diagnosis and advanced-stage cancers, and both babies survived. The main objective in such advanced cancers with poor maternal prognosis is to prolong the delivery to avoid extreme prematurity (1,19).

Oncologists should offer oncofertility counselling and fertility preservation in women before the start of cancer treatment (6,11,19,20). Women with cancer are generally advised to delay pregnancy for up to 2 years following the cancer treatment in order to identify possible relapse, and because of the time needed for the oocyte to recover from the damage caused by chemotherapy and radiotherapy (5,11,19,20). Women who successfully conceive subsequently to the treatment should be monitored throughout their pregnancies by the treating gynaecological oncologist, foetal medicine and obstetrics and reproductive specialist in order to reduce potential pregnancy and birth complications (6,11,19,20).

There are several limitations that should be addressed. Firstly, we describe women presented with a combination of different cancers and treatments without specifying which treatment resulted in a specific reproductive outcome. Furthermore, there were inconsistencies and underreporting in some patients in a dosage of chemo- and radiotherapy, and study population was small. Despite the limitations associated with this study, we reported several interesting findings.

In conclusion, although in small sample, our data demonstrate a favourable obstetric and neonatal outcome for women who have survived cancer. The women considering pregnancy after cancer treatment should not be necessarily afraid, but should be counselled carefully about perinatal risks and risks of recurrence. Prenatal care should be tailored to the specific cancer and risks, and appropriate support should be offered by the obstetrician and oncologist guiding that pregnancy.

FUNNDING

No specific funding was received for this study.

TRANSPARENCY DECLARATION

Conflict of interest: None to declare.

REFERENCES

1. Alıcı Davutoğlu E, Madazlı R, Yılmaz N, Ozel A, Uludag S, Sozen I. Pregnancy in cancer patients and survivors; experience of a university hospital in Turkey. J Obstet Gynaecol 2017; 37:1015-9.
2. Clark H, Kurinczuk JJ, Lee AJ, Bhattacharya S. Obstetric outcomes in cancer survivors. Obstet Gynecol. 2007; 110:849-54.
3. Landa A, Kuller J, Rhee E. Perinatal considerations in women with previous diagnosis of cancer. Obstet Gynecol Surv 2015; 70:765-72.
4. Jeremic K, Stefanovic A, Dotlic J, Kadija S, Kontic O, Gojnic M, Jeremic J, Kesic V. Cancer during pregnancy – clinical characteristics, treatment outcomes and prognosis for mothers and infants. J Perinat Med 2018; 46:35-45.
5. Stensheim H, Cvancarova M, Møller B, Fosså SD. Pregnancy after adolescent and adult cancer: a population-based matched cohort study. Int J Cancer 2011; 129:1225-36.
6. Gerstl B, Sullivan E, Vallejo M, Koch J, Johnson M, Wand H, Webber K, Ives A, Anazodo A. Reproductive outcomes following treatment for a gynecological cancer diagnosis: a systematic review. J Cancer Surviv 2019; 13:269-81.
7. Gerstl B, Sullivan E, Koch J, Wand H, Ives A, Mitchell R, Hamad N, Anazodo A. Reproductive outcomes following a stem cell transplant for a haematological malignancy in female cancer survivors: a systematic review and meta-analysis. Support Care Cancer 2019; 27:4451-60.
8. Sawka AM, Lakra DC, Lea J, Alshehri B, Tsang RW, Brierley JD, Straus S, Thabane L, Gafni A, Ezzat S, George SR, Goldstein DP. A systematic review examining the effects of therapeutic radioactive iodine on ovarian function and future pregnancy in female thyroid cancer survivors. Clin Endocrinol (Oxf) 2008; 69:479-90.
9. Signorello LB, Cohen SS, Bosetti C, Stovall M, Kasper CE, Weathers RE, Whitton JA, Green DM, Donaldson SS, Mertens AC, Robison LL, Boice JD Jr. Female survivors of childhood cancer: preterm birth and low birth weight among their children. J Natl Cancer Inst. 2006; 98:1453-61.
10. van der Kooi ALF, Kelsey TW , van den Heuvel-Eibrink MM , Laven JSE , Wallace WHB, Anderson RA. Perinatal complications in female survivors of cancer: a systematic review and meta-analysis. Eur J Cancer. 2019; 111:126-37.
11. Cerovac A, Ljuca D, Nevacinovic E, Tulumovic A, Iljazovic E. Giving birth after fertility sparing treatment of embrional carcinoma Figo III C: case report and literature review. Med Arch 2018; 72:371-3.
12. Kashima K, Yahata T, Fujita K, Tanaka K. Outcomes of fertility sparing Surgery for women of reproductive age with FIGO stage IC epithelial ovarian cancer. Int J Gynaecol Obstet 2013; 121:53-5.
13. De Sanctis V, Filippone FR, Alfò M, Muni R, Cavalieri E, Pulsoni A, Annechini G, Valeriani M, Osti MF, Minniti G, Enrici RM. Impact of different treatment approaches on pregnancy outcomes in 99 women treated for Hodgkin lymphoma. Int J Radiat Oncol Biol Phys 2012; 84:755-61.
14. Hirsch D, Levy S, Tsvetov G, Weinstein R, Lifshitz A, Singer J, Shraga-Slutzky I, Grozinski-Glasberg S, Shimon I, Benbassat C. Impact of pregnancy on outcome and prognosis of survivors of papillary thyroid cancer. Thyroid 2010; 20:1179-85.
15. Budak A, Gulhan I, Aldemir OS, Ileri A, Tekin E, Ozeren M. Lack of influence of pregnancy on the prognosis of survivors of thyroid cancer. Asian Pac J Cancer Prev 2013; 14:6941-3.
16. Blackburn BE, Ganz PA, Rowe K, Snyder J, Wan Y, Deshmukh V, Newman M, Fraser A, Smith K, Herget K, Kim J, Kirchhoff AC, Porucznik C, Hanson H, Abraham D, Monroe M, Hashibe M. Reproductive and gynecological complication risks among thyroid cancer survivors. J Cancer Surviv 2018; 12:702-11.
17. Hartnett KP, Ward KC, Kramer MR, Lash TL, Mertens AC, Spencer JB, Fothergill A, Howards PP .The risk of preterm birth and growth restriction in pregnancy after cancer. Int J Cancer 2017; 141:2187-96.
18. Marković S, Bogdanović G, Cerovac A. Premature and preterm premature rupture of membranes in adolescent compared to adult pregnancy. Med Glas (Zenica) 2020; 17:136-40.
19. Peccatori FA , Azim HA Jr, Orecchia R, Hoekstra HJ, Pavlidis N, Kesic V, Pentheroudakis G; ESMO Guidelines Working Group. Cancer, pregnancy and fertility: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2013; 24:vi160-70.
20. Barton SE , Najita JS, Ginsburg ES, Leisenring WM, Stovall M, Weathers RE, Sklar CA, Robison LL, Diller L. Infertility, infertility treatment, and achievement of pregnancy in female survivors of childhood cancer: a report from the Childhood Cancer Survivor Study cohort. Lancet Oncol 2013; 14:873-81.