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Cancer During Pregnancy: A Review of 10 Years of Experience

[1]Ali Eishi, [2]Ezat Rahimi, [3]Setareh Akhavan, [3]Sholeh Shahgaibi and [3]Fariba Farhadifar
[1]Department of Internal Medicine, Faculty of Medicine,
Urmia University of Medical Sciences, Urmia, Iran
[2]Kurdistan Digestive Research Center, Faculty of Medicine,
Kurdistan University of Medical Sciences, Sanandaj, Iran
[3]Department of Gynecologic, Faculty of Medicine,
Kurdistan University of Medical Sciences, Sanandaj, Iran

Abstract: Cancer is the second most common cause of death among women who are in reproductive ages; however it is not common during pregnancy. There are few numbers of documents concerning cancer and its related treatment outcomes and prognosis during pregnancy. The aim of this study was to review our experience about gestational cancer. In this retrospective chart review study, 25 pregnant women with any kind of diagnosed malignancy who attended hospitals in Uremia and Sanandaj city since 10 years ago were assessed. Cancer cases were verified by a pathologist using pathology and TNM system for tumors staging. Then survival duration was analyzed using Kaplan-Maier plot. From all, 10 women had gynecologic cancers and 15 had non-gynecologic cancers. Ovarian cancer was the most common malignancy. The mean of survival was 67 months for all patients ($CI_{95\%}$: 23.7-110.3), 67 months for gynecologic cancer group ($CI_{95\%}$: 40.2-93.8) and 69 months for non-gynecologic cancer group ($CI_{95\%}$: 0-159) ($p = 0.51$). According to the results, the cancer complaints and symptoms must be examined thoroughly and do not take them as pregnancy complications since delays in prognosis leads to more severe problems and makes treatment difficult. If cancer is treated carefully after three months of gestation, probably it won't have severe side effects for fetus.

Key words: Cancer, pregnancy, outcomes, chemotherapy, fetus

INTRODUCTION

Cancer is the second most common cause of death among women who are in reproductive ages (Chatterjee, 2011; Safdar and Khan, 2003); however, it is not common during pregnancy. According to published articles its incidence is about 0.02-0.1% (Creasman, 2001; Weisz *et al*., 2001; Pentheroudakis and Pavlidis, 2006; Teran-Porcayo *et al*., 2007). There are two types of cancers during pregnancy: first, new malignant cases that are diagnosed during pregnancy; second, pregnancy of patients with diagnosed cancers (Donegan, 1983). Both cases are rare and lots of medical centers do not have much experience regarding these conditions (Williams and Bitran, 1985; Antonelli *et al*., 1996a).

It seems that because of industrialization and urbanization, pregnancies occur in older ages and increase of pregnancy age will continue in future as well and consequently we will expect more similar cases upcoming (Blackwell *et al*., 2000; Pavlidis, 2002; Teran-Porcayo *et al*., 2008). Diagnosis of cancer during pregnancy generates several questions about mother and fetus health and challenges the selected treatment method affecting fetus; as there is little experience regarding the subject it makes condition more complicated (Pentheroudakis and Pavlidis, 2006; Pentheroudakis, 2008). There is no evidence showing that pregnancy could increase the risk of cancer; causes of cancer during pregnancy are the same genetic and environmental factors which exist in non-pregnant people as well (Ward and Bristow, 2002; Gohar and Mohammadi, 2010).

Most of published articles are either case reports or case series; hence, there is little data about cancer and prognostic and treatment outcomes during pregnancy (Azim and Peccatori, 2010a). This study reviews the results of ten years of experience of dealing with pregnant women with cancer and it assesses and reviews the related findings.

MATERIALS AND METHODS

In this retrospective chart review study, pregnant women with any kind of diagnosed malignancy in Uremia and Sanandaj during 2000-2010 were evaluated. Required

Corresponding Author: Ezat Rahimi, Kurdistan Digestive Research Center, Faculty of Medicine,
Kurdistan University of Medical Sciences, Pasdaran Ave, Sanandaj, Iran Fax: +98-871-3227118

data was collected from gynecologic, surgical and oncology wards in hospitals located in both cities. Clinical conditions and prognosis features of patients were assessed and data about patients were carefully registered. In case of data deficiency, patients or their families were contacted. All patients were diagnosed during pregnancy or child delivery. Collected data included: patients demographic features, data about pregnancy and outcomes, cancer type, clinical stage of cancer, treatment and prognosis and patients final status.

Cancer diagnosis was based on pathology and tumors staging was based on TNM system and it was done by a pathologist. The data about pregnancy including gestational age, parity, gravidity and midwifery side effects was collected. Quantitative data was assessed via Man-Whitney U test. Also using SPSS 11.5 (SPSS Inc., Chicago, IL), Kaplan-Maier curve was used to determine survival duration. Then the Survival durations of two groups with gynecologic and non-gynecologic malignancies were compared and analyzed using Log-Rank test.

RESULTS

In this study 25 pregnant women (10 pregnant women with gynecologic and 15 with Non-gynecologic malignancy) were included. The median age of patients with gynecologic and non-gynecologic cancers and gestational age were 31.5 (21-39) years and 30 (18-39) years and 29 (11-38) weeks, respectively. There was no significant difference between two groups regarding patients age ($p = 0.43$) and gestational age ($p = 0.68$).

From all patients with gynecologic malignancy, six cases had ovarian cancer and two cases had endometrial cancer. A pregnant woman had two types of cancer simultaneously. One of patients had ovarian and endometrial adenocarcinoma cancers simultaneously. Another patient, who previously experienced breast cancer, was affected by endometrial adenocarcinoma. Eight infants (80%) were born alive and healthy. Table 1 presents the characteristics of patients who had cancer in their gynecologic organs during pregnancy and Table 2 shows the characteristics of patients with cancers in their other organs.

Table 1: Characteristic of pregnant women with gynecologic malignancy and their survival duration

Mother age (year)	Type of tumor	Stage	Gestational age (week)*	Pregnancy No.	Fetus outcome	Treatment	Follow up duration (month)	Final situation
23	Ovarian dysgerminoma	III[a]	20	1st	Alive	Surgery with cesarian	32	Dead
29	Ovarian germ cell	I[c]	16	1st	Abortion	Surgery	98	Alive
26	Ovarian germ cell	III[b]	38	1st	Alive	Surgery with cesarian	42	Dead
34	Papillary serous cyst carcinoma	III[b]	38	1st	Alive	Surgery with cesarian	53	Dead
21	Papillary serous cyst carcinoma	III[a]	13	1st	Alive	Surgery with cesarian	67	Dead
37	Mucinous cystadenoma	-	38	2nd	Alive	Surgery after delivery	32	Alive
28	Malignant teratoma	-	14	1st	Alive	Surgery for acute abdomen in 14 week	49	Alive
37	Endometrial adenocarcinoma**	II[b]	34	1st	Alive	Surgery with cesarian	85	Alive
39	Endometrial adenocarcinoma***	II	30	3rd	IUFD****	Surgery after delivery	21	Alive
39	Cervical cancer	CIN	32	2nd	Alive	Surgery after delivery	48	Alive

*Gestational age at diagnosis of malignant condition, **In association with ovarian endometrioid adenocarcinoma, ***History of breast cancer eight years ago, ****Intrauterine fetal death

Table 2: Characteristic of pregnant women with Non-gynecologic malignancy and their survival duration

Mother age (year)	Type of tumor	Stage	Gestational age (week)*	Pregnancy No.	Fetus outcome	Treatment	Follow up duration (month)	Final situation
21	Lung squamous cell carcinoma	IV	31	1st	IUFD**	Conservative treatment	1	Dead
18	Hodgkin's lymphoma	III	19	1st	Alive	Chemotherapy during pregnancy	86	Alive
22	Hodgkin's lymphoma	III	15	1st	Induced abortion	Chemotherapy after pregnancy	51	Alive
20	Burkitt lymphoma	-	33	1st	Alive	Chemotherapy	6	Dead
34	Malignant Neuroblastoma	III	29	3rd	Alive	Surgery and chemotherapy after delivery	113	Alive
27	Malignant Neuroblastoma of nasal cavity	II b	20	1st	Induced abortion	Surgery and chemotherapy	69	Alive
33	Liposarcoma of right thigh	IV	34	2nd	Alive	Surgery, radiotherapy, chemotherapy	2	Dead
35	Breast cancer	III a	29	2nd	Alive	Surgery, radiotherapy, chemotherapy after delivery	100	Dead
32	Breast cancer	III a	32	2nd	IUFD	Surgery after delivery	23	Dead
28	Astrocytoma	-	12	2nd	Induced abortion	Surgery after abortion	18	Alive
37	Glioblastoma multiform	-	35	3rd	Alive	Surgery after delivery	36	Alive
39	Recurrence of colon cancer***	III	38	4th	Alive	Surgery with cesarian	11	Dead
30	Gastric cancer****	II	11	2nd	Induced abortion	Surgery after abortion	89	Alive
36	Gastric cancer	IV	22	3rd	IUFD	Surgery for acute abdomen, diagnosis was gastric cancer	6	Dead
28	AML M3	-	38	2nd	Alive	Chemotherapy during pregnancy	4	Dead

*Gestational age at diagnosis of malignant condition, **Intrauterine fetal death, ***She had history of colon cancer and left sided colectomy 5 years before current pregnancy. She did not consult about the new condition with her doctor and did not take any medical care during pregnancy. Colon perforation and recurrence of tumor were observed in cesarian section, ****She was pregnant at that time

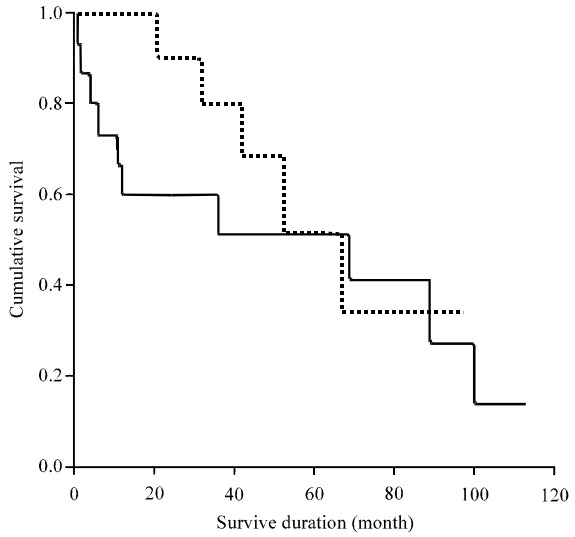

Fig. 1: Survival Kaplan-Maier plot for gynecology and non-gynecology malignancy

In non-gynecologic group, two cases of Hodgkin, two cases of neuroblastoma and two cases of gastric cancer were found. In this group, eight infants (63.3%) were delivered alive. The median of survival duration was 67 months in all patients ($CI_{95\%}$: 23.7-110.3), 67 months in gynecologic group ($CI_{95\%}$: 40.2-93.8) and 69 months in non-gynecologic cancer group ($CI_{95\%}$: 0-159) (Fig. 1). Using Log-Rank test, no significant statistical difference was found among two groups regarding survival duration ($p = 0.51$).

DISCUSSION

Based on the findings, the most common cancer during pregnancy was ovarian cancer. Hodgkin, breast cancer and endometrial ranked as the other most common types of cancer. The most common reported tumors during pregnancy include breast, cervix, leukemia and lymphoma tumors (Pavlidis, 2002; Pentheroudakis and Pavlidis, 2006; Teran-Porcayo *et al*., 2008). In another study, the most common tumors were cervix, breast and ovarian tumor (Teran-Porcayo *et al*., 2007). However, the results of this study were different. We found ovarian cancer more than any other type; maybe it is because of our patients' ages which were younger than most of other studies participants' or maybe it is the result of infrequency of other types of malignancy among our patients (Pentheroudakis and Pavlidis, 2006). Environmental and genetic conditions might be among factors that cause such a sort of difference.

Ovarian cancer is not among cancers that are common during pregnancy. Nevertheless, because of sonographic tests conducted to control the fetus, usually more cases of ovarian cysts are found; however, more than 98% are not malignant (Pentheroudakis and Pavlidis, 2006) and consequently this type of patients have long survival duration. Extreme hormonal changes during pregnancy might provide a good condition for forming ovarian cysts. Reviewing articles shows that 35% of malignant ovarian tumors are epithelial, 30% are interstitial and 35% are germ cells (Oehler *et al*., 2003; Alexander-Sefre *et al*., 2005; Latimer, 2007; Gilani *et al*., 2007).

Two different kinds of malignancy were observed in one of patients. She was a 37 years old who had been infertile for 16 years and she referred to the hospital because of vaginal bleeding in 34th week of gestation. After conducting sonographic tests and cesarian, both endometrial adenocarcinoma and ovarian adenocarcinoma were diagnosed. Such a phenomenon is rare and has never been reported anywhere (Reichert, 2005). Basically, synchronous presence of these two malignancies is not common even among non-pregnant women; till now there has been just few numbers of case studies or case reports talking about this type of patients (Fishman *et al*., 1995; Antonelli *et al*., 1996b; De la Fouchardiere *et al*., 2004; Lou *et al*., 2006; Signorelli *et al*., 2008).

Because of physiologic changes and enlargement of breasts, it is difficult to diagnose breast cancer during pregnancy. Although prognosis of breast cancer is good during early stages, during pregnancy it needs more attention to be diagnosed in progressed stages and its prognosis may become difficult (Lishner, 2003). Two patients died in this study.

One of other remarkable outcomes of this study was diagnosis of endometrial adenocarcinoma during pregnancy in a patient who had experienced breast cancer nine years ago. Two cancers took place in a patient non-simultaneously. Such a case has never been reported in a pregnant woman; there are just some studies reporting concurrent and non-concurrent occurrence of these two malignancies in non-pregnant women (Ichikawa *et al*., 1996; Fletcher *et al*., 2007).

One of patients was a 21 years old who had referred to physicians several times suffering from intense coughs. In every visit physicians prescribed common cold drugs and anti asthma medicines and after three months she was affected by hematuria. Sonographic tests reported two-sided renal tumors and hepatic metastasis and finally lung squamous cell carcinoma was diagnosed. Lung cancer during pregnancy is extremely rare and few cases of cancer during pregnancy have been reported globally. Most of reported cases include adenocarcinoma and carcinoma of small cells (Jackisch *et al*., 2003). Therefore,

the patient that we examined might be the first case of cancer of lung squamous cell carcinoma that has been reported yet. Prognosis of lung cancer during pregnancy is also very infrequent (Chung *et al*., 2005; Azim and Peccatori, 2010b).

One of the most common malignancies during pregnancy is lymphoma, though generally it is not prevalent (Pohlman and Macklis, 2000). Most experiments are about non-Hodgkin lymphoma and few Hodgkin cases are reported (Moore and Martin, 1992; Guven *et al*., 2005). Two Hodgkin cases had been found in our study and one of them started chemotherapy during pregnancy and another patient started it after pregnancy. Fetuses are not really in risk of Intra-uterus Fetal Death (IUFD) or pre-maturity (Lishner, 2003).

Previously, four cases of liposarcoma during pregnancy have had been reported (Matsuda *et al*., 2000; Tebes *et al*., 2001; Jeng *et al*., 2005). The patient who was assessed in this study found a mass around right thigh in the early time of pregnancy. After conducting biopsy lipoma was reported. Two moths later, the mass had grown up again and it had been diagnosed as lipoma again. For the third time, in the late period of pregnancy she referred again with grown up mass together with extensive lung metastasis and finally liposarcoma had been diagnosed. She died two months later after cesarean. A similar case with extensive metastasis was previously reported in 2007 which represent quick progress and bad prognosis of this malignancy during pregnancy (Rouskova *et al*., 2007).

Other malignancies are rarer. Malignant neuroblastoma among pregnant women is extremely rare. According to a report, a case of neuroblastoma was found in adrenal tumors of a 25 year old pregnant woman (Refaat *et al*., 2008). Two cases of neuroblastoma had been found in our study.

The median of survival duration for all patients and for gynecologic and non-gynecologic groups were 67, 67, 69, respectively which did not have significant statistical difference. Based on most of available conducted studies and case reports, prognosis of cancer during pregnancy is poor (Antonelli *et al*., 1996a; Pautier *et al*., 2004). In a study examining cancers during pregnancy in a ten year period, it was reported that about 34% of patients had survival duration of 74 months (Teran-Porcayo *et al*., 2008); this was about 40% in this study.

A limitation of this study was patients' unequal follow up periods; patients must be followed up for longer times. Newborns were not followed up for long periods to be assessed for likely side effects of treatment and it was another limitation of our study. However, like Peres *et al*. (2001) in this study none of newborns had malformation. Unfortunately there are few conducted studies covering this topic. In this study, some of patients whose cancers were diagnosed during first trimester had therapeutic abortions. However, it seems that medical treatments after the first trimester do not make risk for fetus (Weisz *et al*., 2001). Nonetheless, further multi-centered studies with bigger sample size are needed.

CONCLUSION

Based on the results, though malignant conditions are rare among pregnant women it is always essential to consider symptoms and complaints of pregnant women carefully and do not take them as pregnancy complications because delay in diagnosis of cancer leads to poor prognosis and makes treatment more difficult. It is likely that careful initiation of treatment after the first trimester doesn't generate severe side effects for fetus.

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