

Cancer with Pregnancy in a Cancer Hospital

Pariyar J,¹ Shrestha B,¹ Rauniyar BP,² Regmi SC,² Shrestha J,² Jha AK,³ Shrestha S³

¹Gynecologic Oncology Unit, ²Medical Oncology Department, ³Radiation Oncology Department, B.P. Koirala Memorial Cancer Hospital, Chitwan, Nepal.

ABSTRACT

Background: Cancer during pregnancy is rare, occurring one in every 1,000 pregnancies. Cancer itself rarely harms the baby and some cancer treatments are safe during pregnancy. However, treatment dilemmas often occur.

Methods: Descriptive study was conducted at B. P. Koirala memorial cancer hospital. Case records of women with cancer and pregnancy from January 2001 to February 2012 were analyzed regarding their clinical details, treatment, follow-up and feto-maternal outcome.

Results: Nineteen women, of 17 to 40 years had cancer with pregnancy. Observed cancers with pregnancy were: leukemia (4), head and neck (3), ovary (3), cervix (2), rectum (2), breast (1), Non-Hodgkin's lymphoma (1), osteosarcoma (1), spinal cord (1) and vulva (1). Seven women (36%) presented in the second trimester and six women (32%) presented in the first and third trimester each. Seven (36%) women opted for termination of pregnancy for definitive treatment, five (26%) deferred treatment until delivery. Among the seven (36%) that accepted definitive treatment along with pregnancy, fetal demise occurred in three and delivery of healthy baby occurred in four. Nine babies born to mothers with cancer during pregnancy till date have normal growth and development. Total 10 (52%) of the mothers are in remission, six (32%) have died from disease.

Conclusions: Cancers during pregnancy, more common in younger women, posed treatment challenges. Definitive cancer treatment could have greater fetal risk during the first trimester but could be offered with more acceptable risk in the second and third trimesters.

Keywords: cancer; chemotherapy; pregnancy; radiotherapy.

INTRODUCTION

Cancer during pregnancy is rare, but does occur in approximately one out of every 1,000 pregnancies.¹ The most common malignancies diagnosed during pregnancy are gynaecological (mainly uterine or cervical and less frequently ovarian), breast, haematological (leukaemia and lymphoma), and skin (melanoma) cancers.²

Diagnosis of cancer during pregnancy creates a difficult situation to the patient, her family and the treating

medical team due to the concerns of the patient's health and that of the baby. It is known that executing treatment in the form of surgery, chemotherapy or radiation therapy raises the chances of birth defects or even fetal demise.³ Whereas, postponing the treatment, on the other hand, could allow the cancer to spread. True oncological emergencies in pregnant patients are rare (except for leukaemia), and time is required to deliberate and to draw up a personalized treatment

Correspondence: Dr. Jitendra Pariyar, Gynecologic Oncology Unit, B.P. Koirala Memorial Cancer Hospital, Chitwan, Nepal. Email: jpariyar@yahoo.com, Phone: 9855060371.

plan.³ Unnecessary or premature termination of pregnancy should be avoided. The main goal is to offer pregnant patients the same optimum management as non-pregnant patients. Overall survival and recurrence-free survival rates are well documented for most cancers, and survival is not worsened by pregnancy for many of them.⁴

Cancer concurrent with pregnancy has long had ominous implications due to lack of major patient cohorts and large randomized trials.⁵ Inadequate clinical experience in managing a cancer during pregnancy poses a big challenge for the treating physician. Cancer itself rarely harms the baby, and some cancer treatments are safe during pregnancy.⁴ However, the pregnant woman and the treating doctor often face several dilemmas on how to proceed ahead. We report our cases of cancer with pregnancy managed at B. P. Koirala memorial cancer hospital.

METHODS

A descriptive study was conducted in B.P. Koirala memorial cancer hospital. Case records of women with cancer and pregnancy attending the hospital from January 2001 to February 2012 were analyzed regarding their illness history, clinical examination, investigations, treatment and follow-up. Institutional delivery of the women with pregnancy was advised and occurred in medical college teaching hospital or government hospital. Pregnancy outcome was obtained on follow up

visit or through telephone conversation. Patients were followed up with clinical, tumor marker, and radiologic assessments. Follow-up information was recorded up to the date of last contact or death keeping in mind the fetal and maternal outcome. Complete response or cure was defined as complete resolution of all clinically and radiologically measurable diseases. All delivered babies were recommended to be assessed in immunization and pediatrics clinics regarding their growth and development.

RESULTS

Nineteen women had cancer during pregnancy. The age of the patients ranged from 17 to 40 years (with a mean age of: 24.2 years). Types of cancer with pregnancy were: leukemia (4), cervical cancer (2), rectum (2), ovary (3), head and neck (3), breast (1), Non-Hodgkin's lymphoma (1), osteosarcoma (1), spinal cord (1) and vulva (1). Six women (32%) presented in the first trimester, seven (36%) presented in the second trimester and six other (32%) presented in the third trimester (Table 1).

Seven (36%) women opted for immediate termination of pregnancy for definitive treatment among which (57% 4/7 were diagnosed to have cancer in the first trimester. The pregnancy was terminated by manual vacuum aspiration. Two primigravida with ovarian cancer in early pregnancy, desired to continue the pregnancy and the pregnancy outcome was good.

Table 1. Characteristics of patients with cancer during pregnancy (n=19)

First Trimester (n=6)	Age in years	Parity	Cancer Type	Gestation at diagnosis
	20	G2P1+0	CML	8 wks
	20	G2P1+0	CML-CP	9 wks
	40	G3P2+0	Breast- Infiltrating ductal carcinoma	9 wks
	20	G1P0	Ovary-Yolk Sac Tumour, IC	12 wks
	22	G1P0	Ovary-Dysgerminoma, IC	8 wks
	32	G4P3+0	Cervix-Adenocarcinoma, IIIB	9 wks
Second Trimester (n=7)	21	G2P1+0	CML-CP	22+2 wks
	21	G3P2+0	Parotid	24 wks
	30	G2P1+0	Thyroid- Papillary carcinoma	16 wks
	19	G1P0	NHL of Breast	26 wks
	17	G1P0	Rectum-Adenocarcinoma	24 wks
	24	G1P0	Ovary-Adenocarcinoma, IIIC	18 wks
	20	G1P0	Vulva-Squamous cell carcinoma, III	20 wks
Third Trimester (n=6)	22	G2P1+0	Rectum	29 wks
	21	G1P0	Osteosarcoma-femur	28+2 wks
	25	G3P1+1	AML-M2	32+2 wks
	30	G6P5+0	Maxilla	30 wks
	30	G3P2+0	Cervix-Adenocarcinoma, IIB	32 wks
	27	G2P1+0	Spine	34 wks

wks = weeks

Five (26%) women deferred treatment until delivery. Total (80% 4/5) of these women presented in the third trimester of pregnancy. A primigravida with rectal cancer diagnosed at 24 weeks delaying treatment till caesarean delivery at 34 weeks died of progressive disease even after the commencing definitive radiation therapy. The premature baby died as well. The other four women had spontaneous vaginal delivery with good fetal outcome and their definitive treatment was delivered in the postnatal period. There was no change in the stage of cancer in these women even with some weeks of delay in treatment.

Seven (36%) women accepted definitive treatment even with pregnancy among which fetal demise occurred in three and delivery of healthy baby occurred in four. A woman with leukaemia (CML) on chronic phase on Gleevec therapy, delivered through caesarean section at 34 weeks for severe oligohydramnios. At five months of age, the baby has caught up with normal growth and development pattern. Another woman with AML-M2 diagnosed at 32+2 weeks of pregnancy

undergoing induction chemotherapy left treatment against medical advice. She had IUFD at 34 weeks, and died due to severe post-partum haemorrhage. A woman with cervical adenocarcinoma, stage IIIB diagnosed at 9 weeks underwent radiation therapy and had abortion after receiving 20 fractions of external beam radiotherapy. A woman with yolk sac tumour diagnosed at 12 weeks of pregnancy underwent right sided salpingo-oophorectomy with omental biopsy followed by adjuvant chemotherapy (Cisplatin+Etoposide). Another woman with epithelial ovarian cancer, stage IIIC, diagnosed at 18 weeks of pregnancy underwent staging laparotomy. She died while on adjuvant chemotherapy. Two cases underwent radical surgery of maxilla and spine with no adverse effect to the pregnancy. Both of the cases had spontaneous vaginal delivery later on. A case of NHL of breast treated with chemotherapy during pregnancy was on remission and her baby is also doing well till now.

The delivered babies had normal growth and development. Ten (52%) of the mothers were in remission, six (32%) had died from the disease (Table 2).

Table 2. The treatment modality and fetal and maternal outcomes (n=19)

Maternal Status	Cancer Type	Gestation at diagnosis	Definitive Treatment	Fetal Outcome
In Remission (n=10)	CML	8 wks	Gleevac (Imatinib)	Induced Abortion
	CML-CP	9 wks	Gleevac (Imatinib)	Induced Abortion
	CML-CP	22+2 wks	Gleevac (Imatinib)	1900 gm, male, by LSCS
	Parotid	24 wks	Surgery + Radiotherapy	Induced Abortion
	Thyroid	16 wks	Surgery	3300gm, male, by VD
	Maxilla	30 wks	Surgery	Healthy baby, by VD
	NHL of Breast	26 wks	Chemotherapy	Healthy baby, by VD
Living with disease (n=3)	Ovary	12 wks	Surgery+ Chemotherapy	Normal progression of pregnancy
	Ovary	8 wks	Chemotherapy	3000 gm, male, by LSCS
	Spine	34 wks	Surgery	Healthy baby, by VD
	Rectum	29 wks	Surgery (APR)	1100gm, died after birth
	Cervix	9 wks	Radiation Therapy + Hysterectomy	Abortion
Dead (n=6)	Vulva	20 wks	Surgery	Healthy baby by VD
	Osteosarcoma	28+2 wks	Supportive care	700 gm, died after birth
	AML-M2	32+2 wks	Induction Chemotherapy	IUFD
	Breast	9 wks	Surgery+Chemotherapy+ Radiation Therapy	Induced Abortion
	Cervix	32 wks	Radiation therapy with concurrent chemotherapy	2500 gm, male, by LSCS at 34 wks
	Rectum	24 wks	Radiation Therapy	LSCS at 34 wks, NND
	Ovary	18 wks	Surgery- Staging lap.	Abortion

LSCS = lower segment caesarean section, NND = neonatal death, VD = vaginal delivery, wks = weeks,

DISCUSSION

Cancer co-existing during pregnancy is rare. Hospital record shows that only 19 among 9545 women attending the hospital from January 2001 to February 2012 had cancer with pregnancy yielding the hospital incidence of 1.9 per 1000 women with cancer. Our center being the referral cancer center without obstetrical services, incidence of pregnant ladies with cancer could not be estimated. The incidence of pregnancy-associated cancer reported are 1 per 1000 deliveries or ranging from 0.02% to 0.1%.^{1,6}

The cancers that tend to occur during pregnancy are those that are more common in younger people, such as cervical cancer, breast cancer, thyroid cancer, leukemia, Hodgkin's lymphoma, and melanoma.² Similar observation was made in the present study. Pregnancy with breast cancer was noted less often than pregnancy with gynaecological cancers which may be due to the fact that in Nepal, cervical cancer is more common than breast cancer.⁷ The most common gynaecological cancers diagnosed during pregnancy are of cervical and ovarian origin⁷ and this coincided with findings of the present study.

Diagnosis of cancer during pregnancy creates a difficult situation to the patient, her family and the treating medical team due to the concerns of the patient's health and that of the baby. Situation is more exaggerated when the woman is in the first trimester of pregnancy when treatment could lead to higher rate of abortion or development of congenital malformation in the baby. Among the six women (32%) that presented in the first trimester, five women wanted immediate termination of pregnancy for fear of worsening their disease state and also giving birth to baby with birth defects. A primigravida with dysgerminoma of ovary, stage IC, continued pregnancy till term. The delivered child is healthy at five years of age.

Generally, in cancer with pregnancy, the cancer is managed as though the patient is not pregnant. For the various site-specific cancers, surgery is the main modality of treatment; this should be individualized.⁹ Surgery could safely be undertaken during second and third trimester. In our study, three pregnant women with cancer of maxilla, germ cell ovarian cancer and cancer of spinal cord underwent optimal surgery without any adverse effect to pregnancy. Hysterectomy during pregnancy is rarely indicated, unless it contributes significantly to tumor debulking.¹⁰ In our series, a woman underwent hysterectomy during pregnancy for optimal debulking of epithelial ovarian cancer.

Chemotherapeutic agents are potent teratogens and the fetus is most vulnerable to drug-related teratogenicity

during organogenesis.¹¹ However, some organs including the eyes, genitalia, and haemopoietic and nervous systems, are still vulnerable after the first trimester.¹² If the mother's condition necessitates immediate therapy, termination of pregnancy is strongly recommended. Exposure to chemotherapy in the second and third trimesters is less likely to result in teratogenic effects, although it increases the risk of intrauterine growth restriction.¹³ In our study, only one woman with chronic myeloid leukaemia on oral chemotherapy (Imatinib) throughout pregnancy had caesarean delivery at 34 weeks for severe oligohydramnios. The baby, now at five months, has normal growth and development. However, in another study, 12 infants exposed to imatinib during the first trimester had congenital abnormalities, especially of the kidneys, skeleton, heart, brain, and gut (eg, exomphalos).¹⁴ Among the four pregnant women who underwent chemotherapy from second trimester onwards, the one with AML-M2 on induction chemotherapy had intrauterine fetal death at 32 weeks of pregnancy. Non-Hodgkin's Lymphoma on CHOP Regimen, CML on Gleevec and yolk sac tumour on platinum and etoposide chemotherapy had uneventful pregnancy and their babies on follow up were normal.

When cancer is diagnosed during pregnancy and treatment cannot be delayed until delivery, there are concerns as to whether radiotherapy can be given safely.¹⁵ The expected radiation effects are lethality, malformations, mental retardation, and cancer induction.¹⁶ Some clinicians recommend termination of pregnancy when doses higher than 0.05 - 0.10 Gy are to be received by the fetus.^{17,18} In our study, we had had a woman with Adenocarcinoma of cervix stage IIIB diagnosed at 9 weeks of pregnancy. Obtaining the informed consent from the patient, definitive radiation therapy with fetus in utero was delivered. After 20 fractions of external beam radiation therapy, she had abortion.

A primigravida with rectal cancer diagnosed at 24 weeks delayed radiation therapy till caesarean delivery at 34 weeks. She died due to progressive disease even after the commencing definitive radiation therapy. The premature baby also died.

The prognosis for a pregnant woman with cancer is often the same, compared with other women of the same age with the same type and stage of cancer. Pregnancy rarely affects the behavior of some cancers.¹⁹ In the present study, four pregnant women with cancer, diagnosed second and third trimester of pregnancy opted to defer definitive treatment until delivery. There was no change in the stage of cancer in these women even with some weeks of delay in treatment.

CONCLUSIONS

Cancers during pregnancy are rare and are more common in younger women. The treatment of malignancy during pregnancy is challenging and needs to be individualized. In most instances the cancer is treated as though the patient is not pregnant. Therapy, whether by surgery, radiation therapy or with cytotoxic drugs, could have greater fetal risk during the first trimester but could be offered with more acceptable risk in the second and third trimesters.

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