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FROM SURVIVAL TO MOTHERHOOD: PREGNANCY OUTCOMES AFTER TREATMENT FOR MALIGNANCY

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ABSTRACT

Introduction: Around 2 million women of reproductive age are diagnosed with cancer annually. With improved survival and advances in fertility preservation, pregnancies following malignancy treatment are increasing. These pregnancies present unique challenges due to potential effects of prior chemotherapy, radiotherapy and surgery on reproductive and obstetric outcomes. Indian data on such pregnancies is limited. Evaluating maternal and neonatal outcomes in cancer survivors can guide counselling and management. **Objectives:** To evaluate clinical profile, management strategies and maternal and neonatal outcomes in pregnancies following malignancy treatment. **Methodology:** A prospective observational study was conducted at a teaching institution over a period of 46 months. Eight pregnancies following malignancy treatment were analyzed. Data on age at diagnosis, type and treatment of malignancy, age at conception, mode of delivery, obstetric and neonatal outcomes were recorded. **Results:** Prevalence of pregnant women with history of malignancy treatment was about 2.6 per 10,000 (0.026 percent) pregnancies. Mean age at cancer diagnosis was 20.3 years. Five patients (62.5%) had history of germ cell tumours; one each had history of adenocarcinoma colon, gestational trophoblastic neoplasia and epithelial ovarian tumor. The mean interval between diagnosis and conception was 5.8 years. Three patients (37.5%) had preterm delivery, five (62.5%) underwent cesarean section, and one had oncologic complication with ICU admission. **Conclusion:** Maternal outcomes in pregnancies following treatment of malignancy are largely reassuring. However, these pregnancies are associated with increased number of preterm births, low birth weight babies and NICU admissions. Adequate interval between malignancy treatment and pregnancy is associated with better outcomes.

KEYWORDS: Cancer survivorship, Pregnancy after cancer, Maternal outcomes, Cancer survivors

INTRODUCTION

Every year, approximately two million women of reproductive age (15-49 years) are diagnosed with cancer in the world.[1] Nearly one third of these malignancies are breast cancer, followed by thyroid and cervical cancers.[2] Advances in oncology have led to substantial improvements in survival; however, longterm survivors may experience treatment related adverse effects that impact their quality of life. One of the most significant concerns in young women is the effect of cancer therapy on fertility.

Anticancer treatments such as chemotherapy, radiotherapy and extensive surgeries can result in premature ovarian insufficiency and subsequent infertility.[3] Nevertheless, with the advent of fertility preserving treatment options, less gonadotoxic chemotherapy regimens and improved surgical techniques, an increasing number of cancer survivors are able to conceive and successfully complete pregnancy.[4]

Pregnancy following treatment for malignancy presents a unique clinical challenge for both the mother and the fetus, due to the potential longterm sequelae of prior

therapy. Maternal complications may include cardiotoxicity following anthracycline exposure, endocrine dysfunction associated with alkylating agents, renal impairment secondary to cisplatin, hepatic dysfunction and an increased risk of venous thromboembolism.[2] These women may therefore require targeted surveillance including nutritional status, venous thromboembolism and preeclampsia risk evaluation and mental health assessment in addition to routine antenatal care.[2] Despite the existing concerns, the limited available evidence is largely reassuring regarding maternal and fetal outcomes.

Garg et al., in a population based study from Utah, reported a 25% reduction in live birth rates among cancer survivors compared with controls, along with a significantly higher incidence of preterm birth and low birth weight, therefore highlighting the potential impact of prior malignancy and its treatment on pregnancy outcomes.[5]

Another important consideration is the effect of pregnancy on the risk of cancer recurrence. While concerns regarding recurrence persist, some studies suggest a possible protective effect, hypothesized to be mediated through enhanced maternal immune surveillance against malignant cells during pregnancy stated as the "fetal antigen hypothesis."[3]

In this context, the present study was conducted to evaluate maternal and perinatal outcomes of pregnancies occurring after treatment for malignancy, hence contributing to the limited but growing evidence in this important area.

OBJECTIVES

- To evaluate clinical profile and management strategies for pregnancy following treatment of malignancy
- To evaluate maternal and neonatal outcome in pregnancy following treatment for malignancy

METHODOLOGY

This was a prospective observational study conducted in Department of Maulana Azad Medical College and Lok Nayak Hospital over a period of 46 months (January 2022 to October 2025). Antenatal women delivering at Lok Nayak hospital with past history of treated malignancy were included in this study and past records of malignancy were reviewed (Figure 1). Maternal and neonatal outcomes were recorded.

Exclusion criteria

1) Patients in whom malignancy was diagnosed first time during pregnancy.
2) Patients in whom the previous history of malignancy could not be reliably established.

Sample size: 8 patients

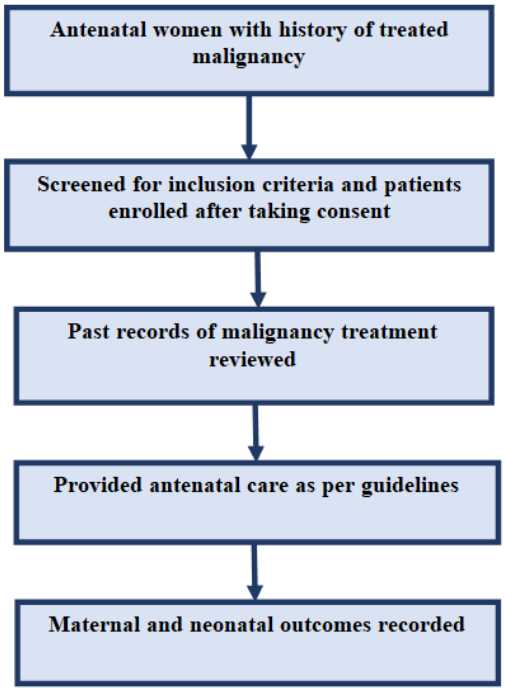

Figure 1: Flow diagram of methodology of study.

OBSERVATION AND RESULTS

Incidence of prior history of malignancy was found in 2.6 patients per 10,000 in women who delivered at Lok Nayak Hospital in the study period. Median age at diagnosis of malignancy was 20.5 years. Table 1 describes parameters like age at delivery, interval from diagnosis of malignancy to conception and parity of patient at conception. In this study, 7 patients (87.5%) had history of gynecological cancers.

Table 1: Different parameters of antenatal women with prior malignancy treatment.

PARAMETER	NUMBER OF PATIENTS	PERCENTAGE
AGE AT DIAGNOSIS OF MALIGNANCY		
≤ 16 YEARS	3	37.5%
16-20 YEARS	1	12.5%
20-24 YEARS	2	25.0%
≥24 YEARS	2	25.0%
AGE AT DELIVERY		
≤22 YEARS	1	12.5%
22-24 YEARS	1	12.5%
24-26 YEARS	1	12.5%
26-28 YEARS	2	25.0%
28-30 YEARS	3	37.5%
INTERVAL DURATION FROM DIAGNOSIS OF MALIGNANCY TO PREGNANCY		
<5 YEARS	5	62.5%
>5 YEARS	3	37.5%
TYPE OF TREATMENT RECEIVED FOR MALIGNANCY		
SURGERY+ ADJUVANT CHEMO	7	87.5%
CHEMOTHERAPY	1	12.5%
OTHER		
PARITY		
NULLIPAROUS	5	62.5%
P1	2	25.0%
>P2	1	12.5%
ASSOCIATED PREGNANCY COMPLICATION		
HTN/PREECLAMPSIA	1	12.5%
GDM	1	12.5%
ANEMIA	3	37.5%
SURGERY DURING PREGNANCY/PUERPERIUM	1	12.5%

The distribution of type of cancer treated before pregnancy is shown in the figure 2.

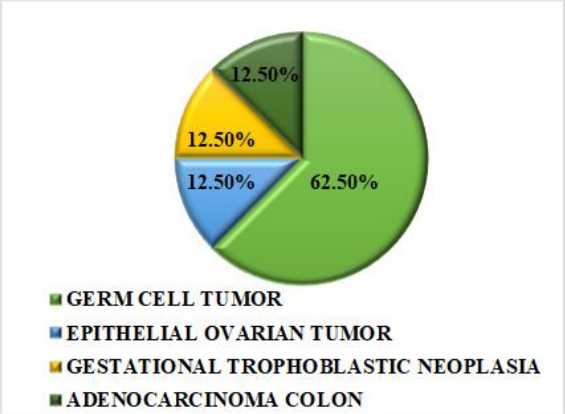

Figure 2: Type of cancer at diagnosis.

Seven patients enrolled in this study required primary surgical staging laparotomy with adjuvant chemotherapy while suction and evacuation was done for 1 patient of Gestational Trophoblastic Neoplasia (GTN) followed by chemotherapy. Surgical interventions included ovariotomy in 3 patients (37.5%), unilateral salpingo-oophorectomy (USO) in 3 patients (37.5%) and hemicolectomy in 1 (12.5%) patient.

Chemotherapeutic agents received by patients were bleomycin, etoposide and cisplatin (BEP) regimen in 5 germ cell malignancy patients (62.5%), 5 Fluorouracil and oxaliplatin (FOLFOX) based regimen in 1 adenocarcinoma colon patient, carboplatin and paclitaxel regimen in 1 epithelial ovarian malignancy patient and Etoposide, Methotrexate, Actinomycin, Cyclophosphamide, Oncovin (EMACO) regimen in 1 GTN patient.

During pregnancy 3 patients developed anemia and required blood transfusion, 1 each had gestational hypertension/preeclampsia and Gestational Diabetes Mellitus (GDM). One patient had deranged liver function test, while no patients had echo changes in liver or kidney disease.

One patient had recurrence of malignancy during pregnancy and required termination of pregnancy in late preterm period for further treatment of malignancy.

Among the study participants, 5 patients (62.5%) delivered by cesarean section while 3 patients (37.5%) delivered by vaginal delivery. Out of 3 study participants delivered vaginally one patient who delivered at term had recurrent ovarian tumor which was operated during postpartum period. She underwent staging laparotomy and ovarian USO for germ cell malignant tumor at the

age of 12 years and received 6 cycles of BEP chemotherapy at this hospital managed by gynecologic oncology unit team. At age of 17 she developed a borderline epithelial tumor on other side and exploratory laparotomy with incomplete resection of tumor was done at this hospital [by other non-gynecologic oncology unit team]. At 25 years of age she again reported to us at gynecologic oncology clinic with a large ovarian tumor [the residual tumor which was operated at age of 17]. All epithelial and germ cell ovarian tumor markers were within normal limit hence she [along with her parents] was counseled properly and advised for early marriage and spontaneous conception so that she can have at least one child as there is risk of remaining ovariotomy and its consequences in 3rd laparotomy. She got married, conceived spontaneously and presented at the age of 28 years with 20 x 15 cm size ovarian tumor which had increased in size during pregnancy. She had uneventful antenatal period and was admitted at 36 weeks of gestation for safe confinement. She had premature rupture of membrane and went into spontaneous labor at 37-38 weeks gestation and delivered vaginally with a healthy term baby. In the postpartum period she developed abdominal pain on and off and her all tumor marker and preoperative investigations repeated and exploratory laparotomy done on 30th day postpartum and repeat ovarian cystectomy of tumor size 20 x 15cm [figure 3] of one side and the other side remnant ovary [for which prior USO done] had 4 x 5 cm dermoid cyst for which cystectomy was done. Histopathology report confirmed benign mucinous cystadenoma of the large tumor and the smaller one as dermoid cyst. Postoperative period was uneventful for this patient.

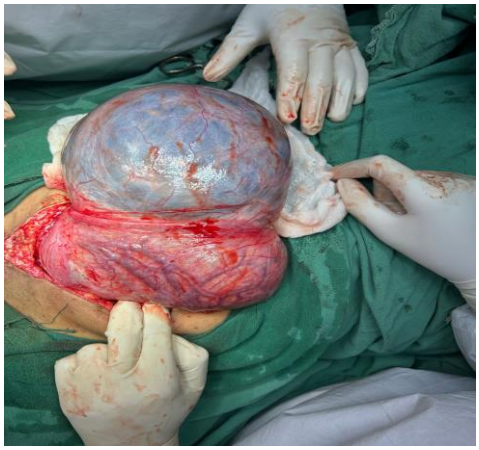

Figure 3: Postpartum laparotomy finding for recurrent ovarian tumor 16 year after surgery for germ cell malignancy with 20 x15 cm epithelial ovarian tumor.

Out of the 5 patients who underwent cesarean section delivery, 4 patients (80%) had obstetric indications (fetal distress in 2, scar tenderness in 1, previous 3 cesarean section in 1) and for one patient cesarean was done for early treatment of malignancy. Infracolic omentectomy was done along with cesarean section for one patient and one patient required classical cesarean section with diversion loop colostomy in view of recurrence of malignancy with metastasis.

About 50% babies had low birth weight, 1 had gross congenital anomaly (dextrocardia) at birth and 3 (37.5%) babies required Neonatal Intensive Care Unit (NICU) admission. Table 2 describes birth weight and gestational age of babies at delivery with mothers who had previous history of malignancy in study population.

Table 2: Neonatal parameters of mothers who had previous history of malignancy.

BIRTH WEIGHT	NUMBER OF BABIES	PERCENTAGE
1500-2000 grams	1	12.5%
2000-2500 grams	3	37.5%
2500-3000 grams	2	50%
3000-3500 grams	2	50%
GESTATIONAL AGE AT DELIVERY		
TERM (≥ 37 weeks)	5	62.5%
EARLY PRETERM (<34 weeks)	1	12.5%
LATE PRETERM (34-37 weeks)	2	25%

The number of term deliveries, number of cesarean sections and birth weight of babies was evaluated against interval from diagnosis and results are shown in Table 3.

Table 3: Association of Fetal outcome distribution in patients with duration of interval between malignancy diagnosis and pregnancy.

	INTERVAL <5 YEARS (n=5)	INTERVAL ≥5 YEARS (n=3)
TERM DELIVERIES	40%	100%
MEAN BIRTH WEIGHT	2.3 Kg	3.1 Kg
CESAREAN SECTION	60%	66%

DISCUSSION

With the rising age at first pregnancy and the increasing incidence of young onset cancers, many women are now diagnosed with malignancy before completing their childbearing plans.[6] Concurrent advances in oncology, fertility preserving strategies and survivorship care have resulted in a growing number of women conceiving after cancer treatment. In the present study, the incidence of pregnancy after malignancy was 2.6 per 10,000 pregnancies.

The median age at diagnosis of malignancy in our cohort was 20.5 years, which is notably younger than that reported in other studies 31-34.2 years in the study by Arecco et al. among breast cancer survivors and a mean age of 28.3 years in the study by Cao et al. involving colorectal cancer survivors.[3,7] This younger age at diagnosis in our population may reflect regional demographic patterns and earlier exposure to risk factors.

The median interval between cancer diagnosis and subsequent pregnancy in the present study was three years, compared with 6.3 years reported by Arecco et al.[3] Current FIGO guidelines recommend a minimum interval of 1-2 years between completion of cancer treatment and conception, as this period corresponds to the highest risk of cancer recurrence.[2] In the present study cohort, four patients (50%) conceived within two years of diagnosis and one of these experienced disease recurrence with metastasis, necessitating extensive treatment and resulting in further complications. Importantly, no recurrences were observed among patients with an interval greater than two years, underscoring the relevance of adherence to the recommended waiting period.

Except for the patient who developed recurrence, maternal outcomes in the remaining patients were largely reassuring. Anemia was observed in 37.5% of patients, while gestational hypertension and gestational diabetes mellitus were each seen in 12.5% of cases which is comparable to the general antenatal population in India.[8-10] These findings suggest that a prior history of malignancy does not necessarily translate into worse maternal outcomes, a conclusion that aligns with observations from studies by Tamauchi et al. Arecco et al., and Cao et al.[3,4,7] Such results have also led to the "healthy mother effect" hypothesis, which states that only women who feel healthy conceive and give birth and those with poorer prognosis do not try to conceive.[3] The POSITIVE trial, which evaluated temporary interruption of adjuvant endocrine therapy to allow pregnancy in breast cancer survivors also demonstrated reassuring maternal outcomes and recurrence rates.[11]

Higher cesarean section rate (60%) was observed among cancer survivors in the present study compared with the overall cesarean rate at our institution. This finding is consistent with the results reported by Cao et al. In contrast an Indian study by Kumari M et al. involving women with a history of non gynecological, non hematological malignancies reported vaginal delivery in all 13 cases.[12] The increased cesarean rate observed in some studies may reflect physician caution, perceived obstetric risk, or institutional practice patterns. FIGO has also acknowledged a possible increased likelihood of cesarean delivery in cancer survivors.[2]

Regarding neonatal outcomes, 37.5% of infants in our study were born preterm and 50% had low birth weight. These findings are in agreement with the study by Garg et al. and FIGO which states that the risk of fetal growth restriction in cancer survivors may be as high as 50%.[2,5] This study also noted 37.5% NICU admission in babies born to mother with previous history of cancer. Study conducted by Jin et al in South Korea also noted significantly increased rates of low birth weight babies, preterm deliveries and NICU admissions.[13] Fetal outcomes appeared to improve with longer intervals between malignancy treatment and pregnancy. As shown in Table 3, women with an interval of more than five years had 100% term deliveries with a mean birth weight of 3.1 kg, compared with only 40% term deliveries and a mean birth weight of 2.3 kg among those with an interval of less than five years.

Data from India on pregnancy outcomes following malignancy remain limited, likely due to the absence of robust population based cancer registries and challenges in long term follow up. Larger multicentric studies with extended follow up are required to better understand maternal and fetal outcomes in this growing population. None of the patients in the present study had received radiotherapy, precluding assessment of its impact on pregnancy outcomes an important limitation that warrants further investigation.

CONCLUSION

Pregnancy following treatment for malignancy is becoming increasingly common with improving cancer survival and wider availability of fertility preserving strategies. Findings from this prospective observational study suggest that outcomes of pregnancy after malignancy are largely reassuring, provided proper interval between malignancy treatment and pregnancy and appropriate antenatal surveillance are ensured.

However, pregnancy after treatment for malignancy is associated with higher rates of preterm birth, low birth weight, and NICU admission, particularly among women who conceived within a shorter interval after cancer treatment. A longer interval between malignancy treatment and conception was associated with improved fetal outcomes.

The observed higher cesarean section rate highlights the need for individualized obstetric decision making, balancing oncological history with obstetric indications rather than default surgical intervention. This study underscores the importance of multidisciplinary care,

involving obstetricians, gynaecologic oncologists and neonatologists in optimizing outcomes for both mother and fetus.

Given the paucity of Indian data on pregnancy outcomes after malignancy, larger multicentric studies with longterm follow up are required to strengthen the evidence base and for formulating regional guidelines.

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