JPESON
Journal of Perinatal Society of Nepal

PROF DSM FIRST PRIZE AWARDED PAPER IN PESCON 2022

Cancer with Pregnancy: Obstetric and Perinatal Outcome

Poonam Lama[1], Pabitra Maharjan[1], Simit Sapkota[2], Subhas Pandit[2], Sameer Neupane[3], Srijana Koirala[3], Rabindra Desar[4], Jitendra Pariyar[1]

[1]Department of Gynecologic Oncology, Civil Service Hospital, Minbhawan, Kathmandu Nepal.
[2]Department of Clinical Oncology, Civil Service Hospital, Minbhawan, Kathmandu Nepal.
[3]Department of Pathology, Civil Service Hospital, Minbhawan, Kathmandu Nepal.
[4]Department of Radiology, Civil Service Hospital, Minbhawan, Kathmandu Nepal.

ISSN: 2976-1050 (Online)
ISSN : 2976-1042 (Print)

Received : 22 Mar, 2023
Accepted : 35 Apr, 2023

Online Access

DOI: 10.59881/jpeson13

Funding Source : None

Conflict of Interest : None

Corresponding Author

Prof Dr. Jitendra Pariyar,
Gynecologic Oncology Unit,
Civil Service Hospital, Kathmandu,
Nepal.

Email: jipariyar@yahoomail.com

ABSTRACT

Background: Cancer occurring one in every 1,000 pregnancies is rare and poses immense challenges in the management. Decision making should involve multidisciplinary approach, always considering detailed perspective into account.

Objectives: The objective of this study is to find obstetrical and neonatal outcomes in pregnancies complicated by cancer.

Methods: A descriptive study was done in women with cancer in pregnancy attending Civil Service Hospital of Nepal from January 2015 to June 2022. Clinical data were collected from hospital registry of past six years and telephonic inquiry followed by in-person interview and thorough relevant investigations regarding their present status in terms of maternal and neonatal wellbeing.

Results: Ten women had cancer with pregnancy. The age of the women ranged from 19 to 35 years (mean age: 28.6 years). Two (20 %) women presented in first trimester, six (60%) in second trimester and two (20%) in third trimester. The types of cancers were leukemia (n=6), non-Hodgkin's lymphoma - NHL (n=2), breast cancer (n=1), thyroid carcinoma (n=1). Four (40%) women terminated the pregnancy before 18 weeks {leukemia: 3[CML (2); CLL (1)] and NHL of breast (1)} followed by Chemotherapy. Of the rest six, delivery occurred in four [vaginal (1) rest Cesarean section (3)]/ [term (1) rest preterm (3)], all the four babies thriving with normal growth and development. Except for thyroid carcinoma, all nine cases received chemotherapy but none underwent surgery or received radiotherapy during pregnancy. Except for two defaulted women with leukemia, lost to follow up, eight women are currently in remission, with ongoing pregnancy:2/6 [Acute promyelocytic leukemia (APML) formerly admitted for postpartum haemorrhage (PPH) 1; a case of chronic myeloid leukaemia (CML)-1].

Conclusions: Cancer management during pregnancy is challenging, yet can be promising with a multidisciplinary team of specialists providing adequate therapy, balancing the potential risks and benefits to mother and unborn fetus.

Keywords: *Cancer, chemotherapy, perinatal outcome, pregnancy, radiotherapy, surgery*

INTRODUCTION

Cancer is the second most common cause of death during reproductive years and complicates between 0.02 and 0.1% of all pregnancies.[1] This incidence is expected to rise with the concomitant increasing age of childbearing. The most common malignant tumors associated with pregnancy include gynaecological conditions (mainly uterine or cervical and less frequently ovarian), breast, haematological (leukemia and lymphoma), and skin (melanoma) cancers.[2]

Cancer treatment during pregnancy is a challenge and imposes a medical-ethical dilemma. Immediate aggressive treatment is often indispensable for maternal survival and on the other hand the used cytotoxic medication threatens fetal well-being by crossing the placenta.[3] Based on the actions,

Citation

Lama P, Maharjan P, Sapkota S, Pandit S, Neupane S, Koirala S, et al. Cancer with Pregnancy: Obstetric and Perinatal Outcome. J. Per. Soc. Nepal. 2023;02(01):3-6. DOI: 10.59881/jpeson13

treatment in the form of surgery, chemotherapy or radiation therapy could be potentially toxic to the developing fetus and thus maternal advantage must be always weighed against the possible risks for the unborn fetus. However, cancer itself rarely harms the baby, and some cancer treatments are safe during pregnancy.[4]

In the past, termination of pregnancy was often the preferred advice due to the fear of adverse effects of cytotoxic drugs on the fetus. This option holds good only in aggressive cancer with pregnancy, diagnosed before fetal viability when the maternal disease requires urgent treatment that is not compatible with continuation of pregnancy. Here, attention is focused on the available data regarding the impact of anti-cancer treatments on the mother and fetus.

METHODS

A descriptive study was conducted in Civil Service Hospital of Nepal. Case records of women with cancer and pregnancy attending the hospital from January, 2015 to June, 2022 were analyzed regarding their illness history, clinical examination, investigations, treatment and follow-up. Inclusion criteria were women diagnosed with any cancers during pregnancy with or without treatment. Women not willing to participate and those diagnosed with cancer before and after pregnancy were excluded.

Data were collected from hospital cancer registry of past six years. Telephonic inquiry followed by in-person interview and relevant investigations were done to all the participants regarding fetal and maternal outcome. Oncologic data included the type of cancer, the date of diagnosis, and the treatment details. Obstetrics data attempted to retrieve included gestational age at diagnosis, obstetric complications, gestational age at delivery and mode of delivery. Pediatric data collected included birth weight, congenital malformations, admission to neonatal intensive care unit (NICU), and reason for admission. All the delivered babies were assessed and followed up by the pediatrician for any defects or deviation from normal developmental milestone.

RESULTS

Between 2015 and 2022, ten women were registered with diagnosis of cancer during pregnancy. The age of the women ranged from 19 to 35 years (mean age: 28.6 years). The timing of cancer diagnosis in pregnancy was distributed as follows: two (20 %) in the first trimester, six (60%) in the second trimester, and two (20%) in the third. The distribution of cancer types is depicted in Table 1 and 2. The types of cancers were leukemia (n=6, 60%), non-Hodgkin's lymphoma (n=2, 20%), breast cancer (n= 1, 10%) and thyroid carcinoma (n=1, 10%).

There were six women with leukaemia in pregnancy and among them, four were cases of chronic myeloid leukaemia (CML), one each were cases of chronic lymphocytic leukaemia (CLL) and acute promyelocytic leukaemia (APML).

The case of APML managed for postpartum hemorrhage (PPH) following preterm stillbirth, who underwent chemotherapy consisting of all-trans-retinoic acid (ATRA) improved and is carrying 20 weeks of pregnancy presently.

While woman with CLL diagnosed at 16 weeks of pregnancy opted for termination of pregnancy which was respectfully complied. (Table1) In addition, pregnancy termination was also carried in two of the four cases of CML [conceived while on oral Imatinib (1) and where diagnosis was made in the first trimester (1)]. (Table1)

While third case CML at 20 weeks of pregnancy treated with Imatinib throughout pregnancy underwent emergency caesarean section (Em CS) for failed induction of labor (IOL) at 35 weeks with outcome of live born baby boy, weight 2.78 kg, is noted having normal growth and development. While fourth woman continuing pregnancy with CML, under chemotherapy, with normal anomaly scan at 22 weeks is at 28 weeks currently. Table 2.

A woman 30 weeks gestation with NHL of neck, successfully treated with combination chemotherapy (CHOP regimen 4 cycles) at 37 weeks underwent Em CS for failed IOL with outcome of alive and well newborn boy with birth weight 3.1kg.

Another success story of pregnancy complicated by breast cancer with outcome of preterm cesarean delivery at 35 weeks with outcome of live born baby boy weighing 2.3 kg, managed in post-partum period surgically by modified radical mastectomy of the right breast followed therapeutically by hormonal, chemotherapy [Total six cycles of FAC regime (5-Flurouracil, Doxorubicin, Cyclophosphamide)] and radiation therapy. The baby, now 3 years of age, has normal growth and development.
Pregnancy at 14 weeks, diagnosed with papillary carcinoma of thyroid, a slow growing tumor, wherein cancer surgery was deferred till puerperium, allowing pregnancy to continue with suppressive treatment of levothyroxine, had vaginal delivery at 35 weeks with the birth of a female baby weighing 1.9 kg. Six months postpartum she underwent total thyroidectomy followed by an ablative dose of radioactive iodine (RAI).

In summary, all four women who opted for continuation of pregnancy had successful delivery, preterm delivery occurred in three and term delivery in one, all with good fetal outcome. No neonate was hospitalized in the NICU. These data do not show an increased incidence of physical malformations at birth. The babies are achieving normal growth curve.

While two cases are ongoing pregnancy.

Nine of ten women except for carcinoma thyroid received chemotherapy during pregnancy, while none underwent surgery or received radiotherapy. Except for two women with leukemia whose status remains unknown, rest eight women are in remission. Chemotherapy was given in all four (40%) pregnancies terminated before 18 weeks in leukemia: 3[CML (2); CLL (1)] and NHL of breast (1).

Table 1. Characteristics of women with cancer during pregnancy with abortion and stillbirth

Age (years)	Parity	Cancer Type	Gestational age at diagnosis	Treatment received	Obstetric outcome	Maternal status
19	G1	CML	10 weeks	Gleevac (Imatinib)	Induced abortion	Unknown
27	G2P1L1	CML	18 weeks	Gleevac (Imatinib)	Induced abortion	In remission
29	G3P0+2	Breast-NHL	10 weeks	Chemotherapy	Induced abortion	In remission
35	G3P2L2	CLL	16 weeks	Gleevac (Imatinib)	Induced abortion	Unknown

Table 2. Characteristics of women with cancer during pregnancy and obstetric outcome

Age (years)	Parity	Cancer Type	Gestational age at diagnosis	Treatment received	Obstetric outcome	Maternal outcome
27	G1	CML	20 weeks	Gleevac (Imatinib)	35 weeks LSCS M/2.78 kg	In remission
29	G2P1L1	Thyroid-papillary carcinoma	14 weeks	Observation Thyroxine supplementation	35 weeks, Vaginal Delivery Female 1.9 kg	In remission
33	G2P1L1	Breast-Ductal carcinoma	32 weeks	Chemotherapy, post-partum surgery, radiation therapy	35 weeks LSCS Male, 2.3 kg	In remission
27	G2P1L1	NHL	30 weeks	CHOP regimen	37 wk Failed IOL Em. LSCS 3.1kg male	Under treatment (Received 4 cycles CHOP regimen)
34	G2P0+1	CML	18 weeks	Gleevac (Imatinib)	28 weeks preg	Under treatment
27	P1	Acute promyelocytic leukemia (APML)	PP	ATO (Arsenic trioxide) and ATRA (All-trans retinoic acid)	Preterm stillbirth (27 weeks) referred PPH	In remission Pregnancy 5 months

DISCUSSION

The most common malignancies: cervix, breast, lymphoma and melanoma account for about 70-80% of pregnancy-associated tumors.[5] Many other sites of primary tumors have been reported in the literature, mainly leukaemia, ovary and thyroid carcinoma.

Cancer diagnosed during pregnancy poses a very difficult challenge to the woman, her family and the medical team. The void between creation of a new life and the tragedy of cancer raises many psychological and ethical problems. In this study, 40% (n=4) women opted for termination of pregnancy before 18 weeks which confers that the women facing cancer during pregnancy were nervous and anxious. They were inclined to terminate pregnancy to eliminate fetal toxicity earlier and to initiate their definitive treatment.

Pregnant women, as much as possible, should be treated as non-pregnant women, in order to preserve maternal prognosis. Depending on gestational age and urgency of treatment, surgery, chemotherapy and radiotherapy are possible during pregnancy with some modifications for fetal reasons.[6] Clear evidence exists for the risk of birth defects when treatment is administered during the first trimester, the crucial timing of organogenesis, which usually occurs from 2 to 8 weeks after conception.[7]

Surgery is the least controversial type of oncologic treatment and can be performed during all three trimesters.[8] In this study, woman with papillary carcinoma of thyroid was offered surgery in postpartum period followed by radioactive iodine therapy. In a woman with breast cancer, surgery was offered in post-partum period. However, current guidelines recommend surgical management like non-pregnant women when discovered in the second or third trimesters with intra-partum radical mastectomy and even adjuvant chemotherapy.[9]

Given the aggressiveness of acute leukemia and the urgency to treat, the common practice is termination of pregnancy when they are diagnosed in the first trimester.[10] Thus, presumably, most of the women in this study, diagnosed in the second and third trimesters of pregnancy and initiated chemotherapy at a safe time. Four women had chronic myeloid leukaemia (CML), one was chronic lymphocytic leukaemia (CLL) and acute promyelocytic leukaemia (APML) each.

A woman referred for postpartum hemorrhage following preterm delivery and stillbirth underwent hematological workup and was diagnosed as APML. She was started on all-trans-retinoic acid (ATRA) and arsenic trioxide (ATO). Currently, she is pregnant for the second time and is at 20 weeks of gestation.

Use of chemotherapy after the first trimester may be

associated with intra-uterine growth restriction, stillbirth, premature delivery and neonatal myelosuppression and sepsis.[7] In the present study, there were no chemotherapy-associated neonatal malformations. Based on these observations immediate termination may not be routinely needed as the maternal and fetal outcomes did not appear to be compromised if chemotherapy is delayed to second trimester and beyond. Although studies are limited and results have been obtained on limited number of women, data regarding the final outcome of children who have received in utero chemotherapy seem reassuring. Previous several studies have compared the effects of cancer during pregnancy on the growth and development of children, and the results are inconsistent. Pariyar J et al. showed that the majority of children who were exposed to chemotherapy in utero did not demonstrate significant complications.[11]

Radiation therapy is not favored during pregnancy owing to its teratogenic effects on the fetus; hence, there is a general agreement to postpone radiotherapy up until after delivery.[12] In general, the expected radiation effects, such as mental retardation, organ malformations and induction of childhood neoplasms probably only arise above a threshold dose of 0.1-0.2 Gy.[13]

In a study of Cardonick et al, eight children (6.9%) were SGA.[7] No significant differences were found for gestational age at delivery or birth weight according to the treatment given during pregnancy similar to this study. As previously observed[14,15] also in our population elective cesarean section was the preferred mode of delivery. In contrast, medically induced labor or elective cesarean section are more frequently performed, due to the need of an early pregnancy termination in order to start surgical or pharmacological treatment.[14]

Data on the long-term outcome of children who are exposed to maternal cancer with or without treatment during pregnancy are lacking. Cancer treatment during pregnancy is associated with low birth weight and preterm delivery. Though iatrogenic fetal prematurity is the commonest complication, fetal outcomes are often good as in our series. Termination of pregnancy may not always be necessary.

CONCLUSION

Cancer management during pregnancy is challenging, yet can be overcome by providing adequate appropriate therapy (adopting relatively safe surgery and chemotherapy after first trimester of pregnancy thereby avoiding unsafe radiation therapy) by multidisciplinary team of specialists, in a specialized center, individualizing each case balancing potential risks and benefits based on gestational age and oncological treatment to mother and unborn fetus mandating frequent obstetric follow-up

REFERENCES

1. Kennedy S, Yudkin P, Greenall M. Cancer in pregnancy. European Journal of Surgical Oncology: the Journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology. 1993 Oct;19(5):405-407. PMID: 8405475.
2. Morice P, Uzan C, Gouy S, Verschraegen C, Haie-Meder C. Gynaecological cancers in pregnancy. Lancet. 2012 Feb 11;379(9815):558-69. doi: 10.1016/S0140-6736(11)60829-5. PMID: 22325661.
3. Calsteren KV, Verbesselt R, Devlieger R, et al. Transplacental transfer of paclitaxel, docetaxel, carboplatin, and trastuzumab in a baboon model. Int J Gynecol Cancer. 2010 Dec;20(9):1456-64. doi: 10.1111/IGC.0b013e3181fb18c8. PMID: 21307819.
4. Stensheim H, Møller B, van Dijk T, Fosså SD. Cause-specific survival for women diagnosed with cancer during pregnancy or lactation: a registry-based cohort study. J Clin Oncol. 2009 Jan 1;27(1):45-51. doi: 10.1200/JCO.2008.17.4110. PMID: 19029418.
5. Haas JF. Pregnancy in association with a newly diagnosed cancer: a population-based epidemiologic assessment. Int J Cancer. 1984 Aug 15;34(2):229-35. doi: 10.1002/ijc.2910340214. PMID: 6469398.
6. Maggen C, Wolters VERA, Cardonick E, Fumagalli M, Halaska MJ, Lok CAR, de Haan J, Van Tornout K, Van Calsteren K, Amant F; International Network on Cancer, Infertility and Pregnancy (INCIP). Pregnancy and Cancer: the INCIP Project. Curr Oncol Rep. 2020 Feb 5;22(2):17. doi: 10.1007/s11912-020-0862-7. PMID: 32025953; PMCID: PMC7002463.
7. Cardonick E, Iacobucci A. Use of chemotherapy during human pregnancy. Lancet Oncol. 2004 May;5(5):283-91. doi: 10.1016/S1470-2045(04)01466-4. PMID: 15120665.
8. Amant F, Han SN, Gziri MM, Vandenbroucke T, Verheecke M, Van Calsteren K. Management of cancer in pregnancy. Best Pract Res Clin Obstet Gynaecol. 2015 Jul;29(5):741-53. doi: 10.1016/j.bpobgyn.2015.02.006.
9. Navrozoglou I, Vrekoussis T, Kontostolis E, Dousias V, Zervoudis S, Stathopoulos EN, Zoras O, Paraskevaidis E. Breast cancer during pregnancy: a mini-review. Eur J Surg Oncol. 2008 Aug;34(8):837-843. doi: 10.1016/j.ejso.2008.01.029. PMID: 18343083.
10. Mahmoud HK, Samra MA, Fathy GM. Hematologic malignancies during pregnancy: A review. J Adv Res. 2016 Jul;7(4):589-96. doi: 10.1016/j.jare.2016.02.001. PMID: 27408762; PMCID: PMC4921778.
11. Pariyar J, Shrestha B, Rauniyar BP, Regmi SC, Shrestha J, Jha AK, et al. Cancer with pregnancy in a cancer hospital. J Nepal Health Res Council 2012 Sept;10(22):224-8. doi: 10.33314/jnhrc.v0i0.337
12. Amant F, Deckers S, Van Calsteren K, et al. Breast cancer in pregnancy: recommendations of an international consensus meeting. Eur J Cancer. 2010 Dec;46(18):3158-68. doi: 10.1016/j.ejca.2010.09.010. PMID: 20932740.
13. Kal HB, Struikmans H. Radiotherapy during pregnancy: fact and fiction. Lancet Oncol. 2005 May;6(5):328-33. doi: 10.1016/S1470-2045(05)70169-8. PMID: 15863381.
14. Lee YY, Roberts CL, Dobbins T, et al. Incidence and outcomes of pregnancy-associated cancer in Australia, 1994-2008: a population-based linkage study. BJOG. 2012 Dec;119(13):1572-82. doi: 10.1111/j.1471-0528.2012.03475.x. PMID: 22947229; PMCID: PMC3533794.
15. Momen NC, Arendt LH, Ernst A, Olsen J, Li J, Gissler M, Ramlau-Hansen CH. Pregnancy-associated cancers and birth outcomes in children: A Danish and Swedish population-based register study. BMJ Open. 2018;8(12):e022946. doi: 10.1136/bmjopen-2018-022946.