ISSN 2282-0930 • Epidemiology Biostatistics and Public Health - 2023, Volume 18, Issue 2

Pregnancy-associated Cancers: A Narrative Review

Giovanna Esposito[(1)], *Carlo La Vecchia*[(1)], *Francesco Fedele*[(1,2)], *Fabio Parazzini*[(1)]

(1) Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy
(2) Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

CORRESPONDING AUTHOR: Giovanna Esposito, Department of Clinical Sciences and Community Health, University of Milan, Via Giovanni Celoria 22, 20133 Milan, Italy. E-mail: giovanna.esposito@unimi.it

SUMMARY

Pregnancy-associated cancers are malignancies diagnosed during pregnancy or within one year of delivery or abortion. These cancers present unique challenges because of the delicate balance required for maternal-fetal health. Diagnosis can be made complex by physiological changes associated with pregnancy, and treatment decisions must take into account potential harm to the fetus. Multidisciplinary collaboration between oncologists and obstetricians is essential. Despite the complexities, early detection and tailored management can optimise outcomes for both the mother and child. A systematic approach is currently lacking; further research into prenatal exposure to maternal cancer is recommended to formulate evidence-based guidelines for the management of cancer in pregnancy.

Keywords: cancer, chemotherapy, pregnancy.

INTRODUCTION

Pregnancy-associated cancers are malignancies diagnosed during pregnancy or within one year of birth or abortion. Neoplasms diagnosed in the first year after the end of pregnancy are presumed to have originated in the previous months of pregnancy.

The clinical management of a pregnant patient with oncological disease is certainly a complex scenario due to the co-presence of the mother and the fetus: an accurate diagnosis and timely treatment may save the life of the mother, but may have irreparable consequences for the fetus. The psychological impact on the woman, the couple, and the family of an oncological disease during pregnancy is also significant.

It is therefore important to quantify this event and assess its impact.

METHODS

This is a narrative review of published data on cancer associated with pregnancy. The Scale for the Assessment of Narrative Review Articles (SANRA) was used to report and qualitatively assess the review [1]. We conducted the review using a narrative review approach [2]. PubMed was searched up to 1 December 2023 for relevant publications in English, focusing on, but not limited to, the use of the keywords listed. Key search terms were: pregnancy associated cancer OR ((cancer OR neoplasm OR chemotherapy OR malignancy) AND (pregnancy OR pregnant OR postpartum)). The most relevant articles providing useful information on definition, diagnosis, treatment options, and clinical management of pregnancy-associated cancers were selected. The bibliography was also analyzed to include articles that could have been missed.

Epidemiology

Cancer complicates approximately 1 in 1000 pregnancies, with about 25% diagnosed during pregnancy and the majority diagnosed after pregnancy [3]. The literature on the incidence or prevalence of pregnancy-associated cancers is difficult to compare. Firstly, many studies have focused on a specific type of cancer. Secondly, there are many differences in study design, inclusion criteria, inconsistent follow-up periods, and different reference populations (i.e., pregnancies or births) between studies.

Northern European countries [4-9] have a tradition of epidemiological studies on this topic, as for North

DOI: 10.54103/2282-0930/22286
Accepted: 23th January 2024

Table 1. Result from selected population-based studies about pregnancy-associated breast cancer

Study	Country	Sample size	Incidence rate per 1000	Post-partum follow-up (months)
Sullivan et al., 2022 [22]	Australia New Zealand	-	0.072 0.090	-
Shechter Maor et al., 2018 [23]	USA	11,846,300	0.065	-
Abenhaim et al., 2012 [24]	USA	8,826,137	0.065	-
Andersson et al., 2009 [25]	Sweden	4,156,190	0.279	24
Rodriguez et al., 2008 [26]	California	4,846,505	0.164	12

America [10-12] and Australia [13, 14]. A few evidence are available also from Asia [15, 16]. Studies from southern Europe, particularly in Italy, are more recent [17-21]. The incidence measures range from 0.65 per 1000 in Finland (1950-1969) [7] to 1.73 per 1000 in Korea (1995-2013) [16].

Pregnant women are more likely to experience cancers that are more common in women of reproductive age, with an incidence generally similar to that of women of the same age who are not pregnant [14]; the most commonly diagnosed is the breast cancer [3].

Table 1 lists selected population-based studies regarding pregnancy-associated breast cancer; specifically, incidence rate, and the postpartum follow-up period are described.

Diagnostic challenge

Regardless of pregnancy status, early diagnosis of cancer is essential for successful treatment. The diagnosis of cancer in pregnancy is often delayed because it can be made complex by the fact that many of the symptoms of malignancy mimic the physiological changes of pregnancy, including nausea, breast changes, abdominal pain, anaemia, and fatigue.

The diagnosis of breast cacer during pregnancy represents a challenging situation for the patient and physicians, because variations in hormone levels can cause changes in the breast that can hide small new formations [27]. Specifically, pregnancy increases breast density and nodularity, complicating clinical and radiological examinations [28]. Although biopsy of a suspected breast lesion can be problematic due to the hypervascularisation and oedema typical of the gravid state, histopathology from core biopsies is the gold standard and should follow standard procedures as for non-pregnant women, but the pathologist needs to be aware of the pregnancy status to properly account for changes that may occur due to the physiology of the breast tissue during pregnancy [29].

The awareness of pregnancy-associated hyperpigmentation can also affect how potential malignant lesions or melanoma are interpreted and manifested. Therefore, any pigmented lesion that changes clinical or dermoscopic characteristics during pregnancy should be considered suspicious [30].

On the contrary, pregnancy favours early diagnosis of cervical cancer: women in this period are strictly monitored and the screening for this type of cancer is considered safe during pregnancy using correct sampling tool to minimize bleeding risk [31]. However, also for cervical cancer, the physiological changes associated with pregnancy can lead to false-positive results, so the cytopathologist must be well informed; a Papanicolaou smear taken from a pregnant woman

Table 2. American College of Obstetricians and Gynecologists (ACOG) guidelines for the use of x-rays, ultrasound, magnetic resonance imaging and radioisotopes during pregnancy and lactation. Source: [32, 33]

"Ultrasonography and magnetic resonance imaging (MRI) are not associated with risk and are the imaging techniques of choice for the pregnant patient, but they should be used prudently and only when use is expected to answer a relevant clinical question or otherwise provide medical benefit to the patient".
"With few exceptions, radiation exposure through radiography, computed tomography (CT) scan, or nuclear medicine imaging techniques is at a dose much lower than the exposure associated with fetal harm. If these techniques are necessary in addition to ultrasonography or MRI or are more readily available for the diagnosis in question, they should not be withheld from a pregnant patient".
"The use of gadolinium contrast with MRI should be limited; it may be used as a contrast agent in a pregnant woman only if it significantly improves diagnostic performance and is expected to improve fetal or maternal outcome".
"Breastfeeding should not be interrupted after gadolinium administration".

ISSN 2282-0930 • Epidemiology Biostatistics and Public Health - 2023, Volume 18, Issue 2

may show squamous metaplasia or trophoblastic cells that could be mistaken for dysplasia [27].

Diagnosis by instrumental examination may have been delayed because exposure to procedures during pregnancy and lactation is avoided in the absence of a strong indication. There are, however, a large number of imaging techniques that can be used as diagnostic tools in pregnancy. Guidelines for the use of x-rays, ultrasound, magnetic resonance imaging, and radioisotopes during pregnancy and lactation are reported in Table 2. In the case of x-rays and nuclear medicine, the exposure of the patient and fetus to ionising radiation must be limited. Other diagnostic procedures such as incisional or excisional biopsies, endoscopies and bone marrow punctures can be performed safely [27, 32, 33].

Treatment options

1. A multidisciplinary approach

A comprehensive assessment is needed when considering how best to manage a pregnant patient with cancer. This involves an analysis of the complex interplay between the progression of the tumour and the decision about whether to continue the pregnancy. This includes a thorough evaluation of the stage and type of cancer, its potential impact on the health of the mother and baby, and the therapies that can be given safely during pregnancy. Equally important is an understanding of how the continuation of the pregnancy may affect the approach to tumour treatment, taking into account the safety of the fetus and the potential need for adjustments to the treatment plan to ensure the best possible outcome for both mother and baby.

Management of this situation requires a joint strategy by a multidisciplinary team of obstetricians, oncologists, surgeons, radiologists, neonatologists, psychologists, and other specialists [34]. It is therefore important that cancers during pregnancy are managed in referreal obstetrics hospitals togher with comprehensive cancer centers, with access to the resources and specialists needed to manage all aspects of treatment. [35]. As for non-pregnant women, the approaches to cancer include: radiotherapy, chemotherapy, and surgery. The choice of treatment and its timing cannot be separated from the wishes of the mother and the couple, and is a challenge for each member of the medical and support team [34].

2. Surgical intervention

Planning surgery during pregnancy is based on assessing the potential risks for both progression of maternal disease and fetus health. Where indicated, the procedure can be performed at any time during the course of the pregnancy [36]. Maternal surgery may result in preterm labour and altered uteroplacental perfusion with a resulting risk of hypoxia, brain injury, and fetal intrauterine death [37]. Complications are more common with major abdominal or pelvic surgery due to the increased blood supply to the pelvis [36]. However, a systematic review including pregnant women who underwent non-obstetric surgery found no increased rate of miscarriage or adverse birth outcomes compared with the general population [38]. In the case of gynaecological malignancies, it is preferably performed in the early second trimester when the risk of miscarriage and the size of the uterus allows access [39].

With regard to anaesthesia, the US Food and Drug Administration suggests minimising the time under general anaesthesia, minimising the dose and concentration of the agent, and avoiding inhalational anaesthetics, propofol, and midazolam [40]. The physiological changes of pregnancy require an adapted anaesthesiological approach with an additional safety margin to keep the blood pressure and the oxygenation of the mother as stable as possible [41].

3. Radiotherapy

Radiotherapy should be limited to a few patients; for others, chemotherapy allows safe deferral of radiotherapy [42]. If strictly recommended, limited upper body use can be considered, as the uterus is out of the field and shielded from radiation, with care taken to protect the patient's abdomen with a shield [37, 43].

Fetal exposure to radiotherapy depends on several factors, including gestational age (the fetus is most vulnerable during the first weeks of organogenesis), target dose (doses between 0.05 and 0.5 Gy are generally considered safe for the fetus during the second and third trimesters), the size of the radiation fields, and the distance from the edges of the fields to the fetus [44, 45].

Careful planning using appropriate shielding techniques or other dose reduction techniques is therefore essential when treating a pregnant patient [46, 47].

In the specific case of breast cancer, breastfeeding during radiotherapy is not recommended because the suckling effect of the infant may potentially increase radiotherapy-induced skin toxicity, leading to discomfort, skin breakdown, and infection [48].

4. Chemotherapy

The physiological changes induced by pregnancy may have an effect on the pharmacokinetics and pharmacodynamics, i.e. the absorption, distribution, metabolism, excretion and mechanism of action of the drug. These changes include an increase in plasma volume by approximately 50%, an increase in renal clearance and an increase in hepatic metabolism. The result is a reduction in the active concentration of the drug in comparison with the same dose in a non-pregnant woman of the same weight [49].

Over the past two decades, the use of chemotherapy during pregnancy has gradually increased [50]. Most chemotherapy is discouraged in the first trimester

as it may lead to increased morbidity, particularly congenital malformations [37, 49, 51-53]. The second and third trimester chemotherapy may be associated with intrauterine growth restriction, preterm delivery, low birth weight, and stillbirth [54]. No consistent evidence of major effects on long-term fetal neurodevelopment has been reported. However, longer and more thorough follow-up is certainly needed to draw firm conclusions [52, 55].

The mechanisms underlying the association between prenatal exposure to chemotherapy and adverse outcomes depend on several factors, including the duration and timing of exposure, the dose delivered to the embryo/fetus, and the disruption of cellular metabolism [56].

Not all chemotherapic drugs are dangerous [57, 58]. Table 3 shows the most commonly used chemotherapic treatment against breast cancer.

As for the potential effects on lactation, more than half of the women who underwent prenatal chemotherapy reported reduced milk production and breastfeeding difficulties, with the need to supplement infant feeding [59].

With evidence limited to a few case reports, little is known about the safety of chemotherapy for infants during breastfeeding. In addition to chemotherapy, cancer patients are usually given other drugs that can pass into breast milk and endanger the health of their babies. Despite the well known benefits for both mothers and their babies, breastfeeding during chemotherapy is discouraged, even though neonatal toxicity depends on the oral bioavailability of the drug, the pharmacokinetics of the newborn, and the amount of milk [60].

Management of pregnancy, delivery, and breastfeeding

The pregnancies in women with a diagnosis of malignancy are considered high-risk and should be monitored in a highly specialised centre with an effective multidisciplinary team. Regular ultrasound scans are required for early detection of malformations, assessment of fetal growth, placental flow, and amniotic fluid regularity [34, 36, 61, 62].

If treatment of the neoplasm is planned, the precautions must be taken. In the case of surgery after 24 weeks, cardiotocographic monitoring of the fetus should be performed in order to ensure his well-being throughout the intervention. In addition, the woman needs to be made aware of the possible complications, so her consent needs to be obtained for an emergency caesarean section [34]. During surgery, the patient should be placed in the left lateral decubitus position from 20 weeks' gestation to avoid compression of the inferior vena cava. Tocolytics should not be administered during surgery unless there is evidence of uterine contractions. Post-operative tocolytics may be considered for 48 hours from late second trimester if uterine manipulation is unavoidable [63].

In the case of chemotherapy, monitoring of fetal well-being is a requirement after each course of treatment. It is desirable to plan these treatments carefully according to gestational age. Chemotherapy is generally avoided in the first trimester and should not be administered later than 35 weeks and stopped approximately three weeks before delivery [34, 41, 49]. This interval allows the drugs to be excreted by the fetus across the placenta. Otherwise, the drugs would remain in the infant's circulation [49].

Wherever possible, delivery should be planned and managed on the basis of obstetric indications, with full-term delivery desirable to avoid the consequences of preterm birth [34, 36, 49, 61]. If a premature birth is necessary, it is important to ensure that the baby adapts well, for example by ensuring that the lungs mature through the administration of cortisone [34]. In general, vaginal delivery is appropriate, but the mode of delivery needs to be assessed on a case-by-case basis, in particular depending on the type of cancer. For those that affect the pelvic-abdominal region, such as colorectal or gynaecological cancers, a caesarean section may be more appropriate. For cervical cancer, caesarean section is recommended if the tumor is more than 3 mm deep because of the risk of bleeding or obstructed labor [37].

Histological examination of the placenta should always be carried out after delivery; this is particularly important for leukaemia and melanoma [34, 36, 61]. However, placental metastases are rare [36].

As for postpartum, a potentially safe combination

Table 3. Most common chemotherapic treatment during pregnancy

Chemotherapic options	Evidence
FAC regimen (5-fluorouracil, doxorubicin, cyclophosphamide)	FAC regimen was commolnly well tollerated. Doxorubicin and epirubicin were used either as single agents or in combination with 5-fluorouracil, in both cases well tollerated.
AC regimen (doxorubicin, cyclophosphamide)	
FEC regimen (5-fluorouracil, epirubicin, cyclophosphamide)	
EC regimen (epirubicin, cyclophosphamide)	
Trastuzumab as HER2/neu targeted agent	Short-term use of trastuzumab did not appear to put pregnancy at risk. Prolonged exposure was associated with adverse events.

ISSN 2282-0930 • Epidemiology Biostatistics and Public Health - 2023, Volume 18, Issue 2

of breastfeeding and chemotherapy with minimal risk to the infant may be achieved by discarding the breast milk. It has been suggested that exposure to cyclophosphamide and paclitaxel is negligible when breast milk was discarded for as little as 2 days, whereas doxorubicin should be discarded for at least 6 days [64, 65].

CONCLUSIONS

Over recent decades, there has been an increase in research into the feasibility and safety of oncological treatment during pregnancy, which has led to an increase in the number of ongoing pregnancies with timely treatment of the mother's cancer. However, a systematic approach is currently lacking due to the relative rarity of this situation. This will be useful in formulating evidence based guidelines for the management of cancer in pregnancy.

CONFLICT OF INTERESTS

The authors declare that they have no conflicts of interest to disclose.

REFERENCES

1. Baethge C, Goldbeck-Wood S, Mertens S: SANRA-a scale for the quality assessment of narrative review articles. Res Integr Peer Rev 2019, 4:5.
2. Gregory AT, Denniss AR: An Introduction to Writing Narrative and Systematic Reviews - Tasks, Tips and Traps for Aspiring Authors. Heart Lung Circ 2018, 27(7):893-898.
3. Dalmartello M, Negri E, La Vecchia C, Scarfone G, Buonomo B, Peccatori FA, Parazzini F: Frequency of Pregnancy-Associated Cancer: A Systematic Review of Population-Based Studies. Cancers (Basel) 2020, 12(6).
4. Eibye S, Kjaer SK, Mellemkjaer L: Incidence of pregnancy-associated cancer in Denmark, 1977-2006. Obstet Gynecol 2013, 122(3):608-617.
5. Lambe M, Ekbom A: Cancers coinciding with childbearing: Delayed diagnosis during pregnancy? Brit Med J 1995, 311(7020):1607-1608.
6. Lundberg FE, Stensheim H, Ullenhag GJ, Sahlgren HM, Lindemann K, Fredriksson I, Johansson ALV: Risk factors for the increasing incidence of pregnancy-associated cancer in Sweden - a population-based study. Acta Obstet Gyn Scan 2023.
7. Nieminen U, Remes N: Malignancy during Pregnancy. Acta Obstet Gyn Scan 1970, 49(4):315-&.
8. Lundberg FE, Stensheim H, Ullenhag GJ, Sahlgren HM, Lindemann K, Fredriksson I, Johansson ALV: Risk factors for the increasing incidence of pregnancy-associated cancer in Sweden - a population-based study. Acta Obstet Gynecol Scand 2023.
9. Andersson TM, Johansson AL, Fredriksson I, Lambe M: Cancer during pregnancy and the postpartum period: A population-based study. Cancer 2015, 121(12):2072-2077.
10. Cottreau CM, Dashevsky I, Andrade SE, Li DK, Nekhlyudov L, Raebel MA, Ritzwoller DP, Partridge AH, Pawloski PA, Toh S: Pregnancy-Associated Cancer: A U.S. Population-Based Study. J Womens Health (Larchmt) 2019, 28(2):250-257.
11. Smith LH, Dalrymple JL, Leiserowitz GS, Danielsen B, Gilbert WH: Obstetrical deliveries associated with maternal malignancy in California, 1992 through 1997. American Journal of Obstetrics and Gynecology 2001, 184(7):1504-1513.
12. Smith LH, Danielsen B, Allen ME, Cress R: Cancer associated with obstetric delivery: Results of linkage with the California cancer registry. American Journal of Obstetrics and Gynecology 2003, 189(4):1128-1135.
13. Lee YYC, Roberts CL, Young J, Dobbins T: Using hospital discharge data to identify incident pregnancy-associated cancers: a validation study. Bmc Pregnancy Childb 2013, 13.
14. Lee YY, Roberts CL, Dobbins T, Stavrou E, Black K, Morris J, Young J: Incidence and outcomes of pregnancy-associated cancer in Australia, 1994-2008: a population-based linkage study. BJOG 2012, 119(13):1572-1582.
15. Kobayashi Y, Tabata T, Omori M, Kondo E, Hirata T, Yoshida K, Sekine M, Itakura A, Enomoto T, Ikeda T: A Japanese survey of malignant disease in pregnancy. Int J Clin Oncol 2019, 24(3):328-333.
16. Shim MH, Mok CW, Chang KH, Sung JH, Choi SJ, Oh SY, Roh CR, Kim JH: Clinical characteristics and outcome of cancer diagnosed during pregnancy. Obstet Gynecol Sci 2016, 59(1):1-8.
17. Parazzini F, Franchi M, Tavani A, Negri E, Peccatori FA: Frequency of Pregnancy Related Cancer: A Population Based Linkage Study in Lombardy, Italy. Int J Gynecol Cancer 2017, 27(3):613-619.
18. Murgia F, Marinaccio M, Cormio G, Loizzi V, Cicinelli R, Bettocchi S, Cicinelli E: Pregnancy related cancer in Apulia. A population based linkage study. Eur J Obstet Gynecol Reprod Biol X 2019, 3:100025.
19. Esposito G, Franchi M, Dalmartello M, Scarfone G, Negri E, Parazzini F, La Vecchia C, Corrao G: Obstetric and neonatal outcomes in women with pregnancy associated cancer: a population-based study in Lombardy, Northern Italy. BMC Pregnancy Childbirth 2021, 21(1):31.
20. Pierannunzio D, Maraschini A, Lopez T, Donati S, Amodio R, Bianconi F, Bruni R, Castaing M, Cirilli C, Fantaci G et al: Cancer and Pregnancy: Estimates in Italy from Record-Linkage Procedures between Cancer Registries and the Hospital Discharge Database. Cancers (Basel) 2023, 15(17).
21. Esposito G, Franchi M, Santucci C, Scarfone G, Parazzini F, La Vecchia C, Corrao G, Negri E: Spontaneous and induced abortions in women with a diagnosis of gestational related neoplasm: a population-based linkage study in Lombardy, 2010-2020.

BMC Womens Health 2023, 23(1):586.
22. Sullivan E, Safi N, Li Z, Remond M, Chen TYT, Javid N, Dickinson JE, Ives A, Hammarberg K, Anazodo A et al: Perinatal outcomes of women with gestational breast cancer in Australia and New Zealand: A prospective population-based study. Birth 2022, 49(4):763-773.
23. Shechter Maor G, Czuzoj-Shulman N, Spence AR, Abenhaim HA: Neonatal outcomes of pregnancy-associated breast cancer: Population-based study on 11 million births. Breast J 2019, 25(1):86-90.
24. Abenhaim HA, Azoulay L, Holcroft CA, Bure LA, Assayag J, Benjamin A: Incidence, risk factors, and obstetrical outcomes of women with breast cancer in pregnancy. Breast J 2012, 18(6):564-568.
25. Andersson TM, Johansson ALV, Hsieh CC, Cnattingius S, Lambe M: Increasing incidence of pregnancy-associated breast cancer in Sweden. Obstet Gynecol 2009, 114(3):568-572.
26. Rodriguez AO, Chew H, Cress R, Xing G, McElvy S, Danielsen B, Smith L: Evidence of poorer survival in pregnancy-associated breast cancer. Obstet Gynecol 2008, 112(1):71-78.
27. Pereg D, Koren G, Lishner M: Cancer in pregnancy: gaps, challenges and solutions. Cancer Treat Rev 2008, 34(4):302-312.
28. Vashi R, Hooley R, Butler R, Geisel J, Philpotts L: Breast imaging of the pregnant and lactating patient: imaging modalities and pregnancy-associated breast cancer. AJR Am J Roentgenol 2013, 200(2):321-328.
29. Amant F, Loibl S, Neven P, Van Calsteren K: Breast cancer in pregnancy. Lancet 2012, 379(9815):570-579.
30. Carter TJ, George C, Harwood C, Nathan P: Melanoma in pregnancy: Diagnosis and management in early-stage and advanced disease. Eur J Cancer 2022, 166:240-253.
31. Kumari S: Screening for Cervical Cancer in Pregnancy. Oncol Rev 2023, 17:11429.
32. Jain C: ACOG Committee Opinion No. 723: Guidelines for Diagnostic Imaging During Pregnancy and Lactation. Obstet Gynecol 2019, 133(1):186.
33. Committee Opinion No. 723: Guidelines for Diagnostic Imaging During Pregnancy and Lactation. Obstet Gynecol 2017, 130(4):e210-e216.
34. Salani R, Billingsley CC, Crafton SM: Cancer and pregnancy: an overview for obstetricians and gynecologists. Am J Obstet Gynecol 2014, 211(1):7-14.
35. Schwab R, Anic K, Hasenburg A: Cancer and Pregnancy: A Comprehensive Review. Cancers (Basel) 2021, 13(12).
36. Peccatori FA, Azim HA, Orecchia R, Hoekstra HJ, Pavlidis N, Kesic V, Pentheroudakis G, Grp EGW: Cancer, pregnancy and fertility: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology 2013, 24:160-170.
37. Eastwood-Wilshere N, Turner J, Oliveira N, Morton A: Cancer in Pregnancy. Asia Pac J Clin Oncol 2019, 15(6):296-308.
38. Cohen-Kerem R, Railton C, Oren D, Lishner M, Koren G: Pregnancy outcome following non-obstetric surgical intervention. Am J Surg 2005, 190(3):467-473.
39. Han SN, Lotgerink A, Gziri MM, Van Calsteren K, Hanssens M, Amant F: Physiologic variations of serum tumor markers in gynecological malignancies during pregnancy: a systematic review. Bmc Med 2012, 10:86.
40. Olutoye OA, Baker BW, Belfort MA, Olutoye OO: Food and Drug Administration warning on anesthesia and brain development: implications for obstetric and fetal surgery. American Journal of Obstetrics and Gynecology 2018, 218(1):98-102.
41. Wolters V, Heimovaara J, Maggen C, Cardonick E, Boere I, Lenaerts L, Amant F: Management of pregnancy in women with cancer. Int J Gynecol Cancer 2021, 31(3):314-322.
42. Mazzola R, Corradini S, Eidemueller M, Figlia V, Fiorentino A, Giaj-Levra N, Nicosia L, Ricchetti F, Rigo M, Musola M et al: Modern radiotherapy in cancer treatment during pregnancy. Crit Rev Oncol Hematol 2019, 136:13-19.
43. Fenig E, Mishaeli M, Kalish Y, Lishner M: Pregnancy and radiation. Cancer Treat Rev 2001, 27(1):1-7.
44. Williams PM, Fletcher S: Health effects of prenatal radiation exposure. Am Fam Physician 2010, 82(5):488-493.
45. Yoon I, Slesinger TL: Radiation Exposure In Pregnancy. In: StatPearls. edn. Treasure Island (FL) ineligible companies. Disclosure: Todd Slesinger declares no relevant financial relationships with ineligible companies.; 2023.
46. Wong YM, Koh CWY, Lew KS, Chua CGA, Nei W, Tan HQ, Lee JCL, Mazonakis M, Damilakis J: A review on fetal dose in Radiotherapy: A historical to contemporary perspective. Phys Med 2023, 105:102513.
47. Magrini SM, Pasinetti N, Belgioia L, Triggiani L, Levis M, Ricardi U, Corvo R: Applying radiation protection and safety in radiotherapy. Radiol Med 2019, 124(8):777-782.
48. Shachar SS, Gallagher K, McGuire K, Zagar TM, Faso A, Muss HB, Sweeting R, Anders CK: Multidisciplinary Management of Breast Cancer During Pregnancy. Oncologist 2017, 22(3):324-334.
49. Cardonick E, Iacobucci A: Use of chemotherapy during human pregnancy. Lancet Oncology 2004, 5(5):283-291.
50. de Haan J, Verheecke M, Van Calsteren K, Van Calster B, Shmakov RG, Mhallem Gziri M, Halaska MJ, Fruscio R, Lok CAR, Boere IA et al: Oncological management and obstetric and neonatal outcomes for women diagnosed with cancer during pregnancy: a 20-year international cohort study of 1170 patients. Lancet Oncol 2018, 19(3):337-346.
51. Esposito S, Tenconi R, Preti V, Groppali E, Principi N: Chemotherapy against cancer during pregnancy: A systematic review on neonatal outcomes. Medicine 2016, 95(38).
52. Cardonick E: Treatment of maternal cancer and fetal development. Lancet Oncology 2012, 13(3):218-220.
53. Wolters V, Amant F: Chemotherapy During Pregnancy: Careful Fetal Growth Monitoring Is Mandatory. JCO Oncol Pract 2020, 16(9):559-560.
54. Ngu SF, Ngan HY: Chemotherapy in pregnancy.

Best Pract Res Clin Obstet Gynaecol 2016, 33:86-101.
55. Korakiti AM, Zografos E, van Gerwen M, Amant F, Dimopoulos MA, Zagouri F: Long-Term Neurodevelopmental Outcome of Children after in Utero Exposure to Chemotherapy. Cancers (Basel) 2020, 12(12).
56. van Gerwen M, Maggen C, Cardonick E, Verwaaijen EJ, van den Heuvel-Eibrink M, Shmakov RG, Boere I, Gziri MM, Ottevanger PB, Lok CAR et al: Association of Chemotherapy Timing in Pregnancy With Congenital Malformation. Jama Netw Open 2021, 4(6):e2113180.
57. Azim HA, Peccatori FA, Pavlidis N: Treatment of the pregnant mother with cancer: A systematic review on the use of cytotoxic, endocrine, targeted agents and immunotherapy during pregnancy. Part I: Solid tumors. Cancer Treatment Reviews 2010, 36(2):101-109.
58. Azim HA, Pavlidis N, Peccatori FA: Treatment of the pregnant mother with cancer: A systematic review on the use of cytotoxic, endocrine, targeted agents and immunotherapy during pregnancy. Part II: Hematological tumors. Cancer Treatment Reviews 2010, 36(2):110-121.
59. Stopenski S, Aslam A, Zhang X, Cardonick E: After Chemotherapy Treatment for Maternal Cancer During Pregnancy, Is Breastfeeding Possible? Breastfeed Med 2017, 12:91-97.
60. Pistilli B, Bellettini G, Giovannetti E, Codacci-Pisanelli G, Azim HA, Jr., Benedetti G, Sarno MA, Peccatori FA: Chemotherapy, targeted agents, antiemetics and growth-factors in human milk: how should we counsel cancer patients about breastfeeding? Cancer Treat Rev 2013, 39(3):207-211.
61. 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(1):35-45.
62. Storgaard L, Greiber IK, Pedersen BW, Nielsen BB, Karlsen MA: Cancer in pregnancy - The obstetrical management. Acta Obstet Gynecol Scand 2023.
63. Amant F, Berveiller P, Boere IA, Cardonick E, Fruscio R, Fumagalli M, Halaska MJ, Hasenburg A, Johansson ALV, Lambertini M et al: Gynecologic cancers in pregnancy: guidelines based on a third international consensus meeting. Ann Oncol 2019, 30(10):1601-1612.
64. Damoiseaux D, Calpe S, Rosing H, Beijnen JH, Huitema ADR, Lok C, Dorlo TPC, Amant F: Presence of Five Chemotherapeutic Drugs in Breast Milk as a Guide for the Safe Use of Chemotherapy During Breastfeeding: Results From a Case Series. Clin Pharmacol Ther 2022, 112(2):404-410.
65. Damoiseaux D, Centanni D, Beijnen JH, Amant F, Huitema ADR, Dorlo TPC: Predicting Chemotherapy Distribution into Breast Milk for Breastfeeding Women Using a Population Pharmacokinetic Approach. Clin Pharmacokinet 2023, 62(7):969-980.