

Breast Cancer in Pregnancy

Quick reference guide

- ❖ Breast cancer is the most common malignancy complicating pregnancy (accounting for 40% of cases), the current incidence rate is estimated at 1 in 1000 pregnancies
- ❖ Numbers of women developing it in pregnancy or in the first year after delivery are rising
→ contributing factors include increasing background incidence of the disease and rising maternal age
- ❖ Diagnosis during pregnancy is associated with a lower prevalence of hormone receptor expression
→ as such, a higher incidence of more aggressive subtypes e.g. triple-negative or HER2-positive disease are seen in this population
- ❖ In addition, presentation may be delayed leading to more advanced clinical staging at diagnosis
- ❖ Management represents a challenging situation, in which healthcare professionals attempt to maximize the curative approach for the patient while minimizing adverse effects on the fetus
- ❖ In order to make risk/benefit decisions an understanding of the safety of each investigation/treatment modality is required

Investigations and Imaging

Tumour markers:

- May be misleading in pregnancy and are therefore not recommended

Ultrasound Scan (USS):

- 1st line imaging modality as lacks ionizing radiation
- Tissue biopsy should be for histology > cytology (proliferative changes in pregnancy render cytology inconclusive)

Mammography:

- Safe and effective in pregnancy
- Minimal risk to developing fetus if appropriate lead shielding is used

Computed Tomography (CT) with/without contrast:

- CT brain and thorax may be used as relative fetal radiation dose is low

Magnetic Resonance Imaging (MRI):

- MRI abdomen and pelvis preferable to CT, as MRI not associated with increased risk of harm to the fetus
- Gadolinium-based contrast should be avoided (associated with adverse neonatal outcomes including rheumatological, inflammatory, infiltrative skin conditions, stillbirth and neonatal death)

Sentinel lymph node biopsy:

- Can be performed throughout gestation, preferably using Technetium-99m colloid solution injection (fetal dose <0.05 mGy)
- A 1-day protocol (solution injected on the morning of the surgery) reduces fetal exposure to radiation
- Avoid blue dye and isosulfan blue through gestation (risk of anaphylaxis 1%)
- Avoid methylene blue in 1st trimester as it is teratogenic

Fetal radiation (mGy) dose during imaging studies

Threshold for fetal damage

=50mGy

CXR	0.0005-0.01
Mammography	0.001-0.01
CT head	0.001-0.01
CT thorax	0.01-0.66
Low-dose perfusion Scintigraphy	0.1-0.5
Technetium-99m Bone scintigraphy	4-5
CT abdomen	1.3-35
CT pelvis	10-50
¹⁸ F PET/CT whole-body scintigraphy	10-50

Other considerations

MDT:

- Involvement of the MDT, including an obstetrician and obstetric physician is important in providing holistic care



VTE prophylaxis should be considered:

- Post-operatively
- If on chemotherapy
- In metastatic disease
- + for 6 weeks post partum



Staging:

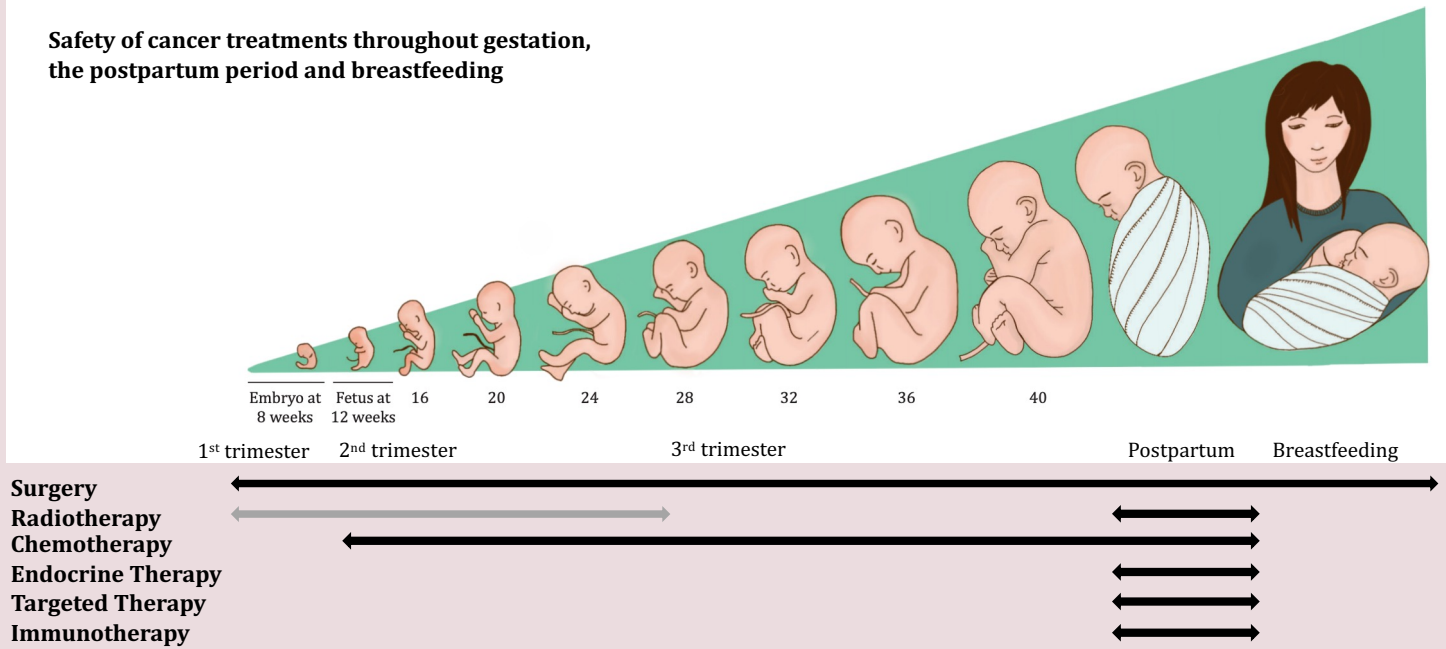
- Should not be withheld if clinically indicated
- Risk/benefit should be discussed with patient

1. Shachar SS et al. Multidisciplinary Management of Breast Cancer During Pregnancy. *Oncologist*. 2017;22(3):324-34.
2. Schwarz EB et al. Contraception for cancer survivors. *J Gen Intern Med*. 2009;24 Suppl 2:S401-6.
3. Knight M et al. Saving Lives, Improving Mothers' Care: Lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2015-17.

4. Poggio F et al. Update on the Management of Breast Cancer during Pregnancy. *Cancers (Basel)*. 2020;12(12).
5. Lowe S. Diagnostic imaging in pregnancy: Making informed decisions. *Obstet Med*. 2019;12(3):116-22.
6. Committee Opinion No. 723 Summary: Guidelines for Diagnostic Imaging During Pregnancy and Lactation. *Obstet Gynecol*. 2017;130(4):933-4.

- ❖ Management decisions can be challenging for both the patient and the healthcare professionals looking after them
- ❖ Increasing numbers of therapeutic options are available to clinicians and their use requires careful consideration of therapeutic benefit vs safety in pregnancy
- ❖ All decisions should be made with the patient at the center, the support of the multidisciplinary team and input from specialists in the field- a low threshold for seeking further expertise should exist

Safety of cancer treatments throughout gestation, the postpartum period and breastfeeding



Surgery:

- Considered safe throughout pregnancy but if possible preferred prior to 24 weeks gestation
- Most anesthetic drugs are safe throughout gestation; suggest liaising with obstetric anaesthetist if any concerns
- Fetal viability should be checked pre- and post- procedure
- Immediate breast reconstruction using tissue expander can be performed after mastectomy, however, due to the physiological changes to the breast, delayed reconstruction should be considered

Radiotherapy (RT):

- Emergency RT may be considered in the 1st/2nd trimester - if beam can be angled distant to the pelvis (e.g. brain/ upper body bony metastasis) but only after discussion with a specialist
- In all other cases RT should be postponed until after delivery, because of potential teratogenic and even lethal effects on the developing fetus. Breast-feeding should be avoided during RT, suckling may be difficult from the irradiated breast

Chemotherapy:

- Cytotoxic agents are teratogenic in the 1st trimester and thus contraindicated during this period
- Anthracyclines, cyclophosphamide, and taxane-based (weekly paclitaxel) regimens can be used after the 1st trimester. There are also reports to support the addition of carboplatin-based regimens if required
- Chemotherapy doses should be calculated using current as opposed to pre-pregnancy weight
- Use published standard dose protocols (neither decrease/increase dose, do not increase treatment intervals)
- A port-a-cath and other central venous access devices/peripherally inserted central catheter lines can be fitted as outside of pregnancy (using local anaesthetic, X-RAY and USS where indicated)
- If possible, stop 3 weeks prior to delivery to allow the bone marrow to recover and prevent hematological complications during delivery. Leave a 14-day interval between last chemotherapy session and start of breastfeeding, if chemotherapy restarted stop breastfeeding

Endocrine Therapy, Targeted Therapies, Immunotherapy:

- Endocrine therapies are contraindicated in pregnancy (risk of malformation) and should be reserved for the postpartum period
- Anti-HER2 agents, CDK4/6 inhibitors and anti-PD-(L)1 inhibitors are all contraindicated during pregnancy and should also be reserved for the postpartum period

Supportive therapies:

- Antiemetics (including ondansetron and metoclopramide) and proton pump inhibitors can safely be used throughout all gestations
- Methylprednisolone, hydrocortisone and prednisolone are favored over dexamethasone
- Neurokinin-1 inhibitors are contraindicated
- G-CSFs should not be withheld if required

Recommended contraception for those under investigation/postpartum:

- Copper coil ✓
- Nexplanon X
- POP X
- Mirena® X

Obstetric Considerations:

- Decisions regarding termination should be individualized with MDT input
- Interpret 1st trimester screening with caution. Women with confirmed metastatic disease may have high serum β -hCG and should not have noninvasive prenatal testing (NIPT) as results can't be accurately interpreted
- If exposed to preconception/1st trimester chemotherapy patient should have fetal medicine specialist scan
- Vaginal delivery is not contraindicated
- Discuss timing of delivery with MDT (aim 38-39 weeks)