Breast cancer and pregnancy: what we know and where we go

A Ives
Centre for Health Services Research,
Department of Public Health,
The University of Western Australia,
Nedlands, WA

J Semmens
Centre for Health Services Research,
Department of Public Health,
The University of Western Australia,
Nedlands, WA

C Saunders
University Department of Surgery, Royal Perth Hospital,
Perth, WA

P Puckridge
Department of General Surgery,
Sir Charles Gairdner Hospital, Nedlands,
WA

Abstract

While breast cancer is a high profile disease, its association with pregnancy is less often reported. Pregnancy-associated breast cancer or gestational breast cancer (GBC) is defined as breast cancer diagnosed during pregnancy or in the 12 months post-partum. GBC is uncommon, but likely to become more common as women delay pregnancy until they are in their thirties and forties when the chance of developing breast cancer begins to rise. Delays in diagnosis mean that the prognosis for GBC is often poor. Women who become pregnant later in life also run the risk of developing breast cancer before they conceive. These breast cancer survivors then have difficult choices to make about conception. Research in these areas is based mainly on reports from single institutions. Further research is needed, and in Western Australia a population-based study to evaluate the epidemiology and management of breast cancer and pregnancy is underway. This work will provide fresh evidence on which to base future practice recommendations, and will enable further research to be conducted about the pathological, biological and imaging characteristics of the malignancies in the pregnant and lactating breast.

Introduction

Because of the high incidence and mortality of breast cancer in the developed world, research in this area has been given a high priority and been widely reported to the general community. Breast cancer’s association with pregnancy, while uncommon, has been less often reported. More women are choosing to delay pregnancy until their thirties and forties, when the incidence of breast cancer rises. This is likely to lead to an increased risk of pregnancy-associated breast cancer, and more women are likely to develop breast cancer before they conceive. This has major implications for both women and the healthcare system.

At present, the association between breast cancer and pregnancy is uncommon, with estimates of it affecting between one in 3,000 and one in 10,000 pregnancies1. Historically breast cancer concurrent with pregnancy, also known as gestational breast cancer (GBC), was thought to carry a poor prognosis2. This adverse outlook, and the fact that most clinicians’ experience and knowledge of GBC is limited, has continued to impact upon the medical psyche3. It has also meant that subsequent pregnancy in breast cancer survivors has not been widely recommended. In this paper we will discuss the evidence available, on which clinicians can base their management of women with GBC and breast cancer survivors who may want to conceive. We will also report on a population-based study of these two groups of women, recently commenced in Western Australia.

Gestational breast cancer (GBC)

GBC is defined as breast cancer diagnosed during or in the 12 months post-partum (including lactation). The reported incidence of GBC, based on mainly single institution reports, ranges from 0.76 – 3.8% of all diagnosed breast cancers4-8. Overall, the incidence appears low, but in premenopausal women, incidence of GBC is reported to be between 7-14%9,10. Pregnancy-associated breast cancers have been reported to have a worse prognosis and are commonly more advanced at presentation (larger tumours and lymph node positive) than non-pregnancy associated breast cancers11,12. However, when matched for age and stage at diagnosis, there is no difference in survival between pregnancy-associated and non-pregnancy associated breast cancers. Ezzat reports on a seven-year survival for GBC of 57% (95% CI, 33-81) and non-GBC of 61% (95%
ARTICLES

that termination of pregnancy is associated with a survival management option in GBC. There is however, no evidence implications for the clinician even in such an uncommon condition, may have medico-legal counterparts have been reported. Similarly, little evidence is available regarding the genetic aspects of GBC, although BRCA1 and BRCA2 mutations have been identified in some cases.

Most young women with operable breast cancer can be offered breast-conserving surgery and postoperative radiotherapy. Radiotherapy is contraindicated during pregnancy due to the high radiation dose to the foetus, thus for many pregnant women mastectomy is the surgical treatment of choice. When breast cancer is diagnosed in the third trimester, it may be possible to perform breast-conserving surgery with radiotherapy delayed until after delivery of the child.

Chemotherapy results in unacceptably high levels of fetal abnormality when administered during the first trimester. Administration of chemotherapy during the second and third trimester is generally safe (a malformation rate of 4% is reported – similar to the 3% risk during a normal pregnancy), although it may be associated with low birth weight and early delivery. Specific agents that should be avoided as treatment during pregnancy include antimetabolites such as methotrexate.

Termination of pregnancy is sometimes considered as a management option in GBC. There is however, no evidence that termination of pregnancy is associated with a survival benefit – it may actually have a deleterious effect. This reporting may be biased, as many women who undergo termination of pregnancy for GBC have more advanced disease and would have a poor prognosis irrespective of whether their pregnancy was terminated or not.

Subsequent pregnancy

Contraception and fertility are two important issues for premenopausal survivors of breast cancer, particularly when their lifespan may be limited. Most clinicians advise against pregnancy in the first two years following treatment. This is mainly to ensure the woman does not develop early recurrence and that all adjuvant treatments have been completed prior to conception. Contraception is therefore likely to be necessary, but hormonal contraception is not recommended. Breast cancer survivors who subsequently conceive have equivalent survival or in some studies better survival matched for stage. This improved survival may be due to bias, with only a select group of healthy women going on to become pregnant – a “healthy mother” effect.

At the other end of the spectrum chemotherapy can induce infertility. Women under 35 years of age are less likely to experience permanent amenorrhoea than women aged over 40. Reports of between 37% and 97% of premenopausal women becoming amenorrhoeic following chemotherapy have been recorded, and this is very much related to age and type of chemotherapy treatment. Various strategies have been proposed to protect the fertility of a woman undergoing chemotherapy, but with little success thus far. It has been estimated that only 7% of fertile women go on to conceive following breast cancer treatment. Whether this is by choice or not is as yet unknown.

Population-based research in Australia

The rarity of GBC means that a randomised controlled trial is not an appropriate method to study the clinical epidemiology and outcomes of the disease. In general, most studies published to date relating to breast cancer and pregnancy have been descriptive, consisting of retrospective, single institution series, where over a long period of time only small numbers of women have been recruited. There are only four published series involving more than 100 women. The results of these studies have given us a greater appreciation of how pregnancy may influence the outcome of breast cancer, but have also led to conflicting and confusing information.

The Gestational Breast Cancer Project that has commenced in Western Australia (WA) will be the first to use a population-based data set to investigate breast cancer and pregnancy. The project involves collaboration between the WA Safety and Quality of Surgical Care Project and the WA Breast Cancer Research Alliance. Initially this study is retrospective, and has used the WA Record Linkage Project to identify women who were diagnosed with GBC or have survived breast cancer and subsequently conceived since 1982. The WA Record Linkage Project brings together around 13 million records and consists of population-based hospital morbidity data, birth and death records, mental health services data, cancer registrations and midwives’ notifications, linked back to 1980. This linkage system is one of only five such projects in the world.

The use of population-linked health data enables us to explore community outcomes and provides additional information for the knowledge base required for evidence-based practice, in areas where it is difficult to gain such data from randomised clinical trials. We expect to identify about 300 cases (approximately 10 GBC and seven subsequent pregnancies per year). The information obtained will be supplemented with data from patient medical records and cancer registry data to provide information on diagnosis, treatment and outcomes of the breast cancer and pregnancy. The project has approval to access named data from the WA Department of Health, and ethics approval from the University of WA and all relevant hospitals. The data file will be de-identified for research purposes.

This work will enable further research to be conducted in the pathological, biological and imaging characteristics of the malignancies in the pregnant and lactating breast. Future prospective studies are envisaged that will look at changes in the management of breast cancer related to pregnancy, and the psychosocial issues (including fertility) which surround such a diagnosis. We anticipate that this study will lead to a greater understanding of breast cancer and pregnancy, providing new, population based evidence to contribute to the body of knowledge about managing breast cancer and pregnancy. And, most importantly, it should enable young women to make informed choices about their health.

Acknowledgements

We would like to thank the Raine Medical Research Foundation for the priming grant, which allows us to carry out this important project.
References