

Original article

Planned and unplanned pregnancies in breast cancer survivors

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ABSTRACT

Background: Nearly 20% of women presenting with breast cancer in the UK are of reproductive age. The aim of our study was to assess fertility outcome in relation to intent to conceive in patients who had completed breast cancer treatment.

Methods: Between July 2011 and December 2013, women, aged less than 43 years at the time of diagnosis, were asked during their follow-up in breast cancer clinic, to complete a questionnaire on intentions to conceive and pregnancy outcome.

Results: A total of 175 women completed the questionnaire at a median time of 6 years from time of diagnosis. Their median age at the time of diagnosis was 37 years and at the time of the survey was 43 years. At the time of the survey, 42% (72/175) had completed their family, 41% (72/175) reported that they would like to have children and 4% (7/175) did not wish to have children. Twenty-seven respondents had actively tried to conceive, and of those 13 (48%) had a live birth. There were 12 unintended pregnancies; the majority of which were terminated (58% (7/12)) with only 3 live births. Among those who did not wish to conceive, only 32% (36/111) reported using contraception.

Conclusion: This is a retrospective study investigating menstrual function, contraceptive methods and fertility outcomes of young breast cancer survivors. This study highlights the need for healthcare professionals to provide long-term contraceptive advice to women who do not wish to conceive.

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Introduction

Breast cancer is the most common cancer of women in the UK, with 1 in 8 developing this disease in their lifetime [1,2]. Approximately 23% of in situ cases and 19% of invasive breast cancer cases are diagnosed in premenopausal women [3].

Despite the increasing incidence, as a result of improved screening programmes and advances in treatment, more than 81% of women with early breast cancer survive more than ten years [4]. Current family planning trends show that women are delaying pregnancies until their late 30–40s [5], which is demonstrated by the rate of live births to mothers aged 35 and over in UK rising from 8.7% in 1990 to 20% in 2012 [6]. Similar trends are demonstrated throughout the USA [7] and the rest of the world [8]. Hence an increasing proportion of women diagnosed with breast cancer now

have not attempted to conceive at the time of their diagnosis.

Despite high rates of women wishing to achieve pregnancy after breast cancer, up to 47% in some cases [9], breast cancer survivors are amongst cancer survivors with the lowest pregnancy rates [10], and 70% lower than the general population [11]. It is thought this is secondary to a number of factors including: the frequent use of gonadotoxic chemotherapy which can cause permanent amenorrhoea with complete loss of germ cells, transient amenorrhoea, menstrual irregularity and subfertility [12]. The degree of damage depends on the type of agent, patient age, original ovarian reserve, dose and duration of treatment [13]. Pregnancy is strongly discouraged during chemotherapy and radiotherapy as there is a higher risk of congenital malformations and spontaneous abortion [14].

In addition to receiving gonadotoxic treatment which can reduce the future conception rate, women are advised to avoid becoming pregnant for at least 18 months to two years when the risk of recurrence is at its highest. Patients often have prolonged treatment periods with tamoxifen in endocrine-sensitive disease

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and current practice is to advise against pregnancy in this period [10]. Finally, patients [15], as well as physicians [16,17], appear to remain concerned that pregnancy could simulate cancer recurrence. Recent studies contradict this hypothesis [18]. Conversely, pregnancy has been hypothesized as a protective factor against breast cancer [19–21]. Iqbal [19] et al. found that the 5 year survival rate amongst women who became pregnant 6 month or more after their breast cancer diagnosis was 96.7% compared with 87.5% for women with no pregnancy. The POSITIVE study is currently investigating the safety of interrupting endocrine therapy to allow patients to attempt to conceive [22].

Although there are data on successful pregnancies after breast cancer, and that childbirth after diagnosis and treatment of early breast outcome does not affect outcome, there are only a few studies in the literature which look at fertility intent. Moreover, to the best of our knowledge none have followed up these women for longer than 10 years.

The aim of our study was to assess fertility outcome in relation to intent in women who had a diagnosis of early breast cancer during reproductive age.

Methods

Between August 2011 and October 2013, female cancer survivors who were diagnosed with early breast cancer up to 42 years of age (inclusive) were approached with a questionnaire during their follow-up visit to the breast clinic at Guy's and St Thomas NHS Foundation Trust.

The questionnaire (Appendix 1) was constructed by a multi-disciplinary team involving medical oncologists, a nurse consultant in breast cancer and a reproductive medicine gynecologist. The questionnaire contained 19 questions covering different aspects of menstrual and reproductive history at the time of diagnosis, and then at the time of the questionnaire: menstrual cycle history, ongoing use of contraception, subsequent pregnancies and their outcomes. In addition, we asked if the patient had completed their family, or wished to have further children in those who had children, or who wanted children or were actively trying to conceive if they had been childless prior to diagnosis. We also explored if patients were told about the potential effect of their cancer treatment on fertility, if they felt they were provided with sufficient information, and if fertility preservation was offered.

This service evaluation was approved by the Guy's and St Thomas' Foundation Trust Audit Committee. Verbal informed consent was obtained from each patient.

Statistical analysis

All data were coded and checked for errors. Missing and ambiguous responses were excluded from analysis. Descriptive statistics (i.e. frequency distribution, mean [standard deviation (SD)], and median [range]) were used to summarise characteristics and outcome variables. Differences between continuous and categorical variables were tested using T-test and the χ^2 test respectively. For all analyses, $p < 0.05$ was considered statistically significant.

Results

Characteristics of responders

We collected questionnaires from 175 patients. The primary diagnosis of breast cancer for these women was made between 1995 and 2012. The details of the responders are given in Table 1. The response rate was 100% as everyone who was approached in

the clinic agreed to fill in a questionnaire, however, not all the responders answered all questions therefore absolute numbers and figures have been given to aid analysis of the results. The median age at diagnosis was 37 (25–42) years. At the time of this survey the median follow-up from diagnosis was 6 (1–21) years. The median age at the time of the survey was 43 (30–55) years. As many as 75% (131/175) of the women had chemotherapy as part of their breast cancer treatment and 33% (55/163) were still undergoing anti-breast cancer hormone treatment at the time of the survey (Table 1).

Fertility history at diagnosis

Prior to the diagnosis of breast cancer, 65% (113/175) of the responders stated they had been pregnant resulting in a live birth in 50% (87/175). In our cohort, the average reported age of conception prior to cancer diagnosis was 25 years.

Menstrual function before and after breast cancer treatment

Most women, 90% (158/175), were having periods at the time of breast cancer diagnosis; four patients were peripartum 2% (4/175). Of the patients who had adjuvant chemotherapy, 56% (74/131) reported that their periods had restarted after chemotherapy (Table 1). 21% (28/131) of patients in this cohort reported no periods after chemotherapy. As expected there was a significant difference ($P < 0.0001$) in age at the time of diagnosis between patients who recovered their menstrual function after chemotherapy (35.9 ± 4.4 years) and those who did not (39.4 ± 2.2 years).

Contraception after treatment

Women were asked about current contraceptive use and their intention to conceive (Table 2). 64% (74/116) reported they were not using any form of contraception at the time of the survey despite not wanting to conceive. Of those not using contraception 46% (53/116) reported having their last period within last month. The median age of women not using contraception was 44 (34–55 years), with 85% (99/116) being under 50 years.

Desire to conceive and pregnancies after diagnosis

At the time of the survey, 42% (74/175) of women had completed their family; 4% (7/175) did not want children. 41% (72/175) wanted to have/or had more children. 20 women did not answer this question. 74% (120/164; 11 did not answer) of women stated they had a discussion with a clinician about their fertility. Of 175 responders, 14 had their embryos/eggs frozen.

Following the diagnosis, at the time of questionnaire, 26 women reported achieving a pregnancy with 16 of them resulting in a live birth (Fig. 1). Not all conceptions were intentional. Among 27 women who had been trying to conceive, 13 had live births (two women were also pregnant at the time of the survey and six women had had a previous miscarriage*, with none of the patients having termination of pregnancy). Conversely, among 12 women who became pregnant unintentionally.

There were seven terminations, two miscarriages and only three live births (see Fig. 2). None of the patients who had termination were receiving tamoxifen or any other endocrine therapy.

Discussion

To the best of our knowledge this is one of the first studies assessing fertility outcome in relation to patients' intent. This study demonstrates that as many as 41% (72/175) of patients wanted to

Table 1
Characteristics of respondents.

Age of patients at the time of cancer diagnosis	
Median age, years	37
Range	25 to 42
Time since diagnosis	
Median, years	6
Range	1 to 21
Age of patients at the time of questionnaire	
Median age, years	43
Range, years	30–55
Menstrual function at diagnosis	
N = 175	
Had periods	158 (90%)
Peripartum	4 (2%)
No periods	4 (2%)
Not answered	9 (5%)
Menstrual function after chemotherapy (n = 131)	
N = 131	
Periods restarted after chemo	74 (56%)
Periods did not restart after periods	28 (21%)
Periods not affected by chemo (did not stop)	21 (16%)
Not answered	8 (6%)
Previous pregnancies before cancer diagnosis	
N = 175	
No	51(29%)
Yes	113 (65%)
Not answered	11 (6%)
Previous live birth	
	87 (50%)
Treatment of breast cancer (reported by patients)	
Chemotherapy for treatment reported by patients	
Current Anti-estrogen Therapy	
Yes	57 (33%)
No	106 (60%)
Not answered	12 (7%)

Table 2
Intention to conceive and reported contraception usage.

Intention to conceive	Contraception reported	No contraception	Not answered	Total
Yes	4 (15%)	22 (81%)	1 (0.04%)	27 (15%)
No	36 (32%)	74 (67%)	1 (1%)	111 (63%)
Not answered	3 (4%)	9 (36%)	13 (52%)	25 (14%)
Not applicable	1 (8%)	11 (92%)	0	12 (7%)
Total	44 (25%)	116 (66%)	15(9%)	175

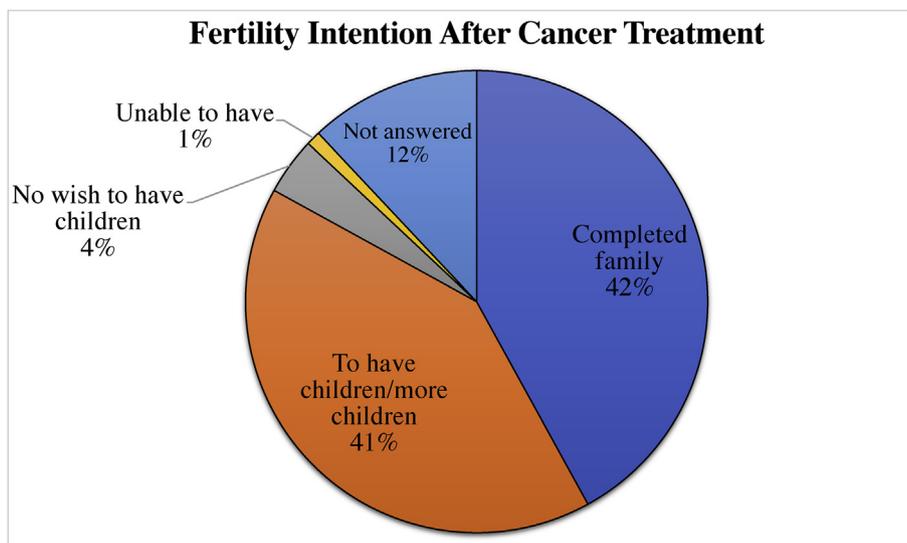


Fig. 1. Intention to conceive after cancer treatment.

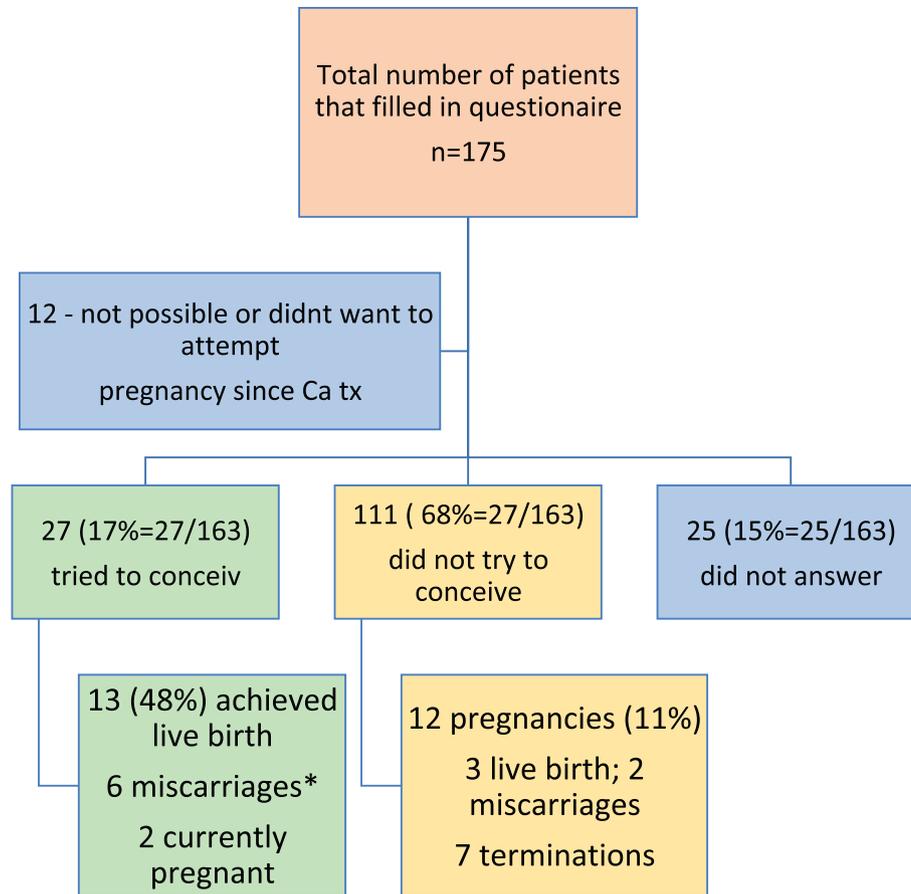


Fig. 2. Pregnancy outcomes in breast cancer patients after treatment.

have children or more children after cancer treatment. However, only 37% (27/72) of those who wanted children have attempted to conceive so far, and of these almost half of them 48% (13/27) have been successful with a live birth.

Conversely, there was a high rate of pregnancy termination in patients who conceived unintentionally. Unexpectedly, a large proportion of patients who reported not using any contraception at the time of the survey, have also acknowledged that they did not want a child or more children.

The particular strength of this study is the length of follow-up of these women at a median of 6 years and up to 21 years. Moreover, 75% (131/175) of the women in our study had chemotherapy as part of their breast cancer treatment and 33% (55/163) were still receiving anti-breast cancer endocrine treatment at the time of the survey. This highlights the need for ongoing discussions with younger patients regarding fertility.

The retrospective nature of our study means that pregnancy age trends in our study may not be representative of trends in 2019. In our cohort the average age of having children was 25.8 years old, which is younger in comparison to the current average of 30.3 years [23]. In our study, 41% (72/175) of the women wanted a baby after breast cancer diagnosis. Due to the increasing trend of delaying pregnancy, a higher rate of women without children at breast cancer diagnosis is to be expected. Therefore, the rate of women wishing to retain fertility at breast cancer diagnosis may now be higher. Furthermore, with the increasing input from Assisted Conception Units over the last 10–15 years the pregnancy rate after breast cancer is likely to be higher. Only 14 women had embryo preservation in our cohort. At the time of questionnaire none of

these patients had used their stored embryos.

A recent systematic review quotes pregnancy rates following breast cancer to be 3–14% [24]. The pregnancy rate after breast cancer in our study was much higher at 52% (14/27) but this is likely to be because our assessment was based on intention to conceive and the long follow-up, whereas the above-mentioned meta-analysis quoted the pregnancy rate in relation to a total number of patients who had breast cancer without adjusting for patients' intention to conceive.

Our study also raises a concern about the rate of unintended pregnancies in this population of patients. Pregnancy during breast cancer treatment should be avoided; not only can cancer treatment be teratogenic to the unborn child but also the emotional distress and difficult decision-making can have adverse psychological consequences for the women involved. A recent meta-analysis of 16 studies showed that 21% of women with a diagnosis of breast cancer terminated their subsequent pregnancies [25].

Contraceptive counselling is important, however little research has been done to establish whether patients take contraception to avoid pregnancies during this time and what advice should be given. Moreover, there is little data on unplanned pregnancies and their outcome. A large Australian population-based study showed that 47% of pregnancies that occurred 2 years following a breast cancer diagnosis were terminated [26], and that the rate of abortion was inversely proportional to the length of time between breast cancer diagnosis and subsequent pregnancy. However, authors could only speculate about the reasons behind this trend, one of which was failure of contraception.

Multiple studies have emphasised the importance of fertility

Table 3Summary of different methods of contraception available adopted from the Faculty of Sexual and Reproductive Healthcare Guidelines <https://www.fsrh.org/home/>.

Type of Contraception	Positives	Negatives
Condoms	Low failure rate Cheap Protects against sexually transmitted infections	Not long-acting form of contraception
Caps	Can be inserted and removed by patient themselves	Not readily available Must not be removed until 6 h post coitus Expensive
Copper IUD	Long term form of contraception Can be used with breast cancer treatment	Can cause menorrhagia, dysmenorrhoea Invasive
LNG-IUS (levonorgestrel- intrauterine system)	Long term form of contraception Counteracts the proliferation effects of tamoxifen in endometrium Can reduce menorrhagia	Little data on use and recurrence of breast cancer. Specialist opinion should be sought before use in past history of breast cancer.
Progesterone only Implant		Contraindicated in current breast cancer treatment Specialist opinion should be sought before use in past history of breast cancer.
Depot medroxyprogesterone acetate		Contraindicated in current breast cancer treatment. Specialist opinion should be sought before use in past history of breast cancer.
Progestogen only pill		Contraindicated in current breast cancer treatment. Specialist opinion should be sought before use in past history of breast cancer.
Combined hormonal contraception		Contraindicated in current breast cancer treatment. Specialist opinion should be sought before use in past history of breast cancer.

counselling, but few have investigated contraceptive counselling in these women [13,26]. A retrospective Swiss study of 100 patients during their first year after breast cancer diagnosis found that circumstances leading to two unintended pregnancies in their cohort included ineffective contraceptive methods, poor communication, and misinterpreting treatment-related amenorrhoea for the menopause [26]. Another cohort study of 104 breast cancer women in Mexico also reported poor counselling and low use of appropriate contraception during chemotherapy [27].

In our study, we found that 66% (116/175) of women at the time of the survey were not using any contraception. More surprisingly, 64% (74/116) of the women who did not use contraception did not intend to conceive, despite 42% (31 out of 74) of them reporting having periods. Clinicians have improved counselling young breast cancer patients about fertility preservation [28–30], but a recent study showed that although oncologists felt the issue of contraception was an important aspect of discussion in breast cancer surveillance, only 30% of respondents said that they actively enquired about use of contraception [31]. Hormonal contraception, in the form of oral contraception or levonorgestrel intrauterine system (LNG-IUS), are relatively contraindicated in women with breast cancer, particularly those with oestrogen receptor positive cancer, and it is usually discontinued. Women may not want to start a new form of contraception whilst undergoing such major changes in their lives, therefore clinicians need to explain to patients the importance of contraception during breast cancer treatment and then plan for long-term contraception after definitive treatment, particularly in those women who have completed their family or do not wish to conceive. Oncologists are not necessarily experts on long-term methods of contraception and women may benefit from referral to gynaecologists. Moreover, better education should be given to general practitioners on contraceptive methods after malignancy as they are the first port of call for the patient for long-term or ongoing contraceptive advice. The current guideline of Faculty of Sexual and Reproductive Health on contraceptive choices after treatment of breast cancer recommends non-hormonal methods [32].

Use of Levonorgestrel Intrauterine System (LNG-IUS) is not usually recommended during breast cancer treatment, but can be

used post breast cancer treatment with specialist advice sought if other more appropriate methods are not available or not acceptable. Table 3 outlines the different methods of contraception and their pros and cons, this is adapted from the Faculty of Sexual and Reproductive Healthcare guidelines.

The limitation of our study was that this was a retrospective questionnaire relying on women to recall facts from sometimes many years ago, and was therefore subject to recall and self-reporting bias. Although the data was collected from a large tertiary unit with a diverse population, the cohort was still limited to those patients living in the South East of England.

This study has highlighted the importance of ongoing fertility counselling in those women who wish to conceive, and in particular contraceptive counselling in those who do not. We must adopt an approach of having frank discussions with our patients at the time of diagnosis, and on follow-up, so we are able to tailor their treatment to encompass issues of fertility and prevent unintended pregnancies.

Specific questions and information regarding fertility and contraception should be part of the routine follow-up care and information offered to all patients of reproductive age following treatment for breast cancer.

Disclosure

The authors have declared no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.breast.2019.05.004>.

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