



Original article

Fertility in Breast Cancer Survivors in the Middle East: A Retrospective Study



Hazem I. Assi^{a,1,*}, Rasha T. Kakati^{b,1}, Rose Mary Attieh^{a,1}, Jessica Khoury^a, Fares Sukhon^a, Juliett Berro^a, Eman Sbaity^c, Ziad Salem^a, Arafat Tfayli^a, Ibrahim A. Alameh^a, Nagi El Saghir^a

^a Department of Internal Medicine, American University of Beirut Medical Center, Beirut, Lebanon

^b Faculty of Medicine, American University of Beirut, Beirut, Lebanon

^c Department of Surgery, American University of Beirut Medical Center, Beirut, Lebanon

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ABSTRACT

Introduction: By the time they complete breast cancer therapy, many young patients are still of child-bearing age. We aim to estimate the incidence of pregnancies in women who completed treatment and examine the percentage of patients who received fertility counseling before initiation of therapy.

Material and methods: Electronic health records of breast cancer patients between 2008 and 2014 at AUBMC were screened for exclusion criteria of having metastatic disease or known infertility, still receiving therapy, and being above 42 years at diagnosis. Data about therapy and tumor characteristics was obtained for the included survivors who were interviewed as well via telephone for information about fertility preservation counseling, pregnancy occurrence, and delivery.

Results: 451 breast cancer patients were identified. 39 patients remained after application of exclusion criteria. 30.76% (n = 12) wanted more children at the time of diagnosis. 10.25% (n = 4) of all 39 patients treated for breast cancer achieved one or more pregnancy after a median time of 3.83 years after completion of therapy. 25% (n = 3) of women who wanted more children at diagnosis (n = 12) were able to conceive. 23.07% (n = 9) of patients discussed fertility with their primary oncologist prior to treatment initiation. 35.89% (n = 14) of patients were aware of fertility preservation technique availability, but none of these patients used one.

Conclusions: The observed rate of pregnancy is comparable to the literature. There is a lack in fertility counseling of breast cancer patients, and the rate of use of fertility preservation techniques is very low despite prior knowledge about their availability.

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Introduction

Breast cancer is the most common cancer among women worldwide. The American Cancer Society estimates that the lifetime risk for developing breast cancer today in an American woman is about 12.3% (1 out of 8 women) with a median age of diagnosis of 61 years [1,2]. In the Arab region, epidemiological studies show a

median age of only 50 years at presentation [3]. This implies that a significant proportion of women who survive breast cancer are still of childbearing age.

Adjuvant chemotherapy and hormone therapy for the treatment of breast cancer significantly impacts fertility [4]. Different regimens used have different levels of toxicity; some have no effect while others may induce transient amenorrhea or even lead to definitive ovarian failure. Subsequently, young women were often advised against pregnancy during their course of adjuvant therapy and soon after cessation, due to risks of teratogenicity and fetal complications, anomalies, preterm birth, and low birth-weight [5,6]. Additionally, ER + patients on adjuvant tamoxifen are often obliged to delay fertility for considerable periods of time while they are maintained on the drug for up to 5–10 years [7,8].

* Corresponding author. Associate Professor of Medicine, Department of Internal Medicine, Division of Hematology and Oncology, Naef K. Basile Cancer Center, American University of Beirut Medical Center, P.O. Box: 11-0236, Riad El Solh, 1107 2020, Beirut, Lebanon.

E-mail address: ha157@aub.edu.lb (H.I. Assi).

¹ Co-First Author.

A growing body of scientific evidence has now demonstrated that pregnancy after breast cancer does not compromise overall survival and that survivors should not be denied the opportunity of future conception [9,10]. Numerous techniques used prior to therapy initiation were developed in an effort to preserve fertility, including embryo or oocyte cryopreservation that are currently the methods of choice [11]. Fertility preservation techniques are more and more readily available, but their use is limited by the lack of appropriate fertility counseling. The importance of fertility counseling was highlighted in the 2013 recommendations of the American Society of Clinical Oncology: “as part of education and informed consent before cancer therapy, oncologists should address the possibility of infertility with patients treated during their reproductive years and be prepared to discuss possible fertility preservation options or refer patients to reproductive specialists” [12].

There remains a significant lack of reproductive counseling prior to breast cancer treatment initiation worldwide [13]. Many women are unaware that their chances of future parenthood might be affected by hormonal therapy or chemotherapy. In fact, a recent study published in October 2016 and conducted at the Cleveland Clinic between 2006 and 2014 showed that less than one-third of women had a documented fertility discussion with their physician prior to treatment. Of those who did receive documented counseling, nearly 90% sought some form of fertility preservation, demonstrating the massive impact of formal education sessions on cancer patients' childbearing choices [13]. Potential barriers to fertility counseling include physicians' level of knowledge about fertility preservation, attitudes and comfort level with the topic, patient preferences, and financial obstacles [14].

Impairment of fertility is a serious consequence of breast cancer treatment, posing significant psychological repercussions on young women which are often overlooked. Nevertheless, fertility preservation remains a major consideration for patients who are about to undergo adjuvant therapy. Senkus E. et al. found that 10% of women were willing to forego any chances of cure from breast cancer in order to preserve their childbearing ability [15].

In our review of the available studies revolving around breast cancer conducted in tertiary care centers from around the world, the incidence of pregnancy after curative therapy has been under-investigated, with only few reports which suggest a range of pregnancy achievement between 7% and 13% [13,16,17].

The primary objective of this study is to estimate the incidence of both planned and unplanned pregnancies in women who have completed adjuvant treatment for breast cancer and are still of reproductive age. The study also aims to determine the percentage of patients who received fertility counseling prior to initiation of therapy, as well as examine the impact of patient and disease characteristics on the likelihood of pregnancy after the end of treatment and evaluate adverse events in the mother and infant following pregnancy. The ultimate endpoint is to set a base for further prospective studies to alleviate the challenges we face with preserving fertility among young breast cancer patients.

Having such information will allow us to identify possible gaps in our current approach to young female breast cancer patients and to find realistic solutions to overcome them, thus improving the likelihood of childbearing in cancer survivors.

Material and Methods

Participants and recruitment

This is a retrospective study conducted at the American University of Beirut Medical Center (AUBMC), a tertiary care center where many cancer patients in Lebanon are treated each year. The

study was approved by the Institutional Review Board (IRB). Women treated for breast cancer between January 1, 2008 and December 31, 2014 were identified. Oral consents were obtained from all patients for future contact by the research team.

Data was collected from patient electronic health records (EHR) concerning demographics, tumor characteristics, and treatment regimens. Patients were not included if they were known to have metastatic disease, whether upon diagnosis or later, or known infertility, were still receiving adjuvant therapy, or were above the age of 42 years at diagnosis. Patients who were not followed up at AUBMC as per their EHR notes were not included in the study.

Subsequently, remaining patients were interviewed through telephone calls, using a questionnaire developed by the research team (see appendix). Information was collected on fertility issues or presence of children prior to diagnosis, desire for more children, and pregnancy achievement. Furthermore, patients were asked whether there was any discussion about the risk of infertility with their primary oncologist before initiation of therapy and their awareness and use of fertility preservation techniques. Patients who then met exclusion criteria or were deceased or out of reach were further excluded after the telephone interviews.

Statistical analysis

Responses to the questionnaire were analyzed using SPSS 25.0 with a p-value of <0.05 for significance. Two outcomes were considered: a primary outcome, achievement, completion of pregnancy and child delivery, and a secondary outcome, fertility discussion.

For each outcome, two-tailed Fischer's exact tests or Chi squared tests were used to analyze categorical variables. Continuous variables such as age, duration of chemotherapy and hormone therapy, as well as time to first achieved pregnancy after treatment cessation were tested for normality; age was normally distributed and analyzed using the independent samples *t*-test and the remaining were analyzed using the Mann-Whitney U independent samples test.

Frequencies and means were used to describe the sample and compare the patient and tumor characteristics as well as treatment regimens of the women who achieved pregnancy compared to those who did not, and p-values were calculated to determine if there is statistical significance between the two groups. Similar analysis was also computed for patient-reported outlook towards children, fertility preservation and choice of therapy, and fertility discussion with primary oncologist. Furthermore, the patients who had intent of pregnancy and wanted more children upon diagnosis were divided according to their achievement of pregnancy and their characteristics were also compared and analyzed for statistical significance between groups. Additionally, outcomes of the pregnancies achieved were reported to describe adverse events in the infants or mothers following the pregnancies.

Results

Sample characteristics

We were able to identify 451 women treated for breast cancer between 2008 and 2014. 138 women with valid data remained after screening the EHR for exclusion criteria. 39 patients remained after further exclusions determined telephone interviews as some were deceased or were out of reach.

The median age at diagnosis was 36 years. Most women fell in the age category of 31–40 years ($n = 27, 69.2\%$). Baseline characteristics of the women included in our study in addition to their corresponding treatment regimens were compiled (Table 1).

Thirty-three (84.61%) women already had children prior to diagnosis, and twelve (30.76%) wanted more children at diagnosis (Table 1).

Fertility discussion

Nine (23.07%) women reported having discussed fertility with their primary treating oncologist prior to treatment initiation, out of which only four (44.44%) felt that it was sufficient. Fourteen (35.89%) were aware of the availability of fertility preservation techniques before starting breast cancer therapy, whether from their oncologist or from other sources, but none of them actually used one. Among the women who had fertility discussion, six women (66.7%), were aware of fertility preservation techniques. Additionally, one woman (2.56%) stated that fertility concerns affected their choice of therapy (Table 1).

Chi squared analysis revealed that estrogen receptor (ER) status ($p = 0.036$) and awareness of fertility preservation techniques prior to initiation of therapy ($p = 0.047$) were significantly correlated with the outcome of having a fertility discussion with the primary oncologist (Table 2).

Pregnancies

Four (10.25%) women were able to achieve pregnancy, with a total of 6 pregnancies ranging between one and two per woman, after a median time of 3.83 years after completion of therapy. Only one (25%) of the women who achieved pregnancy interrupted hormonal tamoxifen treatment in order to get pregnant. Out of a total of 6 pregnancies, 2 (33.33%) were live births and 2 (33.33%) were miscarriages, and 2 (33.33%) of patients who achieved pregnancy were pregnant at the time of conduction of the telephone interviews (Fig. 1). None of the two women experienced breast cancer recurrence or complications during delivery, or resumed treatment after pregnancy, and none of the children delivered had any birth defects or growth impairment.

Of the twelve women who wanted more children and had intent for pregnancy, three (25%) achieved pregnancy. Those who achieved pregnancy had a mean age at diagnosis of 28.33 years (sd 3.055) and were significantly ($p = 0.029$) younger than those who did not achieve pregnancy and had a mean age at diagnosis of 36.67 years (sd 5.268) (Table 1). All women who achieved pregnancy with intent ($n = 3$, 100%) did not receive any hormonal therapy regimen, including tamoxifen. Of those who did not achieve pregnancy while having intent to conceive ($n = 9$), the majority ($n = 8$, 88.9%) did receive tamoxifen hormonal therapy specifically.

Discussion

This is the first study that looks at the chances of pregnancy in breast cancer survivors in Lebanon or the Middle Eastern Arab region in general. This is also the first study in the Middle East to examine the rate of discussion of fertility preservation with their primary treating oncologists and the prevalence of pregnancy achievement among women who completed breast cancer treatment, in addition to the outcome of those pregnancies, a matter which is not sufficiently examined in the literature in the region.

The median age at diagnosis in our study is 36 years many women may considerably still be of reproductive age, have not yet finished their families, and desire more children at diagnosis. Although 84.61% of women already had children prior to diagnosis, this does not necessarily imply that they completed their families by the time they were diagnosed. Our sample shows that 30.76% of women desire more children upon diagnosis, which is comparable to those reported in the literature at 35%–56% and may indicate

concern with fertility and pregnancy achievement [18]. Despite the low rates of fertility concerns affecting treatment choice at 2.56% as compared to 29% reported by King et al, we must acknowledge that knowledge of the impacts on fertility must precede treatment considerations [19].

The rate of pregnancy achievement of 10.25% after a mean duration of 3.87 years after treatment cessation is consistent with that reported in other studies between 7 and 13% after a mean of 3 years [20]. However, it is also necessary to highlight rates in women with pregnancy intent at 25%. Successful pregnancies have shown an equal distribution between pregnancies, live births, and miscarriages. Specifically, 33.33% of women were able to achieve a live birth, as compared to a rate of 5.31% seen in other studies [17].

Among women with pregnancy intent, none of those who received tamoxifen hormone therapy ($n = 8$, 66.7%) were able to achieve pregnancy. However, tamoxifen poses temporary and indirect effects on fertility, and may not have long-term detrimental effects on fertility after its cessation. In our study, no significant correlation was found with receiving the different chemotherapy types.

Younger women were also significantly more likely to achieve pregnancy in our sample, which is consistent with the literature, as several studies reveal that age seems to be the strongest predictor of chemotherapy-induced amenorrhea even after completion of therapy [18,19,21].

The reported rate of fertility discussion with the primary oncologist at 23.07% was comparably lower than those of previous studies ranging from 34 to 72% [13,18]. In addition, less than half of the women who had the discussion subjectively reflected that it was not sufficient. No woman used any fertility preservation techniques, which is striking as compared to rates reported by other studies at 10%, despite the notable level of awareness of their availability reported by 35.89% of women in our sample [18].

Among the nine women who had a fertility discussion with their primary oncologist, five (55.6%) had ER negative tumors, which was slightly more than those who had ER positive tumors ($n = 4$, 44.4%). This finding is in line with the suggestions of the literature which suggest that estrogen receptor status influences physicians' consideration for fertility discussion with patients. Specifically, King et al. reported that physicians would refer a woman with estrogen receptor negativity more than with positivity [19]. The aforementioned strongly implies that disease and patient characteristics are the main determinants, and often patient preferences or desires are overlooked [19].

Additionally, six (66.7%) of those who had the fertility discussion were aware of fertility preservation techniques prior to therapy initiation. It is difficult to discern whether the fertility discussion was initiated by the patient or the oncologist. It is important to note, however, that many women subjectively reported that their source of knowledge was not their oncologist. Also, most ($n = 7$, 58.3%) of the women who wanted more children at diagnosis did not discuss fertility with their oncologist; this may signify that most women were not aware of the risk of infertility caused by their treatment, considering that they would discuss this matter if it is of concern. This sheds light on the importance of patient education on treatment regimens. Moreover, the fact that no woman used fertility preservation techniques questions the quality of the discussions despite their occurrence, which is of utmost importance. However, this could also be attributed to cultural factors interfering with a woman's own decision to use fertility preservation techniques.

Furthermore, the literature describes correlates with the discussion that were not shown to be significant in our study. King et al. also reported that whether women had children prior to diagnosis or a partner were also determinants of the fertility

Table 1

Patient demographics, tumor characteristics, and treatment regimens, in addition to outlook towards children, fertility preservation, and choice of therapy, as well as discussion with primary oncologist among women with breast cancer and their comparison among those who did or did not achieve pregnancy while having pregnancy intent.

| Demographics and Tumor Characteristics | | | | | |
|--|-------------------------------|-------------------------------|----------------------------|-----------------------------------|---------|
| | Total sample | Women with pregnancy intent | | | p-value |
| | Number (%) or Mean (sd) [IQR] | Number (%) or Mean (sd) [IQR] | | | |
| | All women (n = 39) | All women (n = 12) | Achieved pregnancy (n = 3) | Did not achieve pregnancy (n = 9) | |
| Age upon diagnosis in years | 35.77 (4.94) [7] | 34.58 (6.01) | 28.33 (3.055) [<1] | 36.67 (5.268) [5] | 0.029* |
| 21–30 | 6 (15.4) | 3 (25) | 2 (66.7%) | 1 (11.1%) | 0.173 |
| 31–40 | 27 (69.2) | 7 (58.3) | 1 (33.3%) | 6 (66.7%) | |
| 41–42 | 6 (15.4) | 2 (16.7) | 0 | 2 (22.2%) | |
| Nationality | | | | | |
| Lebanese | 32 (82.1) | 10 (83.3) | 3 (100%) | 7 (77.8%) | 1 |
| Syrian | 1 (2.6) | 0 | 0 | 0 | |
| Iraqi | 5 (12.8) | 1 (8.3) | 0 | 1 (11.1%) | |
| Other | 1 (2.6) | 1 (8.3) | 0 | 1 (11.1%) | |
| Type of carcinoma | | | | | |
| In situ | 5 (12.8) | 1 (8.3%) | 1 (33.3%) | 0 | 0.5 |
| Invasive ductal | 27 (69.2) | 4 (33.3%) | 1 (33.3%) | 3 (33.3%) | |
| Invasive lobular | 2 (5.1) | 2 (16.7%) | 0 | 2 (22.2%) | |
| Unspecified | 5 (12.8) | 5 (41.7%) | 1 (33.3%) | 4 (44.4%) | |
| Size in cm | 2.36 (1.2) [2] | 2.044 (0.842) | 1.933 (1.401) [<1] | 2.1 (0.583) [1] | 0.714 |
| <2 | 12 (30.8) | 5 (55.6%) | 2 (66.7%) | 3 (33.33%) | 1 |
| 2–5 | 21 (53.8) | 4 (44.4%) | 1 (33.3%) | 3 (33.33%) | |
| >5 | 2 (5.1) | 3 (25%) | 0 | 3 (33.33%) | |
| Unknown | 4 (10.3) | 0 | 0 | 0 | |
| Estrogen receptor status | | | | | |
| Negative | 10 (25.6) | 3 (25%) | 1 (33.3%) | 2 (22.2%) | 1 |
| Positive | 28 (71.8) | 9 (75%) | 2 (66.7%) | 7 (77.8%) | |
| Unknown | 1 (2.6) | 0 | 0 | 0 | |
| Progesterone receptor status | | | | | |
| Negative | 13 (33.3) | 4 (33.3%) | 2 (66.7%) | 2 (22.2%) | 0.236 |
| Positive | 25 (64.1) | 8 (66.7%) | 1 (33.3%) | 7 (77.8%) | |
| Unknown | 1 (2.6) | 0 | 0 | 0 | |
| HER2 receptor status | | | | | |
| Negative | 14 (35.9) | 5 (41.7%) | 1 (33.3%) | 4 (44.4%) | 1 |
| Positive | 23 (58.9) | 7 (58.3%) | 2 (66.7%) | 5 (55.6%) | |
| Unknown | 2 (5.1) | 0 | 0 | 0 | |
| Lymph node status | | | | | |
| Negative | 24 (61.5) | 5 (41.66%) | 3 (100%) | 2 (22.22%) | 0.061 |
| Positive | 14 (35.9) | 6 (50%) | 0 | 6 (66.66%) | |
| Unknown | 1 (2.6) | 1 (8.33%) | 0 | 1 (11.11%) | |
| Grade | | | | | |
| I | 3 (7.7) | 0 | 0 | 0 | 1 |
| II | 14 (35.9) | 5 (41.66%) | 1 (33.3%) | 4 (44.44) | |
| III | 19 (48.7) | 5 (41.66%) | 2 (66.7%) | 3 (33.33%) | |
| Unknown | 3 (7.7) | 2 (16.66%) | 0 | 2 (22.22%) | |
| Treatment Regimens | | | | | |
| Type of chemotherapy | | | | | |
| Fluorouracil, anthracyclines, and/or cyclophosphamide | 31 (79.5) | 9 (75) | 2 (66.7) | 7 (77.8) | 1 |
| Taxanes | 30 (76.9) | 9 (75) | 2 (66.7) | 7 (77.8) | |
| Trastuzumab (Herceptin) | 18 (46.2) | 3 (25) | 1 (33.3) | 2 (22.2) | |
| None | 6 (15.4) | 2 (16.7) | 0 | 2 (22.2) | |
| Type of hormone therapy | | | | | |
| Tamoxifen | 27 (69.2) | 8 (66.7) | 0 | 8 (88.9) | 0.018* |
| GnRH agonists (goserelin or triptorelin) | 8 (20.5) | 3 (25) | 0 | 3 (33.3) | |
| Aromatase inhibitors | 2 (5.1) | 2 (16.7) | 0 | 2 (22.2) | |
| None | 12 (30.8) | 4 (33.3) | 3 (100) | 1 (11.1) | |
| Type of surgery | | | | | |
| Partial mastectomy | 23 (59) | 7 (58.3) | 3 (100) | 4 (44.4) | 1 |
| Modified radical mastectomy | 11 (28.2) | 4 (33.3) | 0 | 4 (44.4) | |
| Total mastectomy | 5 (12.8) | 1 (8.3) | 0 | 1 (11.1) | |
| Outlook Towards Children, Fertility Preservation, and Choice of Therapy, and Discussion with Oncologist | | | | | |
| Wanted more children at diagnosis | 12 (30.8%) | 12 (100%) | 3 (100%) | 9 (100%) | – |
| Had children before diagnosis | 33 (84.6%) | 11 (91.7%) | 2 (66.7%) | 9 (100%) | 0.25 |
| Discussed risk of infertility with primary treating oncologist prior to therapy initiation | 9 (23.1%) | 5 (41.7%) | 1 (33.3%) | 4 (44.4%) | 1 |
| Aware of available fertility preservation techniques prior to therapy initiation | 14 (35.9%) | 3 (25%) | 1 (33.3%) | 2 (22.2%) | 1 |

(continued on next page)

Table 1 (continued)

| | | | | | |
|--|----------|----------|---|-----------|---|
| Actually used fertility preservation | 0 | 0 | 0 | 0 | 0 |
| Fertility concerns affected choice of treatment | 1 (2.6%) | 1 (8.3%) | 0 | 1 (11.1%) | 1 |

*statistically significant at $p < 0.05$.
[IQR]: Inter-quartile range.

Table 2

Significant correlates with having a fertility discussion with the primary oncologist.

| | Number of women who had fertility discussion (%) (n = 9) | Number of women who did not have fertility discussion (%) (n = 30) | p-value |
|--|---|---|---------|
| ER status | | | 0.036* |
| Positive | 4 (44.4) | 24 (80) | |
| Negative | 5 (55.6) | 5 (16.6) | |
| Unknown | 0 | 1 (3.33) | |
| Patient awareness of fertility preservation techniques | | | 0.047* |
| Aware | 6 (66.7) | 8 (26.7) | |
| Not aware | 3 (33.3) | 22 (73.3) | |

*statistically significant at $p < 0.05$.

Outcome of Pregnancies Achieved

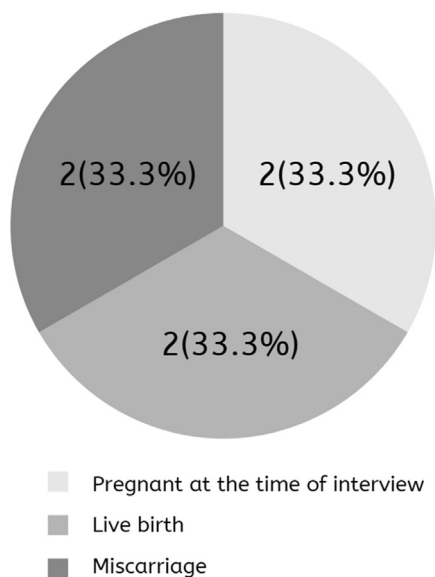


Fig. 1. Outcome of 6 pregnancies among the 4 women who achieved pregnancy.

discussion. Among those who had children prior to diagnosis, most women ($n = 25$, 75.8%) did not have any fertility discussion with their primary oncologist. This may imply that, according to our data, having children prior to diagnosis could play a role in the decision of the oncologist to discuss fertility.

Additionally, the BCY3/BCC 2017 survey carried out at the 2016 3rd European School of Oncology (ESO) – European Society for Medical Oncology (ESMO) Breast Cancer in Young Women Conference (BCY3) and the 15th St. Gallen International Breast Cancer Conference 2017 (BCC 2017) poses several considerations. The survey examined physicians' knowledge, attitudes and practice towards fertility and pregnancy related issues in young breast cancer patients and reported relevant findings. Around 30–47% of respondents agreed or were neutral concerning pregnancy increasing the risk of breast cancer recurrence, or reported never consulting guidelines regarding pregnancy after breast cancer and/or fertility preservation. Moreover, 18% of respondents were unaware if fertility preservation techniques were accessible [22].

These factors may have contributed to the low fertility discussion rates observed in our sample.

This study sheds light that women may still desire to have children despite their disease status. Studies have shown that physicians are highly concerned with possible delays in treatment. However, fertility preservation does not always imply clinical delay, especially with rapid referrals and early stage disease; ideally, fertility discussions should occur soon after diagnosis in order to consider fertility preservation and refer patients to fertility specialists that can best assess whether they are candidates [18]. Some special considerations that may come into play in this region are the lack of comprehensive breast cancer centers involving a multidisciplinary team of oncologists, fertility specialists and psychiatrists on one hand, and on the other hand the tremendous interference of religious and social pressure with a women's choice of therapy. However, recently and outside the window of our study, our institute initiated a new fertility clinic whereby referrals and fertility discussions have increased. Thus, the rates observed may currently differ, a matter which warrants further investigation but may have promising and positive prospects.

The main limitation of this study was the small sample size due to a multitude of exclusion criteria and many lost-to-follow-up patients. This diminished the number of those with positive outcomes, making it difficult to draw generalizable conclusions. Importantly, questions targeting the discussion of fertility with the primary oncologist were subject to recall bias on the part of the interviewee. Additionally, in the case of fertility discussion, it is unknown whether the physician or the patient initiated the topic, making it difficult to accurately locate where the deficits lie. In light of the new fertility clinic and recent advances at our institution, the team has started working on a second branch of this study, a prospective analysis that would serve as a more recent follow up with a larger sample size reaching 200 patients, compensating for the current lack.

Conclusions

Rates of pregnancy achievement among breast cancer survivors in Lebanon are comparable to those reported in the literature and correlate with age upon diagnosis and the type of treatment received. However, the extent of discussion of fertility with primary oncologists remains low, and that of the use of fertility preservation techniques is null up to 2014, as examined in this study. Rates of discussion of fertility risks and the benefits of preservation

techniques, in addition to the rates of use of preservation techniques, is expected to have increased in recent years after 2014, considering the advent of a new fertility clinic at our institution. It is important to note that the discussion of fertility and pregnancy during a time of breast cancer diagnosis is difficult for both the patient and the physician. However, informed consent and patient involvement in the decision-making process of their treatment is essential. Considering that the risk of infertility has notable impacts on the patient in terms of quality of life and psychosocial factors, it is thus necessary to avoid assumptions of patient priorities and engage in educational discussions on the implications on their treatment [18]. Through this study, we shed the light on the importance of informed consent, patient education, and a shared decision-making process between oncologists and their patients.

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Declarations of interest

None.

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Appendix. Telephone Questionnaire with Breast Cancer Survivors

1. Did you have any fertility issues prior to diagnosis? (Yes/No)
2. Did you have children prior to diagnosis? (Yes/No)
3. Did you want more children at the time of diagnosis? (Yes/No)
4. Was there any discussion about the risk of infertility with your primary treating oncologist prior to beginning therapy? (Yes/No)
5. Were you aware of available fertility preservation techniques prior to beginning of therapy? (Yes/No)
6. Were any fertility preservation techniques actually used? (Yes/No) If yes, please specify
7. Do you feel that you received enough counseling regarding the issue of fertility from your primary treating oncologist prior to treatment initiation? (Yes/No) If no, what would you have liked to know?
8. Did you have any planned/unplanned pregnancies following completion of therapy for breast cancer? (Yes/No) If yes, please specify the number of pregnancies and their outcome, and the duration between the end of treatment and first pregnancy. (Planned/Unplanned, Miscarriage/Abortion/Stillbirth/Live Birth, Duration)
9. Were there any complications during delivery of children after completing breast cancer treatment? (Yes/No)
10. Did the children delivered after completion of breast cancer therapy have any medical issues (birth defects, growth impairment, etc)? (Yes/No)
11. Was there treatment interruption in order to get pregnant? (Yes/No)
12. Did fertility concerns affect your choice of cancer treatment? (Yes/No)
13. Did you resume treatment after pregnancy? (Yes/No)

14. Did breast cancer recur after/during pregnancy? (Yes/No) If yes, please specify the time after which recurrence occurred. (Time)

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