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Disparities in Counseling Female Cancer Patients for Fertility Preservation

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Abstract

Background: Female cancer patients who are exposed to gonadotoxic chemotherapy are at risk of future infertility. Research suggests that disparities in fertility preservation counseling (FPC) may exist. Previous research is limited by recall bias; therefore, this study examined objective electronic medical chart data regarding FPC at an academic medical center.

Materials and Methods: This study included reproductive-aged women (18–45 years old) with a diagnosis of breast, gynecological, or hematological cancer and who were exposed to a gonadotoxic chemotherapeutic agent from 2009 to 2013. Chi-square and logistic regression analyses were utilized to analyze disparities in FPC.

Results: Two hundred fifty-nine women met the study criteria. One hundred eighty-one women were diagnosed with breast cancer, 52 with hematological cancer, and 26 with gynecological cancer. 160/259 (62%) women had documented counseling for fertility preservation (FP), 60 (23%) women were not counseled as counseling was determined to be ''not applicable,'' 16 (6%) women were not counseled and no explanation was given for the lack of counseling, and counseling was not documented in 23 (9%) charts. Age, marital status, and racial/ethnic background were related to counseling status. Patients with gynecological or hematological cancer were more likely to be counseled than other patients. Logistic regression results demonstrated that FPC was largely driven by cancer diagnosis.

Conclusions: Although cancer diagnosis was the greatest predictor of FPC, disparities were evident in the counseling of female cancer patients for FP treatment. Equality in counseling female patients for FP treatment is imperative to reduce the risk of emotional harm and future infertility.

Keywords: reproductive health, cancer, health disparities

Introduction

Young female cancer patients are increasingly interested in fertility preservation counseling (FPC).[1,2] Before undergoing gonadotoxic radiation and chemotherapy, many female cancer patients can safely and effectively participate in egg and/or embryo cryopreservation.[3–6] Despite the safety of fertility preservation (FP) treatment, fewer than half of women pursue treatment[7–9] and this decision has been found to lead to regret.[10–12] Feelings of regret may be lessened for those who engage in decision-making after receiving FPC [counseling regarding the risks of cancer treatment (*e.g.*, chemotherapy) on the patient's future fertility] from their oncologist and a fertility specialist.[13]

Unfortunately, research confirms that many oncologists do not discuss FP with their female patients[9,12–16] or do so in ways that are unsatisfactory.[2,17] Research on the FPC of young female cancer patients has also revealed that multiple patient variables, including race, income, education, age, and/or sexual orientation, influence who is counseled for and gains access to FP treatment.[18–21] Physician (*e.g.*, gender, medical specialty, attitude/knowledge about FP, assumptions about patients' desire for FP, discomfort discussing FP, concerns regarding posthumous reproduction, and focus on survivorship issues) and medical (*e.g.*, cancer type, prognosis, immediate need to begin cancer treatment) characteristics may also result in disparate FPC.[15,16,18,19,22]

Disparities in FPC have not been studied extensively thus far; however, it appears that insured nulliparous, young white women with breast cancer may be the most likely to be counseled by a fertility specialist for FP.[23] It is unclear if age, race, or cancer diagnosis contribute equally in the prediction of

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who receives FPC. However, given that FPC is recommended for all patients undergoing gonadotoxic treatment regardless of medical or demographic characteristics,[6,24–26] FPC should be conducted with all cancer patients of reproductive age. Overall, however, the prevention of disparities in FPC for female cancer patients is a relatively understudied topic. What little data exist may be weakened by recall bias or other bias as it have primarily focused on cancer survivor's recollection of FPC, rates of counseling by fertility specialists, or physician's self-reported counseling practices.[16,21,23]

Although little is known about disparities in FPC, a wealth of research supports the existence of socioeconomic-based disparities in counseling and access to fertility treatment among female noncancer patients.[27–29] Many factors influencing disparate counseling and access to treatment begin before the first appointment with a fertility specialist. Factors such as lack of information, mistrust of the medical system, social stigma of infertility, communication/language barriers, access only to low-volume in vitro fertilization (IVF) centers, and poor insurance coverage have all been found to affect access to fertility treatment.[29–34] Those who succeed in accessing treatment may encounter additional communication/language difficulties as well as biases about stereotypic hyperfertility in patient populations, effective/appropriate intended parents, traditional family building, and other sociocultural biases.[33–36] As with infertile patients, disparities in FPC or access to FP may result in unnecessary future impairment in quality of life in women who do not undergo FP.[10–12,21,37–39]

As of 2006, our medical center's electronic medical record (EMR) system has included a field, which requires medical oncologists to indicate whether or not they counseled their patients regarding the risk of cancer treatment on their fertility. Specifically, medical oncologists are asked to indicate with a yes, no, or not applicable to the following question: ''Has the patient been informed about the impact their treatment may have on fertility?'' The purpose of the current study is to assess the rate of documented FPC by oncologists in a sample of breast, gynecological, and hematological cancer patients exposed to chemotherapy utilizing this questionnaire as well as to determine if racial/ethnic, socioeconomic, and demographic variables were associated with FPC among young female cancer patients.

Materials and Methods

Participants

The sample included 259 women with a diagnosis of breast, gynecological, or hematological cancer who were treated at a large private medical center in the United States from 2009 to 2013. Patients who were younger than 18 years; older than 45 years; with no documented exposure to chemotherapy treatment; or with a cancer diagnosis other than breast, gynecological, and hematological cancer were excluded from the study to examine the experiences of patients most frequently counseled for FP, to help ensure a robust sample size, and as the gonadotoxic risk of many chemotherapies is known.

Procedures

EMRs for patients in the sample were retrospectively reviewed. Demographic and medical history data, including age, race, ethnicity, marital status, insurance status, cancer diagnosis, cancer stage, and type of chemotherapy, and FPC status were collected. The study was approved by the Institutional Review Board at the Northwestern University in Chicago, Illinois. There were no conflicts of interest.

Statistical analyses

Statistical analyses using SPSS (IBM, Armonk, NY) were performed using nonparametric tests. Logistic regression analysis was used to test the model for age, marital status, race, cancer diagnosis, and stage as predictors of FPC. Variables found to differentiate counseling status in univariate analyses were included in the hierarchical binomial logistic regression analysis. Demographic variables were entered into the first block, and medical variables were entered into the second block. Analyses are based on available data, sample sizes are provided, and $p < 0.05$ (two-tailed) was considered significant.

Results

The search of EMRs identified 259 patients who met inclusion criteria for this study. The average age of women was 33.99 years (range = 19–42; standard deviation [SD] = 5.32). The majority of women were non-Hispanic white (59.5%), married (53.9%), and with private insurance (78.8%). Patients were relatively evenly distributed across study years with $\sim$20% of patients being diagnosed in each year from 2009 to 2013. The most common diagnosis among women was breast cancer (69.9%, $n = 181$) followed by hematological (*i.e.*, leukemia/lymphoma) cancer (20.1%, $n = 52$) and gynecological cancer (10.0%, $n = 26$). 19.7% of patients presented with stage I cancer, 39.4% with stage II, 13.5% with stage III, 4.2% with stage IV, and cancer stage was unknown for 33.2% of patients.

The majority of breast cancer patients were exposed to doxorubicin/cyclophosphamide chemotherapy (AC; 130/181, 71.8%), doxorubicin/bleomycin/vinblastine/dacarbazine chemotherapy for hematological patients (ABVD; 32/52, 61.5%), and the two most common chemotherapeutic agents for gynecological cancers were carboplatin (8/26; 30.8%) and cyclophosphamide (7/26; 26.9%) ($p < 0.05$). The demographic characteristics of the sample are presented in Table 1.

160/259 (61.8%) known gonadotoxic chemotherapy-exposed women had documented FPC, 60 (23.2%) women were not counseled as FPC was determined to be ''not applicable,'' 16 (6.2%) women's charts indicated ''no'' as they were not counseled and no explanation was given for the lack of FPC, and FPC was not documented in 23 (8.9%) charts.

In univariate analyses, younger women ($p < 0.05$) and women with a diagnosis of gynecological or hematological cancer ($p < 0.05$) were more likely to have documented FPC than older women with breast cancer. Fifty-five percent of breast cancer, 73% of gynecological cancer, and 81% of hematological cancer patients were counseled about FP. The average age of those counseled was 32.96 years, (SD = 5.61), 34.84 years (SD = 4.66) for those not counseled, 35.07 years (SD = 4.49) for those deemed not appropriate for FPC, and 35.07 years (SD = 4.49) for those with no documentation of FPC. Divorced women were less likely to be counseled than women of any other marital status ($p < 0.05$).

Group differences in counseling were also found among patients with diverse racial/ethnic backgrounds ($p < 0.05$)

Table 1. Demographic Characteristics of Patients with Documented Exposure to Gonadotoxic Chemotherapeutic Agents by Counseling Status

Variable	Counseling status: Yes, N (%)	Not applicable, N (%)	No, N (%)
Ethnicity			
Caucasian	96 (60.0)	36 (60.0)	7 (43.8)
African American	20 (12.5)	12 (20.0)	2 (12.5)
Asian	11 (6.9)	5 (8.3)	1 (6.3)
Hispanic	5 (3.1)	1 (1.7)	—
Other/unknown	28 (17.5)	6 (10.0)	6 (37.6)
Marital status			
Single	71 (44.4)	16 (26.7)	9 (56.3)
Married	84 (52.5)	37 (61.7)	7 (43.8)
Divorced	3 (1.9)	6 (10.0)	—
Unknown	2 (1.3)	1 (1.7)	—
Cancer diagnosis			
Breast	99 (61.9)	50 (83.3)	15 (83.8)
Gynecological	19 (11.9)	6 (10.0)	—
Hematological	42 (26.3)	4 (6.7)	1 (6.3)
Cancer stage			
I	18 (11.3)	2 (3.3)	1 (6.3)
II	61 (38.1)	26 (43.3)	8 (50.0)
III	21 (13.1)	12 (20.0)	—
IV	5 (3.1)	3 (5.0)	—
Unknown	55 (34.4)	17 (28.3)	7 (43.8)
Year of diagnosis			
2009	41 (25.6)	19 (31.7)	4 (25.0)
2010	39 (24.4)	8 (13.3)	2 (12.5)
2011	28 (17.5)	6 (10.0)	2 (12.5)
2012	29 (18.1)	11 (18.3)	1 (6.3)
2013	23 (14.4)	16 (26.7)	7 (43.8)
Insurance coverage			
Private insurance	129 (80.6)	47 (78.3)	10 (62.5)
Medicaid/Medicare/ self-pay	26 (16.3)	9 (15.0)	2 (12.5)
Unknown	5 (3.1)	4 (6.7)	4 (25.0)

Table 2. Rate of Fertility Preservation Counseling in Cancer Patients with Documented Exposure to Gonadotoxic Chemotherapeutic Agents by the Year of Diagnosis

Year	Documented FPC: No (%)	Yes (%)	Not applicable	Missing	Total
2009	4 (6)	41 (61)	19 (28)	3 (5)	67
2010	2 (4)	39 (71)	8 (15)	6 (11)	55
2011	2 (5)	28 (64)	6 (14)	8 (18)	44
2012	1 (2)	29 (66)	11 (25)	3 (7)	44
2013	7 (14)	23 (47)	16 (33)	3 (6)	49

Percentages are rounded to tenths and may not add to 100.
FPC, fertility preservation counseling.

with 62% (96/154) of white, 65% (11/17) of Asian, 53% (20/38) of black, 62% (13/21) of unknown race, and 83% (5/6) of Hispanic women with documented FPC. The majority of patients had private insurance ($n=209$ with private insurance, $n=39$ with Medicaid or Medicare, and $n=15$ no information regarding insurance) and having private insurance did not differentiate documentation of counseling. A significant difference in documentation of counseling was also found based on the year of cancer diagnosis ($p<0.05$); 61% of patients were counseled in 2009, 71% in 2010, 64% in 2011, 66% in 2012, and 47% in 2013 (Table 2).

We were interested in examining the relationship between demographic and medical variables in the prediction of FPC in our sample of breast, gynecological, and hematological cancer patients exposed to chemotherapy. Only those variables found to differentiate counseling status using chi-square analyses were included in the hierarchical logistic regression analysis. Logistic regression resulted in unique variance contribution of cancer diagnosis in a model, including age, marital status, race, cancer diagnosis, and year of cancer diagnosis. Demographic variables were entered into the first block, and medical variables were entered into the second block to better assess the contribution of medical variables to the prediction of FPC. FPC was dichotomized into two groups of patients who had either received counseling or who did not receive counseling or were deemed inappropriate for counseling to directly compare the experiences of women who did and did not receive FPC. Racial/ethnic background was also dichotomized into participants who self-reported as white or as other racial/ethnic group due to small subgroups of racial/ethnic minority groups, and this is consistent with previous studies examining race and FPC.[23] Marital status was recorded into two groups of married or unmarried women due to small subgroups of divorced and widowed women. Evaluation of the log-likelihood test of the overall model for FPC was significant ($\chi^2=22.233$, $df=6$, $p=0.001$). The Hosmer–Lemeshow (H-L) goodness-of-fit statistic was not significant ($p=0.728$) suggesting a good model fit. Being counseled for FP was related to having a hematological cancer diagnosis (odds ratio [OR]=4.210, 95% confidence interval [CI]=1.275–13.907), with patients with a hematological cancer being more likely than breast cancer patients to have documented FPC (Table 3). Nagelkerke's R^2, a measure of strength of association between the predictors and the dependent variable, was 0.139 for the entire model (68.9% correctly classified).

Discussion

In the current study, we found that the majority of female breast, gynecological, and hematological cancer patients exposed to gonadotoxic chemotherapy appear to have been counseled for FP treatment by their medical oncologist. While this was an encouraging finding, not all women received counseling. Furthermore, univariate analyses revealed that demographic and medical differences in FPC were evident in the documentation of counseling of a large number of cancer patients for FP treatment. However, the greatest predictor of who received FPC was the patient's cancer diagnosis; women with a hematological cancer diagnosis were more likely to have documented FPC than breast cancer patients. Overall, however, the lack of documented FPC for all female cancer patients in this study heightens the concern about disparate treatment in female chemotherapy-exposed breast, gynecological, and hematological cancer patients as previous studies have identified disparities in referral to FP treatment as well as among those patients who undergo FP treatment.

Although previous studies examining FPC among chemotherapy-exposed female cancer patients have identified sociodemographic and diagnostic disparities in FPC, the

Table 3. Binomial Logistic Regression Predicting Fertility Preservation Counseling from Demographic and Medical Variables

Predictor	*β*	*SE β*	*Wald's* χ^2	*df*	p	*OR (95% CI)*
Race	–0.187	0.147	1.629	1	0.202	0.829 (0.622–1.106)
Marital status	–0.458	0.294	2.421	1	0.120	0.633 (0.355–1.126)
Age at diagnosis	–0.022	0.039	0.329	1	0.567	0.978 (0.907–1.055)
Cancer diagnosis[a]			6.069	2	0.048	
Gynecological	0.479	0.517	0.858	1	0.354	1.614 (0.586–4.446)
Hematological	1.437	0.610	5.559	1	0.018	4.210 (1.275–13.907)
Year of diagnosis	–0.185	0.101	3.327	1	0.068	0.831 (0.682–1.014)
Constant	373.631	203.499	3.371	1	0.066	—

[a]Reference category = breast cancer.
CI, confidence interval; OR, odds ratio.

results of these studies while valuable are also limited in that they (1) did not analyze EMR data regarding FPC and relied primarily on patient and physician recollection of FPC from as many as 17 years before data collection,[21] (2) were based on EMR data that did not appear to include prompts for FPC from incomplete samples of male and female patients in a single year,[40] or (3) focused on EMR documentation of FPC only among patients who had accessed fertility specialists rather than on patients who did or did not receive FPC by their oncologists.[20,23] Unfortunately, the use of select patient data based on patient's long-term memories rather than EMR data may be impaired by recall and/or selection bias. Furthermore, in the United States, a medical oncologist is often the first physician to be able to provide FPC, and disparate counseling from oncologists likely has an effect on the subsequent referral and access to FP treatment. Access to FP treatment may also be limited by patient's health insurance coverage and out-of-pocket costs and/or beliefs about the acceptability of FP among other variables. Thus, the current study examined objective data regarding FPC documented at the time of oncological counseling in a large group of female breast, gynecological, and hematological chemotherapy-exposed cancer patients.

Consistent with previous research on age-related disparities in referral and access to FP treatment in chemotherapy-exposed female cancer patients,[21,23,41] older women, who may have the highest risk of infertility after gonadotoxic treatment, were least likely to be counseled for treatment in our univariate analyses. Although not significant in multivariate analyses, age is an important predicator of baseline fertility, thus, older women are more likely to have baseline decreased ovarian reserve before undergoing cancer treatment. Given the double risk of decreased ovarian reserve at baseline and following chemotherapy exposure in older women, the continued assessment of age-related disparity in FPC is warranted. It is unclear if age differences in documentation for FPC among chemotherapy-exposed female cancer patients are the result of physician assumptions about older women's desire for future family building or if older patients may be more likely to have completed their childbearing and volunteer that information to their medical providers, thus FPC would be deemed not applicable.

The disparity in breast cancer patients receiving counseling compared with other patients in this study is concerning as the majority of these patients were exposed to a known gonadotoxic alkylating agent (cyclophosphamide chemotherapy), and this chemotherapy treatment can have profound effects on fertility.[3,42] Our finding that breast cancer patients were less likely to receive FPC differs from that of Goodman et al.,[23] showing that chemotherapy-exposed breast cancer patients had the greatest probability of receiving FPC. The different outcomes between the studies may be the result of different counseling patterns of oncologists in the two study sites and/or sample differences. For example, the present study had a larger number of breast cancer patients and smaller number of gynecological cancer patients compared with the study of Goodman et al.[23] Furthermore, despite research on the safety of controlled ovarian hyperstimulation in breast cancer patients,[3,43,44] the difference in counseling patterns for breast cancer patients in our study may arise due to oncologist's concerns about the risk of disease recurrence of progression due to hormonal exposure during FP. Differences in counseling patterns may also be the result of different support for FP and/or different documentation behavior of physicians across different units.

This study was possible because of the addition of automated prompt questions regarding FPC in medical oncology progress notes in our medical center's EMR system in 2006. That the majority of the chemotherapy-exposed breast, gynecological, and hematological cancer patients had documented FPC is consistent with the literature on the effectiveness of such prompts in changing medical staff behavior[45–48] and supports the value of prompts in the medical record to encourage the provision of treatment that meets current standard of care minimums. However, in our study, adherence to these prompts appeared to decline over time. This decline could be related to education regarding the prompts which might wane over time.

Given that all patients in this study were likely to have at least a small risk of fertility impairment as a result of gonadotoxic treatment, ideally there should have been 100% positive responses to the EMR prompt. However, if a medical oncologist had not yet decided on the full treatment plan at initial medical visit and therefore did not feel as though a fertility discussion was warranted and/or misunderstood the prompt, this might be a reason to indicate a ''no'' or ''not applicable'' response. It is also possible that the decline in documented FPC might be the result of increased referrals for such counseling by medical oncologists to a different health professional. For example, since being integrated into our program in 2010, medical oncologists have increasingly contacted our division's FP patient navigator after indicating

that they did not provide FPC as they wanted the patient navigator to provide that specialized information. However, given the disparity in documented FPC based on the year of diagnosis, the importance of continued reminders and training on the importance of FPC are warranted.

Initial medical encounters with newly diagnosed cancer patients are deeply complicated, and fertility adds an additional layer of complexity. However, equality in the counseling of female cancer patients for FP treatment is imperative to reduce the risk of emotional harm and future infertility. Consistent with international recommendations that all cancer patients (regardless of medical, demographic, or socioeconomic status) of reproductive age should be informed of the risks of their cancer treatment,[6,24–26] providers should also inform all patients about available FP treatments as well as the risks of delaying cancer treatment to pursue FP. Whether or not patients pursue FP treatment, patient involvement in the decision-making process is necessary to reduce future regret and reduced quality of life for cancer patients.[13]

Limitations of this study include the use of retrospective chart review data from a single, large academic medical center in an urban center in the United States. However, we accessed medical record data from all chemotherapy-exposed breast, gynecological, and hematological female cancer patients presenting to the institution over an extended period and thus were able to gain a broad understanding of FPC across oncological specialties. We were also limited in access to additional data that could strengthen our understanding of disparities in FPC among reproductive-aged female cancer patients. For example, information about the oncologist's gender, patient parity, and expressed desires for child bearing could contribute to a better understanding of counseling differences. In addition, because only one electronic prompt was utilized at a specific time point in care in this study, we did not have access to additional notes or follow-up visits, which may have documented FPC.

Furthermore, the demographics of our institution reflect an urban upper-middle class to wealthy patient population, which might not be reflective of other clinical settings and limited our analyses. The majority of our patients were married (53%), white women (60%), and with private insurance (79%). Interestingly, this is similar to patient populations among infertile women seeking infertility treatment.[28,31] However, neither insurance coverage nor income has been shown to predict FPC in multiple previous multivariate analyses.[21,23] It therefore may be that insurance coverage plays an important role in those who present for cancer treatment in any particular institution, but once patients begin their cancer treatment, their insurance status does not affect FPC. It is also important to note that our sample included only patients with breast, gynecological and hematological cancers who were exposed to chemotherapy. Therefore, caution should be used when comparing the results of this study with studies that include other cancers as well as patients exposed to gonadotoxic radiation.

Finally, a previous multivariate analysis, including cancer diagnosis with a highly racially diverse patient population, found that white women are more likely to receive FPC than other women.[23] Thus, it remains important to assess the degree to which a patient's racial/ethnic background may influence FPC. Regardless of differences in the significance of demographic disparities in FPC across published studies, it appears that these studies have identified possible disparities in FPC. However, the current study is one of the first studies to examine predictors and disparities in documenting FPC in an EMR setting. Our study therefore adds to the growing body of literature on the need for greater understanding of predictors and disparities in FPC among chemotherapy-exposed female breast, gynecological, and hematological cancer patients.

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Author Disclosure Statement

No competing financial interests exist.

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