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Physicians' Attitudes, Knowledge, and Perceived Barriers toward Fertility Preservation in Young Breast Cancer Patients in a Developing Country

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ABSTRACT

Background: In Mexico, up to 15% of breast cancer (BC) patients are 40 years or younger. Therefore, fertility preservation and pregnancy after cancer treatment are major concerns in this population. However, no data are available regarding Mexican physicians' knowledge and attitudes toward these issues. **Objective:** The objective of the study was to describe physicians' attitudes, knowledge, and perceived barriers toward fertility preservation among young women with BC (YWBC) in a developing country. **Methods:** A cross-sectional study was conducted among physicians attending the 2016 Mexican Society of Oncology (SMeO) Annual Meeting or affiliated to SMeO. Chi-squared tests were used to assess factors associated with a higher likelihood of disclosing infertility risks, discussing fertility preservation methods, referring to specialists, and effective counseling. **Results:** Of the 314 participants, 83% reported a high sense of responsibility about informing treatment-related infertility risks, 58% always informed patients about those risks, 38% always discussed fertility preservation procedures, 52% always referred interested patients to fertility specialists, and 24% wrongly considered pregnancy and GnRH analogs detrimental in YWBC. Barriers for discussing fertility preservation were costs, lack of specialists, and prognosis. **Conclusions:** It is crucial to promote physicians' knowledge and to endorse policies to overcome barriers obstructing universal access to fertility preservation for YWBC in Mexico.
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Key words: Breast cancer. Young women. Fertility preservation. Pregnancy. Mexico.

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INTRODUCTION

In Mexico, up to 15% of breast cancer (BC) patients are 40 years or younger at diagnosis[1,2]. International guidelines recommend systemic treatment with chemotherapy and/or hormonal therapy to improve survival in young women with BC (YWBC)[3,4]. However, cancer treatment also poses potential risks to ovarian function and may lead to secondary infertility[5], which has been shown to negatively affect young BC survivors' quality of life[6]. This is particularly relevant considering that a significant proportion of Mexican YWBC might not have fulfilled parity at the time of diagnosis since 26.6% of births occur in women aged 30 years or older[7].

Current international guidelines recommend informing all cancer patients diagnosed during their reproductive years about the possibility of treatment-related premature ovarian failure and infertility, as well as discussing the available fertility preservation options with interested patients[8,9]. Therefore, fertility counseling should be routine clinical practice in all newly diagnosed YWBC[10,11].

However, this issue is not systematically addressed by all physicians[6]. In a previous study by our group, 35% of Mexican YWBC reported not having children, 44% were concerned about treatment-related infertility, and only 31% recalled receiving information regarding such risk[12]. Moreover, these numbers may be over represented considering that patients were treated in two reference centers. Thus, it is relevant to determine if Mexican attending physicians' practice impacts on suboptimal rates of fertility counseling. The objective of this study was to describe physicians' attitudes, knowledge, and perceived barriers toward fertility preservation among YWBC in a developing country.

METHODS

A cross-sectional study was conducted among physicians attending the 2016 Mexican Society of Oncology (SMeO) Annual Meeting, held in Tijuana, or those affiliated to SMeO. All attendees of SMeO's Meeting and its affiliates, regardless of medical specialty, were invited to participate in person or through e-mail, respectively. Attendees of SMeO's Meeting answered a self-report printed questionnaire, while affiliates answered it through a web-based format. The 20-item survey was developed based on prior questionnaires designed by diverse research groups conducted in high-resource settings[13-16]. To address the objective of this study, questions were adapted by a group of healthcare professionals composed of medical oncologists and psycho-oncologists, which are experienced in discussing fertility-related issues in YWBC. The survey evaluated physicians' attitudes and knowledge toward fertility issues using a five-point Likert scale and asked multiple-choice questions regarding perceived barriers toward fertility preservation strategies (expected answers on knowledge regarding fertility issues in YWBC are presented in Supplementary Table 1). Participants included in this study are only those who answered the survey. Invitation to participate in this study was included in the heading of the questionnaire, and by accepting such invitation consent was implied. IRB review was exempted as the participants were anonymous and no intervention was applied.

Answers were dichotomized into "always" versus "not always" (including "almost always," "sometimes," "seldom," and "never"). A $p < 0.05$ was considered statistically significant when comparing "always" versus "not always." Taking into account the questions regarding informing patients about the risk of infertility, informing about fertility preservation procedures before systemic treatment and referring interested patients to a specialist, we developed the new variable "effective counseling" if the participant answered either "always" to the three questions or "always" to two and "almost always" to one question. Primary analyses were descriptive. Chi-squared tests were used to analyze the association of variables of interest and the likelihood of disclosing infertility risks, discussing fertility preservation methods, referring to fertility specialists, and performing effective counseling. Statistical analyses were performed using the Stata version 14.2 statistical software (StataCorp, College Station, Texas).

RESULTS

Of 742 participants attending the 2016 SMeO Annual Meeting, 207 (28%) completed the survey. Among the 1970 affiliated physicians who were

Table 1. Physicians' general characteristics

Variable	Number (%)
Age (years)	
≤ 40	175 (55.7)
41-50	60 (19.1)
51-60	54 (17.2)
≥ 61	24 (7.6)
Missing	1 (0.4)
Gender	
Female	100 (31.9)
Male	214 (68.1)
Specialty	
Medical oncologist	79 (25.2)
Surgical oncologist	122 (38.9)
Gynecologic oncologist	52 (16.6)
Radiation oncologist	23 (7.3)
Other*	38 (12)
Clinical practice	
Private	48 (15.3)
Public	70 (22.3)
Both	195 (62.4)

*"Other" comprises pathologists, radiologists and general physicians.

invited to participate through e-mail, 107 (5%) responded. Therefore, the analysis was performed on the 314 responses. Fifty-six percent of participating physicians were 40 years or younger, 68% were male, 56% were surgical specialists (surgical or gynecologic oncologists), 25% were medical oncologists, and 62% had their clinical practice at both private and public institutions. Physicians' general characteristics are presented in table 1.

Overall, 58% physicians reported always informing patients about treatment-associated infertility risks, 38%, always discussing fertility preservation procedures before treatment, and 52%, always referring interested patients to fertility specialists. Forty-four percent of the participants reported to be performing effective counseling. When planning systemic treatment, 51% reported to always consider patients' interest in fertility preservation, and 45% reported to do so sometimes. However, 73% would not forego chemotherapy at patients' request to preserve fertility, while 20% would. When asked about the degree of responsibility they felt about informing patients on the treatment-related infertility risk, 83% reported high, 12% moderate, and 5% low sense of responsibility.

Physicians with a high sense of responsibility were more likely to inform patients about infertility risks (91.2% vs. 8.8%, $p < 0.001$), advice about preservation options (95.5% vs. 4.5%, $p < 0.001$), refer to fertility specialists (92% vs. 8.0%, $p < 0.001$), and perform effective counseling (94.1% vs. 5.9%, $p < 0.001$). Those aged ≤ 40 years were more likely to inform patients about preservation strategies (61.7% vs. 38.3%, $p < 0.008$) and provide effective counseling (53.3% vs. 46.8%, $p < 0.046$). Physicians who informed patients about infertility risks more frequently discussed preservation strategies (94.1% vs. 5.9%, $p < 0.001$) and made referrals to fertility specialists (64.8% vs. 35.2%, $p = 0.013$). These associations are summarized in table 2.

Regarding physicians' knowledge on fertility preservation, 24% of participants considered pregnancy negatively affects prognosis, 64% considered it does not, and 10% were unsure about its effect. Seventeen percent considered that ovulation inducers negatively affect prognosis in all BC patients, and 23% believed prognosis is negatively affected only in patients with hormone-receptor positive (HR+) disease. Twenty percent believed gonadotropin-releasing hormone agonists (GnRHa) were detrimental in all BC patients, and another 20% considered prognosis is negatively affected only in HR+ disease. When asked about the best time to recommend pregnancy after finishing systemic therapy, more than half (55%) answered 1-2 years, followed by 3-4 years (26%). Results regarding fertility attitudes and knowledge are presented in figures 1 and 2, respectively.

The main reasons listed for not referring patients to fertility specialists included costs (30%), lack of specialists (11%), prognosis (11%), and other (48%). Other reasons included fear of delaying cancer treatment, limited experience, misconception that pregnancy is unsafe, uncertainty about the safety of ovarian induction, and insufficient time in medical visits to address this issue.

Table 2. Physicians' characteristics and fertility-related attitudes*

	Inform about infertility risk		Advice about fertility preservation strategies		Refer to a fertility specialist		Effective counseling	
	n (%)	p-value	n (%)	p-value	n (%)	p-value	n (%)	p-value
Age (years)								
≤ 40	178 (56.5)	0.86	194 (61.7)	0.008	172 (54.9)	0.72	167 (53.3)	0.409
> 40	136 (43.5)		120 (38.3)		142 (45.1)		147 (46.8)	
Gender								
Male	212 (67.6)	0.72	230 (73.1)	0.149	205 (65.4)	0.24	213 (67.9)	0.870
Female	102 (32.4)		84 (26.9)		109 (34.5)		101 (32.1)	
Specialty								
Medical oncologist	95 (30.2)	0.57	98 (31.1)	0.42	89 (28.4)	0.18	99 (31.4)	0.797
Surgical specialist**	182 (57.7)		182 (57.7)		190 (60.5)		181 (57.7)	
Other	37 (12.1)		34 (9.2)		35 (11.1)		34 (10.9)	
Sense of responsibility								
Low-moderate	28 (8.8)	< 0.001	14 (4.5)	< 0.001	25 (8.0)	< 0.001	18 (5.8)	< 0.001
High	286 (91.2)		300 (95.5)		289 (92.0)		296 (94.2)	
Inform about infertility risk								
Always	–	–	295 (94.1)	< 0.001	203 (64.8)	0.013	307 (97.8)	< 0.001
Not always	–		19 (5.9)		111 (35.2)		7 (2.2)	

*Table 2 considers the physicians that answered "always" to the three main questions (vide supra, the percentages represent those physicians). All p-values are the result of chi-squared comparisons between physicians that answered "always" versus "almost always, sometimes, seldom or never." The table reads 56.5% of physicians always informing about infertility risk were 40 years or younger.
**Surgical specialist includes surgical oncologists and gynecologic oncologists.

DISCUSSION

This is the first reported data exploring physicians' attitudes and knowledge toward infertility risk and fertility preservation specifically in YWBC from Latin America. Comparing these findings with previous work was challenging since most of the prior studies were not specific for YWBC, as they included children with cancer[17], both young male and female cancer patients[13,15,18,19], and young women with any type of cancer[14,20]. To the best of our knowledge, the only two previous reports that focused on physicians' attitudes and knowledge on fertility preservation specifically in YWBC are those by Lambertini et al.[21] and Shimizu et al.[22]

In our study, 86% of physicians "always" or "usually" discussed treatment-associated infertility risks, similar to the rates reported by Lambertini et al. (91.6%)[21] and others (95%[14] and 97%[15]). Likewise, a large proportion (72%) of participants "always" or "usually" referred patients to fertility specialists, which is an even higher rate than those reported in the United Kingdom (67%)[15] and United States (47%[19] and 39%[14]). Furthermore, two-thirds of physicians "always" or "usually" informed YWBC about fertility preservation strategies, which is difficult to compare to other studies since they reported the overall rate of informing about fertility options between 18%[17] and 81%[20]. However, effective counseling dropped to 44% when its three components were taken into account.

Physicians aged 40 years or younger and those with a high sense of responsibility were more likely to inform YWBC about preservation strategies in our study. Most participants (83%) felt a high sense of responsibility on discussing these topics, contrasting

Figure 1. Physicians' attitudes about fertility preservation in young women with breast cancer.

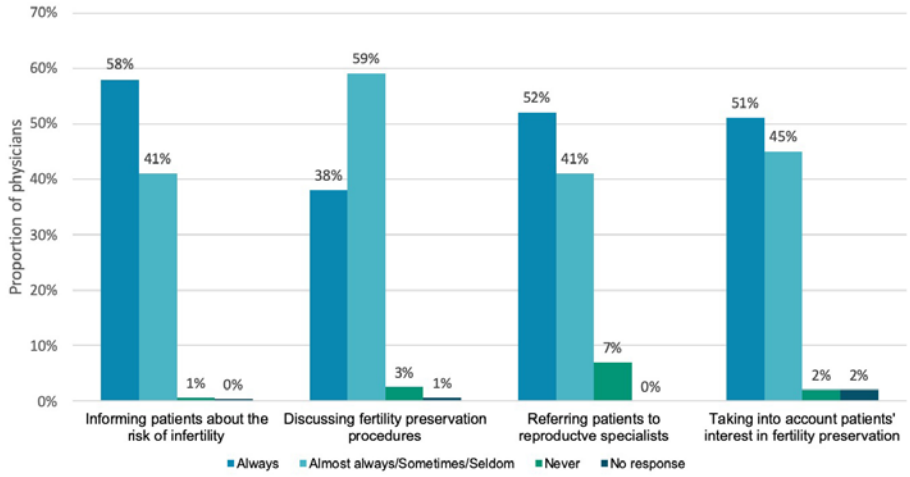
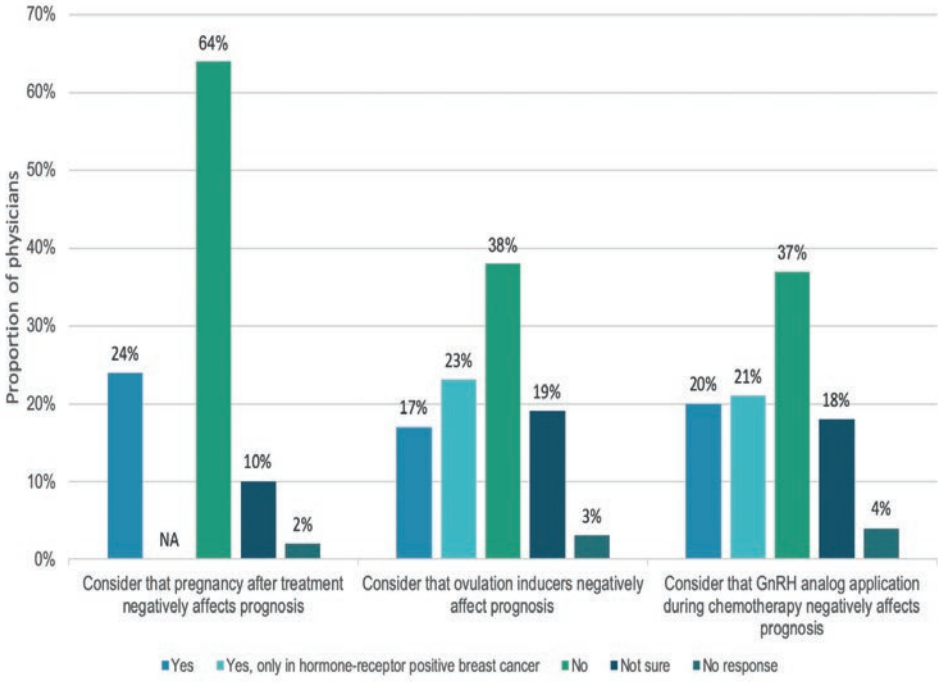


Figure 2. Physicians' knowledge about fertility preservation in young women with breast cancer.



with only 58% of physicians reporting a high sense of responsibility in another study[23]. Similarly, Shimizu et al.[22] reported that physicians aged 50 years or younger discussed fertility issues more often. Although female physicians[19,22] and gynecologic oncologists[14,19] have been reported to be more likely to enclose fertility discussions in previous studies, these associations were not observed in our survey. Likewise, another study found no associations between physicians' fertility-related attitudes and gender, age, or specialty[15].

In our study, the most commonly mentioned barriers for discussing fertility preservation were costs, lack of fertility specialists, patients' prognosis and limited

knowledge, as reported in previous studies[13,15,18,19,22,23]. Likewise, Shimizu et al. reported that poor prognosis or high recurrence risk (51%), lack of reproductive specialists (45%), and lack of time (45%) were major barriers for discussing fertility issues[22]. Other studies have also found barriers such as time constraints[15,18,19] and perceived poor preservation success rates[13,15].

In particular, limited knowledge may be a determining barrier among Mexican physicians. Despite current data supporting the long-term safety of pregnancy after BC[24-26], 24% of participants considered that pregnancy after BC negatively affects prognosis, as compared to 12.5% of physicians in the study by Lambertini et al.[21]. Deficient knowledge was also evident in the use of GnRHa, regardless of current recommendations on temporary ovarian suppression during chemotherapy with GnRHa for ovarian protection and fertility preservation[27,28], as 20% considered their use negatively affects prognosis in all BC patients, and another 20% believed that prognosis is negatively affected only in HR+ disease. This rate is higher than that reported by Lambertini et al., where 14.3% of participants agreed that ovarian suppression with GnRHa during chemotherapy should be proposed only to women with hormone-receptor negative BC[21]. As for physicians' knowledge on the safety of concomitant administration of letrozole or tamoxifen during controlled ovarian hyperstimulation to avoid the possible detrimental impact of high estradiol levels on cancer cells[25], 17% of our participants considered that ovulation inducers negatively affect prognosis in all BC patients, and 23% believed prognosis is negatively affected only in HR+ disease, which highly resembles the numbers found by Lambertini et al.[21]

Even though referrals to oncofertility specialists in Mexico are higher than those reported in other countries[14,18-20,22], it is presumed that a very low proportion of patients actually undergoes preservation procedures, as shown in our previous study[12]. Limited access to fertility preservation could be tackled through public health policies granting universal access to preservation strategies to all Mexican YWBC. This strategy has been previously effective in Argentina[29], where access to assisted reproductive techniques is covered, as well as Italy[30] and Australia[31], in which 6-month treatment with GnRHa is reimbursed. Furthermore, specialized programs, such as "Joven & Fuerte" ("Young & Strong") in Mexico, are currently addressing the unmet needs of YWBC by providing comprehensive cancer and supportive care in Mexico City and Monterrey. Since November 2014, 57 of 633 patients included in the program have undergone embryo/oocyte preservation[32]. However, more efforts are needed to ensure a larger coverage of YWBC. Moreover, further research is required regarding the preferences of Mexican YWBC on fertility preservation, their risk perception and the limitations that presumably withdraw them from preservation decision-making. Likewise, education initiatives should be implemented to enhance Mexican physicians' knowledge concerning fertility preservation strategies in YWBC.

Our study has the following limitations: first, evaluated physicians were affiliated to a medical association or attended a medical conference, which might translate into a selection bias and results may not be generalizable, as respondents could be more updated and more willing to participate in surveys. Second, since the majority of participants were surgical specialists [surgical oncologists and gynecologic oncologists] (56%), male (68%), and young physicians (56%), the population is not homogenous and the results obtained by this survey might not portray the attitudes and knowledge of the general population of cancer physicians, particularly those involved in the systemic treatment of YWBC. Nonetheless, the survey was designed to assess the overall population of physicians involved in cancer care in Mexico. Third, results regarding participants' attitudes may not be representative of their real-life clinical practice, as physicians may have exhibited a response bias and modified their answer in response to their awareness of being evaluated. Fourth, additional information regarding the approximate number of YWBC cared for by these physicians is unknown, however, as it would have been interesting to know if physicians attending a larger number of young cancer patients might be more aware of these issues.

In conclusion, this is the first survey to explore Mexican physicians' attitudes, knowledge, and perceived barriers toward fertility preservation specifically in YWBC. Results regarding discussions on infertility risk and preservation strategies and referrals to fertility specialists were similar to previous studies. However, a considerable proportion of participants wrongly

regarded pregnancy after BC and the use of GnRHa unsafe. Furthermore, physicians reported that access barriers were the most prevalent factors that hindered appropriate referrals. Physicians play a major role in the timely detection of patients' interest in future fertility; thus, it is crucial to promote knowledge and endorse policies to provide universal access to fertility preservation strategies for YWBC.

SUPPLEMENTARY DATA

Supplementary data are available at Revista de Investigación Clínica online (www.clinicalandtranslationalinvestigation.com). These data are provided by the corresponding author and published online for the benefit of the reader. The contents of supplementary data are the sole responsibility of the authors.

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