

The role of Indian gynecologists in oncofertility care and counselling

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Received: 21.04.2016
Review completed: 15.06.2016
Accepted: 22.06.2016

ABSTRACT

Oncofertility is gaining importance because of increasing cancer incidence, high survivorship, the need to provide a good quality of life to survivors and the desire of patients to preserve their fertility. Disseminating information about the effect of cancer and cancer treatment on fertility and the availability and effectiveness of fertility preservation techniques is critical. Gynaecologists in India act as family physicians and are in a unique position to guide cancer patients on issues of fertility and fertility preservation. Their contribution in oncofertility is vital to improve the quality of life of many young survivors. This paper presents the result of a survey done with Indian gynaecologists. The aim of this survey was to ascertain awareness and knowledge of reproductive damage by cancer therapy, knowledge of fertility preservation techniques and an understanding of the barriers to fertility preservation. This information would assist in planning programs to improve oncofertility care and counselling.

KEY WORDS: Counseling, fertility preservation, oncofertility

INTRODUCTION

Worldwide, millions of individuals in the reproductive age group are affected by cancer. Improved chemotherapy regimens have increased survival rates, and offering a good "quality of life" (QOL) to survivors has become the need of the hour. It is well acknowledged that cancer therapy can lead to subfertility in both males and females and that cancer survivors who face infertility as a result of cancer treatment are at an increased risk for emotional distress.^[1] This has led to the recognition of oncofertility, a discipline that deals with preserving future fertility of cancer survivors and improving their QOL.^[2]

Why fertility preservation services are important in India: The overall incidence of new cancer cases in India was reported to be 1.19 million in 2011, 0.603 million cases were women and 0.589 million were males. This figure is set to rise to 0.934 million for females and 0.935 for males by 2026 (ICR). Considering that 65% of India's population is <35 years of age and 50% is <25 years a significant number of cancer patients would be in the reproductive age group. The Indian Cancer Registry has

suggested figures between 11% and 25%. Among females, cancer of the breast and cervix are the leading sites of cancer in 18 of 25 population-based cancer registries in India, followed by cancer of the ovary and uterus. Breast cancer is the most common cancer in urban registries and second commonest in rural registries of India.^[3]

These figures would suggest that there is a sizeable population of cancer survivors in India who may suffer from subfertility as a consequence of their cancer treatment. A study conducted on long-term effects of cancer treatment in childhood cancer survivors (CSS) in South India found that 24% of CSS were diagnosed with infertility (Rajendranath *et al.* 2014).^[4]

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How to cite this article: Mahajan N, Patil M, Kaur S, Kaur S, Naidu P. The role of Indian gynecologists in oncofertility care and counselling. J Hum Reprod Sci 2016;9:179-86.

Access this article online

Quick Response Code:



Website:

www.jhrsonline.org

DOI:

10.4103/0974-1208.192061

Being childless is a huge stigma in most Asian cultures. Knowing that a woman's reproductive capacity is compromised can lead to the inability to find a suitable partner, divorce or simply abandonment of the woman.

Technological advances in the field of assisted reproductive technology have offered reproductive hope to women about to undergo ovariotoxic chemo-radiotherapy and fertility-damaging surgical treatments. Timely intervention and preservation of gametes, embryos, or ovarian tissue can give these patients hope of biological and genetic parenthood.

The American Society of Clinical Oncology (ASCO) and the European Society for Medical Oncology have formulated guidelines for oncologists to adequately discuss possible consequences of cancer therapy on future fertility of patients of reproductive age and refer patients desirous of fertility preservation (FP) to specialists. The American Society for Reproductive Medicine (ASRM) has also endorsed the requirement to offer FP to cancer patients.^[5] Despite these guidelines, very few oncologists actually refer patients for FP counseling.^[6,7] Constraints of time and the need to focus on treatment have been identified as important barriers to discussion on fertility. It has been suggested that physicians, nurses, psychologists, and social workers should play a role in imparting information so that patients may benefit from individualized expertise.^[8]

Indian gynecologists play the unique role of family physicians and are often consulted on any medical problems occurring within the extended family unit and even close friends. Gynecologists are also typically the first to be consulted for breast disease in addition to gynecological malignancies. Thus, gynecologists in India are an important link between cancer patient, oncologists, and fertility specialists. Their background knowledge of reproduction suggests that they can play a vital role in counseling and guiding cancer patients regarding fertility issues and FP.

This paper presents the result of a survey done with Indian gynecologists. The aim of this survey was to ascertain awareness and knowledge of reproductive damage by cancer therapy, knowledge of FP techniques, and an understanding of the barriers to FP. This information would assist in planning programs to improve oncofertility care and counseling.

MATERIAL AND METHODS

Searching e-mail addresses publicly available on the websites of Gynaecology Departments and procured from the Federation of Obstetrics and Gynaecology Society created a database of gynecologists. Surveys were subsequently

emailed to respondents in March 2015. However, the electronic survey received limited response (<10 responses till May). In view of this, copies of survey sheets were printed and junior doctors and medical representatives were sent to various hospitals personally to collect data in all five zones of India. Two-hundred fifty forms could be delivered personally. We took guidance from previous surveys done on oncologists to formulate the questions keeping in mind our ethnic, social, and cultural differences.^[9,10] Data were collected from March 2015 to August 2015. It was analyzed using Cloud Cherry, a proprietary online analysis tool. Descriptive statistics were employed to assess survey results using pivot table and pivot charts functionality within the Microsoft Office 365 suite.

The survey consisted of 28 questions under four domains. These included (1) demographic information (age, gender, religion, and regional ethnicity), (2) practice behavior (whether they discuss the impact of female patient's type of cancer and treatment on her future fertility, their agreement with the ASCO guidelines, considering patient's desire for future fertility, designing less effective treatment regimens to preserve fertility, their referrals to IVF specialist or accredited centers), (3) current knowledge (regarding impact of multidrug regimens and effect of therapy on fertility, awareness about FP techniques, whether they attended a continuing medical education [CME] on FP), and (4) attitude, perceptions, and barriers (reasons for not discussing the impact on fertility, reasons for not referring patients, their agreement to refer patient if reproductive specialist is available in-house). Most of the questions listed by the authors included either binary choice questions (yes/no or true/false) or multiple options. However, in some questions that inquired reasons for not always discussing fertility or the ones who do not refer their patients to fertility specialists, 4-point Likert Scale (always, usually, rarely, and never) were used.

RESULTS

The response rate via email was <1% (7/1000) whereas it increased to 62.5% after including the data collected from personal visit (157/250).

Demographics

Most respondents were below the age of 50 with 39.9% being under 40 years. 82.4% female gynecologists participated while only 17.6% males answered the questionnaire [Table 1]. Younger female gynecologists showed a willingness to participate and discuss FP. Quinn *et al.* 2009 reported that "female physicians appear to think more about a patients' desire for family- and fertility-related issues."^[11] This is not surprising as motherhood is inherently more important to women. Gynecologists from the South

Table 1: Demographics

	<i>n</i> (%)
Age	
<40	65 (39.9)
40-50	53 (32.5)
50-60	38 (23.3)
>60	7 (4.3)
Gender	
Male	26 (17.6)
Female	122 (82.4)
Religion	
Hindu	135 (83.9)
Muslim	7 (4.3)
Christian	4 (2.5)
Others	15 (9.3)
Regional ethnicity	
North	18 (17.3)
South	34 (32.7)
East	9 (8.7)
West	42 (40.4)
Central	1 (1.0)

and West of India answered in larger numbers 32.7% and 40.4%, respectively [Table 1]. Only 17.3% of gynecologists from the North of India participated reflecting a more conservative attitude and possibly a slower acceptance of change amongst North Indians [Table 1].

Practice behavior

Even though majority (81%) of the gynecologists were in agreement with ASCO guidelines on the need for FP discussion with all patients in the reproductive age group, only 42% routinely discuss the impact of the type of cancer on future fertility and only 37% discuss the impact of cancer treatment on fertility [Figure 1a and b]. While 65% gynecologists would consider a patient's desire for future fertility, when planning surgical treatment for cancer, only 23% were actually willing to provide fertility-sparing surgery to preserve future fertility and 31% would not consider it at all [Figure 1c]. This would imply that the issue of fertility is important but concerns about the need for close follow-up and compliance of the patient after conservative surgery for cancer prevents them from offering such treatment.

Most cited reasons for not discussing the impact of cancer treatment on fertility included poor prognosis (29.6%), need for immediate therapy (18.3%), already having children (30.3%), lack of available FP services in the city (35.9%), not aware of FP options (30.3%), too expensive (34.5%), and social reasons 16.2% [Figure 1d]. Cost, availability of services, knowledge of FP options, and poor prognosis emerged as the major barriers to discussion on fertility.

Knowledge of the effect of cancer treatment

While 51.6% gynecologists were aware of effect of alkylating agents on fertility, <40% had knowledge regarding multidrug regimens in specific cancers [Figure 2a-d]. Thirty-nine percent felt that the resting follicle was affected more by chemotherapy than the growing follicle and 29% replied that ovaries of older women required higher dose of radiation to cause sterility [Figure 2e and f]. Understanding oncology regimens and the effect they have on the reproductive axis needs to be incorporated into basic gynecology training, given the growing desire of oncofertility patients to preserve their fertility. This would improve the magnitude and quality of FP counseling.

Knowledge of fertility preservation techniques

Regarding awareness of the FP techniques 45% gynecologists were aware of all the available techniques in postpubertal women [Figure 3a]. 36.9% felt that only oocyte freezing could be offered and 6.7% believe that embryo freezing is the only technique that can be suggested, 11.4% were aware of ovarian tissue cryopreservation (OTC) [Figure 3a]. Knowledge of FP options in prepubertal girls was low, and only 16.9% were aware that the ovarian tissue freezing was the only option that could be considered [Figure 3a]. The use of GnRH agonist for ovarian protection was promoted by 36.7% while 26.5% believed that it did not protect the ovaries and one-third of gynecologists (36.7%) were not sure about its efficacy [Figure 3b]. Lacunae in knowledge of the effects of cancer therapy and FP techniques exist among gynecologists and this area needs to be addressed.

Only 41.5% of the gynecologists had ever attended a CME on FP [Figure 3c]. Most common cited reasons for not attending a CME on FP included no information received on oncofertility CMEs (58.6%) and lack of time (23%). 18.4% were not interested in the topic and therefore did not feel the need to attend. Requirement for improvement in the area of information dissemination was identified. There is a need to understand why 20% of doctors were not interested in oncofertility.

Perception and barriers - referral practice

Only 28.8% gynecologists routinely refer cancer patients for FP [Figure 4a]. Over 60% said that they refer sometimes while approximately 2% rarely or never refer [Figure 4a]. More than 80% agree that they would consider referral to specialized centers for FP and would want these centers to be accredited [Figure 4b]. An overwhelming majority (89.7%) felt that an FP specialist should be associated with an oncology unit [Figure 4b]. The need for immediate consultation was suggested by 58.6% gynecologists, 22.4% suggested that FP specialist should see the patient within 24 h while 19.1% felt that a consult

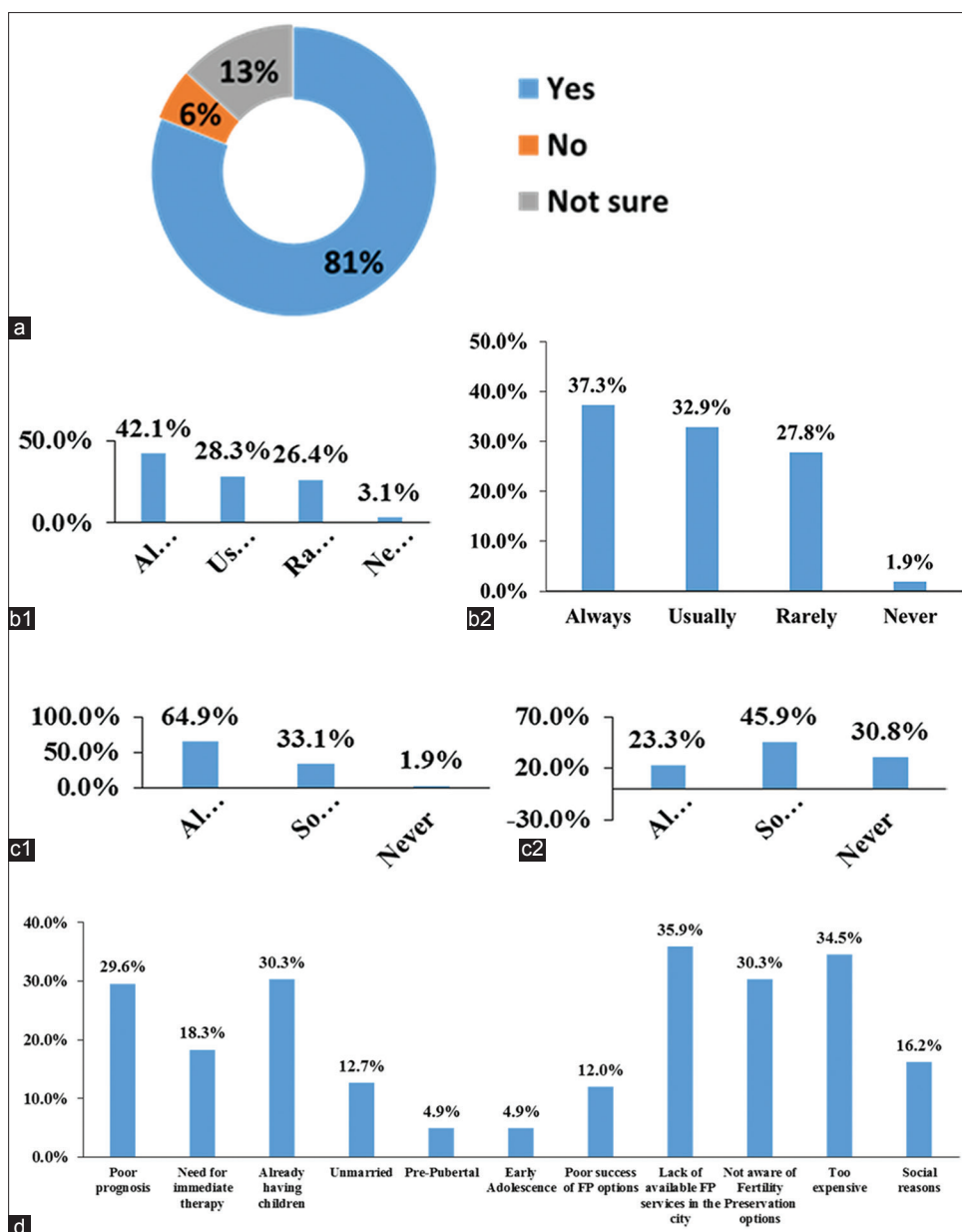


Figure 1: Practice behavior of general gynecologists toward fertility preservation. (a) Do you agree with American Society of Clinical Oncology guidelines that fertility preservation should be discussed with all young patients before starting chemotherapy?. (b1) How often do you discuss the impact of female patient's type of cancer on her future fertility?. (b2) How often do you discuss the impact of female patients cancer treatment on her future fertility?. (c1) How often do you consider a patient's desire for future fertility when planning treatment for cancer?. (c2) Are you ever willing to provide a less effective treatment to attempt to preserve fertility?. (d) Reasons for not discussing the impact on fertility?

within 48 h was acceptable [Figure 4c]. Having an in-house FP specialist and FP services would make it easier to refer and create less physical burden for the patient [Figure 4c]. This intervention would, however, require administrative involvement and financial input. Accredited centers increase physicians' confidence to refer the patient.

Most cited reasons for not referring patients included, not interested in FP (33.8%), lack of available FP services in the city (33%), do not know where service is available (40.6%),

too expensive (39.8%) [Figure 4d]. Similar to other studies, cost and availability of FP services were found to be important barriers to referral. 13.5% doctors were worried about the poor success rate of FP options [Figure 4d]. Live birth rate (LVB) per embryo transfer according to SART registry 2010 is 38.7% for thawed embryos and 34.8% thawed oocyte donor cycles.^[12]

Other reasons that have been identified for nonreferral to reproductive specialists are physician's specialty, age,

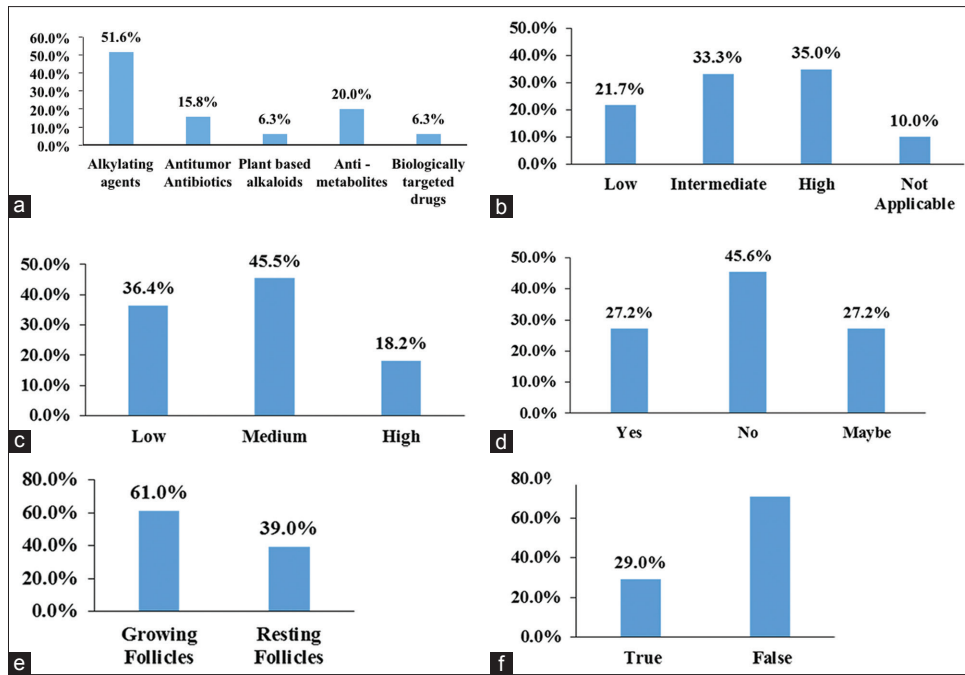


Figure 2: Knowledge regarding effect of cancer treatment on fertility. a) Which group of chemotherapy drugs affect fertility the most?. (b) Risk of amenorrhea with doxorubicin, bleomycin, vinblastine and darcabazine for Hodgkin's disease is?. (c) Risk of permanent amenorrhea with chemotherapy regimen four cycles in breast cancer in 30-year-old woman?. (d) Hematopoietic stem cell transplant treatment can cause sterility. (e) What stage of follicles is most affected by chemotherapy?. (f) Ovaries of older women need higher dose of radiation to cause sterility?

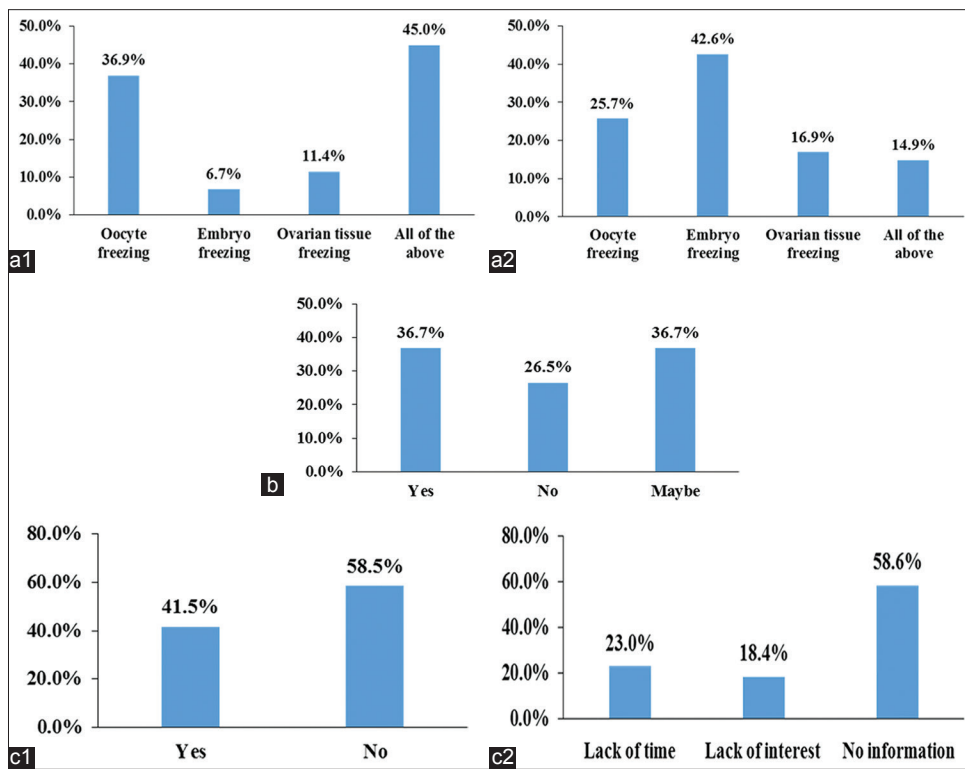


Figure 3: Knowledge regarding fertility preservation techniques. (a1) What fertility preservation technique can be used in postpubertal women?. (a2) What fertility preservation technique can be used in prepubertal girls?. (b) Is GnRH agonist helpful in protecting ovaries?. (c1) Have you ever attended a continuing medical education on fertility preservation?. (c2) Why not?

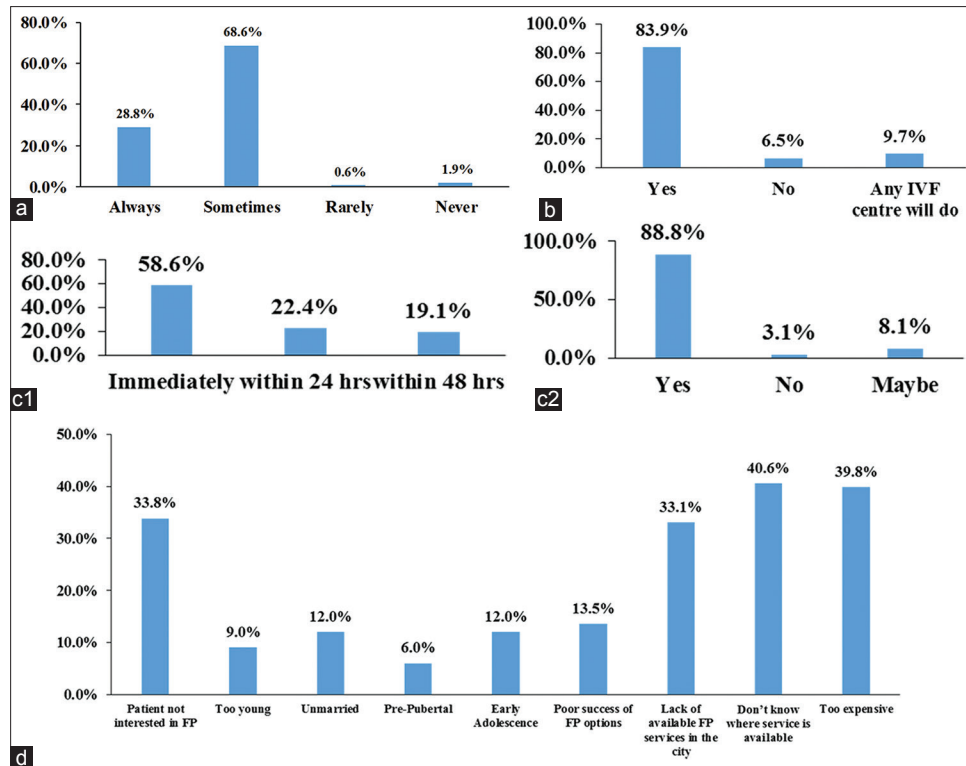


Figure 4: Perception and barriers toward referral practice. (a) Do you ever refer patients to an IVF specialist?. (b) Would you prefer to refer such patients to a specialized center for IVF and fertility preservation?. (c1) How fast would you want the fertility preservation specialist to see the patient?. (c2) If reproductive specialist is available in-house would you refer patient for counseling. (d) Reasons for not referring

and comfort with the topic.^[13,14] Our survey revealed that there was a perception among gynecologists that patients were not interested in discussion on FP because they did not ask about it. It is important that physicians raise the topic as patients may feel hesitant to ask or may not be aware of the possibility of FP. Quinn *et al.* 2009 found that one key predictor of referral was having a patient who asked about FP.^[15]

DISCUSSION

Cancer therapy can have a damaging effect on the reproductive axis in young girls and women, leading to premature menopause, premature ovarian failure, and infertility. Diagnosis of infertility has an immense psychological and emotional impact on cancer survivors. Reproductive dysfunction postcancer therapy is associated with depression, distress, and “posttraumatic stress disorder”.^[16,17] QOL studies have shown that patients who do not receive information regarding the effect of cancer treatment on their fertility have feelings of anger and distress.^[18] Carter *et al.* 2010 demonstrated higher depression and distress scores for women with perceived unmet informational needs.^[19] They also found that female cancer survivors showed evidence of greater sexual dysfunction and lower physical QOL compared with noncancer-afflicted

infertile women.^[20,21] Failure to inform patients of their fertility options or refer them to FP units may also lead to medico-legal settlements.^[22,23]

Success of FP procedures and reproductive outcome are a concern as FP techniques are invasive and require use of gonadotropins for ovarian stimulation and ovarian tissue collection requires laparoscopy. Data on reproductive outcome in oncofertility patients using preserved gametes/embryos are sparse and counseling is done by extrapolating data from infertile patients and oocyte donor-recipient IVF cycles.

Among the FP techniques available, embryo cryopreservation is an established technique but necessitates the woman to be married, have a partner or be willing to use donor sperms. Oocyte cryopreservation offers more reproductive autonomy while OTC is still considered experimental. Technical expertise, age of the woman, and number of oocytes recovered determine success of the oocyte freezing. Randomized controlled trials have shown that implantation and clinical pregnancy rates are similar using fresh or frozen oocytes.^[24,25] Cil *et al.* reported an LVB of 21.4–24.1% for a 30-year-old woman who has 2–6 oocytes to thaw. If 1–3 embryos are available for transfer, the chance of LVB is 9.7–24.9%. The age cutoff for determining success was 35 years in their study.^[26]

In a recent study, Martinez *et al.* 2014^[27] reported on the obstetric outcome after oocyte cryopreservation in cancer patients. They reported an oocyte survival rate of 92.3%, fertilization rate of 76.7%, an implantation and clinical pregnancy rate of 31.8% and 54.5%, respectively, and an ongoing PR of 36.4%. No obstetric complications or congenital anomalies were found in these patients. Although the number of patients in the study was small (11 patients), the data on reproductive outcome are reassuring.

OTC is a promising technique and offers the opportunity of natural conception. It is still considered experimental by ASRM though more than forty babies have been born from transplanted ovarian tissue.^[28] Many of these conceptions have been spontaneous highlighting the advantage of this procedure. Additional benefits of OTC relate to the steroid production ability of ovarian tissue. Ovarian tissue has been transplanted to induce puberty^[28] and alleviate menopausal syndrome.^[29]

ASCO suggests that oncologists should discuss possible consequences of cancer therapy on future fertility and refer patients to an FP specialist if they desire FP. Results of various surveys show that most oncologists do not discuss FP with their patients and referrals to specialists are low.^[9,11] ASCO puts the onus of counseling on the oncologists for whom cancer treatment is the priority. If family/primary care physicians and paramedical staff share this burden, more patients might receive the benefit of FP counseling.^[11,15]

Gynecologists in India act as family physicians and are likely to interact with patients throughout their treatment. Apart from taking care of basic medical requirements such as pain management, they offer emotional support both to the patient and caregivers. They are, thus, in a unique position to promote a discussion on fertility and offer FP counseling. They can educate the patients about oncofertility so that the patient initiates the discussion with the oncologist. To do this effectively, they need to have updated information themselves. Results of our survey showed gaps in knowledge of FP techniques and the negative effect of cancer therapy on fertility. More multidisciplinary CME's need to be conducted for updates on oncofertility.

CONCLUSION

This survey shows that gynecologists are keen to discuss fertility issues with cancer patients, but currently, there is a lack of awareness of FP techniques, their availability and efficacy and centers providing good FP services. Options for FP in prepubertal children are also not well known. Cost remains an important factor preventing referrals. A need for FP specialists to hold clinics within oncology units and to have in-house FP services was also identified.

Oncofertility is gaining importance because of an increased cancer incidence, high survivorship, the need to provide a good QOL to survivors, and the desire of patients to preserve their fertility. Recognizing the barriers to physician-patient communication and disseminating information on the effects of cancer on fertility and availability and effectiveness of FP techniques is critical. Addressing these issues will improve oncofertility care and counseling. Religious, social, and cultural barriers may differ between countries and have to be kept in mind.

Gynecologists in India act as family physicians and are in a unique position to guide cancer patients on issues of fertility and FP. Their contribution in oncofertility is vital to improve the QOL of many young survivors. Results of FP from Europe and America provide encouragement on the efficacy of FP procedures.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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