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Oncofertility: knowledge, attitudes, and barriers among Indian oncologists and gynecologists

Citation for published version:

Tholedti, P, Uppangala, S, Bhat, V, Udupa, KS, Kumar, V, Patted, S, Pandiyan, N, Spears, N, Kalthur, G, Woodruff, TK & Adiga, SK 2020, 'Oncofertility: knowledge, attitudes, and barriers among Indian oncologists and gynecologists', *Journal of Adolescent and Young Adult Oncology*.
<https://doi.org/10.1089/jayao.2020.0034>

Digital Object Identifier (DOI):

[10.1089/jayao.2020.0034](https://doi.org/10.1089/jayao.2020.0034)

Link:

[Link to publication record in Edinburgh Research Explorer](#)

Document Version:

Peer reviewed version

Published In:

Journal of Adolescent and Young Adult Oncology

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Title: Oncofertility: knowledge, attitudes, and barriers among Indian oncologists and gynecologists.

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Running head: Oncofertility trends among healthcare providers in India

Key words: Fertility preservation; oncofertility; oncologists; gynecologists

Abstract:

Purpose: Recommendations from American Society of Clinical Oncology (ASCO) emphasize the critical need to understand current trends in fertility preservation (FP) among the two sets of primary healthcare providers involved in oncofertility: the oncologists and the gynecologists. This study is aimed at understanding the healthcare providers' knowledge, attitudes and barriers in oncofertility across India.

Methods: An eighteen-item oncofertility survey was designed and directed to 77 oncologists and 214 gynecologists across India. The responses were analysed using descriptive statistical methods and the oncofertility trends between the two groups was studied.

Results: The total response rate was 34% with 49 of 214 oncologists (23%) and 49 of 77 gynecologists (64%), participating in the survey. The awareness of ASCO fertility preservation guidelines among oncologists and gynecologists was 53% and 59.5%, respectively. About 48% of oncologists felt knowledgeable about sperm banking while 52% knew about oocyte freezing but not about other options. On the other hand, among gynecologists, 38% reported inadequate knowledge of testicular or ovarian tissue cryopreservation. About 85% of oncologists reported routine referral of cancer diagnosed patients for FP, while 75% of gynecologists reported routine FP discussion with patients. Healthcare providers from both groups perceived the major barriers in oncofertility to be, 'financial burden on the patient' (73-86%) and, 'lack of patient awareness' (71-79.5%).

Conclusion: Effective collaboration between oncologists and gynecologists is essential to establish a successful fertility preservation program. Economic burden on the patient and lack of patient and physician awareness are limiting factors which need to be overcome.

Introduction:

The estimated cancer incidence in India is 1.15 million new diagnoses as of 2018, with diagnoses expected to almost double by 2040.¹ With advancements in cancer treatment, early diagnostics, and increased investment in healthcare technology, there has been an increase in cancer survival rates, especially in developed countries.² However, survival rate does not equate to improved quality of life. A follow-up study on a cohort of childhood cancer survivors in India reported impaired reproductive capacity as a common long-term effect in approximately 25% of patients.³ This brings about an urgent need for awareness and effective implementation of oncofertility services before the commencement of cancer treatment.

Oncofertility is a rapidly emerging field that aims to increase awareness of fertility preservation (FP) among cancer patients and healthcare providers on a global scale.⁴ Along with a well-orchestrated involvement of various medical experts to address the needs of fertility problems in cancer patients, oncofertility demands a merger of two medical specialties: oncology and reproductive medicine.⁴ Despite the American Society of Clinical Oncology (ASCO) recommending guidelines to offer fertility preservation services to oncological patients,⁵ 85% of childhood cancer survivors in India reported that no information was provided to them about the possible risk of infertility due to treatment.⁶ This lack of information dissemination resonates the need to understand the attitudes, knowledge and barriers in oncofertility among healthcare providers, given the important role they play in FP decision making.⁷ To the best of our knowledge, there have been no studies in India addressing the oncofertility trends among oncologists nor an assessment of these trends between oncologists and gynecologists, to reflect the exchange of communication and practice behaviors between the two specialties. Hence, the present study is aimed at assessing the knowledge levels, perceptions, and current

challenges in oncofertility among the two most important groups of healthcare providers involved in an oncofertility program: oncologists and gynecologists.

Methods:

An 18-item survey was designed constituting four domains – knowledge about fertility preservation (FP) techniques, attitudes, existing barriers in oncofertility, and demographics (Supplementary Table 1). The survey design was based on review of literature from developed countries,⁸⁻¹¹ and in collaboration with the Oncofertility Consortium. Content validity for the survey was performed by five experts in the fields of medical oncology and gynecology. A pilot survey was administered to a small group of healthcare providers to confirm the comprehensibility of the questions, the unpublished results of which are not included in the present study. The survey was then randomly distributed to oncologists and gynecologists attending various national conferences or academic meetings across the country (specific to the field of oncology and gynaecology) or even visits to the practitioners' clinics between May to November 2019. The first page of the survey contained aims of the survey along with a consent form; healthcare providers willing to participate were requested to sign the informed consent before beginning the survey.

The survey contained a total of 18 questions of which 10 were aimed at understanding the knowledge, attitudes, practice trends in oncofertility, existing barriers, and suggestions for effective use of FP; the remaining 8 questions covered the demographics of the survey responder and contextual details such as the number of new cancer patients treated in a month and the patient age groups. Two questions were dichotomous, 8 were multiple choice where only 1 response could be selected; 1 question was multiple response where more than one answer could be selected and 1 was an open-ended question with space provided for

respondents to give their suggestions. 6 questions were assessment tools with 3- or 4-point grading scales to ascertain the levels of knowledge or attitude. The multiple response question had a list of nine common oncofertility barriers from which a participant could select more than one option.

The survey responses were analysed using IBM SPSS Statistics Software after assigning numerical values to the responses (Yes=1, No=0). The data was analysed using descriptive statistics and percentages were calculated based on number of responses for each of the questions. For analysis of certain questions that contained grading scales or multiple choice (Q2, Q4, Q5, Q7), the response options such as 'not aware', 'aware but not adequate knowledge', 'knowledgeable' and 'very knowledgeable' were combined into two categories such as, 'inadequate knowledge' and 'knowledgeable'. Questions with high variation in responses, such as more than half of the respondents not answering, were not analysed in the present study. The study was approved by the Institutional Ethics committee of Kasturba Medical College & Kasturba Hospital, Manipal (No: IEC 880/2017).

Results:

The total response rate to the survey was 34% with 49 out of 77 responses (64%) received from gynecologists and 49 out of 214 responses from oncologists (23%), across various subspecialties such as pediatric hematology and oncology, medical oncology, radiation and surgical oncology. The demographics of the healthcare providers participating in the survey are listed in Table 1 describing characteristics such as age, gender, work setting, and experience in their field.

Awareness and attitudes towards fertility preservation: In the present study, 53% of oncologists (26 of 49) and 59.5% of gynecologists (28 of 47) reported awareness of the current

ASCO guidelines regarding fertility preservation. However, a considerable number in both the groups (40-47%) seemed to be unaware (Fig 1A). In order to assess attitudes towards fertility preservation, the survey participants were asked to give their opinion on the statement, ‘offering fertility preservation compromises cancer treatment’. About 71% of oncologists (34 of 48) and 75% of gynecologists (36 of 49) disagreed with the statement, while 22-25% in both groups felt that cancer treatment is compromised. 2-4% of the participants from both groups chose not to respond to the statement.

Knowledge of fertility preservation options: When asked about their knowledge of different fertility preservation options currently available for both prepubertal and adult cancer patients, 52% of oncologists (25 of 48) reported adequate knowledge of sperm banking and 48% (23 of 48) had knowledge of oocyte freezing, but >60% of the participants in this group did not have adequate knowledge of other fertility preservation options. On the other hand, the reproductive specialists were knowledgeable of the most widely available options for adult cancer patients such as sperm banking (41 of 49 - 83.6%), oocyte freezing (44 of 49 - 89.7%), *in vitro* fertilization followed by embryo freezing (IVF) (44 of 49 - 89.7%) and Gonadotropin releasing hormone agonist (GnRHa) pre-treatment (39 of 48 - 81.2%). Interestingly, about 39-41% of gynecologists reported inadequate knowledge of prepubertal/pubertal FP options such as immature testicular tissue and ovarian tissue cryopreservation (Fig 1B).

Patient referral for fertility preservation: To determine the practice trends in oncofertility among oncologists and gynecologists, participants were asked about the frequency of initiating a fertility preservation discussion with their cancer-diagnosed patients. Among oncologists, 81.6% (40 of 49) stated that they routinely, if not mostly, initiated FP discussions, and 85% (39 of 46) of them even reported referring their patients for FP services immediately after

diagnosis. A similar trend was seen among gynecologists, with 75% (36 of 48) of them reporting routine fertility preservation discussions with cancer patients (Fig 1C).

Comfort level to discuss fertility preservation with patients: When asked to rate the comfort level in discussing the various FP options with cancer patients, about 87% oncologists (42 of 48) reported being comfortable in discussing sperm banking, and 79% (38 of 48) with oocyte banking. There appeared to be a decline in their comfort level, however, when discussing the other options such as testicular tissue cryopreservation (30 of 45 - 67%), ovarian tissue freezing (32 of 46 - 69.5%), IVF (30 of 46 - 65%) or GnRHa pre-treatment (30 of 45 - 67%). About 90-94% gynecologists felt comfortable discussing most options, but even among this group a small proportion were not at ease when discussing testicular (15%), ovarian (11.5%) tissue freezing or GnRHa pre-treatment (12%) options (Fig 1D).

Barriers and suggestions for effective oncofertility implementation in India: In the present study, nine common barriers were listed in the questionnaire with the responder allowed to select more than one option. The study revealed an overall consensus among participants in perception of oncofertility barriers, with 73-82% of healthcare providers from both groups perceiving 'financial burden on patient' as an important barrier to fertility preservation, followed by 'lack of patient awareness' (71-80%). Other major barriers perceived by oncologists and reproductive specialists alike were 'lack of physician awareness' (55-57%) and 'time to treatment' (40-43%), referring to the time from diagnosing a cancer to commencement of treatment (Fig 2). However, opinions seemed to differ between the two groups for certain barriers, such as, 'lack of FP facilities' (oncologists – 61%; Gynecologists - 26.5%), 'cultural and religious barriers' (oncologists – 35%; gynecologists - 16%), and 'age of patient' (oncologists – 43%; gynecologists - 16%).

Among the survey participants (56%), 25 of 49 oncologists (51%) and 31 of 49 gynecologists (63%) suggested that there was a need to strengthen utilization of FP in India. The primary suggestion given by 61-64% of the healthcare providers in both the groups was ‘awareness and sensitization of healthcare providers in fertility preservation’, and 52% of oncologists felt there was a need for availability of more FP units closer to cancer hospitals for immediate intervention and minimum discomfort to the patients. ‘Creating a social awareness to educate the general public’, was suggested by 29% of gynecologists for effective implementation of oncofertility programs. Other suggestions included, ‘affordable costs’ (8-13%), ‘need for fertility preservation counselling’ (8-13%) and a need for consensus guidelines (13-16%), among participants from both groups.

Discussion:

The present study investigated oncofertility attitudes, knowledge, and practice trends amongst Indian oncologists and gynecologists, along with their perception of oncofertility barriers. Despite reduced awareness of the international guidelines and inadequate knowledge of some of the available services, majority of the oncologists were found to routinely refer their oncological patients for FP services, soon after cancer diagnosis. Similarly, gynecologists reported routine FP discussions with patients before the commencement of cancer therapy. While this is a promising finding, it highlights the need for oncofertility awareness programs among oncologists and reproductive specialists to enable effective oncofertility counselling and referral. The common oncofertility barriers perceived by both the groups were, economic burden to the patient and lack of patient and physician awareness on fertility preservation. To the best of our knowledge, this is the first study in India to assess oncofertility knowledge and attitudes among oncologists and relate their practice trends with that of gynecologists.

In the present study, only 50-53% of the healthcare providers from both medical specialities were aware of the ASCO fertility preservation guidelines⁵ that recommend routine discussion of FP options with cancer diagnosed patients. This finding is in line with a Dutch study on 23 medical professionals that included oncologists and gynecologists, citing lack of awareness of FP guidelines among healthcare providers as one of the significant barriers, despite availability of this information in journals and websites.¹² Also, the perspectives of healthcare providers towards oncofertility played a key role in FP discussions. In the present study, majority of the oncologists (70.8%) and gynecologists (75%) did not perceive that fertility preservation compromises cancer treatment. This finding is in contrast to a Canadian interview-based qualitative study on 22 clinicians, including oncologists and fertility specialists, which reported that clinicians perceived patient survival as the primary factor and infertility as non-fatal, therefore, fertility preservation is secondary and could interfere or even delay cancer treatment.¹³

Despite the reduced awareness of guidelines, it was interesting to see that a majority of oncologists and reproductive specialists participating in the present study reported routine fertility preservation discussions and referrals to FP services, before commencement of cancer therapy. However, this is in stark contrast with the reality of oncofertility consultations in India, where only 15% of 21 childhood cancer survivors reported to have received counselling on infertility risks despite treatment plans involving alkylating chemotherapy, radiotherapy or gonadal surgery.⁶ The need for FP counselling after a cancer diagnosis is emphasized further with the findings of a study on newly cancer diagnosed patients in India, which reported that 87% of cancer patients wish to know the future risks associated with their disease and treatment, to allow for positive decision-making.¹⁴ Individuals who have been counselled for FP have been shown to cope better and have lower distress pertaining to fertility, along with an improved quality of life.¹⁵ Inadequate or lack of information from the healthcare providers

could add to the complexities of decision making during emotionally vulnerable times such as soon after a cancer diagnosis.

The role of oncologists and gynecologists is pivotal in a successful oncofertility program, as the former is the first point of contact for cancer diagnosed patients and the latter plays a key role in fertility preservation discussion with the patients.⁴ Their knowledge of FP options and comfort in discussing adult and prepubertal options would likely correlate directly with the frequency of these discussions with their patients.¹⁶ In the present study, knowledge gaps were seen among oncologists and even the reproductive specialists, particularly with prepubertal options such as testicular and ovarian tissue cryopreservation. This finding correlated with their admittance of reduced comfort level in discussing these options with their oncological patients. Further, the lack of comfort among oncologists to discuss IVF or GnRHa pre-treatment could reflect the dearth of knowledge in this area. In concurrence with our finding, a study from the UK reported that oncologists felt knowledgeable mainly about sperm cryopreservation and knew little about other options, but referred patients for FP nevertheless, as they perceived it as a priority.⁸ While in-depth knowledge on gonadal toxicity and infertility may not be required for counselling, identifying the need for fertility preservation and awareness of the nearest FP unit is essential.⁸ Disparity of knowledge and lack of ease in discussing FP, even among reproductive specialists for prepubertal options, highlights the need for further education and awareness in this field. Providing healthcare providers with educational resources such as toolkits, brochures or through Continuing Medical Education (CME) programs would improve the frequency and quality of fertility preservation discussions with their patients.^{9,12,17}

Barriers in oncofertility hinder the effective execution of fertility preservation services leading to their under-implementation. In India, insurance coverage is not provided for FP procedures,¹⁰ making financial burden to the patient one of the biggest challenges to overcome

in the country. Economic burden to the patient is one of the significant barriers perceived by both groups of healthcare providers participating in the present study, followed by lack of patient and physician awareness. These findings can be corroborated by another study conducted in India among gynecologists who also reported social and medical barriers such as lack of patient interest, physician awareness and unavailability of fertility preservation services.¹⁸ Lack of insurance coverage or funding and high costs to patients appear to be common economic barriers in developing countries^{19,20} that need to be addressed. Similar barriers have been reported in developed countries as well, along with other religious or cultural restrictions and legal barriers.^{10,21}

Other important barriers cited by healthcare providers participating in the present study include the physician's lack of awareness, and 'time to treatment'. Although FP plays a crucial role in the quality of life post-treatment, the options may not always be offered, especially to prepubertal children and women, due to the urgency to initiate cancer treatment.^{22,23} Kohler *et al*, reported gender disparity in oncofertility referrals, with around 50% healthcare providers referring male pubertal patients for FP but only 13% referrals for female pubertal patients which could be attributed to lack of knowledge among physicians, as well as inadequate time prior to treatment for services such as IVF or oocyte banking.²⁴ A similar finding was reported by Peddie *et al*, where one of the reasons why fertility preservation was not discussed with cancer diagnosed patients was the belief that treatment had to start urgently and that the delay due to FP could not be justified, however, not all the medical professionals were certain of the time taken for each of the FP procedures.²⁵

In addition to the barriers cited in the present study, healthcare providers also gave their suggestions, some of which are potential solutions for a successful establishment of oncofertility in the country. Suggestions included increasing awareness and sensitization of

healthcare providers about FP, an availability of more FP units, a need for consensus guidelines, and affordable costs. These suggestions are in line with earlier studies, which also included developing reliable referral pathways and training of patient navigators and oncology nurses about fertility issues and available options.^{7,12,16}

In conclusion, this study shows that the two primary healthcare providers involved in an oncofertility program, i.e, oncologists and gynecologists, agree upon the importance of preserving fertility before cancer therapy. It also reveals the necessity of more information on FP options. The study highlights the major barriers perceived between the two specialties in India, which brings about a need to develop strategies for increased medical and social awareness for effective implementation of FP services. One of the strategies for an effective nationwide implementation of oncofertility programs could include the formation of a network similar to the National Physicians Cooperative (NPC), a network that includes 83 institutions within the USA committed to FP for oncological and non-oncological medical conditions that could impact fertility.²⁶ Also, the creation of fertility preservation consortiums along the lines of the Oncofertility Consortium, that also includes NPC, would facilitate global networking, knowledge sharing, and resource distribution in fertility preservation among medical professionals, thereby helping establish a standard-of-care in oncofertility practice²⁷ in India.

The present study has its limitations, one of which is the random recruitment of participants attending oncology and gynecology national conferences or meetings, rendering it likely to have a selection bias. Another limitation is the inclusion of all gynecologists, not all of them being experts in fertility management or andrology, whose awareness of the various FP options may be limited. Details pertaining to the types of cancers treated by oncologists, the frequency of treating adolescent and young adult patients requiring oncofertility services, and whether

gynecologists also treated cancer patients are areas that need to be focused upon in future studies.

Acknowledgement: This work was supported by the Indian Council of Medical Research (ICMR # 5/10/FR/10/2014-RCH). The authors thank all the oncologists and gynecologists who participated in the survey. Authors thank the subject experts for validating the content of the survey and Mr Vishwas Adiga for language editing of the manuscript.

Disclaimers: None

Author disclosure statement: No competing financial interests exist.

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Figure legends:

Figure 1: Trends in fertility preservation among oncologists and gynecologists in India.

(A) Awareness of ASCO- fertility preservation guidelines among healthcare providers. (B) Healthcare provider's knowledge of various fertility preservation options. The various fertility preservation options in X axis are Sperm freezing (SF), Testicular tissue cryopreservation (TTC), Oocyte banking (OB), Ovarian tissue cryopreservation (OTC), IVF followed by embryo freezing (IVF) and GnRHa pre-treatment (GnRHa). (C) Frequency of initiating fertility preservation discussions with cancer patients. (D) Proportion of healthcare providers comfortable in discussing the various fertility preservation options with cancer patients.

Figure 2: Barriers to effective utilization of fertility preservation services in India.

Table 1: Demographics of healthcare providers participating in the survey.

Characteristics	Percentage of oncologists (n=49)	Percentage of gynecologists (n=49)
Age (in years)		
< 30	10.2 (5)	16.3 (8)
31-40	59 (29)	32.6 (16)
41-50	24.5 (12)	22.4 (11)
51-60	4.1 (2)	10.2 (5)
>60	2.1 (1)	18.3 (9)
Gender		
Male	40.8 (20)	22.4 (11)
Female	59.1 (29)	77.6 (38)
Practice setting		
University/Institution	53.1 (26)	51 (25)
Govt/Aided institution	20.4 (10)	4.1 (2)
Private practice with institutional affiliation	14.3 (7)	16.3 (8)
Exclusive private practice	12.2 (6)	28.5 (14)
Experience (in years)		
<5	38.8 (19)	30.6 (15)
5-10	34.7 (17)	14.3 (7)
11-15	14.3 (7)	16.3 (8)
16-20	8.2 (4)	12.2 (6)
>20	4.1 (2)	26.5 (13)

Figure 1

Figure 2

Supplementary Table 1: The 18-item questionnaire administered to oncologists and gynaecologists to assess the healthcare provider knowledge, attitudes and barriers in fertility preservation.

Q1. Are you familiar with the American Society of Clinical Oncology (ASCO) guidelines regarding fertility preservation for cancer patients?

- a. Yes
- b. No

Q2. How would you grade your knowledge of fertility preservation options available for patients affected with cancer? *Please tick the appropriate box.*

Fertility preservation options	Not aware	Aware but not adequate knowledge	Knowledgeable	Very knowledgeable
a. Semen cryopreservation				
b. Testicular tissue cryopreservation				
c. Oocyte cryopreservation				
d. Ovarian tissue cryopreservation				
e. <i>In vitro</i> fertilization with embryo cryopreservation				
f. Pre-treatment with GnRH agonists				

Q3. Offering fertility preservation to patients before cancer therapy compromises their oncological treatment.

- a. Agree
- b. Disagree
- c. Do not know

Q4. How often do you initiate a discussion on effects of cancer treatment on fertility?

- a. Never
- b. Only when asked
- c. Occasionally
- d. Most of the time
- e. Routinely

Q5. When do you refer your patients for fertility preservation consultation?

- a. Immediately after diagnosis

- b. Before planning treatment
- c. During cancer treatment
- d. After cancer therapy

Q6. How long do you feel is the time required for a cancer patient to complete the fertility preservation procedure? *Please tick the appropriate box.*

Fertility preservation options	<1 week	2-3weeks	1 month	Do not know
a. Semen cryopreservation				
b. Testicular tissue cryopreservation				
c. Oocyte cryopreservation				
d. Ovarian tissue cryopreservation				
e. <i>In vitro</i> fertilization with embryo cryopreservation				
f. Pre-treatment with GnRH agonists				

Q7. How comfortable are you to discuss the fertility preservation options with your patients? *Please tick the appropriate box.*

Fertility preservation options	Not comfortable at all	Comfortable	Very comfortable
a. Semen cryopreservation			
b. Testicular tissue cryopreservation			
c. Oocyte cryopreservation			
d. Ovarian tissue cryopreservation			
e. <i>In vitro</i> fertilization with embryo cryopreservation			
f. Pre-treatment with GnRH agonists			

Q8. What is the proximity to the nearest fertility preservation unit you can refer your patients to?

- a. Same hospital
- b. Same city
- c. <100kms
- d. >100 kms
- e. Don't know

Q9. Which factors may be considered as barriers for providing fertility preservation to cancer patients? (*More than one option may be selected.*)

- a. Time to treatment
- b. Financial burden on patient
- c. Lack of patient awareness on importance of fertility preservation
- d. Lack of awareness among healthcare providers about availability of fertility preservation options
- e. Lack of fertility preservation facilities nearby
- f. Lack of referrals
- g. Cultural/religious restrictions
- h. Age of patient
- i. Emotional status of patient
- j. Others .....

Q10. Please give your recommendations for effective utilization of fertility preservation services by cancer patients, in India.

Details of survey participant

Q11. Age of the participant (in years)

- a. ≤ 30
- b. 31-40
- c. 41-50
- d. 51-60
- e. >60

Q12. Gender of participant

- a. Male
- b. Female

Q13. Area of specialization

- a. General Medicine
- b. Medical Oncology
- c. Paediatrics
- d. Paediatric surgery
- e. Gynaecology
- f. Reproductive specialist
- g. Others .....

Q14. Which setting would best describe your practise?

- a. University/Academic Institution
- b. Government/Aided Institution
- c. Private practice affiliated with Institution
- d. Exclusive private practice
- e. Others .....

Q15. Work experience in your specialization (in years).

- a. <5
- b. 5-10
- c. 11-15
- d. 16-20
- e. >20

Q16. How many new cancer diagnoses are made by you in a month, gender-wise?

Please tick the appropriate box.

No. / Gender	<5	5-15	16-25	>25
a. Male				
b. Female				

Q17. How many of the above new diagnoses are in the following age groups?

Please tick the appropriate box.

Age/Gender	<15yrs	15-20yrs	21-25yrs	26-30yrs	31-35yrs	>35yrs
a. Male						
b. Female						

Q18. How many of the cancer patients come for follow-up? *Please tick the appropriate box.*

No. /Gender	<5	5-15	16-25	>25
a. Male				
b. Female				