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*March, 2019*



**International And National Review  
Of Uptake Of Oncofertility**

**ONCOFERTILITY  
COMMUNICATIONS**

**An academic initiative by IFS**

**Supported by AstraZeneca Pharma Ltd**



**Dr M Gouri Devi**

President - IFS

Fertility preservation is an important aspect of care provided by fertility experts to patients undergoing cancer treatment. We have tried to bring in more awareness on this aspect.

I hope that you may have enjoyed first volume of this series where an overview was presented. We present the second volume of this series where we present uptake of fertility preservation in India and also review efforts put in this sub-specialized field by various countries worldwide.



**Prof (Dr) Pankaj Talwar**

Secretary General - IFS

Oncofertility-Fertility preservation: an important aspect of care given by reproductive medicine specialist.

It has been endeavor of all of us to counsel, educate the masses about the nuances of fertility preservation and the outcome of the procedures. Many of them are experimental and have not an efficient outcome. Indian Fertility Society and Astra Zenac initiated bulletin- “Oncofertility Communications” to educate you all to do something for these unfortunate fighters and survivors and ease their pain and anxiety.

Continuing this educative endeavour forward, we present here the second volume of this series in which we discuss the understanding and uptake of this speciality in India and also review on various work done globally.



## **Dr Puneet Rana Arora**

Guest Editor

Oncofertility communications was started with view to increase awareness among medical faternity regarding oncofertility services provided to patients underfoing cancer treatment. First volume was released in january, 2019. It is my absolute privelege to present the second volume of “Oncofertility Communications”.

Any new subspecilaised field comes with its challenges and logistics. It is important to understand these challenges so that uptake can be maximised to larger poulation without any difference in economic status. In this volume we compare the Indian data and the western data with regards to understanding and avialability of oncofertility services.

I hope this edition brings in further understanding from last overview volume.

Happy Reading!.



## **Dr Jayesh Amin**

SIG Chair - ONCOFERTILITY

Fertility preservation is an innovative technique which requires multi disciplinary approach. Our colleagues in the field of oncology as well as general public need more awareness about the subject and therefore lot of scope for training is the requirement.

## PUBLISHED TOPICS

1.	<b>Fertility Preservation : An Overview</b>	<b>January-2019</b>
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## UPCOMING TOPICS

1.	<b>Ethical, Logistic and Legal aspects of Fertility Preservation</b>	<b>April-2019</b>
2.	<b>Breast diseases and Fertility Preservation</b>	<b>June-2019</b>
3.	<b>Fertility preservation in Males</b>	<b>August-2019</b>
4.	<b>Fertility preservation in Gynaecological Malignancies</b>	<b>October-2019</b>
5.	<b>Non-malignant conditions and role of fertility preservation</b>	<b>November-2019</b>
6.	<b>Childhood cancers and fertility preservation</b>	<b>December-2019</b>

## INDEX

S.NO.	CONTENT	PAGE
i.	Introduction	6
ii.	Why is it important to discuss uptake of Oncofertility Care?	7
iii.	Barriers on uptake of Oncofertility services	10
iv.	Data on publications related to fertility preservation/Oncofertility	12
v.	Conclusion	12
vi.	Recommended reading	13

## International and National Review of uptake of Oncofertility

### I. INTRODUCTION

Fertility preservation has moved from providing services related to preserving gametes (sperms/oocytes) and embryos to “Oncofertility Care”. “Oncofertility Care” is a broad term including not only fertility preservation discussion and management, but also discussion regarding management of sexual dysfunction, hormonal dysfunction, complex contraception and fertility related psychosocial support. These effects are related to cancer and its treatment.

As per national cancer registry of India by 2020, 11.4 lakh people will have some form of cancer out of which 30-75% of males and 40-80% of females have problems with fertility at some point after completion of cancer treatment.

### II. WHY IMPORTANT TO DISCUSS UPTAKE OF ONCOFERTILITY CARE

As the number of long-term cancer survivors are increasing, fertility has become an increasingly important quality of life issue. However, aggressive cancer treatment, especially with alkylating agents or ionizing radiation can cause premature ovarian failure. The loss of reproductive potential is one of the most distressing adverse consequences of successful cancer treatment and can affect the quality of life of cancer survivors and can lead to psychological distress in some. Therefore, wherever possible, oncofertility care should be an integral part of cancer care from diagnosis through to survivorship.

If the risks of infertility are not discussed properly before cancer treatment, cancer survivors may experience prolonged anger and grief when they are unable to conceive.

Currently, several options are available for fertility preservation in young cancer patients; however, the only established option for male patients is sperm cryopreservation. For women both embryo cryopreservation and oocyte cryopreservation are considered as well established methods, but not ovarian tissue cryopreservation at the moment. Nevertheless, ovarian tissue cryopreservation is a good alternative option for women who cannot delay cancer treatment or with hormone dependent tumor. It is the only option for pre-pubertal girls who want to preserve fertility before cancer treatment.

There are various guidelines till date enforcing Oncofertility care naming few such as-

- Multi-disciplinary Working Group convened by the British Fertility Society, 2003
- French Association for the Care of Oncological Support, 2011
- National Comprehensive Cancer Network, 2011; von Wolff et al., 2011; Cardoso et al., 2012; Kim et al., 2012

# International and National Review of uptake of Oncofertility

- National Institute for Health and Care Excellence, 2013
- Scottish Intercollegiate Guidelines Network, 2013; Sudour-Bonnange et al., 2013
- Fertility preservation for AYAs diagnosed with cancer: Guidance for health professionals, 2014.
- Practice Committee of American Society for Reproductive Medicine, 2014

Despite above extensive recommendations, fertility preservation care is often under-implemented.

## III. BARRIERS TO UPTAKE OF ONCOFERTILITY SERVICES

Several barriers have been found to thwart the implementation of comprehensive and equitable fertility preservation practice. These include:

1. A lack of referral pathways and model of care for oncofertility services and collaboration between cancer and fertility doctors to deliver services;
2. Inequitable access based on cost;
3. Health literacy;
4. Lack of trained staff who can deliver these services; and
5. No consensus about the best way to deliver information to patients

All the guidelines recommends that health care providers should discuss fertility with their patients as a part of their counseling before cancer therapy, and should be prepared to refer for fertility preservation.

Even though fertility has been a significant issue expressed by cancer survivors, uptake of fertility preservation offered at the time of diagnosis is 10-12%.

There are several clinician and patient barriers which exist in providing oncofertility care and these barriers need to be quantified more accurately .

While fertility preservation is recognized as an important issue, work still needs to be done to educate care providers along with patients about the issues and options for fertility preservation.

A retrospective cohort study of female cancer patients aged 18-42 years in 2012 showed that overall referral rates for fertility preservation consultation are low (20.6%), with significant discrepancies in referral based on patient ethnicity, age, parity, and cancer type.

A population based study published in 2015 showed that the proportion of patients who were discussed about fertility preservation options before cancer treatment was 71% in young males and 44% in young women with cancer. However, actual fertility preservation arrangement was made only in 31% of males and 6.8% of females. Indeed, these low referral rates (confirmed by other studies) and under-utilization of fertility preservation are problematic even by now.

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The main barriers among all include lack of knowledge on fertility preservation, attitude and behaviors of health care providers, and time constraint before cancer treatment.

In developing countries like India, the financial barrier (such as high cost and no insurance coverage) is a very significant issue. In spite of many barriers, a new global trend for fertility preservation is encouraging.

Rates of referral for fertility preservation remain relatively low, averaging 20–30% (Cohen et al., 2016; Scanlon et al., 2012), with women reporting lower uptake rates of fertility preservation (14.9%) compared to men (31.5%) in a recent study (Wang, Chen, Ruan, & Cheung, 2016). These low rates are a matter of concern, as clinicians have a 'duty of care to provide the option of fertility preservation' to patients of reproductive age (Logan, Perz, Ussher, Peate, & Anazodo, 2018b), and uptake of fertility preservation can improve quality of life and wellbeing post-treatment (Letourneau et al., 2012; Sobota & Ozakinci, 2014).

In addition, a lack of private health insurance or public healthcare funding for fertility preservation is associated with lower rates of uptake, due to financial barriers to accessing services (Inhorn et al., 2018; Shnorhavorian et al., 2015).

A lack of information about the consequences of cancer treatment on fertility from health professionals has been identified as one of the major barrier to accessing fertility preservation (Logan, Perz, Ussher, Peate, & Anazodo, 2018a).

### IV. DATA ON PUBLICATIONS RELATED TO FERTILITY PRESERVATION/ ONCOFERTILITY SERVICES

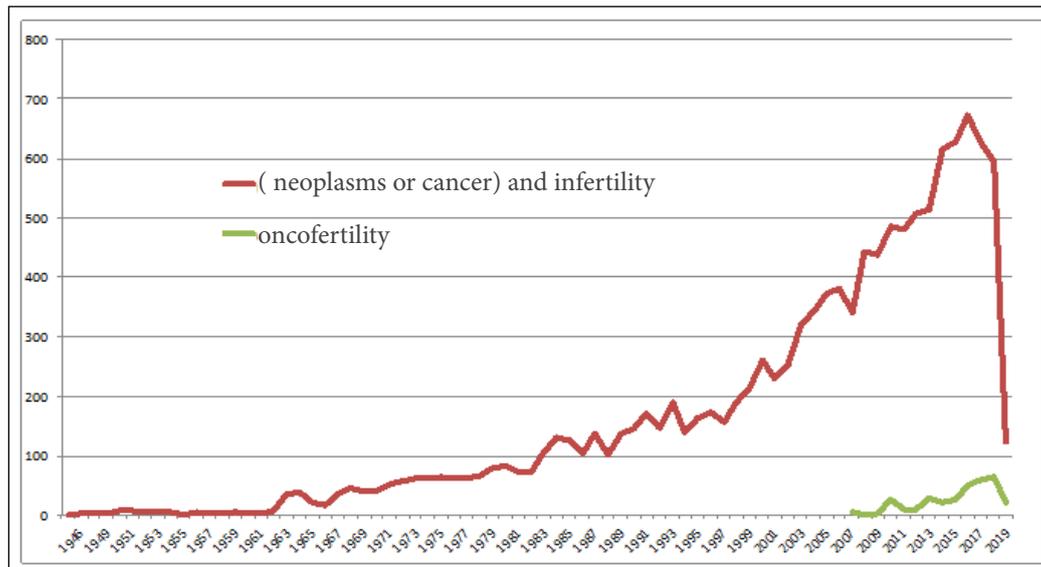
Figure 1,2,4 depicts the total number of literature found on single source search engine-Pubmed. There were more articles with Neoplasms and infertility. Oncofertility search revealed few articles and were commonly after 2007 when this specific nomenclature was used formally. Number of studies in India were less in both categories. But still published data on other hand of whatever grade means the awareness and availability of Oncofertility service is available and what is needed is to streamline the services so that mass population can utilise when needed.

Existing research examining fertility preservation after cancer has focused on Western countries, with most studies conducted in the United Kingdom, United States of America, Canada and Australia. Figure 3 shows the different types of studies published related to Oncofertility or Neoplasms with fertility. Clinical Trials and laboratory based work was found less in Indian scenario than in western world. This is in line with other specialities of medicine. Studies have examined the distribution and quality of information by health professionals, utilisation of fertility services, as well as patient

# International and National Review of uptake of Oncofertility

satisfaction and psychological distress as outcomes of fertility-related care (Deshpande et al., 2015; Letourneau et al., 2012; Ussher, Cummings, Dryden, & Perz, 2016; Yeomanson, Morgan, & Pacey, 2013).

## GLOBAL LITERATURE ON CANCER AND FERTILITY



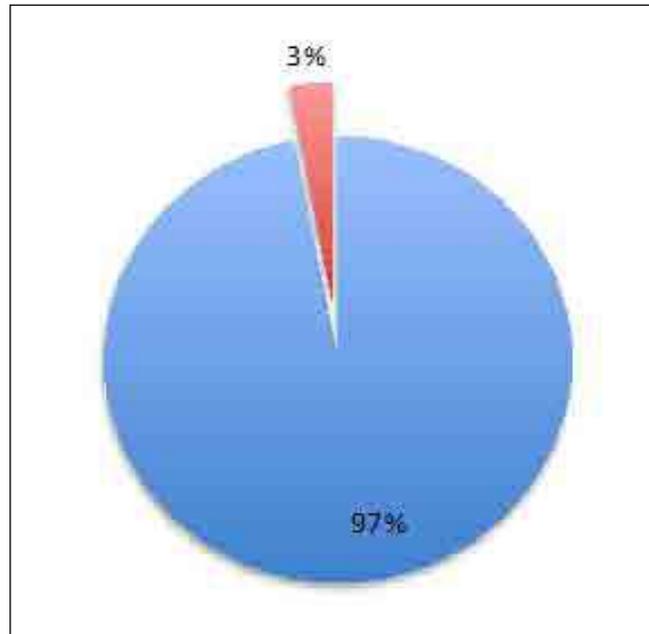
**Figure:1- Literature published based on kew words Neoplasms/Cancer/Infertility/Oncofertility**

Many people with cancer report receiving no information, or inadequate information from healthcare professionals about fertility (Benedict, Thom, et al., 2016; Ussher & Perz, 2018). Furthermore, fertility information from healthcare professionals is not uniformly distributed across gender, age group and cancer type (Shnorhavorian et al., 2015). Men, those who are nulliparous, heterosexual, with reproductive cancers, and who are AYA at the time of diagnosis, are the groups most likely to receive information from healthcare professionals and take part in fertility preservation studies/surveys (Barlevy et al., 2016; Logan et al., 2018a; Wang et al., 2016).

While previous studies have focused on health professional information and referral for specialist fertility care, other factors may influence uptake of fertility preservation (Flink et al., 2017). For example, the desire to have a biological child and being in a stable relationship at the time of cancer can motivate people with cancer to take part in fertility preservation (Baysal et al., 2015; Treves et al., 2014). Conversely, limited clinic times, urgency to act on fertility during cancer treatment, the wish to preserve survival for an existing child, and for women, the physical burden of fertility preservation, can act as barriers to uptake (Baysal et al., 2015; Flink et al., 2017; Lee et al., 2011)

Referral pathways between cancer and fertility clinicians can vary between different regions/countries and also institutions, relying sometimes on particular relationships between centers, between doctors rather than a formal referral system.

## ONCOFERTILITY AND INDIA (10 OUT OF 331)



**Figure:2- Literature Search of studies on Oncofertility from India**

Fertility preservation strategies were initially developed and applied in Western Europe and North America, but ISFP (International society of fertility preservation) committee recommends that fertility issue should be addressed to all patients in reproductive age before cancer treatment, hence these applications are no longer limited to certain geographic areas or socio-economic classes.

A review of literature until December 2014 highlighted the lack of published data internationally from FP databases or registries collecting “whole of care” oncofertility information from male and female pre and post - pubertal cancer patients:

- The International Society of Fertility Preservation (ISFP) launched the Ovarian Cortex freezing registry in 2014, which is designed to collect ovarian cortex cryopreservation data.
- The Northwestern Oncofertility Consortium has an observational fertility information research study (FIRST Registry) collecting annual questionnaire data from women aged 18–44 years on the impact of cancer treatment on the reproductive health of young survivors.
- The Human Oocyte Preservation Experience (HOPE) is a prospective multicenter, observational oocyte cryo- preservation registry; however, this registry has not collected data from cancer patients.
- The FertiPROTEKT Network is the European oncofertility consortium set up in 2006 to provide expertise in oncofertility and standardized support and FP treatment recommendations for female cancer patients. Seventy registered centers in Germany, Switzerland, and Austria collect

# International and National Review of uptake of Oncofertility

and report on FP data before cancer treatment.

- A number of countries produce national reports about the success of assisted reproductive technologies, however, to date, these reports have not included specific data on FP in cancer patients.

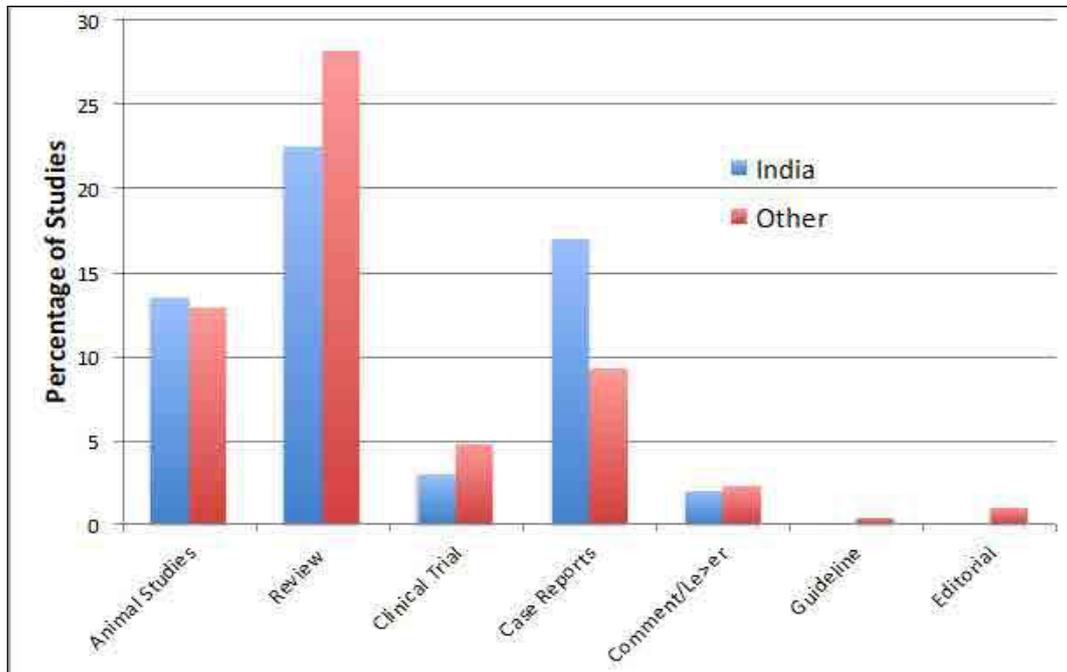


Figure:3- Type of studies publishes globally and in India

(NEOPLASMS OR CANCER) AND INFERTILITY AND INDIA (200 OUT OF 12315)

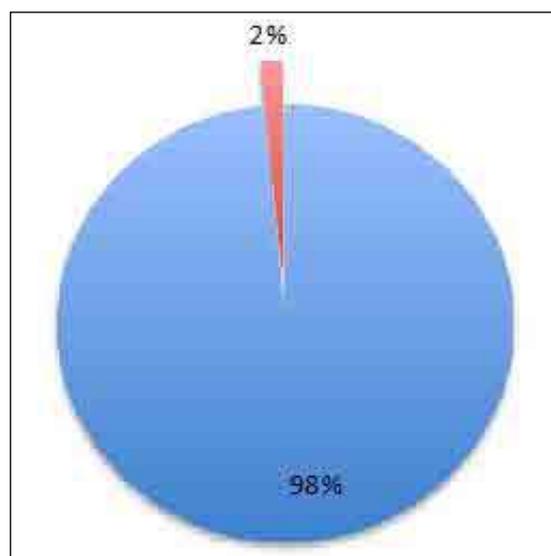


FIGURE:4- Literature review with key words as Neoplasms/Cancer from india

## V. CONCLUSION

Oncofertility Care/Fertility preservation is one of the most important quality of life issues in young cancer survivors worldwide. It is imperative to promote the global awareness of fertility preservation, to improve the global collaboration for fertility preservation and to expand fertility preservation service beyond the boundaries of geographic areas, socioeconomic status, ethnicity, nationality, age, parity, and cancer type.

One of the ways of promoting awareness among healthcare providers is publication of work being done on fertility preservation in various geographic areas. This is one of the good ways to connect between health care providers of various nationalities. Also publication data is more directly co-related to work done in a particular region, it may not necessarily reflect the workload in an area.

Network between oncologist and reproductive medicine specialist is must for a successful fertility preservation program .

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Pregnancy and Lactation. **PRECAUTIONS:** Children: Zoladex is not indicated for use in children, as safety and efficacy have not been established in this group of patients. Males: Use in patients at particular risk of developing ureteric obstruction or spinal cord compression should be considered carefully and patients monitored during first month of therapy. Females: Exclude pregnancy before treatment. Non-hormonal contraception should be employed during therapy. Loss of bone mineral density, which may recover on cessation of therapy. Caution in women with known metabolic bone disease. Increase in cervical resistance, requiring care of fitting the cervix. Currently, there are no clinical data on the effects of treating benign endometriosis conditions with Zoladex for periods in excess of six months. An increase in benign pituitary tumours has been observed in male rats following long-term repeated dosing. (Relevance to man not established). Pancreatic islet cell hyperplasia and a benign proliferative condition in the pyloric region of the stomach observed in mice following long-term repeated dosing with human dose (relevance to man is unknown). There is no evidence that Zoladex results in impairment of ability to drive or operate machinery. **PREGNANCY AND LACTATION:** Although reproductive toxicology in animals gave no evidence of teratogenic potential, Zoladex should not be used in pregnancy, as there is a theoretical risk of abortion or foetal abnormality if LHRH agonists are used during pregnancy. Potentially fertile women should be examined carefully before treatment to exclude pregnancy. Non-hormonal methods of contraception should be employed during therapy. The use of Zoladex during breast-feeding is not recommended. **SIDE EFFECTS:** Rarely, hypersensitivity, skin rashes, generally mild. Arthralgia. Changes in blood pressure. Occasional mild bruising at injection site. Males: Hot flushes, decrease in potency, infrequently breast swelling and tenderness. Temporary increase in bone pain. Isolated case of ureteric obstruction and spinal cord compression have been recorded. Females: Hot flushes and sweating, change in libido, headaches, mood changes including depression, change in breast size. Temporary increase in signs and symptoms. Degeneration of fibroids. **LIST OF EXCipients:** Lactide/glycolide copolymer. **PRESENTATION:** A sterile depot containing goserelin 3.6mg (as acetate) in a SafeSystem™. **PRECAUTION FOR STORAGE:** Store below 25°C. Zoladex is a Trade Mark of the AstraZeneca Group of Companies.   
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