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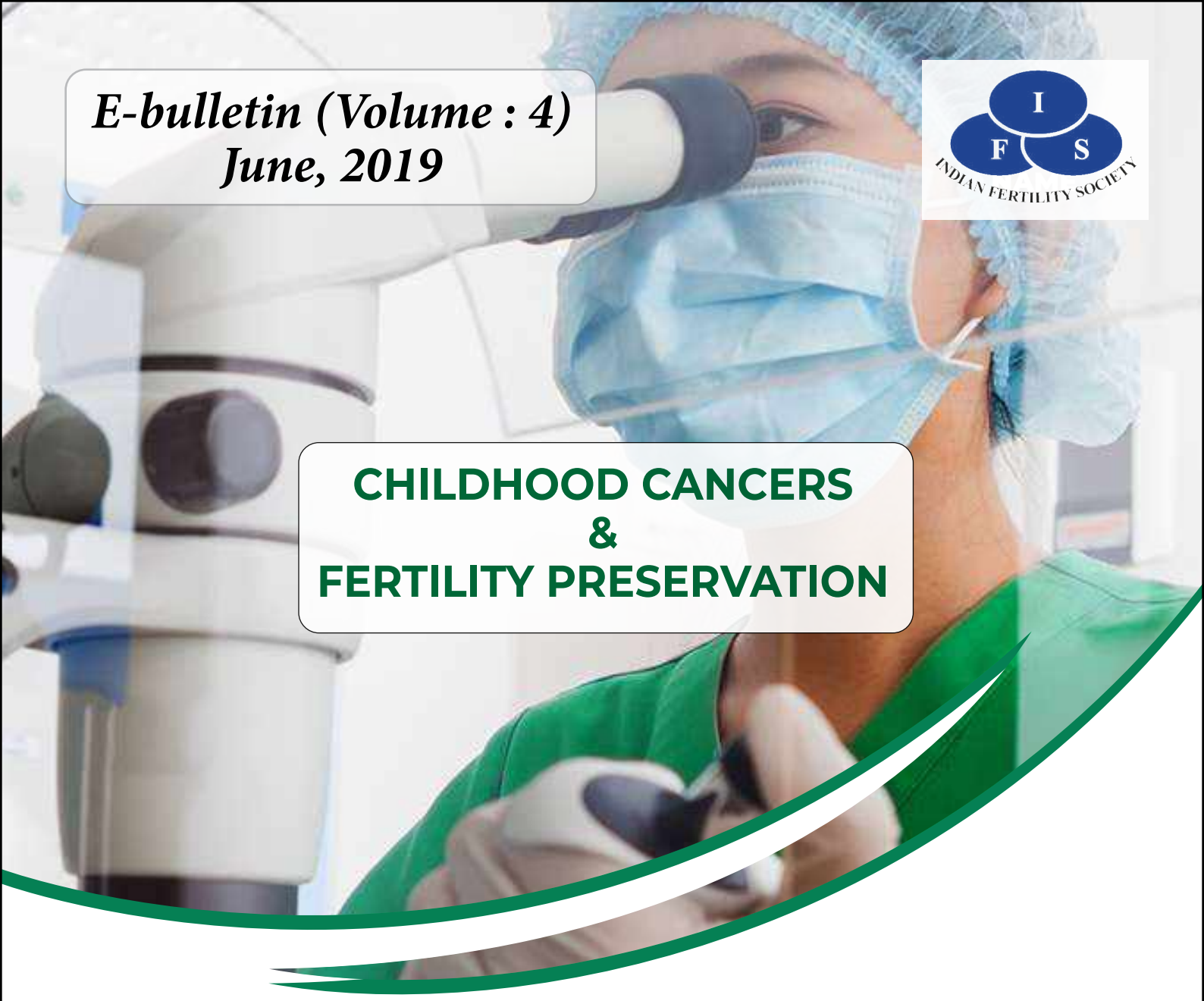

CHILDHOOD CANCERS & FERTILITY PRESERVATION

ONCOFERTILITY COMMUNICATIONS

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Dr Puneet Rana Arora
Executive Editor

It's my privilege to present 4 th edition of oncofertility communications . This month focus is on Children with cancer and Fertility Preservation. Children wil cancer represent a special group where they will be heading towards adulthood and fertility may become a very important quality of life aspect for them. They may experience the remanants of effects of cancer and it's treatment on their fertility.

But ethical dilemma includes the diagnosis of cancer and hence decision of fertility preservation is at an age when they are minors. Parents or care takers play a major role in their decision making. So in this group both children and their care taker needs counseling and awareness.

Hope this edition answers all your questions on Children with cancer and aspects of fertility preservation in this group.

I would like to extend my special thanks to Dr Sweta Agarwal for contribution for this edition.

Happy Reading !

Dr Sweta Agarwal
Guest Editor

Childhood cancer treatment is getting better with improved survival rate & full recovery. A major quality of life parameter in survivors is ability to live a fuller life, including reproduction. It is only if we are geared up for it and inform the family of current fertility preservation options, it is possible to fulfill this important aspect of life.

Happy reading !!

PUBLISHED TOPICS

1.	Fertility Preservation : An Overview	January-2019
2.	International And National Review Of Uptake Of Oncofertility	March-2019
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UPCOMING TOPICS

1.	Breast diseases and Fertility Preservation	June-2019
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INTRODUCTION

The treatment of children and adolescents with cancer has become increasingly successful.

About 78% of all patients diagnosed before 15 years of age will survive for 5 years.[1] The most common types of cancer diagnosed in children aged between 0 to 14 years are leukemias, brain and other central nervous system (CNS) tumors, and lymphomas.Survivors of these cancers can develop health problems months or years after cancer treatment, known as late effects. These late effects cover the spectrum from life altering to life-threatening conditions.

The gonadotoxic impact of treatments for cancers have concerns, anxiety, and embarrassments due to the impact of therapy on sexual and reproductive function, which have the potential to adversely impact quality of life.[2] Infertility remains one of the most common life-altering treatment effects experienced by long-term childhood survivors[3] Infertility, not only involves the individual, but also a partner, a spouse, or other family members.[4,5,6] In these patients, fertility preservation maximizes long-term quality of life.

One of the issues is that the patient or their families do not receive proper information about the possible gonadotoxic impact of cancer therapy. Unless patients are informed or properly referred before treatment, options for later reproduction may be lost. Thus, it is essential for pediatric oncologists to consider the potential impacts of treatment on every patient's fertilityand inform patients and/or their families of options, benefits, and risks, and referring them to fertility specialists for fertility preservation prior to initiation of gonadotoxic therapy.

However, for several children and adolescents diagnosed with cancer, fertility preservation is not possible due to its cost or investigational nature. In some cases, fertility preservation may not be a priority because of the desire or necessity to initiate cancer treatment urgently. Many childhood cancer survivors who maintain fertility have concerns about the potential effects of cancer treatment on their health during pregnancy and health of their offspring. Cancer and reproduction raises ethical issues for both oncologists and fertility specialists, including issues of experimental vs. established therapies, the ability of minors to give consent and the welfare of expected children.[7] All of these factors have to be taken into consideration while discussing with the patient and their parents.

EFFECTS OF CANCER THERAPY ON FERTILITY

Recent reports from ChildhoodCancer Survivor Studyobserved that, compared to a sibling cohort, female participants were less likely to become pregnant (relative risk of ever pregnant 0.81; 95% Confidence Interval [CI], 0.73-0.90).[8] In another report from the Childhood Cancer Survivor Study, the risk of infertility was 2.5 times higher in male cancer survivors compared to healthy siblings (46% vs. 17.5%).[9]

Surgery, radiation, or chemotherapy that has a negative impact on any component of the hypothalamic-pituitary-gonadal axis may compromise the reproductive outcomes in childhood cancer.[10] Pediatric cancer treatment protocols often prescribe combined modality therapy, thus the additive effects of gonadotoxic exposures may need to be considered in assessing reproductive potential. The most harmful regimens to the ovaries and testes are alkylating agent-based chemotherapy and high doses of cranial radiotherapy that impair hypothalamic pituitary function, resulting in the depletion of gonadotropin-releasing hormone (GnRH)

EFFECT OF SURGERY ON FERTILITY

Gonadal and extragonadal germ cell tumors account for only 1% of primary tumors in children younger than 15 years and 10% of primary cancer sites in adolescents and young adults 15 to 29 years.[11] Orchidectomy or oophorectomy performed for the management of these relatively rare pediatric cancers may reduce germ cell numbers. Fertility may also be adversely impacted in survivors with autonomic nerve damage and/or vascular injury resulting from pelvic or spinal surgery. Sexual dysfunction associated with these procedures may be exacerbated in survivors with androgen or estrogen insufficiency. [12]

EFFECT OF CHEMOTHERAPY

Alkylating agents are used to treat a variety of pediatric hematological and solid malignancies.Factors influencing the risk of gonadal injury in children treated with alkylating agent chemotherapy include cumulative dose, the specific alkylating agent, the length of treatment, age at treatment, and sex.[13, 14] Prepubertal status does not provide protection from gonadal injury.[15, 16]

Females are more likely to be at risk for long-term premature ovarian failure rather than acute ovarian failure. Acute ovarian failure develops in a small subset ranging from 6% to 12% in childhood cancer survivors. Ovarian damage caused by treatment can lead to amenorrhea during or immediately after treatment and it could be temporary or permanent. Furthermore, regular menstruation cannot be concluded to have no damage to the ovarian reserve, so ovarian function should be judged not only by menstruation but also by anti-Mullerian hormone (AMH), follicle stimulating hormone (FSH), and ultrasound. In the childhood cancer survivor study, secondary amenorrhea rate of post-pubertal girls was higher than the primary amenorrhea rate of prepubertal girls. Adolescents have about 2 to 3 times higher risk of premature ovarian insufficiency than those under 12 years of age.

Thus, a female pediatric cancer patient is more likely to have a window of fertility after completion of treatment, although alkylating agents may reduce her overall fertility span. The most detrimental effects were observed in alkylating agents including chlorambucil, cyclophosphamide, ifosfamide, melphalan, busulfan, and procarbazine. Furthermore, myeoblastive chemotherapy regimens such as

high-dose cyclophosphamide with busulfan or Thiotepa-based high-dose therapy has been shown to increase the incidence of ovarian failure.
In males, spermatozoa-producing germ cells are more sensitive to chemotherapy and radiation compared to the testosterone-producing Leydigcells. In males, Leydig cell function is preserved, but germ cell failure is very common when treated with high cumulative doses of cyclophosphamide (≥ 7500 mg/m2) and more than 3 months of combination alkylating agent therapy.Therefore, infertility is more often a late effect of cancer therapy in males, while sexual function is relatively spared. [16,17,18]

EFFECT OF RADIOTHERAPY

Direct irradiation of the hypothalamus and/or pituitary may produce impaired secretion of follicle-stimulating hormone (FSH) and luteinizing hormone (LH), especially when the dose is greater than 35 Gy. Lower-dose exposures (18 to 24 Gy), such as those employed for prophylactic cranial irradiation of children with acute lymphoblastic leukemia, did not appear to produce major abnormalities in FSH or LH release.

In women treated for childhood cancer, the potential for primary gonadal injury exists if treatment fields involve the lumbo-sacral spine, abdomen, pelvis, or total body. As with chemotherapy-induced gonadal injury, the ovaries of younger patients are more resistant to radiation damage than are those of older women. Permanent ovarian failure uniformly occurs in childhood cancer patients treated with ovarian radiation doses > 20 Gy.[19]

Combined modality therapy with alkylating agent chemotherapy and radiation treatment volumes that include the ovaries increases the risk for both acute ovarian failure and premature menopause. [20,21] Prepubertal girls treated with 20 to 30 Gy abdominal radiation may fail to undergo or complete pubertal development. Ovarian transposition to a region that is lateral or medial to the planned radiation volume may preserve ovarian function in young girls and adolescents who require pelvic radiation therapy for lymphoma.[22] Moreover, radiation can affect reproductive organs, such as the uterus, with subsequent issues related to implantation and carrying a pregnancy.

Among men treated for childhood cancer, the potential for primary gonadal injury exists if radiation treatment fields include the pelvis, gonads or total body. Sperm production is reduced in a dose-dependent fashion following radiation. Azoospermia may be reversible at doses of 1 to 3 Gy, but doses in excess of 3 Gy typically produce irreversible azoospermia. Radiation injury to Leydig cells is related to the dose delivered and age at treatment.[18,23] Testosterone production may be normal in prepubertal boys treated with < 12 Gy fractionated testicular radiation, but elevated plasma concentrations of luteinizing hormone observed in this group suggest subclinical injury. Gonadal failure typically results when prepubertal boys are treated with > 20 Gy radiation to the testes; androgen therapy is required for masculinization. Leydig cell function is usually preserved in sexually mature males if radiation doses do not exceed 30 Gy.[24]

WHEN TO DISCUSS ABOUT FERTILITY PRESERVATION?

Cancer survivors and their families value a frank discussion about fertility at the time of diagnosis. At first glance, one might wonder why even bother bringing up the issue in the dramatic setting of disclosing a cancer diagnosis and the pressing need to start treatment for a patient that is far from planning to have a family of his or her own. In a multicentre Canadian study looking at the perspectives of survivors, parents, and providers, found that parents and survivors would like to be informed at the time of diagnosis, regardless of the actual risk of fertility impairment, and despite other factors, such as cost, experimental nature of interventions, and likelihood of surviving. Furthermore, non-disclosure was noted to be associated with future negative feelings, such as resentment and anger.[25]

Several international guidelines have already recommended early referral of young patients diagnosed with cancer to infertility specialists, as soon as possible, after diagnosis and it would decrease time spent making decisions and undergoing procedures.[3,6,9,25] Early counseling can provide a positive psychological effect for the patient and their parents, and can be accepted even when realistic fertility options are not available.

WHICH MEMBER OF HEALTHCARE TEAM SHOULD DISCUSS FERTILITY

The development of a multidisciplinary oncofertility group with participation of nurses, oncologists, urologists, gynecologist, ethicists, administrators, and reproductive specialists can assist with implementation of best practices and counselling, being mindful of cultural issues, financial constraints, and individual preferences and beliefs.[2]

MINOR PATIENTS & CONSENT

Ethical and legal norms require that procedures done on minors serve their best interests. If invasive procedures are necessary, minors who are able to understand the choice presented must give their assent (permission less than full consent). This means that the procedure can be done if they agree and their parents consent, but not if they object.[7]

FERTILITY PRESERVATION IN MALE CHILDREN

In male patients who have attained puberty, cryopreservation of sperm is now standard practice. Cryopreservation of sperm should be done prior to initiating cancer therapy, as even small doses of gonadotoxic agents can affect the quality of the sperm.[26,27,28]
Clinicians should recommend sperm banking for all males with newly diagnosed malignancies, regardless of planned treatment intensity. This approach maximizes fertility options for patients who

might relapse prior to sperm count recovery and therefore face more gonadotoxic chemotherapy.
The least invasive method for sperm collection is masturbation. When masturbation is not a viable option, other methods are available for obtaining a semen sample. Electroejaculation, a method often employed in adult patients with neuropathic dysfunction, can be offered to collect sperm. This, however, would require general or regional anesthesia, and education to accept the need to use a rather large rectal probe to stimulate emission and ejaculation.The published experience with this technique in the adolescent age group is still limited, but success rates close to 50% have been reported.[29] If electroejaculation fails to produce a sperm sample or in patients unwilling or unable to tolerate the procedure, microsurgical epididymal sperm aspiration, where in sperm is removed from the epididymal tubule and in testicular sperm extraction, sperm is retrieved via a needle biopsy of the testis.[30] Numerous recent improvements in sperm storage techniques and advances in assisted reproductive technology using intracytoplasmic sperm injection (ICSI) can facilitate successful pregnancies using banked sperm, which is documented to remain viable for up to 28 years, if stored properly.[31]

Prepubertalmales, cannot produce semen for cryopreservation. In prepubertal testis, germ cells include spermatogonial stem cells (SSCs), mature spermatozoa are not yet present. In these patients cryopreservation of testicular tissue for eventual restoration of spermatozoa production can be done. Ideally, in prepubertalmale's testicular biopsy should be done and tissue should be banked prior to initiating gonadotoxic cancer therapy. After completion of cancer therapy, once the patient is ready to begin a family, this tissue could then be thawed and the stored germ cells reimplanted into the patient's own testes to continue full maturation in situ.[32,33,34] Moreover, contaminating cancer cells must be detected and removed from testicular biopsy samples.

One innovative strategy utilizes in vitro culture methods to expand and purify gonadal SSCs, guide their differentiation into viable spermatids, then achieve fertilization through ICSI. This is still in experimental phase.

FERTILITY PRESERVATION IN FEMALE CHILDREN

Embryo cryopreservation is one of the most well-established technique of fertility preservation. However, this option may not to suitable for all cases of childhood cancers. In these cases, alternative options such as oocyte cryopreservation, ovarian tissue cryopreservation or suppression of the effects of anticancer drugs on the ovaries through ovarian suppression can be advised.

EMBRYO OR OOCYTE CRYOPRESERVATION

Invitro fertilization (IVF) has now become a standardized procedure and embryo cryopreservation is one of the most well-established technique of fertility preservation.

This method involves ovarian hyperstimulation for the in vivo maturation of oocytes and subsequent retrieval of mature oocytes prior to beginning chemotherapy. The oocytes are then fertilized and the

resultant embryo is cryopreserved. Years later, the embryo can be thawed and transferred into either the patient's own uterus or that of another woman (gestational surrogate).A spouse, partner, or the patient's willingness to use donor sperm for this purpose is also necessary.

For post pubertal girls without a male partner,who have the time to undergo a stimulation cycle would benefit from oocyte cryopreservation. As such, recent studies have demonstrated that transfer of embryos originated from frozen-thawed oocytes had comparable pregnancy rates compared to those using fresh oocytes. As freezing and thawing techniques have been improved currently, oocyte cryopreservation is no longer considered as an experimental method.[35,36,37]

Even if improved technique of Oocyte cryopreservation has resulted in more than 900 births in last 30 years, there are some limitations to establish this as a standard method for childhood and adolescent cancer patients. Firstly, oocyte cryopreservation requires time for ovarian stimulation and follicular growing, which can be especially a problem in pediatric cancers, which often require urgency to start cancer treatment. Random-start controlled ovarian stimulation protocol can result in shortening the time from consultation to cryopreservation, but even a 2-week delay is often not feasible in cancer treatment because of characteristics of childhood cancer with aggressive prognosis. Secondly, oocytes are retrieved through transvaginal approach, which is accompanied by damage such as hymen rupture. Pediatric and adolescent patients who have never had sexual relationship or vaginal procedure previously, even if they were sexually mature, may find this processes emotionally and physically unbearable in the absence of anesthesia. Finally, oocyte cryopreservation cannot be used in prepubertal girls whose hypothalamic-pituitary axis not mature or ovulation does not occur.[38-41]

OVARIAN TISSUE CRYOPRESERVATION

Ovarian tissue cryopreservation seems to be advantageous as it can be performed at any time, with less delay to initiating cancer treatment. This represents the only potential option available to preserve fertility in prepubertal girls or pubertal girls who cannot delay their cancer treatment. More than 60 cases of successful live births using tissue cryopreservation have been reported worldwide, however, it should still be considered experimental because there is no standard protocol or report with robust success rates.

Minimally invasive laparoscopic surgery is preferred and in this process, strips of ovarian cortical tissue, which contains vast amounts of primordial follicle, are harvested. The ovarian tissue should be evaluated for evidence of metastasis or malignant disease. In pediatric patients, it is preferred to freeze strips from the ovarian cortex than the whole ovary, the ovarian cortex is dissected into 1- to 2-mm-thick strips after separation from medulla.

If ovarian insufficiency is diagnosed and the patient wants to be pregnant after complete cure of malignancy, orthotopic or heterotropic transplantation may be performed. Restoration of ovarian function was observed 3–6 months after reimplantation, documented blood level of several hormones

changes - increased estradiol and decreased FSH levels. After ovarian tissue transplantation, additional assisted reproductive techniques may be often required. A recent meta-analysis has reported a CPRs of 57.5% and a live birth rate of 37% after ovarian tissue transplantation.

One of the major concerns with ovarian tissue cryopreservation is the potential risk of reimplanting tissue contaminated with cancer. Ovarian transplantation might be most concerning in patients withovarian and hematological malignancies, where contaminating cancer cells theoretically seed ovarian tissue.

OTC is the only fertility preservation option for prepubertal females, but tissue from pre-pubertal girls contains only immature follicles. In vitro maturation, in which immature oocytes could be harvested and matured entirely in vitro and support the mature oocytes until in vitro fertilization, is more appealing, as it would remove the danger of reimplanting cancer cells back into the patient. Methods of growing human oocytes from primordial follicles is still experimental. However, there are 2 case reports of live births in patients who underwent tissue cryopreservation prior to menarche, indicating promising procedure in this population.[42-49]

OVARIAN SUPPRESSION

Ovarian suppression using gonadotropin-releasing hormone (GnRH) analogues, during chemotherapygenerates a pseudoprepubertal hormonal state. Although a pseudoprepubertal hormonal state may make ovaries less vulnerable to gonadotoxic treatment, the protective effect of GnRH agonist during chemotherapy is under debate and still considered investigational. This treatment has been studied in adult (postpubertal) population and such treatments are not recommended for prepubertal girls who lack of maturity of the ovarian cycle.[50,51]

CONCLUSION

With the advances of cancer treatments and increase in survival rates following cancer therapy, fertility has emerged as a highly significant quality-of-life issue for childhood cancer survivors. Pediatric or adolescent patients with malignancy should be referred to a reproductive endocrinologist as soon as possible upon receiving a cancer diagnosis. Early referral will make patients and parents to consider an appropriate method of fertility preservation. Currently available options for fertility preservation for pediatric or adolescent female patients with malignancy include cryopreservation of oocytes or embryos, and ovarian tissue freezing before commencing cancer therapy. Also GnRH analogues can be considered as another option during chemotherapy, but this is still experimental. In post pubertal male patients, sperm cryopreservation is a standard option. In some patients, microsurgical epididymal sperm aspiration, testicular sperm extraction or testicular tissue cryopreservation can be done whenever indicated. An appropriate option of fertility preservation should be chosen through discussion between individual patients, their parents and healthcare providers with analyses of possible options.

REFERENCES & RECOMENDEED READING

1. **Ries LA, Melbert D, Krapcho M, et al** (eds): SEER Cancer Statistics Review, 1975-2005.
2. **Jeruss JS, Woodruff TK.** Preservation of fertility in patients with cancer. N Engl J Med. 2009;360(9):902–11.
3. **Schover LR.** Patient attitudes toward fertility preservation.Pediatr Blood Cancer.2009 Aug; 53(2): 281–4.
4. **Mariotto AB, Rowland JH, Yabroff KR, et al.** Long-term survivors of childhood cancers in the United States. Cancer Epidemiol Biomarkers Prev. 2009 Apr; 18(4):1033– 40.
5. **Diller L, Chow EJ, Gurney JG, et al.** Chronic disease in the Childhood Cancer Survivor Study cohort: a review of published findings. J ClinOncol. 2009 May 10; 27(14):2339–55.
6. **Oeffinger KC, Hudson MM.** Long-term complications following childhood and adolescent cancer: foundations for providing risk-based health care for survivors. CA Cancer J Clin. 2004 Jul-Aug; 54(4):208–36.
7. Ethics Committee of American Society for Reproductive Medicine Fertility preservation and reproduction in patients facing gonadotoxic therapies: a committee opinion. FertilSteril. 2013; 100:1224-31.
8. **Green DM, Kawashima T, Stovall M, et al.** Fertility of female survivors of childhood cancer: a report from the childhood cancer survivor study. J ClinOncol. 2009 Jun 1; 27(16):2677–85.
9. **Green DM, Kawashima T, Stovall M, et al.** Fertility of male survivors of childhood cancer: a report from the Childhood Cancer Survivor Study. J ClinOncol. 2010 Jan 10; 28(2):332–9.
10. **Hudson MM.** Survivors of childhood cancer: coming of age. HematolOncolClin North Am. 2008 Apr; 22(2):211–31. v–vi.
11. **Bleyer A, Viny A, Barr R.** Cancer in 15- to 29-year-olds by primary site. Oncologist. 2006 Jun; 11(6):590–601.
12. **Huddart RA, Norman A, Moynihan C, et al.** Fertility, gonadal and sexual function in survivors of testicular cancer. Br J Cancer. 2005 Jul; 2593(2):200–7.
13. **Muller J.** Impact of cancer therapy on the reproductive axis. Horm Res. 2003; 59(Suppl 1):12–20.
14. **Thomson AB, Critchley HO, Kelnar CJ, Wallace WH.** Late reproductive sequelae following treatment of childhood cancer and options for fertility preservation. Best Pract Res ClinEndocrinolMetab. 2002 Jun; 16(2):311–34.
15. **Mackie EJ, Radford M, Shalet SM.** Gonadal function following chemotherapy for childhood Hodgkin's disease. Med PediatrOncol. 1996 Aug; 27(2):74–8.
16. **Whitehead E, Shalet SM, Jones PH, Beardwell CG, Deakin DP.** Gonadal function after combination chemotherapy for Hodgkin's disease in childhood.Arch Dis Child. 1982 Apr; 57(4): 287–91
17. **Shalet SM, Tsatsoulis A, Whitehead E, Read G.** Vulnerability of the human Leydig cell to radiation damage is dependent upon age. J Endocrinol. 1989;120(1):161–5.
18. **Sklar C.** Reproductive physiology and treatment-related loss of sex hormone production. Med PediatrOncol. 1999 Jul; 33(1):2–8.
19. **Thomson AB, Critchley HO, Kelnar CJ, Wallace WH.** Late reproductive sequelae following treatment of childhood cancer and options for fertility preservation. Best Pract Res ClinEndocrinolMetab. 2002 Jun; 16(2):311–34.
20. **Chemaitilly W, Mertens AC, Mitby P, et al**. Acute ovarian failure in the childhood cancer survivor study. J ClinEndocrinolMetab. 2006 May; 91(5):1723–8.
21. **Sklar CA, Mertens AC, Mitby P, Whitton J, Stovall M, Kasper C, et al.** Premature menopause in survivors of childhood cancer: a report from the childhood cancer survivor study. J Natl Cancer Inst. 2006 Jul 5; 98(13):890–6.
22. **Thibaud E, Ramirez M, Brauner R, et al.** Preservation of ovarian function by ovarian transposition performed before pelvic irradiation during childhood. J Pediatr. 1992 Dec; 121(6):880–4.
23. **Izard MA.** Leydig cell function and radiation: a review of the literature. RadiotherOncol. 1995 Jan; 34(1):1–8.
24. **Hahn EW, Feingold SM, Simpson L, Batata M.** Recovery from aspermia induced by low-dose radiation in seminoma patients. Cancer. 1982 Jul 15; 50(2):337–40.
25. **Loren AW, Mangu PB, Beck LN, et al.** Fertility preservation for patients with cancer: American Society of Clinical Oncology clinical practice guideline update. J ClinOncol. 2013; 31:2500–10.
26. **Ginsberg JP, Ogle SK, Tuchman LK, et al.** Sperm banking for adolescent and young adult cancer patients: sperm quality, patient, and parent perspectives. Pediatr Blood Cancer. 2008;50(3):594–8.

27. **Lass A, Akagbosu F, Abusheikha N, et al.** A programme of semen cryopreservation for patients with malignant disease in a tertiary infertility centre: lessons from 8 years' experience. Hum Reprod. 1998;13(11):3256–61.
28. **Chung K, Irani J, Knee G, et al.** Sperm cryopreservation for male patients with cancer: an epidemiological analysis at the University of Pennsylvania. Eur J ObstetGynecolReprod Biol. 2004;113: S7–11.
29. **Adank MC, van Dorp W, Smit M, et al.** Electroejaculation as a method of fertility preservation in boys diagnosed with cancer: A single-centre experience and review of the literature. FertilSteril. 2014; 102:199–205
30. **Gupta AA, Donen RM, Sung L, et al.** Testicular biopsy for fertility preservation in prepubertal boys with cancer: Identifying preferences for procedure and reactions to disclosure practices. J Urol. 2016; 196:219–24.
31. **Feldschuh J, Brassel J, Durso N, Levine A.** Successful sperm storage for 28 years. FertilSteril. 2005;84(4):1017.
32. **Levine J, Canada A, Stern CJ.** Fertility Preservation in Adolescents and Young Adults with Cancer. J ClinOncol. 2010 May
33. **Brinster RL.** Male germline stem cells: from mice to men. Science. 2007;316(5823):404–5.
34. Brinster RL, Zimmermann JW. Spermatogenesis following male germ-cell transplantation. ProcNatlAcadSci U S A. 1994;91(24):11298–302.
35. **Revel A, Revel-Vilk S.** Fertility preservation in young cancer patients. J Hum Reprod Sci. 2010;3(1):2–7. Fertility preservation options are discussed in this review.
36. **Wennerholm UB, Soderstrom-Anttila V, Bergh C, et al.** Children born after cryopreservation of embryos or oocytes: a systematic review of outcome data. Hum Reprod. 2009;24(9):2158–72.
37. **Oktay K, Cil AP, Bang H.** Efficiency of oocyte cryopreservation: a meta-analysis. FertilSteril. 2006 Jul;86(1):70–80.
38. **Burns KC, Hoefgen H, Strine A, Dasgupta R.** Fertility preservation options in pediatric and adolescent patients with cancer. Cancer. 2018; 124:1867–76.
39. **Borini A, Lagalla C, Bonu MA, et al.** Cumulative pregnancy rates resulting from the use of fresh and frozen oocytes: 7 years' experience. Reprod Biomed Online. 2006; 12:481–6.
40. **Grifo JA, Noyes N.** Delivery rate using cryopreserved oocytes is comparable to conventional in vitro fertilization using fresh oocytes: potential fertility preservation for female cancer patients. FertilSteril. 2010; 93:391–6.
41. **Hashim Kim, Hoon Kim, Seung-Yup Ku.** Fertility preservation in pediatric and young adult female cancer patients. Ann PediatrEndocrinolMetab.2018 Jun; 23(2): 70–74.
42. **Poirot C, Vacher-Lavenu MC, Helardot P, et al.** Human ovarian tissue cryopreservation: indications and feasibility. Hum Reprod. 2002;17(6):1447–52.
43. **Smitz J, Dolmans MM, Donnez J, et al.** Current achievements and future research directions in ovarian tissue culture, in vitro follicle development and transplantation: implications for fertility preservation. Hum Reprod Update. 2010;16(4):395–414.
44. **Dolmans MM, Marinescu C, Saussoy P, et al.** Reimplantation of cryopreserved ovarian tissue from patients with acute lymphoblastic leukemia is potentially unsafe. Blood. 2010 Jul
45. **Sanchez-Serrano M, Crespo J, Mirabet V, et al.** Twins born after transplantation of ovarian cortical tissue and oocyte vitrification. FertilSteril. 2010;93(1):268, e11–3.
46. Ethics Committee of American Society for Reproductive Medicine Fertility preservation and reproduction in patients facing gonadotoxic therapies: a committee opinion. FertilSteril. 2013; 100:1224–31.
47. **De Bruin ML, Van Dulmen-den Broeder E, Van den Berg MH, Lambalk CB.** Fertility in female childhood cancer survivors. Endocr Dev. 2009; 15:135–58.
48. **Jadoul P, Dolmans MM, Donnez J.** Fertility preservation in girls during childhood: is it feasible, efficient and safe and to whom should it be proposed? Hum Reprod Update. 2010; 16:617–30.
49. **Salama M, Isachenko V, Isachenko E, Rahimi G, Mallmann P.** Updates in preserving reproductive potential of prepubertal girls with cancer: systematic review. Crit Rev OncolHematol. 2016; 103:10–21.
50. **Blumenfield Z.** How to preserve fertility in young women exposed to chemotherapy? The role of GnRH agonist cotreatment in addition to cryopreservation of embryo,oocytes or ovaries. Oncologist. 2007; 12:1044-54
51. **Okatay K, Rodriguez-wallbergK, Munster P.** Ovarian protection during adjuvant chemotherapy. N Engl J Med. 2015; 372:2268-9

Organised by

INDIAN FERTILITY SOCIETY

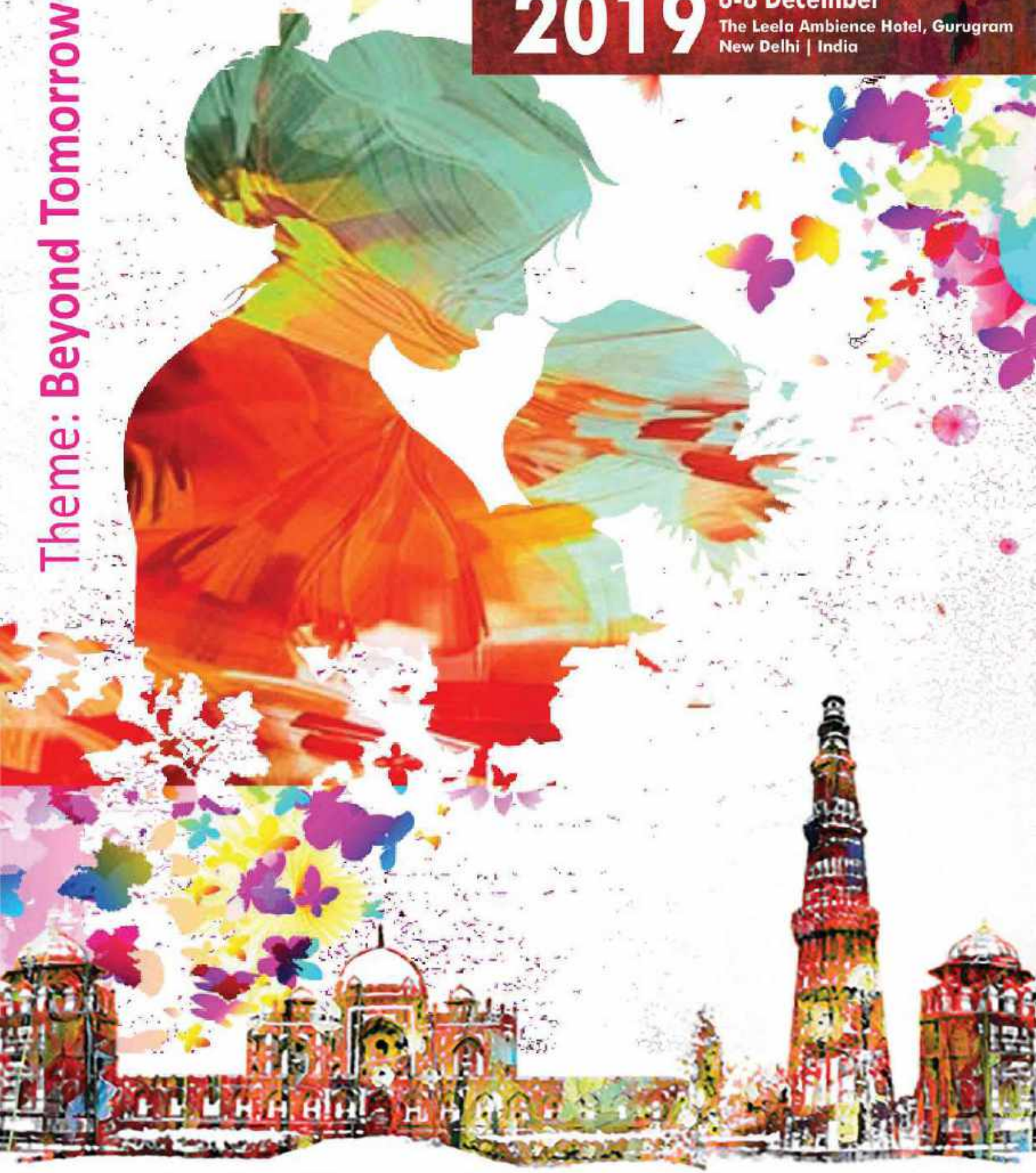
15th Annual Congress of Indian Fertility Society

FERTIVISION 2019

6-8 December

The Leela Ambience Hotel, Gurugram
New Delhi | India

Theme: Beyond Tomorrow



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Invitation

Dear Friends, Welcome to *FERTIVISION 2019*

On behalf of the Indian Fertility Society (IFS), we are extremely pleased to announce and cordially invite you to the much awaited academic event – the **15th National Annual Conference - Fertivision 2019**, to be held on **6th, 7th & 8th December 2019** at Hotel **The Leela Ambience, Gurugram, New Delhi / NCR, India**.

This conference is aimed to provide the most comprehensive academic platform in the field of Infertility and Assisted Reproductive Technology (ART)" befitting the theme of the meeting **"Beyond Tomorrow"**

Renowned and leading expert faculty from around the world would gather and deliver talks in our cutting edge scientific program which will not only enrich your current knowledge and clear all doubts faced in day-to-day clinical practice, but will also enlighten you about the latest innovations and ongoing research.

A large number of renowned international faculties have already confirmed their participations till date. The pre-congress workshops on 6th December are specially designed for informal in-depth training with hands on sessions on simulators and live, where ever feasible. There will be 4 simultaneous running streams on 7th & 8th December covering a wide variety of topics, enabling you to choose the deliberations specific to your area of interest and clinical practice. We are having a dedicated hall for the esteemed embryologist friends.

The best oral and poster presenters under various categories and the quiz winners will be honoured with special awards and prizes. Do join us in large numbers and update your knowledge with most updated current standards in clinical practice, as well as get inspired to innovate further to overcome remaining enigmatic issues!

The three days of scientific program will encompass didactic lectures, keynote presentations, panel discussions and orations. There will be 9 Preconference workshops based on Ovulation Induction, Ultrasound, Andrology, Embryology, Hands on Embryo Transfer, Ovum Pickup and more. These workshops will be in addition to the special state of the art workshops by the faculty from IFFS and ESHRE. We expect delegates across India, Sri lanka, Bangladesh, Nepal, Middle - East Countries and African Nations and the arrangements are being made to accommodate more than 2500 delegates.

The exhibition area will be one of the highlights of the conference. Exhibiting provides tremendous benefits to both participating industry and the society. Tea, coffee and lunch will be served confluent with the trade area to allow optimal interaction between the trade companies and delegates during beverage and lunch breaks.

We invite you to participate in the Fertivision 2019 and exchange your expertise with more than 2500 specialists in the field of Assisted Reproduction.

We look forward to your active participation and suggestions for successful conduct of the conference.

With Our Best Regards

Dr. M Gouri Devi
Organizing Chairperson
FERTIVISION 2019

Dr. Pankaj Talwar
Organizing Secretary
FERTIVISION 2019

and All Executive Committee of Current IFS team

15th Annual Congress of Indian Fertility Society

FERTIVISION 2019

6-8 December The Leela Ambience Hotel Gurugram, New Delhi, NCR | India

Organised by IFS Indian Fertility Society

Registration Form

Title Prof/ Dr/ Mr/ Ms _____ Gender : Male ☐ Female ☐

First Name _____ Last Name _____

Institution _____ IFS Member No. _____

Correspondence Address _____

_____

City _____ Pin Code _____ State _____

Mobile No. _____ Email _____

(All the above fields are mandatory)

Limited Seats

Choose from 10 Pre Conference Workshops | 6 December — Choose Any 1 Workshop

1)	☐ IFFS Workshop on Do's and Don'ts in Ovarian Stimulation	7)	☐ QA / QC
2)	☐ Reproductive Surgery		Pre Lunch Workshop (0900 - 1300 Hrs)
3)	☐ Ultrasonography Imaging In Infertility	8 A)	☐ Counselling & Psychological Support
4)	☐ Andrology & Semenology		Post Lunch Workshop (1400 - 1700 Hrs)
5)	☐ Ovum Pickup and Embryo Transfer (With Simulators)	8 B)	☐ Research Methodology
6)	☐ Cryobiology	9)	☐ PGT and Genomics

Registration Fees

Inclusive of 18% GST

Please tick the appropriate checkbox

Category	Early Bird Fees Till 15th July 2019	Regular Fees Till 15th October	Onspot
IFS Member	INR 10500 ☐	INR 12500 ☐	INR 14500 ☐
Non IFS Member	INR 12500 ☐	INR 14500 ☐	INR 16500 ☐
Conference Registration plus Life Time IFS Membership	Embryologist INR 14500 ☐ Gynaecologist INR 15500 ☐	Embryologist INR 16500 ☐ Gynaecologist INR 17500 ☐	Embryologist INR 18500 ☐ Gynaecologist INR 19500 ☐
PG Students (No Dinner)	INR 6000 ☐	INR 7000 ☐	INR 8000 ☐
Accompanying Person	INR 10500 ☐	INR 11500 ☐	INR 12500 ☐
Foreign Delegates	$ 350 ☐	$ 400 ☐	$ 500 ☐

Inclusive of 18% GST

Conference Registration Fees Includes

- 18 Hrs of World Class Academic Program with Access to Best & Brightest International & National Faculty
- 3 Lunches and 6 Tea / Coffee Served During the Conference on 6, 7 & 8 December
- Banquet Dinner on 7 December
- Conference Kit (Including Bag, Badge, Notepad, Certificate & Pen)
- 1 Pre Conference Workshop
- Accompanying Person is Entitled for Food Coupons Only

Mode of Payment

1. Bank Draft/Cheque - To be made in favor of "INDIAN FERTILITY SOCIETY"

2. Bank Transfer Details

IFS Account Name : Indian Fertility Society
Account Number: 50562010067180
IFSC Code : ORBC0100179
Bank Name: Oriental Bank of Commerce
Branch: Connaught place, New Delhi- 110001

Cancellation Policy

- Cancellation till 31st October, 2019 – 50% Refund.
- Cancellation from 1st November, 2019 – No Refund.
- All refunds will be made after the congress.

Cheque / Draft No. _____ **Total Amount** _____

Note: Kindly email us bank deposit slip / UTR number once you made the payment for our record.
Payment confirmation will take 7-10 working days post deposit of cheque, DD or RTGS

3. To Register online log on to www.fertivision2019.com

Congress Manager's

Mr. Vikas Sharma
Conferences International
B-220/2, 2nd Floor,
Opposite Kali Masjid, Savitri Nagar
New Delhi – 110017
M: +91-9560493999
Email: fertivision2019@gmail.com

Please send Registration Form along with cheque / draft at the following address

www.fertivision2019.com

IFS SECRETARIAT
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